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SYNTHESIS OF INNOVATIVE MULTIFUNCTIONAL THERMALLY ACTIVATED REACTIVE SPECIES FOR ELASTOMERIC NANOCOMPOSITE TECHNOLOGY

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Preface

The Scotsman Robert William Thomson in 1846 patented an invention that would change the history of the world of transport. The idea was called "Application of elastic supports around the wheels of vehicles, in order to reduce the effort necessary to tow them, make their movement easier and muffle the noise they make when they move". Unfortunately, his intuition was so revolutionary that it was not considered. In fact, there were still no vehicles or bicycles and the fantastic properties linked to a new material, the rubber, was recently being realized. During the same period, some Brazilian planters had intuited the properties and malleable capacities of “Hevea brasiliensis”, also known as rubber tree. The objects that could be obtained hot working this latex were many, but it was soon noticed that the characteristics of this material remained unchanged at room temperature, melted in the heat and stiffened in the cold. The remedy to this problem came from Charles Goodyear who, in 1839, succeeded in adding sulfur to the rubber compound to obtain a product resistant to climatic changes which he used to coat the wheel rims. The thread that connects the previous inventors is the limited success of their discoveries. John Boyd Dunlop was the man who invented the tire in its modern conception, in 1888. He was trying to please his son who was complaining of having a very slow tricycle and decided to fill the tires with air to lighten the weight. The experiment gave brilliant results and so he decided to file a patent that same year, achieving great success. From that moment the main companies that produce tires began to arise and some of them still exist today.

The growing use of cars and auto vehicles led to a boom in tire sales. At the same time, while the demand for tires was increasing, the tire industry start investing heavily in research and development to improve their performances. Therefore, important steps have been taken in the understanding of the filler-rubber interactions and of the dynamic mechanical properties connected to them, with attention to the nature of the filler and its functionalization, to make it more compatible with the polymer matrix.

In the last years, a complementary approach attracted more interest and this project was born under this light, with the idea of functionalizing the elastomers with functional groups able to make the matrix more compatible with the inorganic fillers, used as reinforcing agents, or to cross-link the matrix in a different way respect to the classic vulcanization process.

Finding new methods to functionalize the elastomeric matrix, which is the main ingredient of any rubber-based composite, is an extremely fascinating challenge. Mainly because the recipes used for compound formulation have been optimized in over one hundred years of research and they have reached a high degree of complexity. Furthermore, during compounding phase, several different ingredients interacts with each other to give to the product peculiar proprieties and changing or adding some components can trigger unknown processes that can overturn established conventions, forcing the research to re-evaluate the optimization process.

This doctoral project was a continuum of the collaboration between my research group, which deals with organic synthesis, and Pirelli as industrial partner. The possibility to start from a clean sheet has allowed us to explore the world of polymer synthesis and functionalization but, at the same time, it has been necessary to invest time to acquire knowledge on polymer reactivity, to gain practical experience in compound formulation and to learn the mechanical dynamic behavior.

Moreover, formulation and characterization of the compounds was carried out in the laboratories of the company, using equipment bigger respect to the laboratory scale standards and more suitable for the characterization of the materials obtained.

Structure of the thesis

The **First chapter** will describe the ideal characteristics that a suitable functionalization should have. Particular attention will be given to 1,3-dipolar cycloadditions, to nitrilimines as reactive species and to tetrazoles as their sources. The notions present in the literature and the results obtained by investigating these systems during these years of doctorate will be described.

The **Second chapter** will provide an overview over the ingredients used in tire compounding, a theoretical introduction on the compound formulation and on their dynamical-mechanical characteristics.

In the **Third chapter** the project concerning the synthesis of new compatibilizers will be described, including their application in rubber compounds, with their chemical, physical and mechanical properties.

In the **Fourth chapter** the project concerning the synthesis of new elastomeric cross-linking agents will be described, including their application in rubber compounds, with their chemical, physical and mechanical properties.

In the **Fifth chapter** the project concerning the synthesis of new initiator/terminator for anionic polymerization will be described.

In the **Sixth chapter** the project developed at the University of Strasbourg will be described, concerning the study of non-covalent interactions in functionalized polymers.

Finally, there is an additional chapter, the **Experimental Part**, where all the synthetic procedures will be described, as well as the characterization of the compounds.

Chapter 1

This chapter will describe the background of knowledge used to develop the PhD project. Starting from the functionalization of polymers, passing through 1,3 dipolar cycloadditions, nitrilimines and tetrazoles to arrive at the description of the work carried out during the project.

1.1 Polymer functionalization

In the field of polymer science, the possibility of using appropriately functionalized polymers has attracted more and more attention over the years and, in particular, to use them in the synthesis and production of innovative materials, whose properties can be modified according to technological and application interest[1].

The previous century was characterized by the development of new synthetic ways to produce polymers on a large scale, starting from monomers suitably chosen on the basis of the final properties of the desired material, while in recent decades post-polymerization modification has become increasingly popular, thanks to the possibility of obtaining tailored complex structures. The debate on which approach is the best still exists today: pre-polymerization or post-polymerization functionalization. In the first case specific functional groups are inserted along the chain in two ways: 1) by acting on the terminal functions[2], which are head (or α-position) and tail (or ω position), but in this way the number of features inserted is limited; 2) directly inside the polymer backbone by choosing the appropriate monomers[3]. This latter approach allows both to obtain a higher number of functionalization within the polymer and to plan the synthesis of new monomers carrying a wide range of functional groups. The main problem correlated with these approaches is the polymerization condition itself, which must be compatible with the functionalizer used; moreover, as regards the new monomers used, their reactivity must be studied in order to predict their behavior during polymerization and the properties that they can confer to the final polymer, such as degree of polymerization, molecular weight, tacticities etc. While using the post functionalization approach, through chemical modification, it is possible to obtain a certain degree of functionalization along the chain without considering the reactivity of the functional groups inserted during polymerization process and therefore without having to modify the common industrial production procedures[4,5]. This type of approach also allows to obtain a wider class of functionalized polymers starting from the same precursor, which can be a commercially available polymer at low cost; ensuring that all polymers will have identical degrees of polymerization, molecular weight, tacticities etc. The post polymerization also allows to obtain

functionalized polymers with pendant groups that would not be possible to obtain through other techniques, avoiding side reactions.

The recent development of new post functionalization methodologies such as “click chemistry”[6] and reversible-deactivation radical polymerization[7] (RDRP) have allowed the introduction of many different functionalizations and, consequently, paved the way to new complex structures. However, attention must be paid to the following criteria that should drive the selection of suitable systems:

- High yield and efficiency
- Very fast
- Easy to conduct (mild conditions, simple purifications)
- Selective
- Versatile
- Non-toxic
- Cheap
- Industrially scalable

In this contest, some of the most important chemical transformations investigated over the past decades within polymer science are thiol-X modification[8], isocyanate modification[9], cycloaddition reactions[10,11]. In addition, to be implemented in the manufacture of tires, these systems must also be applicable to dienic polymers such as polyisoprene (IR), polybutadiene (BR), styrene-butadiene copolymer (SBR).

The functionalization of the elastomers is driven by the opportunity to improve their compatibility with the other components constituting the final compound, in particular with the fillers[12]. Within this doctorate, it was developed an original approach to polymer post-functionalization and such approach was then exploited to propose new cross-linker and functionalization agents not including sulfur. Additional challenges included in this project involved the development of selective and thermally activable reactions which can occur only at suitable temperatures involved in the tire technology.

In a previous PhD project, some promising classes of reactions were identified for an efficient elastomer functionalization namely: 1,3 dipolar cycloadditions, thiol-ene, aza-ene reactions and within them the 1,3 dipolar cycloadditions were those that better matched the prerequisites for thermal activation at the required temperatures.

1.2 1,3 Dipolar cycloadditions

This chemical reaction, which belongs to pericyclic reactions, involves a 1,3 dipole and a dipolarophile to give a regio- and stereoselective synthesis of five-membered heterocycles. The dipolarophile is typically an alkene or alkyne but can be other π-systems. When the dipolarophile is an alkyne, heteroaromatic rings are generally produced. The earliest 1,3-dipolar cycloadditions were described in the late 19th century to the early 20th century, following the discovery of 1,3-dipoles, but it was Rolf Huisgen[13] who gave a detailed description of the reaction mechanism, assuming a concerted single-step reaction, that could explain its stereospecificity. To this first mechanistic explanation was then added that of Firestone[14], namely a stepwise mechanism involving two-steps and a diradical intermediate.

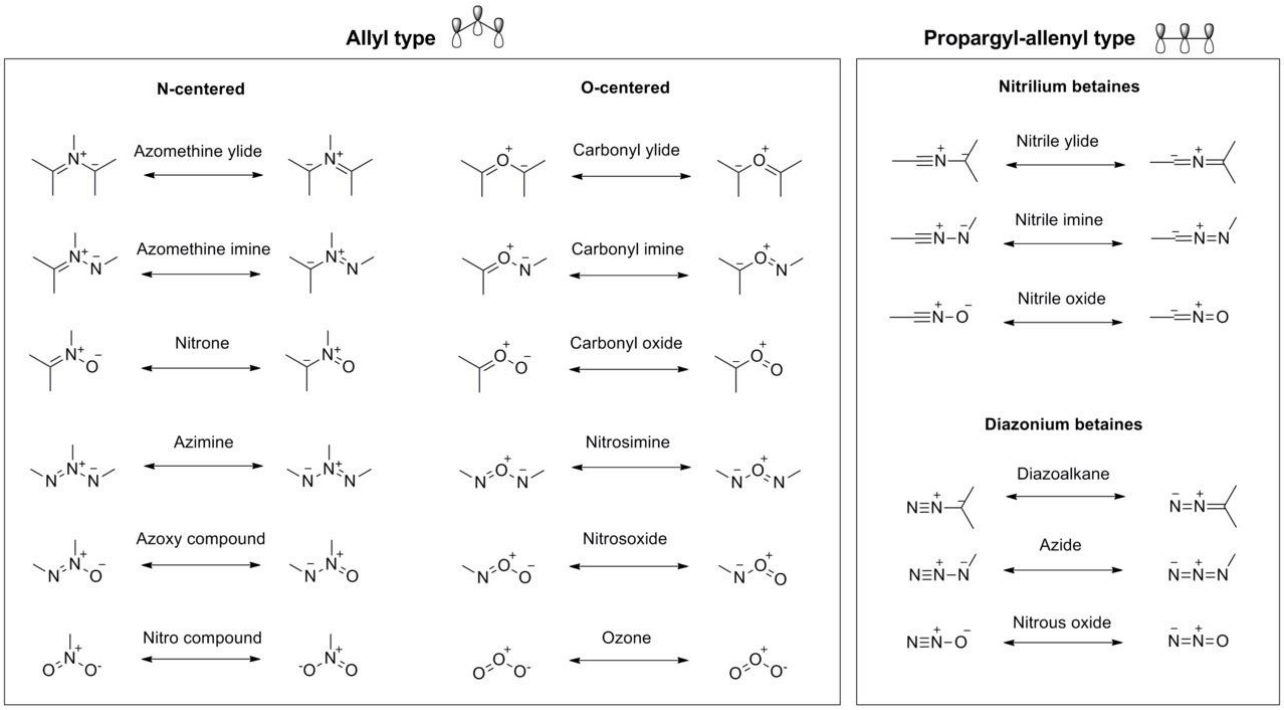
Around these two theories there have been many discussions but, to date, the most accredited one involves the 1,3-dipole reacting with the dipolarophile in a concerted and asynchronous way, although there are exceptions of stepwise mechanisms involving 1,3-dipole such as thiocarbonyl ylides[15] or nitrile oxides[16].

The observations made by Huisgen in support of the pericyclic mechanism are as follows:

- **Substituent effects**: different substituents on the dipole do not exhibit a large effect on the cycloaddition rate, suggesting that the reaction does not involve a charge-separated intermediate.
- **Solvent effects**: solvent polarity has little effect on the cycloaddition rate, in line with the pericyclic mechanism where polarity does not change much in going from the reactants to the transition state.
- **Stereochemistry**: 1,3-dipolar cycloadditions are always stereospecific with respect to the dipolarophile (i.e., cis-alkenes giving syn-products), supporting the concerted pericyclic mechanism in which two sigma bonds are formed simultaneously.
- **Thermodynamic parameters**: 1,3-dipolar cycloadditions have an unusually large negative entropy of activation similar to that of the Diels-Alder reaction, suggesting that the transition state is highly ordered, which is a signature of concerted pericyclic reactions.

At this point it is important to give a more detailed description of the two key players involved in this type of reaction: the 1,3 dipole and the dipolarophile. A dipole 1,3 is an organic molecule in

which there is a charge separation, in which 4 π-type electrons are delocalized on three atoms to form the dipole. Usually these compounds have in their structure a heteroatom that can be nitrogen, oxygen, sulfur or phosphorus. It is possible to distinguish dipoles in two types[17]: allyl-type or propargyl-type, and the most important are reported in the Scheme 1.



Scheme 1- Class of dipoles listed by their geometry

To these two types correspond two different geometries: bent or linear.
Since the position of the charge is delocalized on more atoms it is not correct to use a unique structure formula, but it is better to represent resonance structures. Nevertheless, there are examples reported in literature in which one of the mesomeric forms significantly contribute to the energy of the ground state and is possible to determine it, both through experiments and computationally.

Resonance structures can be drawn to represent delocalized negative and positive charges onto any terminus of a 1,3-dipole, consequently, this ambivalence means that the ends of a 1,3-dipole can be treated as both nucleophilic and electrophilic at the same time[18]. The extent of nucleophilicity and electrophilicity at each end can be evaluated using the frontier molecular orbitals, which can be obtained computationally[19]. In general, the atom that carries the largest orbital coefficient in the HOMO acts as the nucleophile, whereas that in the LUMO acts as the electrophile. The most nucleophilic atom is usually, but not always, the most electron-rich atom.

Depending on the alignment and on the gap of energy levels, three types of behavior were identified. To the first type, defined as HOMO-controlled dipole (or nucleophilic dipole), belong dipoles like azomethine ylide, nitril ylide, carbonyl ylide, azomethine imine, carbonyl imine and diazoalkane. In this case the HOMO of the dipole tends to align with the LUMO of the dipolarophile. For this reason, any electron-attractor substituent able to lower the LUMO allows an approach of the levels, speeding up the reaction. On the contrary, an electron-donor group will increase the spacing between the levels, slowing the reaction or even preventing it. To the second type, defined as HOMO-LUMO-controlled dipole (or ambiphilic dipole), belong dipoles such as nitrile imide, nitrone, nitril oxide, carbonyl oxide and azide[20]; in this case the two frontiers molecular orbitals can both move in direction of their target orbital and any substituent helps to close this gap allows to increase the reaction speed . To the third, defined LUMO-controlled dipole one (or electrophilic dipole), belong dipoles such as nitrous oxide and ozone[21], in which the dipole LUMO is characterized by a low energy value that allows it to align with the HOMO of the target dipolarophile. The introduction of a substituent on the dipolarophile produces an opposite effect to that seen for the reactivity of the first type: the electron donor groups accelerate the reaction while the attracting groups slow it down.

The progress of the reaction is affected by other factors, mainly related to the characteristics of dipolarophile and reaction intermediate:

- Conjugation of the target molecule: the aromaticity of the substrate can stabilize the partial charges of the transition state during the formation of the sigma bonds between the reactants.
- Polarizability of dipolarophiles: the polarizability of the substrate regulates the reactivity of the compound, since diffuse electron clouds make the system more prone to exchange electrons.
- Angle strain & steric hindrance: ground state energy levels of tensioned systems are higher and therefore the molecules are more reactive. For the same reason the passage through a high hindered reaction intermediate slows down the reaction rate.
- Hetero-dipolarophiles: they have slower addition rates compared to C,C-dipolarophiles, due to a lower gain in sigma bond energy to offset the loss of a π-bond during the transition state.

- Isomerism of the dipolarophile: Trans-isomers are more reactive because during the reaction, the 120° bond angle shrinks to 109°, bringing eclipsing *cis*-substituents towards each other for increased steric clash.

All the theoretical considerations previously made regarding the 1,3 dipolar cycloadditions were taken into consideration choosing the most suitable species to study during this doctoral project. In this case the use of an activated dipolarophile could not be contemplated, since the starting point has necessarily to be a commercial polymer, among the elastomers commonly used for tires production. The range is, therefore, limited to olefins such as polybutadiene (PB), polyisoprene (IR) or to styrene-butadiene copolymers (SBR), in which the dienophiles are constituted by the double bonds present on the polymeric backbone. The attention was focused on the possibility to functionalize selectively only the terminal double bonds of vinyl type.

Regarding the choice of the appropriate 1,3 dipoles, after a thorough bibliographic research, the nitrilimines were chosen as the most promising species for the PhD project purposes.

The reasons at the base were:

- The possibility to form covalent bonds with the polymer matrix
- The capability to selectively functionalize vinyl bonds
- The possibility to generate these species at high temperatures, starting from very stable precursors

In the following paragraphs the choice to use nitrilimines and, consequently, tetrazoles as their precursors will be amply motivated.

1.3 Nitrilimines

Nitrilimines (NIs) belong to the class of 1,3 dipoles[22]. Their generation was firstly reported in the early part of the twentieth century, but for many years they could not find application because of their high reactivity and their difficult characterization. It was Huisgen, in 1959, who first reported an in-depth study of these species[23], describing their generation from various precursors, their kinetics, their ability to react with dipolarophiles and nucleophiles and their chemoselectivity[24].

NIs have a structure that is isoelectronic with that of the allyl anion with 4 π-type electrons distributed over three atoms[17]. For this reason, they cannot be represented with a single form but have different forms of resonance[25], the contribution of each is important for understanding the reactivity of those species (Figure 1).

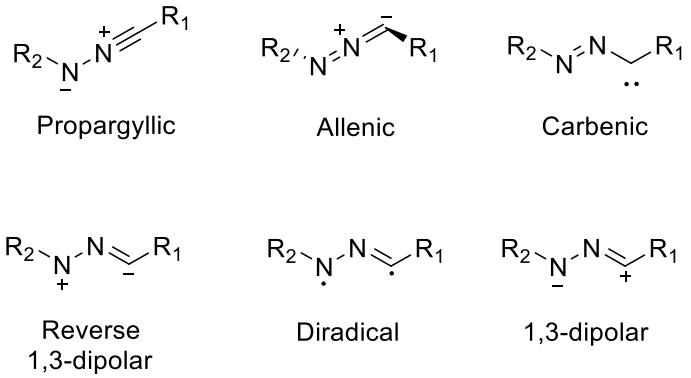


Figure 1- NI resonance forms

The two forms of resonance that contribute most are the propargylic and the allenic one[26]; the presence of different substituents on the sides of the NI affects which of the two forms prevails. The most important factor is the electronegativity of the terminal nitrogen atom: a higher electronegativity gives prevalence to the propargyl structure and forms a more electrophilic dipole with a low LUMO level, while for the allenic form it is the opposite[27]. After years of studies on which was the dominant structure of formyl nitrilimine, it was concluded, supported by computational calculations, that it exists almost exclusively in the allenic form, while the propargyl form is only a transition state[28]. The presence of substituents with different electronic properties on the NI is however able to give rise to both structures, as reported in the literature[29,30]. Given the difficulties encountered in isolating this reactive species, its characterization was not easy at all.

Following are reported the techniques used for the detection of NI and their characteristic signals:

- The UV[31,32] spectra present a large signal around 240-275 nm (heteroatom-substituted) or 370-465 nm (diaryl substituted).
- The IR[33,34] is the most suitable technique for identifying the structure (propargylic or allenic) of the NI. The most prominent peak corresponds to the C-N antisymmetric stretch. Frequency below 2100 cm^{-1} indicate an allenic form while frequency above 2200 cm^{-1} indicate propargylic form. Value between 2100 and 2200 cm^{-1} indicate NI with both

characters. Heteroatom-substituted NIs tipically show allenic form with C-N stretches in the range 1990-2170 cm^{-1}. Using this technique, it was shown that diaryl-NIs species have a propargylic structure and the presence of functional groups (ED or EW) on both aromatic rings will lower the stretching frequency.

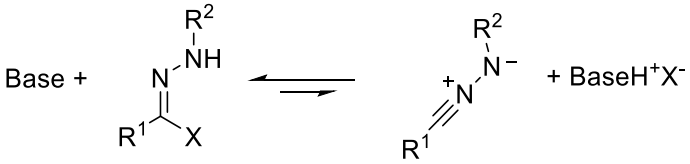
- The NMR[35] characterization is less used to detect NIs, due to the particular conditions required, to register a spectrum (NIs are too unstable). In special situations, using ^{13}C resonances between 70 and 45 ppm were observed, while using ^{14}N resonances between 215 and 170 ppm were observed.

1.3.1 NI generation

As it emerged from the discussion previously made, NIs are unstable under standard conditions, then they must be generated in situ through different methods[22]. In this paragraph only a few examples will be reported, those that are more efficient. The use of tetrazoles as a source of nitrilimine will be explained in more detail in a separate chapter, given that it constitutes the species investigated during this doctoral project.

Hydrazonyl halides

They are one of the most common NI-precursors[36]. Nitrilimines are generated from those species in presence of a base, that causes the deprotonation and the subsequent elimination of the halide[37] (Scheme 2).

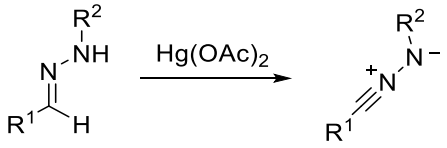


Scheme 2- Hydrazonyl halides

This process of NI liberation has been demonstrated to be reversible. Those hydrazonyl halides can act as "storage site" of NIs and release them at a rate dependent on the reactivity of the dipolarophile involved in the cycloaddition. Another aspect that can influence the reaction rate is the type of base involved to generate NI species, in literature are reported many examples of both organic and inorganic bases with effective results[38]. The synthesis of hydrazonyl halides involves halogenation with an electrophilic halogen source[39] (bromination with Br_2, chlorination with $POCl_3$) of the corresponding hydrazide.

Hydrazones

NIs can also be generated directly from the corresponding aldehyde hydrazine through oxidation with heavy metal salts (lead acetate[40], mercury acetate[41]) (Scheme 3). In this case there is a loss of H_2 rather than HX (as in the previous case).

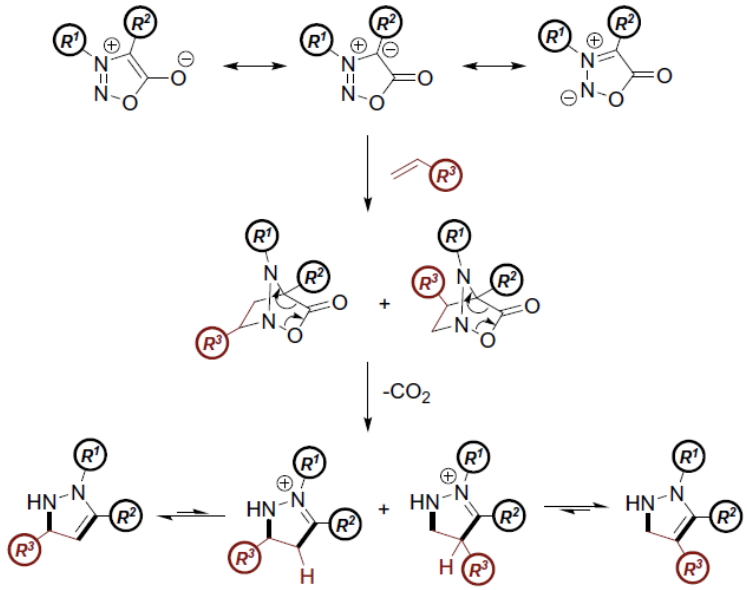


Scheme 3- Hydrazones

The problem with this approach is the use of acetate as a counter ion, which can limit the subsequent reactivity of the NI thus generated. Oxidation of hydrazones[42] can be employed, generating it in situ, without the isolation of any intermediate between the starting aldehyde and the cycloadduct of the NI. It was shown that atmospheric oxygen can facilitate the formation of NIs on particular occasions[43].

Sydnones

They are mesoionic heterocyclic chemical compounds possessing a 1,2,3-oxadiazole core with a keto group in 5-position[44]. They are known to participate in 1,3 dipolar cycloaddition reactions[45] due to their zwitterionic nature, releasing CO_2 and forming pyrazoline/pyrazole product (Scheme 4). While thermal cycloaddition does not proceed through an NI intermediate (a 5,5 fused ring system is formed), the photolysis of arylsydnones gives NIs intermediate after CO_2 release[46]. Applications of sydnones are known but limited respect to the hydrazine and tetrazole derivatives, mainly because of the lower tolerance to different functional groups and the numerous side reactions that limit their use in organic synthesis[47]. Furthermore, the quantum yields of sydnones in photochemical reactions are ten times lower than those of tetrazoles[31].



Scheme 4 – Sydnones reactivity, from *C. Jamieson and K. Livingstone, The Nitrile Imine 1,3-Dipole*

1.3.2 Nitrilimine reactivity

Nitrilimines, unlike other 1,3-dipoles, have the peculiar characteristic of reacting differently with different types of substrates, generating very different compounds. For this reason, the main reaction products with double bonds and nucleophiles will be described below.

1.3.2.1 1,3 Dipolar cycloadditions

This type of reaction has already been introduced previously (Paragraph 1.2), here the focus is limited to the use of nitrilimine as 1,3-dipole and on some important aspects such as regioselectivity and rate of reaction.

1.3.2.2 Regioselectivity

The cycloaddition of nitrilimine with an asymmetrical dipolarophile can lead to the formation of two adducts (substitution in 4 or 5 position), even if the formation of the regioisomer with the more bulky substituent in 5-position on the pyrazoline ring formed is generally favored[48]; even if examples of formation of substituted compounds in 4-position are known[49]. In order to better understand the electronics of regioselectivity, it is necessary to consider the theory of molecular

orbitals[50,51] (FMO), to calculate the electronic densities of the HOMO and LUMO orbitals. The FMO therefore explains how the favored species is the one replaced in 5-position, with the sole exception of strongly electron withdrawing groups that form a mixture of regioisomers or compounds substituted in 4-position. More recently the density functional theory (DFT) has been used as a tool to study the reactivity of cycloadditions[52]. Even this theory, however, is not entirely able to predict with certainty the reactivity of nitrilimines, which continues to present numerous exceptions that are difficult to predict accurately.

1.3.2.3 Rate of reaction

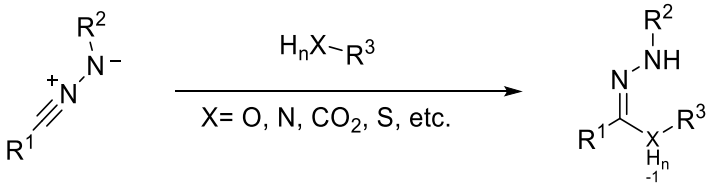
The reaction rate corresponding to the reaction of a nitrilimine with a dipolarophile is strongly influenced by steric and electronic effects. In this case, by applying the FMO theory, excellent results can be obtained predicting the reactivity of a particular substrate. Nitilimines are considered type II dipoles, which means that both the HOMO dipole-LUMO dipolarophile interaction and the LUMO dipole-HOMO dipolarophile interaction affect the rate of reaction[53]. For this reason, each type of substituent on the dipolarophile will increase the reaction rate. Indeed, ethene is the least reactive double bond in NI cycloaddition and all alkenes with no conjugative electron activation require more stringent conditions to form the product. The nature of substituents on nitrilimine profoundly affects its straightness, for example the presence of electron-donating groups can transform the dipole into a pseudo type I[54] (the LUMO is raised to such an extent that the interaction LUMO dipole-HOMO dipolarophile is no longer relevant). The steric hindrance also influences the cycloaddition rate. In fact, by using strained cyclic systems instead of the corresponding linear analogues, the rate increases by 20-50 times[55]. Increasing the steric bulk has a detrimental effect on the reaction rate. In fact, considering alkenes as dipolarophiles, mono and disubstituted are commonly used as substrates for this type of reactions, while the trisubstituted react much more slowly and the tetrasubstituted do not react at all.

Other considerations that must be made concern trans-alkenes that are better substrates than the analogous cis and that alkenes have a reactivity different orders of magnitude higher than the alkynes. These effects have not yet been fully understood but should be explained by the overlap of the orbitals in their respective transition states. Finally, entropy can also influence the rate of reaction[56]. Intramolecular cycloadditions between nitrilimines and electronically neutral alkenes

give reactions rates similar to those of intermolecular cycloadditions with electronically activated alkenes, even if the cyclisation of a single molecule negates the significant entropy penalty during the highly ordered transition state formed between dipole and dipolarophile. In fact, inactivated dipolarophiles can be cyclized in mild conditions, without using high temperature or excess of reagents.

1.3.2.4 Nucleophiles

Nitrilimines react with different types of nucleophiles, although not in a prolific way such as dipolar 1,3 cycloadditions[22]. The formation of these adducts were reported by Huisgen during his years dedicated to the study of nitrilimines. The general reaction scheme is shown below (Scheme 5).



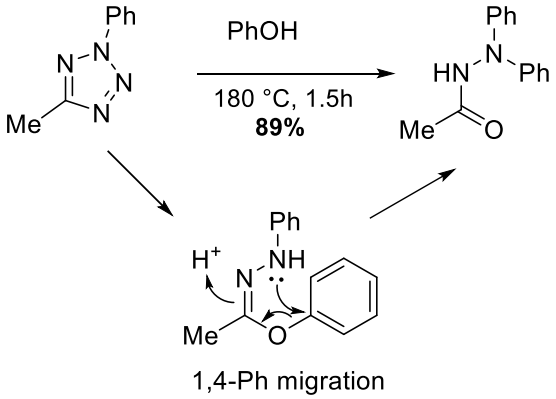
Scheme 5- NI reactivity with nucleophiles

The primary product given by this reaction shows the formation of a carbon-heteroatom bond on the C-terminus of nitrilimine, while the N-terminus is protonated. At this point, depending on the type of nucleophile used, there may be intramolecular arrangements that lead to the formation of new species. The rate of reaction with nucleophiles is however much lower than reactivity with dipolarophiles, even if there are particular cases in which some peculiar functional groups give rates in competition with those of cycloadditions[57].

The products obtained from the reaction between nitrilimine and some important nucleophiles will be listed and briefly described below.

Alcohols

After the formation of the intermediate previously reported to give the corresponding hydrazonyl ester, there is a migration of the aryl group onto the nitrogen, which leads to the formation of a thermodynamically favored amide bond[58](Scheme 6).

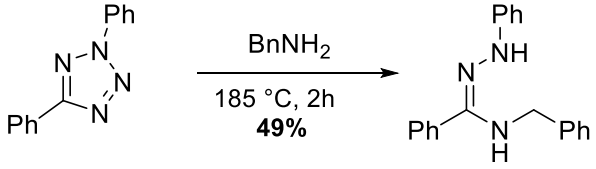


Scheme 6- NI + alcohol

The reactivity of alchols with nitrilimines is very low compared to other nucleophiles and dipolarophiles and also much less efficient[57]; in fact, the cases reported in the literature require a large excess of alcohol[59].

Amine

Also, in this case the first intermediate is like the one described above but here, subsequently, there is no spontaneous rearrangement because the product is stable[58] (Scheme 7).

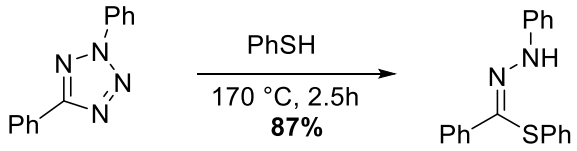


Scheme 7- NI + amine

Nitrogen-based nucleophiles are much more reactive towards nitrilimines and therefore an excess of amine is not necessary for the reaction to take place[57] and for this reason there are many more examples reported in the literature. In addition to the amines, hydrazines and hydrazones can also be used as nucleophiles[60]. The latter are a good example of the competitiveness of the reaction between nitrilimines and nucleophiles compared to that with dipolarophiles; since in this case the nucleophilic addition can compete with the cycloaddition with the double C-N bond[61].

Thiols

The mechanism of addition to nitrilimine is always the same as previously described, to form an α-mercaptohydrazones[58] (Scheme 8).

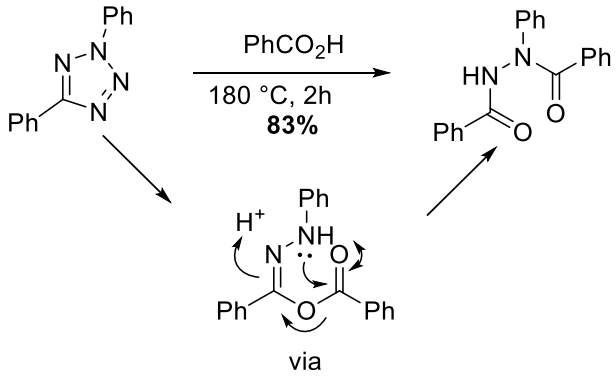


Scheme 8- NI + thiol

The reactivity of thiols is comparable to that of amines. The high efficiency of this reaction and the formation of compounds that are not very useful from a synthetic point of view has meant that this reaction was often considered as a parasitic reaction capable of forming by-products during cycloadditions[62]. The reaction with thiols is capable of out competing the reaction with amines and is comparable to that with carboxylic acids[63]. It was demonstrated in recent studies that the order of reactivity of NIs with nucleophiles follows this order: acids ≈ thiols > amines.

Carboxylic acids

The reaction of a nitrilimine with a carboxylic acid leads to the formation of an adduct which, given the poor stability, tends to rearrange through a 1,4-acyl shift to form a stable product with two amide bonds[58] (Scheme 9).

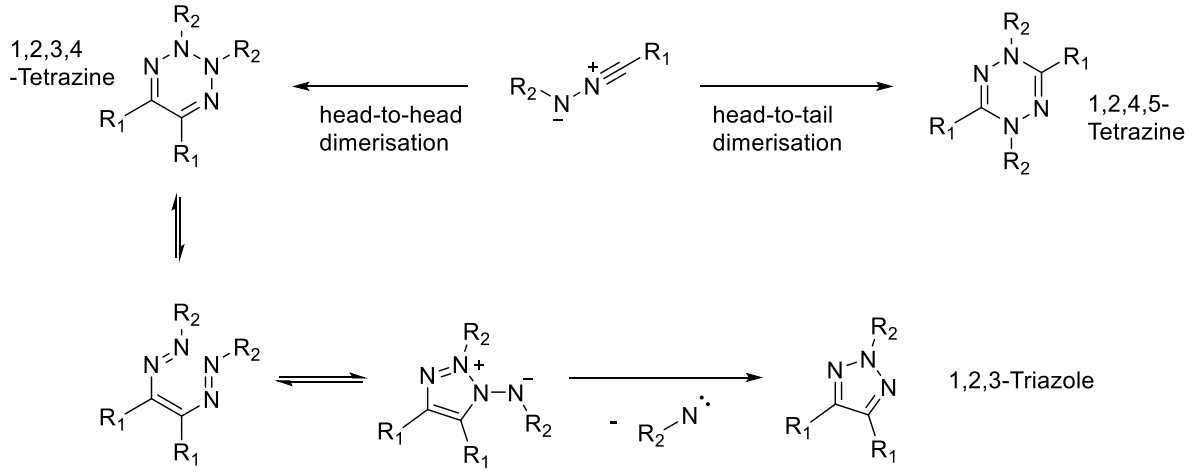


Scheme 9- NI+ carboxylic acid

Carboxylic acids are among the most reactive nucleophiles and can compete and beat even many dipolarophiles. This is because nitrilimine can deprotonate the acid, generating the most reactive carboxylate, before the addition to the electrophilic center, making this species more reactive than the neutral ones[64].

1.3.2.5 Dimerization

When nitrilimine is generated in the absence of a dipolarophile or a nucleophile with which to react, it is possible that two equivalents of the react with each other, forming a dimerization product. The selected reaction conditions can influence the product formed, since both 1,2,3-triazole and 1,2,4,5-dihydrotetrazine can be obtained[65] (Scheme 10).

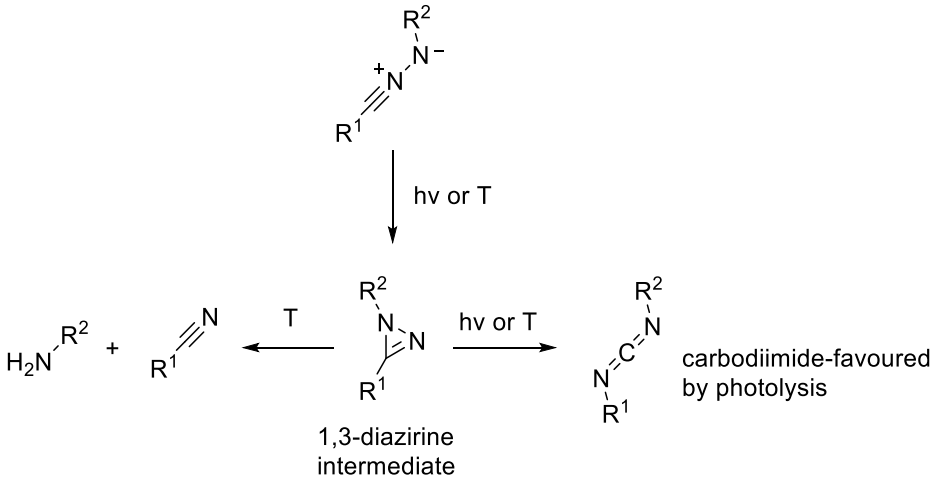


Scheme 10- NI dimerization process

There are two ways in which dimerization can occur, namely head-tail or head-head. Both form dihydrotetrazine (1,2,4,5 or 1,2,3,4), but 1,2,3,4 is not stable and undergoes cycloreversion to generate a bis-azoethylene, which subsequently gives a thermally ring closure or photochemically, generating a 1,2,3 triazole and a nitrene[66]. Both species are in most cases unwanted by-products formed during the reaction of nitrilimines with dipolarophiles or nucleophiles.

1.3.2.6 Decomposition

In the absence of a partner to react with (dipolarophile, nucleophile) and at high dilutions that inhibit dimerization, nitrilimines decompose into a series of simpler components (Scheme 11). Decomposition can only occur using irreversible methods of generating nitrilimines, i.e. starting from sydnones and tetrazoles.



Scheme 11- NI decomposition

The main product resulting from the decomposition is the corresponding carbodiimide which can be generated both thermally[67] and photochemically[25], even if photolysis is able to accelerate this process more. It has recently been shown that this rearrangement goes through the formation of a diazirine intermediate[68]. Once this species is formed, there are two possible degradation pathways. The main one is the formation of carbodiimide, but there is also the possibility that the corresponding nitrile will be formed from the C-terminal substituent. While the corresponding nitrene is formed from the N-terminal substituent, which subsequently generates the corresponding aniline[68].

1.3.3 Nitrilimine derivatives and their application

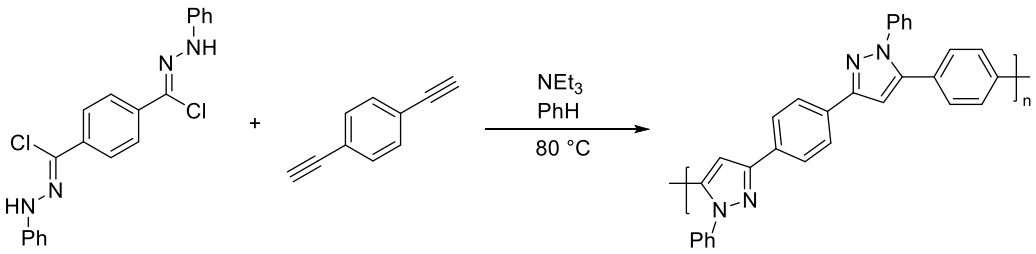
The reactivity of nitrilimines leads to a wide variety of derivatives that allowed these compounds to be applied in various scientific fields[22] with interesting results. Most of these applications use the 1,3-dipolar cycloaddition between nitrilimine and a substituted alkene, thanks to the ease with which it occurs and the possibility of having orthogonality. Some examples from the literature describing the application of these dipoles in the field of materials science, bio-orthogonal chemistry and their contribution to organic synthesis of biomolecules and natural products for medicinal applications will be reported below.

1.3.3.1 Material chemistry

Nitrilimines have been widely used in materials science, where their ability to undergo cycloaddition has been exploited. The precursors that gave the best results are 2,5-disubstituted tetrazoles, photochemically activated in selective reactions for surface patterning.

1.3.3.2 Polymer synthesis

Species capable of generating nitrilimines have been used for the synthesis of polymers, using species of the type A-A and B-B, such as bis 2,5-tetrazoles and bis-dipolarophiles containing double or triple bonds[69–71] (Scheme 12). Photochemical or thermal activation of these species allows to form the desired polymer. In addition, nitrilimine-containing monomers of type A-B have also been developed, also capable of forming polymers in the same way[72].



Scheme 12- NI copolymerization

Another application in this area concerned the extension of polymer chains: nitrilbutadiene rubber was modified with a tetrazole, allowing the subsequent photochemical dimerization in the presence of a bis-maleimide-based linker[73]. This method allowed to grow linear chains, minimizing the possibility of cross-linking and thus obtaining polymers with a high molecular weight with low dispersity, difficult to obtain through other synthetic ways. This approach is also applicable for the synthesis of copolymers[74].

1.3.3.3 Polymer cross-linking

Cycloaddition reaction by nitrilimines found application also in polymer cross-linking. Scope of the reticulation reaction is the formation of a branched tridimensional polymeric structure having tailored properties, owing to the elasticity of the network or to the segmental chain length and mobility, or else to the porosity of the 3D structure. For this purpose, nitrilimine precursors were

inserted into the monomers as side chains, subsequently polymerized by radical polymerization. Once the functionalized polymer was obtained, it was possible to carry out cross-linking both by photochemical and thermal methods[75,76] (Fig.2). The advantage of this technique lies in the fact that an external cross-linking agent is not required, and any additional step is not necessary.

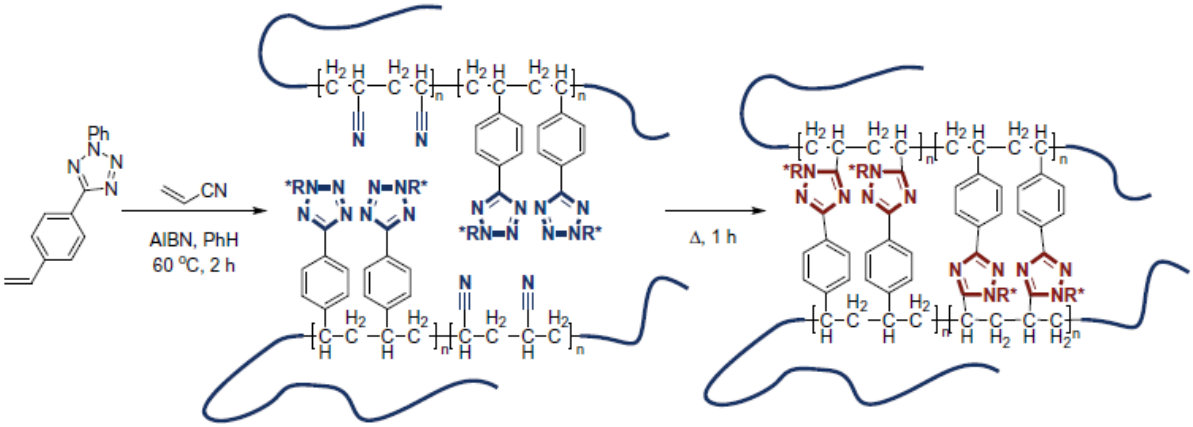


Figure 2- NI polymer cross-linking, from *C. Jamieson and K. Livingstone, The Nitrile Imine 1,3-Dipole*

In some cases, however, it was useful to introduce a cross-linking agent containing a double system capable of generating nitrilimines, to be subsequently reacted with the polymer. This approach was used to expand the use of this cross-linking technique, particularly with commercially available polymers such as cellulose[77]. Moreover, the formation of the fluorescent pyrazoline ring has allowed to find a further application of this technique: fluorescent patterns drawn onto polymer surfaces (laser writing), generating the cross-linking selectively in space[78].

1.3.3.4 Reaction with carbon allotropes

The well-known reactivity of nitrilimines with carbon-carbon double bonds made it possible to use these species for the functionalization of carbon-based nanoparticles. Most publications in this field involve the use of fullerene C-60 (Fig.3), which can be considered an electron deficient alkene owing to the degree of conjugation within its π-electron system[79].

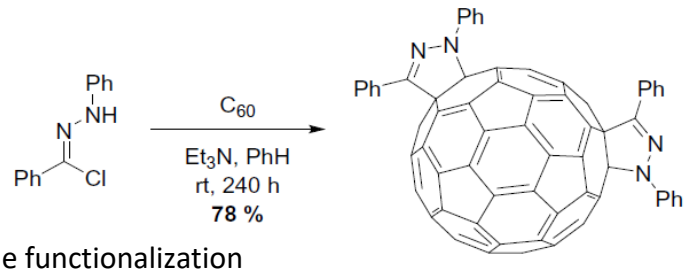


Figure 3- NI- Fullerene functionalization

This fullerene can undergo 1,3-dipolar cycloaddition with many different dipoles, including nitrilimines. The tetrazoles can react thermally or photochemically forming pyrazolino-fullerene systems in good yields. Pyrazoline is a linking moiety, which allows functional groups such as amines[80] or aldehydes[81] to be attached to the fullerene in order to subsequently modify the surface of the particle. Examples of functionalization of C-70 and C-80 fullerenes are also known even if the examples are very limited[82]. The fullerenes thus morphed found use in donor-acceptor or push-pull systems in which the fullerenes act as an electron-rich species[83]. Functionalization by reaction with nitrilimine does not break the π-system, as other types of functionalization often do, maintaining a reduction potential similar to that of unmodified C-60 fullerenes[84]. Other allotropic forms of carbon have also been shown to be reactive towards nitrilimines, such as carbon nanotubes[85] and graphene[86].

1.3.3.5 Surface chemistry

Even in the field of surface chemistry nitrilimines have found fertile ground[87], thanks to their ability to functionalize in a rapid and orthogonal way, exploiting the possibility of using tetrazoles as photochemically activable precursors. The simplest example concerns the anchoring of a polymer on a silicon wafer surface, using a 2,5-tetrazole exposed to UV light in the presence of a polyacrylate derivative capped with a maleimide[88] (dipolarophile). A similar reactivity has also been demonstrated in the attack of an enzyme on the surface of a polymersome[89]. The photochemical activation of tetrazoles allows the use of templates and shadow masks, to selectively irradiate part of the surface to perform patterning with the product of the reaction with nitrilimine[90](Fig.4). An alternative method concerns a microcontact chemistry in which a reagent is selectively applied to some parts of the surface, through a special mold, reacting only on the exposed parts[91].

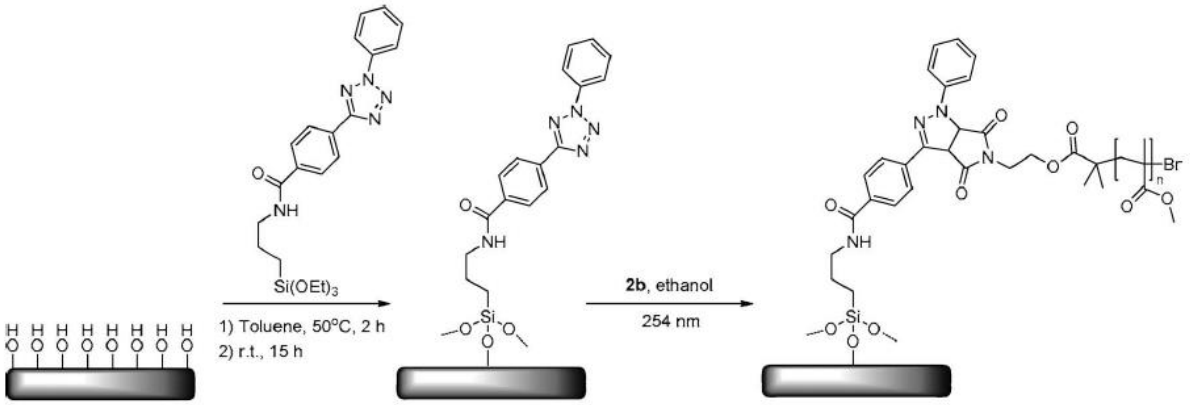


Figure 4- NI surface modification, from *Adv. Funct. Mater. 2012, 22, 304–312*

Through this technique it is possible to attack biomolecules on a surface, even peptide sequences of tens of units[92]. It is also possible to use cellulose substrates, modified with nitrilimine precursors, instead of the common silicon-based substrates[93]. It is also possible to functionalize nanoparticles, for example gold, by using 2,5-diaryl tetrazoles capped with alkyl thiols and subsequently making them react with maleimide derivatives containing biomolecules or polymers[94].

1.3.3.6 Medicinal applications

Nitrilimines have been used for the synthesis of compounds of pharmaceutical interest, containing five-membered heterocycles, formed by the 1,3-dipolar cycloaddition with an alkene or alkyne[95]. The most common moiety is the pyrazole, which is rarely formed starting from an alkyne as dipolarophile (not very reactive), but usually this problem is avoided by using a modified alkene which is subsequently converted into the desired product by oxidation or tautomerism of pyrazoline[96,97]. Another approach uses an enamine as a dipolarophile (very reactive and with a regioselective attack); the subsequent treatment with acid or base generates the desired pyrazoline[98].

1.3.3.7 Bioorthogonal chemistry

The 1,3-dipolar cycloaddition between a nitrilimine and an alkene, often referred to with the generic term "click chemistry", have proven to be an effective method for obtaining bioorthogonality[99]. The term bioorthogonal chemistry refers to a chemical reaction that can occur

within living systems without interfering with native biochemical processes, and without being toxic to cells. The preferred reactivity involves the photolysis of 2,5-diaryl tetrazoles, due to the traceless nature of the reaction (minimal formation of by-products).

1.3.3.8 Protein ligation

Cycloaddition of nitrilimines has recently also been used for protein ligation, using 2,5-disubstituted tetrazoles. In Figure 5 is reported how the incorporation of O-allyltyrosine into Z-domain protein gives the dipolarophile that, after subsequent photochemical reaction with a tetrazole forms a pyrazoline derivative which, being fluorescent, can easily show attachment to the protein[100]. Subsequently, based on this work, further studies were published in which, by modifying the tetrazole with the appropriate substituents, it was possible to modify the reaction rate[54].

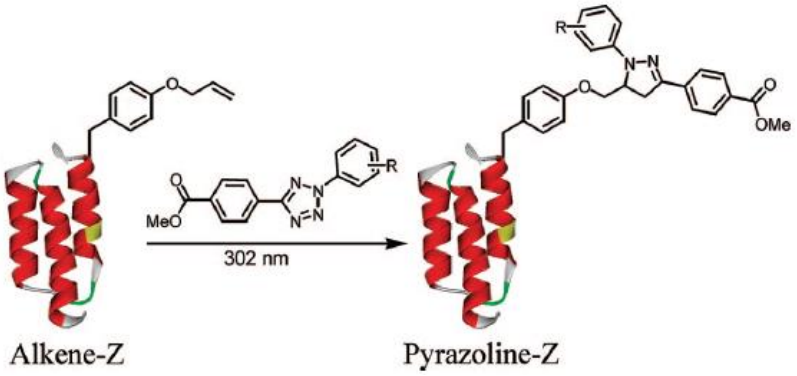


Figure 5- NI protein ligation, from *J. AM. CHEM. SOC. 2008, 130, 9654–9655*

To obtain even more reactive systems, methodologies have been developed in which tetrazole reacts with previously substituted amino acids in order to contain a terminal double bond[100] (e.g. amidation of lysine or allylation of tyrosine with acrylic acid). Supported by these results, in recent years increasingly complex methods have been developed to introduce species capable of generating nitrilimines (especially tetrazoles) within biomolecules. For example, through genetic encoding of an artificial amino acid inside the protein of interest, by an engineered E. Coli bacterium[101]. The strength of this technique lies in the fact that the photolysis of tetrazole is a non-invasive technique and, by appropriately modifying the activation wavelength, it is possible to reduce the risk of damage within biological systems such as DNA. Studies on the reactivity of nitrilimines with nucleophiles were also carried out, demonstrating that the presence of

substituents in ortho on the C-aryl ring allows to maintain the selectivity of the reaction with the double bonds to the detriment of the nucleophiles, whose attack is sterically prevented[102].

1.3.3.9 Chemosensors

Nitrilimines can be used as a detector of analytes present in living systems, exploiting the fluorescence of their derivatives in turn-on imaging. In these situations, probes (e.g. pyrazolines) are formed as products of the photochemical reaction between the nitrilimine and a double bond. An example concerns the accumulation of fumarate, due to a poor regulation of the metabolism, which can be discovered through this technique[103]. The fumarate reacts photochemically with a biomolecule containing a tetrazole, forming a highly fluorescent pyrazoline, which makes it possible to quantitatively measure the level of fumarate (Fig.6).

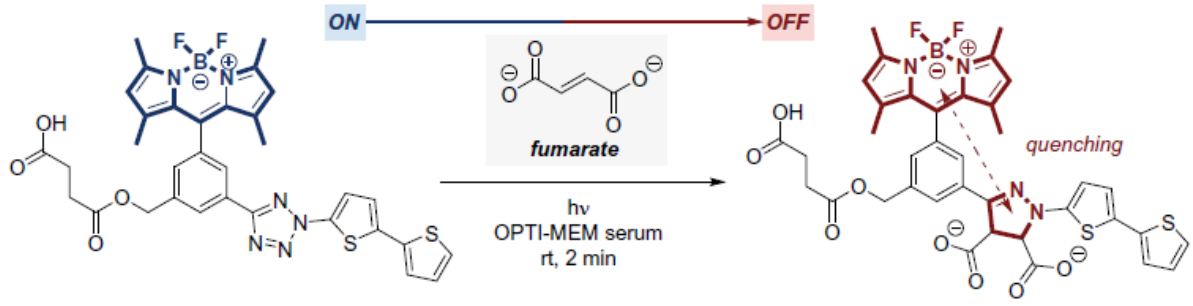


Figure 6- BODIPY-NI chemosensor, from *C. Jamieson and K. Livingstone, The Nitrile Imine 1,3-Dipole*

1.4 Tetrazoles

Tetrazoles are the most common precursors of NIs that can be found in literature[104]. They are a class of synthetic organic heterocyclic compounds, consisting of a 5-member ring of four nitrogen atoms and one carbon atom. The synthesis of tetrazoles was first reported[105] in 1885 by Bladin group at Uppsala University but, at that time, these compounds were considered of little use from a synthetic and applicative point of view. Several years later, during the 1950s, interest in tetrazoles grew when it was demonstrated the great stock of chemical energy accumulated in the tetrazole ring. From that moment many approaches to the synthesis were proposed and the applicability of these compounds was discovered in several research fields. Over the past 20 years this interest has continued to grow, as demonstrated by the increase in publications on this topic

concerning the development of efficient and safe methods for their synthesis, the study of the physicochemical properties and their reactivity[106,107].

1.4.1 Structure

Tetrazole is a structure with tunable aromaticity. In fact, its aromaticity depends on the nature and position of the substituents, or on the prototropic form in which it is found[108](Fig.7).

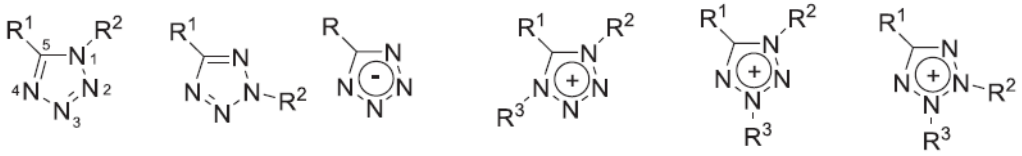


Figure 7- Tetrazole prototropic forms

The two forms with greater aromaticity correspond to the tetrazole anion and to the 2,5 disubstituted one (which was chosen by us as the structure to work on). The high aromaticity of tetrazoles, compared to other azoles, is underlined by the strong chemical and thermal stability of this system[109]. As shown by computational calculations, the presence of a substituent on the carbon of the ring influences the value of the charges on the nitrogen atoms and the dipole moment of the system. The non-substituted NH tetrazoles, but also the disubstituted 1,5 and 2,5, in addition to the 1H and 2H, have a pyrrolinic nitrogen atom and three pyridine nitrogen atoms in the ring. The latter are strong nucleophilic centers, with the highest negative charge located on the N4-nitrogen atom. Regarding the tetrazole cations, the unprotonated nitrogen atoms can react with various electrophiles (e.g. carbocation or metal ions). Tetrazole anions are symmetrical structures, despite the presence of a delocalized charge. While, as regards unsubstituted tetrazoles or substituted tetrazoles in position 5 containing an electron-donor or a weak acceptor, the 1-H form turns out to be more polar than the 2-H form[108]. The tetrazole ring is a strongly electron-acceptor system and the protonated tetrazole ring turns out to be extraordinarily electron-acceptor. The tetrazole ring is planar in both neutral and ionic forms, with a bond length between the atoms within the cycle between 1.26 and 1.36 Å, with the N2-N3 bond being the shortest[110].

1.4.2 Synthesis

Given the vast number of synthetic pathways for the synthesis of tetrazoles, we will focus only on those that lead to the formation of the tetrazoles used during this doctoral project: 1H-unsubstituted and 2,5-disubstituted.

1.4.2.1 1H-unsubstituted

These tetrazoles are of particular interest as intermediates in the synthesis of many compounds. The most popular preparation for the synthesis of 1H-unsubstituted tetrazoles is based on the reaction of a nitrile with the salts of hydrazoic acid (or other derivatives). Usually the formation of tetrazole can proceed by two ways[111]: [3 + 2] cycloaddition of a dipolarophile (RCN) with a 1,3-dipole (XN_3) via the intermediate A, or by nucleophilic attack of the azide on the carbon of the nitrile to form an aridoazomethinic intermediate (B) which subsequently cyclizes to form tetrazole (Fig.8).

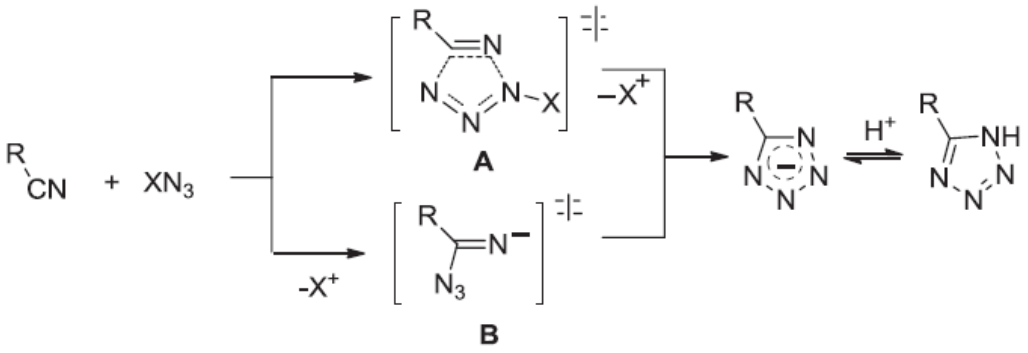
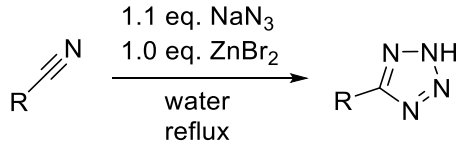


Figure 8- 1H-unsubstituted tetrazoles formation

The choice of a suitable solvent catalyst can influence the course of the reaction according to one of the two mechanisms mentioned above.

Several variants for the synthesis of 1H-unsubstituted tetrazoles have been developed in the past decades. In particular, the synthesis proposed by K.B. Sharpless[112] has found great success. This method allows to solve three problems related to the synthesis of tetrazoles: the use of tin or silicon azide, the use of strong Lewis acids and the use of acidic media. The drawbacks connected to these procedures are the use of toxic and expensive metals, severe water sensitivity, the use of organic solvents and the presence of hydrazoic acid, which is explosive, toxic and volatile.



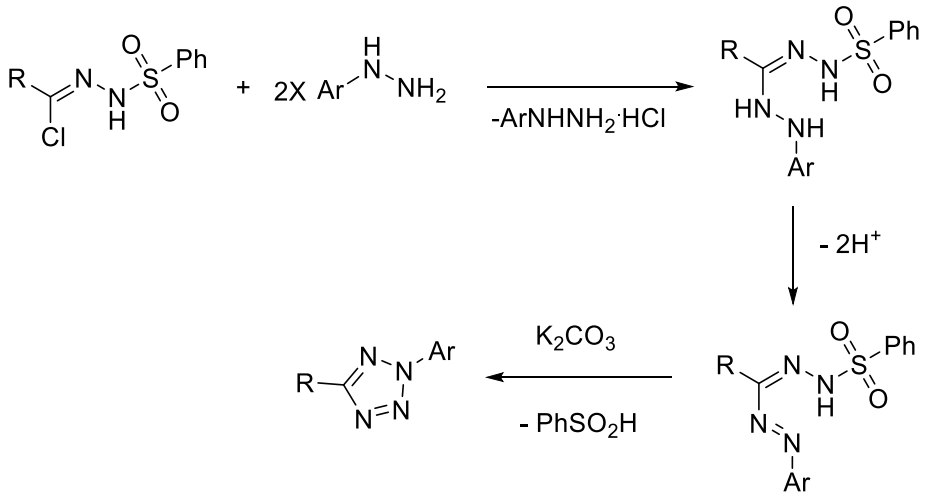
Scheme 13- Sharpless 1H unsubstituted tetrazole

The new procedure proposed instead provides for the use of water as a solvent and the presence of zinc salts to make the reaction take place with excellent yields (Scheme 13). Furthermore, the method is applicable to a large number of nitriles and has been found to be scalable on large quantities at an industrial level.

1.4.2.2 2,5-disubstituted tetrazole synthesis

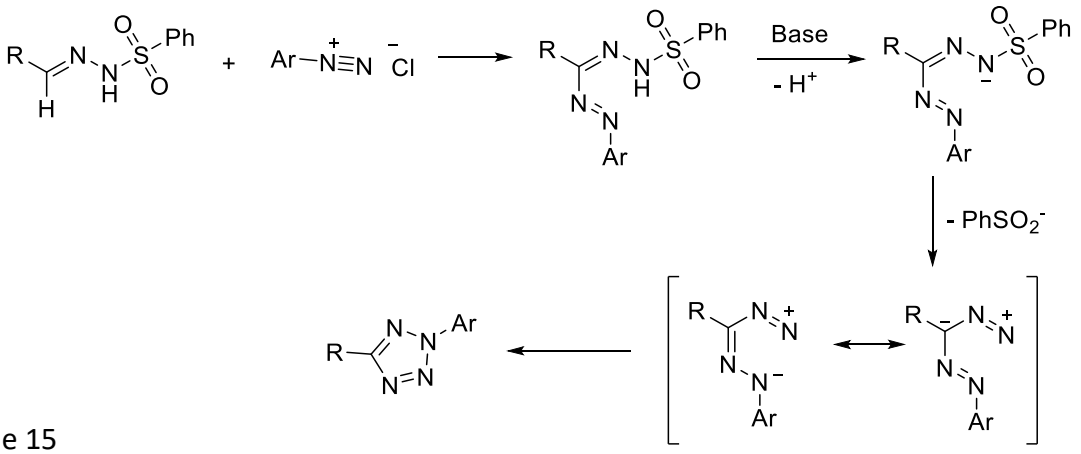
The synthesis of 2,5-disubstituted tetrazoles can be carried out by various pathways. The most widespread methods coincide with the oldest, dating back to the mid-1970s and were proposed by A. Kakehi.

Two methods for obtaining tetrazoles in two steps are reported in his publications. The first method[113] involves the reaction between an N-phenylsulfonylbenzhydrazidoyl chlorides and an arylhydrazine, with subsequent action of the potassium carbonate to form the 2,5-disubstituted tetrazole through a concerted mechanism that provides for the elimination of the benzenesulfinate ion from the intermediate 1,3-diaryl-5-phenylsulfonylformazanide anion (Scheme 14).



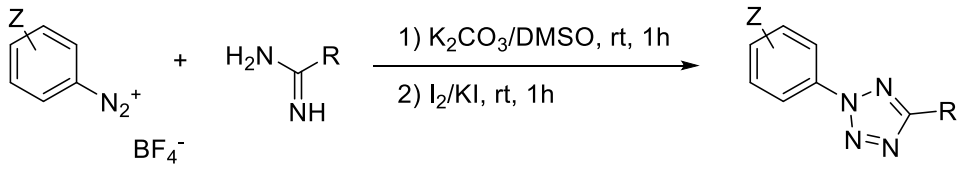
Scheme 14

The second method[114] involves the reaction between an aromatic aldehyde and the phenylsulfonylhydrazones to form an intermediate which subsequently reacts with an arendiazonium salt, under basic conditions. This second method has established itself as the best for obtaining 2,5-disubstituted tetrazoles thanks to the great variety of starting aromatic aldehydes, the simplicity of the procedure, the mild reaction conditions and the high reaction yields (Scheme 15).



Scheme 15

Recently a variant to Kakehi synthesis has been proposed, to obtain the same tetrazoles. It involves a one-pot sequential reaction of amidines with aryldiazonium salts, followed by the addition of I_2 / KI under basic conditions to give the desired compound, via oxidative ring closure[115](Scheme 16).

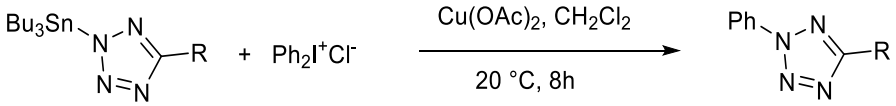


Scheme 16

This synthesis turns out to be a valid alternative to the previous one thanks to the mild rection conditions, the short reaction times and the high yields obtainable. It also turns out to be easy-to-handle and atom efficient, even on gram scale. The only defect lies in the limited commercial availability and the high cost of the starting materials, which limits their use.

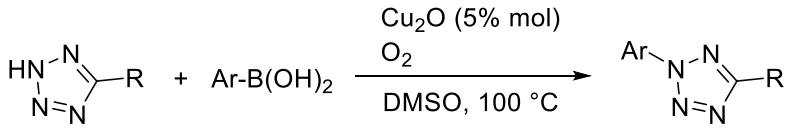
The synthesis of tetrazoles proposed by Kakehi is still considered the best for the synthesis of 2,5-disubstituted derivatives, for the reasons listed above; however, other syntheses relating to these compounds have recently been proposed, involving cross-coupling reactions. The difference of

these recent methodologies lies in the fact that they start from 1H-unsubstituted tetrazoles (the synthesis of which was described above) and involve a subsequent attack of a substituent group in position 2 of the tetrazole. These syntheses are relevant because they allow to obtain more complex molecules (containing a tetrazole inside them) and are often used in multistep procedures, while the Kakehi synthesis remains the most used to obtain 2,5-disubstituted tetrazoles without particular synthetic complexity. One of these methodologies[116] involves the arylation of N-tributylstannylated 5-substituted tetrazoles with diaryliodonium salts, in the presence of stoichiometric amounts of $Cu(OAc)_2$ (Scheme 17).



Scheme 17

This reaction has various drawbacks: the use of stannyls which are toxic, the need for stoichiometric quantities of copper salts and above all the difficulty in preparing some diaryliodonium salts as well as the need to prepare the starting reagents, lengthening the number of steps. The last synthesis to mention provides the direct C-N coupling of H-tetrazole and boronic acid in aerobic conditions with copper-catalysis[117,118](Scheme 18).



Scheme 18

This procedure, although better than the previous one with the stannyls, has similar drawbacks, to which is added the need to carry out the reaction in an oxygen atmosphere.

For the reasons listed above these synthetic routes were mentioned only for the record but were not used to obtain the compounds made during this PhD project. The desired compounds were synthesized through a variant of Kakehi's synthesis for 2,5-disubstituted tetrazoles and through Sharpless reaction for 1H-unsubstituted tetrazoles.

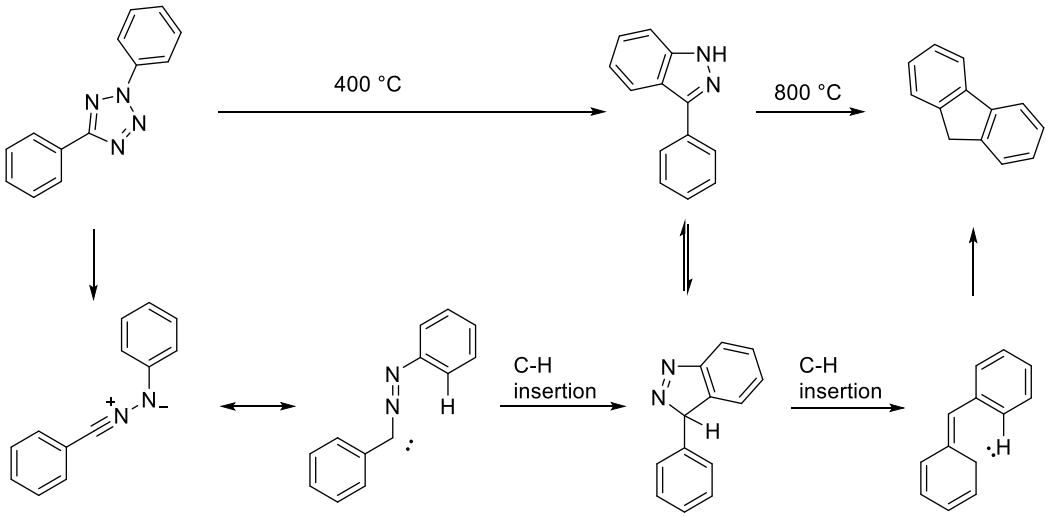
1.4.3 Reactivity

Among the various methods in which 2,5-disubstituted tetrazoles can react, the most used involves the breaking of the ring, with consequent loss of nitrogen, to form nitrilimine. This peculiar reactivity allows to obtain an enormous number of synthetic derivatives, since the nitrilimine formed can react with many functional groups. Before seeing some of the most interesting products of this reactivity, we will focus on the method by which tetrazoles are activated. In the literature the methods described are mainly two: thermal and photochemical. It must be mentioned that only 2,5-disubstituted tetrazole regioisomer expel nitrogen through nitrilimine intermediate, while 1,5-disubstituted tetrazole does not form the nitrilimine during decomposition process[119].

1.4.3.1 Thermolysis

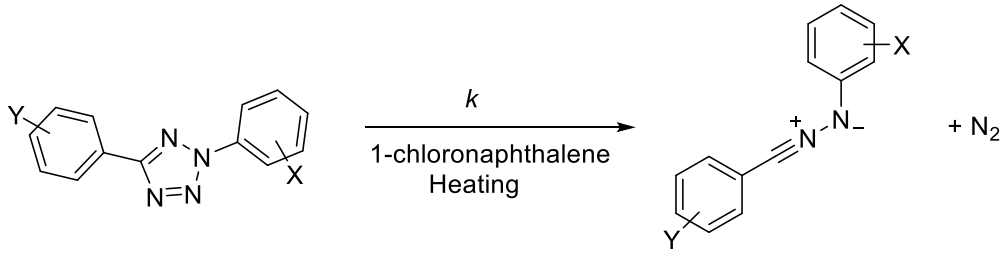
Thermal activation of 2,5-disubstituted tetrazoles to form nitrilimines was first reported in 1959 by Huisgen[23] and is also the first method of generating NI described in the literature. This method is particularly useful because it requires the use of only two species, the tetrazole and the molecule with which you want to react it, without exogenous reagents. The stumbling block that has severely limited the application of this type of reactivity is the temperature required for the activation of tetrazole, which, in the case of 2,5-disubstituted tetrazoles, is usually above 160 °C[120]. This requires that the reaction products are stable at these temperatures and furthermore prevents the use of this reactivity in fields where the high temperature is not applicable, as in the biological field.

These high temperatures, however, may be advantageous in some cases, such as pyrolysis of tetrazoles at temperatures above 400 °C which leads to the formation of compounds that are inaccessible at lower temperatures. For example, by taking 2,5-diphenyl tetrazole and performing a flash vacuum pyrolysis, it is possible to instigate an insertion (carbene-like) in position 2 of the N-aryl ring, with the formation of an indazole. This compound, if heated to 800 °C expels another nitrogen molecule generating the fluorene[121](Scheme 19).



Scheme 19- Pyrolisis mechanism

In addition to this example, other reactions that occur at high temperatures and lead to the formation of compounds that cannot be obtained with more conventional approaches are reported in the literature[122]. The substituents present in positions 2 and 5 can influence both the activation temperature and the rate of thermolysis[123] (or NI formation). As described in the literature, the nitrilimine formation rate was studied by modifying the substituents with electron withdrawing or electron donating groups on both aromatic rings of a 2,5-diphenyl tetrazole, selected as the reference structure. It has therefore been observed that the presence of electron donating groups on the C-aryl ring leads to faster decomposition, as well as the presence of electron withdrawing groups on the N-aryl ring. This direct impact on the reaction rate shows that the cleavage of the N2-N3 and N4-C5 bonds is not symmetrical and that therefore there is a residual charge present in the transition state formed in the pyrolysis of tetrazole[124]. Furthermore, considering the Hammett plot (Fig. 9) of this reaction it can be deduced how the effect of the substituent on the N-aromatic ring is five times more influential on the reaction rate than the substitution of the C-aryl ring.



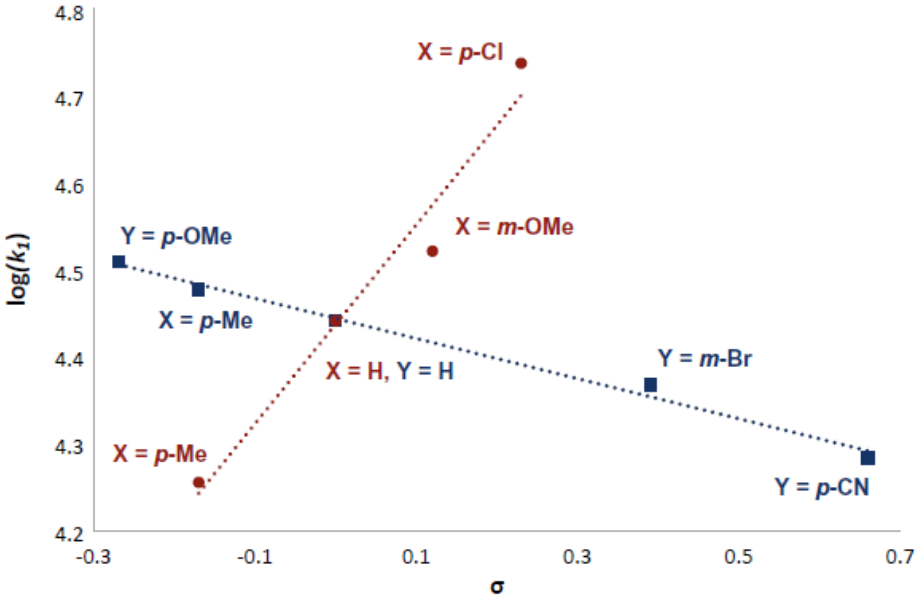
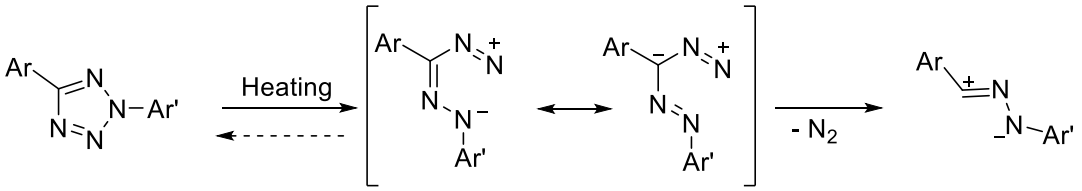


Figure 9- Hammet plot, from *C. Jamieson and K. Livingstone, The Nitrile Imine 1,3-Dipole*

This led to the hypothesis that the N2-N3 bond may be the first to break, probably due to the rate determining step of the process, according to the following proposed mechanism (Scheme 20).



Scheme 20- Thermal activation mechanism

1.4.3.2 Photolysis

This method for the activation of 2,5-disubstituted tetrazoles, discovered about ten years after thermolysis, has the advantage of not requiring high temperatures to form nitrilimines[125]. The wavelengths needed to stimulate the decomposition of the system is usually around 250-300 nm. In order to obtain light in the UV-B range of the electromagnetic spectrum, it is necessary to use high-energy mercury lamps, which were not a common lighting system, especially in the past and, this fact, has limited their use for many years.

But, when an article[126] was published in 2007 describing the activation of a tetrazole using a 300nm hand-hold UV lamp (the classic used in the laboratory for TLC), this technique came back into vogue. In particular, it found application in the field of material and bioorthogonal chemistry,

thanks to the possibility to avoid any exogenous reagent. With the spread of this technique, the first questions also arose regarding the mechanism of photolysis of tetrazoles. At first it was assumed[127] that these species were generated by a forbidden π-π* transition to the first excited singlet state. Furthermore, the measurement of the quantum yield, which turns out to be good compared to that of other photochemical reactions, indicates an efficient photolytic process. The quantum yield of the process was also found to be weakly influenced by the substrate, the presence of substituents on the C-aryl ring and other parameters such as the concentration and polarity of the solvent. The only parameter capable of significantly influencing it is the type of substituent on the N-aryl ring, in particular, similarly to what was discovered on thermal activation, the presence of electron withdrawing groups is able to improve the quantum yield, further confirming that also the photolysis of tetrazoles is not a symmetrical process[128]. Furthermore, the non-influence of the substituent on the C-aryl ring confirms the proposed thermolysis mechanism: the N2-N3 bond is broken in the rate determining step of the process. Only recently, thanks to the development of computational methods combined with experimental data, was it possible to discover and propose a new mechanism for the photolysis of tetrazole and the subsequent formation of nitrilimine[129]. Initially, the excitation of tetrazole involves the π-π* transition to the first excited state (S_1). HOMO is positioned on both the tetrazole and the N-aryl ring, justifying the observations made experimentally on the effect of the substituents on that ring on the quantum yield. Subsequently, nitrilimine is generated through the first triplet state (T1) formed by intersystem crossing (ISC) from S1. The triplet state of the tetrazole decomposes into a radical intermediate, from which the nitrilimine is produced by a conical intersection (Figure 10).

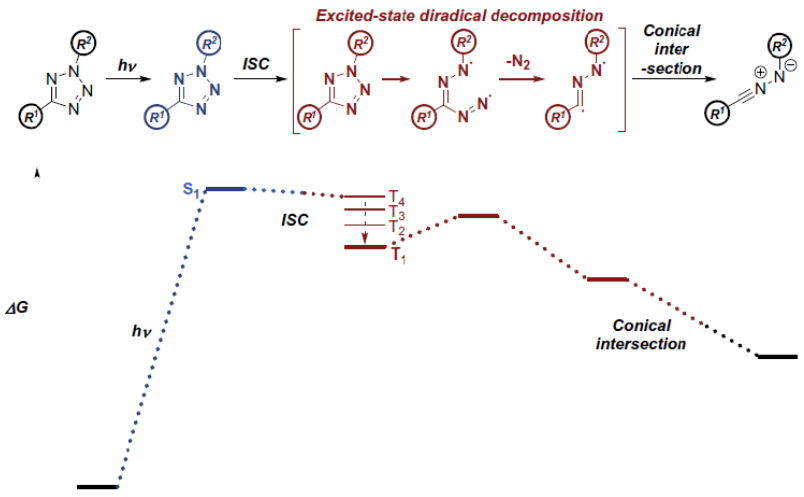


Figure 10- Photochemical process, from *C. Jamieson and K. Livingstone, The Nitrile Imine 1,3-Dipole*

Thanks to these studies it was possible to identify which are the important parameters in this process, that is, that the excitation from the S_1 state must be obtained by irradiation with a suitable and defined wavelength. But also, that the chemical properties of tetrazole that determine the nitrilimine quantum yield is the fast ISC at the expense of competitive relaxation processes (Fig.11). In conclusion, the exact quantum yield value at which the formation of nitrilimine takes place from the corresponding tetrazole is not simple and requires both computational calculations and experimental data, case by case, to find out if the formation of nitrilimine is favored or not. Fortunately, the cases in which the nitrilimine is not formed are limited to a few tetrazole species[129,130] (e.g. containing nitro and dimethylamino functional groups). As for all the other tetrazoles described in the literature, however, they are particularly reactive to photolysis, generating nitrilimines in good quantum yields.

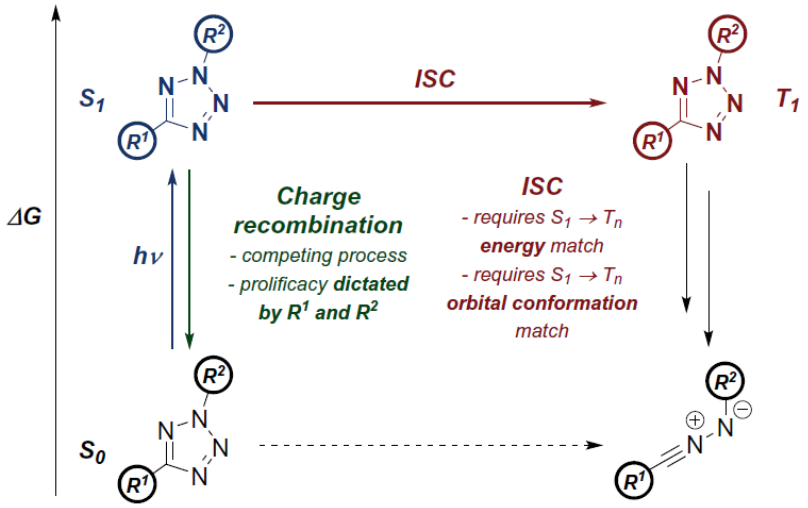


Figure 11- Photochemical mechanism, from *C. Jamieson and K. Livingstone, The Nitrile Imine*

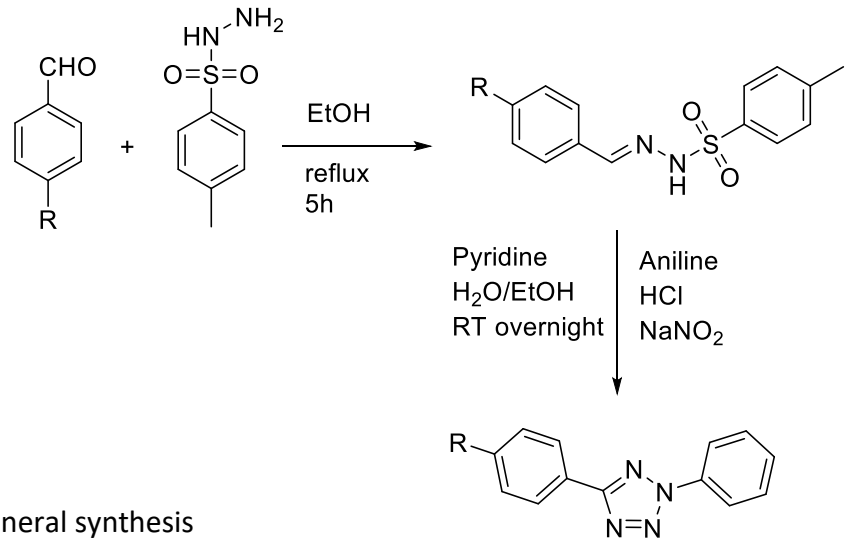
1.5 Our proposal

The target proposed by Pirelli concerned the development of organic systems capable of functionalizing the polymer matrix. Particular interest laid in being able to functionalize commercially available polymers already used for tires applications at temperatures above 100 °C, even better if in a range between 140 and 200 °C, which corresponds to the range in which rubber can be processed and vulcanized. For this reason, after a careful search of the literature, we identified tetrazoles as the most promising class of compounds for our purpose.

As mentioned above, the thermal activation of tetrazoles was not investigated in detail within the scientific community, essentially due to the high temperatures involved in the process. In fact, there are few research fields in which high temperatures can be used and even in these cases photochemical activation is often preferable. One of the few applications in which the thermal reactivity is preferable to the photochemical one is the application in the tires field, as reaction shall occur in the bulk and such bulk is usually black. In fact, we decided to thoroughly study this technique in order to functionalize commercially available polymers directly during the process and in particular the vulcanization phase, which requires temperatures above 150 °C. On the contrary, the use of the photochemical activation of tetrazoles was of little use to our purpose. Indeed, this technique can only be applied in solution (while we are concerned with bulk reactivity) or on very thin layers where light can penetrate, something that cannot be applicable to a tire. Starting from the information collected in literature, it was decided to study the synthesis of tetrazoles and their thermal reactivity, focusing on the 1,3-dipolar cycloaddition reaction between the generated nitrilimines and the polymer double bonds.

1.5.1 Tetrazole synthesis

Regarding the synthesis of tetrazoles, we decided to focus on the one reported by Kakehi[114], which allows to obtain 2,5-disubstituted derivatives through a 2-step synthesis. The reason that led us to choose this synthesis is the extreme protocol simplicity which does not require special experimental reaction conditions, the relative cheapness of the reagents and the possibility to scale-up. Below is reported the reaction scheme and the synthesis of a generic tetrazole according to this procedure (Scheme 21).



Scheme 21- General synthesis

Step 1: An aromatic aldehyde (1 eq) is dissolved in ethanol. Tosylhydrazide (1 eq.) is added and the reaction is stirred for 5h at reflux. Then the mixture is cooled, and water added. The precipitate formed was collected in a funnel. The product was used for the next step without any further purification.

Step 2: The solid of the first step is dissolved in pyridine to give solution A. In parallel, a solution of $NaNO_2$ (1 eq.) in water is added dropwise to a cooled mixture of aniline (1 eq.) dissolved in water/ ethanol (1:1) and concentrated HCl to give solution B. Solution A is cooled with an ice bath and solution B is then slowly added. The mixture was allowed to react overnight. Then is poured to an acid solution (HCl) and the precipitate formed collected by filtration. The crude was purified with the appropriate method (different for each tetrazole).

1.5.2 Thermal activation study

Thanks to this methodology, the synthesis of various tetrazoles, relevant for our purposes, was planned and realized. Given that there are not many examples in the literature, we wanted to study the effect of the substituents in position 2 and 5 of tetrazole on the activation temperature (generation T of nitrilimine). To do this, each compound was subjected to thermogravimetric analysis (TGA), with this technique it was possible to see the temperature of nitrogen loss in weight from the tetrazole to form nitrilimine. In Fig. 12, is reported the decomposition temperature of a tetrazole bearing a carboxylic function in para position of the phenyl ring

connected to the tetrazole carbon atom; this is around 210 °C with a sharp weight decrease.

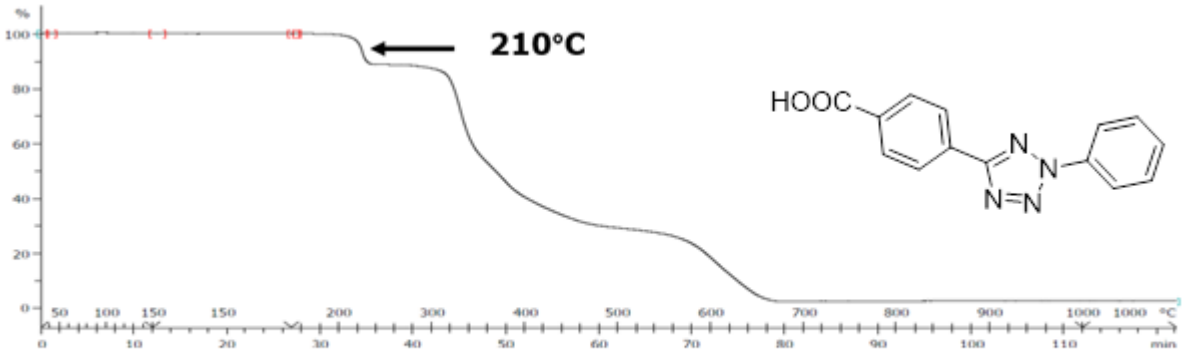
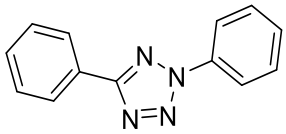
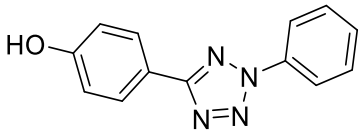
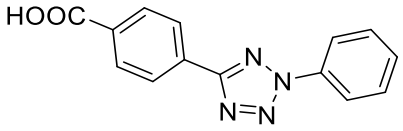
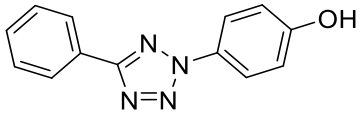
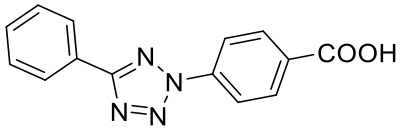
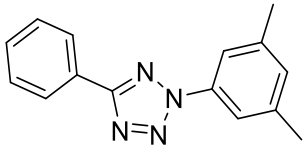


Figure 12- Tetrazole TGA

The following table (Table 1) shows the synthesized tetrazoles and the activation temperature.

N°	Formula	Molecular Formula	M.W. (g/mol)	Activation Temperature (°C)
1		$C_{13}H_{10}N_4$	222.25	170
2		$C_{13}H_{10}N_4O$	238.25	190
3		$C_{14}H_{10}N_4O_2$	266.26	210
4		$C_{13}H_{10}N_4O$	238.25	150
5		$C_{14}H_{10}N_4O_2$	266.26	180
6		$C_{15}H_{14}N_4$	250.31	165

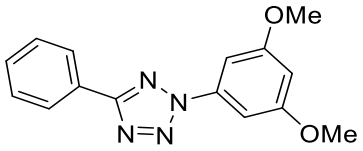
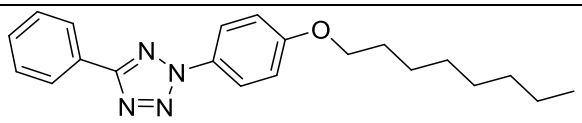
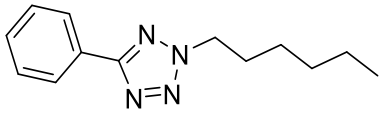
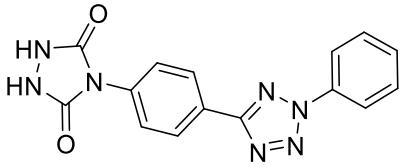
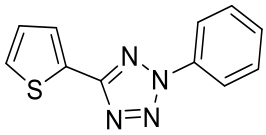
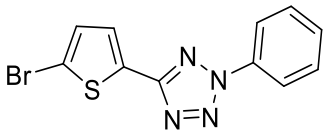
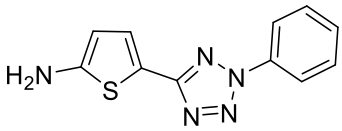
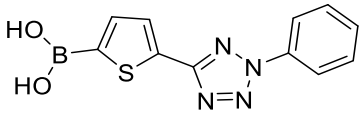
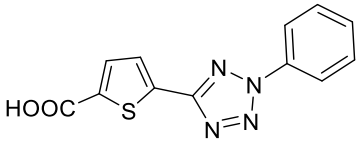
7		$C_{15}H_{14}N_4O_2$	282.30	160
8		$C_{21}H_{26}N_4O$	350.47	180
9		$C_{13}H_{18}N_4$	230.32	---
10		$C_{15}H_{11}N_7O_2$	321.30	200
11		$C_{11}H_8N_4S$	228.27	150
12		$C_{11}H_7BrN_4S$	307.17	150
13		$C_{11}H_9N_5S$	243.29	165
14		$C_{11}H_9BN_4O_2S$	272.09	140
15		$C_{12}H_8N_4O_2S$	272.28	175

Table 1

The collected data demonstrate the effect of the substituents on the two aromatic rings of tetrazole. For the substituents on C-aryl, the presence of electron donor groups lowers the activation temperature (e.g. thiophene), while electron withdrawing groups raise the activation temperature (e.g. carboxylic acid). Regarding the N-aryl unit, the presence of the substituents on the ring has similar effects on the activation T, even if the effect is much less marked (the temperature varies by 10-15 °C). Take for example the carboxylic acid substituent which, if attached to the ring on the C-aryl (compound 3), raises the T to 210 °C, while if attached to the

ring on the N-aryl (compound 5) it is 180 °C (a little bit higher respect to the 170 °C of unsubstituted tetrazole 1). It should be noted that these results concern the activation temperature and not the reaction kinetics (discussed in the previous paragraph on thermolysis). The trend of the two parameters as a function of the substituents is often similar, but not always. As can be seen in compound 5, the presence of carboxylic acid on the N-aryl raises the activation temperature (respect to compound 1) and at the same time the nitrogen release rate should rise.

1.5.3 Polymer functionalization

At this point, after having studied how to modify the activation temperature of the tetrazoles to generate the nitrilimine, it was investigated the effectiveness of the reaction between the nitrilimine and the double bonds of the polymer. The selectivity of cycloaddition on vinyl and terminal double bonds, with respect to internal ones, was already well known, due to accessibility effects. Regarding the polymers we expected similar behavior, indeed even more accentuated by the fact that a polymer is a macromolecule which tends to organize itself in space in a convoluted way, leaving the vinyl double bonds more exposed.

1.5.3.1 POLYVEST® 130

To demonstrate polymer functionalization, we used POLYVEST® 130 (purchased from Evonik, Fig.13), a polybutadiene stereospecific oligomer, with low viscosity and unsaponifiable, with a mean molar mass of 4,600 g / mol. The microstructure of this compound is so composed:

- 1,4-cis double bonds approx. 77% (p)
- 1,4-trans double bonds approx. 22% (n)
- 1,2-vinyl double bonds approx. 1% (m)

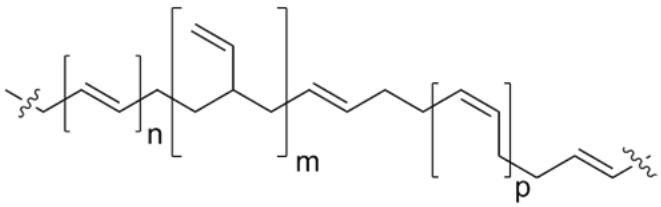
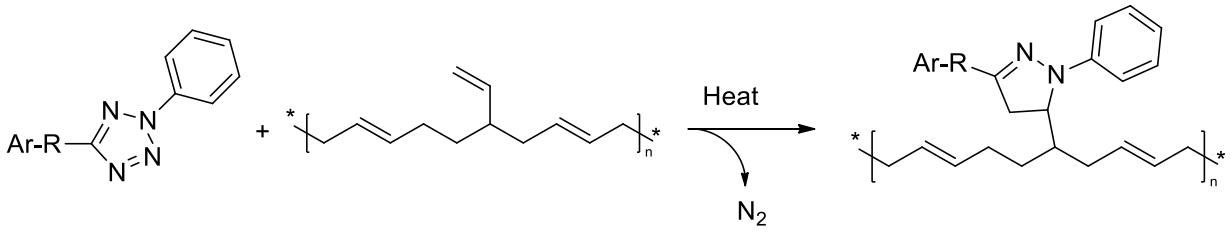


Figure 13- Polyvest 130

Its characteristic of being liquid and soluble in both aliphatic and aromatic solvents permits to the aforementioned polymer to be very useful to work with on laboratory scale, overcoming the characteristic problems of solubility and viscosity experienced dissolving a long chain polymer in an organic solvent. This polymer presents a low vinyl content (about 1%), allowing a qualitative assessment of the selectivity of the chosen reaction. Furthermore, it gives the possibility to analyze the cyclization product between nitrilimine and polymer double bonds through NMR spectroscopic techniques in solution.

1.5.3.2 Polymer functionalization test and characterization

A few milligrams of tetrazole were homogeneously dispersed in Polyvest 130 in a 1: 1 molar ratio with respect to vinyls, heating to 70 °C to homogenize the dispersion. Then the mixture was heated at the tetrazole activation temperature for about 30 minutes. During the reaction it was possible to observe nitrogen bubbles developing, proof that the tetrazole was thermally activated releasing the nitrilimine. The reaction scheme concerning the functionalization of the polymer is reported below (Scheme 22).



Scheme 22- Functionalization mechanism

At the end of the reaction the polymer was observed under the UV light of a handlamp, showing a strong fluorescence due to the presence of the pyrazoline ring formed during the cycloaddition.

Furthermore, in addition to these empirical observations, the polymer was purified from any unreacted trace of tetrazole by dissolving it in a little amount of dichloromethane, precipitating in methanol and centrifuging (procedure performed 3 times). The purified polymer was then characterized using IR and NMR (Fig.14) to demonstrate effective functionalization.

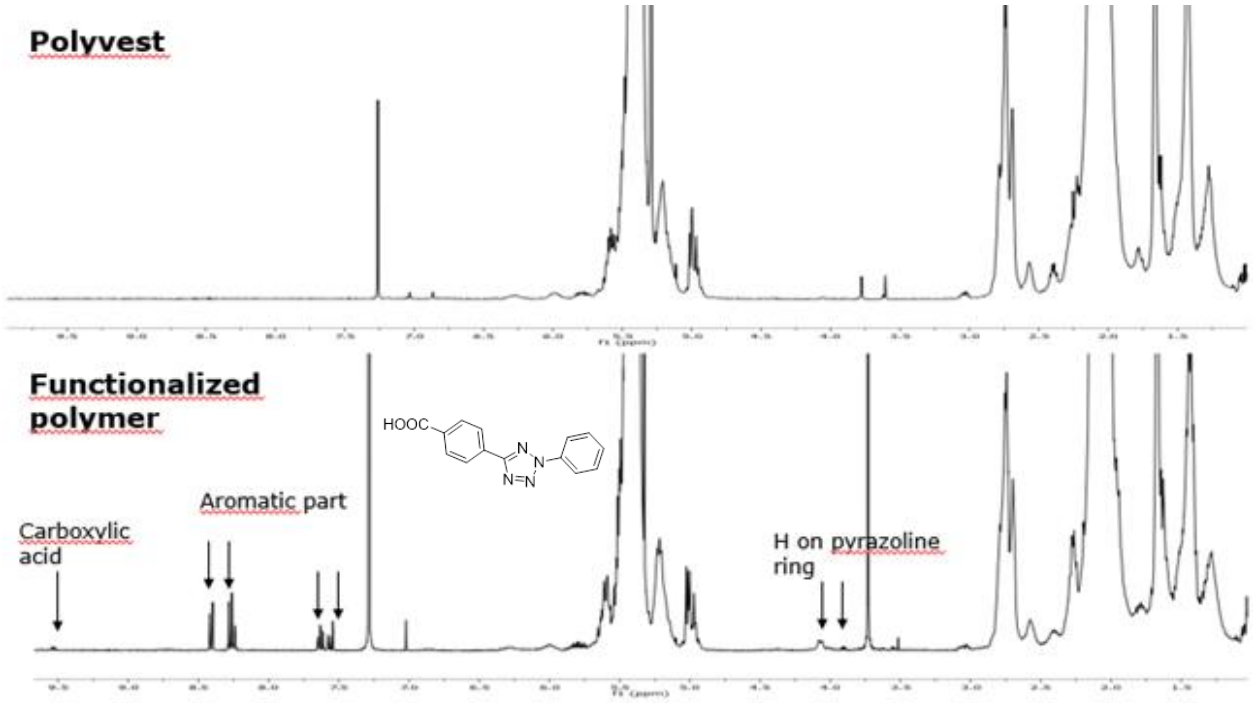


Figure 14- NMR spectra of pristine and functionalized Polyvest 130

Below is an image showing the fluorescence of the functionalized polymer, due to the presence of the pyrazoline ring formed by the reaction between nitrilimine and vinyl of the polymer (Fig.15).

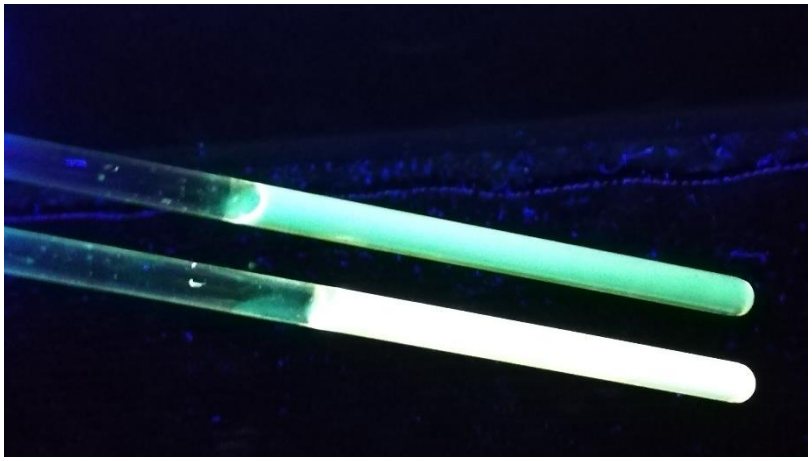


Figure 15- Fluorescence of functionalized Polyvest 130 in solution

After the synthesis of a series of tetrazoles, some of which not known in the literature, and having studied their thermal activation and reactivity with the polymer, the attention was focused on the possible applications of the results obtained in the field of tires. Therefore tetrazole-based systems, containing specific functional groups that could perform useful functions (such as acting as compatibilizers and cross-linking agents) were developed.

Four specific applications of tetrazoles were identified, which will be dealt with later in the respective chapters:

- Compatibilizers
- Cross-linking agents
- Reactive chain end
- Non-covalent interaction mediators

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2. Rubber compounding

This chapter describes the principal type of ingredients used for the preparation of a rubber compound (e.g. rubbers, fillers, vulcanizing agents). Moreover, some concepts concerning the reinforcing effect of fillers in a polymeric matrix will be introduced.

2.1 Formulation of rubber compounds

Formulation is the heart of rubber compounding. It is an industrial process based on a set of operations necessary to mix all the ingredients according to a recipe[1]. An example of a rubber formula is given in Table 1.

Ingredient	***phr***
Crude rubber	100
Filler	50
Softener	5
Antioxidant	1
Stearic acid	1
Zinc oxide	5
Accelerator	1
Sulphur	2
Total	*165*

Table 1- General tire formulation

The main part of a rubber compound is the elastomeric matrix[2], generally either one or a blend of two or more elastomers, chosen to achieve the desired properties required for the final product. The total amount of elastomer in a recipe is usually defined in 100 parts, while all the other ingredients are rationed against the 100 parts of rubber (phr). Each ingredient is added for a specific purpose based on its chemical reactivity and physical properties[3], which can be exploited either in processing, vulcanization or end use of the product. In addition to rubber there are dozens of different ingredients[4] that can be divided into classes according to their specific functions: fillers (silica or carbon black); plasticizers and softeners (processing aids, oil extenders); antidegradants (antioxidants, antiozonants, age resistors, radical scavengers); vulcanizing and curing ingredients (vulcanizing agents, activators, co-activators, accelerators); special ingredients

for specific purpose (pigments, flame retardants, antistatic agents, odorants, retarders, blowing agents). However, many ingredients can act in more than one manner.

The formulation process is not trivial because each ingredient must be added in a specific order, during the mixing phase, to avoid premature interactions with the others. The time and temperature of mixing are defined by a balance between a good solubilization/dispersion of the ingredients and their thermal and mechanical stability. The following figure (Fig. 1) shows some of the ingredients that can be found in a composite[4,5].

Figure 1- Ingredients used in tire

2.1.1 Rubber

"Rubber"[6] is a generic term that indicates an amorphous polymer with high molecular weight (M_n > 100000), a random-coil arrangement and a glass transition temperature far below typical use temperature. Usually those polymers can undergo significant deformations if stressed, returning to their original size once the stress has ended. Due to their unique elastic properties it is also possible to refer to those materials with the term "elastomers"[7]. The elastomers are essential in several industrial sectors due to their main characteristics such as elasticity, flexibility, and toughness. Beyond these common features, each rubber has its own peculiar properties[8]. Although the processing and final properties of rubber compounds are highly dependent on the elastomer, the properties can be extensively manipulated by appropriate choice of compounding ingredients[9]. The elastomers commonly used are divided into two main categories: natural or

synthetic. The most used natural elastomer is natural rubber (NR, Fig.2). NR is obtained by coagulation of the latex harvested from different tropical trees (Hevea Brasiliensis is the most exploited source). Since it is a natural product, a small percentage of proteins, fatty acids, resins and salts could be found alongside the polymer itself, which is cis-1,4 polyisoprene, into the colloid where the dispersed phase is mainly rubber and the dispersion medium is water.

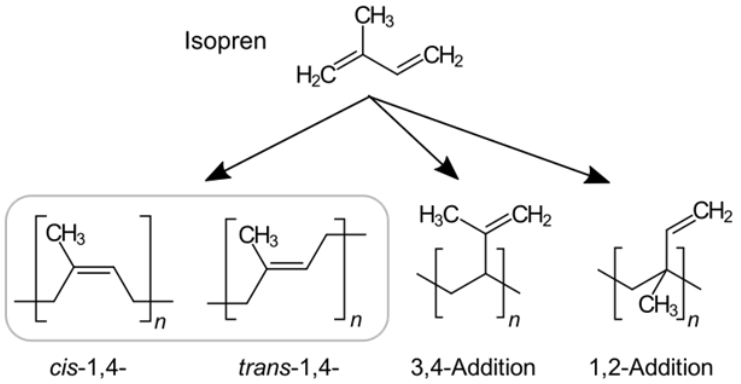

Figure 2- Isoprene and its four possible isomers

The other class of polymers, the synthetic rubbers, is much wider. Synthetic elastomers are produced by polymerization of monomers generally coming from petroleum-derived hydrocarbons. The most relevant for tire applications are briefly introduced hereafter. The first one is the synthetic analogue of the natural rubber: polyisoprene (IR). Its synthesis for industrial applications was possible only after the discovery of the stereospecific catalysis. Depending on the polymerization conditions it is possible to insert isoprene into a polymer chain in different isomeric forms: 1,4-trans, 1,4-cis, 1,2 and 3,4 (these last two are less important for industrial applications). 1,4-cis polyisoprene is the most used polymer for the mechanical and elastic properties that gives to the vulcanize compounds. After vulcanization, polyisoprene shows aging properties and resistance to chemicals like those of natural rubber, while the physical properties are not as good as those of NR.

Another example of general-purpose elastomers is butadiene rubber (BR). BR constitutes about 10% of yearly global rubber production, 70% of which is used for tires making. Butadiene monomer can add in different ways but, it has fewer accessible configurations, due to lack of lateral substituents. This allows the formation of only three isomers: 1,4-cis, 1,4-trans and 1,2 addition. This latter structure introduces a stereogenic center in the polymer chain with three possible types of vinyl structures: isotactic, syndiotactic and atactic. Changing the polymerization conditions, it is possible to obtain polymers with different microstructures, either pure or made by

a blend of different isomers. The high cis-polybutadiene, which is a soft and easily soluble material with excellent dynamic characteristics, low hysteresis, good resistance to abrasion and high resilience. The production of pure BR compound is not trivial, mainly because of his high degree of crystallinity and so compounds are commonly made of blends with NR or SBR.

SBR is a copolymer of styrene and butadiene, typically containing from 15% to 45% styrene. The copolymerization of styrene-butadiene results in a synthetic rubber that covers about 35% of the market. SBR production is dominated by a cold emulsion process (E-SBR), but in 1960 the synthesis in solution with anionic polymerization (S-SBR) has eroded important shares of the market (15-20%) especially for construction of original equipment tires, which must meet stricter specifications on the rolling resistance. The anionic polymerization in a hydrocarbon solvent of a mixture of styrene and butadiene does not provide a copolymer with comonomers distributed in a random manner, but a block copolymer. Acting on monomer concentration and on the type of modifiers (polar substances that determines a variation in the reactivity ratios values) it is therefore possible to obtain S-SBR containing up to 35-40% by mass of styrene well distributed along the polymer chain, but it is not possible to keep the amount of 1,2 units at low levels (i.e. tires with 25% of styrene contain 60-65% of 1,2 units). With this type of polymerization, it is therefore possible to modify in a controlled way the molecular structure together with the microstructure (abundance of 1,2 unit) and composition (styrene quantity), molecular weight and weight distribution. In ideal conditions (i.e. statistical comonomers distribution) is possible to control the Tg, acting on both the quantity of vinyl and styrene. The ability to change the Tg of the material varying the quantity of the vinyl unit is an important feature which differentiates the S-SBR from the E-SBR, at constant content of 1,2 unit. The increase of the vinyl unit, with constant styrene, determines an increase in the value of the Tg without penalizing excessively the value of the damping factor (tanδ measured at typical tire rolling frequencies); this means that it is possible to improve the grip without compromising the low rolling resistance.

SBR does not develop high tensile strengths without the aid of reinforcing fillers. SBR rubber has tread-wear and heat-ageing properties superior to those of NR, but inferior resilience and low-temperature behavior. This kind of rubber is generally used in many applications, particularly the principal end uses are passenger car tires. During this doctoral project we focused on SBR rubber, choosing it as the main component of our compounds.

2.1.2 Fillers

Fillers are the principal compounding ingredient after elastomers[4,5,10]. They are usually added in large amount (30-70phr) as a powder to the crude rubber, at the first stage of the mixing process. Fillers are groupable in two classes: carbon black and non-black fillers.

Carbon black (CB) is essentially elemental carbon in a 'graphitic' form of agglomerated spherical particles, produced by incomplete combustion or thermal decomposition of petroleum product. The carbon black grades differ from one another regarding their particle size, surface area, aggregate form and shape. It is the oldest filler for tires compounding, and it is still used nowadays. CB fillers can give high resistance to abrasion and wear to the compound besides having relatively good heat and electrical conduction properties.

Non-black fillers for rubber exist in a wide variety. The principal non-black fillers are silicas and calcium carbonates. Other major fillers are clays, talc, mica, zinc oxide, magnesium oxide, magnesium carbonate, titanium oxide, barites and many others. Short fibers of nylon, glass, polyester, aramid and carbon are also used in rubber compounds. However, the most common one is silica, because it can provide extremely high reinforcement values. After the discovery of coupling agents[11] (e.g. silanes), in 1980s, silica started to replace CB in rubber compounding for tires application. Silica was able to guarantee excellent mechanical performances, to lower the rolling resistance without losing wear, to give abrasion and heat resistance and to enhance wet grip.

2.1.3 Antidegradants

The main problem that causes rubber goods to lose performance in time, not strictly related to their use, is attributable to degradation phenomena triggered by exposure to atmospheric agents (oxygen, ozone, moisture, heat, light). The addition of antidegradant[9] agents during the compounding can prevent, or slow down, those degradation processes. Typically, the compound added are radical scavengers and antioxidants that can inhibit oxidation by oxygen or ozone, that can break polymer chains.

2.1.4 Vulcanizing agents

In 1839 Charles Goodyear made the discovery that revolutionized rubber technology. By adding sulfur to natural rubber and heating (Fig.3), he discovered that the material obtained had completely different characteristics: elasticity, impermeability, solvent resistance.

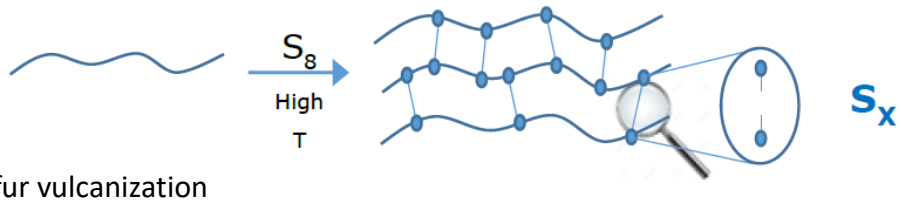

Figure 3- Sulfur vulcanization

From that discovery began a series of studies on the vulcanization, a chemical process that allows to form bonds between the chains in a polymer matrix. The addition of these bridges radically transmutes the elastic properties of the material, making it useful for technological applications. The protocol developed by Goodyear, i.e. a vulcanization carried out simply by adding 8 phr of sulfur and heating at 140 °C for 5 hours, was not particularly efficient. For this reason, over the years, the study and research on this process made it possible to obtain more efficient, rapid and homogeneous systems, with reduced amount of sulfur, permitting to obtain a better quality of the final product. These new systems are made up of various components which, together with sulfur, give a much more controlled process. The various components grouped by function are listed below:

- **Vulcanizers**: they are responsible of the bridge formation among the polymer chains. The most common agent is elemental sulfur, but there are also other compounds (e.g. peroxydes).
- **Accelerants**: their function is to lower the activation energy of the process, increasing drastically the reaction rate. There are dozens of accelerators, each one characterized by different time of curing and scorch. Usually they are classified by their chemical composition: sulfonamides (e.g. CBS), thiazoles (e.g. MBT), guanidines, thiurams, dithiocarbamates and dithiophosphates.
- **Activators**: they form complexes with accelerators and co-activators, influencing the curing rate and the degree of cross-linking. Generally, they are metal oxides[12], ZnO is the most common.
- **Co-activators**: they react with the activators, forming complexes containing cations that will react with accelerators. They also promote the solubilization of the activator into the

polymer matrix, making the cations more available. They are organic molecules such as stearic acid.

2.2 Filler reinforcement

To meet market needs and legislative requirements, a tire must respect certain characteristics, for example it must have sufficient grip in all conditions (both wet and dry), have low rolling resistance, be resistant to wear and abrasion, give precise feedback during the steering phase. The composition of the compounds used to produce a tire is one of the parameters that most influences the characteristics of the final product, obviously together with the construction of the tire itself and the tread pattern design. The task is not at all simple because some desired features contrast with each other (e.g. improve traction on wet surfaces without losing wear resistance) and is commonly indicated by researchers with the term "magic triangle" (Fig.4).

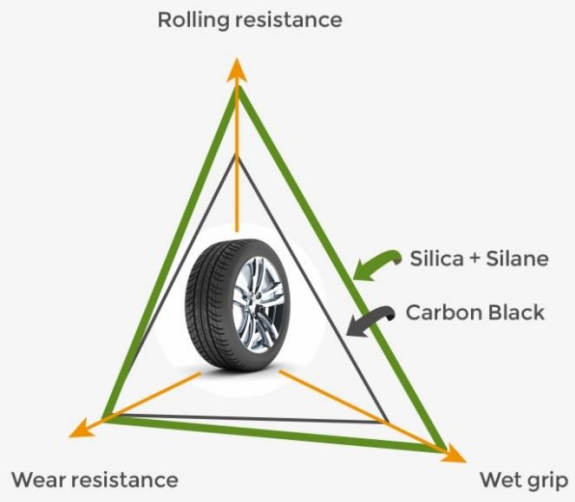

Figure 4- Magic triangle

The rubber, in order to improve its properties, needs to be mixed with other components[10,13]. The final characteristics of the material, however, are not the simple sum of the contributions of the various components, but rather the result of the interactions between these components. The behavior of rubber-based composite is complex, but as a first approximation it can be considered as a viscoelastic material whose behavior can be described by some simple theoretical concepts[7,8].

Applying a sinusoidal tangential deformation γ(t) with an angular frequency ω, the equation describing its behavior is:

$$\gamma(t) = \gamma_0 \sin(\omega t)$$

Where γ_0 corresponds to the maximum value of strain and t to the time. To which is correlated an out-of-phase sinusoidal stress described by the equation:

$$\sigma(t) = \sigma_0 \sin(\omega t + \delta) = (\sigma_0 \cos\delta)\sin(\omega t) + (\sigma_0 \sin\delta)\cos(\omega t)$$

Where δ is the phase angle. G', G" can be defined as follows:

$$\sigma(t) = \gamma_0[G' \sin(\omega t) + G" \cos(\omega t)]$$

$$G' = \frac{\sigma_0}{\gamma_0}\cos\delta$$

$$G" = \frac{\sigma_0}{\gamma_0}\sin\delta$$

Where G' represents the elastic component of the shear modulus and is most influenced by the reinforcement contribution given by the filler (filler-polymer interaction) and the curing level, while G" represents the viscous component of the shear modulus, most influenced by the filler-filler interactions and by non-crosslinked components. Given these relationships we can then write a complex equation that describes the shear modulus G *:

$$G^* = G' + iG"$$

and the phase angle formula:

$$\tan\delta = \frac{G"}{G'}$$

Tan δ is particularly important because it is directly related to the hysteretic behavior of the mixture, primary cause of rolling resistance, that is the energy consumed per unit of distance traveled. The values of G', of G" and $\tan\delta$ depend on both the temperature and the frequency and it is possible to obtain valuable information about the mechanical dynamic behavior of the material analyzing their dependency on these conditions, which reflect different situations experienced by the tire during its service life. As previously mentioned, the addition of the filler strongly influences the mechanical behavior of the nanocomposite. The reinforcement contribution that the filler brings, is partly given by its intrinsic nature (i.e. the modulus of the lone-standing filler particle), its chemical nature, the size of the particles, the surface reactivity and the state of aggregation. For this reason, it is essential to know how to predict the different types of interactions that are formed. Below we will focus on the filler-filler and filler-rubber interaction,

as well as the hydrodynamic effects. The reinforcement effect obtained will be given by the sum of the individual contributions, as shown in the Figure 5.

The shear modulus G* (Y axis) is reported as a function of the deformation. Payne was the first one to provide an interpretation of these curves, describing in his work the dependence of G' and G" from the strain and correlating it with the size of the filler aggregates in the composite (Fig.5).

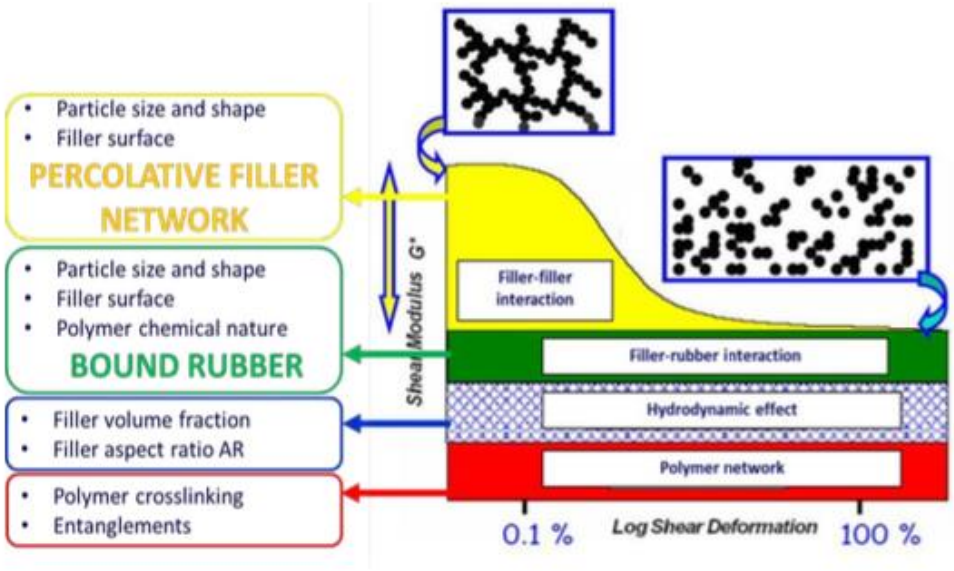

Figure 5- Model of stress-strain curve of a rubber nanocomposite

2.2.1 Filler-filler interaction

In his works, Payne explains how, during cyclic deformation, the breaking of the filler network follows a sigmoidal-like pattern that decreases from an initial value (G'_0) at low strain to a plateau (G'_∞) for high elongation values.

This breakdown is caused by the destruction of the weak forces (e.g. hydrogen bonds and Van der Walls interactions) that hold together the filler particles. Notably, this network destruction and reconstruction occurs at very low deformations (about 1%), far lower than the critical strain above which failure of the material may occur.

The difference between G'_0 and G'_∞ is commonly called “Payne effect” and is one of the most important parameters to consider. Being able to keep this value under control, i.e. to keep G’ substantially independent from deformation would improve the hysteretic properties of the material, with a direct reduction of rolling resistance and better control in heat generation.

Over the years, different models have been proposed to explain this type of interaction, and among the most recent theories, the one proposed by Klüppel[14] and collaborators is the most relevant. They suggest two alternative approaches, a link-blob-nodes (LBN) model and one based on cluster-cluster aggregation (CCA). Their model considers not only the interaction between the filler particles, but also the filler-rubber interaction, in a more complete approach.

2.2.2 Filler-rubber interaction

Filler-polymer interaction is the main responsible of the reinforcing action in a composite material. This contribution is elongation independent and it is related to the superficial interphase formed between the filler particles and the rubber surrounding them. Usually this interaction is improperly called bound rubber, in fact there might be no covalent bond between the surface of the particles and the polymeric matrix. This would only be true if a coupling agent was used, which can form these bridges (e.g. silane-silica systems) at rubber-filler interface, but in general it would be more correct to describe this part of rubber as if it was immobilized. Moreover, because of this interaction between the two components, the local mechanical properties are twisted. In their model Medalia[15] and Kraus[16], hypothesize that the rubber could be trapped inside a filler cage, with an elastic behavior like the filler itself at low strain values.

Smit[17] and Pliskin[18] proposed a similar model but a slightly different description of this phenomenon. According to them the rubber coated the filler agglomerates, forming a chemisorbed shell on the surface of the filler.

2.2.3 Polymer network effect

This contribution[4,7,8], independent from the elongation, can be considered as the mutual interaction between polymeric chains, which are physically linked through entanglements or real chemical bonds introduced into the polymeric network after the vulcanization process.

The equation that describes this contribution is the following:

$$G_0 = \nu \cdot K_b \cdot T$$

Where K_b is the Boltzmann constant, T the temperature and ν the concentration of elastically active chains per unit volume.

2.2.4 Hydrodynamic effect

The hydrodynamic effect[3,19] is a consequence of the increase of viscosity determined by the addition of particles. Einstein was the first one to theorize this behavior, describing the viscosity variation as follows:

$$\eta = \eta_0(1 + k_e\phi)$$

where η is the viscosity of the suspension, η_0 is the viscosity of the pure liquid, k_e is a coefficient related to the shape and aspect ratio of the filler and ϕ the volume fraction of the filler. This hypothesis could be considered true only applying strong approximations to the system, for example considering particles as spheres, a wettability of the total surface and diluted particle concentration. Guth and Gold then modified this equation semi-empirically to make it suitable for the description of highly concentrated dispersions, which is the case of rubber compounds:

$$\eta = \eta_0(1 + 2.5\phi + 14.1\phi^2)$$

where the parameter ϕ^2 accounts for the effect given by a dense solution of particles. Finally, Guth corrected the equation introducing the parameter "a", to consider also the aspect ratio of the particles:

$$G' = G'_0(1 + 0.67a\phi + 1.62a^2\phi^2)$$

Guth-Gold equation considers interparticle interactions but not the formation of the network associated with typical behavior before, during and after percolation.

2.2.5 The key role of interface in filler-rubber interaction

Concerning the filler-rubber interaction[13,20,21], this should be maximized at the expense of the filler-filler interaction. All the proposed theories converge on one point: the interface between filler and polymer is crucial and influences and explains the rheological behavior of the final product. Due to the importance of the interface, it is fundamental to understand what kind of affinity exists between the surface of the filler and the rubber, paying attention to the surface

reactivity and the presence of functional groups exposed by the filler particles. Of course, it is quite clear how it is not possible to treat all fillers similarly and it is necessary to make a distinction between them considering two main classes: silica and carbon black.

Regarding to silica, the one used is an amorphous silica, consisting of spherical particles produced through precipitation processes from an aqueous medium. The size of the particles is around 15nm in diameter but, usually, aggregates are formed organized in more complex structures, such as strings or pearls with sizes ranging from 50 to 500 nm; these latter do not completely disaggregate on mixing with the elastomer. In addition, they can assemble into larger clusters which are responsible of previously mentioned filler network. The driving force of the aggregation phenomena consists of weak attractive forces (e.g. hydrogen bonds, VdW forces, dipole-dipole interactions) formed by the terminal polar groups present on the particle surface. In fact, the particles surface is decorated with silanol units of various kinds (e.g. isolated silanols, geminal silanols, vicinal silanols or siloxanes). Those groups are weak Brönsted acids, but they are stronger than aliphatic silanols or hydrocarbon alcohols, for that reason they can form hydrogen bonds with polar molecules such as alcohols, amines, water or other silanol groups[22]. The surface polarity makes the silica particularly hydrophilic (high surface energy), a characteristic that certainly does not help the dispersibility of the particles in a hydrophobic matrix such as polymers (low surface energy).

Donnet et al.[13] considered the surface energy as the sum of two components:

$$\gamma_s = \gamma_s^d + \gamma_s^p$$

Where γ_s^d describes the tendency of silica to be dispersed in the rubber (hence the dispersion component name) and γ_s^p is the aggregation surface energy. These two values can be measured by evaluating the interaction of silica particles (nominally at infinite dilution) with a probe with variable polarity. Using this technique[23], it was possible to evaluate the dispersibility of silica in the most common polymeric matrices, which follows the subsequent scale:

NBR> SBR> NR> BR> high vinyl BR> EPDM> IIR

Where NBR is the acronym of acrylonitrilebutadiene rubber, IIR is butyl or isobutylene isoprene rubber and EPDM is ethylene propylene diene rubber.

2.2.6 How to increase compatibility

Due to their non-polar nature, carbon black fillers are inherently more compatible with the polymer matrix, but the composites obtained still have a hysteretic character and a marked Payne effect[17]. For many years they were the technological standard used in industry, without the use of any type of compatibilizer; while recently various treatments have been proposed[24] (e.g. chemical, electrochemical, plasma, ozone, and heat treatment) to oxidize the carbon black surface and to allow further compatibilization reactions like for the silica-silane system. To overcome the limits related to carbon black and to move towards environmentally sustainable production, researchers has focused on the progressive replacement of carbon-based fillers in favor of silica-based fillers. However, the use of silica alone is not enough to guarantee the required performances, or at least without using a coupling agent capable to modify the particles surface, in order to increase their dispersion in the polymer matrix. The most important discovery in this field was the introduction of bifunctional organosilanes, able to graft to the surface, reacting with the hydroxyl groups of silica, and at the same time able to bind covalently the polymer during vulcanization phase. Wolff and collaborators[13] were able to synthesize more than 100 compounds, but only two were industrially adopted for the purpose, in particular the bis (triethoxysilylpropyl) tetrasulfide (TESPT) and the bis (triethoxysilylpropyl) disulfide (TESPD) (Fig.6).

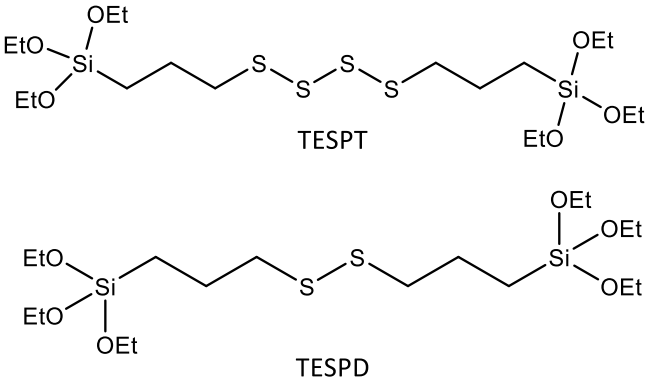

Figure 6- Silane coupling agents

All the methods reported in literature, move in the direction of making the filler more compatible with the polymer matrix. However, the approach used within our research group was radically different, unusual and ambitious: to modify the polymer matrix to make it more compatible with the filler, but without modifying it too much in its fundamental properties. The results of this work will be described later in the chapter on compatibilizers.

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3. Compatibilizers

This chapter concerns one of the applications of tetrazoles in the field of tire compounding: tetrazole compatibilizing agents characterized by suitable activation temperatures. This work allowed us to file a patent in this field.

3.1 State of the art

In the rubber industry, and particularly in the tire industry, it is known that adding reinforcing fillers to elastomeric compositions improves their mechanical properties[1–4]. They are usually particulate nanomaterials whose industrial availability is higher than 1000 Tons/Year. Thanks to its high reinforcing power, carbon black is the most used filler, providing also a marked hysteresis, i.e. increases the heat dissipated under dynamic conditions. Alternatively, the so-called "white" reinforcing fillers are in use, such as gypsum, talc, kaolin, bentonite, titanium dioxide, and especially silica; fillers these that can partially or completely replace carbon black in elastomeric compositions and, at the same time, give a lower rolling resistance, good wet grip and sufficient reinforcement. For these reason white fillers, silica in particular, are advantageously used in elastomeric compounds targeted to different performances such as high-performance HP, summer and for all seasons or winter tires.

For such uses, silicas with different characteristics are commercially available or can be prepared according to known processes[1]. For the elastomeric compound to have the desired properties, however, it is important that the reinforcing nanofiller is distributed homogeneously in the elastomer and that it remains over time, avoiding the formation of agglomerates as much as possible. Even more important is that the reinforcing nanofiller is chemically linked during curing to the polymer matrix. The distribution and dispersion of the filler in the matrix depend both on their chemical compatibility and on the mechanical energy used to mix them. A better distribution and dispersion are achieved, more similar is their chemical nature (in terms of compatibility) and the greater the mechanical mixing work applied. Typically, in compounds for tires, to improve the dispersion and the compatibility between the "white" fillers, i.e. inorganic fillers which have surface hydroxyl groups (such as silicates, carbonates or amorphous silica) and the rubber, agents called compatibilizers or coupling agents are used[5–9]. The most used coupling agents are polysulphide silane coupling agents, such as for example bis (3-triethoxysilyl-propyl) tetrasulphide

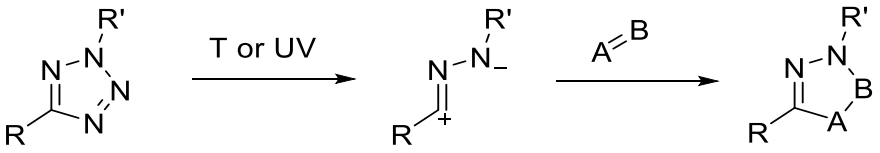
TESPT and bis (3-triethoxysilyl-propyl) disulfide TESPD. These agents have an alkoxyl-silanic head, capable of reacting with the surface hydroxyl groups of the fillers, and a polysulphide units which, by heating and interaction with the curing package, can react with the elastomer, but not always with optimal results. In fact, it is known that the thermal decomposition of these polysulphide systems is difficult to control, as it can already occur at mixing temperatures, well before the vulcanization phase. In addition, the radical species thus generated have high reactivity and poor selectivity leading to the formation of mixtures of mono, di- and poli-sulfides[1]. To best use these polysulphide compatibilizers, it is necessary to check carefully the mixer internal temperature to prevent reactions with the elastomer starting before the curing stage. Typically, this mixing phase - called non-productive phase or first phase - is carried out at temperatures not higher than 140 °C.

However, despite the use of compatibilizers and high energy mixes, it is not always possible to reach and overall to maintain the optimal dispersion of the reinforcement charges in the elastomeric matrix. A good dispersibility of the reinforcing fillers is an important requirement for obtaining compositions suitable for use in tires. In fact, a non-homogeneous dispersion, with the formation of numerous and/or bulky aggregates, negatively reflects on the performance of the material itself, resulting for example in excessive hysteresis or poor tearing behavior. Furthermore, in the case of mixtures of elastomers with different polarity, migration and accumulation of fillers can occur mainly in the more affine phases, raising problems related to the lack of homogeneity of the composite, such as high abradibility and uncontrolled hysteresis of the compound, as well as potential crack triggers. At the process level, it would also be advantageous to be able to extend the mixing until the desired distribution is achieved without having to strictly control the temperature and to be able to fix the well-dispersed charges stably to the matrix only later, for example in vulcanization.

3.2 Summary of the research project

The main aim of the research project was to study how to improve the affinity of the fillers for the elastomeric materials of the compounds and to stabilize the dispersion of the same obtained at the end of the mixing. For this purpose, the attention was focused on compatibilizing agents capable, on one hand, of interacting with the selected reinforcement filler and, on the other, of covalently binding in a controlled manner to the elastomeric component of the compounds.

As discussed in chapter 1, it is known from the literature[10] that tetrazoles 2,5 disubstituted, following heating or irradiation with ultraviolet light, evolve, with development of nitrogen, generating intermediate species highly reactive (nitrilimine) capable of reacting with double bonds (A = B), with the formation of stable substituted pyrazolines, easy to recognize by their strong fluorescence, as depicted in Scheme 1 (for more details see chapter 1).



Scheme 1- NI formation and reactivity

The temperature at which the disubstituted tetrazole 2,5 decomposes, referred here as the activation temperature, depends on the nature of the groups present in the 2,5 positions of the tetrazole, as it was discussed by Otomo et al.[11] and as investigated by our research group and described in the first chapter.

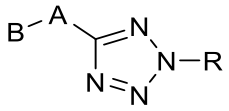
Only few studies have been conducted on the use of tetrazoles in relation to elastomeric materials and are shown below.

One patent[12] deals with an elastomeric composition for tires, comprising silica, a conventional silane coupling agent and a mono-substituted tetrazole derivative in position 5. That composition showing an improved affinity of silica for rubber and an increased vulcanization rate. This document does not mention the possible thermal decomposition of those mono-substituted tetrazoles, nor use 2,5-disubstituted tetrazoles. In this regard, we have experimentally verified that tetrazoles substituted only in 5 such as those shown in this document decompose at very high temperatures, well above 220 °C and are thus of little practical interest (activation temperature is too high for tire application).

A second patent[13] describes an elastomeric composition - comprising in addition to a silane coupling agent also a tetrazole having a sulfur atom outside the ring - which would have a better reactivity between the silane coupling agent and the rubber. The description does not involve thermal activation of that compound at certain temperatures. Also, in this case, the reported 5-mercapto-substituted tetrazoles, on heating do not decompose sharply with release of nitrogen but slowly degrade.

The studies carried out in this PhD project, have underlined that not only certain particular tetrazoles prove to be compatibilizers of reinforcing fillers for better elastomers but also that their activation, at a very precise and tunable temperature, allows to continue the mixing process up to achievement of the desired dispersion and proceeding to anchor the charges on the elastomer only later. Moreover substituents on the tetrazole can be chosen to raise the activation temperature (Ta) of the same, making possible to carry out the mixing phases with the elastomer without having to rigidly control times and temperatures for fear of early reactions, reactions that can already occur around 140 °C using classic polysulphide-based compatibilizers. Furthermore, it was found that using the present tetrazole compatibilizers it is possible to maintain, if not even improve the mechanical properties of the final compounds that incorporate them.

The general formula of tetrazole compatibilizer is as follows:



In which A represents an organic group linker (chain or aromatic ring), covalently linked to position 2 of the tetrazole; R is a group, usually an aromatic ring, bound in position 5 of the tetrazole, appropriately substituted with an electron-attractor or one electron-donor group to change the activation temperature of the tetrazole. B represents a group with high affinity for the desired reinforcement charge, such as silane or boronic acid (interaction with silica), or a polycondensed aromatic ring (interaction with carbon black). This tetrazole-based compatibilizing agent, when incorporated and vulcanized in elastomeric compounds for tires, gives static and dynamic mechanical properties comparable to those found with the classic polysulphide compatibilizers. Moreover, by varying the type of substituents on the tetrazole ring, it is possible to suitably tune the activation temperature Ta of the tetrazole and obtain process advantages that cannot be achieved with conventional thermally unstable polysulphide compatibilizers.

3.3 Description of the project

The following table shows the synthesized tetrazoles (Table 1).

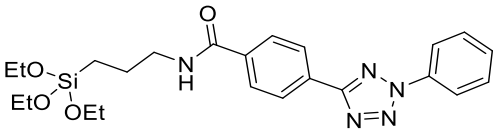
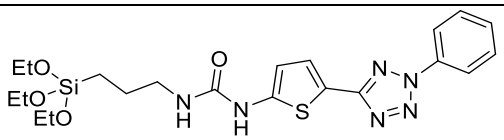
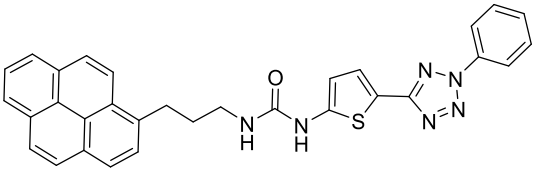
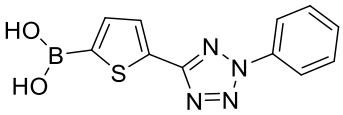
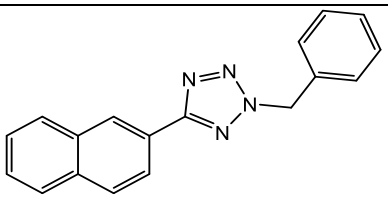
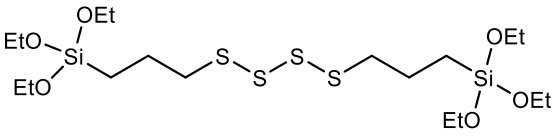
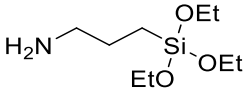
N°	Formula	Molecular Formula	M.W. (g/mol)	Activation Temperature (°C)
1		$C_{23}H_{31}N_5O_4Si$	469.61	190
2		$C_{21}H_{30}N_6O_4SSi$	490.65	150
3		$C_{31}H_{24}N_6OS$	528.63	180
4		$C_{11}H_9N_4O_2BS$	272.09	140
5		$C_{18}H_{14}N_4$	286.33	230
TESPT		$C_{18}H_{42}O_6S_4Si_2$	538.95	150
APTES		$C_9H_{23}NO_3Si$	221.37	--

Table 1

By suitably choosing the substituents, it is possible to modulate ad hoc the activation temperature Ta of the tetrazole compatibilizer, its affinity for the specific reinforcement charge and its solubility in the chosen elastomeric matrix.

Preferably the tetrazole compatibilizer agent should have an activation temperature (Ta) between 140 °C and 200 °C, to allow higher temperatures to be reached during mixing and consequently

allowing to obtain a better dispersion of the various components in the composite. Activation temperature should be chosen so that the tetrazole is not activate too early and reacts only when subjected to conventional vulcanization conditions.

Depending on the activation temperature of the tetrazole, which can be modulated, the reaction can take place with the elastomer before, during or after vulcanization. A tetrazole compatibilizer with an activation temperature (Ta) lower than approximatively 130-140 °C is to be avoided because it could react with the elastomer from the preliminary mixing phases of the components prior to vulcanization, before reaching a homogeneous dispersion. The early reaction could lead to the concentration of the compatibilizer and therefore of the reinforcing filler in particular areas to the detriment of the performance of the material and it would also lead to an increase in the viscosity of the raw mix, making it difficult to process in the subsequent extrusion and/or calendering phases.

The preparation process of the elastomeric mixture comprises:

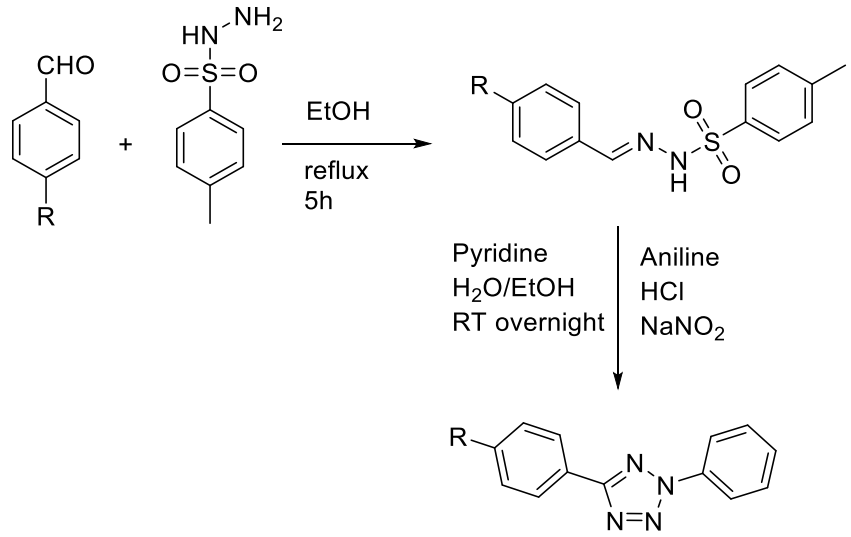
1) Mixing, in one or more phases, all the components of the composition keeping the temperature at a value lower than the activation temperature Ta of the tetrazole compatibilizing agent, to give a mixture comprising the unreacted tetrazole. During the first mixing phase, the reinforcing filler and the compatibilizers are dispersed in the elastomeric matrix. Under these conditions, the tetrazole ring of the compatibilizer remains substantially stable and does not undergo significant decomposition, while one or more groups B of the compatibilizer react or interact with the charge.

2) Heating the mixture to a temperature higher than the activation temperature Ta of the tetrazole compatibilizer, to give a new mixture wherein the tetrazole compatibilizer has at least partially reacted by decomposition of tetrazole and subsequent addition to the elastomeric diene polymer. This second heating temperature preferably coincides with the vulcanization phase of the tire. At this point he tetrazole ring of the compatibilizer decomposes and reacts with the elastomer, anchoring the filler to the matrix.

3.4 Experimental part

3.4.1 Tetrazole synthesis

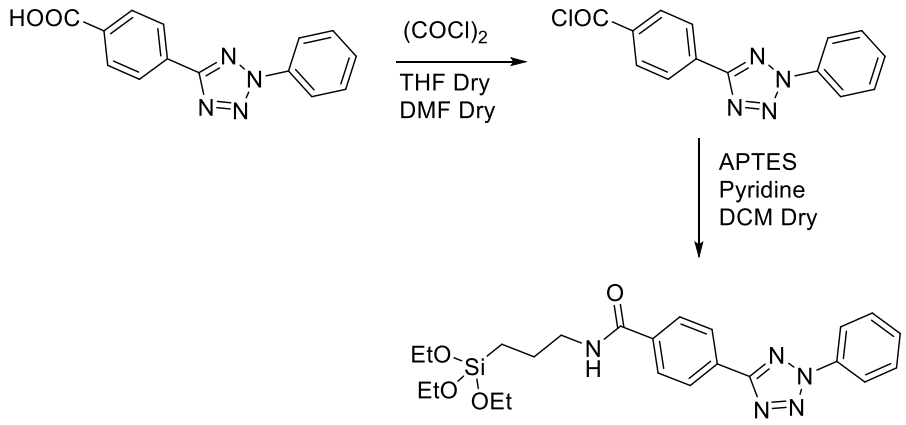
The tetrazole compatibilizing agent can be prepared according to the conventional synthesis (Scheme 2).



Scheme 2- General synthesis

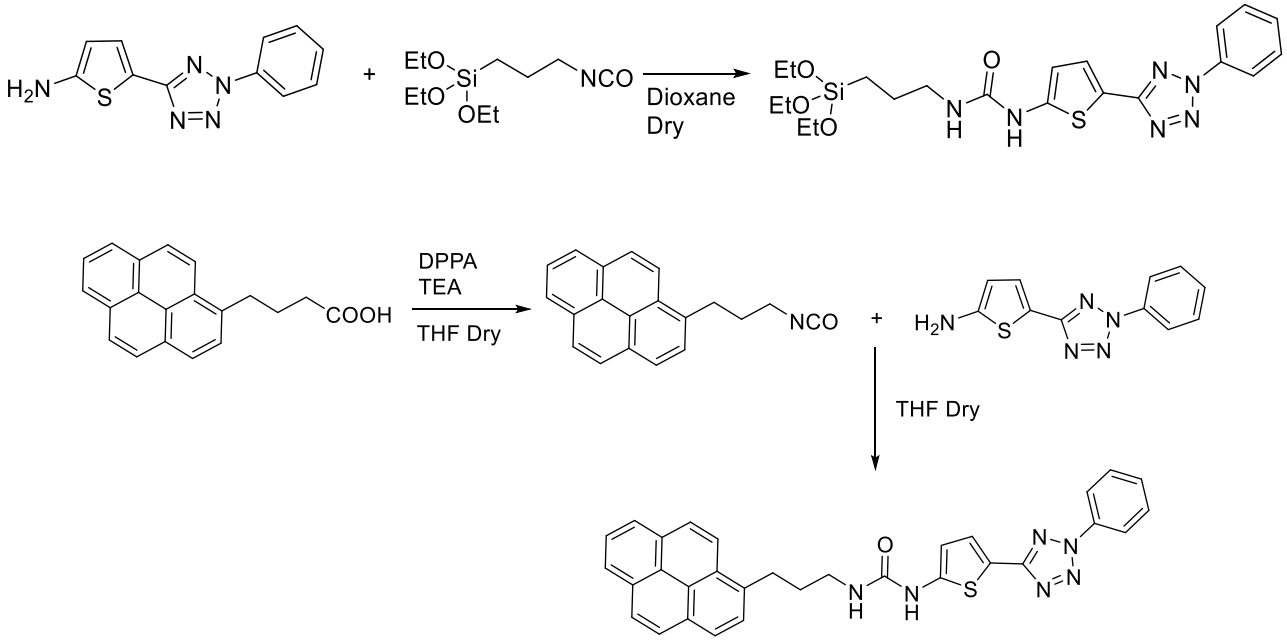
All the synthetic procedures are reported in detail in the last chapter (experimental part).

Starting from this methodology intermediates for compounds 1,2,3 and 4 were synthesized. Compound 1 was synthesized starting from the tetrazole-carboxylic acid derivative using two additional steps. The first one consists in the formation of the correspondent acyl chloride while the second involves APTES to form the final compound (Scheme 3).



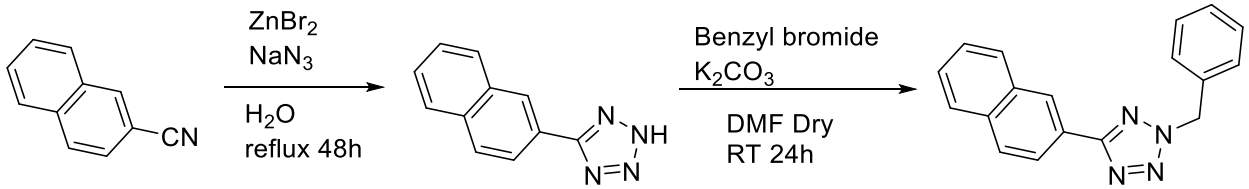
Scheme 3- Compound 1

Compounds 2 and 3 comes from the same intermediate (aminothiophene-tetrazole). The reaction with the appropriate isocyanate (Scheme) derivative leads to the formation of the desired product (Scheme 4).



Scheme 4- Compound 2 and 3 synthesis

Synthesis of compound 5 involves Sharpless tetrazole procedure followed by alkylation of the N position (Scheme 5).



Scheme 5- Compound 5 synthesis

All the synthetic procedures are reported in detail in the last chapter (experimental part).

Tetrazoles 1, 2 and 4 appear to be suitable compatibilizers for silica and silicate fibers while the monotetrazoles 3 and 5 are suitable for compatibilizing the carbon black given the high affinity of the pyrene and naphthalene nucleus for this charge.

3.4.2 Preparation of elastomeric compounds with silica

Elastomeric compounds have been prepared comprising equal equivalents of a classic silane-compatible TESPT (having two siloxane groups per molecule and sulphides for anchoring on the elastomer through sulfur bridges, e.g. 3.1 and 3.5 comparatives), of APTES (Silane having only a siloxane group, and an NH_2 group, e.g. 3.2 and 3.6 comparatives) or a tetrazole compatibilizer (3.1 with a siloxane group or 3.4 with a boronic group, e.g. 3.3, 3.4 and 3.7).

The quantities of the various components expressed in phr (percentage by weight) are reported in Table 2:

Ingredients phr (% pp)	**Ex. 3.1**	**Ex. 3.2**	**Ex. 3.3**	**Ex. 3.4**	**Ex. 3.5**	**Ex. 3.6**	**Ex. 3.7**
SBR (100 phr)	137	137	137	137	137	137	137
Silica	60	60	60	60	60	60	60
Tetrazole 1	--	--	5.2*	--	--	--	8.5**
Tetrazole 4	--	--	--	3*	--	--	--
TESPT	3	--	--	--	4.8	--	--
APTES		2.5*				3.9**	
6PPD	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Stearic Acid	1	1	1	1	1	1	1
ZnO (80%)	2	2	2	2	2	2	2
CBS	3	3	3	3	3	3	3
Sulfur (67%)	1	1	1	1	1	1	1

Table 2

Where:

- SSBR: extended solution styrene-butadiene copolymer with 37.5 phr of TDAE oil for every 100 phr of Dow dry polymer SE SLR-4630 dry elastomeric polymer.

- Silica: Zeosil 1165 MP. Supplier: Solvay Rhodia Operations.

- Stearic acid: Supplier: Temix Oleo SRL.

- 6PPD: N- (1,3-dimethylbutyl) -N`-phenyl-p-phenylenediamine, Supplier: Eastman.

- ZnO (80): 80% zinc oxide, 20% polymeric binder and dispersing agent, Supplier: Lanxess Add.

- Silane: TESPD Bis- (3-triethoxy-silyl-propyl) -disulfide, Supplier: Jingzhou Jianghan Fine Chem.

- CBS: N-cyclohexyl-2-benzothiazylsulfenamide, cyclohexylamine content <1%, Supplier Dulso.

- Sulfur: Crystex OT33 amorphous sulfur, insoluble in CS2 and in toluene. 33% treated with hydrotreated heavy naphthenic distillate (petroleum), Supplier: Eastman.

Mixing procedure

The mixing was carried out in several stages using an internal laboratory mixer with Brabender tangential rotors (60 ml mixing chamber).

1) In the first phase 50% of the elastomer was introduced and chewed for 30 seconds at 140 °C.

2) In the following phase the tetrazole compatibilizer, the silane TESPT or the APTES, the silica, and the remaining elastomer were added. The mixing was continued for 2 minutes, at 140 °C. Subsequently the antioxidant, ZnO and stearic acid were introduced. The mixing was continued for about 2 minutes, until the reaction between stearic acid and zinc was completed, always at 140 °C, after which the compounds - called first phase compounds - were discharged and tested for their rheological properties.

3) After 12-24 hours, in second phase, carried out using the same mixer, the vulcanizer (sulfur) and the accelerator CBS were introduced, and the mixing continued for about 3 minutes at 90 °C. Then final compounds were unloaded and tested again for their rheological and dynamic properties.

3.4.3 Dynamic mechanical properties

The obtained compounds, after first mixing phase and final mixing phase, were subjected to analysis of the dynamic rheological and mechanical properties according to the following conditions.

Test method 1:

1) Deformation cycle up to 100% at 70 °C, 10 Hz to determine the rheological properties of raw compounds.

2) Heating at 170 °C for 30 minutes.

3) Deformation cycle up to 10% at 70 °C, 10 Hz to determine again the dynamic properties.

Test method 2:

1) Deformation cycle up to 100% at 70 °C, 10 Hz to determine the rheological properties of raw compounds.

2) Heating at 190 °C for 30 minutes.

3) Deformation cycle up to 10% at 70 °C, 10 Hz to determine again the dynamic properties.

Figures 1 - 3 show the trend of the curves of the rheogram S '(dNm) / time (min.).

- Figure 1 shows the S 'torque curve measured on samples heated to 170 °C of first phase composite of the comparative examples 3.5 (TESPT) and 3.6 (APTES) and of the example 3.7 (tetrazole 1) 8% by weight compared to silica.

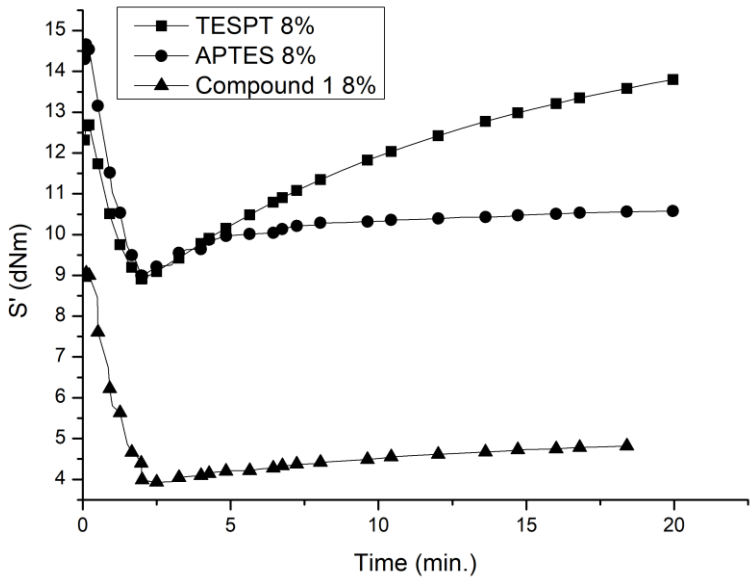


Figure 1

From the S' curve, measured in the absence of a sulfur vulcanizing system, the effect of the compound by the silane alone can be assessed. As expected TESPT silane releases sulfur which cross-links the mix, as demonstrated by the increase in S'. APTES silane normally acts as a catalyst for the vulcanization package but does not cross-link, and in fact the value of S' is unchanged once the operating temperature is reached, as vulcanization package is not present in such first-phase compounds. As regards tetrazole 1, the very low starting value of S' testifies to the high degree of compatibilization of the silica in the compound and the suppression of the interaction between the silica particles that is typically obtained when dispersion is excellent. At 170 °C the tetrazole is stable and in fact a constant S 'value is observed over time once the test temperature is reached.

- Figure 2 shows the S' curve of samples heated to 190 °C of final compound of the comparative examples 3.5 (TESPT) and 3.6 (APTES) and 3.7 (tetrazole 1) at 8% by weight with respect to silica.

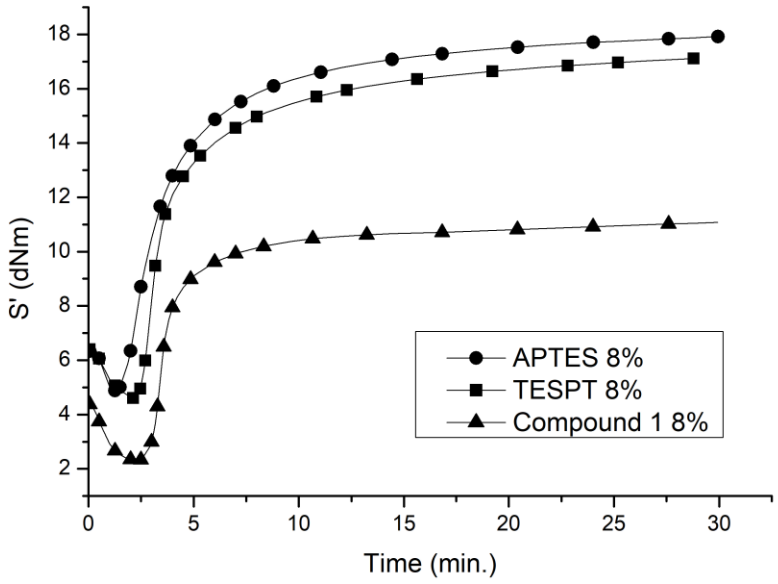


Figure 2

Table 3 shows the measured values of elastic modulus G' and viscous G'' for the comparative samples of Ex 3.5 and 3.6 and of Ex 3.7:

Final composite		**Ex. 3.5**	**Ex. 3.6**	**Ex. 3.7**
		TESPT	**APTES**	**Tetrazole 1**
Crude	G'9% (KPa)	611.05	720.09	427.23
	ΔG (0.5-10%)	134.47	305.17	174.48
Vulcanized (190°C x 30 min.)	G'9% (KPa)	1260.23	1526.42	713.47
	ΔG (0.5-10%)	347.01	727.57	242.14
	G'' 9% (KPa)	128.05	210.79	104.83

Table 3

From the data reported in Table and from the curve of Figure 2, it was observed that the sample containing the tetrazole 1 had a modulus of raw final compounds reduced compared to the comparison compounds. This behavior is attributable to a good compatibilization and dispersion of the charge. The vulcanization curve of Figure 2 testifies to a kinetic profile of the compound, containing tetrazole 1, comparable with those of the reference compounds. By comparing the modules before and after vulcanization it can be seen that the increase in the modulus to 9% deformation, following vulcanization, of the samples containing the two reference compounds (of about 700 KPa) is more marked than that of the second sample containing tetrazole (of about 300 KPa). This result may depend on the fact that the reference compounds, with different mechanisms, can increase the cross-linking of the elastomer unlike the tetrazoles. It is in fact known that TESPT silane can act as a sulfur donor and contribute to the formation of the disulfide bridges of the lattice. It is also known from literature[14] that APTES silane can contribute to the formation of the sulfur grafting since it acts as a vulcanization accelerator. Regarding the tetrazole 1, the reactivity of the silane is independent of the sulfur cross-linking reaction, therefore its contribution to the mechanical reinforcement of the vulcanized product is lower.

- Figure 3 shows the curve S' of samples heated to 190 °C of final compound of the examples 3.1 (TESPT) and 3.2 (APTES) and 3.3 (tetrazole 1) and 3.2 (tetrazole 4) at 5% by weight with respect to silica.

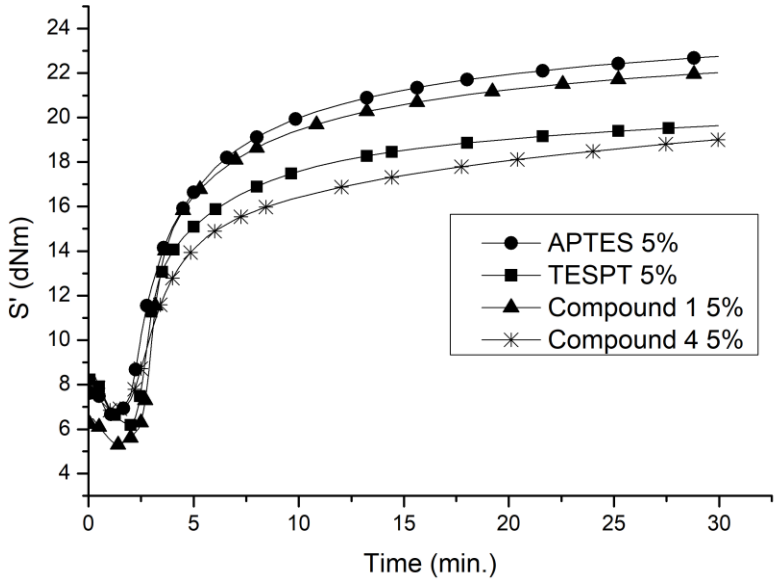


Figure 3

Table 4 shows the measured values of elastic modulus G' and viscous G'' for the comparative samples of ex 3.1 and 3.2 and containing tetrazole of ex 3.3 and 3.4:

Final composite		**Ex. 3.1**	**Ex. 3.2**	**Ex. 3.3**	**Ex. 3.4**
		TESPT	**APTES**	**Tetrazole 1**	**Tetrazole 4**
Crude	G'9% (KPa)	784.46	967.57	758.76	934.07
	ΔG (0.5-10%)	210.63	442.95	628.70	449.69
Vulcanized (190°C x 30 min.)	G'9% (KPa)	1486.75	2017.30	1631.10	1933.43
	ΔG (0.5-10%)	413.21	970.82	1237.11	1057.93
	G'' 9% (KPa)	151.24	269.41	269.61	283.89

Table 4

From the values reported in Table, it can be observed that at more reduced quantities of compatibilizer with respect to the samples of Figure 2 (ex. 3.5 - 3.7), the G' values of the raw samples of the compounds containing APTES (ex. 3.2), tetrazole 4 (ex. 3.4) are higher than the sample containing TESPT (ex. 3.1). This behavior could depend on the greater polarity, compared to TESPT, of APTES and of tetrazole 4 which would make the latter more similar to silica, leading to a stronger filler network.

From the vulcanization curves of Figure 3, a comparable kinetic profile is observed again for all the samples. The modulus G' and G'' values of the vulcanized product shown in Table are in line with the G' values of the raw material and testify differences mainly due to the dispersion state. In summary, the tetrazole compatibilizers demonstrate the classic behavior of a surface modifier, and that the modification is particularly effective with higher quantities of modifier (see examples with TESPT equal to 8% of the silica).

In conclusion, in line with the dynamic and rheological properties, the tetrazole compatibilizers allow to proceed with the compatibilization of the charge without affecting the cross-linking, unlike the classic compatibilizers, where the two functions are present together and where the trigger is poorly controllable sulfur cross-linking can occur early in situations of dispersion of the charge which are not optimal. With these tetrazole agents, it is instead possible to proceed to the ideal dispersion of the filler without interfering with the cross-linking, even without exercising a tight control of the mixing temperatures, with advantages both in terms of processing and in terms of improved mechanical performance of the materials.

3.4.4 Static mechanical properties

Samples containing tetrazoles and their comparatives, vulcanized at 190 °C for 30 minutes, were also subjected to the evaluation of static mechanical properties. The results of these tests are shown in Table 5:

	Ex. 3.1	Ex. 3.2	Ex. 3.3	Ex. 3.4	Ex. 3.5	Ex. 3.6	Ex. 3.7
Compatibilizer	**TESPT***	**APTES***	**3.1***	**3.4***	**TESPT****	**APTES****	**3.1****
Ca0.5 (MPa)	2.0	1.5	1.4	1.5	1.7	1.5	1.0
Ca1 (MPa)	3.5	1.9	1.4	1.9	3.1	2.0	2.7
Ca3 (MPa)	7.6	5.0	5.4	5.3	13.3	5.8	4.6
CR (MPa)	15.8	14.4	18.5	18.9	17.5	14.7	13.8
AR %	347	612	659	699	368	547	589

Table 5
Where: *5% vs silica; **8% vs silica.

The punctual load values at the deformations of 50%, 100% and 300% shows higher modulus for the samples containing the TESPT, due to its ability to contribute to sulfur vulcanization. On the other hand, the elongations at break are far lower than those obtainable with all the other compatibilizers. Considering that in general it is difficult to obtain a good compromise between mechanical reinforcement (expressed for example as Ca3) and elongation at break, the tetrazole compatibilizers are of great interest.

In conclusion, from the tests carried out and from the results of the tests described above it appeared that the tetrazole compatibilizing agents incorporated in tire compounds had a marked compatibilization effect, especially at higher concentrations, as demonstrated by the values of G' of raw and vulcanized compounds, and present benefits on the breaking properties of the vulcanized compound, in comparison with the commercial silanes APTES and TESPT. These results pave the way to potential future use of the tetrazole compatibilizers in compounds for tires as an alternative to traditional compatibilizers, adding an undoubted advantage in the simplification of the preparation process linked to the possibility of being able to trigger the reaction of the compatibilizing agent with the elastomer to a precise predetermined temperature, for example only during vulcanization, and therefore to be able to work the mixture longer without having to exercise a tight temperature control. The final compounds containing tetrazole compatibilizers have interesting properties, combining remarkable mechanical reinforcement and excellent ultimate properties.

3.5 Bibliography

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4. Elastomeric cross-linkers

This chapter regards the application of polytetrazole as cross-linking agents, characterized by precise activation temperatures, for curing of elastomeric compounds in tires. The results of this work are filed in a patent.

4.1 State of the art

In the tire industry, sulfur cross-linking is a process commonly used to control the mechanical properties of compounds[1]. Cross-linking influences the hardness, elasticity, hysteresis of elastomeric materials and, consequently, the properties and behavior of the tire that incorporate them[2].

Over the years, several additives were proposed to improve the cross-linking process such as activators, accelerators and retarding agents[3–6]. Even with the use of additives, conventional cross-linking system[7–9] (in particular based on sulfur) are however not completely satisfactory since they are not very versatile and difficult to control both in terms of degree and homogeneity of cross-linking and in activation temperatures. These latter aspects introduce problems of scorching due to early cross-linking or of materials with poor hysteretic properties due to the not optimal dispersion of sulfur in the elastomeric material.

Typically[10], the cross-linking agent (sulfur) and the cross-linking additives are incorporated into the mix in one or more stages of the production process, at controlled temperature, generally not exceeding 110 °C, and for limited mixing times to avoid triggering the cross-linking reactions early. However, the low solubility of sulfur in elastomeric compounds together with the mild mixing conditions adopted for its incorporation - controlled temperature and short times - make not always optimal the sulfur dispersion. For example, in the case of mixtures of elastomers with different polarity, undesired accumulation of sulfur can occur in the affine elastomeric phase.

Because of an unsatisfactory distribution of sulfur, the cross-linked final material may not have the desired properties, in particular it can be characterized by a marked hysteresis, i.e. showing an increase in the heat dissipated under dynamic conditions. Furthermore, the ultimate properties such as breaking load and elongation at break can be compromised by a non-homogeneous distribution of the vulcanizers. Finally, the migration of some components of the vulcanization

system to the interface between different compounds can cause problems of stiffening of the interfaces themselves and therefore reduce their mechanical strength. The problem appears where there is contact between compounds rich in accelerators but poor in sulfur and compounds rich in sulfur and poor in accelerators (example tread/substrate). In tires this translates into high rolling resistance, and overall, greater fuel consumption, increased polluting emissions and higher costs, greater tire wear and in general in a lower useful life than that potentially achievable in the absence of the aforementioned problems.

Currently, most vehicle manufacturers increasingly require their suppliers to develop low rolling resistance tires to reduce fuel consumption and environmental impact.

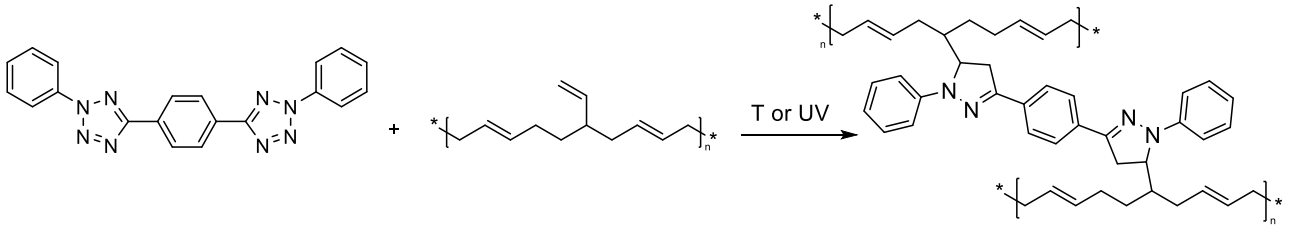
A possible approach to decrease the hysteresis of elastomeric materials is based on the use of special reinforcing fillers that can partially or completely replace standard fillers such as carbon black and silica and give less hysteresis while maintaining enough reinforcement. However, the need remains to further reduce the rolling resistance of the tires and therefore to produce increasingly eco-compatible tires and to increase the useful life of the tire by maximizing the breaking resistance of all its parts.

4.2 Summary of the research project

The studies carried out in this PhD project focused on the possibility to improve both the cross-linking process and the final product of the elastomeric compounds, with the aim of having fewer constraints in operating conditions, greater versatility and possibly improving the dynamic properties of the cross-linked materials, so as to reduce the rolling resistance of the tires that include them.

For this purpose, focus was put on alternative cross-linking systems, consisting of polytetrazole systems, capable of reacting with the double bonds present in the elastomeric component of the tire, the addition of which, besides simplifying and making the compounding process more versatile, unexpectedly led to an improvement in the hysteretic properties of the same and to the reduction of the non-linearity of the dynamic behavior, i.e. the dependence of the dynamic module of the cross-linked compound by deformation, also known as "Payne effect".

The mechanism by which tetrazoles are thermally and photochemically activated to generate nitrilimines was extensively discussed in the previous chapters. Here the idea was to have systems containing more than one tetrazole, capable of simultaneously activating and cross-linking the elastomer, as shown in the following Scheme 1.



Scheme 1- Polytetrazole reactivity with polymer

Only few studies were found in the use of tetrazoles in relation to elastomeric materials and are shown below.

Among these, an article from Stille et al.[11] show the preparation of synthetic elastomers which incorporate tetrazole pendants in the polymeric skeleton. In particular it describes the copolymerization of styrenes substituted with tetrazoles with isoprene to give the block copolymer or with styrene and butadiene a give the terpolymers. According to the article, these elastomers if heated around 200 °C led to materials with physical properties comparable to those of conventional SBR elastomers cross-linked with sulfur and zinc oxide. The authors do not present any comment or result on the dynamic properties of cross-linked materials. Furthermore, the prepared materials did not require cross-linking additives since the tetrazole functionalized elastomers work as self-cross-linkers. Nothing is also reported about any possible interaction of the materials with the fillers and with the other materials typically present in a technical compound. Finally, a large number of tetrazole functional groups (> 20) were present for each chain.

Another article[4], describes the synthesis of nitrile butadiene rubbers with high molecular weight by coupling short NBR chains terminated with a 2,5-disubstituted tetrazole on a maleimide linker. This tetrazole is photochemically decomposed to give a nitrilimine which reacts selectively with the double bonds of the linker and not with the much more numerous ones of the NBR. The article does not deal with the cross-linking of these NBR nor the dynamic properties of the cross-linked materials.

In our studies, it was found not only that certain polytetrazole compounds prove to be very effective, selective, versatile and modifiable cross-linkers, but also that after cross-linking they improve the hysteretic properties and linearity of dynamic behavior (Payne effect reduction) of the final composite, with potential application advantages.

The general formula of the polytetrazole cross-linking agents consists of an organic linker A (chain or aromatic ring), covalently linked to two or more tetrazoles. Usually, the compound has the tetrazoles replaced with a substituted aromatic ring R, to modify the activation temperature.

In some of the synthesized linkers (compounds 4 and 5) the two tetrazoles are bound to A in position 2 and replaced in position 5 with the same substituent R, as shown in Figure.

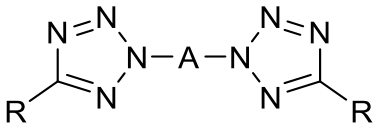


Figure 1

Some other linkers (compounds 1, 2, 3, 6, 7, 8, 9) instead have the two tetrazoles linked to A in position 5 and replaced in position 2 with the same substituent R, as shown in Figure 2.

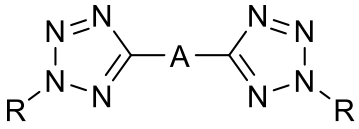


Figure 2

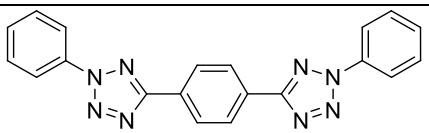
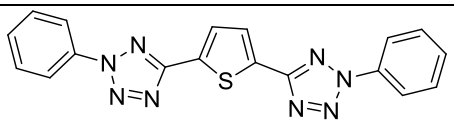
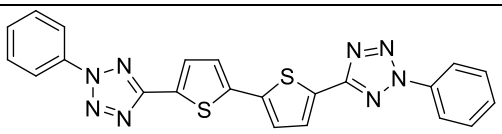
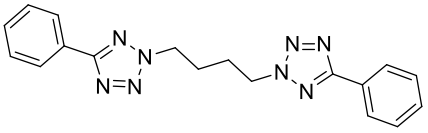
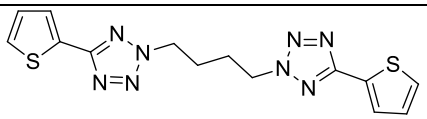
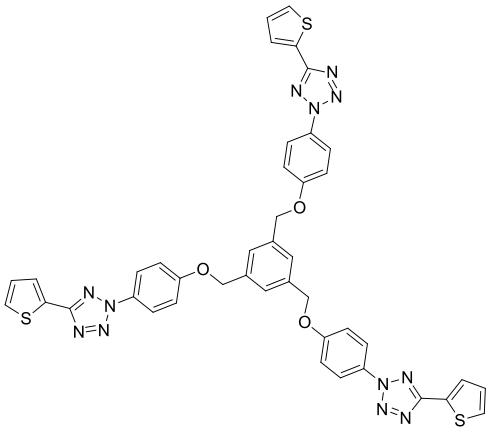
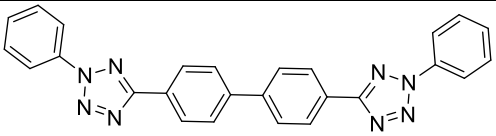
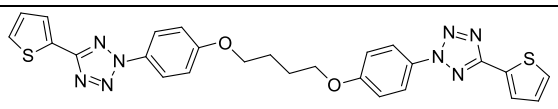
The initial idea was to use systems containing two or more tetrazole units linked together, so that they could act as cross-linking agents within polymer matrices. Those compounds can in fact be thermally activated according to the aforementioned methodology, so that each tetrazole releases nitrogen, generating the corresponding nitrilimine. The latter, should have been able to react with the vinyls of the elastomer, forming new and irreversible bonds, which could modify the properties of the pristine polymer.

It was discovered that polytetrazole compounds, when incorporated in elastomeric compounds for tires, after cross-linking impart better hysteretic properties to them.

Furthermore, the reactivity and versatility in the activation temperature of these cross-linkers, depending on the type of substituents on the tetrazole ring, allow to obtain further advantages not achievable with conventional sulfur-based cross-linkers.

4.3 Description of the project

The following table shows the synthesized polytetrazoles (Table 1).

N°	Formula	Molecular Formula	M.W. (g/mol)	Activation Temperature (°C)
1		$C_{20}H_{14}N_8$	366.38	185
2		$C_{18}H_{12}N_8S$	372.41	170
3		$C_{22}H_{14}N_8S_2$	454.53	190
4		$C_{18}H_{18}N_8$	346.39	210
5		$C_{14}H_{14}N_8S_2$	358.44	190
6		$C_{42}H_{30}N_{12}O_3S_3$	846.96	190
7		$C_{26}H_{18}N_8$	442.47	185
8		$C_{26}H_{22}N_8O_2S_2$	542.64	190

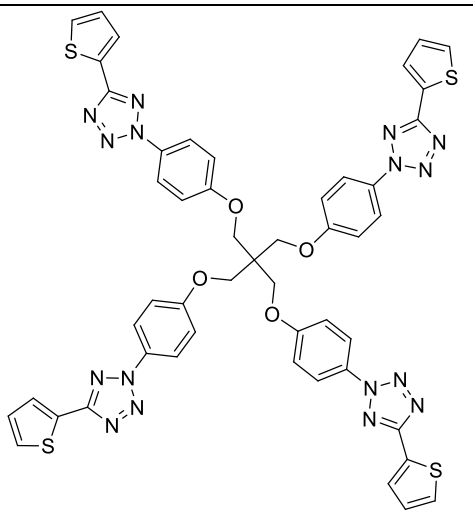
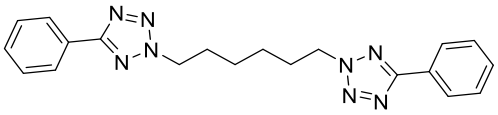
9		$C_{49}H_{36}N_{16}O_4S_4$	1041.17	190
10		$C_{20}H_{22}N_8$	374.45	230

Table 1

By suitably choosing the substituents, it is possible to modulate ad hoc the activation temperature Ta of the polytetrazole and its solubility in the chosen elastomeric matrix.

The polytetrazole cross-linking agent should have an activation temperature not lower than 100 °C, since it could give rise to cross-linking reactions too early, already during the mixing phases of the components prior to vulcanization. Early cross-linking would make the compound difficult to work with, both in the unloading phases from the internal mixer and in the extrusion processes of the semi-finished products, also compromising the integrity of the finished tire. The polytetrazole cross-linking agent should not have an activation temperature higher than 210 °C, to avoid degradation of the elastomer.

Depending on the specific application, the polytetrazolic cross-linking agent may have a lower activation temperature, similar or higher than the vulcanization temperature of a conventional sulfur-based cross-linker possibly present in the mixture, typically between 140 °C and 170 °C, with possible advantages both for the materials and for the preparation processes.

The polytetrazolic cross-linker can be selected on the basis of its activation temperature and the high solubility, to allow a good dispersion in the elastomeric mass and the subsequent cross-linking in energy saving conditions.

To improve the dispersion of the present polytetrazolic crosslinker in the elastomeric material, one with a higher activation temperature can be selected, thus being able to use prolonged hot mixing phases, without running the risk of triggering the cross-linking early and thus scorching the compound. On the other hand, if in addition to the polytetrazolic cross-linker there is also a sulfur-based vulcanizer, different situations can be thought according to the activation temperature of the present polytetrazolic cross-linker.

- A lower activation temperature, between 100 °C and 130 °C, allows to partially pre-crosslink the compound, increasing its viscosity in a controlled way before conventional vulcanization. In this case, the mixing phases will be carried out at controlled temperature, preferably not higher than the activation temperature itself. In particular, such a low activation temperature allows pre-crosslinking of the thinner semi-finished products, improving their handling without compromising their adhesiveness and ability to covulcanise with the other layers of the tire and with the reinforcement elements.

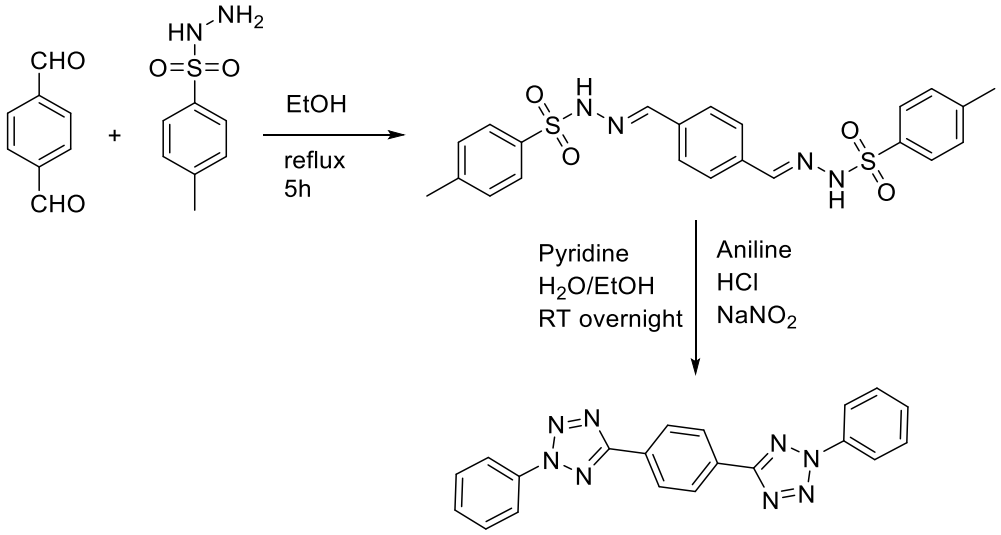
- An activation temperature similar to a classic curing system (between 130 °C and 170 °C), allows the mixture to be crosslinked with both cross-linking systems (conventional sulfur-based and polytetrazoles) in a single step, making the cross-linking more uniform and increasing its level.

- An activation temperature higher than typical sulfur cure (from 170 °C to 210 °C) allows to proceed with the conventional preparation steps without having to strictly control the T, if not to avoid the early sulfur vulcanization of the mixture (mixing T preferably below 120 °C). Such a high activation temperature allows to prepare an elastomeric compound already vulcanized with sulfur but at the same time still capable of cross-linking when, for example, subjected to particularly stressful conditions of use, with overheating beyond that specific activation temperature. In this way it is possible to remedy the degradation of the material under stress thanks to the formation of new bonds originated by the reaction of the polytetrazolic cross-linking agent during the use of the tire.

4.4 Experimental part

4.4.1 Polytetrazole synthesis

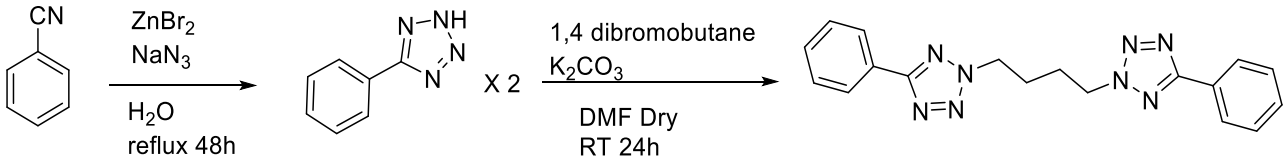
The polytetrazole cross-linking agent can be synthesized following the classic methods adopted for the synthesis of the analogous monotetrazole systems previously described. Compounds 1,2,3 and 7 were synthesized using the following procedure, changing only the starting aromatic dialdehyde (Scheme 2).



Scheme 2- General synthesis

All the synthetic procedures are reported in detail in the last chapter (experimental part).

Compound 4 and 5 were prepared using a different procedure, according to Scheme 3 (for compound 5 the aromatic ring is a thiophene instead of a phenyl):



Scheme 3- Compound 4 and 5 synthesis

All the synthetic procedures are reported in detail in the last chapter (experimental part).

This procedure for the alkylation was used also to synthesize compounds 6,8 and 9, starting from the appropriate intermediate.

4.4.2 Preparation of elastomeric compounds with silica

Comparative elastomeric compounds have been prepared, free of polytetrazolic cross-linkers (example 4.1), or using a certain amount of polytetrazole (examples 4.2 -4.3). In example 4.2 was used compound 1, while in example 4.3 was used compound 2 (see the Table 1). The quantities of the various components expressed in phr are reported in the following Table 2:

Ingredients (phr)	**Ex. 4.1**	**Ex. 4.2**	**Ex. 4.3**
SSBR	137	137	137
Silica	60	60	60
Polytetrazole (1)	---	4.2	---
Polytetrazole (2)	---	---	4.3
6PPD	2.5	2.5	2.5
TESPD	4.8	4.8	4.8
Stearic acid	1	1	1
ZnO (80%)	2	2	2
CBS	3	3	3
Zolfo (67%)	1	1	1

Table 2

Where:

- SSBR: extended solution styrene-butadiene copolymer with 37.5 phr of TDAE oil for every 100 phr of Dow dry polymer SE SLR-4630 dry elastomeric polymer.

- Silica: Zeosil 1165 MP. Supplier: Solvay Rhodia Operations.

- Stearic acid: Supplier: Temix Oleo SRL.

- 6PPD: N- (1,3-dimethylbutyl) -N`-phenyl-p-phenylenediamine, Supplier: Eastman.

- ZnO (80): 80% zinc oxide, 20% polymeric binder and dispersing agent, Supplier: Lanxess Add.

- Silane: TESPD Bis- (3-triethoxy-silyl-propyl) -disulfide, Supplier: Jingzhou Jianghan Fine Chem.

- CBS: N-cyclohexyl-2-benzothiazylsulfenamide, cyclohexylamine content <1%, Supplier Dulso.

- Sulfur: Crystex OT33 amorphous sulfur, insoluble in CS2 and in toluene. 33% treated with hydrotreated heavy naphthenic distillate (petroleum), Supplier: Eastman.

Mixing procedure

The mixing was carried out in several stages using an internal laboratory mixer with Brabender tangential rotors (60 ml mixing chamber).

1) In the first mixing phase, 50% of the elastomer was introduced and chewed for 30 seconds at 140 °C (set temperature).

2) In the following mixing phase, polytetrazole, silica, silane and the remaining elastomer were added. The mixing was continued for 2 minutes, at 140 °C. Subsequently, the antioxidant, ZnO and stearic acid were introduced. The mixing was continued for about 2 minutes, until the reaction between silica and silane was completed, always at 140 °C after which the compounds, called first phase compounds, were discharged, and tested for their dynamic properties.

3) After 12-24 hours, the vulcanizer (sulfur) and accelerator were introduced into the first phase compounds, and the mixing continued for about 3 minutes, at 90 °C obtaining the final compounds. Then final compounds were re-tested for their dynamic properties.

4.4.3 Dynamic mechanical properties

The first phase and final phase compounds were subjected to analysis of the dynamic mechanical rheological properties according to these conditions:

1) Deformation cycle up to 100% at 70 °C, 10 Hz to determine the rheological properties of raw compounds.

2) Heating at 190 °C for 30 minutes to obtain the cross-linking.

3) Deformation cycle up to 10% at 70 °C, 10 Hz to determine the dynamic properties after the cross-linking.

Figures 1 (A-H) show the dynamic characterization at 70 °C (G' and tan Delta) vs deformation (strain%) of samples of materials obtained from the reference composition (e.g. 4.1) and containing the polytetrazole (e.g. 4.2) at various levels of mixing, and cross-linking and the S' vs time curve in the cross-linking carried out at 190 °C.

- Fig. 1A: elastic modulus G ’at 10 Hz, 70 °C measured on first phase compound samples of the examples 4.1 and 4.2.

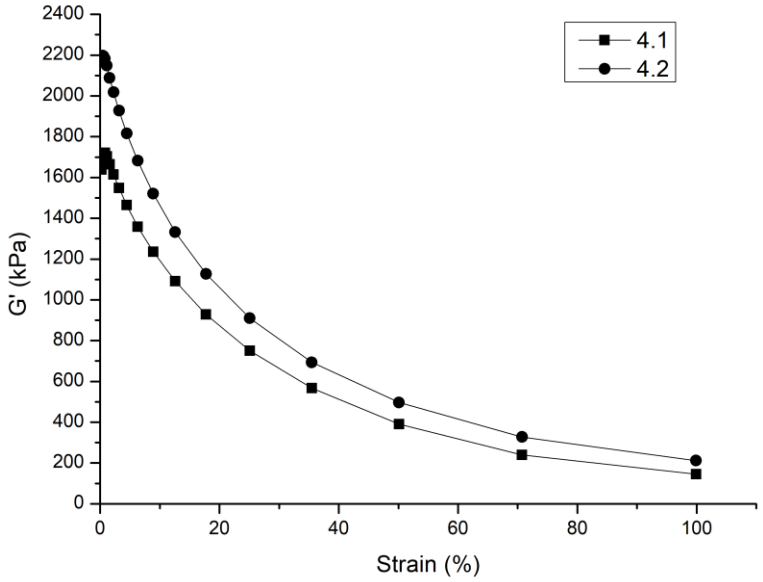


Figure 1A

- Fig. 1B: torque cross-linking curve S 'at 190 °C measured on raw samples of the first phase compounds of examples 4.1 and 4.2.

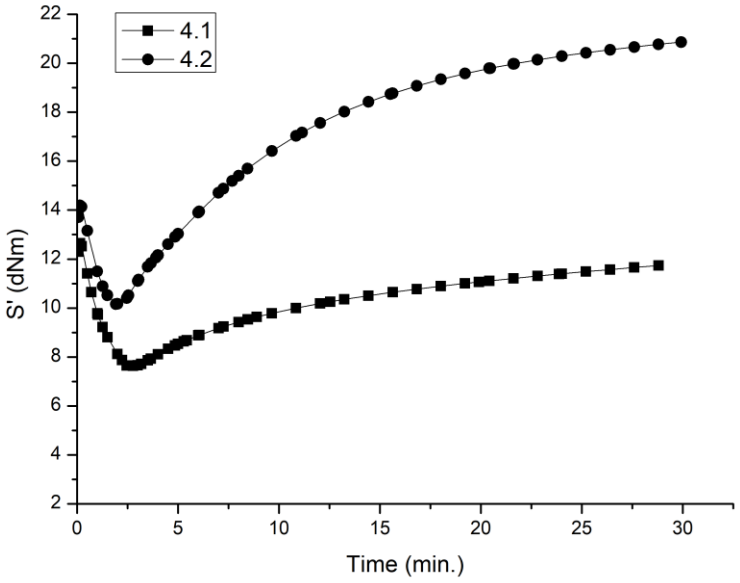


Figure 1B

- Fig. 1C: elastic modulus G 'at 10 Hz, 70 °C measured on samples of first phase compounds samples heated at 190 °C for 30' of examples 4.1 and 4.2.

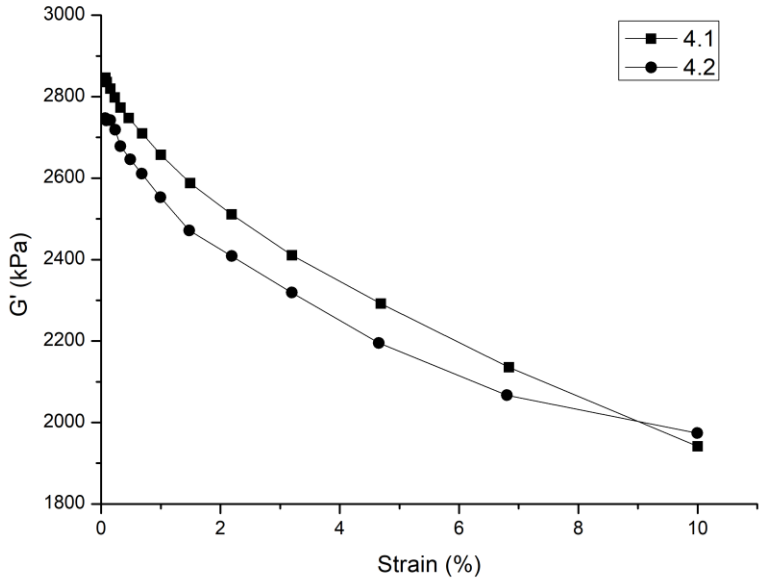


Figure 1C

- Fig. 1D: tan delta at 10 Hz, 70 °C measured on samples of first phase compounds heated to 190 °C for 30 min. of the examples 4.1 and 4.2.

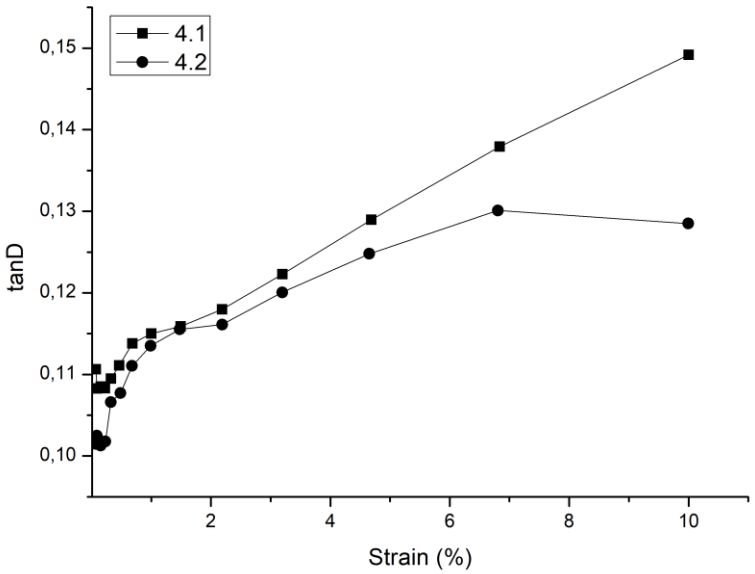


Figure 1D

- Fig. 1E elastic modulus G ’at 10 Hz, 70 °C measured on raw final compound samples of the examples 4.1 and 4.2.

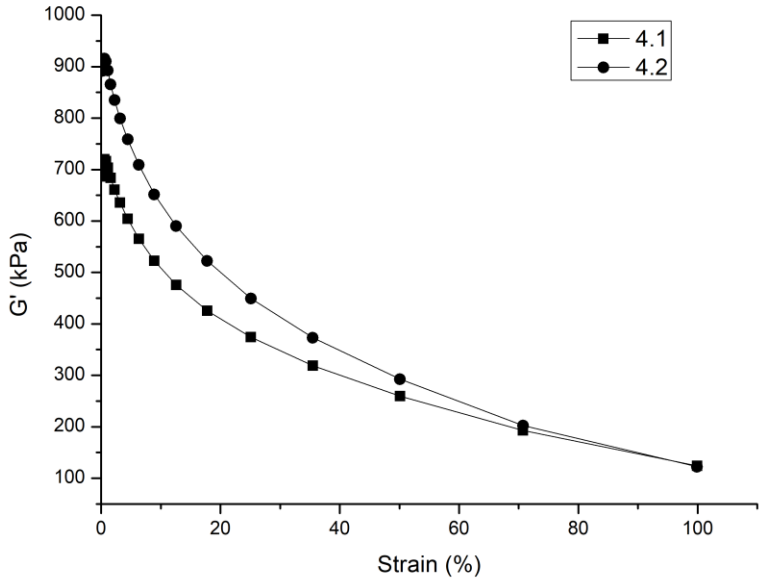


Figure 1E

- Fig. 1F: torque cross-linking curve S 'at 190 °C measured on samples of final compounds of the examples 4.1 and 4.2.

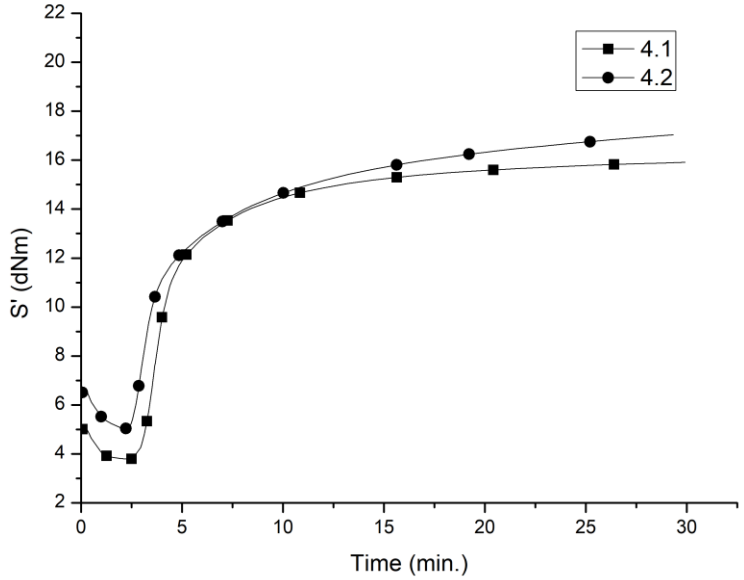


Figure 1F

- Fig. 1G: elastic modulus G 'at 10 Hz, 70 °C measured on samples of final compounds heated to 190°C for 30' of the examples 4.1 and 4.2.

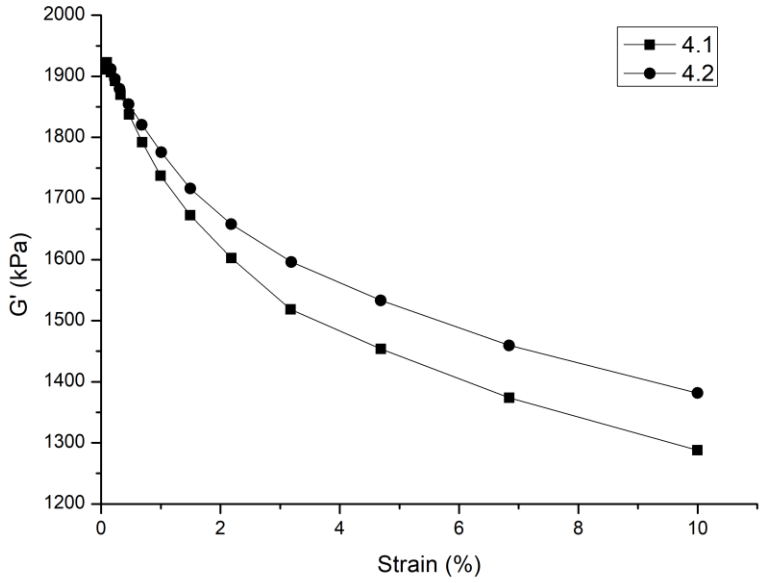


Figure 1G

- Fig. 1H: tan delta at 10 Hz, 70 °C measured on samples of final compounds heated to 190 °C for 30 min. of the examples 4.1 and 4.2.

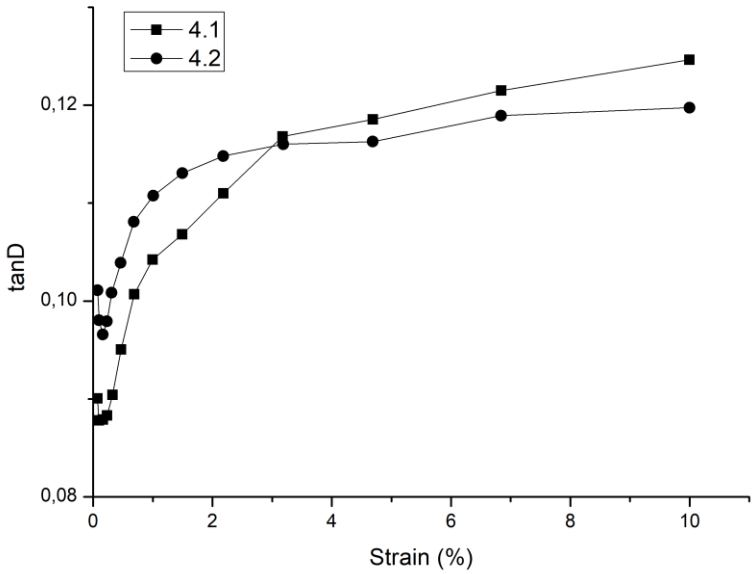


Figure 1H

It was observed that:

1) In both first phase compounds and final compounds, the addition of the tetrazole cross-linking agent 1 leads compound 4.2 to have an elastic modulus at low deformations higher than that of the respective reference compound 4.1. The difference in elastic modulus in

these raw compounds tends to decrease with increasing deformation: as evident from figures 1A and 1E in raw compounds, the tetrazole cross-linking agent tends to increase the Payne effect. This effect could be due to the fact that the tetrazole cross-linker is not so soluble in the mixture at 70 °C and therefore behaves like a filler. The increased Payne effect of the raw compound does not have negative consequences and can indeed be useful in some semi-finished products, translating into a greater "green strength", which reduces the risk of deformation of the semi-finished product during its handling and storage.

2) The crosslinking curves measured at 190 °C shown in figures 1B for the first phase compounds and 1F for the final compounds show the effectiveness of the tetrazole cross-linking agent: in the case of the first phase compounds there is a very significant increase in torque with respect to the reference, and also in the case of final compounds also including standard vulcanizing agents, the final torque is higher for the inventive compound.

3) Figures 1C and 1G show that in the compounds (respectively first phase and final) after a heating cycle to the activation temperature of the polytetrazole, the addition of this agent leads to a marked decrease in the effect Payne in the cross-linked compound. The decrease in the Payne effect in the vulcanized compound is unexpected, given that the crosslinks between the polymer chains should increase the modulus both at low and high deformations. It was hypothesized that the decrease in the Payne effect is linked to the homogeneity of the network that is formed in the presence of the tetrazole cross-linking agent, which could reduce the possibility of interaction of the filler with itself. The decrease in the Payne effect is of technological interest as it is often associated with less hysteresis and as an indicator of lower non-linearity of the mechanical response of the tire. A tire with a more linear response is more predictable and more precise and therefore safer.

4) Figures 1D and 1H show that in the compounds (respectively first phase and final) after a heating cycle to the activation temperature of the polytetrazole, the addition of this agent leads to a significant reduction of the hysteresis to 70 °C of the cross-linked compound, at least at deformations greater than about 3%, which are those of technological interest (the tire under load easily reaches local deformations of the order of 10% and higher). The

hysteresis at 70 °C is considered a predictor of the rolling resistance of the tire, so this effect is certainly interesting.

4.4.4 Separate temperature test

The final compounds were also subjected to analysis of the dynamic mechanical rheological properties by a different procedure heating at two different temperatures, according to these conditions:

1) Deformation cycle up to 100% at 70 °C, 10 Hz to determine the rheological properties of raw compounds.

2) Heating at 150 °C for 40 minutes to obtain a first low T cross-linking in which only the sulfur vulcanization system is activated.

3) Deformation cycle up to 10% at 70 °C, 10 Hz to determine the dynamic properties after the first cross-linking.

4) Heating at 190 °C for 30 minutes to complete the cross-linking, also making the tetrazole cross-linking agent come into play.

5) Deformation cycle up to 10% at 70 °C, 10 Hz to determine the dynamic properties after the second cross-linking.

The first heating at 150 °C induced sulfur cross-linking, the second at 190 °C the further cross-linking due to the polytetrazolic cross-linking agent 1.

Figures 2 (A-D) show the dynamic characterization at 70 °C (G 'and tan Delta) (strain %) of samples of materials obtained from the reference composition (e.g. 4.1) and containing tetrazole 1 (e.g. 4.2) after heating to 150 °C (Fig. 2A, 2B) and at 190 °C (Fig. 2C, 2D).

- Fig. 2A: elastic modulus G ’at 10 Hz, 70 °C measured on samples of final compounds after a 40 min. thermal cycle at 150 °C of examples 4.1 reference and 4.2 with tetrazole (phase 3 of the procedure described above).

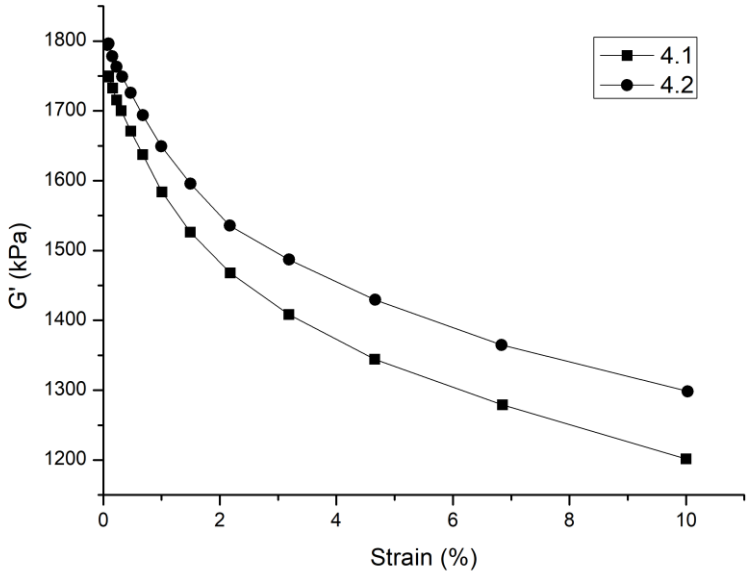


Figure 2A

- Fig. 2B: tan delta at 10 Hz, 70 °C measured on samples of final compounds after a 40 min. thermal cycle at 150 °C of the examples 4.1 and 4.2 (phase 3 of the procedure described above).

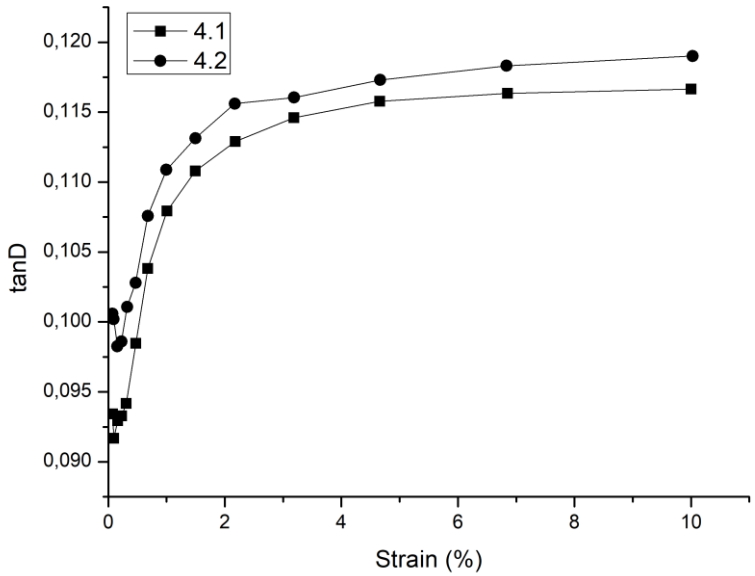


Figure 2B

- Fig. 2C: elastic modulus G 'at 10 Hz, 70 °C measured on samples of final compounds after a 30 min. thermal cycle at 190 °C of the examples 4.1 and 4.2 (step 5 of the procedure described above).

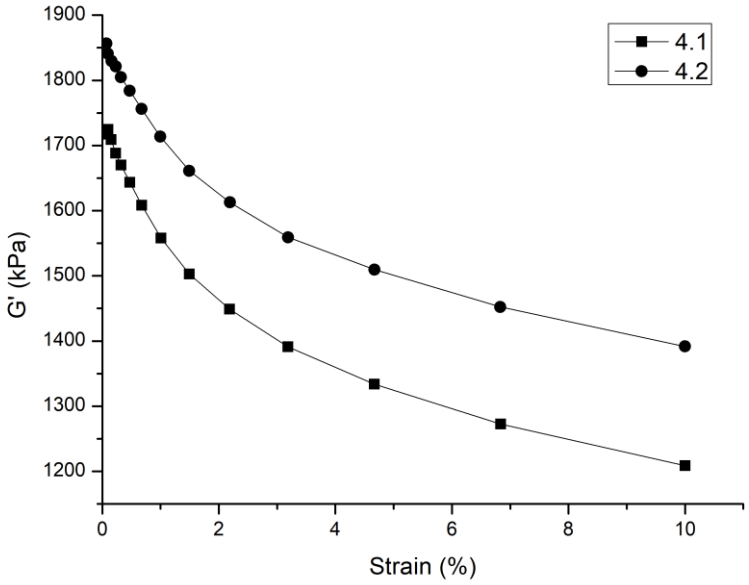


Figure 2C

- Fig. 2D: tan delta at 10 Hz, 70 °C measured on samples of final compounds after a 30 min. thermal cycle at 190 °C of the examples 4.1 and 4.2 (step 5 of the procedure described above).

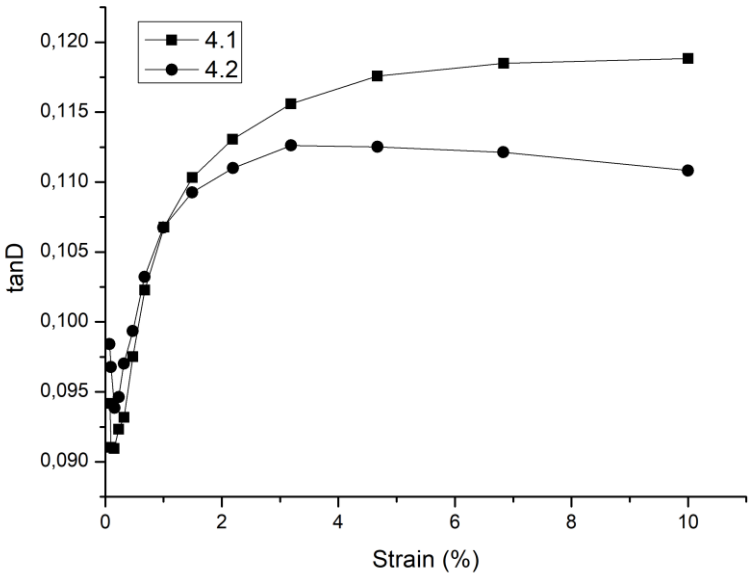


Figure 2D

It was observed that:

After the first cross-linking at 150 °C (phase 2 of the procedure described above), the measurement of the dynamic properties at 70 °C (phase 3) shows that:

- The hysteresis of the compounds of the examples 4.1 and 4.2 are very similar, as shown in figure 2A, but the mixture 4.2 tends to be a little more hysteretic, as expected for the addition of a small molecule, which if it remains unreacted it should behave like a plasticizer.

- The dynamic module G' of the compounds are relatively similar (figure 2B), but a decrease in the Payne effect for the compound 4.2 is already noted. This could be interpreted as indicative of a partial reaction of the tetrazole cross-linking agent, although at temperatures lower than the activation one, which can be explained by the interaction with the complex compound matrix.

After the second cross-linking at 190 °C (phase 4 of the procedure described above), the measurement of the dynamic properties at 70 °C (phase 5) shows that:

- The hysteresis of the compound of example 4.2 is much lower than that of the reference compound 4.1, as shown in figure 2C.

- The dynamic modulus G' of the compound 4.2 is much higher than that of the reference compound 4.1 while there is a sharp decrease in the Payne effect for the compound 4.2.

Table 3 summarizes the dynamic properties measured in the compounds of examples 4.1, 4.2, 4.3.

		Ex. 4.1	**Ex. 4.2**	**Ex. 4.3**
Uncured final compound (70 °C, 10 Hz)	**G' 9%**	522.74	651.7	524.07
	ΔG (0.5-10%)	197.61	262.88	200.06
Final compound after heating 150 °C x 40 min. (70 °C, 10 Hz)	**G' 9%**	1201.65	1298.28	1218.21
	ΔG (0.5-10%)	469.38	427.74	488.54
	tanD 9%	0.117	0.119	0.133
Final compound after heating 190 °C x 30 min. (70°C, 10 Hz)	**G' 9%**	1208.6	1391.65	1215.87
	ΔG (0.5-10%)	614.8	392.38	422.80
	tanD 9%	0.133	0.111	0.122

Table 3

It was noted that:

- The trend of the dynamic properties using the tetrazole cross-linking agent 2 in the compound of example 4.3 are completely analogous to those observed in detail above for the agent 1 in the compound 4.2: the addition of the tetrazolic cross-linking agent brings, at a temperature at least

equal to that of activation of the cross-linker itself, to a reduction of both the hysteresis and the Payne effect of the final cross-linked compound.

In the respective compounds raw or only vulcanized at temperatures lower than those of activation of the tetrazole agent, the effects are much lower and in some cases in the opposite direction, as is expected for the addition of a molecular species in the compound.

4.4.5 Static mechanical properties

The compound of example 4.3, in comparison with the reference compound of example 4.1, was also subjected to the evaluation of the static mechanical properties, shown in Table 4.

It was noted that the tetrazole cross-linking agent 2 in the compound of example 4.3 has a marked effect of increasing the high elongation modules (modulus at 300% CA3), without decreasing the breaking modulus of the mixture, as it would be instead expected for an increase in the standard vulcanizer: this data can also be interpreted assuming that the tetrazole agent leads to a higher homogeneity of the lattice compared to standard vulcanizers.

		Ex. 4.1	**Ex. 4.3**
Vulcanization (190 °C x 30 min.)	**Ca0.1 (Mpa)**	0.55	0.57
	Ca0.5 (Mpa)	1.54	1.60
	Ca1 (Mpa)	2.81	3.20
	Ca3 (Mpa)	11.75	14.44
	CR (Mpa)	15.64	15.94

Table 4

It can therefore be concluded that the tetrazolic cross-linking agents 1 and 2 have a positive effect on the dynamic properties of the compound and lead to a decrease in the hysteresis and in the Payne effect of the vulcanized product. Furthermore, it can be concluded that these effects occur both when the tetrazole cross-linking agent is used in the absence of sulfur vulcanizers, and when the latter are present and that in both cases the activation temperature of the tetrazoles in cross-linking remains the one determined by thermogravimetric tests.

4.5 Example with carbon black

Comparative elastomeric compounds were prepared, without polytetrazolic cross-linkers (example 4.4), or with the polytetrazolic cross-linker 2 (example 4.5). The quantities of the various components expressed in phr are reported in the following Table 5:

Ingredients (phr)	**Ex.4.4**	**Ex. 4.5**
SSBR	137	137
CB 234	60	60
Polytetrazole 2	---	4.3

Table 5

Where:

- SSBR: extended solution styrene-butadiene copolymer with 37.5 phr of TDAE oil for every 100 phr of Dow dry polymer SE SLR-4630 dry elastomeric polymer.

- CB 234: Birla Carbon grade N234 carbon black.

The mixing was carried out using an internal laboratory mixer with Brabender tangential rotors (60 ml mixing chamber).

1) In the first phase, 50% of the elastomer was introduced and chewed for 30 seconds at 140 °C (set temperature).

2) In the following phase, polytetrazole, carbon black and the remaining elastomer, were added. The mixing was continued for 2 minutes, at 140 °C.

4.5.1 Dynamic mechanical properties

The first phase compounds 4.4 and 4.5, respectively comparative and containing polytetrazole 2, have been subjected to analysis of the dynamic mechanical rheological properties, according to these conditions:

1) Deformation cycle up to 100% at 70 °C, 10 Hz to determine the rheological properties of raw compounds.

2) Heating at 190 °C for 30 minutes to obtain the cross-linking.

3) Deformation cycle up to 10% at 70 °C, 10 Hz to determine the dynamic properties after the cross-linking.

Figures 3 (A-D) show the dynamic characterization at 70 °C (G' and tan Delta) vs deformation (strain%) of samples of materials obtained from the reference composition (e.g. 4.4) and containing polytetrazole 2 (e.g. 4.5) before and after cross-linking, as well as the S' vs time curve in the crosslinking carried out at 190 °C.

- Fig. 3A: elastic modulus G’ at 10 Hz, 70 °C measured on samples of green compounds of the examples 4.4 and 4.5.

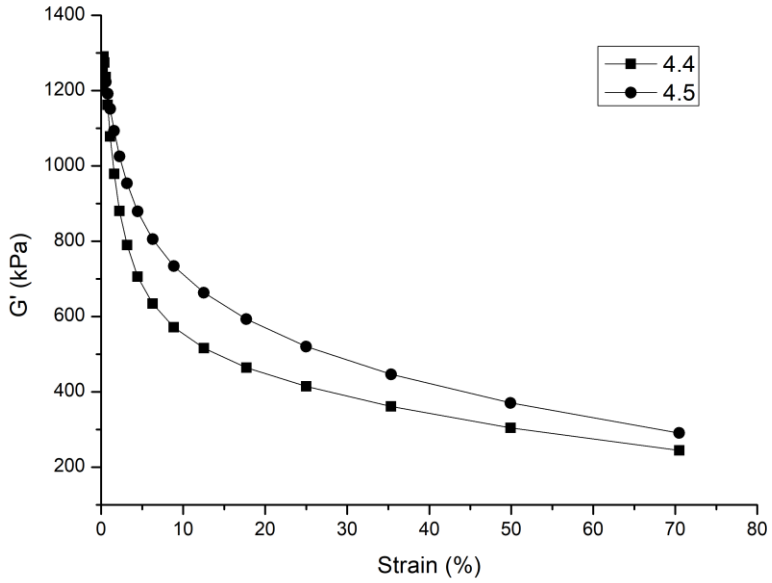


Figure 3A

- Fig. 3B: torque cross-linking curve S' at 190 °C measured on samples of green compounds of the examples 4.4 and 4.5.

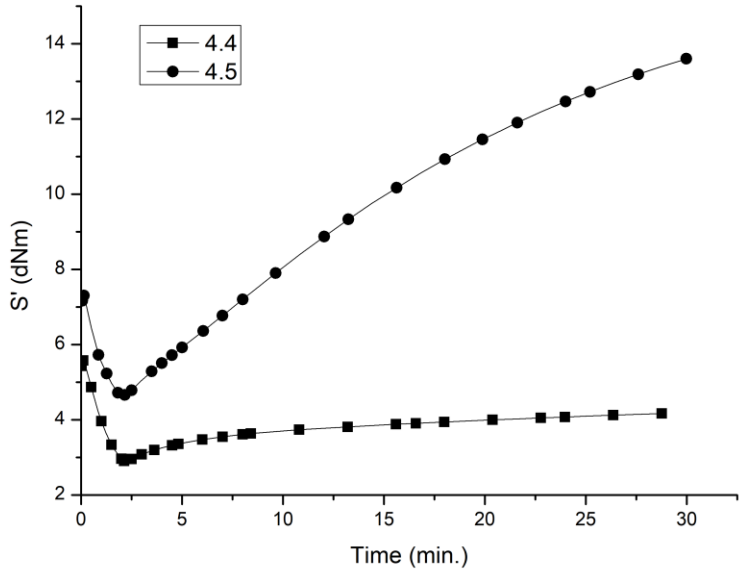


Figure 3B

- Fig. 3C: elastic modulus G' at 10 Hz, 70 °C measured on samples of compounds heated to 190 °C for 30 min. of the examples 4.4 and 4.5.

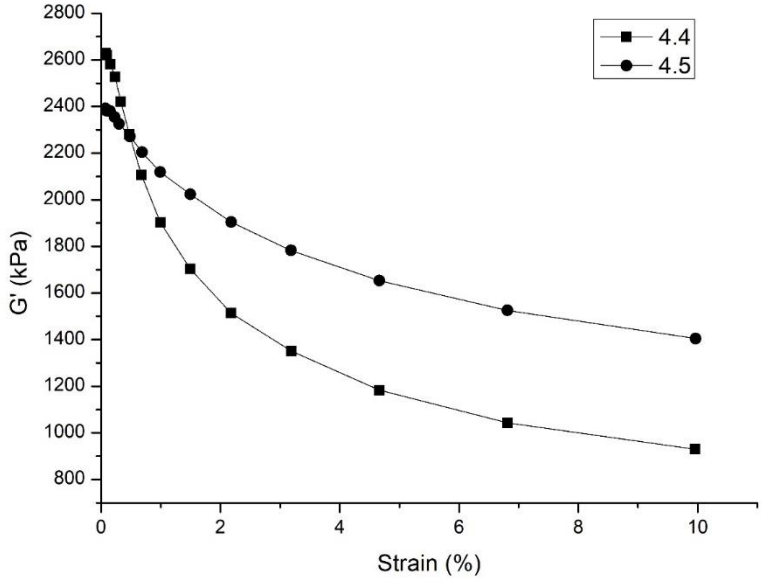


Figure 3C

- Fig. 3D: tan delta at 10 Hz, 70 °C measured on samples of compounds heated to 190 °C for 30 min. of the examples 4.4 and 4.5.

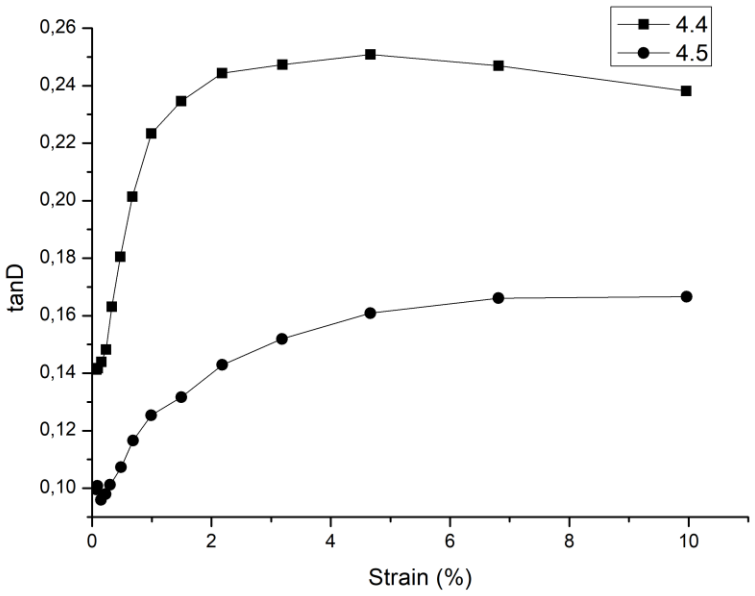


Figure 3D

It was observed that

1) In the raw mix, the addition of the tetrazole cross-linking agent 2 leads the compound 4.5 to have an elastic modulus at low deformations higher than that of the respective reference compound 4.4 (figure 3A), similarly to what has been observed for example 4.2.

2) The cross-linking curves measured at 190 °C shown in figure 3B show the effectiveness of the tetrazolic cross-linking agent: the final torque is higher for the example 4.5, as observed for example 4.2 - the increase of torque for the reference compound can be interpreted as the effect of the flocculation of the filler.

3) After a heating cycle at the activation temperature of the tetrazole cross-linking agent, the addition of this agent leads to:

- A marked decrease in the Payne effect in the cross-linked compound, as shown in figure 3C.

- A significant reduction of the cross-linked mix hysteresis at 70 °C, as shown in Figure 3D. The hysteresis at 70 °C is considered a predictor of the rolling resistance of the tire, so this effect is certainly interesting.

It cannot be excluded that there is a reaction between a tetrazole unit with carbon black, also leading to its better dispersion in the elastomeric matrix. Moreover, it is known in the literature that nitrilimines react with fullerene and carbon nanotubes (Chapter 1).

4.6 Swelling tests

Swelling tests with solvent were carried out on samples of raw and cross-linked composite to verify the contribution of the tetrazole cross-linking on the restrictions that the solvent encounters in swelling the mix. Swelling tests on the raw mix are possible since the filler is present in such a quantity that a physical gel is formed, and the rubber is not soluble in the solvent as its mobility is restricted by the filler[12]. A weighed sample (about 400 mg) of the mix was immersed in 10 mL of solvent (Toluene) and left to soak away from light and heat. The solvent was changed with fresh toluene every 24 h. After 72 h the solvent was removed, and the solvent swollen compound gel is weighed. The gel was dried in an oven and weighed. Swelling percentage (SW%) was reported as swollen gel mass/dried gel mass.

4.6.1 Carbon black test

In this test, Carbon Black-based composites were prepared, containing different quantities of polytetrazole 2 (Table 6), as well as a reference without cross-linking agent (SBR Standard), according to the recipe described in paragraph 4.5 (Table 5). The table shows the average values obtained by repeating the swelling test three times for each compound, after curing process (190°C 30 min.).

	First phase SBR Standard (mg)	**First phase + compound 2 3phr (mg)**	**First phase + compound 2 4phr (mg)**	**First phase + compound 2 5phr (mg)**
Initial weight	406.25	334.67	348.42	372.47
First wash	1848.30	1603.60	1413.18	1344.17
Second wash	1846.57	1695.32	1465.15	1394.21
Third wash	1829.64	1704.59	1491.36	1405.98
Dry	220.51	228.92	245.89	267.56
ΔW	1608.75	1476.33	1246.12	1137.69
SW%	731%	645%	507%	425%

Table 6

The results obtained show a decreasing swelling trend as the amount of cross-linking agent increases, which is in agreement with our assumptions. Composites containing increasing amounts of polytetrazole have a more compact polymer matrix. This feature allows for less weight loss and less swelling. Furthermore, the difference between the reference and the samples containing polytetrazole is accentuated by the fact that in the chosen composites there were no sulfur-based

vulcanizing agents and therefore the only component capable of giving chemical cross-linking the polytetrazole.

4.6.2 Silica test

In this test, Silica-based compounds were prepared (Table 7), containing different polytetrazole (2 and 7) as well as a reference without polytetrazole (SBR Standard), according to the recipe described in paragraph 4.4.2 (Table 2). The table shows the average values obtained by repeating the swelling test three times for each compound, after curing process (190°C 30 min.).

	Final compound SBR Standard (mg)	**Final compound compound 2 3phr (mg)**	**Final compound compound 7 3phr (mg)**
Initial weight	336.67	294.35	283.51
First wash	950.56	797.42	740.78
Second wash	967.33	808.61	749.27
Third wash	972.38	807.72	747.43
Dry	283.25	245.37	236.33
ΔW	689.40	562.45	510.62
SW%	244%	229%	216%

Table 7

The results obtained show a decreasing swelling when the polytetrazoles are present, which is in agreement with our assumptions. In this case it should be noted that we are referring to final compounds in which, in addition to polytetrazole, there is also the classic sulfur-based vulcanizing package. For this reason, the SW% values between the reference and the samples containing the polytetrazoles are closer to each other even if, in case of polytetrazole-based composite, the value is still lower.

4.7 Final considerations

From this evidence it can be concluded that the present polytetrazolic cross-linkers, both used as single cross-linkers and together with classic sulfur-based cross-linkers, are able to significantly reduce the hysteresis of the elastomeric compounds with potential advantages in terms of lower rolling resistance of the tire and, last but not least, vehicle consumption. Furthermore, it can be concluded that the present polytetrazolic cross-linkersare able to significantly reduce the Payne

effect of the vulcanized compounds, with potential advantages on driving precision and therefore on the safety of the tire. Furthermore, by appropriately selecting the substituents present on the tetrazoles, it is possible to modify their activation temperature bringing it to similar or decidedly different values from those necessary to trigger the classic sulfur cross-linking, thus creating advantageous application opportunities. For example, by choosing a tetrazole crosslinker with high activation temperature as the sole or main crosslinker of an elastomeric compound, it is possible to minimize the risk of scorching the compound, or of unwanted pre-crosslinking in the preliminary stages of mixing the components and preparing the semi-finished products (e.g. extrusion, calendering), even in the event of an increase in temperature, provided that it remains below the activation temperature of the cross-linker. This allows to simplify the preparation process of the compound and semi-finished products, no longer having to strictly control the temperatures during the mixing phase and the subsequent operations that lead to the green tire.

In fact, the cross-linking conducted with the present cross-linkers appears much more controllable than the classic sulfur cross-linking, allowing to prolong the mixing until optimum dispersion and homogeneity are obtained. In the case of mixtures of tetrazole cross-linkers and sulfur based cross-linkers in the same compound, they can be activated at the same time or at a later time, even far away, and in different sequence by choosing the tetrazole cross-linker with the appropriate activation temperature - equal, higher or lower compared to the sulfur cross-linker - and the appropriate thermal process conditions, depending on the particular applications of the tire. For example, in sports competitions, the tire overheats and degrades, worsening in performance as the race progresses. In these cases, if there are tetrazole cross-linkers in the tire components that have not reacted - because they have higher activation temperature and, therefore, resistant to vulcanization conditions - they will trigger crosslinking reactions when the activation temperature is reached during use in the tire, with the formation of new bonds and consolidation of the material, thus counteracting their degradation. The polytetrazole cross-linker therefore could be used as an auxiliary system that comes into play to repair damage in the material when it degrades, activating only when the tire reaches certain critical temperatures in intensive use.

In other applications it may be advantageous to use tetrazole crosslinkers at an activation temperature lower than that of the classic sulfur cross-linkers for semi-finished pre-reticulation. For example, some semi-finished products, such as carcass plies for car applications, risk being

deformed in the tire manufacturing stages and above all risk being penetrated by the liner mix during the molding phase at the buttress level: it is known to overcome this problem with a pre-crosslinking induced by ionizing radiation (electron beam), which however requires a lot of energy and a considerable investment: the use of low activation T tetrazole cross-linkers has potential to obtain a similar pre-crosslinking simply by thermal means, without compromising neither the adhesiveness of the carcass nor substantially the standard sulfur vulcanization, which will take place during the vulcanization phase.

Another advantage of the present polytetrazole cross-linkers, compared to the classic sulfur-based crosslinkers, is the possibility, by choosing the appropriate substituents on the tetrazoles, to optimize their solubility and therefore their dispersion, which can be homogeneous or aimed at a specific phase, in the compound. Consequently, it is possible to obtain a homogeneous cross-linking throughout the mass or a higher cross-linking density in particular areas, for example near the filler's particles, if the tetrazole cross-linker carries groups with high affinity for the same, such as for example silanes or polyalkoxyl groups in the case of silica.

In conclusion, in addition to conferring less hysteresis to the compounds, the present polytetrazole cross-linkers could be more modulable in terms of reaction temperatures and solubility than the more traditional crosslinker, sulfur. Advantageously, these compounds allow in principle selective cross-linking to take place in certain components, at certain temperatures and therefore in specific phases of the tire production or use process.

4.8 Interference tests

At the end of this chapter some tests, although still partial, are reported to find any component present in the composite that could interfere with the cross-linking process of our polytetrazoles.

This question arose from looking at the vulcanization curves (S') relating to the tests carried out on the final compound at a single temperature (Fig. 1F). In fact, the degree of cross-linking of compounds containing polytetrazole were higher than those without, but not as much as it was expected. In the tests on the first phase samples (Fig. 1B) the difference was indeed much greater. It was therefore investigated which of the components added in the final phase could interfere with the formation of the nitrilimine or with its reaction with the polymer.

4.8.1 Investigation of tetrazole reactivity as a function of ratio to vinyls

Before proceeding with the tests, it should be explained that not all the nitrilimine formed after thermal treatment actually reacts with the vinyl double bonds of the polymer. This was demonstrated in the experiment below, in which Polyvest (1% vinyl polybutadiene) was taken as a reference and thermally reacted with various amounts (0.5, 1 and 2 eq. respect to the vinyl content) of tetrazole 12 (Table 1, Chapter 1). This tetrazole was chosen for its high dispersibility in the Polyvest, which made it possible to obtain a homogeneous system. The polymer was then heated to the tetrazole activation temperature (150 °C) for 30 minutes and subsequently underwent a washing process (dissolving it in DCM, precipitating it in methanol and centrifuging three times), in order to obtain the functionalized polymer clean from any trace of by-products. Assuming that vinyls are the only double bonds that react with nitrilimine (see chapter 1, paragraph 1.4.3), the NMRs of the three polymers at different degrees of functionalization were observed, focusing on the ratio between the integrals of the thiophene proton (1H) (6.9 ppm) compared to 1,2-PB vinyl protons (3H) (4.95 ppm). The ratios result in 2.3% vinyl functionalized using 0.5 eq. of tetrazole 12 (Fig.4), 4.3% functionalized vinyl using 1 eq. of tetrazole 12 (Fig.5) and 6.3% vinyl functionalized using 2 eq. of tetrazole 12 (Fig.6).

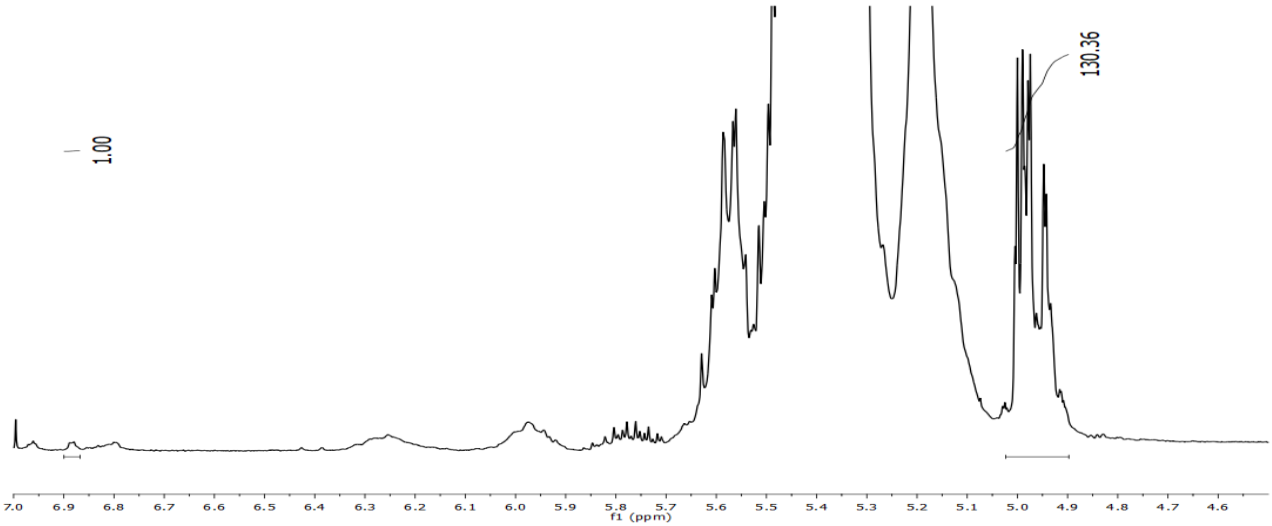


Figure 4- Polyvest + 0.5 eq. of tetrazole

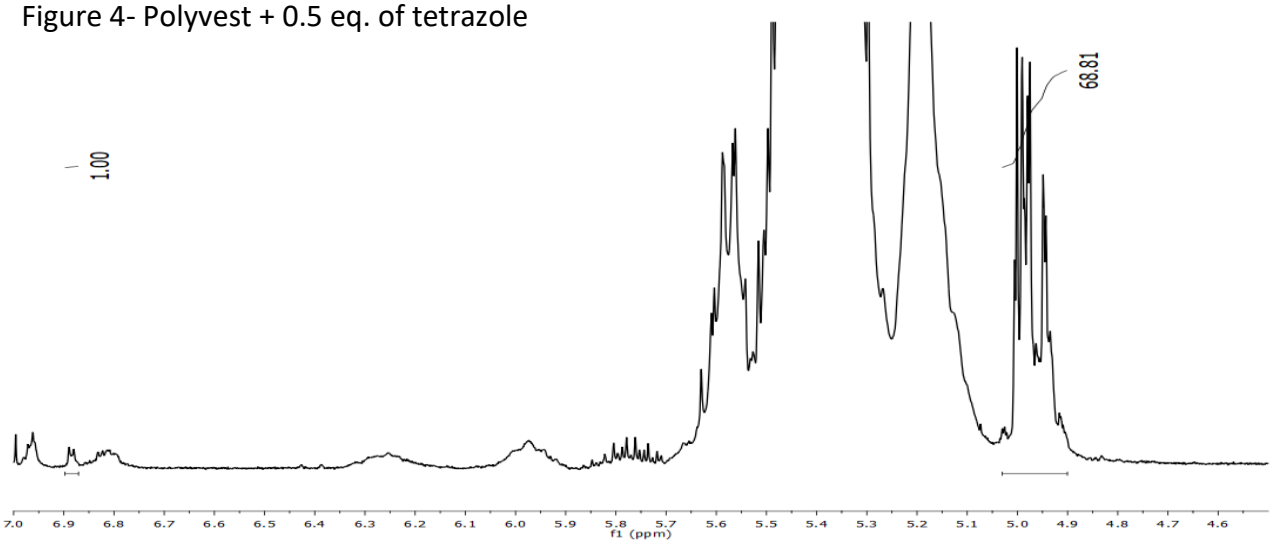


Figure 5- Polyvest + 1 eq. of tetrazole

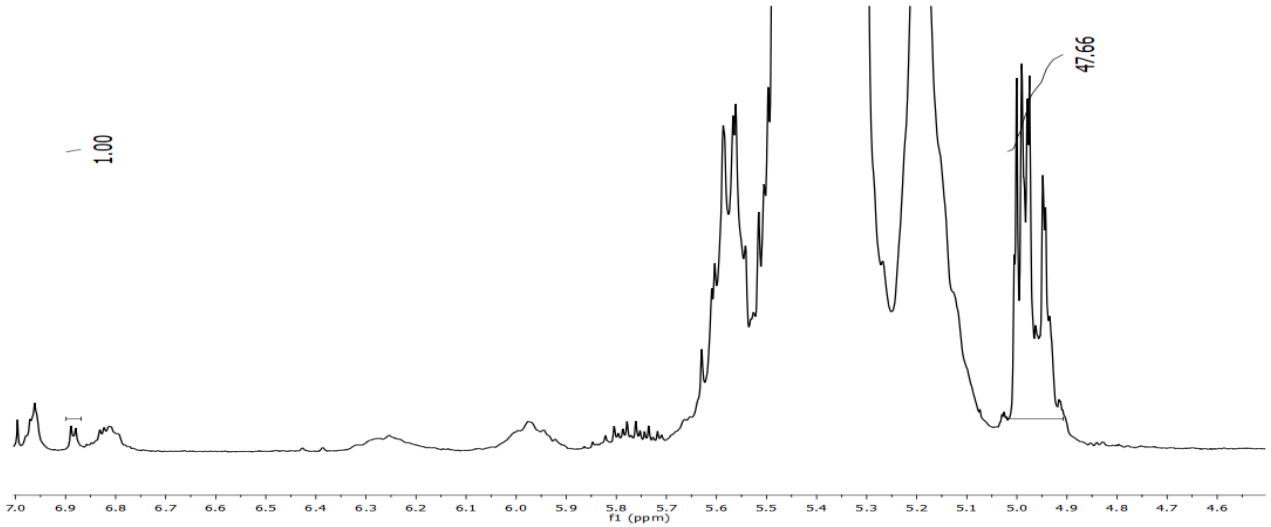


Figure 6- Polyvest + 2 eq. of tetrazole

Given these results, it was hypothesized that, as regards the case of a low vinyl content polymer such as polyvest, it is useless to increase tetrazole beyond a certain amount. This is because, once some of the vinyls have reacted, it becomes less and less likely for the nitrilimine to find a free vinyl and therefore it becomes more likely that the NI will react with itself, dimerizing (as described in Chapter 1).

In the case of the tested compounds, on the other hand, SBRs with a high vinyl content were used, and therefore the amount of tetrazole can be increased.

Below, the possible reactivity of nitrilimines with the various components present in a rubber compound will be investigated.

4.8.2 TGA interference test

It was initially decided to study the phenomenon by thermogravimetric analysis (TGA), preparing samples containing compound 2 and each of the other components (6PPD, Zn Neodecanoate, CBS, sulfur) taken individually, with or without a polymer matrix (in this case Polyvest 130).

The samples for the TGA were prepared, by mixing the components and loading them into the pan. As a method it was used a 160-220 °C ramp, since the activation temperature of this tetrazole was around 170 °C. Then the graphs of each test were plotted to identify any differences. Test in bulk (Fig.7), Test with polymer (Fig.8)

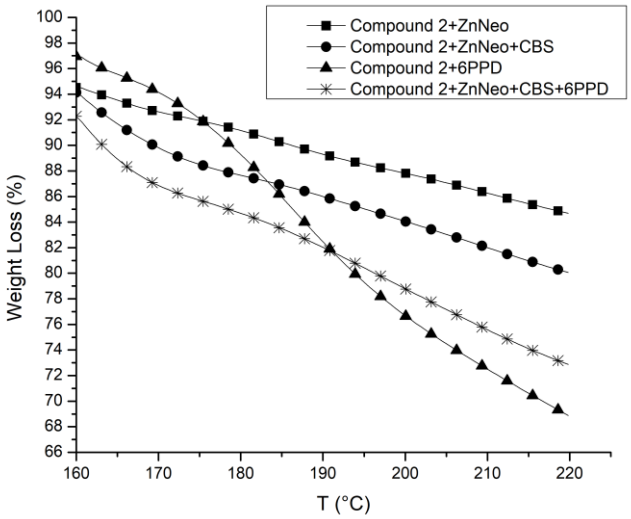


Figure 7

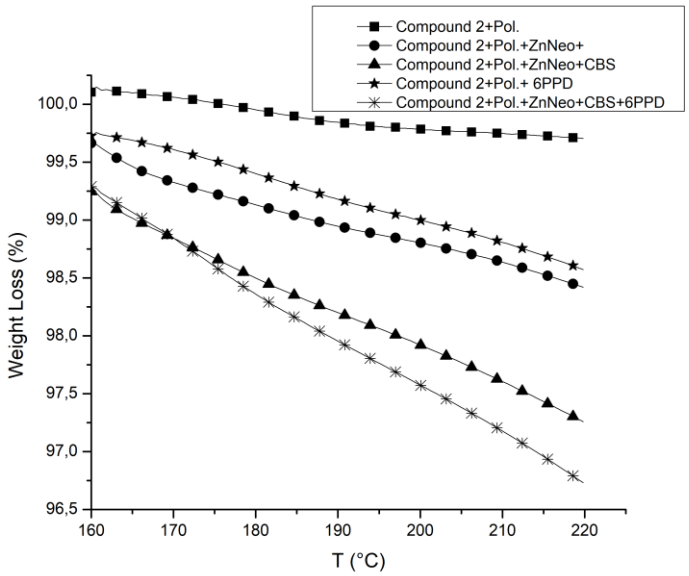


Figure 8

Since a loss in weight occurs in the presence of each ingredient, it was concluded that there is no interference in the formation of nitrilimine, which is formed after activation of tetrazole and by release of nitrogen.

Of course, this test was not enough to identify the 'killer' candidate within the composite and therefore further tests were required.

4.8.3 RPA tests

It was decided to reproduce a similar test using the rheometer. Compound samples were prepared containing polymer, silica or carbon black, polytetrazole 1 and adding the other ingredients one at a time. The vulcanization curves (S') were measured for each sample at 190°C.

Silica test: compounds without CBS (Fig.9), compounds with CBS (Fig.10).

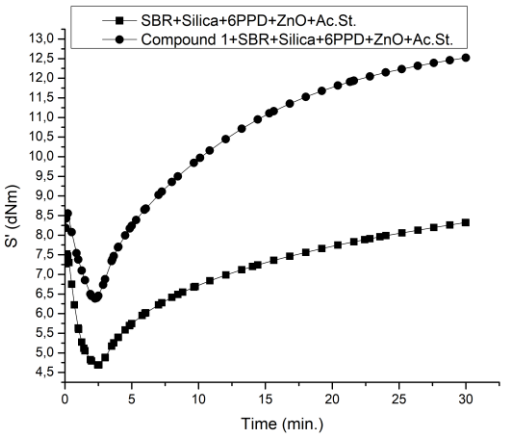


Figure 9

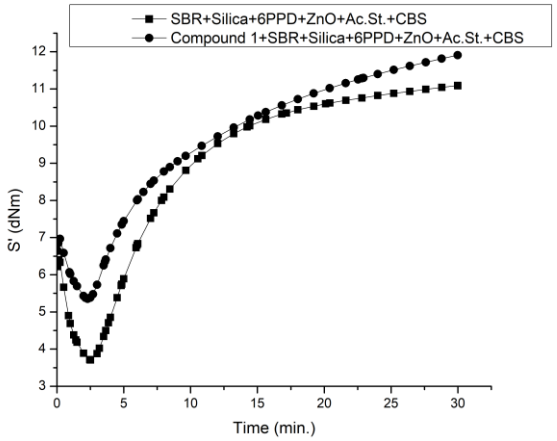


Figure 10

Table 8 shows the MH, ML and Δ(MH-ML) values corresponding to each S 'curve for all the samples, with or without polytetrazole 1. Moreover, for each addition step is reported a Δ between the Δ(MH-ML) values with and without polytetrazole 1.

	MH	**ML**	**Δ(MH-Ml)**	**Δ(ΔT-ΔR)**
SBR+Silica+6PPD	10.46	6.37	4.09	5.11
Compound 1+SBR+Silica+6PPD	17.18	7.98	9.20	
SBR+Silica+6PPD+ZnO+Ac.St.	8.32	4.69	3.63	2.51
Compound 1+SBR+Silica+6PPD+ZnO+Ac.St.	12.52	6.38	6.14	
SBR+Silica+6PPD+ZnO+Ac.St.+CBS	11.09	3.71	7.38	- 0.85
Compound 1+SBR+Silica+6PPD+ZnO+Ac.St.+CBS	11.91	5.38	6.53	

Table 8

Carbon black test: compounds without CBS (Fig.11), compounds with CBS (Fig.12).

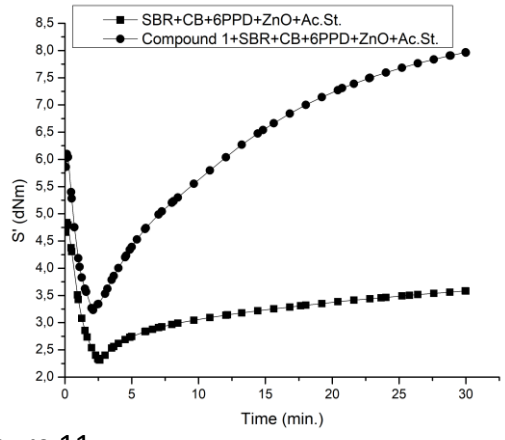


Figure 11

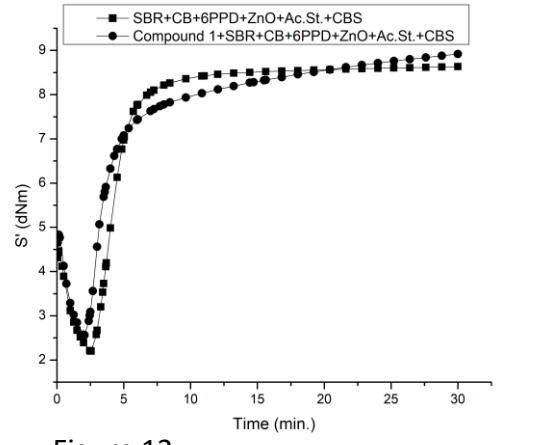


Figure 12

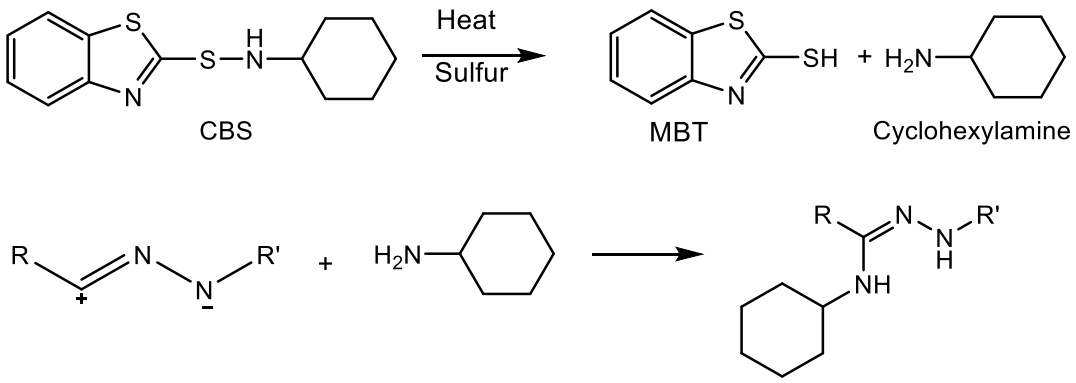
Table 9 shows the MH, ML and Δ(MH-ML) values corresponding to each S 'curve for all the samples, with or without polytetrazole 1. Moreover, for each addition step is reported a Δ between the Δ(MH-ML) values with and without polytetrazole 1.

	MH	**ML**	**Δ(MH-Ml)**	**Δ(ΔT-ΔR)**
SBR+CB+6PPD	3.99	2.59	1.40	5.92
Compound 1+SBR+CB+6PPD	10.93	3.61	7.32	
SBR+CB+6PPD+ZnO+Ac.St.	3.58	2.31	1.27	3.46
Compound 1+SBR+CB+6PPD+ZnO+Ac.St.	7.96	3.23	4.73	
SBR+CB+6PPD+ZnO+Ac.St.+CBS	8.63	2.20	6.43	-0.07
Compound1+SBR+CB+6PPD+ZnO+Ac.St.+CBS	8.92	2.56	6.36	

Table 9

With these results, it seemed possible that the 'killer' candidate was CBS. As it can be seen, in fact, in its presence, the values of S' of the compounds containing polytetrazole 1 are lower and comparable with the curves relative to the reference compound. Given that S' can be interpreted as an indication of the degree of cross-linking of the system and given that, apart from the case of a complete composite, in the other cases there is no other cross-linking agent apart from polytetrazole, the curve of the sample containing CBS is much lower. It was hypothesized that CBS, interacting with the nitrilimines, poisons a part of them, preventing them from reacting with the polymer matrix and therefore from cross-linking it. Another evidence to support this thesis is the marked reduction in fluorescence observable by comparing the various compounds containing polytetrazole 1. The one in which CBS is also present, after vulcanization, is clearly less fluorescent than the others, demonstrating how nitrilimine formed reacts with the CBS instead of with the vinyls, so that the pyrazoline (responsible for the fluorescence) is not formed.

Taking up the considerations made previously (chapter 1) on the reactivity of nitrilimines, it was hypothesized that CBS, by thermally decomposing, forms nucleophilic species capable of reacting with nitrilimine according to Scheme 4.



Scheme 4- Proposed CBS interference mechanism

It was proposed that the cyclohexylamine formed as a side product of the reaction could interfere.

Tests are still in progress to understand this interference phenomenon. Among the various hypotheses, it seems interesting to split the activation temperatures of the vulcanizing package (containing CBS) from the polytetrazole. In this case a first vulcanization at 150°C would allow to obtain the classic cross-linked matrix, making the whole CBS react and then raise the temperature to activate the polytetrazoles and obtain the formation of the second lattice. In this way the formation of the cyclohexylamine is not avoided but, by vulcanizing the elastomer, the diffusion of the components, which are more bound, is slowed down. Another possible solution could be to use different types of accelerators which, once thermally activated, release different types of amines. This is because the cyclohexylamine released by CBS is a primary amine, and therefore more reactive but, in the case of aromatic amines, not primary amines or sterically hindered amines, their reactivity would drastically decrease.

4.9 Bibliography

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5. Cross-linkable chain-end

5.1 State of the art: chain-end and anionic polymerization

This chapter will describe the project, in collaboration with an external partner, aimed at the synthesis by anionic polymerization of elastomers terminally functionalized with thermally activable tetrazole species. The purpose of using these materials is to reduce the hysteresis deriving from the presence of the free chain-ends within an elastomeric matrix. The concepts relating to hysteresis in rubbers and anionic polymerization will then be described and, subsequently, the results obtained so far, which are partial, as the project is not yet concluded.

5.1.1 Chain-end contribution to hysteresis

The hysteresis comes from several mechanisms associated with the polymer, the filler (silica or carbon-black) and their interaction[1] (Fig.1). Hysteresis can also be influenced by other compounding ingredients and by the state of cure. It has also been found that rubber hysteresis can be reduced when functional groups, are attached to the polymer chain ends[2–5]. Since polymer and filler are the major weight components of the composite, the two materials play a fundamental role in rubber hysteresis. Filler contribution to rubber hysteresis is associated with a continuous, three-dimensional network formed by the particles[6].

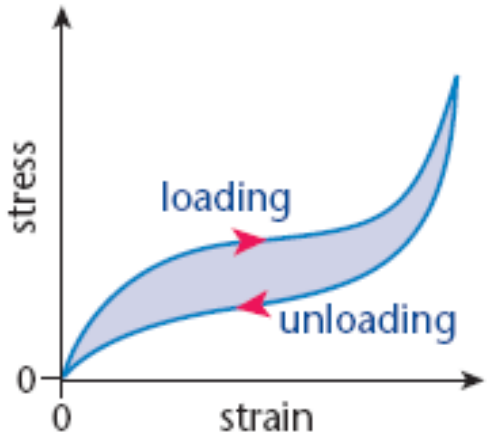


Figure 1- Rubber hysteresis

This network, which was studied by Payne[1], breaks down at increasing dynamic strain amplitude. For that reason, the dynamic mechanical properties such as hysteresis, shear loss modulus (G'') and tan δ, are strain dependent.

For the polymers, the major factors in rubber hysteresis are the glass transition temperature[7,8] (Tg) and molecular weight. The glass transition is the gradual and reversible transition that occurs in amorphous materials, or in amorphous regions within semicrystalline materials, from a hard and relatively brittle glassy state into a viscous or rubbery state as the temperature is increased. It is always lower than the melting temperature (Tm) of the crystalline state of the material, if one exists. Hard plastics, like polystyrene and poly(methyl methacrylate), are used well below their Tg because their Tg values are above room temperature, both at around (around 100 °C).

Rubber elastomers, like polyisoprene and polyisobutylene, are used above their Tg, where they are soft and flexible, and cross-linking prevents free flow of their molecules, endowing rubber with a set shape at room temperature. The Tg is associated with a reduction of molecular mobility, as the temperature falls, while molecular mobility and free volume increase as the temperature rises above Tg. Moreover, the monomeric friction coefficient or the frictional force encountered by a small chain segment as it moves through its surroundings, decreases. With the term chain friction, it is possible to refer to the extent to which chain mobility and the monomeric friction coefficient influence polymer hysteresis, at a particular temperature. It has also been demonstrated[1,2] that the hysteresis of compounded elastomers decreases increasing molecular weight and that the hysteresis tends to be proportional to 1/Mn, which itself is proportional to the number of chain ends. That is why hysteresis reduction at increasing number-average molecular weight (Mn) might also come from reduced energy losses associated with the chain ends. After vulcanization process, a cross-linked polymer network is formed, and the linear polymer is divided by cross-links into shorter chains (respect to the pristine polymer). Chains terminated with a cross-link at each end are considered effective network chains; while chains terminated with a cross-link at only one end, are considered ineffective network chains, like the two terminal chains at either polymer end. Since the ineffective network chains are free at one end, their dynamic property contributions are designated “free chain end" contributions. The free chain ends can be seen as a deviation from a perfect network, and so their contributions to G’ and G'' would be additive. For these reasons, G’ and G'' can be considered as the sum of contributions from three additive sources: the filler network, the polymer free chain ends and the polymer effective network chains[2] (Fig. 2 and 3).

G’ and G’’ are the value at finite strain and finite Mn.

G’∞ and G’’∞ are the value at infinite strain and finite Mn.

G’∞,∞ and G’’∞,∞ are the value at infinite strain and infinite Mn.

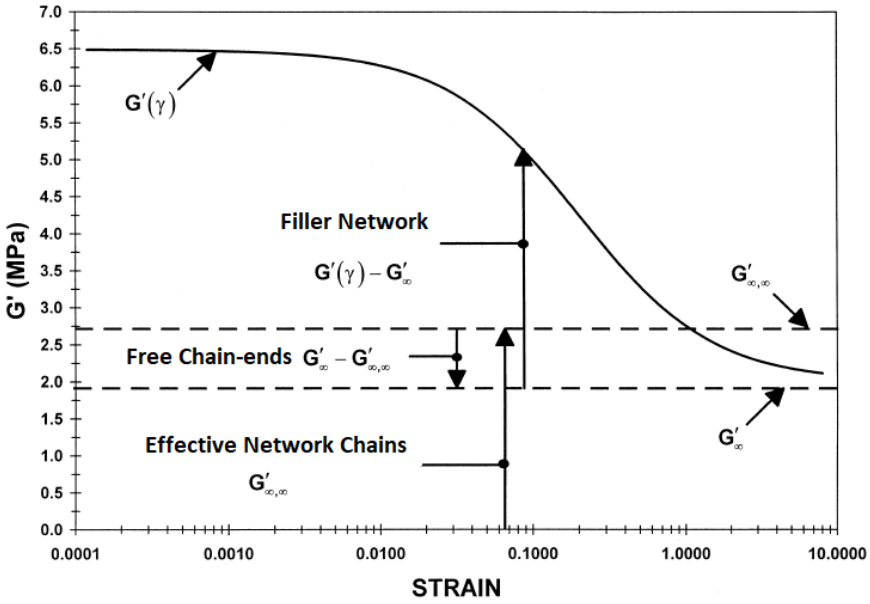


Figure 2- Contributions to G’, from *Ulmer, J. D., Hergenrother, W. L. & Lawson, Rubber chemistry and technology vol. 71 637-667 (1998).*

Where the dashed line G’∞ is the asymptote approached by G’ at infinite strain. The dashed line labeled G’∞, ∞ is the value of G’∞ at infinite molecular weight.

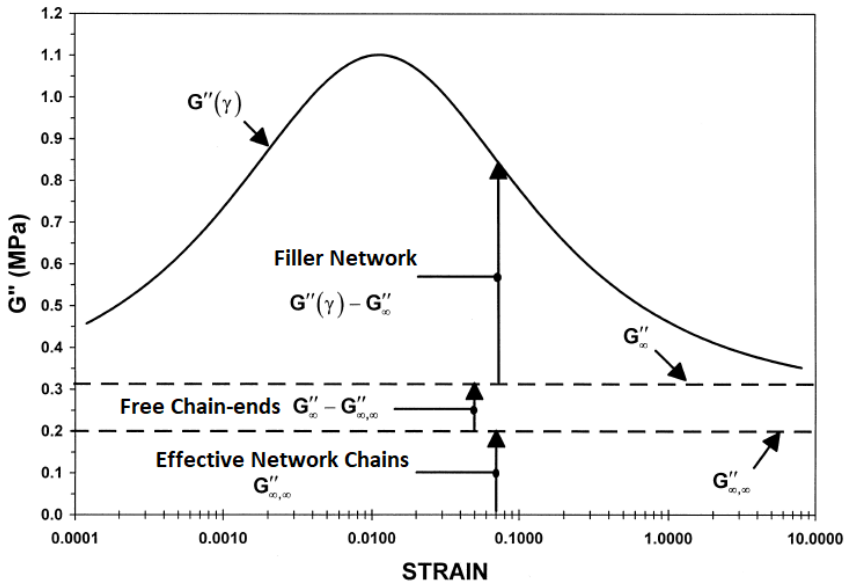


Figure 3- Contributions to G’’, from *Ulmer, J. D., Hergenrother, W. L. & Lawson, Rubber chemistry and technology vol. 71 637-667 (1998).*

Where the dashed line G''$_\infty$ is the asymptote approached by G'' at infinite strain. The dashed line labeled G''$_{\infty,\infty}$ is the value of G''$_\infty$ at infinite molecular weight.

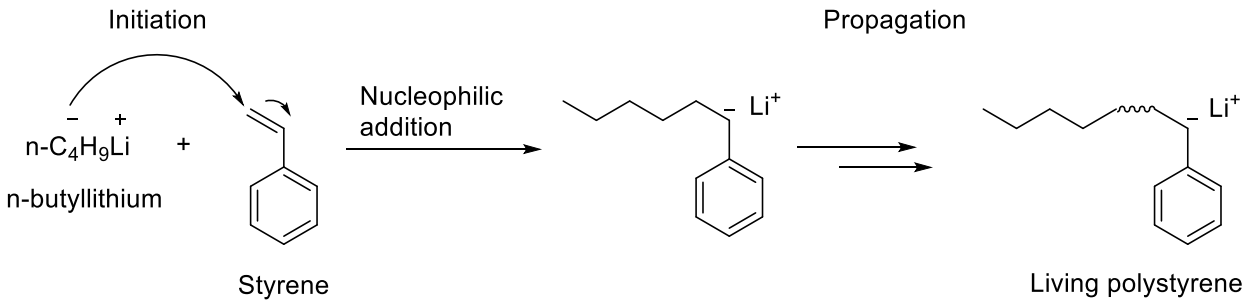
A feature associated with free chain ends is their negative contribution to G', and is less than zero because chains with free ends do not fully support the applied load and in the limit of zero frequency, the terminal chains provide no support at all. Consequently, above a certain strain amplitude, G' is less than G'$_{\infty,\infty}$ (infinite strain and infinite Mn), where the strain depends on the filler network contribution and the number of free chain ends. As the number of free chain ends decreases, the entire G' curve increases uniformly until, in the limit of a perfect polymer network, its asymptote becomes G'$_{\infty,\infty}$.

The contribution of free chain ends is correlated with the hysteresis reduction that accompanies a reduction in free chain ends. Free chain end reduction may be achieved by increasing Mn, or by modification of chain ends. Moreover, for every free chain end eliminated (every elimination of an ineffective polymer network chain), a new effective network chain is created. Thus, the reduction in free chain-end contributions is the net effect of an increase in effective network chains and a decrease in ineffective network chains.

The terminal functionalization of polymer with special chain ends, able to react with the polymer itself or with the filler, has been proposed as an additional mechanism to reduce rubber hysteresis. In addition to the effect of free chain ends, also called ineffective polymer network chains, hysteresis can arise from the effective polymer network chains, through chain friction.

5.1.2 Anionic polymerization

Anionic polymerization[9] is a chain polyaddition process (Scheme 1) in which the active center responsible for propagation, to which the monomer molecules are added one after the other, is an ion with a partial or total negative charge on a carbon atom or on a heteroatom. The anion, which is strongly associated with a positively charged counterion (usually a cation of an alkaline or alkaline earth metal), has a nucleophilic reactivity (kinetic property) which derives from its basic Lewis character (thermodynamic property). The strength of the interactions between the growing macro-anion and its counterion depends on the nature of the ions and the reaction medium. There is also the possibility of pseudo-anionic polymerizations, in which the active centers are made up of strongly polarized covalent entities.



Scheme 1- Living polymerization of styrene

Monomer

The monomers capable of anionic polymerization can be divided into three types: alkenes, heterocycles, aldehydes. The first two types include species with acid electrophilic behavior (Lewis acid) and therefore sensitive to nucleophilic activation. A stabilization of the anion is achieved by delocalization of the negative charge, as in styrene and butadiene in which the carbon-carbon double bonds are conjugated, or as in heterocyclic compounds in which the negative charge can be delocalized to atoms that are more electronegative than carbon. It has been seen that the fundamental requirement of an anionically polymerizable monomer is its ability to generate an anion species sufficiently stabilized for inductive and/or mesomeric effects. Based on their reactivity, they can be divided into five groups with increasing reactivity, as listed here with some examples of the most representative monomers:

- Group 1: styrene, α-methyl styrene, butadiene, isoprene, 2- and 4-vinylpyridine
- Group 2: acrylates, methacrylates
- Group 3: ethylene oxide, ethylene sulphide, propylene sulphide
- Group 4: acrylonitrile, methacrylonitrile
- Group 5: nitroethylene, vinylidene cyanide

Each anion can start the polymerization of the monomers included in its own group or in the following ones, but it cannot start the polymerization of monomers present in the previous groups. In this way, for example, the order of formation of the sequences in the anionic syntheses of block copolymers can be established.

Anions capable of initiating polymerization by reaction on the carbon-carbon double bond of the monomer are strong bases. However, if the growing macro-anion is an extremely strong base, it

will be converted to the corresponding hydrocarbon by transfer of a proton from the solvent or any other less basic species present in the reaction medium. In these cases, the kinetic chain will be terminated since the anions thus produced will not be sufficiently basic to restart the propagation sequence. Anionic polymerizations, therefore, in practice require the use of relatively stable macro-anions under the reaction conditions.

Solvent

Solvents with high polarity cannot be used in anionic polymerizations. In fact, protic liquids such as alcohols or amines are sufficiently acidic to destroy the active carbanionic centers, while very polar aprotic solvents can form stable complexes with the anions, preventing the addition of monomers.

Consequently, the anionic polymerizations are carried out in weakly basic solvents (electron attractor) or, better still, non-polar, whose relative permittivity is between 2 and 10. Two types of solvents are commonly used: aliphatic and aromatic hydrocarbons and ethers. The former does not intervene at all in the reaction mechanisms, the latter play a role of solvation of the ionic species and therefore of their stabilization. In particular, the macro-anion and its counterion in relatively non-polar solvents will be mainly in the form of associated ion pairs of different types depending on the degree of solvation of the ions. The nature of the reaction medium and the counter-ion will strongly influence the degree of proximity between the ions and, consequently, the course of polymerization; in some cases, also the microstructure of the polymer can be influenced by the above parameters. In aliphatic and aromatic hydrocarbon solvents the ionic pairs are not solvated but can exist in the form of aggregates. In more polar media, such as ethers and, in particular, cyclic ethers, the ionic pairs are instead solvated and partially dissociated.

The main peculiarities of anionic polymerizations are the following:

• The initiation reactions, contrary to what happens in radical polymerizations, can be very fast with respect to subsequent propagation reactions. This fact can facilitate the preparation of polymers with very narrow distribution of molecular masses

• Acidic impurities (including water and alcohols) can destroy propagating species, preventing the anionic polymerization reaction from taking place

• 'Spontaneous' termination reactions in the absence of impurities are in fact absent in many anionic polymerizations. It is therefore possible to produce block copolymers by adding a second

monomer after the complete consumption of the first (living polymerizations). Alternatively, polymers with terminal functional groups can be produced by adding suitable terminating agents to the reagent system

• The choice of the initiator defines the nature of the counterion derived from it and, consequently, also influences the anionic propagation reaction, unlike what happens in radical polymerizations

• The choice of the solvent (reaction medium) is much more important in anionic (and cationic) polymerizations than in radical processes, since this choice can influence the nature of the growing active center (more or less solvated ion pair)

• The geometric isomerism of polymers formed by conjugated diolefins can be well controlled in some anionic polymerizations, while the tacticity of vinyl polymers is much less so (almost always atactic polymers, as in radicals).

A characteristic of the anionic polymerizations of styrenes and conjugated dienes is the appearance of intense colors associated with the active centers present in the solutions, which disappear immediately if traces of water, methanol, etc. are introduced. The persistence of the color is therefore a good indication of the absence of the impurities indicated above and the establishment of conditions compatible with living polymerizations.

Chain initiator

The initiators of anionic polymerizations are all electron-donors of varying basic strength. The type of initiator required for a particular anionic polymerization depends on the ease with which an anion can be formed from the monomer, which acts as an electron acceptor. Sodium methoxide, which is a relatively weak base, can polymerize acrylonitrile as this monomer contains the electronegative group -CN which decreases the electron density on the double bond C=C and increases the reactivity towards anions. The vinylidene cyanide carries two -CN groups on the same carbon atom and can be polymerized from even weaker bases such as water and amines. Similarly, cyanoacrylates have two electron-attracting groups on the same carbon atom (-CN and -C=O(OCH_3) and are polymerized by water. On the contrary, the polymerization of non-polar monomers such as conjugated diolefins requires an initiation reaction by very strong bases such as metal alkyls.

The two main initiation processes in anionic polymerizations are: nucleophilic attack on the monomer and electron transfer. Nucleophilic attack is essentially the addition of a negatively charged species to the double bond of the monomer with the formation of a covalent bond at one end and a carbanion at the other, and mainly involves metal alkyls of alkali metals, living polymers, metal alkoxides, metal amides and Grignard reagents. Among these, the metal alkyls and living polymers are the most important polymerization initiators for vinyl monomers (reaction 1). The group of electron transfer initiators includes alkali metals and complexes of these metals with hydrocarbons (reaction 2).

$$Me\text{-}B + CH_2{=}CH(X) \rightarrow B\text{-}CH_2\text{-}CH^{\ominus}(X)\ Me^{\oplus} \qquad (1)$$

$$Me + CH_2{=}CH(X) \rightarrow {\cdot}CH_2\text{-}CH^{\ominus}(X)\ Me^{\oplus} \qquad (2)$$

Chain terminator

Chain transfer reactions in anionic polymerizations are not very usual and occur only under particular reaction conditions. Water, oxygen, CO2 and any other impurities capable of reacting with the growing anionic active centers must not be present in the reaction medium. In particular, the water adsorbed on the internal surface of the glass equipment used in laboratory syntheses must be eliminated in advance, for example by flame treatment under high vacuum. In industrial reactors the problem is much less relevant since the surface / volume ratio is much lower. Polymers with specific terminal groups can be prepared by deliberately introducing reagents into the reaction medium capable of terminating (killing) living macromolecular chains. For example, in the anionic polymerization of butadiene with bifunctional initiators it is possible to obtain carboxylic end groups by termination with CO2 or hydroxyl end groups by termination with ethylene oxide. This is also the way used industrially to produce the so-called liquid rubbers, characterized by low molecular masses (3,000 ÷ 10,000).

5.1.3 SSBR

Styrene-butadiene rubber (SBR) is one of the most produced synthetic rubber and it is mostly used for the manufacture of tires and rubber goods. The process types utilized for SBR production are two: emulsion polymerization and solution polymerization. In emulsion polymerization the monomers polymerize in water in the presence of an emulsifier (fatty acid or rosin acid soap) by a

radical mechanism. The SBR obtained by solution polymerization, commonly indicated as SSBR, is by far the most used in tires. SSBR is obtained by anionic polymerization usually conducted in n-hexane or cyclopentane. The polymerization is terminated by adding chain terminators agent to the reactor effluent to allow chain length to be controlled and the introduction of functional end groups as outlined above. Unreacted butadiene and styrene are then recovered in a flash tank and/or a stripping column. The polymer slurry is then sent to the finishing section for blending to make the product meet the required specifications.

5.2 Summary of proposal

The main aim of the research project was to study new compounds able to functionalize the terminal positions of polymers directly during the polymerization phase. New chain initiators/terminators for anionic polymerization were therefore developed, to insert functional groups that can react, after activation, with the polymer obtaining a polymeric matrix without free chain ends. Moreover, compounds able to post-functionalize polymers with specific chain ends (e.g. R-OH) were developed.

The importance of functionalization of chain terminals is described in the literature to find the best balance between the demands for low rolling resistance and high traction, as well as with wet grip. It was reported by Ueda et al. that it was possible to obtain a remarkable reduction of hysteresis modifying the chain end of high-vinyl polybutadiene with 4,4'-bis(dimethylamino)-benzophenone by the reaction of the living lithium end group. Similar reduction of hysteresis was reported by Oshima et al.[5], coupling the chain-end of SBR rubber with $SnCl_4$. This reduction was a consequence of an improved carbon-black dispersion due to interactions between carbon-black and terminally functionalized chains. Compared to unfunctionalized solution SBR, the modified chain-end compounds showed improved rolling resistance, wet skid resistance and wear resistance.

Current mainstream approach to SSBR chain end functionalization aims to the introduction of groups which are able to anchor to the filler: the stronger the interaction with the filler, the better the immobilization of the chain end and the final properties of the cured compound.

The main limit of SSBR chain end functionalization with groups interacting with the filler is the green rubber compound processability: interaction with the filler develops during mixing, with

beneficial effects on dispersion, but with critical effects on green compound elasticity: in worst cases, the rubber compounds behaves as a cured compound and is thus not further processable.

The studies carried out in this PhD project, have shown that not only certain particular tetrazoles prove to functionalize elastomer chain-ends (Fig.4) but also that their activation allows to anchor the chain-ends on the polymer backbone, giving a gelation process. Moreover, substituents on the tetrazole can be chosen to tune the activation temperature (Ta).

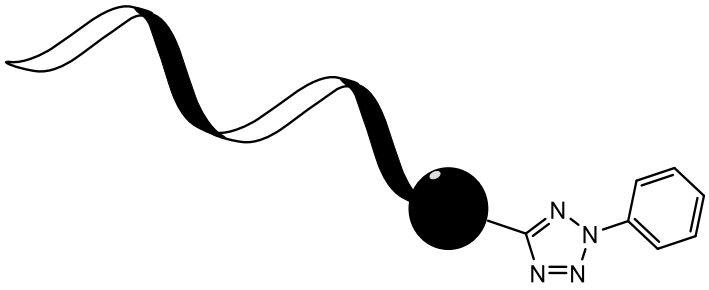
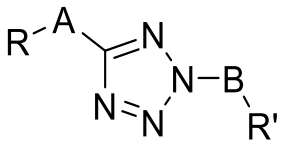


Figure 4- Tetrazole as polymer chain-end

The general formula of tetrazole initiator/terminator is as follows:



In which A and B represents an organic group linker (chain or aromatic ring), covalently linked to position 2 and 5 of the tetrazole. R and/or R' are groups able to react with lithium derivatives (BuLi) to form the anion and start the anionic polymerization, acting as a chain initiator or they can be function groups that can react with living anions and stop the anionic polymerization, acting as a chain-terminator. Substitution with different aromatic rings or with an electron-attractor or an electron-donor group helps to change the activation temperature of the tetrazole, while the presence of alkyl chains can improve the solubility of the compound in SSBR aliphatic solvent. Alternatively, R and/or R' are groups able to react with specific polymer chain ends groups (e.g. R-OH) after polymer synthesis.

5.3 Description of the project

Table 1 shows the synthesized tetrazoles.

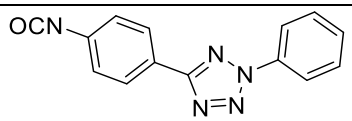
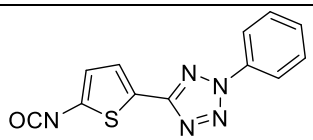
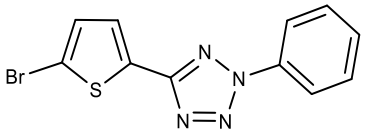
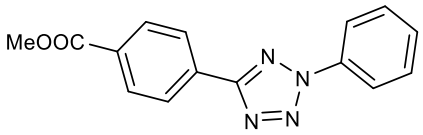
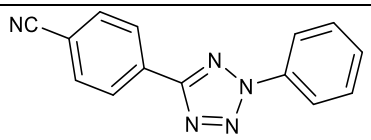
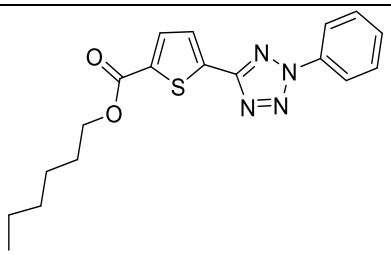
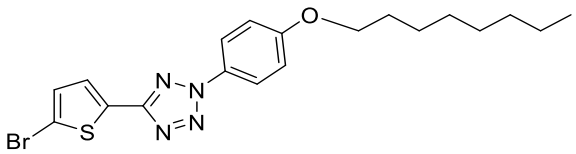
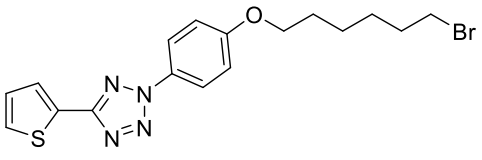
N°	Formula	Molecular Formula	M.W. (g/mol)
1		$C_{14}H_9N_5O$	263.26
2		$C_{12}H_7N_5OS$	269.28
3		$C_{11}H_7LiN_4S$	234.21
4		$C_{15}H_{12}N_4O_2$	280.29
5		$C_{14}H_9N_5$	247.26
6		$C_{18}H_{20}N_4O_2S$	356.44
7		$C_{19}H_{23}BrN_4OS$	435.38
8		$C_{17}H_{19}BrN_4OS$	407.33

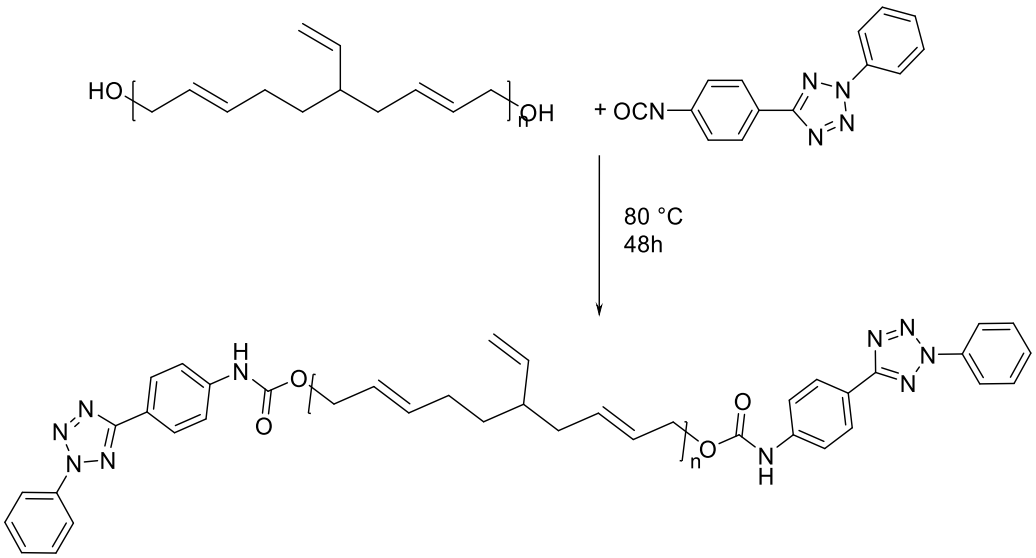
Table 1

The derivatives with isocyanates (compounds 1 and 2) were used to functionalize polymers terminated with OH or NH_2 after polymer synthesis. The compounds with esters and nitriles (compounds 4, 5 and 6) have reactive groups useful in quenching anionic polymerizations and thus

introduce the tetrazole reactive functionality as chain end in living SSBR polymers. Derivatives containing bromine can act as potential initiators of anionic polymerization via lithium-halogen exchange (compounds 3,7 and 8) and thus introduce the tetrazole reactive functionality as the beginning of the living SSBR chain. Regarding compound 8 it is possible that the lithium from the chain passes into α-position to thiophene.

5.3.1 Krasol tests

The first step in studying the effects of tetrazoles as chain terminators was to start from a commercially available hydroxy terminated polymer, Krasol LBH 2000, and to functionalize it with a tetrazole carrying an isocyanate group. Krasol was chosen because it is a low molecular weight polybutadiene oligomer (2100) with high vinyl content, it is liquid and easily workable on a laboratory scale and has two hydroxyl functionalities at the ends of the chains that lend themselves to subsequent modifications. The polymer was then functionalized with tetrazole 1 (Scheme 2), heating at 80 ° C for 48h, to give the functionalized derivative. The reaction was monitored with IR (the NCO band disappears).



Scheme 2- Krasol functionalization with tetrazole 1

The polymer thus obtained was characterized by NMR, IR and TGA (to study tetrazole activation temperature and thermal stability). At this point a sample of the polymer was heated for 30 minutes at the tetrazole-polymer activation temperature (190 °C). After heating above the nitrilimine activation temperature, the polymer becomes gelatinous and insoluble, demonstrating

the successful cross-linking. The polymer becomes fluorescent, which indicates the presence of the pyrazoline moiety formed by the cycloaddition of the nitrilimine with the polymer double bond (Fig.5).

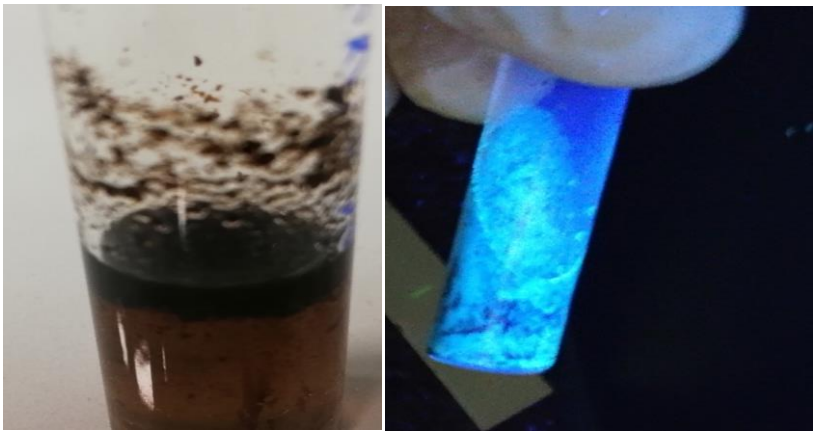


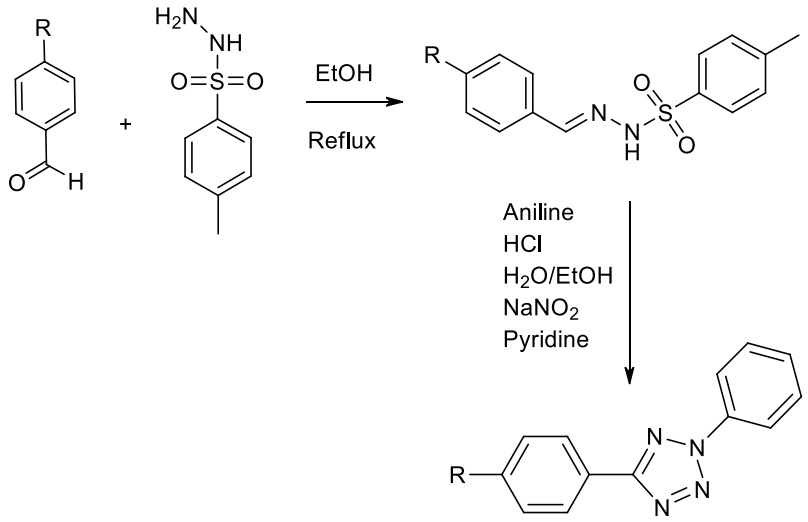
Figure 5- Functionalized Krasol, gelation and fluorescence

Similarly, a test was made by functionalizing Krasol with tetrazole 2, obtaining the same results. Tetrazole 2 has a thiophene ring instead of phenyl, which imparts a lower activation temperature (180 °C).

5.4 Experimental part

5.4.1 Initiator/Terminator synthesis

The tetrazole chain-end can be prepared according to the conventional synthesis (Scheme 3).

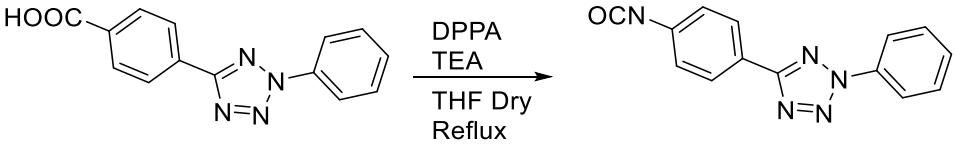


Scheme 3- General synthesis

All the synthetic procedures are reported in detail in the last chapter (experimental part).

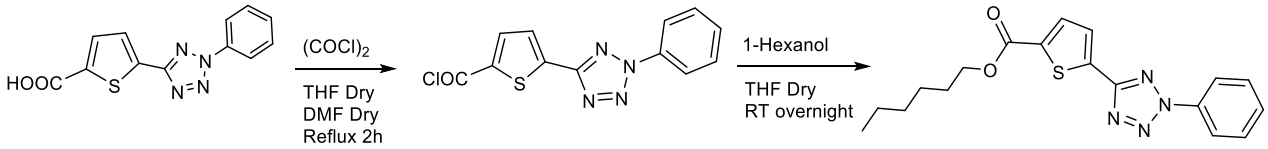
Compounds 3, 4, 5, 7 were synthesized according to the previous procedure, choosing the appropriate aromatic aldehyde and aniline derivatives.

Compounds 1 and 2 were synthesized starting from the carboxylic acid derivative after a functional group modification to form the corresponding isocyanate (Scheme 4).



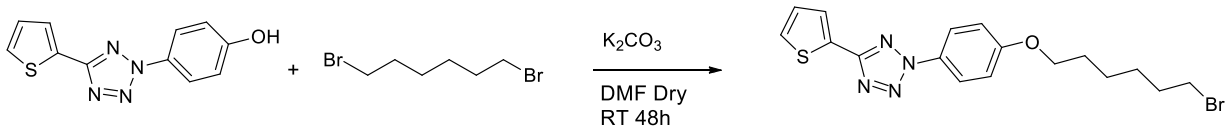
Scheme 4- Compund 1 and 2 synthesis

Compound 6 was synthesized starting from the carboxylic acid tetrazole derivative, forming the corresponded acyl chloride and then the final ester (Scheme 5).



Scheme 5- Compund 6 synthesis

Compound 8 was synthesized starting from the tetrazole hydroxy functionalized after alkylation with 1,6-dibromohexane in large excess, to form the monosubstituted compound (Scheme 6).



Scheme 6- Compund 8 synthesis

All the synthetic procedures are reported in detail in the experimental part.

5.4.2 First-generation

Compounds 2, 3 and 4 are the compounds that were synthesized first. They have been designed to be able to react with lithium alkyls to form a reactive anion capable of initiating polymerization (compound 3) or to react with the live anions of the growing polymer chains to terminate the polymerization (compound 4 and 5).

Solubility and reactivity tests were carried out before delivering them to the external partner for testing on a polymer batch.

Solubility Test

Solubility tests are necessary to establish if the compounds are soluble in cyclohexane, the solvent used for the anionic polymerization in solution and have shown the following results:

1mg of each component was added to 0.5 ml of cyclohexane:

- Compound 3 is completely soluble at room temperature.

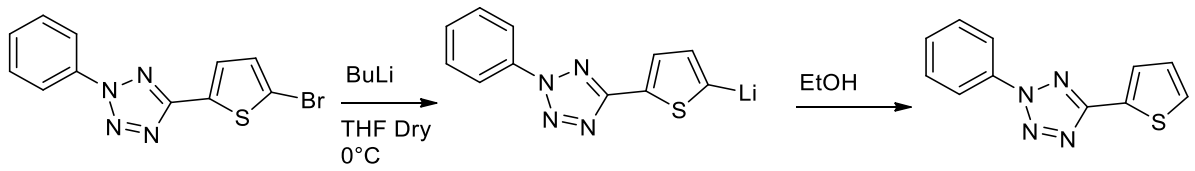
- Compound 4 is partially soluble at room temperature, completely soluble if heated for 2-3 min. at 70°C.

- Compound 5 is partially soluble at room temperature, completely soluble if heated for 2-3 min. at 50°C.

Reactivity test

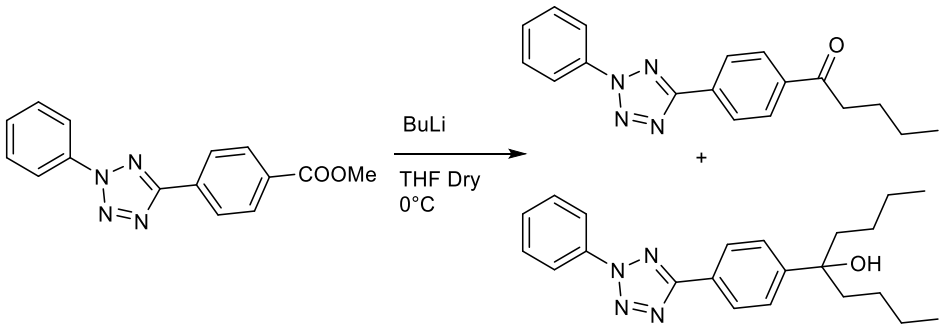
To prove the effective reactivity of the compounds, laboratory-scale tests were carried out using buthyllithium.

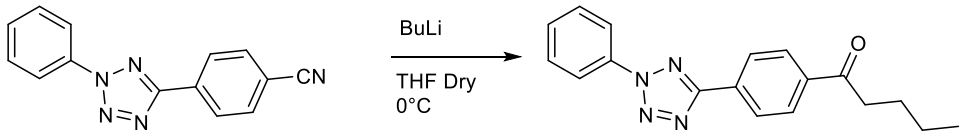
The reactivity of initiator 3 was initially tested by making it react with buthyllithium to generate the derived lithium by lithium-halogen exchange and subsequently the formed anion was quenched with ethanol (Scheme 7). The NMR of the obtained product showed only the presence of the debrominated product, demonstrating the conversion of all the starting reagent.



Scheme 7- Reactivity test compound

The reactivity of terminators 4 and 5 was tested by adding buthyllithium (Scheme 8) and looking at the alkylation products formed by NMR. Compound 4, which is an ester, has the formation of two different products, the ketone resulting from the mono alkylation and the tertiary alcohol from the double alkylation. Compound 5, which is a nitrile, has the formation of only the ketone, the monoalkylation product, as it is less reactive and therefore unable to form the double alkylation product.





Scheme 8- Reactivity test compound 4 and 5

Subsequently, the compounds were sent to the external partner for further tests but were found to be too poorly soluble under the conditions used at industrial level to perform anionic polymerizations. For this reason, further studies were carried out to obtain more soluble compounds, called second-generation.

5.4.3 Second-generation

The second-generation compounds were studied by modifying the first-generation ones with the addition of alkyl chains to improve the solubility in organic solvents.

Compound 6 is a structural analog of compound 4, but with a C6 chain in place of a methyl on the ester. Compound 7 is a structural analog of compound 3 with the addition of a C8 chain. Compound 8 is also similar to compounds 3 and 7 but with a C6 chain terminated with a bromine. In fact, the presence of bromine on an alkyl chain instead of on an aromatic ring such as thiophene should allow the formation, after the lithium-halogen exchange, of a less stable anion and therefore more likely to react as an initiator in anionic polymerization.

Solubility test

1mg of each component was added to 0.5 ml of cyclohexane:

- Compound 6 is completely soluble at room temperature.

- Compound 7 is completely soluble at room temperature.

- Compound 8 is completely soluble at room temperature.

As has been shown by the solubility tests, the second-generation compounds are more soluble than their predecessors.

5.4 Conclusion

At the moment the second-generation compounds have not yet been tested by our partners and therefore there are no results. The tests carried out on the first-generation ones have highlighted problems of solubility in hexane and lower than expected reactivity. In particular the reaction product of BuLi and initiator 3 precipitated in hexane (reaction performed at 50 °C, at 2wt% concentration), in a very fast reaction. It was anyway tried to initiate the reaction with utility of such initiators, but no reaction was observed.

So, it was reconsidered the mechanism of reaction, firstly it was proposed this path:

Initiator-Br + Bu-Li -> Initiator-Li + Bu-Br

But the Wurtz reaction (easy in the preparation Na-alkyls, less common in lithium alkyl preparation) could happen:

Initiator-Br + Bu-Li -> Initiator-Bu + Li-Br

This would explain the non-reactivity of the initiator and the formation of a precipitate. New tests will then be carried out in the laboratory to understand the reaction mechanism, as well as the development of new even more soluble systems.

5.5 Bibliography

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6. Non-Covalent interactions

6.1 Introduction

This chapter describes the activity carried out during the period abroad at the University of Strasbourg, in the research group of Professor Luisa De Cola. During these months it was investigated a new approach regarding polymer functionalization and the interaction between polymeric chains. In particular, the focus was on systems able both to functionalize the polymer chain and to introduce, at the same time, functional groups able to give non-covalent interactions (i.e. hydrogen bonds) aimed to modify the properties of the polymer itself. It was decided to focus on the field of self-healing polymers to get inspiration on the systems to be used. However, the main idea was not to obtain polymers with self-healing properties like the ones described in the literature, where the aim is to joint together two parts of cut material. Indeed, in this contest the goal is to obtain certain properties working with short oligomers or even with small molecules, which show capabilities to quickly reorganize themselves in space. The idea of this project was to transfer some of these features to the world of elastomers, polymers with higher molecular weight, hoping to observe similar behaviors. In details, it was investigated the possibility of introducing, along the polymer chain, functionalities able to form reversible interactions strong enough to modulate some properties such as the viscosity and elastomeric properties.

6.2 General overview on self-healing materials

The new challenge in material development, concerning the synthesis of novel materials capable of responding to internal or external stimuli, was extensively studied in the last decades. Among them, the most promising are the materials capable of autonomously self-heal[1–3].

A mechanical damage of polymer networks leads to chain cleavage and subsequent formation of reactive groups, which may form a wounded area with conformational changes[2,4,5]. The reactivity of these groups determines if they can auto-assembly or not, repairing the damage[6]. Bond reformation and physical network repair occur, in addition to reactive groups behavior, if segmental chain mobility and diffusion brings such reactive groups in contact with each other before the occurrence of other reactions[7]. There are reactive groups (pendant or chain ends) that may facilitate rebonding to achieve successful self-healing. They include radicals, –C=C–, –COOH, –NH_2, –OH, –SH, –Si–O, S–S, –C=O, and formation of cyclic structures[8]. Using these entities, a

significant number of synthetic efforts leading to self-healing networks have been developed. The classes of reactions that offer self-healing of polymers include covalent bonding, supramolecular chemistry, H-bonding, ionic interactions, and π-π stacking.

6.2.1 Thioureas

In a recent work of T. Aida[2] it is reported that low-molecular weight polymers, when cross-linked by dense hydrogen bonds, yield mechanically robust and readily repairable materials, despite their extremely slow diffusion dynamics. The key is to use thiourea units, which forms a zig-zag hydrogen-bonded structure, that induces the formation of amorphous materials (Fig.1) different from crystalline or semi-crystalline materials obtained when urea units are used.

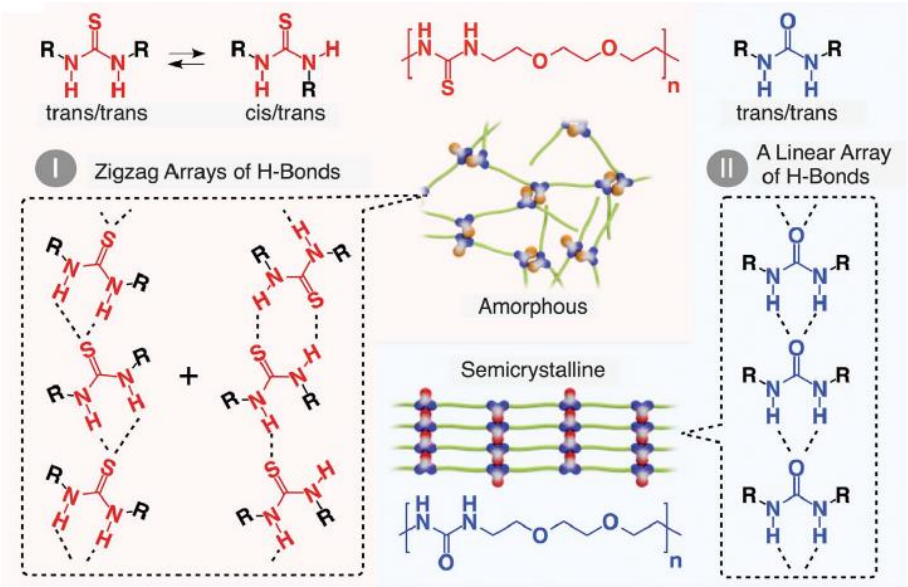


Figure 1- urea vs thiourea bonds, from *Science 359, 72–76*

In general, non-crystalline, high-molecular weight polymers form mechanically robust materials due to the entanglement of long polymer chains. However, once the materials are fractured, they are difficult to repair unless by heating at high enough temperatures, because the entangled polymer chains diffuse too slowly and can't unite fractured portions within reasonable time scale. For this reason, high mechanical robustness and healing ability tend to be mutually exclusive.

In the article, it is reported that poly(ether-thioureas) anomalously form amorphous materials, despite carrying dense H-bonding thiourea units. The reason is that H-bonded thioureas are geometrically nonlinear (less ordered), so that they do not induce crystallization. The obtained

materials are highly mechanically robust and can be readily repaired by compression at fractured surfaces.

6.2.2 Pyrimidones

The properties of low-molecular-weight polymers at room temperature can be improved by functionalization with chain end interacting groups[9,10]. Association between end groups can be obtained through non-covalent interactions: van der Waals, hydrophobic or ionic interactions and hydrogen bonding. Without other interaction, by raising the temperature[11] the end groups tend to dissociate, resulting in viscosity reduction[7]. However, if these relatively weak interactions are also associated to the formation of crystalline domains resulting in physical cross-links, the final polymeric material often shows improved properties[12].

Polymers functionalized at chain ends with specific units that dimerize without forming crystalline structures will lead to concatenation within the polymer with the formation of long linear chains[9,13]. A high dimerization constant of the unit allows to obtain high degree of polymerization[8,14]. It is reported in literature that, thanks to the strong dimerization of 2-ureido-4[1H]-pyrimidinones by quadruple hydrogen bonding (Fig.2), if one consider that the energy involved in one hydrogen bond is about 5-7 Kcal/mole, two of this units are kept together by about 30Kcal/mol, a significant high interaction), long linear polymeric chains are obtained with polymers terminated with this unit.

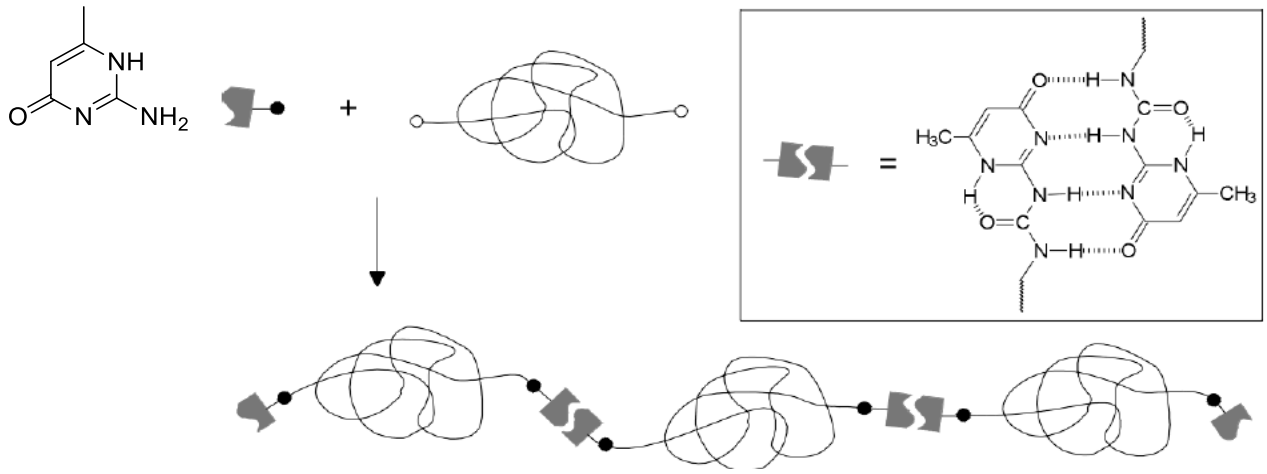


Figure 2- Pyrimidone H-bonds, from *Adv. Mater. 2000, 12, No. 12*

Some examples of these polymers are described on large scale starting from cheap commercially available reagents, where the UPy-unit is linked by reaction with isocyanate derivative (Fig.3).

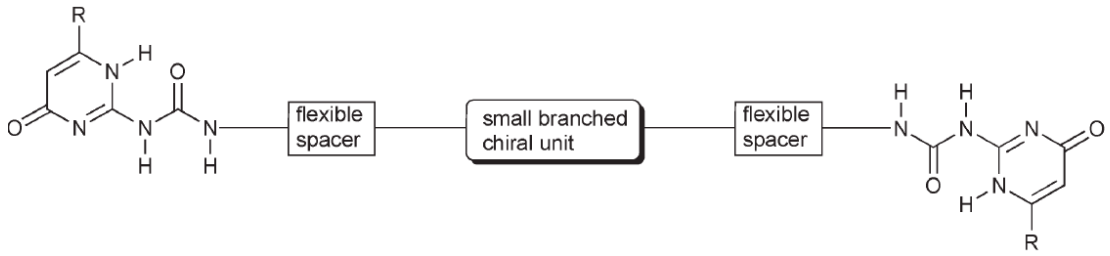


Figure 3- Terminal functionalization with pyrimidone, from *Chem. Commun., 2006, 2173–2175 | 2173*

6.2.3 Metal complexes

Finally, another possibility is to exploit metal mediated interaction. In the last decade, a new area of special interest has been identified in metallo(supramolecular) polymers[3]. These materials have been utilized to fabricate stimuli-responsive structures, resulting in reversible polymeric materials highly dependent on the environment. For these reasons, metallopolymers have been discussed in the context of self-healing materials. The aforementioned properties (reversibility and stimuli-responsiveness) are directly related to the metal–ligand binding strength. By changing the metal ion and the ligand the intrinsic properties of the final material can be adjusted within a certain range. Ciardelli was the first one to classify the architecture of metallopolymers into three types (Figure 4):

- Type I: the metal–ligand pairs can be attached to the polymer as a side chain or as an end group of the backbone by electrostatic interactions, covalent bonds or metal–ligand coordination.
- Type II: the metal complexes are included into the main chain by coordinative or covalent associations.
- Type III: the assembling of metal ions into the polymer matrix is carried out through physical interactions.

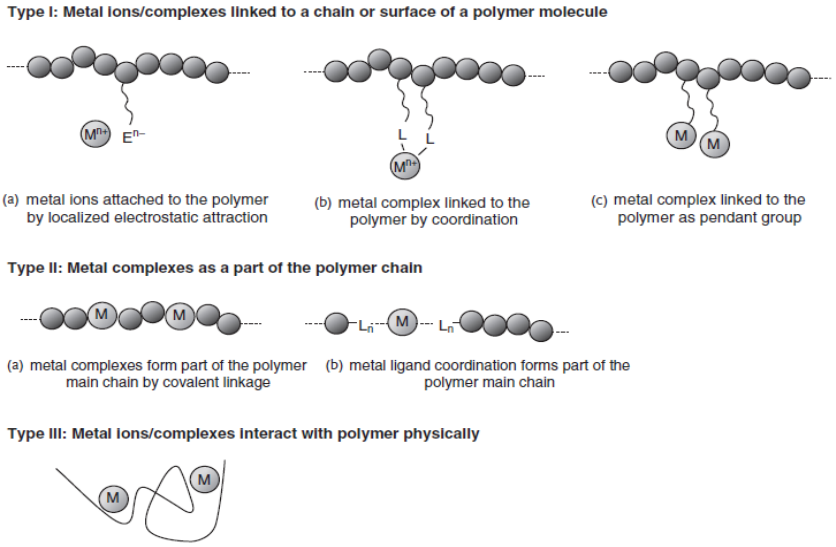


Figure 4- Metallopolymer types, from *Binder, W.H. Self-Healing*

Polymers of Types I and II are interesting candidates for applications in self-healing polymers.

The most important task for metal–ligand interactions is the conjunction of a high binding constant with the reversibility of the process. The stability of a certain complex is a thermodynamic property, represented by the individual binding constant K. Thermodynamically stable polymers are formed in case of a very high binding constant between the ligands and the corresponding metal ion, to give polymers with properties comparable to classical covalent polymers. While, for a low binding constant, polymers assemble only in the solid state, not in solution. On the contrary, medium binding constants enable the formation of macromolecular assemblies also in solution. The binding constant (K) depends on the ligand design and the corresponding metal ion and on external parameters such as pH, solvent, temperature. The binding constant can be increased by multiple interacting binding sites, such as chelating ligands or multivalent metal ions.

Among the various opportunities described, it was decided to investigate the field of metal incorporation in side-group metallopolymers, which was achieved by attaching a ligand moiety to a polymeric backbone. The polymer was previously functionalized with a binder and, once the resulting polymer was prepared, the addition of a metal precursor led to complete the synthesis of the side-group organometallic polymer. Moreover, complexation of these polymers with metal ions led to cross-linked networks.

Based on this background, it was decided first of all to investigate introduction of the H-bonding groups in elastomers commonly used in rubber compounding, by modifying them with thiourea or pyrimidine units. Three different approaches were identified:

1) Chain-end polymer functionalization
2) Functionalizers with different number of thioureas/pyrimidones units
3) Multibranched systems

In addition, the introduction of metal-ligands on elastomeric matrixes was explored together with the investigation of the interaction between chains triggered or activated by adding metals.

6.3 Pyrimidone-based functionalized polymers

The synthesis of these polymers was planned to start from cheap commercially available reagents individuating as strategic intermediate an UPy-moiety bearing a reactive isocyanate group (Compound 1, Fig.4)

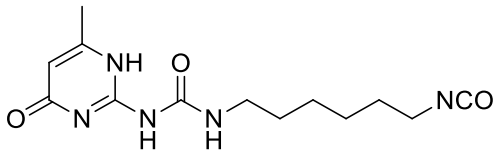


Figure 4- Pyrimidone based isocyanate, compound 1

Indeed, exploiting the reactivity of the isocyanate group towards common oxygen and nitrogen centered nucleophiles, the UP group can be easily introduced in polymers bearing hydroxy or amino groups. In literature is described the versatility of this approach, in which several OH telechelic polymers (poly(ethylene/butylene, polyethers, polyesters, and polycarbonates) are functionalized this reagent, leading to a new set of supramolecular materials.

6.3.1 Polymer functionalization

Krasol LBH 2000 is a polymeric molecule (Fig. 5) used as additive in elastomeric compounding to improve the compatibility between the elastomeric matrixes and the silica and is a suitable test molecule for introducing the UP moiety onto a polymeric material.

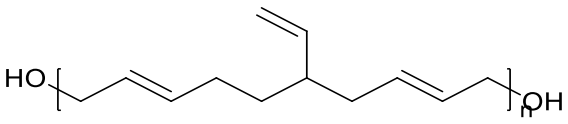
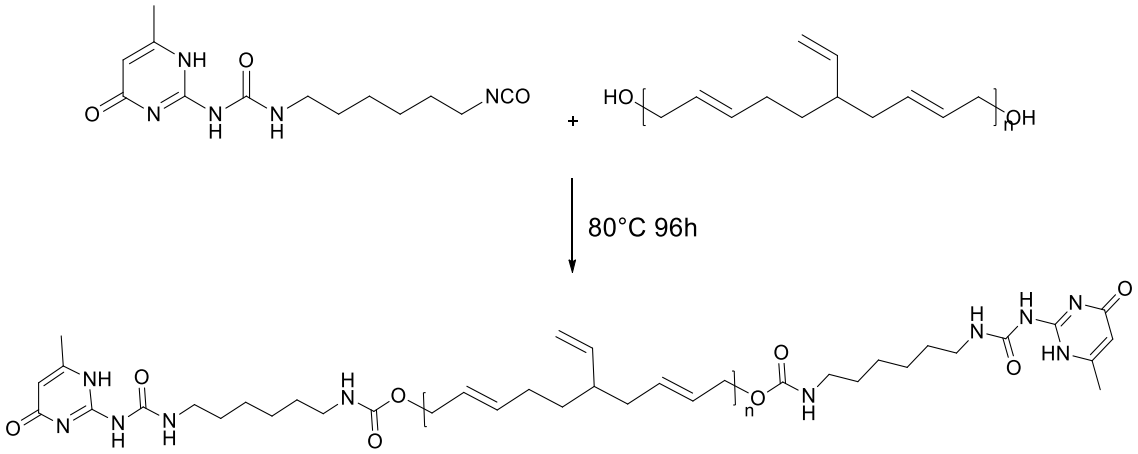


Figure 5- Krasol LBH 2000

The first attempts performed to functionalize Krasol LBH 2000, were carried out by adding 1 to Krasol preheated at 80 °C to reduce its viscosity. Then the mixture was allowed to react for 96h at this temperature (Scheme 1).



Scheme 1- Krasol functionalization using pyrimidone isocyanate

The progression of the reaction was controlled using FT-ATR (rection was considered complete when -NCO band at 2200 cm^{-1} disappeared). It was later demonstrated that using dibutyltin dilaurate as catalyst it is possible to speed up the reaction to 24h. The polymer was dissolved in DCM, precipitated in MeOH and centrifuged (x 3 times). The polymer was characterized with HNMR. In the spectrum are present the signals of the pyrimidine moiety. There is also a shift (Fig.6) of the signals attributable to the terminal CH_2 of the polymer (blue line, next to the OH, 4 ppm) with respect to the CH_2 of the functionalized polymer (red line, next to the formed urethane,

3.3 ppm).

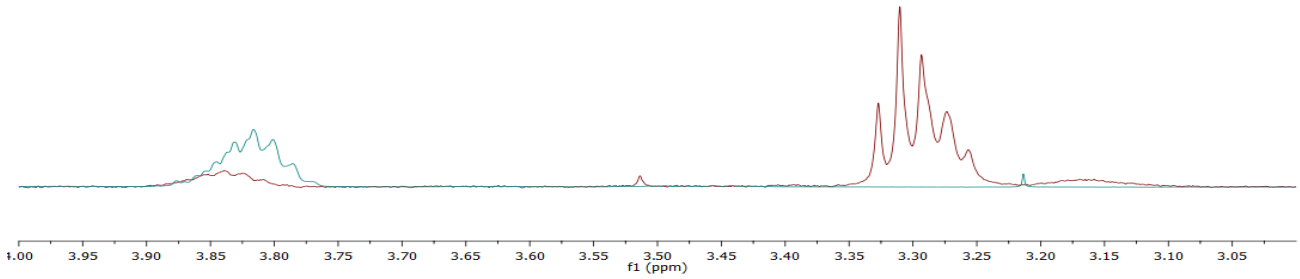


Figure 6- NMR signals comparison

Thermal stability of the functionalized compound was measured using thermogravimetric analysis (Ramp: 20-500 °C, 5 °C/min.), showing a weight loss of 21% starting above 200 °C, attributable to the breaking of the two urethane bonds. This data is of great importance given that, for applications in tire compounding, there is a need for stable systems under the vulcanization conditions (at least up to 170 °C).

6.3.2 Rheometric data

All the rheometric data presented in this chapter were collected using an HAAKE RheoWin instrument. Geometry: parallel plates (cone-plate), method: rotational steps, steady state, constant shear stress along the gap (CS), 25° C. Data reported as dynamic viscosity (Pas) vs shear stress (Pa).

The dynamic viscosity (η) of the synthesized polymer (sample 6.2) was measured with the rheometer and compared with the viscosity of Krasol LBH 2000 (sample 6.1) (Fig.7).

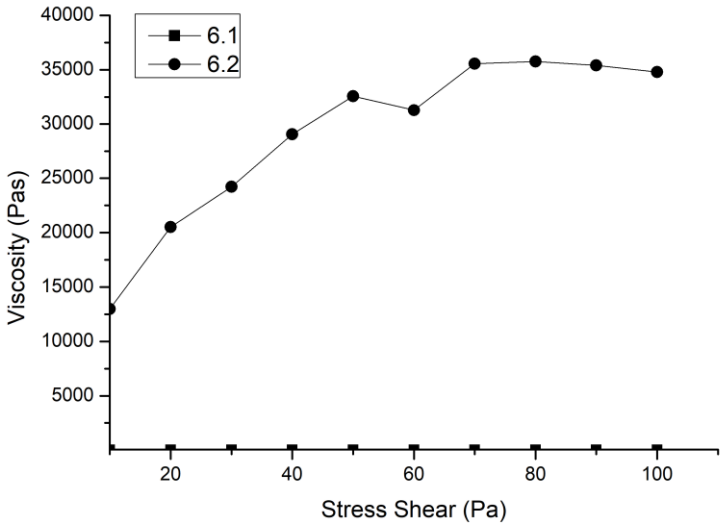


Figure 7

As can be seen, there was a huge increment of the viscosity, from 12 Pa*s (6.1 pristine Krasol) to a maximum of 35760 Pa (6.2, functionalized Krasol) due to the formation of H-Bonds. From the point of view of the physical aspect the sample (6.2) appears as a semi-solid while the starting polymer (6.1) is a viscous liquid.

6.3.3 Solubility test

Since the interactions formed are of non-covalent type (H-bonds), measurements of the solubility of the functionalized polymer at different pH were performed, in order to demonstrate the stimuli responsive nature of the polymer.

In Fig.8 the left vial contains the functionalized polymer dispersed in dichloromethane (poorly soluble), while the right vial contains the functionalized polymer, dichloromethane and few drops of trifluoroacetic acid (completely soluble). As it is easily ascertained, the presence of an acid can break the H-bonds network formed by pyrimidones.

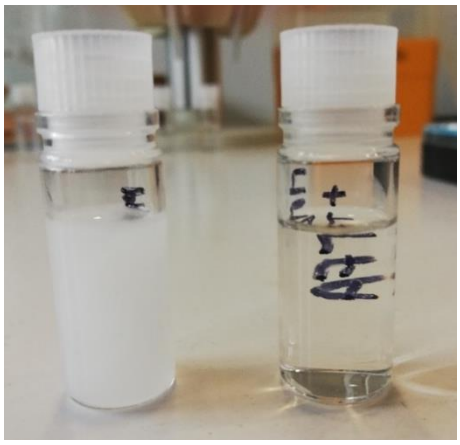


Figure 8- Functionalised Krasol in DCM (left), and in DCM + TFA (right)

Adding a base to neutralize the TFA permits to the H-bonds to reform their network and the functionalized polymer returns insoluble (Fig.9).

Figure 9- Functionalised Krasol after TFA neutralization

6.4 Functionalizers with different number of thioureas/pyrimidones

In this case the idea was to prepare functionalized polymer with pyrimidone or thiourea moieties starting directly from SSBR (solution styrene/butadiene copolymers), a polymer employed in tire compounding. Since the most accessible functionalizable part in this polymer is represented by vinyl units, the attention was focused on the synthesis of new tetrazole derivatives, bearing pyrimidone or thiourea functionalities (Table 1).

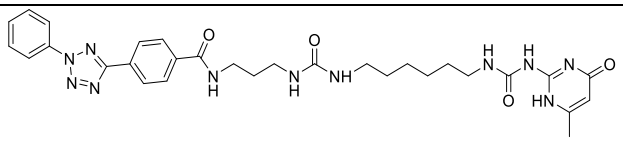
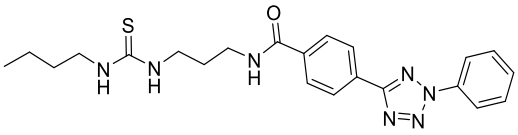
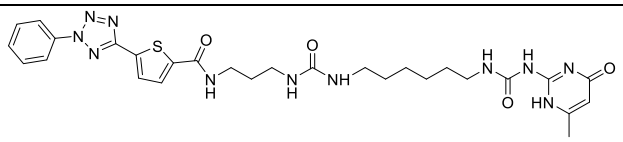
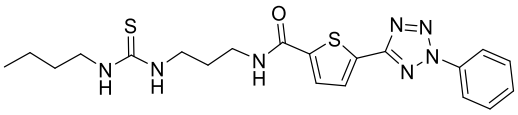
N°	Formula	Molecular Formula	M.W. (g/mol)	Activation Temperature (°C)
2		$C_{30}H_{37}N_{11}O_4$	615.70	190
3		$C_{22}H_{27}N_7OS$	437.57	190
4		$C_{28}H_{35}N_{11}O_4S$	621.72	180
5		$C_{20}H_{25}N_7OS_2$	443.59	180

Table 1

These tetrazoles, after thermal activation, can undergo 1,3 dipolar cycloaddiction with vinyls, anchoring to the polymer matrix, following the normal mechanism previously shown (see Chapter 1), to give thiourea (Fig.10) or pyrimidone side-chain functionalized polymers, that can interact through H-bonds. Due to stronger hydrogen bonding higher interchain interactions are expected with pyridine-functionalized polymer.

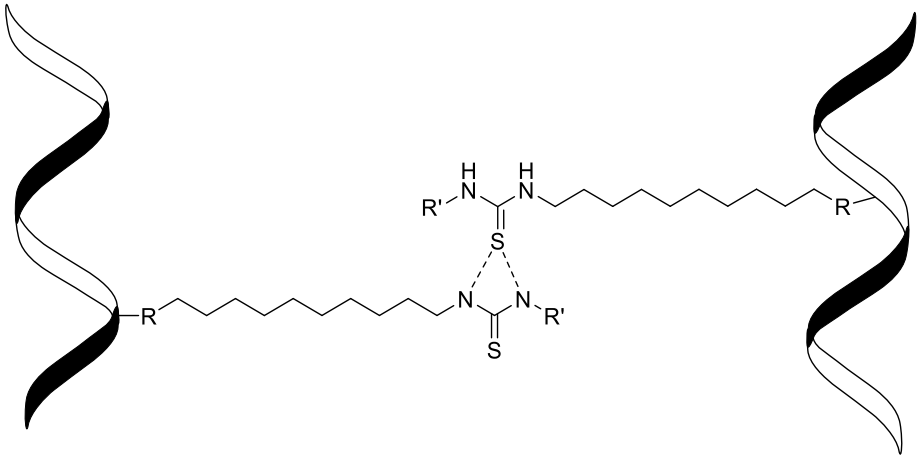
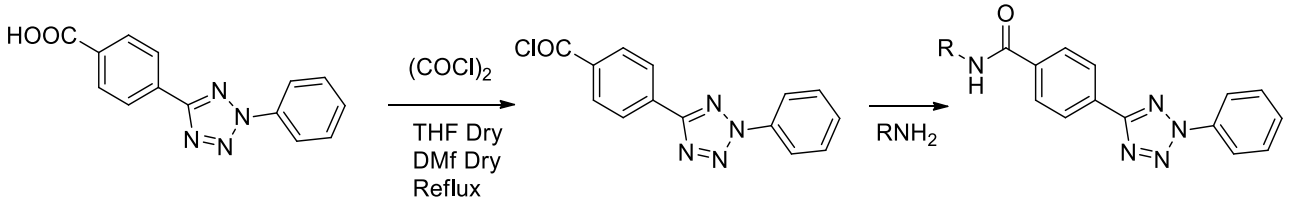


Figure 10- Thiourea H-bonds between polymer chains

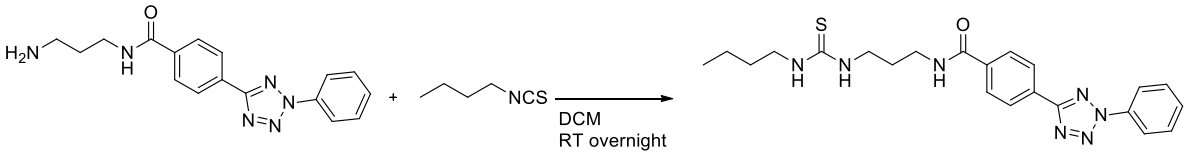
6.4.1 Synthetic part

Starting from the tetrazole with a carboxylic acid moiety it is possible to synthesize the desired compounds following the scheme below (Scheme 2).

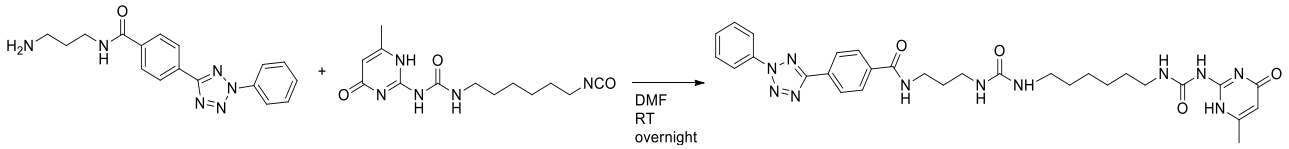


Scheme 2- Synthesis of tetrazole-amide intermediates

The first step consists in the transformation of the carboxylic function in the acyl chloride using $(COCl)_2$ and the second, the reaction of the latter with an amine giving the corresponding amide. For the synthesis of all compounds reported in the table 1, the amine use was N-Boc-1,3-diaminopropane. Boc deprotection, followed by reaction with 1-butyl-isothiocyanato led to the thiourea derivative (Scheme 3). While the addition of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)-urea gives the pyrimidone derivative (Scheme 4).



Scheme 3- Synthesis of thiurea-tetrazole derivative



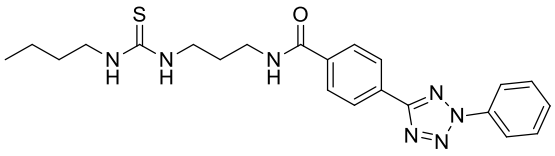
Scheme 4- Synthesis of pyrimidone-tetrazole derivative

6.4.2 Polymer functionalization

At laboratory scale, liquid Krasol LBH 2000 (Mw: 2100 g/mol), was selected as polymer since it contains a high number of vinyls potentially reactive with thermal generated nitrilimine.

Starting from a liquid polymer, the best way to investigate changing properties due to the presence of the H-bond network was to measure the viscosity of the functionalized polymer. The functionalization of Krasol was carried out employing different amount of functionalizer (0.2 eq., 0.4 eq., 1 eq. respect to the polymer). The synthetic procedure was simple: polymer was heated at 80 °C to make it more fluid, then the functionalizer was added under stirring. After the complete dispersion of tetrazole, the temperature was raised at the activation T (characteristic for each tetrazole, see Table 1) for 30 minutes. The occurrence of the reaction was proved by observing the formation N_2 bubbles, by bright fluorescence due to the pyrazoline formed and confirmed by NMR. Subsequently the viscosity tests were carried out.

6.4.3 Thiourea derivative



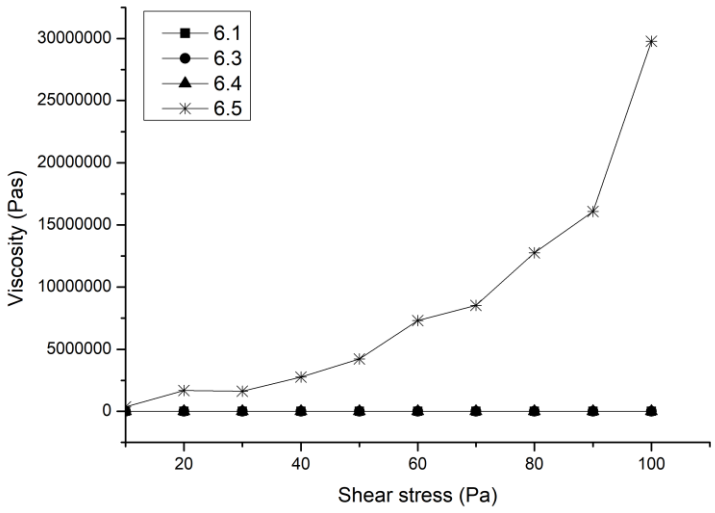
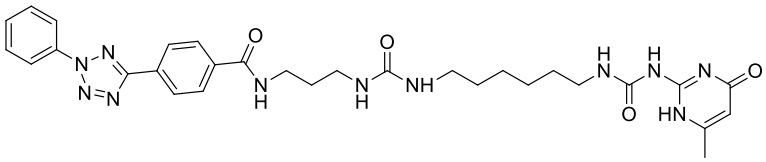


Figure 11

The functionalization using 0.2 eq. (sample 6.3) and 0.4 eq. (sample 6.4) led to a slight increase of the viscosity with respect to the pristine polymer while, using 1:1 ratio (sample 6.5) the viscosity increased incredibly (Fig.11). Visually the polymer was more similar to a gel.

6.4.4 Pyrimidone derivative



Since in this case the increase of viscosity was bigger respect to the previous case (even at low amount of functionalization), the viscosity changes were divided in two graphs. The first one (Fig.12) refers to the difference between pristine polymer (6.1) and 0.2 eq. of functionalizer (6.6).

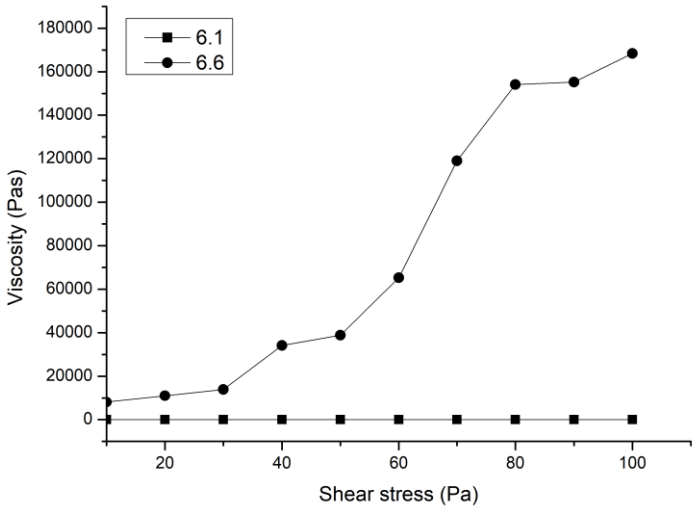


Figure 12

At this functionaliser concentration, the viscosity was already quite high, thus the measure with 0.4 eq. was not performed, going directly the one with 1 eq. of functionalizer (6.7). In that case the increase of viscosity was impressive (Fig.13). Furthermore, as the stress increases the viscosity continues to increase, indicating how the system responds strongly to the increase in the distance between the chains being pulled.

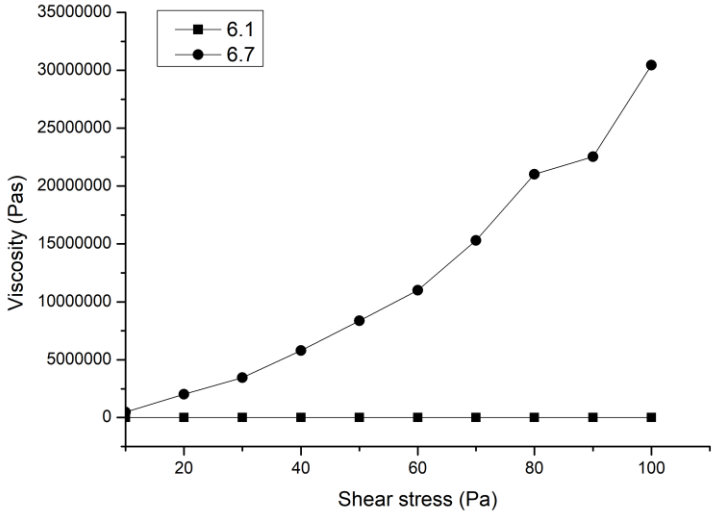
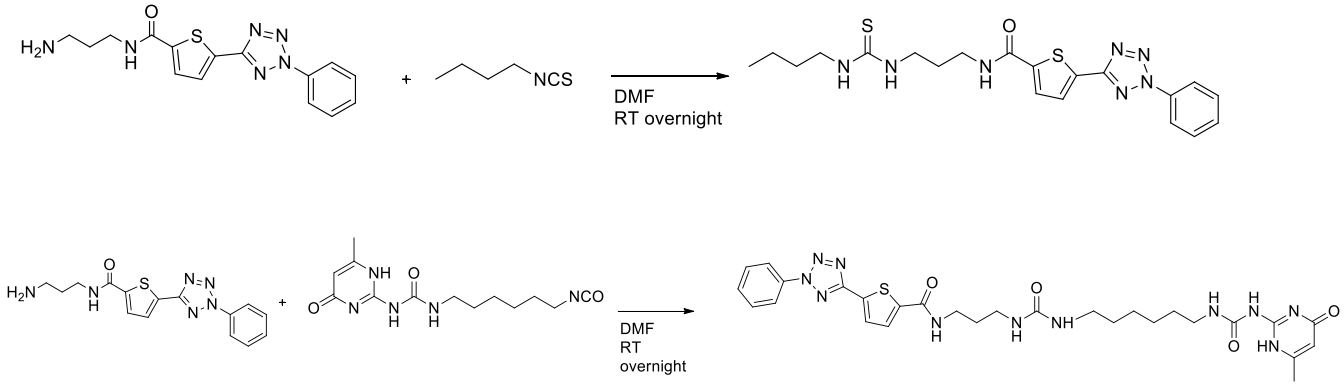


Figure 13

6.4.5 Thiophene derivatives

Analogous thiophene derivatives were synthesized (Scheme 5) in order to obtain different activation temperature of the tetrazoles, since it was previously demonstrated that the presence of the thiophene ring (electron-donor system) lower the activation temperature. For these compounds it was not tested the reactivity with the polymer and so there are no rheometric data, only their synthesis is reported. However, based on previous experience, we expect a similar result to that of the compounds previously investigated, since the presence of the thiophene should not affect the other properties. The synthesis is identical to those of the analogs with phenyl as a substituent.



Scheme 5

As can be seen from the table shown above, by inserting thiophene it is possible to lower the activation temperature by 10 °C, passing from 190 to 180 °C.

6.5 Multibranched systems

It was thought to prepare systems containing from two to four units capable of giving hydrogen bonds and conceived as cross-linking systems between polymer chains functionalized with one of the units already described. These systems can be placed between two or more functionalized polymer chains, acting as knot points (Fig.14) and should improve the connection between the chains and therefore also the self-healing property. Furthermore, they must be added in very small concentrations, to avoid high level of cross-linking.

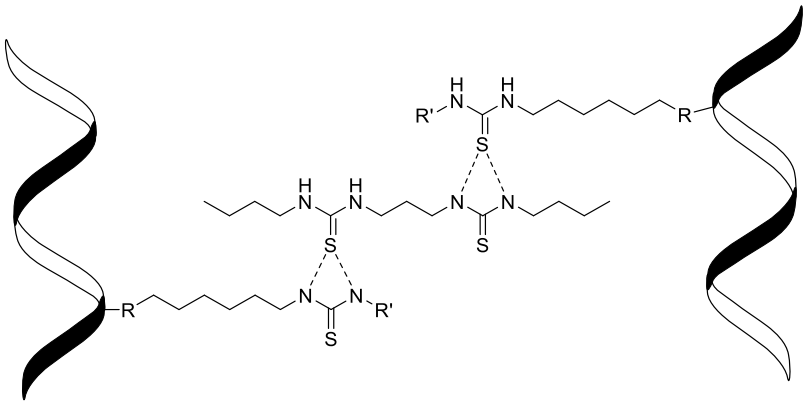
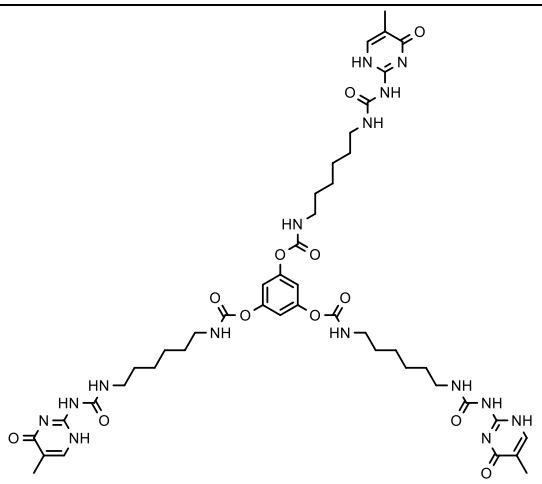


Figure 14- Multibranched systems H-bonding with functionalized polymer

Multi-branched systems containing both thioureas and pyrimidones were synthesized (Table 2), so that they could be used in addition to each of the functionalized polymers described above.

N°	Formula	Molecular Formula	M.W. (g/mol)
6		$C_{45}H_{63}N_{15}O_{12}$	1006.09

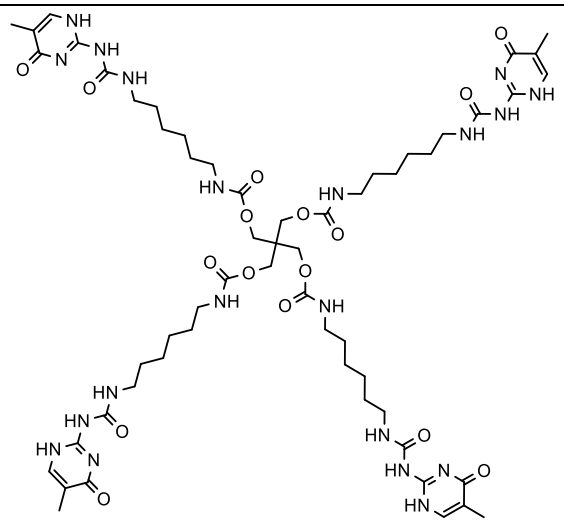
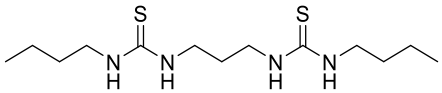
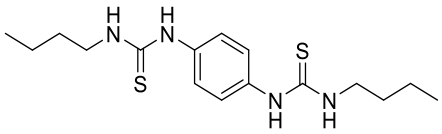
7		$C_{57}H_{88}N_{20}O_{16}$	1309.46
8		$C_{13}H_{28}N_4S_2$	304.52
9		$C_{16}H_{26}N_4S_2$	338.53

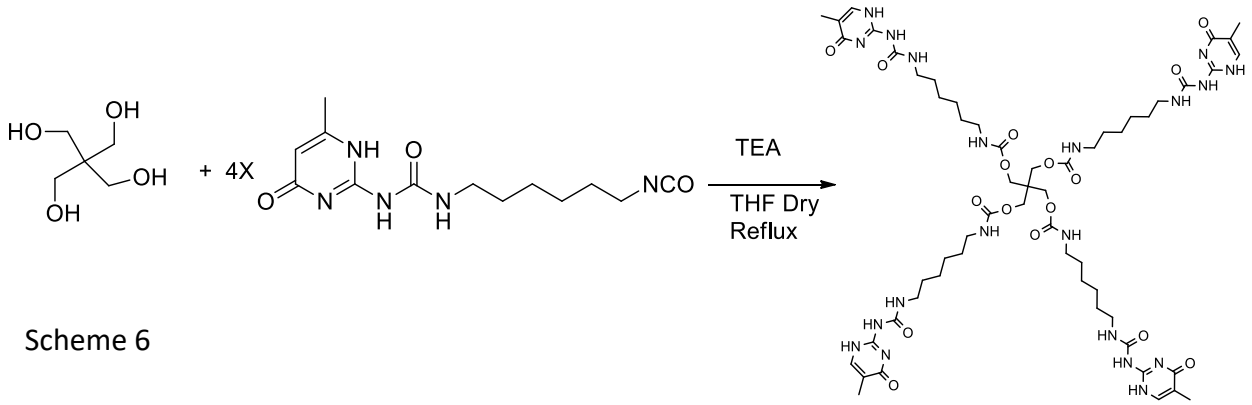
Table 2

6.5.1 Synthetic part

Starting from commercially available branched alcohols it was possible to obtain multi-branched pyrimidone while, using diamines, it was possible to obtain thiourea systems. The synthesis requires a one-step reaction.

Synthesis of pentaerytritol derivative

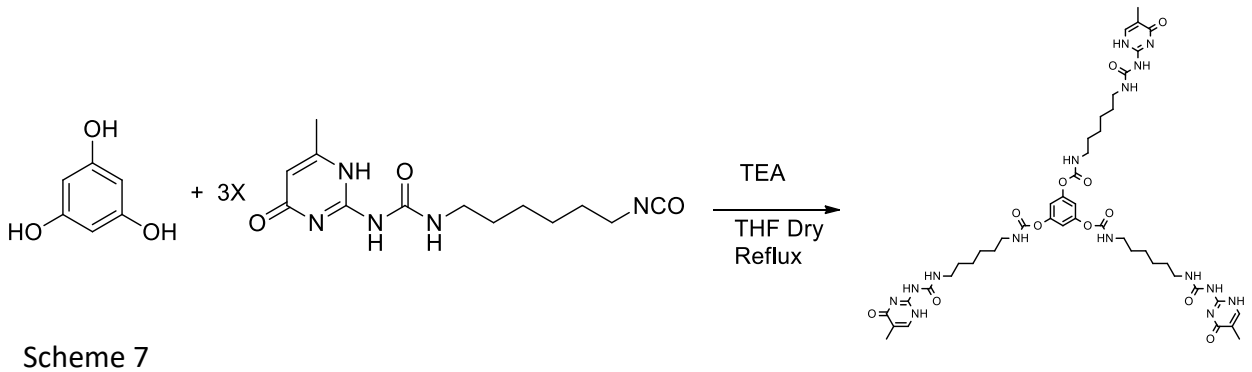
All the synthetic procedures are reported in detail in the experimental part.



Scheme 6

Synthesis of phloroglucinol derivative

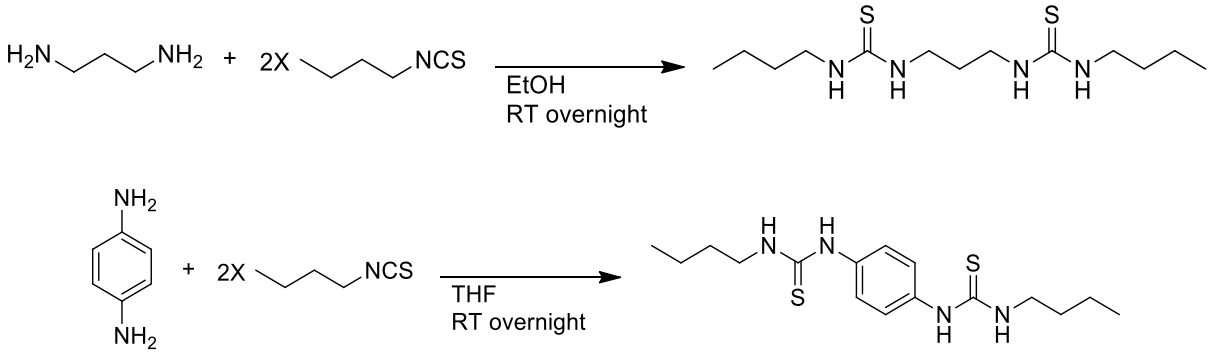
All the synthetic procedures are reported in detail in the experimental part.



Scheme 7

Synthesis of thiourea derivatives

All the synthetic procedures are reported in detail in the experimental part.



Scheme 8

6.5.2 Pentaerytritol derivative rheometric test

As already explained, these compounds are to be considered as extra cross-linking agents, to be used in addition to previously functionalized polymers with similar groups, in order to form further knot points, increasing the cross-linking of the material. Krasol functionalized with pyrimidone (sample 6.2) was used as functionalized polymer (Fig.15).

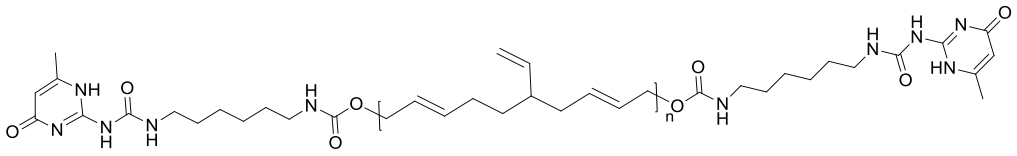


Figure 15

The tetrameric linker was added 10% by weight respect to the polymer stirring the functionalized polymer at 80 °C for 30 minutes.

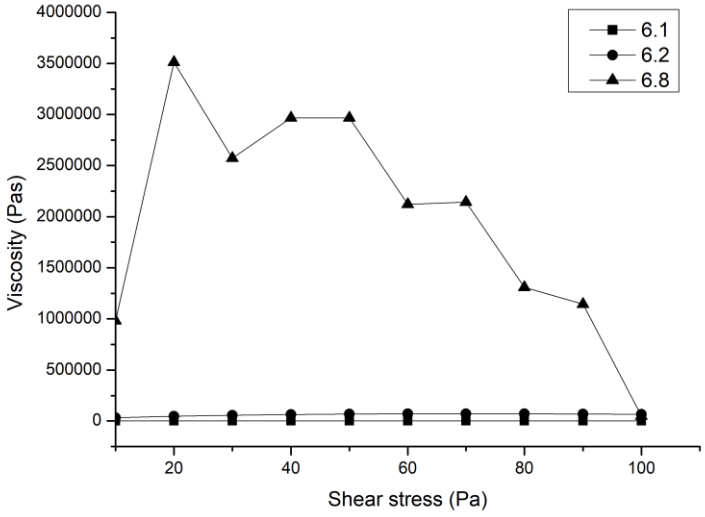


Figure 16

The presence of the linker gives an extra-degree of H-bonds to the functionalized polymer, raising the viscosity (Fig.16). After 20 Pa there is a decrease in viscosity. Perhaps the additive begins to make bonds with itself, breaking the formation of the extra lattice and thus decreasing the viscosity of the system. Further experiments would be needed to see if the original situation is restored after some time.

6.5.3 Phloroglucinol derivative rheometric test

Krasol functionalized with pyrimidone (Fig. 17) was used.

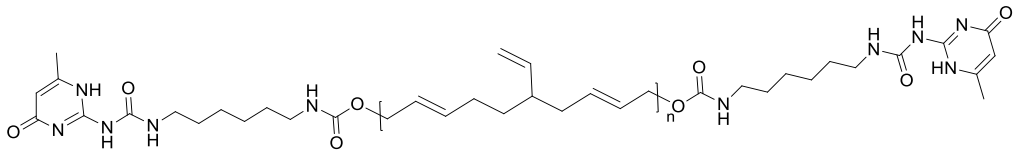


Figure 17

The trimeric linker was added 10% by weight respect to the polymer stirring the functionalized polymer at 80 °C for 30 minutes.

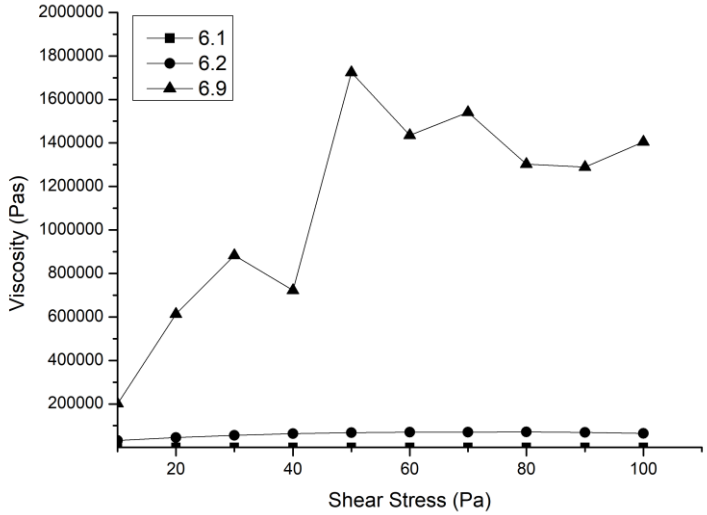
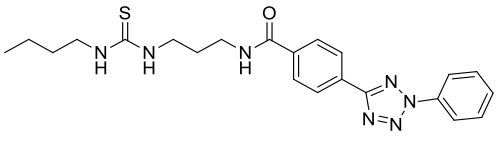


Figure 18

The presence of the linker gives an extra-degree of H-bonds to the functionalized polymer, raising the viscosity (Fig.18). In this case, at high strain the viscosity reaches a plateau. Perhaps the application of a greater stress helps to better mixing, but after a certain stress the system reaches a situation of equilibrium in which the balance between H-bond forming and breaking gives a more or less constant viscosity.

6.5.4 Bis-thiourea derivatives rheometric test

Krasol functionalized with thiourea-tetrazole (sample 6.5) was used.



The bis-thiourea linker was added (0.5 eq. respect to the tetrazole-thiourea molecule) stirring the functionalized polymer at 80 °C for 30 minutes.

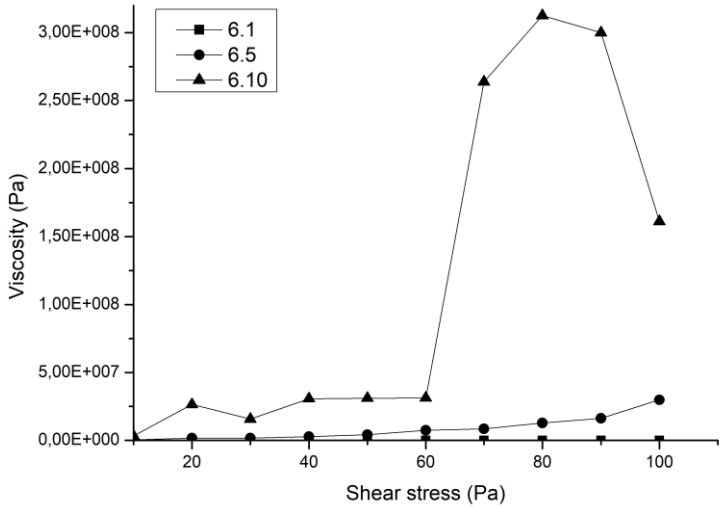


Figure 19

The presence of the linker gives an extra-degree of H-bonds, raising the viscosity (Fig.19). Here the polymer and thiourea-linker mixing could be better by increasing the stress, resulting in a significant increase in viscosity after a certain amount of stress. At high stress the interaction is broken, probably polymer chains are too far and the bis thiourea linker self-assembly instead of interacting with the functionalized polymer.

6.6 Metal-mediated self-healing

The idea is to functionalize the polymer matrix with tetrazoles bearing some functional groups able to complex a metal Ion (Fig. 20). In particular it would be interesting to find something which could interact with Zinc (2^{+}), which is already present in tire compounds.

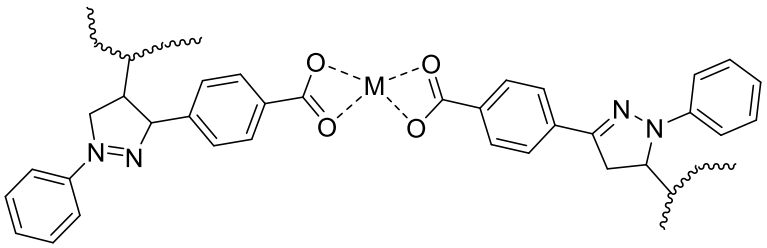
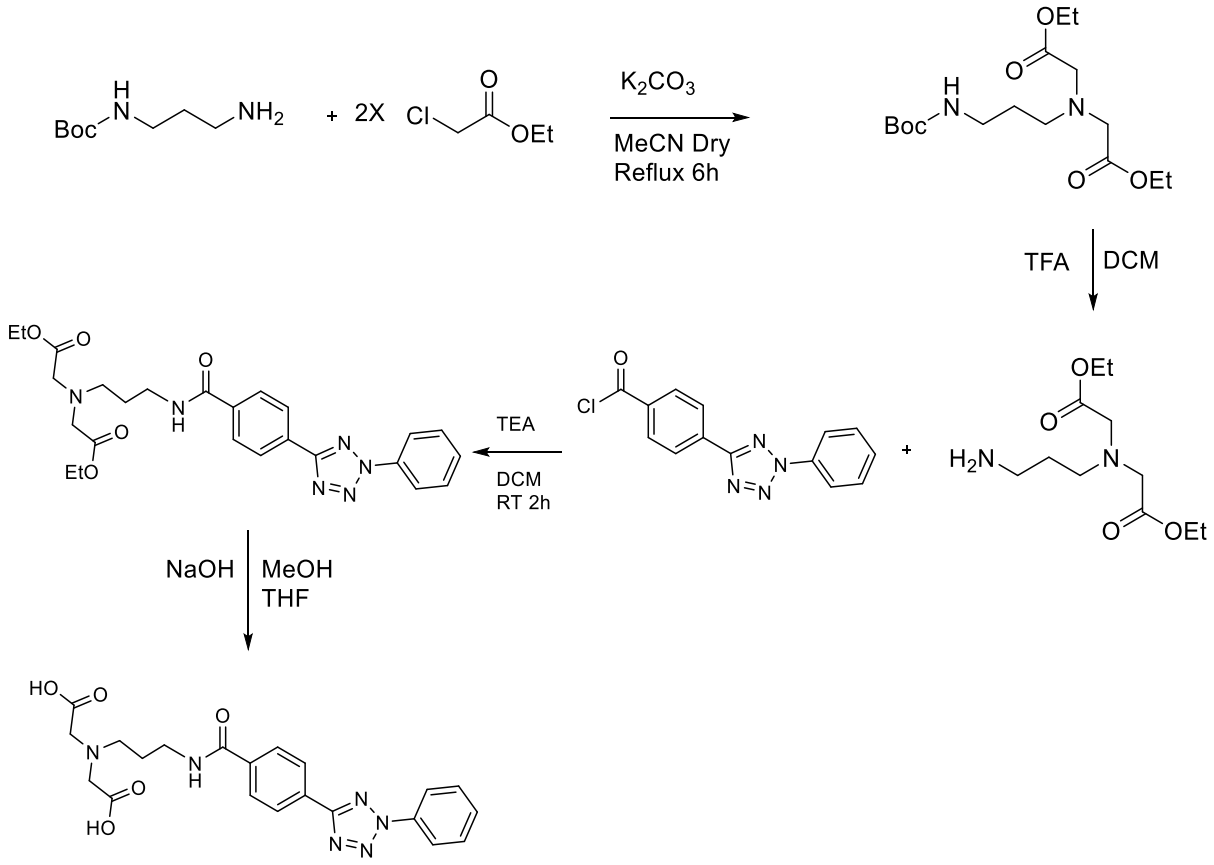


Figure 20

6.6.1 Synthetic part

Scheme 9 shows the synthesis of the chelant (compound 10) that could functionalize the polymer matrix.



Scheme 9

The first step involves the formation of the chelating agent through a double alkylation, then a Boc cleavage occurs, to form the chelating functional group which is attached to the acyl chloride-tetrazole. The last step is a hydrolysis in basic conditions to give the chelating tetrazole. All the synthetic procedures are reported in detail in the experimental part.

6.6.2 Polymer functionalization

The chelating was added 20% by weight respect to the polymer stirring the Krasol LBH 2000 at 80 °C for 30 minutes.

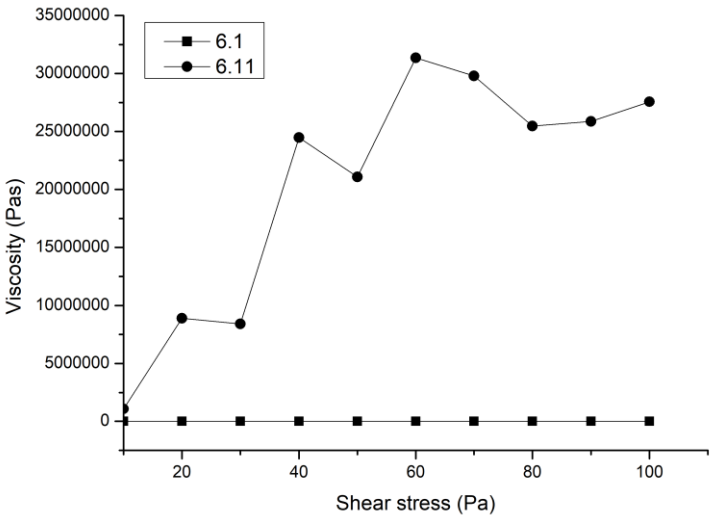


Figure 21

The presence of two carboxylic groups per each functionalizer molecule give the formation of H-bond network that increase the viscosity of the polymer, which remains high even at high stress; where it seems to reach a plateau that can indicate an equilibrium between the interaction formed and broken (Fig.21).

The final idea was to add a metal cation in order to create a complex (Fig. 22) between two functionalizer molecules and so to cross-link the polymer matrix and will be performed in the future. Subsequent studies could be performed changing the nature of the cation, to investigate the variation of the metal-ligand interaction.

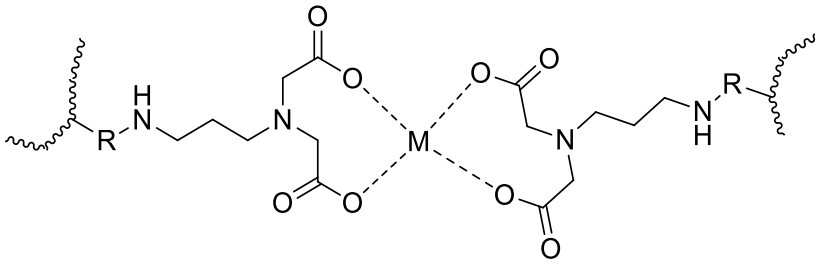


Figure 22

6.6.3 Tetrazoles bearing a carboxylic acid group

In Fig.23 are reported the tetrazole derivatives bearing a carboxylic acid group.

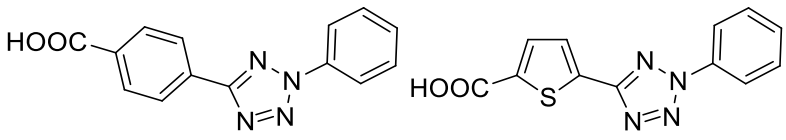


Figure 23

Since the activation temperature of the tetrazole with the phenyl substituent is 210 °C (too high), the experiment was performed only using the tetrazole-thiophene carboxylic acid, which has an activation temperature consonant with the application (185 °C).

Krasol LBH 2000 was functionalized with different amount of tetrazole: 0.2 eq. (sample 6.12), 0.4 eq. (sample 6.13), 1 eq. (sample 6.14) respect to the polymer.

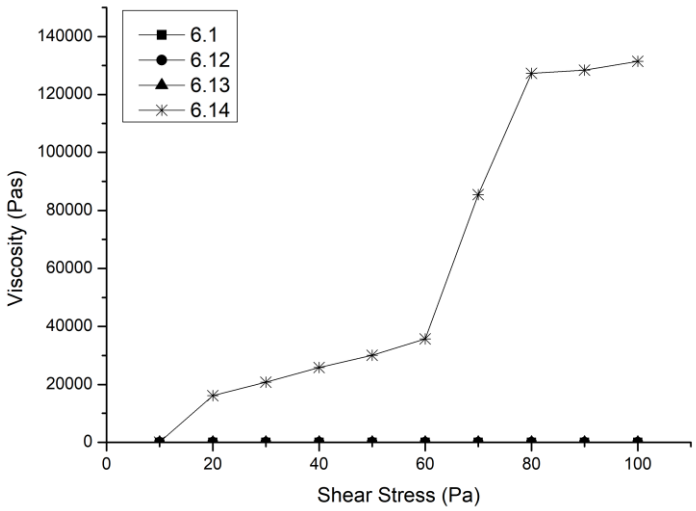


Figure 24

Functionalization with 0.2 eq. and 0.4 eq. led to a negligible increase in while, for 1 eq. functionalization, there was an increase (Fig.24).

To the functionalized polymers (6.12, 6.14, 6.14) 0.5 eq. (with respect to the acid groups) of $Zn(OAc)_2$ dissolved in aqueous NH_3 were added followed, by heating at 120 °C, in order to form the Zn complex (Fig.25).

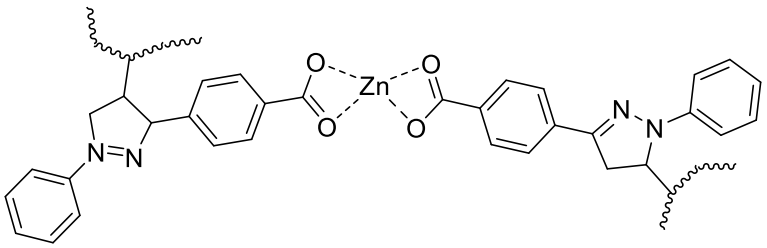


Figure 25

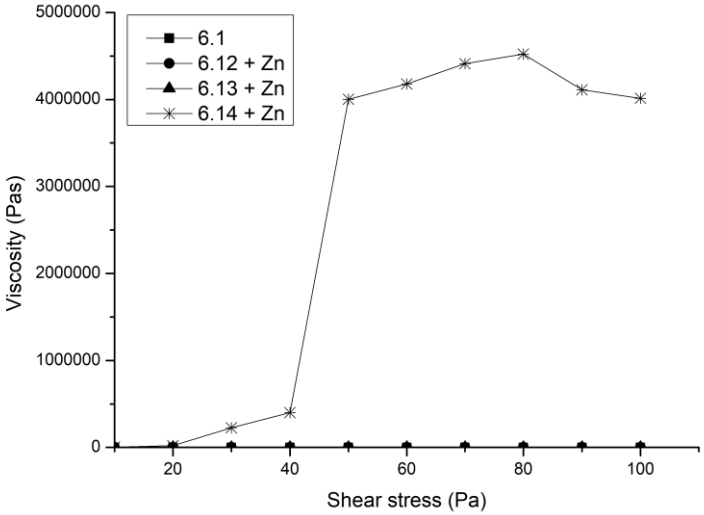
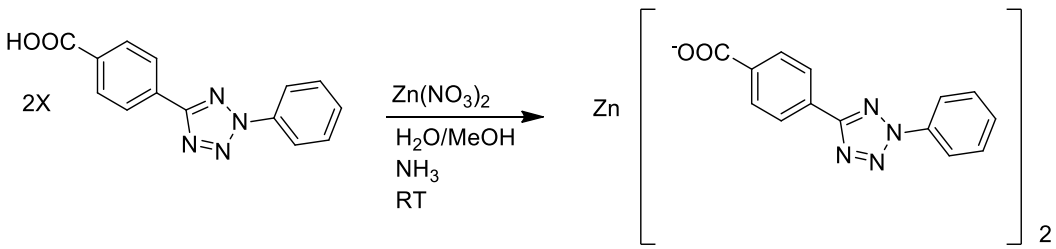


Figure 26

For all the functionalized polymer it was possible to notice an increase of viscosity that, after a certain stress tends to oscillate around the same value (Fig.26). Probably the system is in a state of equilibrium between bonds formed and broken.

6.6.4 Zinc Complex

Given the previous result, it was decided to use the tetrazole-zinc complex as cross-linker. The tetrazole-zinc salt has been prepared by deprotonating the tetrazole-carboxylic acid derivative with NH_3 and reaction with $Zn(NO_3)_2$, as reported in the Scheme 10.



Scheme 10- Synthesis of the Tetrazole-Zinc complex

The Zinc complex present an activation temperature (180 °C) lower than the corresponding tetrazole, and therefore it represents an advantage from the application point of view. Furthermore, the complex could function as a modulable cross-linking agent, that is, it changes the strength of the interaction between tetrazole and zinc ion as the temperature varies.

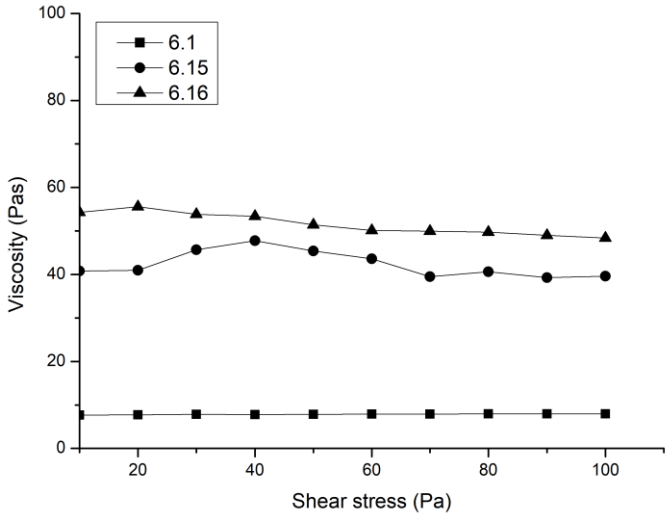
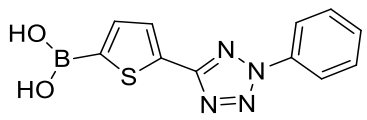


Figure 27

There is an increase of viscosity moving from pristine polymer to 0.5 eq. functionalization to 1 eq. functionalization but not so high as it was expected (Fig.27). Probably the reaction time was not enough, maybe for tetrazole-metal complexes is necessary a longer heating time respect to the classic 30 minutes. Solubility problems are not excluded.

6.6.5 Boronic acid derivative



Boronic acid can interact with itself or with boric acid, forming cycloadducts and giving an enhancement in cross-linking degree[5,15].

Krasol LBH 2000 was functionalized with different amount of tetrazole: 0.2 eq. (sample 6.17), 0.4 eq. (sample 6.18), 1 eq. (sample 6.19) respect to the polymer.

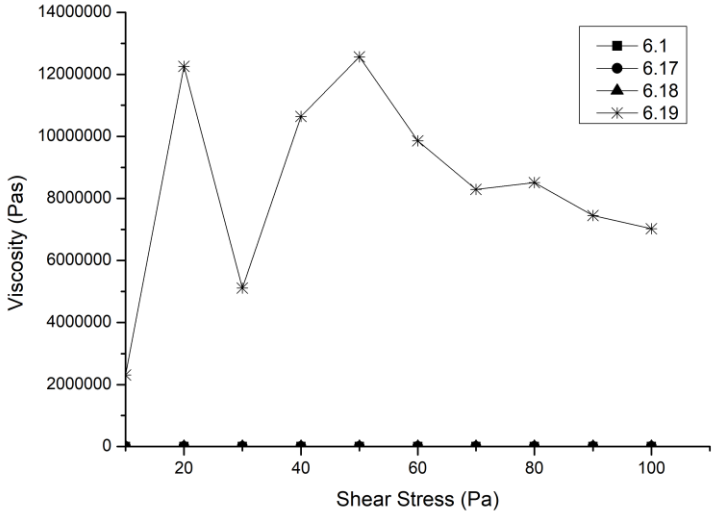
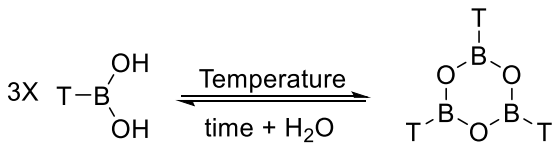


Figure 28

With 0.2 eq. and 0.4 eq. of functionalizer the increase in viscosity was linear but not so high, while with 1 eq it was huge (Fig.28). After a certain stress the viscosity oscillates around a narrow range. Probably there is an equilibrium between bonds formed and broken.

The curious aspect is that the polymer, after the heating, becomes solid (that's the reason of the increadibly high viscosity) but, after 24h, it returns liquid. The process seems to be reversible. The hypothesized mechanism is reported in the scheme 11. Boronic acid thermally trimerizes to form boroxine, resulting in a loss of water. This process is reversible over time, in the presence of environmental humidity.



Scheme 11- Reversible boroxine formation

So rheometric analysis was performed also after 24h (sample 6.20), demonstrating the reversibility of the process as a loss in viscosity (Fig.29).

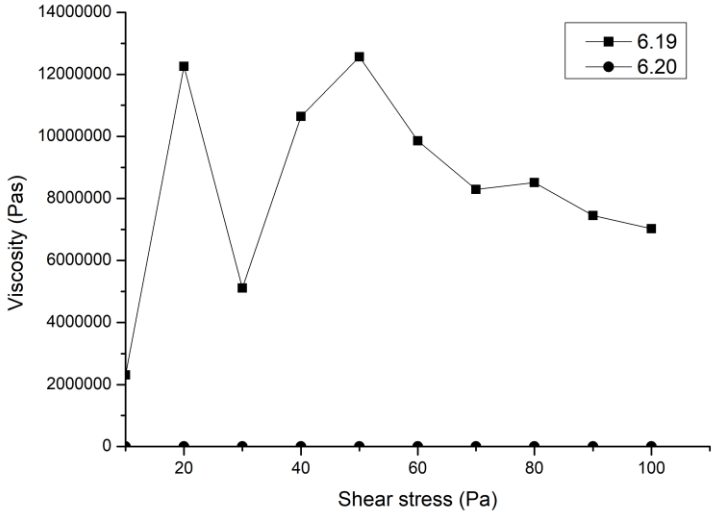


Figure 29

Re-heating the polymer at 170 °C permits to obtain again a solid-like polymer.

6.6.6 Boric acid tests

Some experiments were performed adding H_3BO_3 to the already functionalized polymer (see paragraph 6.6.5). Results similar to the previously obtained using tetrazole-boronic acid derivative by itself were expected, maybe with a little increment.

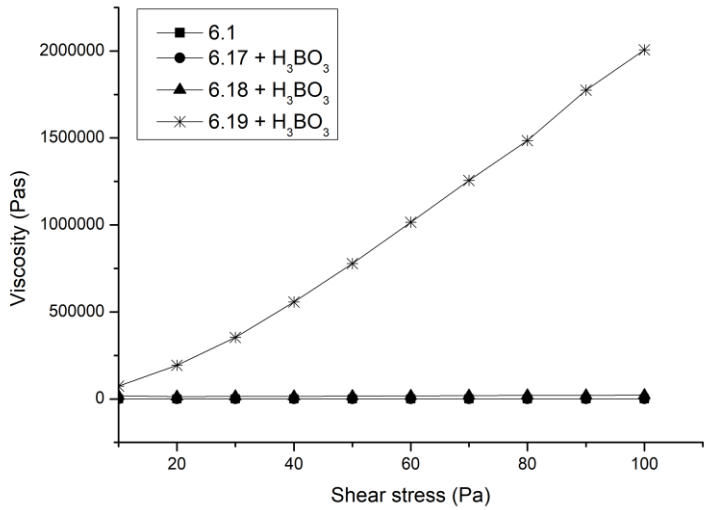


Figure 30

It was hypothesized that the addition of H_3BO_3 gives an extra-crosslinking, increasing the viscosity (Fig.30). Here the value raises with the stress applied so, maybe the higher stress helps the dispersion of the boric acid, increasing the interaction with the functionalized polymer.

As in the previous case, concerning the 1:1 functionalization (sample 6.19), a solid-like polymer was obtained which, after 24h became liquid again with a lower viscosity (Fig.31).

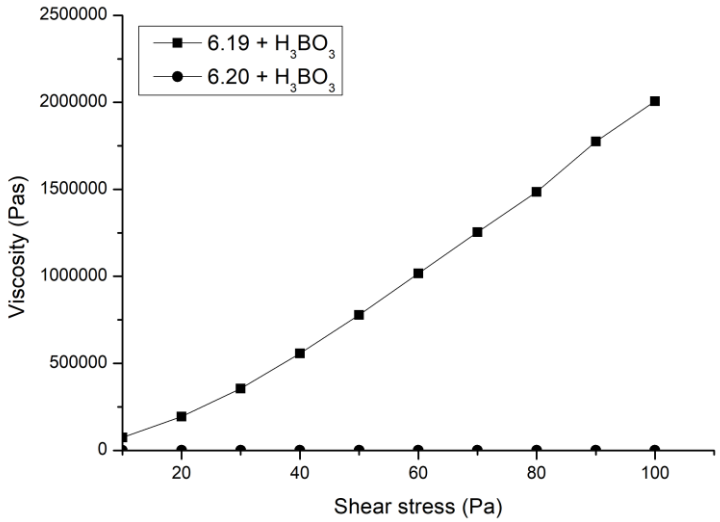


Figure 31

6.6.7 Final conclusions

During the period abroad new systems were developed, in which the previous knowledge in the field of tetrazoles was combined with the field of non-covalent interactions (hydrogen bonds), taking inspiration from the systems used for the self-healing of polymers. The data collected allowed us to begin to understand the behavior of these hydrogen-bonded functionalizers as a side chain of polymers. Unfortunately, it has not yet been possible to investigate these effects on a larger scale, using them in real elastomeric compounds. For each of the systems used, an increase in viscosity was registered respect to the pristine polymer as well as an increase due to the presence of a greater quantity of functionalizer, interpretable as a greater formation of hydrogen bonds.

The most promising systems are those containing pyrimidones, as they can form a greater number of hydrogen bonds per functionalizing unit. Regarding systems with thioureas, it is necessary to introduce more functionalities on the chain to obtain comparable results. Multi-branched systems

are very effective, even in small quantities, in increasing the interactions between already functionalized polymers and will be used for tests on a larger scale. Finally, further tests will be carried out on systems containing boronic acids to study their peculiar behavior reversible over time, which looks very promising for elastomer applications.

The results obtained, even if preliminary, were still encouraging and will be taken as a starting point for a subsequent PhD project within our research group.

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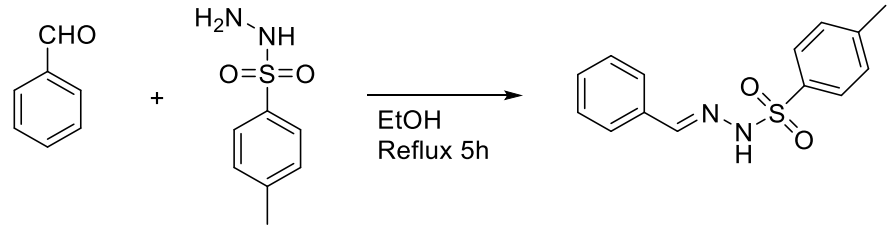
7. Experimental part

All reagents and solvents were purchased from commercial sources (Fluorochem Co.; Tokyo Chemical Industry Co. and Aldrich Chemical Co.;) and used as received. Chromatographic purifications were performed using Merck 9385 silica gel, pore size 60 Å (230–400 mesh). IR spectra were recorded with a Perkin Elmer Spectrum 100 FT-IR spectrometer equipped with universal ATR sampling accessory. NMR were recorded with a Bruker AVANCE III HD 400 MHz spectrometer. Chemical shifts (δ) are expressed in parts per million (ppm), and coupling constants are given in Hz. Splitting patterns are indicated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. TGA analysis was performed using Mettler Toledo TGA/DSC1 StarE.

The synthesized compounds were reported in the order of appearance in the chapters. The main compounds are indicated with the identification number used in the tables in each chapter.

Chapter 1

Synthesis of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide

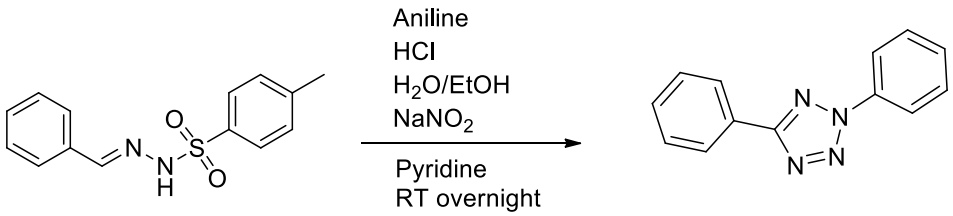


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
benzaldehyde	106.13	5	47.00	1
p-Toluenesulfonyl hydrazide	186.23	8.78	47.00	1

Solvent: EtOH

5.00g (47.00 mmol) of benzaldehyde, 8.78 g (47.00 mmol) of p-Toluenesulfonyl hydrazide and 60 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (12.51g, yield:97%). The product was used for the next step without any further purification. **Physical aspect**: Solid, white powder

Synthesis of 2,5-diphenyl-2H-tetrazole (compound 1)

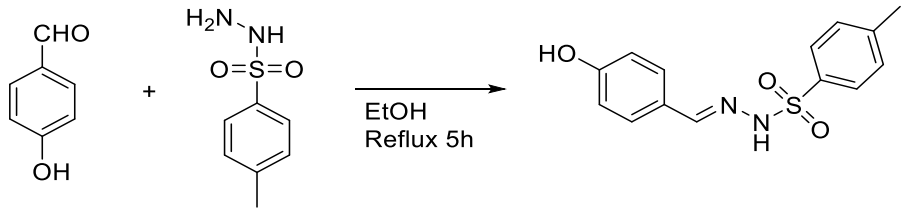


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D (g/ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1		
Aniline	95.126	0.34	3.65	1	0.64	1.02
$NaNO_2$	69.00	0.25	3.65	1		
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91	

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (340mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (DCM) to give the pure product (446g, yield:55%). **Physical aspect**: Solid, orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.31 – 8.27 (m, 2H), 8.23 (ddd, *J* = 3.7, 3.1, 2.0 Hz, 2H), 7.64 – 7.58 (m, 2H), 7.57 – 7.50 (m, 4H) **FTIR-ATR** (cm^{-1}): 3098, 3067, 3051, 3028, 2590, 2553, 2160, 1968, 1900, 1892, 1827, 1811, 1774, 1750, 1713, 1678, 1639, 1596, 1531, 1497, 1472, 1460, 1448, 1373, 1368, 1321, 1282, 1257, 1216, 1185, 1158, 1137, 1105, 1074, 1018, 993, 925, 915, 853, 840, 814, 789, 761, 728, 714, 691, 676, 616, 580, 568 **TGA analysis**: 170 °C

Synthesis of (E)-N'-(4-hydroxybenzylidene)-4-methylbenzenesulfonohydrazide

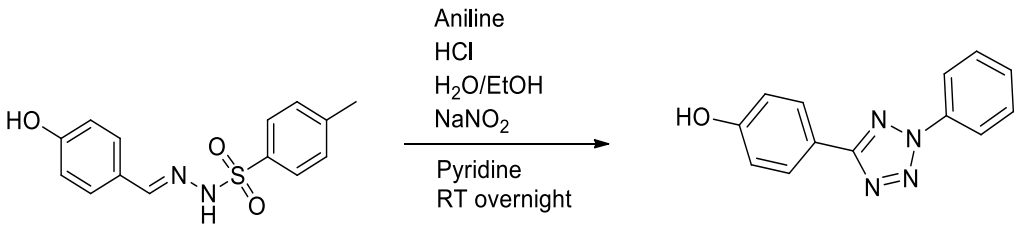


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-hydroxybenzaldehyde	122.12	5.00	41.00	1
p-Toluenesulfonyl hydrazide	186.23	7.63	41.00	1

Solvent: EtOH

5.00g (41.00 mmol) of 4-hydroxybenzaldehyde, 7.63 g (41.00 mmol) of p-Toluenesulfonyl hydrazide and 60 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (11.90g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, pale yellow powder

Synthesis of 4-(2-phenyl-2H-tetrazol-5-yl)phenol (compound 2)

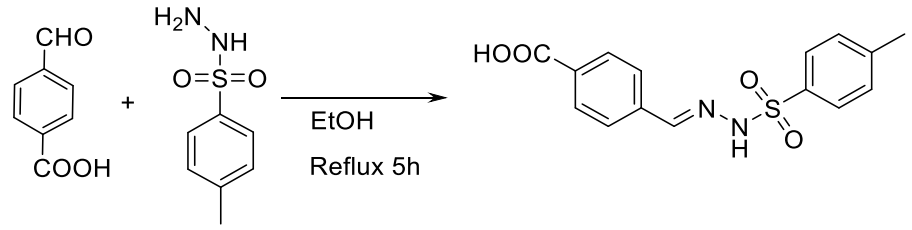


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-N'-(4-hydroxybenzylidene)-4-methylbenzenesulfonohydrazide	290.34	11.90	41.00	1		
Aniline	95.126	3.82	41.00	1	0.64	1.02
$NaNO_2$	69.00	2.83	41.00	1		
HCl (37%, 12M)	36.46	4.48	123.00	3	10.2	

Solvent: Pyridine

11.90g (41.00 mmol) of (E)-N'-(4-hydroxybenzylidene)-4-methylbenzenesulfonohydrazide was dissolved in pyridine (100ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (2.83g, 41.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (3.82g, 41.00mmol) and concentrated HCl (4.48g, 123.00mmol) dissolved in 20 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was washed with MeOH to give the pure product (5.18, yield:53%). **Physical aspect**: Solid, white powder **^{1}HNMR** (500 MHz, DMSO) δ 10.16 (s, 1H), 8.19 – 8.10 (m, 2H), 8.06 – 7.97 (m, 2H), 7.75 – 7.66 (m, 2H), 7.66 – 7.58 (m, 2H), 7.02 – 6.92 (m, 1H) **FTIR-ATR** (cm^{-1}): 3127, 3077, 3027, 2817, 2611, 1979, 1887, 1823, 1753, 1678, 1613, 1592, 1548, 1489, 1459, 1436, 1385, 1363, 1317, 1276, 1244, 1236, 1211, 1196, 1174, 1164, 1147, 1103, 1080, 1069, 1031, 1021, 1012, 998, 941, 917, 832, 755, 703, 676, 625, 575 **TGA analysis**: 190 °C

Synthesis of (E)-4-((2-tosylhydrazono)methyl)benzoic acid

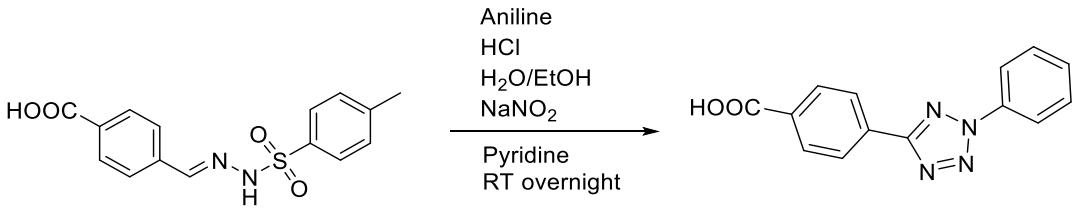


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-formylbenzoic acid	150.13	1.50	9.99	1
p-Toluenesulfonyl hydrazide	186.23	1.86	9.99	1

Solvent: EtOH

1.50g (9.99 mmol) of 4-formylbenzoic acid, 1.85 g (9.99 mmol) of p-Toluenesulfonyl hydrazide and 25 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (3.12g, yield:98%). The product was used for the next step without any further purification. **Physical aspect**: Solid, white powder

Synthesis of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid (compound 3)

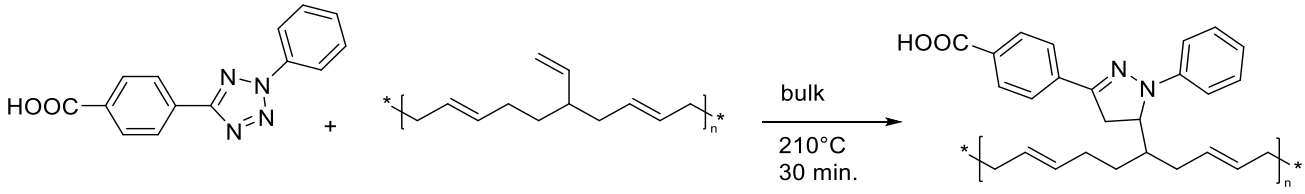


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-4-((2-tosylhydrazono)methyl)benzoic acid	318.35	3.01	9.45	1		
Aniline	95.126	0.68	9.45	1	0.64	1.02
$NaNO_2$	69.00	0.65	9.45	1		
HCl (37%, 12M)	36.46	1.03	28.35	3	2.4	

Solvent: Pyridine

3.01g (9.45mmol) of (E)-4-((2-tosylhydrazono)methyl) benzoic acid was dissolved in pyridine (40ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (0.65g, 9.45mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (0.68g, 9.45mmol) and concentrated HCl (1.03g, 28.35mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was washed with MeOH to give the pure product (1.76g, yield:70%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO): δ 13.35 (s, 1H), 8.34 – 8.27 (m, 2H), 8.23 – 8.13 (m, 4H), 7.73 (tt, *J* = 8.8, 1.8 Hz, 2H), 7.70 – 7.62 (m, 1H) **FTIR-ATR** (cm^{-1}): 3098, 3066, 2923. 2853, 2676, 2593, 2552, 1690, 1617, 1594, 1575, 1557, 1541, 1496, 1460, 1431, 1417, 1392, 1315, 1285, 1215, 1186, 1137, 1124, 1112, 1076, 1014, 995, 920, 869, 844, 815, 798, 785, 759, 736, 690, 679, 558 **TGA analysis**: 210 °C

Thermally functionalized PB oligomer with 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid	266.29	0.07	0.25	1
Polyvest	54.09	1.37	2.50	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

1.37g (0.25mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 67 mg (2.50mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid was added to the reaction mixture and heated at 210°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

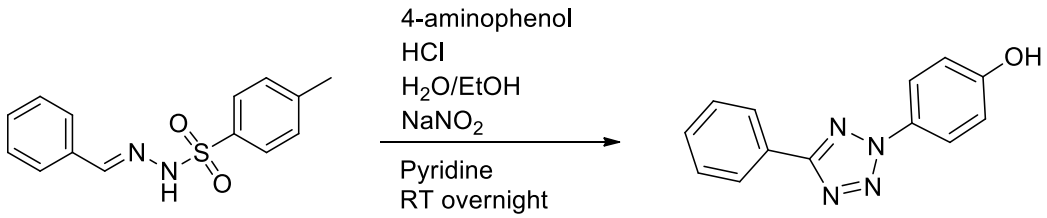
The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of dichloromethane used in dissolving functionalized Polyvest.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’.
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure.

Physical aspect: yellowish viscous liquid

Synthesis of 4-(5-phenyl-2H-tetrazol-2-yl)phenol (compound 4)

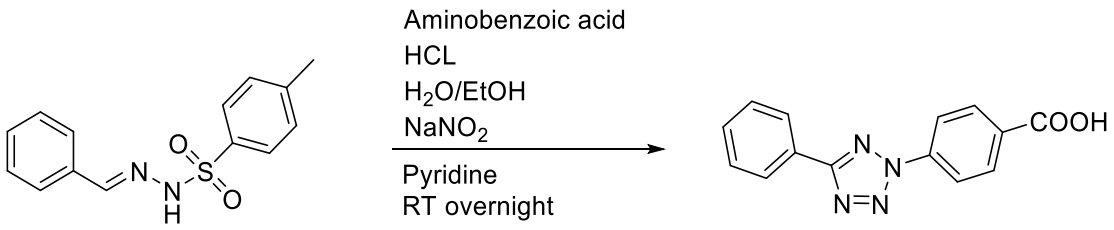


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1	
4-aminophenol	109.13	0.40	3.65	1	
$NaNO_2$	69.00	0.25	3.65	1	
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (40ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of 4-aminophenol (400mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (DCM) to give the pure product (408mg, yield:47%). **Physical aspect**: Solid, purple powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.31 – 8.22 (m, 3H), 7.61 – 7.55 (m, 3H), 7.43 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H), 7.26 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.12 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H) **FTIR-ATR** (cm^{-1}): 3260, 3084, 3047, 2924, 2853, 2627, 1976, 1915, 1825, 1797, 1769, 1711, 1595, 1532, 1496, 1463, 1449, 1401, 1368, 1333, 1317, 1306, 1287, 1262, 1234, 1207, 1155, 1139, 1117, 1071, 1060, 1030, 1013, 1003, 973, 940, 923, 852, 829, 790, 774, 756, 727, 703, 687, 666, 621, 566 **TGA analysis**: 150 °C

Synthesis of 4-(5-phenyl-2H-tetrazol-2-yl)benzoic acid (compound 5)

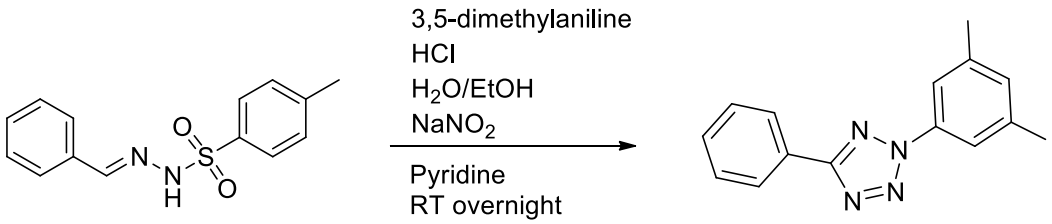


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1	
Aminobenzoic acid	137.14	0.50	3.65	1	
$NaNO_2$	69.00	0.25	3.65	1	
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of Aminobenzoic acid (500mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was crystallized using diisopropyl ether to give the pure product (515mg, yield:53%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 13.37 (s, 1H), 8.34 – 8.30 (m, 2H), 8.26 – 8.23 (m, 2H), 8.22 – 8.19 (m, 2H), 7.67 – 7.61 (m, 3H) **FTIR-ATR** (cm^{-1}): 3113, 3070, 3034, 2984, 2955, 2885, 2845, 2821, 2730, 2675, 2595, 2551, 2165, 2103, 1951, 1897, 1820, 1680, 1605, 1532, 1512, 1488, 1466, 1450, 1432, 1381, 1317, 1292, 1214, 1174, 1133, 1115, 1070, 1018, 991, 937, 863, 812, 783, 770, 725, 682, 609, 559 **TGA analysis**: 180 °C

Synthesis of 2-(3,5-dimethylphenyl)-5-phenyl-2H-tetrazole (compound 6)

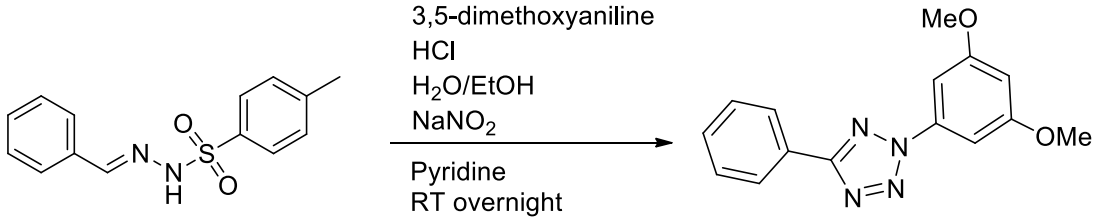


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1	
3,5-dimethylaniline	124.13	0.44	3.65	1	
$NaNO_2$	69.00	0.25	3.65	1	
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of 3,5-dimethylaniline (440mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (DCM) to give the pure product (274mg, yield:30%). **Physical aspect**: Solid, Pale orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.32 – 8.25 (m, 2H), 7.84 (s, 2H), 7.59 – 7.50 (m, 3H), 7.15 (s, 1H), 2.47 (s, 6H) **FTIR-ATR** (cm^{-1}): 3293, 3072, 3034, 2969, 2918, 2854, 2339, 2165, 1965, 1916, 1896, 1824, 1768, 1717, 1657, 1620, 1594, 1564, 1529, 1463, 1447, 1398, 1379, 1362, 1321, 1287, 1210, 1174, 1155, 1132, 1097, 1069, 1038, 1022, 990, 928, 902, 851, 842, 815, 788, 756, 728, 691, 678, 624, 563 **TGA analysis**: 165 °C

Synthesis of 2-(3,5-dimethoxyphenyl)-5-phenyl-2H-tetrazole (compound 7)

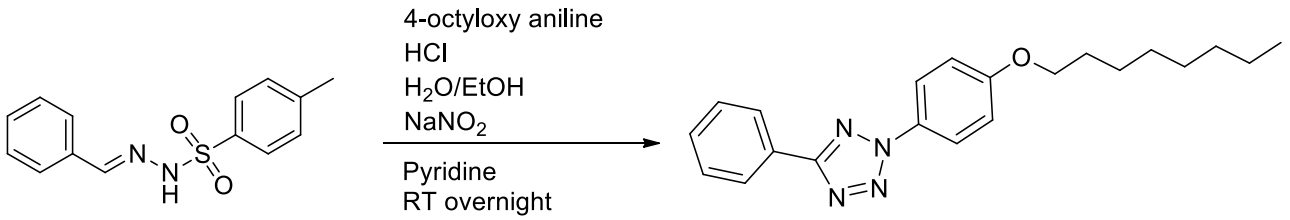


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1	
3,5-dimethoxyaniline	153.18	0.56	3.65	1	
$NaNO_2$	69.00	0.25	3.65	1	
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of 3,5-dimethoxyaniline (560mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (DCM) to give the pure product (422mg, yield:41%). **Physical aspect**: Solid, orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ8.21 – 8.15 (m, 2H), 7.49 – 7.41 (m, 3H), 7.31 (d, *J* = 2.3 Hz, 2H), 6.50 (t, *J* = 2.3 Hz, 1H), 3.83 (s, 6H) **FTIR-ATR** (cm^{-1}): 3124, 3077, 3032, 3010, 2974, 2947, 2929, 2848, 2589, 2314, 2050, 1977, 1955, 1901, 1825, 1762, 1627, 1615, 1596, 1530, 1489, 1481, 1465, 1445, 1431, 1386, 1365, 1331, 1276, 1203, 1179, 1158, 1086, 1063, 1044, 1029, 1019, 1000, 928, 832, 813, 791, 727, 691, 670, 636, 613, 594, 580, 574, 552 **TGA analysis**: 160 °C

Synthesis of 2-(4-(octyloxy)phenyl)-5-phenyl-2H-tetrazole (compound 8)

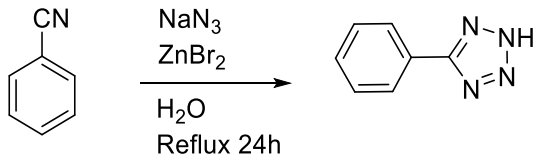


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-benzylidene-4-methylbenzenesulfonohydrazide	274.34	1.00	3.65	1	
4-octyloxy aniline	221.34	0.80	3.65	1	
$NaNO_2$	69.00	0.25	3.65	1	
HCl (37%, 12M)	36.46	0.40	10.95	3	0.91

Solvent: Pyridine

1.00g (3.65 mmol) of (E)-N'-benzylidene-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (250mg, 3.65 mmol) in water was added dropwise to a cooled (0°C) mixture of 4-octyloxy aniline (800mg, 3.65 mmol) and concentrated HCl (400mg, 10.95 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (Hexane/ACOEt 9:1) to give the pure product (511mg, yield:40%). **Physical aspect**: Solid, red powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.17 (ddd, *J* = 5.7, 4.1, 2.3 Hz, 2H), 8.02 (d, 2H), 7.50 – 7.39 (m, 3H), 6.97 (d, 2H), 3.96 (t, *J* = 6.6 Hz, 2H), 1.80 – 1.70 (m, 2H), 1.46 – 1.36 (m, 2H), 1.35 – 1.16 (m, 8H), 0.82 (t, *J* = 6.9 Hz, 3H) **FTIR-ATR** (cm^{-1}): 3072, 3034, 2962, 2940, 2918, 2867, 2852, 1893, 1609, 1603, 1597, 1529, 1513, 1466, 1449, 1395, 1378, 1368, 1307, 1264, 1212, 1179, 1132, 1113, 1074, 1043, 1021, 998, 921, 891, 872, 833, 812, 801, 783, 761, 722, 705, 689, 661, 630, 571 **TGA analysis**: 180 °C

Synthesis of 5-phenyl-2H-tetrazole

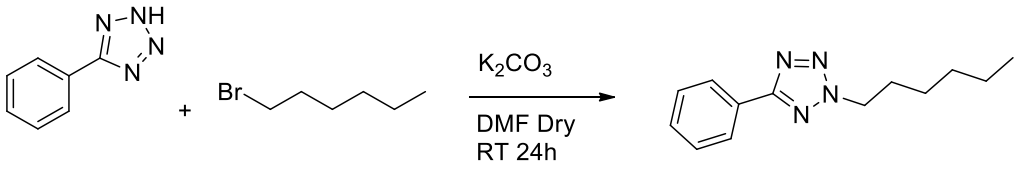


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
benzonitrile	103.12	2.50	24.00	1	2.48	1.01
Sodium azide	65.01	1.73	24.00	1		
Zinc Bromide	225.19	5.46	24.00	1		

Solvent: H_2O

2.5g (24.00 mmol) of benzonitrile, 1.73 (24.00 mmol) of Sodium azide, 5.46g (24.00 mmol) of Zinc Bromide and 50ml of H_2O were added to a round bottom flask equipped with a water condenser. The mixture was heated at reflux under magnetic stirring for 24 hours (a white precipitate forms). Afterwards 30 ml of HCl (3M) were added, until pH=1. The mixture was extracted with ethyl acetate (3X 30 ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give a white powder. The compound was dissolved in 200ml of NaOH (0.25M). The zinc salts formed were filtered. The aqueous phase was acidified with HCl (3M) to precipitate the product which was filtered in a buchner (2.64g, yield: 76%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 8.08 – 8.04 (m, 2H), 7.64 – 7.57 (m, 3H) **FTIR-ATR** (cm^{-1}): 3130, 3056, 2980, 2905, 2834, 2794, 2763, 2684, 2649, 2601, 2543, 2480, 2450, 1898, 1857, 1824, 1765, 1713, 1609, 1563, 1485, 1466, 1439, 1409, 1288, 1256, 1084, 1055, 1035, 1015, 989, 956, 925, 840, 790, 784, 725, 703, 685

Synthesis of 2-hexyl-5-phenyl-2H-tetrazole (compound 9)

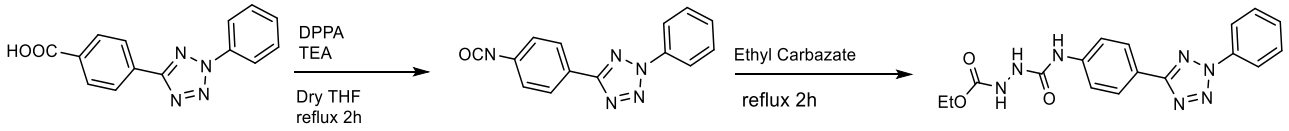


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-phenyl-2H-tetrazole	146.15	0.200	1.37	1		
1-bromoesane	165.08	0.225	1.37	1	0.19	1.17
Potassium carbonate	138.21	0.208	1.50	1.2		

Solvent: Dry DMF

200mg (1.37 mmol) of 5-phenyl-2H-tetrazole and 5ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 208mg (1.50 mmol) of Potassium carbonate were added and, after 10 min. 225mg (1.37mmol) of 1-bromoesane were added. The reaction mixture was stirred for 24 hours. The mixture was extracted with ethyl acetate (2X 10ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (283mg, yield:90%). **Physical aspect**: colorless oil **^{1}HNMR** (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.51 – 7.42 (m, 3H), 1.33 (ddd, *J* = 12.2, 7.3, 4.1 Hz, 10H), 0.87 (t, *J* = 7.0 Hz, 3H) **TGA analysis**: undetectable, the compound isn't stable and decomposes during the analysis at T>150 °C.

Synthesis of ethyl 2-((4-(2-phenyl-2H-tetrazol-5-yl)phenyl)carbamoyl)hydrazinecarboxylate

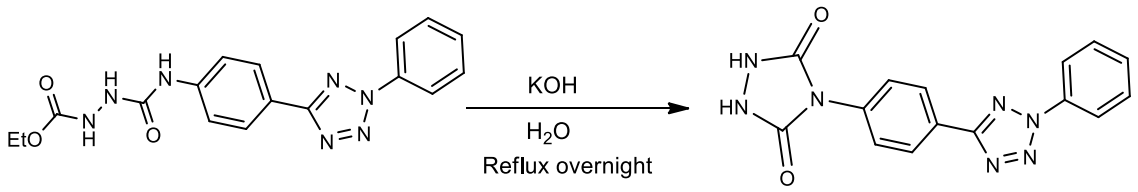


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid	266.25	0.20	0.75	1		
Diphenylphosphoryl azide	275.20	0.23	0.83	1.1	0.18	1.28
Triethylamine	101.19	0.08	0.83	1.1	0.11	0.73
Ethyl Carbazate	104.11	0.07	0.75	1	2.4	

Solvent: Dry THF

200mg (0.75 mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid and 25 ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. The reaction mixture was cooled at 0°C, then 230mg (0.83mmol) of DPPA were added and, after 10 min., 80 mg (0.83mmol) of TEA were added. The reaction mixture was heated at reflux under magnetic stirring for 2 hours. Afterwards 70mg (0.75mmol) of ethyl carbazate was added dropwise and the reaction mixture was heated for and additional 2h at reflux. The solvent was evaporated under reduced pressure. The reaction mixture was extracted 3 times with ethyl acetate, then washed with $NaHCO_3$ (aq.), H_2O an HCl (1M). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the desired compound (209mg, yield:76%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of ethyl 4-(4-(2-phenyl-2H-tetrazol-5-yl)phenyl)-1,2,4-triazolidine-3,5-dione (compound 10)

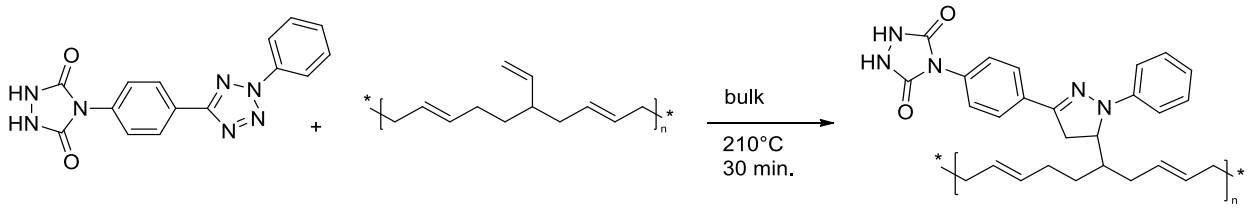


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	[C]
2-((4-(2-phenyl-2H-tetrazol-5-yl)phenyl)carbamoyl)hydrazinecarboxylate	367.36	0.1	0.27	1	
KOH	56.11			1.1	5M

Solvent: H_2O

100mg (0.27 mmol) of 2-((4-(2-phenyl-2H-tetrazol-5-yl)phenyl)carbamoyl)hydrazinecarboxylate and 10 ml of KOH solution (5M) were added to a round bottom flask equipped with a water condenser. The reaction mixture heated at reflux overnight, under magnetic stirring. The reaction mixture was allowed to cool down to room temperature, then HCl was added until pH=2. The precipitate formed was filtered to obtain the product (86mg, 99% yield). **Physical aspect**: Solid, white powder. Since the product was insoluble in the common deuterated solvent it was formed the corresponding sodium salt (1 eq. of Na_2CO_3). **^{1}HNMR** (400 MHz, D_2O) δ 8.32 – 8.29 (m, 2H), 8.17 – 8.13 (m, 1H), 7.70 – 7.63 (m, 4H), 7.59 – 7.56 (m, 2H) **TGA analysis**: 200 °C

Thermally functionalized PB oligomer with 4-(4-(2-phenyl-2H-tetrazol-5-yl)phenyl)-1,2,4-triazolidine-3,5-dione

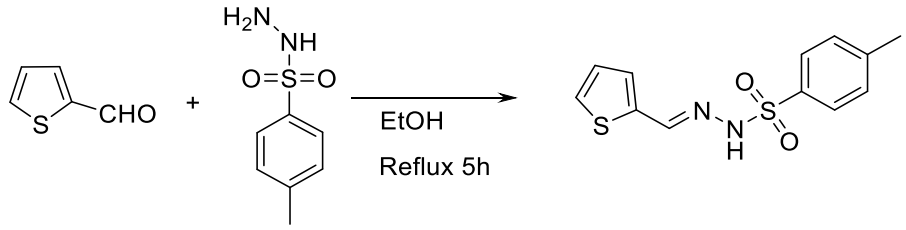


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-(4-(2-phenyl-2H-tetrazol-5-yl)phenyl)-1,2,4-triazolidine-3,5-dione	228.27	0.01	0.03	1
Polyvest	54.09	0.17	3.11	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

170mg (3.11 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 10 mg (0.03mmol) of 4-(4-(2-phenyl-2H-tetrazol-5-yl)phenyl)-1,2,4-triazolidine-3,5-dione was added to the reaction mixture and heated at 210°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence. It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. The 4-(4-(2-phenyl-2H-tetrazol-5-yl)phenyl)-1,2,4-triazolidine-3,5-dione attached to the polymer forms hydrogen bonds that can crosslink the polymer matrix. **Physical aspect**: orange gelatin

Synthesis of (E)-4-methyl-N'-(thiophen-2-ylmethylene)benzenesulfonohydrazide

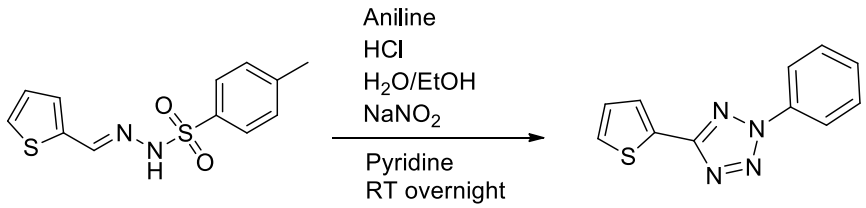


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
2-Thiophenecarboxaldehyde	112.15	1.00	8.92	1
p-Toluenesulfonyl hydrazide	186.23	1.66	8.92	1

Solvent: EtOH

1.00g (8.92 mmol) of 2-Thiophenecarboxaldehyde, 1.66 g (8.92 mmol) of p-Toluenesulfonyl hydrazide and 25 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (2.4g, yield:96%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of 2-phenyl-5-(thiophen-2-yl)-2H-tetrazole (compound 11)

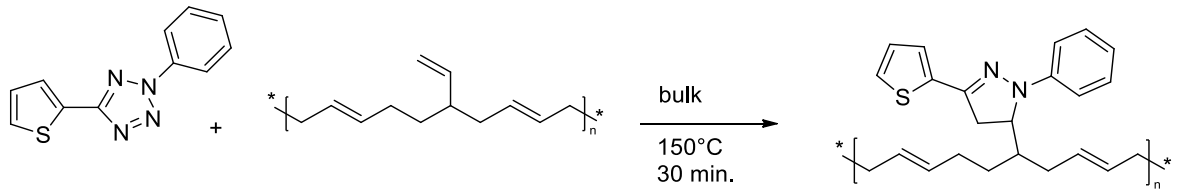


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-4-methyl-N'-(thiophen-2-ylmethylene)benzenesulfonohydrazide	280.36	2.30	8.20	1		
Aniline	95.126	0.76	8.20	1	0.74	1.02
$NaNO_2$	69.00	0.57	8.20	1		
HCl (37%, 12M)	36.46	0.89	24.60	3	2	

Solvent: Pyridine

2.30g (8.20 mmol) of (E)-4-methyl-N'-(thiophen-2-ylmethylene)benzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (0.57g, 8.20 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (0.76g, 8.20 mmol) and concentrated HCl (0.89g, 24.60mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (50% hexane 50% DCM) to provide the desired compound (1.03g, yield:55%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.24 – 8.18 (m, 2H), 7.94 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.56 – 7.50 (m, 2H), 7.25 – 7.20 (m, 1H) **FTIR-ATR** (cm^{-1}): 3304, 3194, 3106, 3068, 2920, 2855, 1965, 1813, 1745, 1674, 1596, 1572, 1494, 1464, 1410, 1365, 1340, 1302, 1263, 1227, 1206, 1162, 1117, 1090, 1067, 1040, 1003, 963, 920, 849, 812, 761, 746, 702, 674, 664, 580 **TGA analysis**: 150 °C

Thermally functionalized PB oligomer with 2-phenyl-5-(thiophen-2-yl)-2H-tetrazole



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
2-phenyl-5-(thiophen-2-yl)-2H-tetrazole	228.27	0.04	0.16	1
Polyvest	54.09	0.12	1.6	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

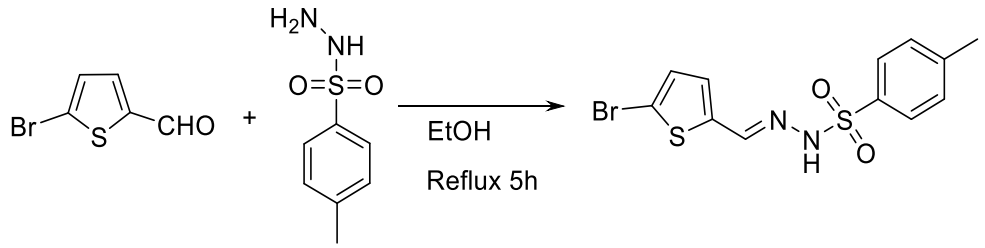
120mg (1.6mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 40 mg (0.16mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid was added to the reaction mixture and heated at 150°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.After washing procedure, the sample was collected and dried under reduced pressure.

Physical aspect: yellowish viscous liquid

Synthesis of (E)-N'-((5-bromothiophen-2-yl)methylene)-4-methylbenzenesulfonohydrazide

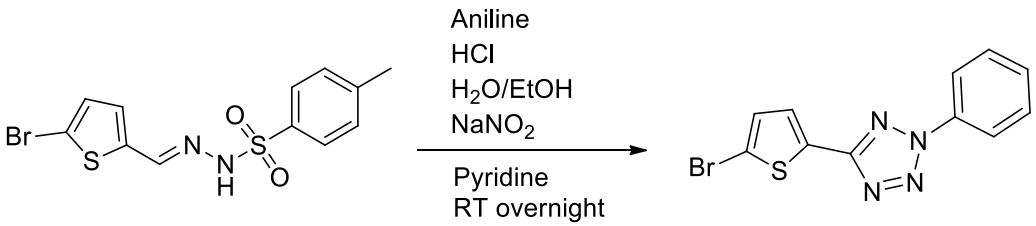


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-bromothiophene-2-carbaldehyde	191.05	2	10.5	1
p-Toluenesulfonyl hydrazide	186.23	1.95	10.5	1

Solvent: EtOH

2g (10.5 mmol) of 5-bromothiophene-2-carbaldehyde, 1.95 g (10.5mmol) of p-Toluenesulfonyl hydrazide and 35 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (2.9g, yield:77%). The product was used for the next step without any further purification. **Physical aspect**: Solid, pale yellow powder

Synthesis of 5-(5-bromothiophen-2-yl)-2-phenyl-2H-tetrazole (compound 12)

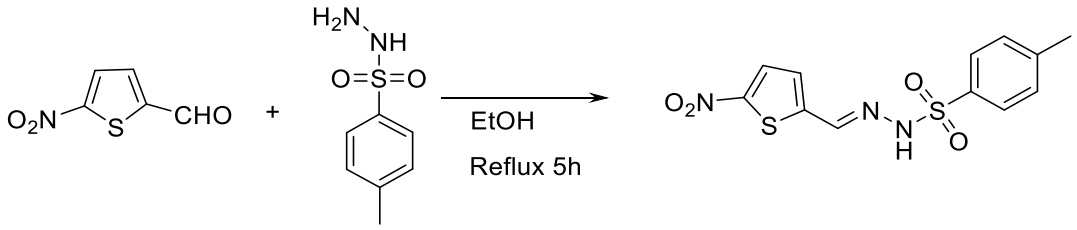


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-N'-((5-bromothiophen-2-yl)methylene)-4-methylbenzenesulfonohydrazide	360.36	2.90	8.10	1		
Aniline	95.126	0.76	8.10	1	0.74	1.02
$NaNO_2$	69.00	0.56	8.10	1		
HCl (37%, 12M)	36.46	0.89	24.30	3	2	

Solvent: Pyridine

2.90g (8.10 mmol) of (E)-N'-((5-bromothiophen-2-yl)methylene)-4-methylbenzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (0.56g, 8.10mmol)in water was added dropwise to a cooled (0°C) mixture of aniline (0.76g,8.10mmol) and concentrated HCl (0.89g, 24.30mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (50% hexane 50% DCM) to provide the desired compound (1.30, yield:53%). **Physical aspect**: Solid, pale yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.19 – 8.14 (m, 2H), 7.66 – 7.65 (m, 1H), 7.60 – 7.55 (m, 2H), 7.54 – 7.49 (m, 1H), 7.15 (d, J = 3.9 Hz, 1H) **FTIR-ATR** (cm^{-1}): 3144, 3107, 3091, 3066, 3049, 3027, 2535, 2171, 2048, 1978, 1956, 1881, 1771, 1750, 1717, 1692, 1596, 1574, 1496, 1478, 1464, 1408, 1376, 1296, 1215, 1200, 1176, 1108, 1068, 1056, 1003, 981, 948, 910, 885, 799, 760, 743, 704, 690, 674, 667, 615 **TGA analysis**: 150 °C

Synthesis of (E)-4-methyl-N'-((5-nitrothiophen-2-yl)methylene)benzenesulfonohydrazide

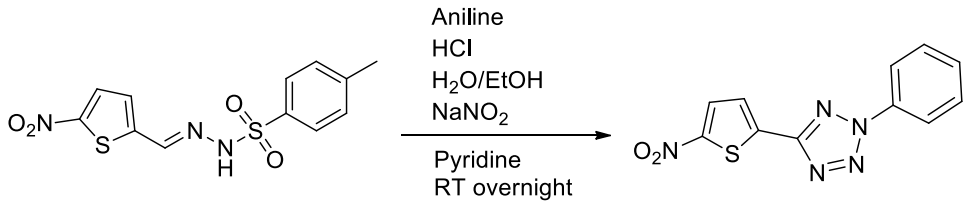


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-nitrothiophene-2-carbaldehyde	157.15	2	12.73	1
p-Toluenesulfonyl hydrazide	186.23	2.37	12.73	1

Solvent: EtOH

2g (12.73 mmol) of 5-nitrothiophene-2-carbaldehyde, 2.37g (12.73 mmol) of p-Toluenesulfonyl hydrazide and 50 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (3.7g, yield:89%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of 5-(5-nitrothiophen-2-yl)-2-phenyl-2H-tetrazole

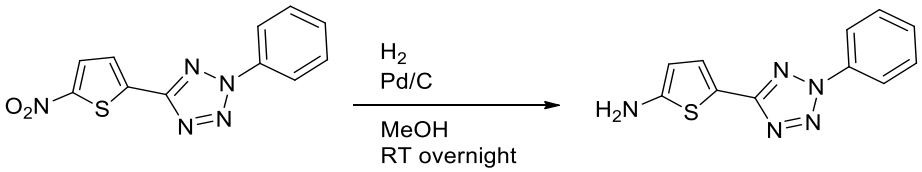


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-4-methyl-N'-((5-nitrothiophen-2-yl)methylene)benzenesulfonohydrazide	327.38	2.8	8.55	1		
Aniline	95.126	0.80	8.55	1	0.78	1.02
$NaNO_2$	69.00	0.59	8.55	1		
HCl (37%, 12M)	36.46	0.93	25.65	3	2	

Solvent: Pyridine

2.80g (8.55 mmol) of (E)-4-methyl-N'-((5-nitrothiophen-2-yl)methylene)benzenesulfonohydrazide was dissolved in pyridine (60ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (0.59g, 8.55 mmol)in water was added dropwise to a cooled (0°C) mixture of aniline (0.76g,8.10mmol) and concentrated HCl (0.93g, 26.65 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel.The crude product was crystallized with diisopropyl ether to provide the desired compound (1.30, yield:55%). **Physical aspect**: Solid, pale orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.21 – 8.17 (m, 2H), 7.99 (d, J = 4.3 Hz, 1H), 7.84 (d, J = 4.3 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.58 – 7.53 (m, 1H) **FTIR-ATR** (cm^{-1}): 3250, 3217, 3107, 1594, 1569, 1518, 1489, 1466, 1414, 1383, 1334, 1293, 1225, 1212, 1163, 1123, 1090, 1072, 1034, 1010, 966, 931, 912, 828, 816, 780, 759, 745, 730, 700, 680, 669

Synthesis of 5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-amine (compound 13)

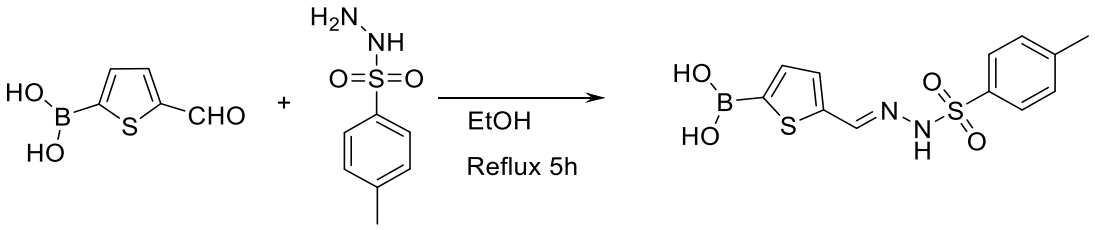


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-(5-nitrothiophen-2-yl)-2-phenyl-2H-tetrazole	273.27	0.20	0.73	1
Pd/C		7		Cat.

Solvent: MeOH

200mg (0.20 mmol) of 5-(5-nitrothiophen-2-yl)-2-phenyl-2H-tetrazole and 30 ml of MeOH were added to a round bottom flask under nitrogen atmosphere. Afterwards 7mg (catalytic amount) of Pd/C were added and after H_2 was poured into the flask. The reaction mixture was stirred overnight. Afterwards the mixture was filtered in a funnel with a pad of Celite to remove de catalyst. Then the solvent was evaporated under reduced pressure to give the desired product (175mg, yield:98%). **Physical aspect**: Solid, brown powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.17 – 8.11 (m, 2H), 7.58 – 7.51 (m, 3H), 7.49 – 7.47 (m, 1H), 6.22 (d, J = 3.8 Hz, 1H), 4.11 (s, 2H) **FTIR-ATR** (cm^{-1}): 3419, 3309, 3193, 3076, 2935,2832, 2543, 2194, 2159, 2015, 1968, 1889, 1841, 1748, 1582, 1494, 1464, 1447, 1381, 1350, 1312, 1296, 1260, 1229, 1203, 1185, 1116, 1070, 1036, 1000, 953, 913, 872, 832, 758, 741, 701, 688, 671, 599, 571 **TGA Analysis**: 165 °C

Synthesis of (E)-(5-((2-tosylhydrazono)methyl)thiophen-2-yl)boronic acid

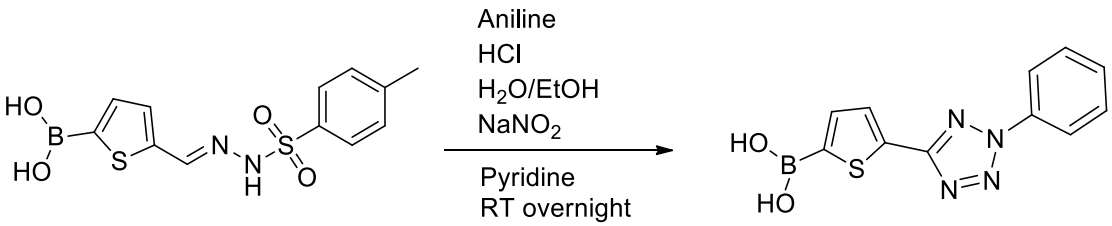


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
(5-formylthiophen-2-yl)boronic acid	155.97	0.50	3.21	1
p-Toluenesulfonyl hydrazide	186.23	0.58	3.21	1

Solvent: EtOH

500mg (3.21 mmol) of (5-formylthiophen-2-yl)boronic acid, 580 mg (3.21 mmol) of p-Toluenesulfonyl hydrazide and 20 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (1.04g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, dark yellow powder

Synthesis of (5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)boronic acid (compound 14)

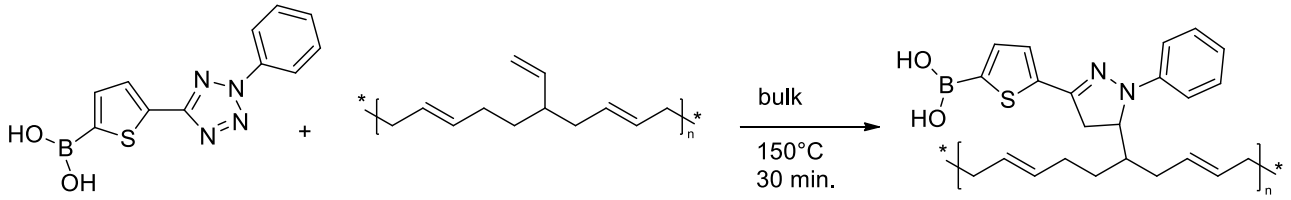


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-(5-((2-tosylhydrazono)methyl)thiophen-2-yl)boronic acid	324.18	0.74	2.28	1		
Aniline	95.126	0.21	2.28	1	0.21	1.02
$NaNO_2$	69.00	0.16	2.28	1		
HCl (37%, 12M)	36.46	0.25	6.84	3	0.6	

Solvent: Pyridine

740mg (2.28 mmol) of (E)-(5-((2-tosylhydrazono)methyl)thiophen-2-yl)boronic acid was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (0.21g, 2.28 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (0.16g, 2.28mmol) and concentrated HCl (0.25g, 6.84mmol) dissolved in 7 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was washed with dichloromethane to provide the desired compound (285mg, yield:46%). **Physical aspect**: Solid, pale orange powder **^{1}HNMR** (400 MHz, DMSO) δ 8.51 (s, 2H), 8.14 (ddd, J = 3.8, 3.3, 2.0 Hz, 2H), 7.93 (dd, J = 3.6, 2.2 Hz, 1H), 7.78 (d, J = 3.6 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.67 – 7.60 (m, 1H) **FTIR-ATR** (cm^{-1}): 3334, 3070, 1874, 1791, 1595, 1566, 1492, 1466, 1421, 1398, 1379, 1328, 1284, 1224, 1207, 1187, 1121, 1057, 1008, 983, 963, 913, 828, 809, 773, 747, 705, 676, 648, 620, 571 **TGA analysis**: 140 °C

Thermally functionalized PB oligomer with (5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)boronic acid



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)boronic acid	228.27	0.01	0.04	1
Polyvest	54.09	0.200	4.0	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

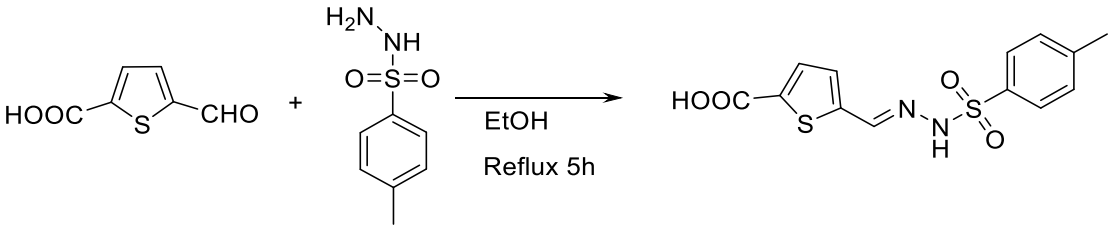
200mg (4.0 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 10 mg (0.04mmol) of (5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)boronic acid was added to the reaction mixture and heated at 150°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure. **Physical aspect**: dark yellow/brown viscous liquid

Synthesis of (E)-5-((2-tosylhydrazono)methyl)thiophene-2-carboxylic acid

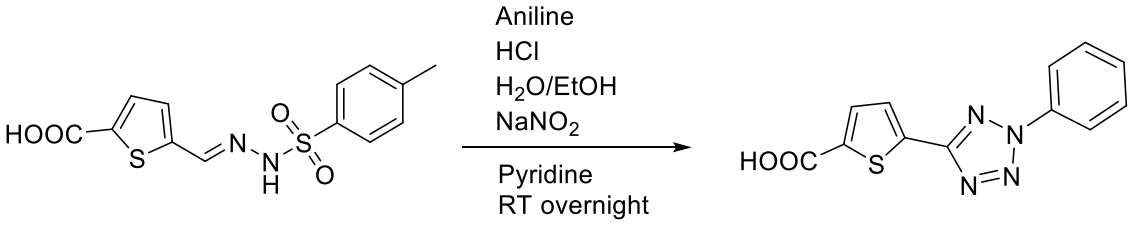


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-formylthiophene-2-carboxylic acid	156.16	2.5	16.00	1
p-Toluenesulfonyl hydrazide	186.23	2.98	16.00	1

Solvent: EtOH

2.5g (16.00 mmol) of 5-formylthiophene-2-carboxylic acid, 2.98g (16.00 mmol) of p-Toluenesulfonyl hydrazide and 70 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (5.19g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylic acid (compound 15)



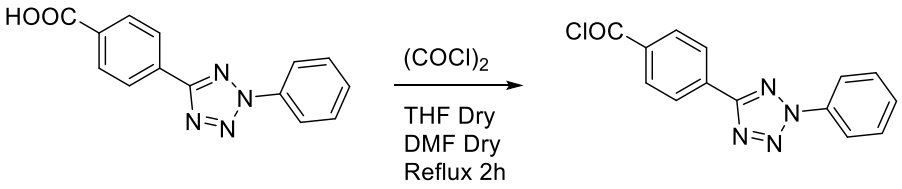
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-5-((2-tosylhydrazono)methyl)thiophene-2-carboxylic acid	324.38	5.19	16.00	1		
Aniline	95.126	1.49	16.00	1	0.74	1.02
$NaNO_2$	69.00	1.10	16.00	1		
HCl (37%, 12M)	36.46	1.75	48.00	3	4.00	

Solvent: Pyridine

5.19g (16.00 mmol) of (E)-5-((2-tosylhydrazono)methyl)thiophene-2-carboxylic acid was dissolved in pyridine (70ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (1.10g, 16.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (1.49g, 16.00 mmol) and concentrated HCl (1.75g, 48.00 mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified adding K_2CO_3 and forming the salt, then the impurities were extracted with DCM (2X 40ml). The aqueous phase was acidified with HCl to precipitate the pure product (1.03, yield:55%). **Physical aspect**: Solid, pale pink powder **^{1}HNMR** (400 MHz, DMSO) δ 8.15 (d, *J* = 7.8 Hz, 2H), 7.93 (d, *J* = 3.9 Hz, 1H), 7.84 (d, *J* = 3.9 Hz, 1H), 7.72 (dd, *J* = 10.2, 4.9 Hz, 2H), 7.65 (dd, *J* = 8.4, 6.2 Hz, 1H) **FTIR-ATR** (cm^{-1}): 3086, 2974, 2866, 2678, 1548, 2328, 2163, 2050, 1868, 1842, 1680, 1653, 1596, 1567, 1515, 1494, 1466, 1436, 1409, 1382, 1305, 1288, 1269, 1228, 1207, 1155, 1125, 1104, 1072, 1043, 1006, 968, 932, 913, 839, 754, 751, 701, 676, 620, 585 **TGA analysis**: 175 °C

Chapter 3

Synthesis of 4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride

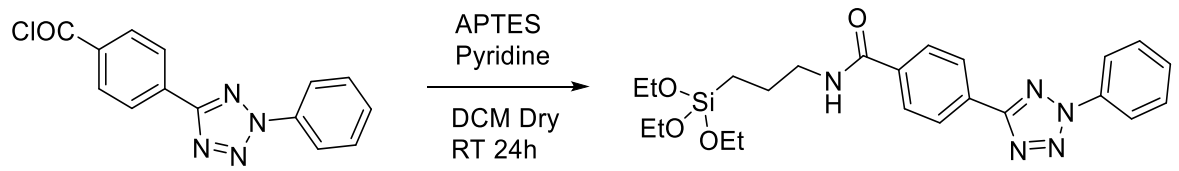


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid	266.25	0.10	0.38	1		
Oxalyl chloride	126.93	0.09	0.76	2	0.06	1.48
Dry DMF	73.10				2 drops	

Solvent: Dry THF

100mg (0.38 mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid and 10ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. After 2 drops of Dry DMF were added and then 90mg (0.76mmol) of oxalyl chloride were added. The reaction mixture was heated at reflux under magnetic stirring for 2 hours. The proceeding of the reaction was monitored using IR (C=O band shifts). The solvent was evaporated washing with DCM to remove the excess of oxalyl chloride to give the compound (105mg, yield:97%). The product was used for the next step without any further purification. **Physical aspect**: Solid, orange powder **FTIR-ATR** (cm^{-1}): 3086, 2955, 2926, 2854, 2792, 1974, 1951, 1770, 1733, 1693, 1663, 1613, 1597, 1535, 1495, 1470, 1459, 1419, 1371, 1318, 1286, 1217, 1202, 1178, 1133, 1076, 1019, 997, 882, 855, 753, 720, 692, 677, 645, 634

Synthesis of 4-(2-phenyl-2H-tetrazol-5-yl)-N-(3-(triethoxysilyl)propyl)benzamide (compound 1)

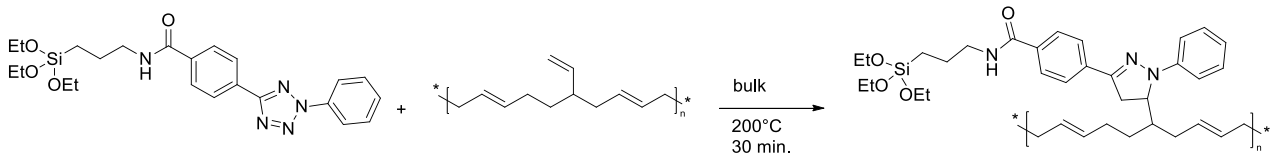


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride	284.70	0.11	0.38	1		
(3-Aminopropyl)triethoxysilane	221.37	0.79	0.36	0.95	0.08	0.95
Pyridine	79.10	0.30	0.38	1	0.03	0.98

Solvent: Dry DCM

110mg (0.38 mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride and 15 ml of Dry DCM were added to a round bottom flask under nitrogen atmosphere. After 30mg (0.38 mmol) of Pyridine were added and, after 10 min. 79mg (0.36mmol) of APTES were added. The reaction mixture was stirred for 24 hours. Afterwards the solvent was removed under reduced pressure and the crude was washed with dichloromethane to give the desired product (140mg, yield:83%). **Physical aspect**: Solid, brown powder **^{1}HNMR** (400 MHz, $CDCl_3$) 8.32 (d, *J* = 8.4 Hz, 2H), 8.21 (d, *J* = 7.3 Hz, 2H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.59 (dd, *J* = 8.5, 6.7 Hz, 2H), 7.55 – 7.47 (m, 1H), 6.69 (d, *J* = 6.1 Hz, 1H), 3.84 (q, *J* = 7.0 Hz, 6H), 3.51 (q, *J* = 6.6 Hz, 2H), 1.86 – 1.73 (m, 2H), 1.23 (t, *J* = 7.0 Hz, 9H), 0.80 – 0.69 (m, 2H). **FTIR-ATR** (cm^{-1}): 3401, 3044, 2921, 2897, 2718, 2271, 2071, 1634, 1597, 1549, 1496, 1461, 1379, 1305, 1283, 1213, 1203, 1099, 1028, 1012, 996, 948, 913, 863, 839, 796, 757, 744, 692, 680 **TGA analysis**: 190 °C

Thermally functionalized PB oligomer with 4-(2-phenyl-2H-tetrazol-5-yl)-N-(3-(triethoxysilyl)propyl)benzamide



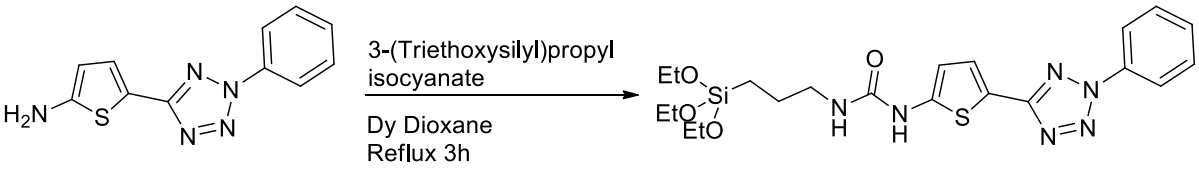
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-(2-phenyl-2H-tetrazol-5-yl)-N-(3-(triethoxysilyl)propyl)benzamide	469.61	0.15	0.03	1
Polyvest	57.09	0.18	3.00	100
Polyvest vinyl double bonds	57.09			1

No Solvent: Bulk

180mg (3.00mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 15 mg (0.03mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)-N-(3-(triethoxysilyl)propyl)benzamide was added to the reaction mixture and heated at 200°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. Probably the silanols groups, after thermal treatment, form a network that can cross-link the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(triethoxysilyl)propyl)urea (compound 2)

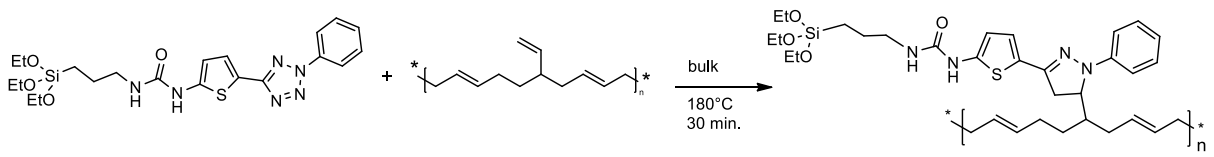


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-amine	243.29	0.170	0.70	1		
3-(Triethoxysilyl)propyl isocyanate	247.37	0.172	0.70	1	0.17	0.99

Solvent: Dry Dioxane

170mg (0.70 mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-amine and 15 ml of Dry Dioxane were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. Afterwards 172mg (0.70 mmol) of 3-(Triethoxysilyl)propyl isocyanate were added and the reaction mixture was heated at reflux for 3 hours, under magnetic stirring. Afterwards the solvent was evaporated under reduced pressure to give the desired product (325mg, yield:94%). **Physical aspect**: brown oil **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.16 – 8.10 (m, 2H), 7.69 (s, 1H), 7.63 (d, J = 4.0 Hz, 1H), 7.54 (ddd, J = 8.0, 4.6, 1.3 Hz, 2H), 7.47 (dt, J = 9.5, 4.3 Hz, 1H), 6.56 (d, J = 4.0 Hz, 1H), 3.86 – 3.77 (m, 6H), 3.30 (dt, J = 16.0, 8.0 Hz, 2H), 1.74 – 1.64 (m, 2H), 1.26 – 1.18 (m, 9H), 0.70 – 0.63 (m, 2H) **FTIR-ATR** (cm^{-1}): 3330, 2973, 2926, 2884, 1695, 1642, 1582, 1543, 1501, 1467, 1445, 1389, 1367, 1274, 1241, 1192, 1166, 1102, 1079, 1001, 957, 874, 791, 760, 702, 678 **TGA Analysis**: 170 °C

Thermally functionalized PB oligomer with 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(triethoxysilyl)propyl)urea



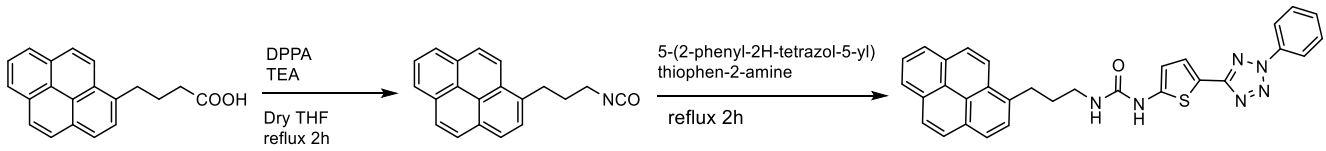
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(triethoxysilyl)propyl)urea	490.65	0.025	0.05	1
Polyvest	54.09	0.140	5.00	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

140mg (5.00mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 25 mg (0.05mmol) 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(triethoxysilyl)propyl)urea was added to the reaction mixture and heated at 180°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. Probably the silanols groups, after thermal treatment, form a network that can crosslink the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(pyren-1-yl)propyl)urea (compound 3)

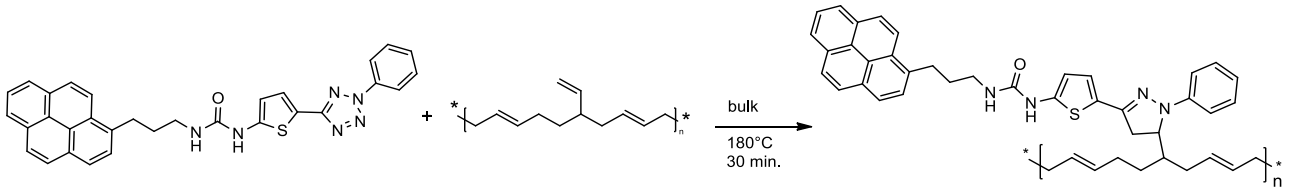


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
1-Pyrenebutyric acid	288.34	0.474	1.64	1		
Diphenylphosphoryl azide	275.20	0.497	1.81	1.1	0.39	1.28
Triethylamine	101.19	0.183	1.81	1.1	0.25	0.73
5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-amine	243.29	1.644	1.64	1		

Solvent: Dry THF

474 mg (1.64 mmol) of 1-Pyrenebutyric acid and 25 ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. The reaction mixture was cooled at 0°C, then 497mg (1.81mmol) of DPPA were added and, after 10 min. 181 mg (1.81mmol) of TEA were added. The reaction mixture was heated at reflux under magnetic stirring for 2 hours. Afterwards 1.64g (1.64mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-amine was added dropwise and the reaction mixture was heated for and additional 2h at reflux. The solvent was evaporated under reduced pressure. The reaction mixture was extracted 3 times with ethyl acetate, then washed with $NaHCO_3$ (aq.), H_2O an HCl (1M). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude compound was extracted with a Soxhlet using ethyl acetate to give the desired compound (480mg, yield:55%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 10.02 (s, 1H), 8.15 (d, J = 2.8 Hz, 1H), 8.12 (t, J = 1.7 Hz, 4H), 8.10 (dd, J = 1.6, 0.9 Hz, 1H), 8.07 (t, J = 7.6 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 4.0 Hz, 1H), 6.77 – 6.61 (m, 1H), 6.57 (d, J = 4.0 Hz, 1H), 3.44 – 3.36 (m, 2H), 2.08 – 1.96 (m, 2H). **FTIR-ATR** (cm^{-1}): 3310, 3277, 3039, 2936, 2869, 2324, 2167, 1786, 1735, 1689, 1635, 1586, 1560, 1532, 1497, 1466, 1435, 1373, 1261, 1243, 1209, 1180, 1092, 1068, 1041, 1003, 960, 914, 839, 805, 755, 744, 703, 675, 619 **TGA Analysis**: 180 °C

Thermally functionalized PB oligomer with 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(pyren-1-yl)propyl)urea



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(pyren-1-yl)propyl)urea	530.64	0.015	0.243	1
Polyvest	54.09	0.130	2.43	100
Polyvest vinyl double bonds	54.09			1

No Solvent: Bulk

130mg (2.43 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 15 mg (0.243mmol) of 1-(5-(2-phenyl-2H-tetrazol-5-yl)thiophen-2-yl)-3-(3-(pyren-1-yl)propyl)urea was added to the reaction mixture and heated at 180°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

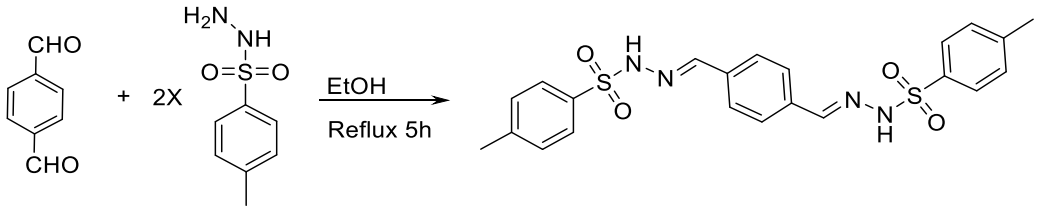
The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure. **Physical aspect**: dark yellow/brown viscous liquid

Chapter 4

Synthesis of (N',N''E,N',N''E)-N',N''-(1,4-phenylenebis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)

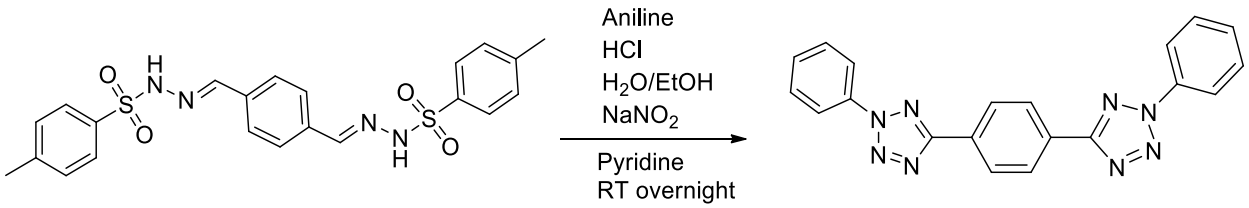


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
terephthalaldehyde	134.13	1.00	7.50	1
p-Toluenesulfonyl hydrazide	186.23	2.92	15.00	2

Solvent: EtOH

1.0g (7.50 mmol) of terephthalaldehyde, 2.92 g (15.00 mmol) of p-Toluenesulfonyl hydrazide and 35 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours.The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (3.30g, yield:94%). The product was used for the next step without any further purification. **Physical aspect**: Solid, white powder

Synthesis of 1,4-bis(2-phenyl-2H-tetrazol-5-yl)benzene (compound 1)

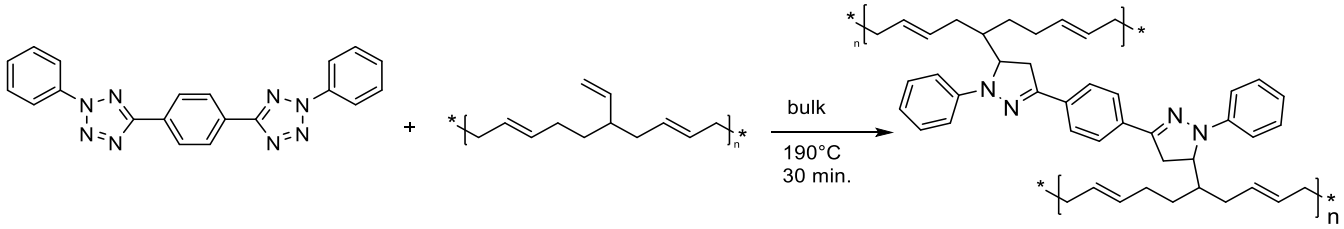


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(N',N''E,N',N''E)-N',N''-(1,4-phenylenebis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)	470.56	1.00	2.13	1		
Aniline	93.126	0.396	4.26	2	0.64	1.02
$NaNO_2$	69.00	0.293	4.26	2		
HCl (37%, 12M)	36.46	0.466	12.78	6	1.06	

Solvent: Pyridine

1.0g (2.13mmol) of (N',N''E,N',N''E)-N',N''-(1,4-phenylenebis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (293mg, 4.26 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (396mg, 4.26mmol) and concentrated HCl (466mg, 12.78 mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was crystallized using ethyl acetate to give the pure product (428mg, yield:55%) **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.44 (s, 4H), 8.26 – 8.22 (m, 4H), 7.64 – 7.58 (m, 4H), 7.57 – 7.50 (m, 2H). **FTIR-ATR** (cm^{-1}): 3191, 1596, 1560, 1492, 1471, 1450, 1425, 1361, 1322, 1300, 1277, 1213, 1187, 1165, 1093, 1053, 1011, 994, 954, 913, 854, 835, 811, 759, 739, 702, 677,571, 553 **TGA analysis**: 185 °C

Thermally functionalized PB oligomer with 1,4-bis(2-phenyl-2H-tetrazol-5-yl)benzene

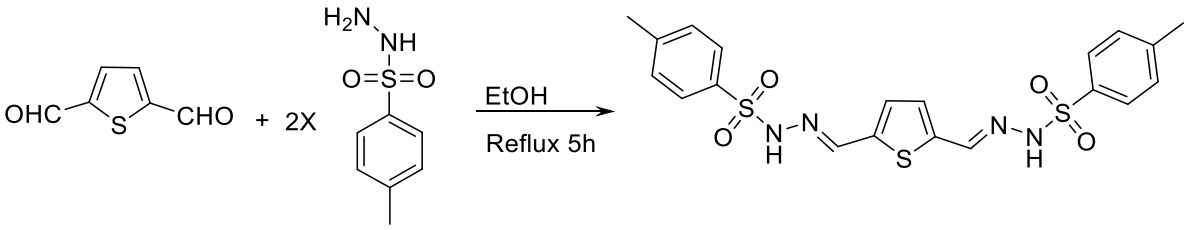


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,4-bis(2-phenyl-2H-tetrazol-5-yl)benzene	366.38	0.006	0.017	1
Polyvest	54.09	0.180	3.330	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

180mg (3.330 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 6mg (0.017 mmol) of 1,4-bis(2-phenyl-2H-tetrazol-5-yl)benzene was added to the reaction mixture and heated at 190°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence. It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of (N',N''E,N',N''E)-N',N''-(thiophene-2,5-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)

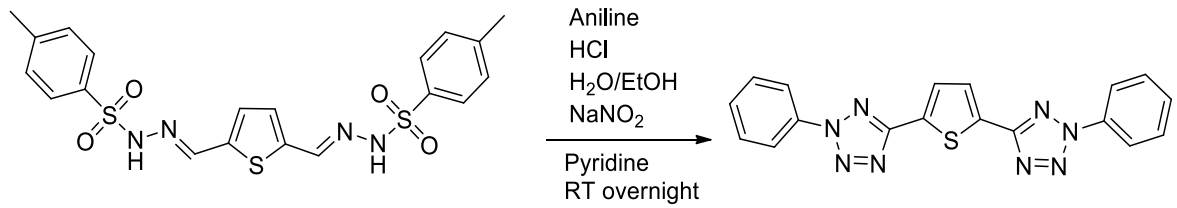


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
thiophene-2,5-dicarbaldehyde	140.16	2.50	18.00	1
p-Toluenesulfonyl hydrazide	186.23	6.64	36.00	2

Solvent: EtOH

2.5g (18.00 mmol) of thiophene-2,5-dicarbaldehyde, 6.642 g (36.00 mmol) of p-Toluenesulfonyl hydrazide and 60 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (8.50g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of 2,5-bis(2-phenyl-2H-tetrazol-5-yl)thiophene (compound 2)

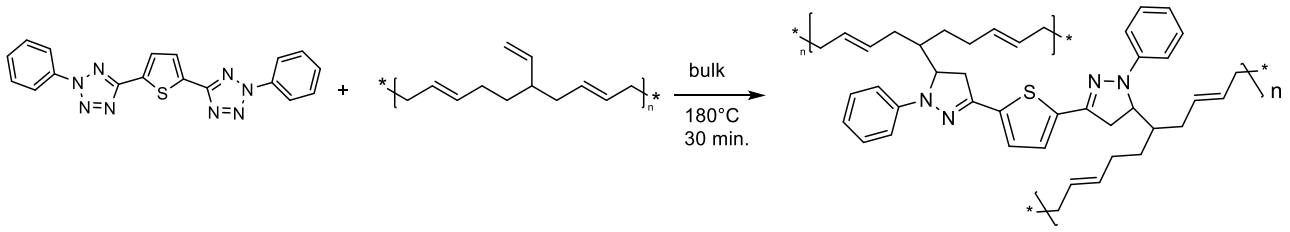


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(N',N''E,N',N''E)-N',N''-(thiophene-2,5-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)	476.59	8.50	18.00	1		
Aniline	95.126	3.32	36.00	2	3.25	1.02
$NaNO_2$	69.00	2.48	36.00	2		
HCl (37%, 12M)	36.46	3.94	108.00	6	9.00	

Solvent: Pyridine

8.50g (18 mmol) (N',N''E,N',N''E)-N',N''-(thiophene-2,5-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide) was dissolved in pyridine (100ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (2.48g, 36.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (3.32g, 36.00mmol) and concentrated HCl (3.94g, 108.00 mmol) dissolved in 20 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was crystallized using ethyl acetate to give the pure product (3.02g, yield:45%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.21 (d, 4H), 7.98 (s, 2H), 7.60 (dd, *J* = 10.3, 4.9 Hz, 4H), 7.56 – 7.50 (m, 2H) **FTIR-ATR** (cm^{-1}): 3085, 2962, 2891, 2879, 2323, 2168, 2051, 1977, 1949, 1886, 1799, 1747, 1674, 1652, 1596, 1581, 1495, 1462, 1458, 1422, 1363, 1353, 1335, 1315, 1296, 1266, 1240, 1226, 1197, 1187, 1167, 1158, 1123, 1095, 1048, 1008, 967, 954, 935, 926, 912, 815, 749, 702, 673, 589, 575, 554 **TGA analysis**: 170 °C

Thermally functionalized PB oligomer with 2,5-bis(2-phenyl-2H-tetrazol-5-yl)thiophene

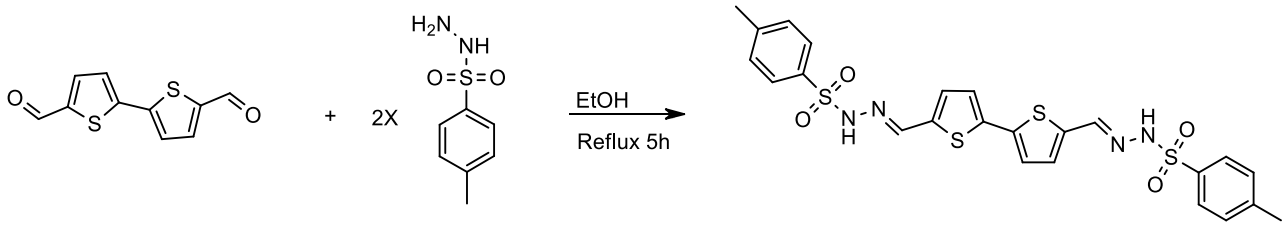


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,4-bis(2-phenyl-2H-tetrazol-5-yl)benzene	372.41	0.007	0.02	1
Polyvest	54.09	0.204	3.70	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

204mg (3.70 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 7mg (0.020 mmol) of 2,5-bis(2-phenyl-2H-tetrazol-5-yl)thiophene was added to the reaction mixture and heated at 180°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright orange fluorescence. It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of (N',N''E,N',N''E)-N',N''-([2,2'-bithiophene]-5,5'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)

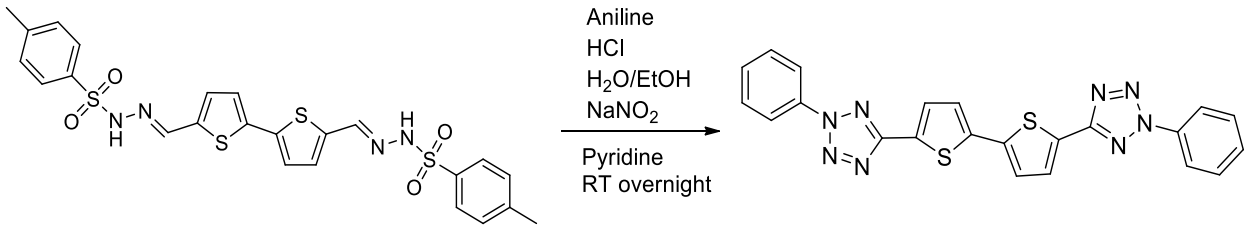


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
[2,2'-bithiophene]-5,5'-dicarbaldehyde	222.28	2.50	11.00	1
p-Toluenesulfonyl hydrazide	186.23	4.19	22.00	2

Solvent: EtOH

2.5g (11.00 mmol) of [2,2'-bithiophene]-5,5'-dicarbaldehyde, 4.19 g (22.00 mmol) of p-Toluenesulfonyl hydrazide and 90 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (6.02, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, yellow powder

Synthesis of 5,5'-bis(2-phenyl-2H-tetrazol-5-yl)-2,2'-bithiophene (compound 3)

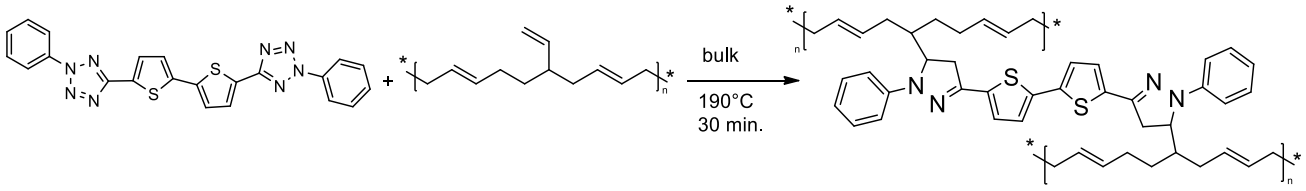


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(N',N''E,N',N''E)-N',N''-([2,2'-bithiophene]-5,5'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)	558.72	6.28	11.00	1		
Aniline	95.126	2.10	22.00	2	2.06	1.02
$NaNO_2$	69.00	1.55	22.00	2		
HCl (37%, 12M)	36.46	2.41	66.00	6	5.50	

Solvent: Pyridine

6.28g (11.00 mmol) of (N',N''E,N',N''E)-N',N''-([2,2'-bithiophene]-5,5'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide) was dissolved in pyridine (100ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (1.55g, 22.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (2.10g, 22.00mmol) and concentrated HCl (2.41g, 66.00 mmol) dissolved in 12 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was washed with dichloromethane to give the pure product (2.23g, yield:45%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.23 – 8.17 (m, 4H), 7.86 (d, J = 3.8 Hz, 2H), 7.63 – 7.56 (m, 4H), 7.56 – 7.49 (m, 2H), 7.36 (d, J = 3.8 Hz, 2H) **FTIR-ATR** (cm^{-1}): 3065, 3051, 1980, 1941, 1873, 1786, 1661, 1596, 1564, 1498, 1481, 1464, 1424, 1368, 1317, 1296, 1263, 1214, 1181, 1131, 1069, 1058, 1006, 967, 910, 879, 810, 753, 743, 701, 673, 573 **TGA analysis**: 190 °C

Thermally functionalized PB oligomer with 5,5'-bis(2-phenyl-2H-tetrazol-5-yl)-2,2'-bithiophene



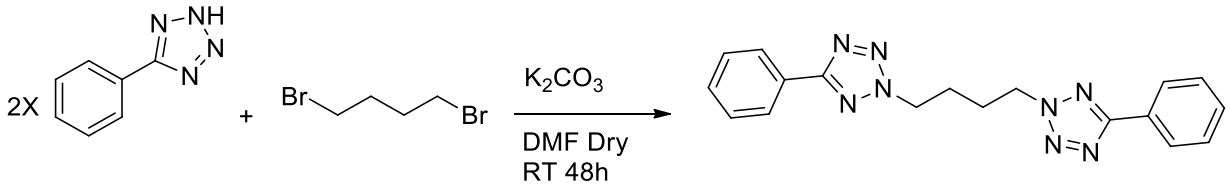
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5,5'-bis(2-phenyl-2H-tetrazol-5-yl)-2,2'-bithiophene	454.53	0.08	0.018	1
Polyvest	54.09	0.195	3.600	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

195mg (3.600 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 8mg (0.018 mmol) of 5,5'-bis(2-phenyl-2H-tetrazol-5-yl)-2,2'-bithiophene was added to the reaction mixture and heated at 190°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright white fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of 1,4-bis(5-phenyl-2H-tetrazol-2-yl)butane (compound 4)

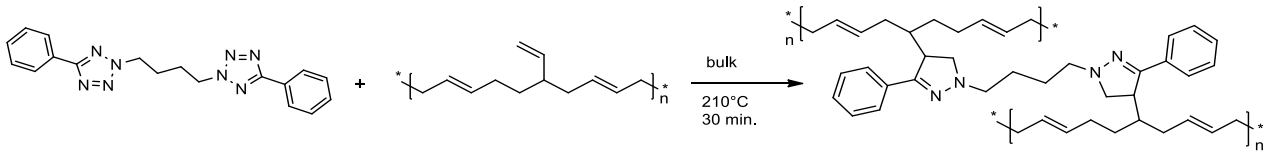


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-phenyl-2H-tetrazole	146.15	0.200	1.37	2		
1,4-dibromobutane	215.91	0.148	0.68	1	0.08	1.81
Potassium carbonate	138.21	0.208	1.50	2.2		

Solvent: Dry DMF

200mg (1.37 mmol) of 5-phenyl-2H-tetrazole and 5ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 208mg (1.50 mmol) of Potassium carbonate were added and, after 10 min. 148mg (0.68mmol) of 1,4-dibromobutane were added. The reaction mixture was stirred for 48 hours. The mixture was extracted with ethyl acetate (2X 10ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (188mg, yield:80%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 4H), 7.41 (dd, *J* = 5.1, 1.9 Hz, 6H), 4.72 – 4.63 (m, 4H), 2.16 – 2.05 (m, 4H) **FTIR-ATR** (cm^{-1}): 3070, 3033, 2953, 2865, 1954, 1891, 1818, 1767, 1736, 1675, 1611, 1584, 1530, 1493, 1463, 1446, 1386, 1349, 1330, 1307, 1294, 1273, 1255, 1226, 1194, 1173, 1155, 1140, 1109, 1091, 1072, 1045, 1029, 1009, 998, 926, 848, 804, 787, 726, 707, 690, 655, 616, 567, 558 **TGA analysis**: 210 °C

Thermally functionalized PB oligomer with 1,4-bis(5-phenyl-2H-tetrazol-2-yl)butane



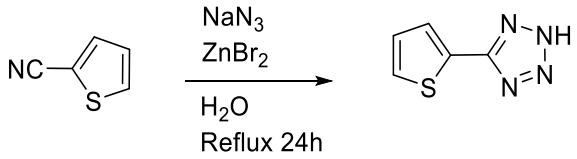
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,4-bis(5-phenyl-2H-tetrazol-2-yl)butane	346.39	0.007	0.02	1
Polyvest	54.09	0.218	4.04	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

218mg (4.04 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 7mg (0.02 mmol) of 1,4-bis(5-phenyl-2H-tetrazol-2-yl)butane was added to the reaction mixture and heated at 210°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of 5-(thiophen-2-yl)-2H-tetrazole

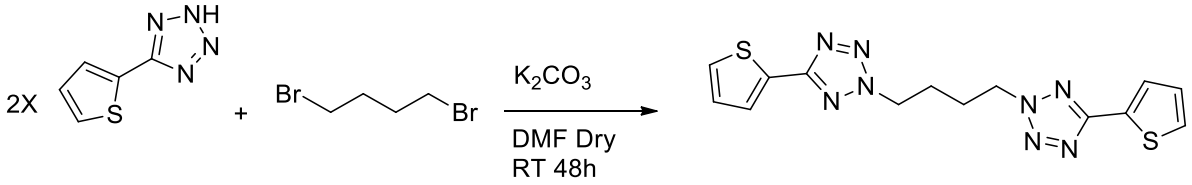


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
thiophene-2-carbonitrile	109.15	2.62	24.00	1	2.24	1.17
sodium azide	65.01	1.73	24.00	1		
zinc Bromide	225.19	5.46	24.00	1		

Solvent: H_2O

2.62g (24.00 mmol) of thiophene-2-carbonitrile, 1.73 (24.00 mmol) of sodium azide, 5.46g (24.00 mmol) of zinc Bromide and 50ml of H_2O were added to a round bottom flask equipped with a water condenser. The mixture was heated at reflux under magnetic stirring for 24 hours (a white precipitate forms). Afterwards 30 ml of HCl (3M) were added, until pH=1. The mixture was extracted with ethyl acetate (3X 30 ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give a white powder. The compound was dissolved in 200ml of NaOH (0.25M). The zinc salts formed were filtered. The aqueous phase was acidified with HCl (3M) to precipitate the product which was filtered in a buchner (2.70g, yield: 74%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 7.89 (d, *J* = 5.0, 1.0 Hz, 1H), 7.84 (d, *J* = 3.0 Hz, 1H), 7.30 (dd, *J* = 5.0, 3.7 Hz, 1H)

Synthesis of 1,4-bis(5-(thiophen-2-yl)-2H-tetrazol-2-yl)butane (compound 5)

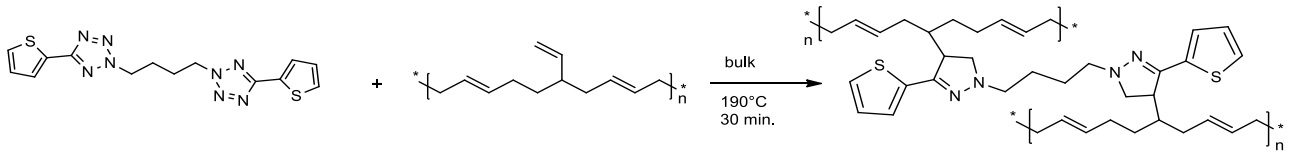


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(thiophen-2-yl)-2H-tetrazole	152.18	0.200	1.31	2		
1,4-dibromobutane	215.91	0.141	0.66	1	0.08	1.81
potassium carbonate	138.21	0.199	1.45	2.2		

Solvent: Dry DMF

200mg (1.31 mmol) of 5-(thiophen-2-yl)-2H-tetrazole and 5ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 199mg (1.45 mmol) of potassium carbonate were added and, after 10 min. 148mg (0.68mmol) of 1,4-dibromobutane were added. The reaction mixture was stirred for 48 hours. The mixture was extracted with ethyl acetate (2X 10ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (194mg, yield:82%). **Physical aspect**: Solid, pale yellow powder **^{1}HNMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 3.6, 1.0 Hz, 2H), 7.45 (d, *J* = 5.0, 0.9 Hz, 2H), 7.15 (t, *J* = 4.9, 3.7 Hz, 2H), 4.68 (t, *J* = 6.9 Hz, 4H), 3.45 (t, *J* = 6.5 Hz, 4H) **TGA analysis**: 180 °C

Thermally functionalized PB oligomer with 1,4-bis(5-phenyl-2H-tetrazol-2-yl)butane



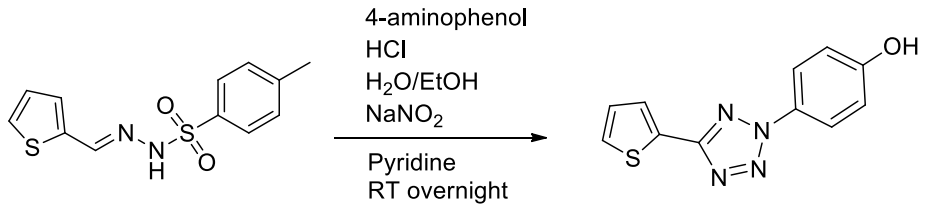
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,4-bis(5-(thiophen-2-yl)-2H-tetrazol-2-yl)butane	358.44	0.008	0.022	1
Polyvest	54.09	0.241	4.463	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

241mg (4.463 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 8mg (0.022 mmol) of 1,4-bis(5-(thiophen-2-yl)-2H-tetrazol-2-yl)butane was added to the reaction mixture and heated at 180°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright yellow fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: brown gelatin

Synthesis of 4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol

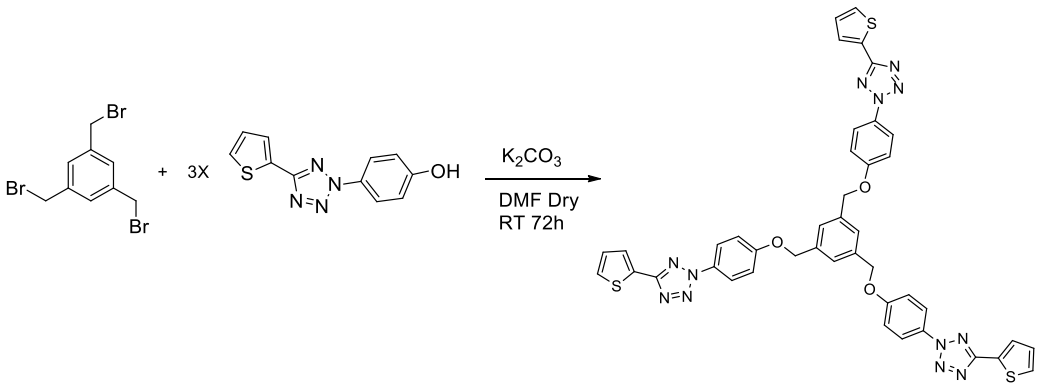


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-4-methyl-N'-(thiophen-2-ylmethylene)benzenesulfonohydrazide	280.36	2.00	7.10	1		
4-aminophenol	109.13	0.78	7.10	1	0.74	1.02
$NaNO_2$	69.00	0.49	7.10	1		
HCl (37%, 12M)	36.46	0.78	21.30	3	1.80	

Solvent: Pyridine

2.00g (7.10 mmol) of (E)-4-methyl-N'-(thiophen-2-ylmethylene)benzenesulfonohydrazide was dissolved in pyridine (30ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (490mg, 7.10 mmol) in water was added dropwise to a cooled (0°C) mixture of 4-aminophenol (780g, 7.10 mmol) and concentrated HCl (780mg, 21.30mmol) dissolved in 12 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (DCM/AcOEt 95:5) to provide the desired compound (520mg, yield:30%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 2H), 7.89 (d, J = 3.7, 1.2 Hz, 1H), 7.49 (d, J = 5.0, 1.2 Hz, 1H), 7.19 (t, J = 5.0, 3.6 Hz, 1H), 7.04 – 6.99 (m, 2H) **FTIR-ATR** (cm^{-1}): 3177, 3108, 3093, 2983, 2952, 2925, 2847, 2701, 2632, 1883, 1811, 1743, 1680, 1644, 1618, 1600, 1575, 1569, 1516, 1474, 1410, 1368, 1340, 1328, 1281, 1254, 1230, 1221, 1201, 1187, 1168, 1124, 1106, 1089, 1074, 1053, 1018, 1005, 971, 939, 908, 851, 833, 747, 714, 705, 688, 669, 635, 628, 572 **TGA analysis**: 160 °C

Synthesis of 1,3,5-tris((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)benzene (compound 6)

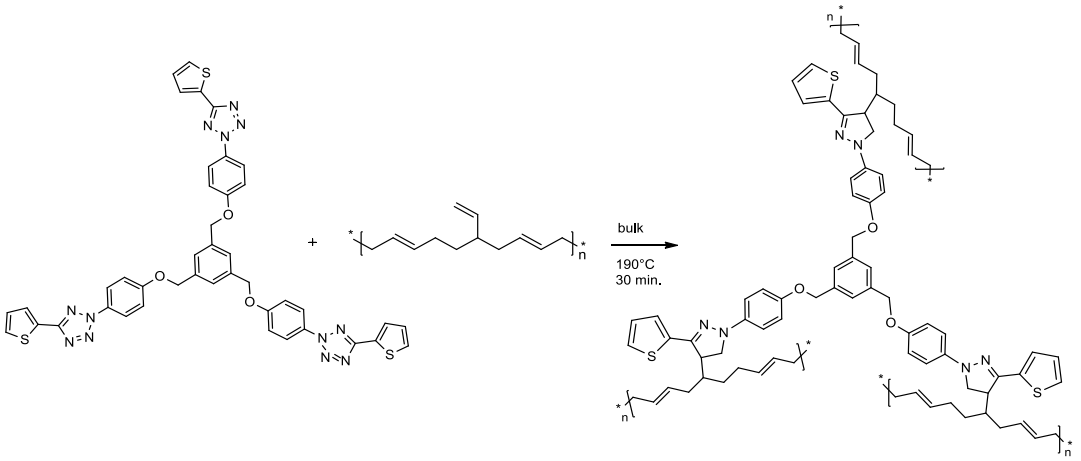


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol	244.27	0.200	0.82	3.5		
1,3,5-tris(bromomethyl)benzene	356.88	0.083	0.23	1		
potassium carbonate	138.21	0.129	0.94	4		

Solvent: Dry DMF

200mg (0.82 mmol) of 4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol and 8ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 129mg (0.94 mmol) of potassium carbonate were added and, after 10 min. 83mg (0.23mmol) of 1,3,5-tris(bromomethyl)benzene were added. The reaction mixture was stirred for 72 hours. The mixture was extracted with ethyl acetate (2X 15ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (123mg, yield:63%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.10 (d, J = 9.2 Hz, 6H), 7.88 (dd, J = 3.6, 1.2 Hz, 3H), 7.49 (dd, J = 5.0, 1.1 Hz, 3H), 7.18 (dd, J = 5.0, 3.6 Hz, 3H), 7.14 (d, J = 9.2 Hz, 3H), 5.22 (s, 6H) **FTIR-ATR** (cm^{-1}): 3107, 3082, 2925, 2854, 2558, 1885, 1805, 1729, 1680, 1608, 1596, 1572, 1509, 1475, 1457, 1440, 1409, 1373, 1300, 1247, 1225, 1203, 1175, 1112, 1066, 1043, 1012, 1002, 964, 893, 867, 850, 835, 807, 747, 701, 688, 673, 632, 587, 574 **TGA analysis**: 190 °C

Thermally functionalized PB oligomer 1,3,5-tris((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)benzene



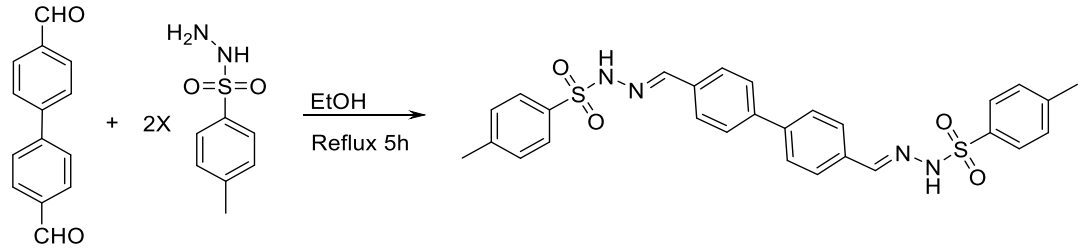
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,3,5-tris((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)benzene	846.96	0.006	0.007	1
Polyvest	54.09	0.122	2.250	300
Polyvest vinyl double bonds	54.09			3

No Solvent: Bulk

122mg (2.250 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 6mg (0.007 mmol) of 1,3,5-tris((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)benzene was added to the reaction mixture and heated at 190°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright yellow fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: brown gelatin

Synthesis of (N',N''E,N',N''E)-N',N''-([1,1'-biphenyl]-4,4'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)

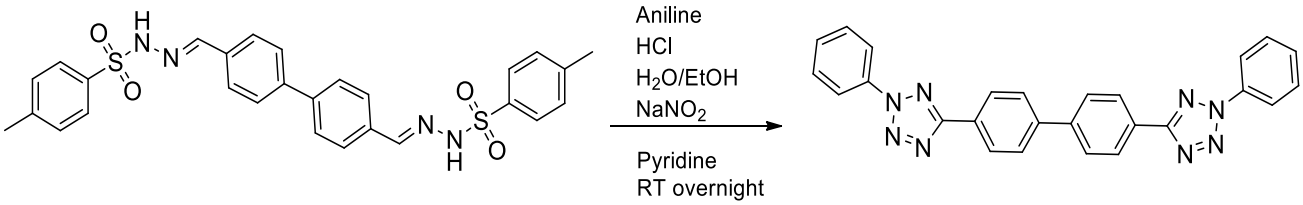


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
[1,1'-biphenyl]-4,4'-dicarbaldehyde	210.23	2.50	12.00	1
p-Toluenesulfonyl hydrazide	186.23	4.43	24.00	2

Solvent: EtOH

2.50g (12.00 mmol) of [1,1'-biphenyl]-4,4'-dicarbaldehyde, 4.43g (24.00 mmol) of p-Toluenesulfonyl hydrazide and 80ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (6.50g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, pale yellow powder

Synthesis of 4,4'-bis(2-phenyl-2H-tetrazol-5-yl)-1,1'-biphenyl (compound 7)

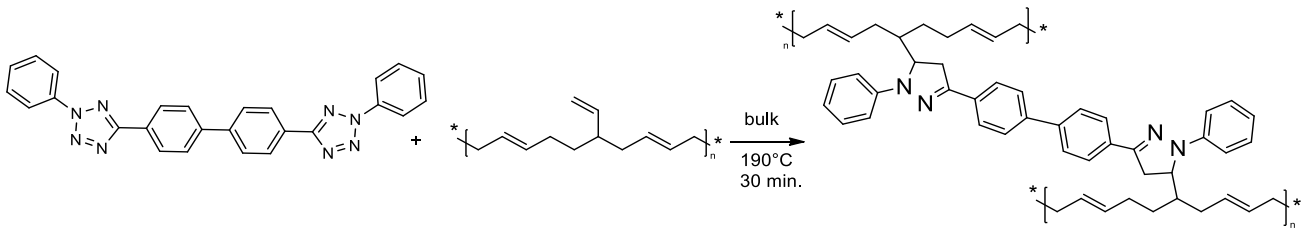


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(N',N''E,N',N''E)-N',N''-([1,1'-biphenyl]-4,4'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide)	546.66	6.50	12.00	1		
Aniline	93.126	2.22	24.00	2	0.64	1.02
$NaNO_2$	69.00	1.65	24.00	2		
HCl (37%, 12M)	36.46	2.62	72.00	6	6.00	

Solvent: Pyridine

6.50g (12.00 mmol) of (N',N''E,N',N''E)-N',N''-([1,1'-biphenyl]-4,4'-diylbis(methanylylidene))bis(4-methylbenzenesulfonohydrazide) was dissolved in pyridine (90ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (1.65g, 24.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (2.22g, 24.00 mmol) and concentrated HCl (2.62mg, 71.00 mmol) dissolved in 10 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was crystallized using ethanol to give the pure product (2.39g, yield:45%). **Physical aspect**: Solid, red powder The compound was not soluble in the common organic solvents **FTIR-ATR** (cm^{-1}): 3065, 3032, 2050, 1697, 1615, 1597, 1535, 1494, 1458, 1431, 1409, 1374, 1360, 1318, 1293, 1253, 1210, 1184, 1165, 1139, 1106, 1087, 1075, 1033, 1013, 992, 909, 863, 825, 748, 731, 715, 692, 675, 575 **TGA analysis**: 185 °C

Thermally functionalized PB oligomer with 4,4'-bis(2-phenyl-2H-tetrazol-5-yl)-1,1'-biphenyl

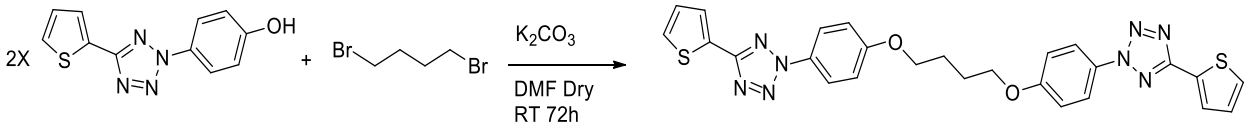


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4,4'-bis(2-phenyl-2H-tetrazol-5-yl)-1,1'-biphenyl	442.27	0.007	0.016	1
Polyvest	54.09	0.171	3.200	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

171mg (3.200 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 8mg (0.017 mmol) of 4,4'-bis(2-phenyl-2H-tetrazol-5-yl)-1,1'-biphenyl was added to the reaction mixture and heated at 190°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence. It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Synthesis of 1,4-bis(4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)butane (compound 8)

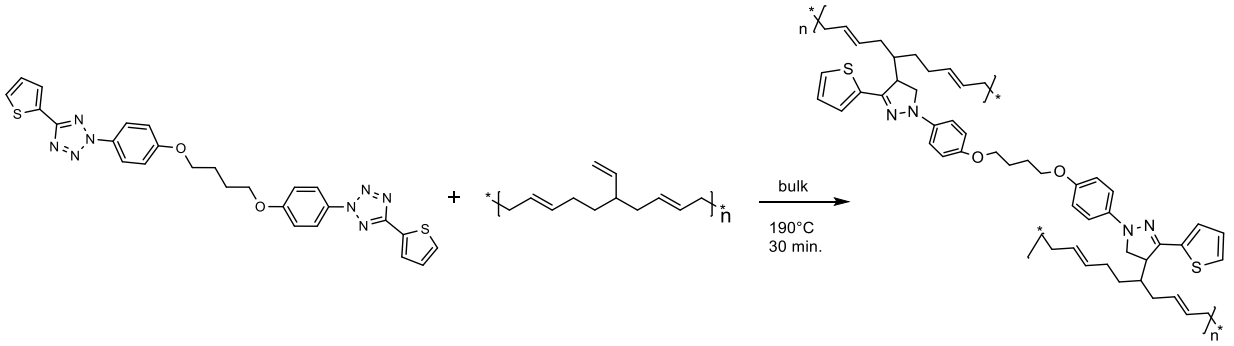


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol	244.27	0.405	1.66	2		
1,4-dibromobutane	215.91	0.179	0.83	1	0.10	1.81
potassium carbonate	138.21	0.252	1.82	2.2		

Solvent: Dry DMF

405mg (1.66 mmol) of 4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol and 10ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 252mg (1.82 mmol) of potassium carbonate were added and, after 10 min. 179mg (0.83mmol) of 1,4-dibromobutane were added. The reaction mixture was stirred for 72 hours. The mixture was extracted with ethyl acetate (2X 15ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (392mg, yield:87%). **Physical aspect**: Solid, pale yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.08 (d, J = 9.2 Hz, 4H), 7.89 (d, J = 3.7, 1.2 Hz, 2H), 7.49 (d, J = 5.0, 1.2 Hz, 2H), 7.18 (t, J = 5.0, 3.7 Hz, 2H), 7.04 (d, J = 9.2 Hz, 4H), 3.51 (t, J = 6.5 Hz, 4H), 2.17 – 2.05 (m, 4H) **FTIR-ATR** (cm^{-1}): 3075, 2957, 2939, 2869, 1980, 1888, 1808, 1732, 1609, 1600, 1570, 1517, 1471, 1437, 1431, 1406, 1397, 1376, 1351, 1302, 1276, 1258, 1225, 1204, 1182, 1114, 1066, 1042, 1015, 1001, 965, 852, 843, 827, 788, 748, 734, 704, 686, 682, 654, 638, 575 **TGA analysis**: 190 °C

Thermally functionalized PB oligomer with 1,4-bis(4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)butane



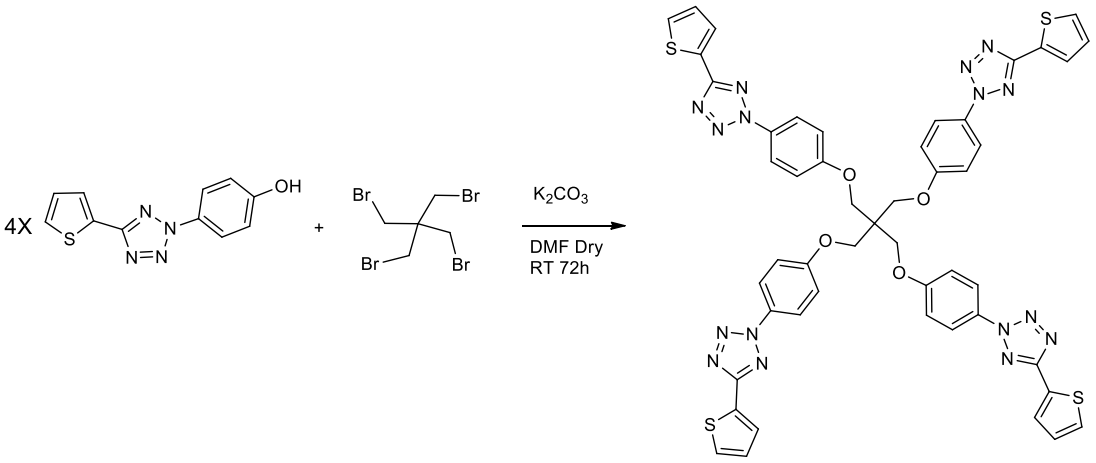
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,4-bis(4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)butane	542.64	0.007	0.012	1
Polyvest	54.09	0.130	2.400	200
Polyvest vinyl double bonds	54.09			2

No Solvent: Bulk

130mg (2.400 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 7mg (0.012 mmol) of 1,4-bis(4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)butane was added to the reaction mixture and heated at 190 °C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright yellow fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective cross-linking of the polymer matrix. **Physical aspect**: brown gelatin

Synthesis of 2,2'-(((2,2-bis((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)propane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(5-(thiophen-2-yl)-2H-tetrazole) (compound 9)

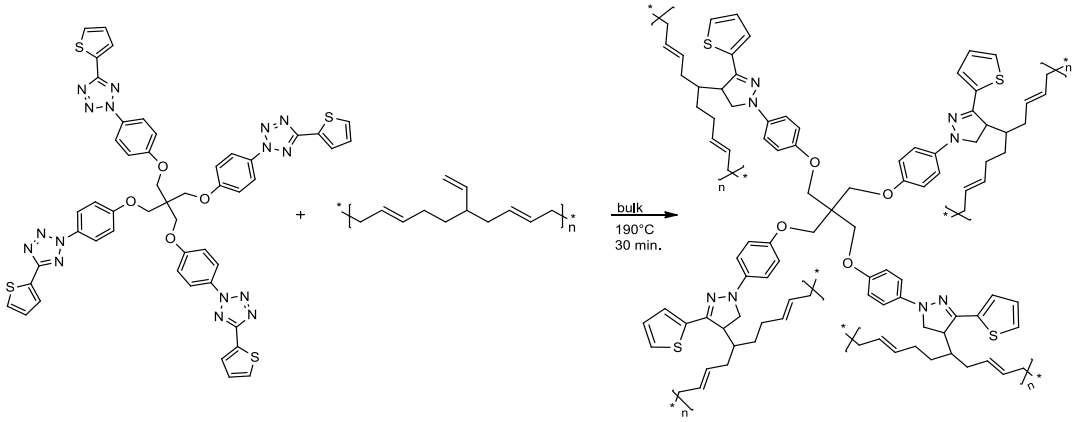


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol	244.27	0.200	0.82	4.5		
1,3-dibromo-2,2-bis(bromomethyl)propane	387.74	0.071	0.18	1		
potassium carbonate	138.21	0.126	0.91	5		

Solvent: Dry DMF

200mg (0.82 mmol) of 4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol and 8ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 126mg (0.91 mmol) of potassium carbonate were added and, after 10 min. 71mg (0.18mmol) of 1,3-dibromo-2,2-bis(bromomethyl)propane were added. The reaction mixture was stirred for 72 hours. The mixture was extracted with ethyl acetate (2X 15ml), washing with brine (2X10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (Hexane→DCM/AcOEt 4:) to give the pure product (28mg, yield: 15%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 9.1 Hz, 8H), 7.90 (d, *J* = 3.6, 1.1 Hz, 4H), 7.50 (d, *J* = 5.0, 1.1 Hz, 4H), 7.19 (t, *J* = 5.0, 3.7 Hz, 4H), 7.10 (d, *J* = 9.1 Hz, 8H), 4.15 (s, 8H) **TGA analysis**: 190 °C

Thermally functionalized PB oligomer 2,2'-(((2,2-bis((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)propane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(5-(thiophen-2-yl)-2H-tetrazole)



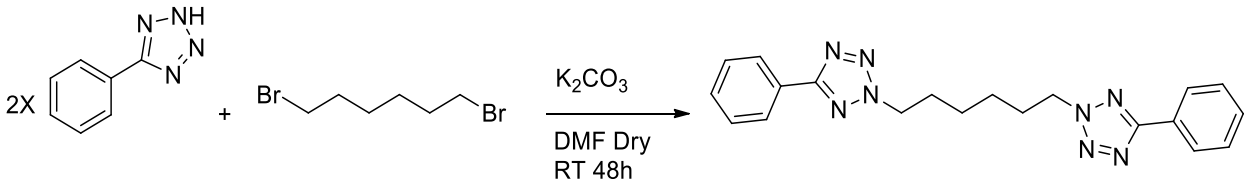
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
2,2'-(((2,2-bis((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)propane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(5-(thiophen-2-yl)-2H-tetrazole)	1041.17	0.006	0.006	1
Polyvest	54.09	0.130	2.400	400
Polyvest vinyl double bonds	54.09			4

No Solvent: Bulk

130mg (2.400 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 6mg (0.006 mmol) of 2,2'-(((2,2-bis((4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenoxy)methyl)propane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(5-(thiophen-2-yl)-2H-tetrazole) was added to the reaction mixture and heated at 190°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright yellow fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: brown gelatin

Synthesis of 1,6-bis(5-phenyl-2H-tetrazol-2-yl)hexane (compound 10)

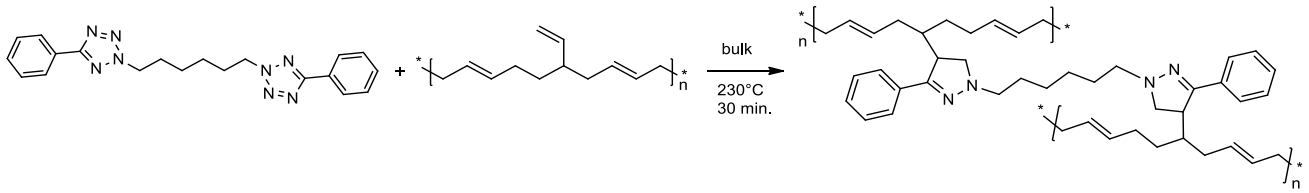


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-phenyl-2H-tetrazole	146.15	0.763	5.20	2		
1,6-dibromohexane	243.97	0.637	2.60	1	0.40	1.61
potassium carbonate	138.21	0.794	5.70	2.2		

Solvent: Dry DMF

763mg (5.20 mmol) of 5-phenyl-2H-tetrazole and 20ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 794mg (5.70 mmol) of potassium carbonate were added and, after 10 min. 637mg (2.60 mmol) of 1,6-dibromohexane were added. The reaction mixture was stirred for 48 hours. The mixture was extracted with ethyl acetate (2X 20ml), washing with brine (2X20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (507mg, yield:52%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.17 – 8.11 (m, 4H), 7.52 – 7.45 (m, 6H), 4.65 (t, *J* = 7.0 Hz, 4H), 2.13 – 2.02 (m, *J* = 7.2 Hz, 4H), 1.49 – 1.42 (m, 4H) **FTIR-ATR** (cm^{-1}): 3067, 3034, 2947, 2872, 2863, 2165, 1981, 1962, 1895, 1822, 1767, 1716, 1653, 1610, 1585, 1528, 1463, 1449, 1397, 1365, 1352, 1339, 1306, 1286, 1251, 1206, 1177, 1131, 1103, 1070, 1042, 1030, 1000, 997, 921, 855, 787, 759, 729, 689, 617 **TGA analysis**: 230 °C

Thermally functionalized PB oligomer with 1,6-bis(5-phenyl-2H-tetrazol-2-yl)hexane



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1,6-bis(5-phenyl-2H-tetrazol-2-yl)hexane	374.44	0.008	0.02	1
Polyvest	54.09	0.218	4.04	200
Polyvest vinyl double bonds	54.09			2

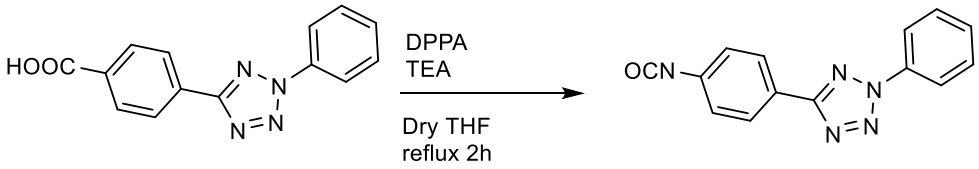
No Solvent: Bulk

218mg (4.04 mmol) of Polyvest was heated at 80°C to make it more fluid. The system was kept under vigorous stirring for 10 minutes, then 8mg (0.02 mmol) of 1,6-bis(5-phenyl-2H-tetrazol-2-yl)hexane was added to the reaction mixture and heated at 210°C for 30 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence.

It wasn't possible to apply the usual procedure for purification, since the functionalized polymer wasn't soluble in DCM. It is an evidence of the effective crosslinking of the polymer matrix. **Physical aspect**: dark gelatin

Chapter 5

Synthesis of 5-(4-isocyanatophenyl)-2-phenyl-2H-tetrazole

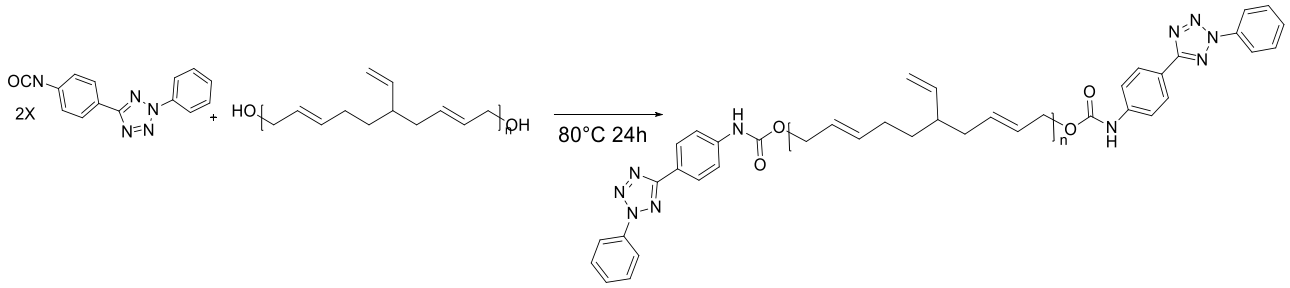


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid	266.25	0.300	1.13	1		
Diphenylphosphoryl azide	275.20	0.341	1.24	1.1	0.27	1.28
Triethylamine	101.19	0.125	1.24	1.1	0.17	0.73

Solvent: Dry THF

300mg (1.13 mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoic acid and 20 ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. The reaction mixture was cooled at 0°C, then 341mg (1.24 mmol) of DPPA were added and, after 10 min. 125mg (1.24mmol) of TEA were added. The reaction mixture was heated at reflux under magnetic stirring for 2 hours. The proceeding of the reaction was monitored using IR (NCO band forms). The solvent was evaporated under reduced pressure.
The product was used for the next step without any further purification. **Physical aspect**: Red viscous oil **FTIR-ATR** (cm^{-1}): 3065, 2974, 2861, 2338, 2272, 2256, 2170, 2134, 1954, 1792, 1692, 1614, 1594, 1537, 1490, 1471, 1458, 1422, 1374, 1365, 1309, 1288, 1238, 1204, 1180, 1131, 1110, 1092, 1068, 1027, 1011, 986, 968, 912, 898, 861, 757, 730, 694, 678, 633, 617, 595, 561

Functionalization of hydroxy-terminated PB oligomer with 5-(4-isocyanatophenyl)-2-phenyl-2H-tetrazole



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-(4-isocyanatophenyl)-2-phenyl-2H-tetrazole	263.25	0.298	2.26	2
Krasol LBH 2000	2100	0.920	1.13	1

No Solvent: Bulk

920mg (1.13 mmol) of Krasol LBH 2000 and 298mg (2.26 mmol) of 5-(4-isocyanatophenyl)-2-phenyl-2H-tetrazole were mixed. The system was heated at 80°C under vigorous stirring for 24 hours. The proceeding of the reaction was monitored using IR (NCO band disappears).

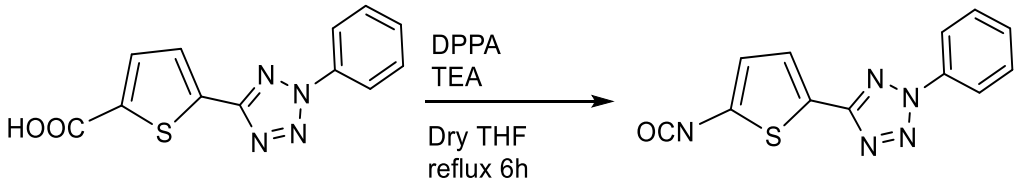
The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure. **Physical aspect**: dark red viscous liquid **TGA Analysis**: 190 °C

A small amount of the polymer was heated at 200°C for 10 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence. The polymer is also insoluble, proving the effective crosslinking.

Synthesis of 5-(5-isocyanatothiophen-2-yl)-2-phenyl-2H-tetrazole (compound 2)

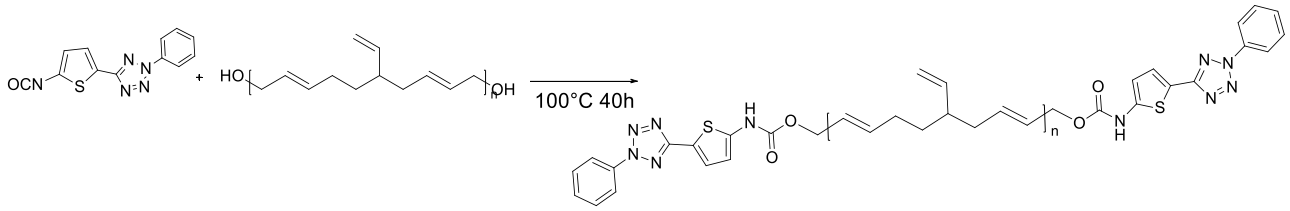


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylic acid	272.28	1.30	4.77	1		
Diphenylphosphoryl azide	275.20	1.46	5.30	1.1	1.14	1.28
Triethylamine	101.19	0.54	5.30	1.1	0.74	0.73

Solvent: Dry THF

1.30g (4.77 mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylic acid and 120ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. The reaction mixture was cooled at 0°C, then 1.46g (5.30 mmol) of DPPA were added and, after 10 min. 540mg (5.30 mmol) of TEA were added. The reaction mixture was heated at reflux under magnetic stirring for 6 hours. The proceeding of the reaction was monitored using IR (NCO band forms).The solvent was evaporated under reduced pressure to give the product (1.22g, yield:99%) . The product was used for the next step without any further purification. **Physical aspect**: Red viscous oil **FTIR-ATR** (cm^{-1}): 3090, 3067, 3052, 2978, 2855, 2309, 2274, 2170, 2130, 1980, 1958, 1941, 1682, 1588, 1568, 1491, 1468, 1456, 1420, 1377, 1333, 1304, 1283, 1263, 1244, 1231, 1211, 1169, 1153, 1113, 1099, 1074, 1054, 1026, 1007, 989, 916, 892, 832, 778, 762, 745, 715, 688, 673, 617, 595, 569

Functionalization of hydroxy-terminated PB oligomer with 5-(5-isocyanatothiophen-2-yl)-2-phenyl-2H-tetrazole



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
5-(5-isocyanatothiophen-2-yl)-2-phenyl-2H-tetrazole	269.28	1.22	4.54	2
Krasol LBH 2000	2100.0	4.77	2.27	1

No Solvent: Bulk

4.77g (2.27 mmol) of Krasol LBH 2000 and 1.22g (4.54 mmol) of 5-(5-isocyanatothiophen-2-yl)-2-phenyl-2H-tetrazole were mixed. The system was heated at 100°C under vigorous stirring for 40 hours. The proceeding of the reaction was monitored using IR (NCO band disappears).

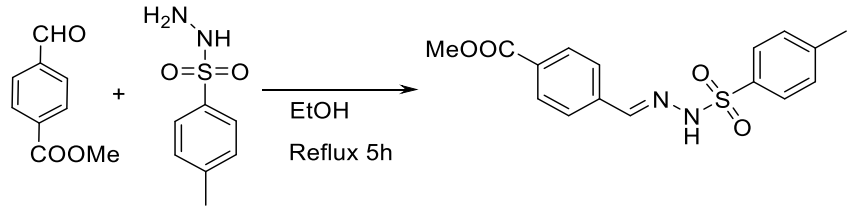
The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure. **Physical aspect**: dark red viscous liquid **TGA analysis**: 180 °C

A small amount of the polymer was heated at 180°C for 10 minutes. Then the fluorescence was checked using an UV-lamp (λ=365nm), the polymer shows a bright blue fluorescence. The polymer is also insoluble, proving the effective crosslinking.

Synthesis of (E)-methyl 4-((2-tosylhydrazono)methyl)benzoate

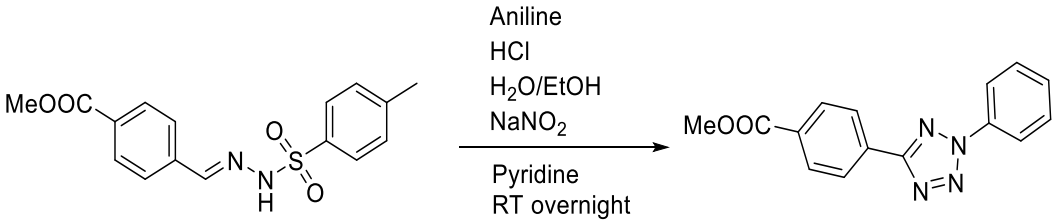


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
methyl 4-formylbenzoate	164.16	2.02	12.30	1
p-Toluenesulfonyl hydrazide	186.23	2.29	12.30	1

Solvent: EtOH

2.02g (12.30mmol) of 4-formylbenzoic acid, 2.29g (12.30mmol) of p-Toluenesulfonyl hydrazide and 40 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (4.09g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, white powder

Synthesis of methyl 4-(2-phenyl-2H-tetrazol-5-yl)benzoate (compound 4)

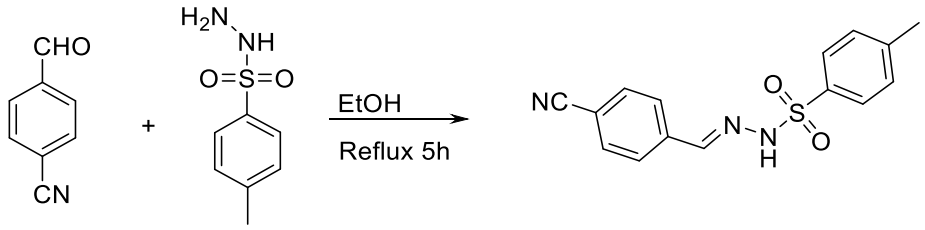


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-methyl 4-((2-tosylhydrazono)methyl)benzoate	332.27	4.09	12.30	1		
Aniline	95.126	1.15	12.30	1	0.64	1.02
$NaNO_2$	69.00	0.85	12.30	1		
HCl (37%, 12M)	36.46	1.34	36.90	3	3.07	

Solvent: Pyridine

4.09g (12.30 mmol) of (E)-methyl 4-((2-tosylhydrazono)methyl)benzoate was dissolved in pyridine (60ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (1.15g, 12.30 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (850mg, 12.30 mmol) and concentrated HCl (1.34g, 36.90 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The compound was purified over a pad of silica eluting with DCM to give the pure product (2.30g, yield:67%). **Physical aspect**: Solid, orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.37 – 8.33 (m, 2H), 8.24 – 8.18 (m, 4H), 7.64 – 7.56 (m, 2H), 7.56 – 7.50 (m, 1H), 3.97 (s, 3H) **FTIR-ATR** (cm^{-1}): 3072, 3028, 2955, 2851, 1773, 1721, 1619, 1596, 1577, 1542, 1496, 1476, 1462, 1452, 1440, 1418, 1374, 1315, 1291, 1278, 1213, 1200, 1161, 1136, 1111, 1077, 1028, 1013, 994, 963, 925, 866, 830, 781, 740, 696, 678, 568

Synthesis of (E)-N'-(4-cyanobenzylidene)-4-methylbenzenesulfonohydrazide

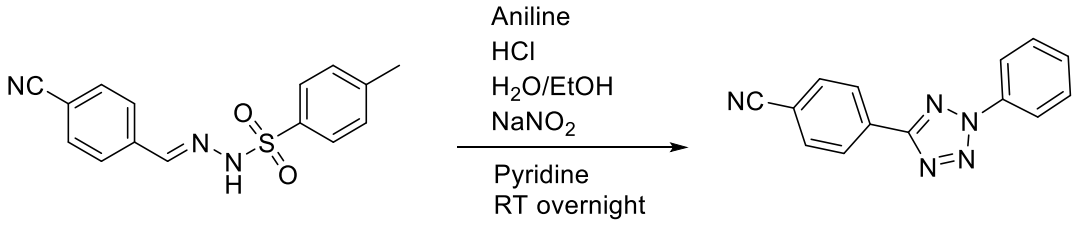


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
4-formylbenzonitrile	131.34	5.00	38.00	1
p-Toluenesulfonyl hydrazide	186.23	7.10	38.00	1

Solvent: EtOH

5.00g (38.00 mmol) of 4-formylbenzoic acid, 7.10g (38.00 mmol) of p-Toluenesulfonyl hydrazide and 80 ml of EtOH were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at reflux under magnetic stirring for 5 hours. The reaction mixture was allowed to cool down to room temperature, then was poured into cold water. The precipitate formed was collected filtering in a filter funnel, to give the desired compound (11.26g, yield:99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, white powder

Synthesis of 4-(2-phenyl-2H-tetrazol-5-yl)benzonitrile (compound 5)

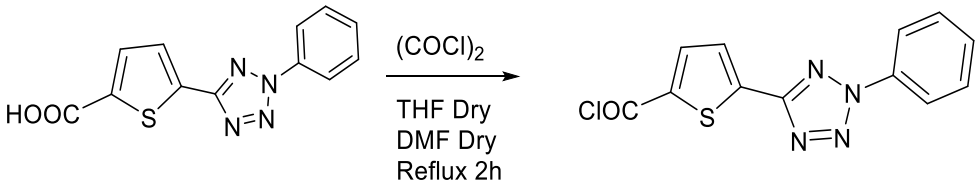


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
(E)-N'-(4-cyanobenzylidene)-4-methylbenzenesulfonohydrazide	299.35	11.40	38.00	1		
Aniline	95.126	3.55	38.00	1	3.47	1.02
$NaNO_2$	69.00	2.63	38.00	1		
HCl (37%, 12M)	36.46	4.16	114.00	3	9.50	

Solvent: Pyridine

11.40g (38.00 mmol) of (E)-N'-(4-cyanobenzylidene)-4-methylbenzenesulfonohydrazide was dissolved in pyridine (120ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (2.63g, 38.00 mmol) in water was added dropwise to a cooled (0°C) mixture of aniline (3.55g, 38.00 mmol) and concentrated HCl (4.16g, 114.00 mmol) dissolved in 15 ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (Hexane/DCM 4:1) to give the pure product (4.89g, yield:52%). **Physical aspect**: Solid, red powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.6 Hz, 2H), 8.23 – 8.18 (m, 2H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.64 – 7.58 (m, 2H), 7.56 (dd, *J* = 4.9, 3.6 Hz, 1H) **FTIR-ATR** (cm^{-1}): 3083, 3065, 3038, 2920, 2395, 2226, 2165, 1803, 1743, 1681, 1594, 1538, 1491, 1472, 1459, 1418, 1370, 1319, 1293, 1277, 1217, 1179, 1145, 1134, 1121, 1106, 1075, 1067, 1013, 1002, 910, 841, 754, 715, 700, 676, 613, 596, 575 **TGA analysis**: 180 °C

Synthesis of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carbonyl chloride

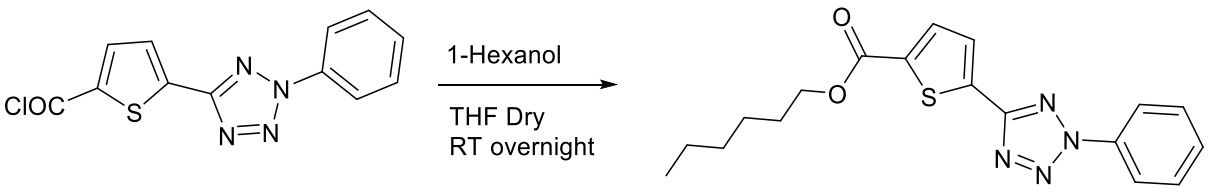


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylic acid	272.28	0.10	0.35	1		
Oxalyl chloride	126.93	0.09	0.70	2	0.06	1.48
Dry DMF	73.10				2 drops	

Solvent: Dry THF

100mg (0.35 mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylic acid and 7ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. After 2 drops of Dry DMF were added and then 90mg (0.70 mmol) of oxalyl chloride were added. The reaction mixture was heated at reflux under magnetic stirring for 2 hours. The proceeding of the reaction was monitored using IR (C=O band shifts). The solvent was evaporated washing with DCM to remove the excess of oxalyl chloride to give the product (101mg, yield: 99%). The product was used for the next step without any further purification. **Physical aspect**: Solid, orange powder **FTIR-ATR** (cm^{-1}): 3101, 2960, 2872, 2337, 2163, 1983, 1886, 1717, 1664, 1594, 1562, 1490, 1469, 1443, 1415, 1377, 1321, 1289, 1223, 1195, 1171, 1124, 1073, 1053, 1010, 1005, 969, 912, 858, 819, 805, 758, 747, 702, 691, 677, 666, 573

Synthesis of hexyl 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxylate (compound 6)

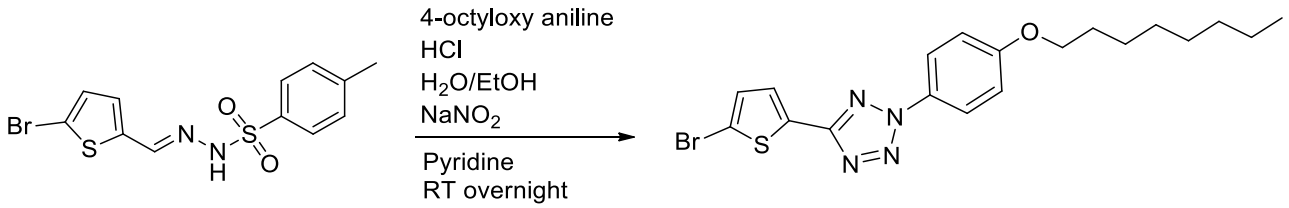


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carbonyl chloride	290.73	0.102	0.35	1		
1-Hexanol	102.10	2.042	0.70	5	0.23	0.80

Solvent: Dry THF

102mg (0.35 mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carbonyl chloride and 7ml of Dry THF were added to a round bottom flask under nitrogen atmosphere. Then 2.042g (0.70 mmol) of 1-Hexanol were added. The reaction mixture was heated under magnetic stirring overnight. The proceeding of the reaction was monitored using IR (C=O band shifts). The solvent was evaporated, and the crude product was purified by silica gel chromatography (Hexane/DCM 1:1) to give the pure product (108mg, yield: 87%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.18 (d, J = 7.9 Hz, 2H), 7.87 (d, J = 3.9 Hz, 1H), 7.84 (d, J = 3.9 Hz, 1H), 7.59 (t, 2H), 7.53 (t, 1H), 4.34 (t, J = 6.7 Hz, 2H), 1.84 – 1.71 (m, 2H), 1.45 (dd, J = 10.0, 5.0 Hz, 3H), 1.36 (td, J = 7.2, 3.6 Hz, 4H), 0.92 (t, J = 7.0 Hz, 2H) **FTIR-ATR** (cm^{-1}): 3322, 3102, 2956, 2929, 2859, 1718, 1595, 1562, 1491, 1469, 1416, 1378, 1329, 1290, 1223, 1197, 1171, 1124, 1073, 1054, 1011, 969, 912, 857, 819, 804, 758, 747, 702, 691, 677, 666, 577

Synthesis of 5-(5-bromothiophen-2-yl)-2-(4-(octyloxy)phenyl)-2H-tetrazole (compound 7)

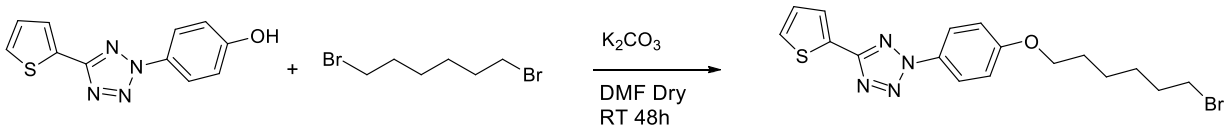


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)
(E)-N'-((5-bromothiophen-2-yl)methylene)-4-methylbenzenesulfonohydrazide	360.36	3.26	9.04	1	
4-octyloxy aniline	221.34	2.00	9.04	1	
$NaNO_2$	69.00	0.62	9.04	1	
HCl (37%, 12M)	36.46	0.99	27.12	3	2.3

Solvent: Pyridine

3.26g (9.04 mmol) of (E)-N'-((5-bromothiophen-2-yl)methylene)-4-methylbenzenesulfonohydrazide was dissolved in pyridine (90ml) in a round bottom flask to give solution A. In parallel, a solution of $NaNO_2$ (620mg, 9.04 mmol) in water was added dropwise to a cooled (0°C) mixture of 4-octyloxy aniline (2.00g, 9.04 mmol) and concentrated HCl (990mg, 27.12 mmol) dissolved in 30ml of H_2O/EtOH (1:1) to give solution B. Solution A was cooled with an ice bath and solution B was then slowly added. The reaction was carried out overnight. The mixture was poured into an acid solution (HCl) and the precipitate formed was collected with a filter funnel. The crude product was purified by silica gel chromatography (Hexane/ACOEt 9:1) to give the pure product (1.38g, yield:35%). **Physical aspect**: Solid, orange powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 9.2 Hz, 2H), 7.63 (d, *J* = 3.9 Hz, 1H), 7.14 (d, *J* = 3.9 Hz, 1H), 7.04 (d, *J* = 9.2 Hz, 2H), 4.03 (t, *J* = 6.6 Hz, 2H), 1.82 (dt, *J* = 14.5, 6.6 Hz, 2H), 1.47 (dd, *J* = 15.4, 7.3 Hz, 2H), 1.41 – 1.26 (m, 8H), 0.95 – 0.85 (m, 3H) **FTIR-ATR** (cm^{-1}): 3080, 2939, 2919, 2852, 1980, 1896, 1749, 1609, 1598, 1573, 1516, 1484, 1467, 1442, 1410, 1396, 1368, 1305, 1284, 1264, 1215, 1201, 1177, 1145, 1129, 1112, 1072, 1043, 1027, 1004, 981, 953, 893, 876, 828, 796, 756, 744, 720, 688, 671, 660, 631, 574, 560

Synthesis of 2-(4-((6-bromohexyl)oxy)phenyl)-5-(thiophen-2-yl)-2H-tetrazole (compound 8)



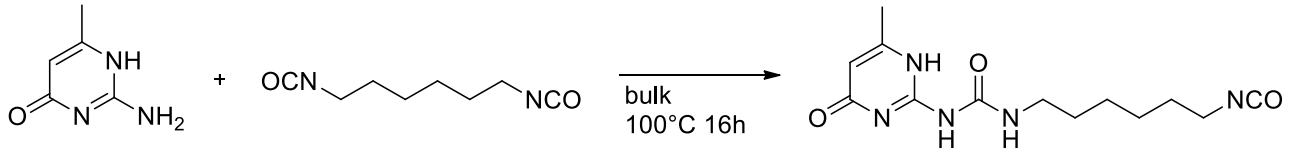
Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol	244.27	0.500	2.05	1		
1,6-dibromohexane	243.97	1.99	8.20	4	1.24	1.61
potassium carbonate	138.21	0.340	2.45	1.2		

Solvent: Dry DMF

500mg (2.05 mmol) of 4-(5-(thiophen-2-yl)-2H-tetrazol-2-yl)phenol and 20ml of Dry DMF were added to a round bottom flask, under nitrogen atmosphere. Then 340mg (2.45 mmol) of potassium carbonate were added and, after 10 min., 1.99g (8.20 mmol) of 1,6-dibromohexane were added. The reaction mixture was stirred for 48 hours. The mixture was extracted with ethyl acetate (2X 20ml), washing with brine (2X 20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM) to give the pure product (818mg, yield:98%). **Physical aspect**: Solid, yellow powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.07 (d, J = 9.1 Hz, 2H), 7.89 (d, J = 3.7, 1.2 Hz, 1H), 7.49 (d, J = 5.0, 1.2 Hz, 1H), 7.18 (t, J = 5.0, 3.7 Hz, 1H), 7.04 (d, J = 9.2 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.44 (t, J = 6.7 Hz, 2H), 1.96 – 1.89 (m, 2H), 1.85 (dt, J = 16.2, 6.9 Hz, 2H), 1.59 – 1.50 (m, 4H)

Chapter 6

Synthesis of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea (compound 1)

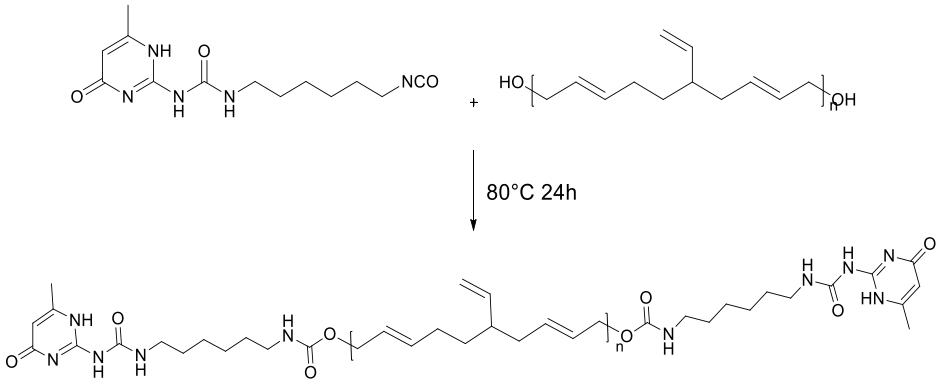


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
2-amino-6-methylpyrimidin-4(1H)-one	125.13	1.00	7.99	1		
1,6-diisocyanatohexane	168.19	9.68	57.50	7.2	9.20	1.05

No solvent: Bulk

1.00g (7.99 mmol) of 2-amino-6-methylpyrimidin-4(1H)-one and 9.68g (57.50 mmol) of 1,6-diisocyanatohexane were added to a round bottom flask equipped with a water condenser. The reaction mixture was heated at 100°C, stirring for 16 hours. The reaction mixture was allowed to cool down to room temperature, then the precipitate was filtered on a filter funnel, washing with pentene to give the pure product (2.20g, yield:95%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 13.13 (s, H), 11.88 (s, 1H), 10.20 (s, 1H), 5.84 (s, 2H), 3.40 – 3.20 (m, J = 5.5 Hz, 4H), 2.25 (s, 2H), 1.75 – 1.57 (m, 2H), 1.53 – 1.33 (m, 4H) **FTIR-ATR** (cm^{-1}): 3325, 3216, 3144, 3026, 2934, 2856, 2334, 2283, 1698, 1663, 1571, 1522, 1461, 1441, 1410, 1382, 1359, 1311, 1253, 1176, 1141, 1095, 1073, 1045, 1021, 1007, 981, 938, 872, 855, 812, 793, 779, 766, 739, 684, 665, 601, 565

Functionalization of hydroxy-terminated PB oligomer 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea	293.32	0.97	3.30	2
Krasol LBH 2000	2100.00	3.15	1.50	1

No Solvent: Bulk

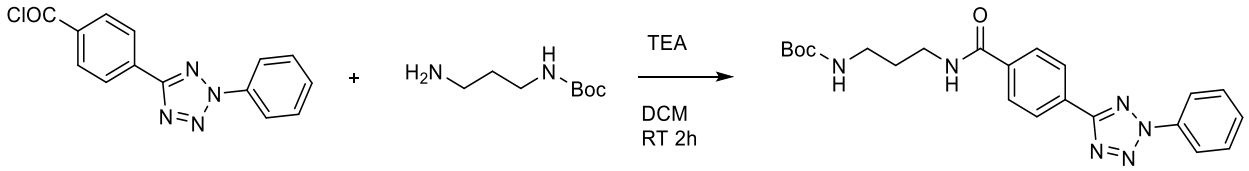
3.15g (1.50 mmol) of Krasol LBH 2000 and 970mg (3.30 mmol) of 5-(4-isocyanatophenyl)-2-phenyl-2H-tetrazole were mixed. The system was heated at 80°C under vigorous stirring for 24 hours. The proceeding of the reaction was monitored using IR (NCO band disappears).

The work up procedures was performed by repeating three times the following purification protocol:

- Solubilization in DCM - The amount of dichloromethane used was few ml.
- Precipitation in MeOH - The amount of methanol used was 20 to 30 times the volume of the reaction solvent.
- Centrifugation - The suspension was centrifuged at 12'000 rpm for 30’
- Skimming – The solvent mixture was removed from the centrifuge tube.

After washing procedure, the sample was collected and dried under reduced pressure. **Physical aspect**: white very viscous liquid

Synthesis of tert-butyl (3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)carbamate

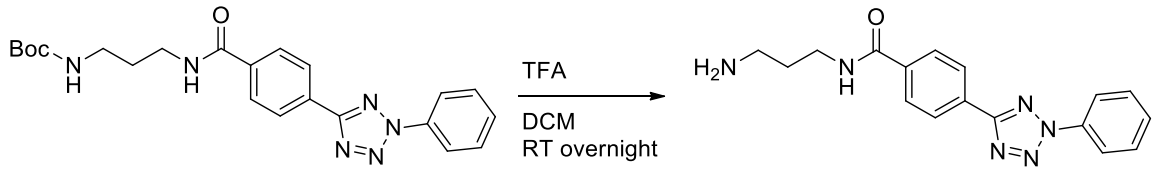


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride	284.71	0214	0.75	1		
tert-butyl (3-aminopropyl)carbamate	174.24	0.131	0.75	1		
TEA	101.19	0.076	0.75	1	0.10	0.720

Solvent: DCM

214mg (0.75 mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride and 15 ml of DCM were added to a round bottom flask. After 76mg (0.75 mmol) of TEA were added and, after 10 min. 131mg (0.75 mmol) of tert-butyl (3-aminopropyl)carbamate were added. The reaction mixture was stirred for 2 hours. The mixture was extracted with DCM (2X 20ml), washing with NaOH (1M) (2X10ml) and brine (2X 10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM/AcOEt 4:1→3:2) to give the pure product (301mg, yield:95%). **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.4 Hz, 2H), 8.24 (d, J = 7.7 Hz, 2H), 8.06 (d, J = 8.2 Hz, 2H), 7.62 (t, J = 7.6 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.47 (s, 1H), 3.58 (dd, J = 12.2, 6.1 Hz, 2H), 3.31 (dd, J = 11.9, 6.2 Hz, 2H), 1.85 – 1.71 (m, 2H), 1.50 (s, 9H)

Synthesis of N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide

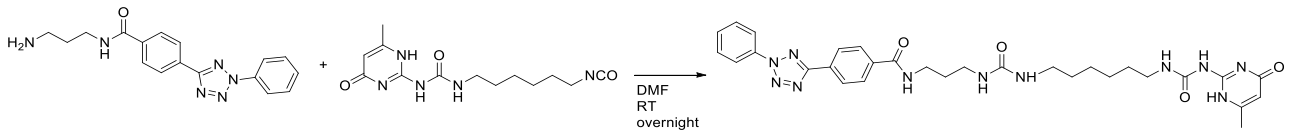


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
tert-butyl (3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)carbamate	422.48	0.250	0.59	1		
TFA	114.02	0.673	5.90	10	0.45	1.49

Solvent: DCM

250mg (0.59 mmol) of tert-butyl (3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)carbamate and 10 ml of DCM were added to a round bottom flask. After 673mg (5.90 mmol) of TFA were added. The reaction mixture was stirred overnight. The mixture was quenched with NaOH (6M) in order to neutralize the excess of TFA (until pH=7), then was extracted with DCM (2X 20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the pure product (184mg, yield:97%). **Physical aspect**: Solid, red powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.4 Hz, 2H), 8.24 (d, 2H), 8.07 (s, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.62 (t, J = 7.6 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 3.70 – 3.63 (m, J = 11.5, 5.8 Hz, 2H), 3.04 – 2.98 (m, 2H), 1.86 – 1.76 (m, J = 11.9, 5.9 Hz, 2H)

Synthesis of N-(3-(3-(6-(3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)hexyl)ureido)propyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide (compound 2)

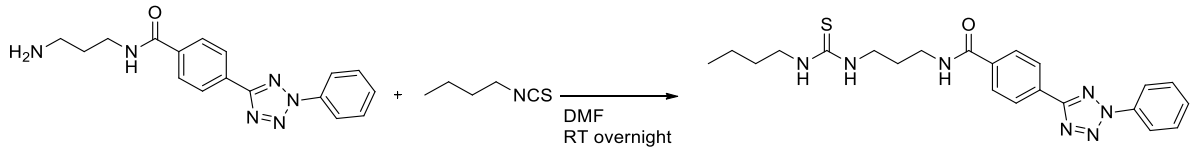


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide	322.36	0.480	1.49	1
1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea	293.32	0.437	1.49	1

Solvent: DMF

480mg (1.49mmol) of N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide and 50 ml of DMF were added to a round bottom flask. After 437mg (1.49mmol) of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (820mg, yield:89%). **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, DMSO) δ 11.56 (s, 1H), 9.64 (s, 2H), 8.68 (t, J = 5.5 Hz, 1H), 8.27 (d, J = 8.3 Hz, 2H), 8.19 (d, J = 7.6 Hz, 2H), 8.07 (d, J = 8.2 Hz, 2H), 7.72 (t, J = 7.6 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 5.95 – 5.83 (m, 2H), 5.76 (s, 1H), 3.18 – 3.10 (m, J = 5.9 Hz, 2H), 3.10 – 3.04 (m, 2H), 3.04 – 2.93 (m, J = 6.1 Hz, 2H), 2.09 (s, 3H), 1.69 – 1.58 (m, 2H), 1.53 – 1.40 (m, 2H), 1.40 – 1.33 (m, 2H), 1.33 – 1.22 (m, 4H) **FTIR-ATR** (cm^{-1}): 3329, 3041, 2933, 2860, 1698, 1645, 1568, 1549, 1520, 1496, 1460, 1442, 1417, 1377, 1304, 1250, 1135, 1074, 1014, 995,972, 946, 915, 859, 845, 799, 758, 739, 679, 602, 557 **TGA analysis**: 190 °C

Synthesis of N-(3-(3-butylthioureido)propyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide (compound 3)

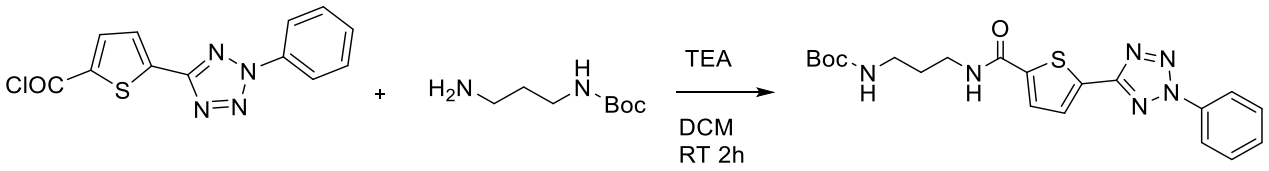


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide	322.36	1.20	3.47	1		
1-isothiocyanatobutane	115.20	0.40	3.47	1	0.42	0.955

Solvent: DMF

1.20g (3.47 mmol) of N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide and 50 ml of DMF were added to a round bottom flask. After 400mg (3.47 mmol) of 1-isothiocyanatobutane were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (726mg, yield:48%). **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, DMSO) δ 8.69 (s, 1H), 8.28 (d, J = 8.3 Hz, 2H), 8.19 (d, J = 7.6 Hz, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.72 (t, J = 7.6 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.43 (d, J = 17.2 Hz, 2H), 3.55 – 3.38 (m, J = 25.8 Hz, 6H), 1.83 – 1.70 (m, 2H), 1.46 (dt, J = 14.4, 7.2 Hz, 2H), 1.29 (td, J = 14.8, 7.3 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H) **FTIR-ATR** (cm^{-1}): 3330, 3284, 3087, 2955, 2932, 2872, 2858, 1632, 1596, 1551, 1496, 1481, 1459, 1438, 1419, 1386, 1358, 1334, 1295, 1282, 1261, 1213, 1184, 1156, 1132, 1116, 1093, 1075, 1014, 995, 972, 933, 916, 858, 836, 819, 777, 757, 737, 724, 693, 679, 598, 575, 553 **TGA analysis**: 190 °C

Synthesis of tert-butyl (3-(5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamido)propyl)carbamate

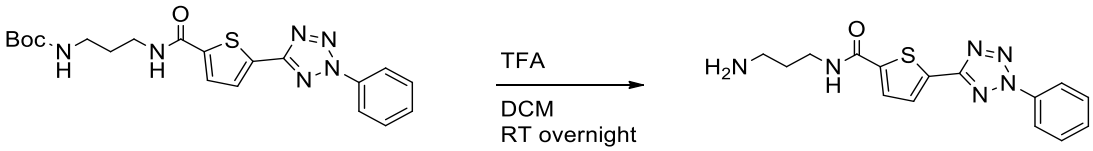


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carbonyl chloride	290.73	1.07	3.67	1		
tert-butyl (3-aminopropyl)carbamate	174.24	0.640	3.67	1		
TEA	101.19	0.371	3.67	1	0.51	0.726

Solvent: DCM

1.07g (3.67mmol) of 5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carbonyl chloride and 30 ml of DCM were added to a round bottom flask. After 371mg (3.67mmol) of TEA were added and, after 10 min. 640mg (3.67mmol) of tert-butyl (3-aminopropyl)carbamate were added. The reaction mixture was stirred for 2 hours. The mixture was extracted with DCM (2X 20ml), washing with NaOH (1M) (2X10ml) and brine (2X 10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM/AcOEt 4:1→3:2) to give the pure product (1.49g, yield:95%). **Physical aspect**: Solid, red powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.7 Hz, 2H), 7.89 (d, J = 3.9 Hz, 1H), 7.65 (d, J = 3.8 Hz, 1H), 7.61 (t, J = 7.6 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.48 (s, 1H), 3.54 (dd, J = 12.0, 6.1 Hz, 2H), 3.31 (d, J = 5.8 Hz, 2H), 1.82 – 1.70 (m, 2H), 1.50 (s, 9H)

Synthesis of N-(3-aminopropyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide

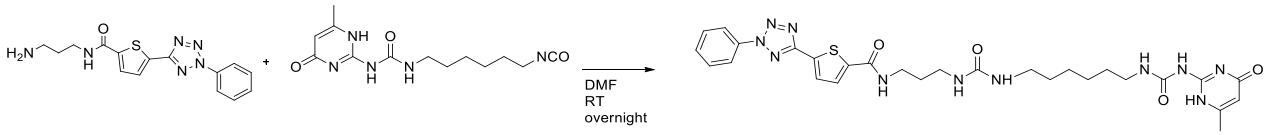


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
tert-butyl (3-(5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamido)propyl)carbamate	428.51	1.49	3.49	1		
TFA	114.02	3.98	34.9	10	2.67	1.49

Solvent: DCM

1.49g (3.49 mmol) of tert-butyl (3-(5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamido)propyl)carbamate and 30 ml of DCM were added to a round bottom flask. After 3.98g (3.49 mmol) of TFA were added. The reaction mixture was stirred overnight. The mixture was quenched with NaOH (6M) in order to neutralize the excess of TFA (until pH=7), then was extracted with DCM (2X 20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the pure product (1.15g, yield:95%). **Physical aspect**: Solid, red powder **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.20 (d, J = 7.6 Hz, 2H), 7.86 (d, J = 3.8 Hz, 1H), 7.65 – 7.50 (m, J = 11.6, 7.5 Hz, 4H), 3.63 (dd, J = 11.6, 5.7 Hz, 2H), 3.04 – 2.95 (m, 2H), 1.83 – 1.72 (m, 2H)

Synthesis of N-(3-(3-(6-(3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)hexyl)ureido)propyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide

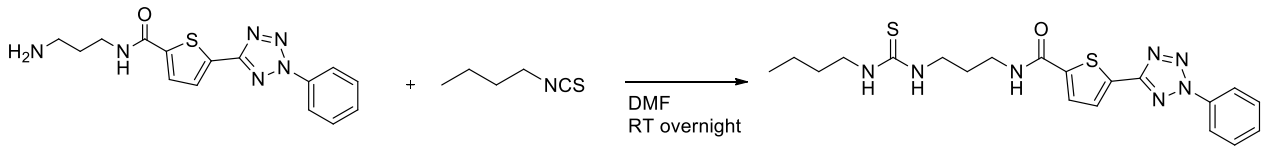


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
N-(3-aminopropyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide	328.39	0.794	2.42	1
1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea	293.32	0.710	2.42	1

Solvent: DMF

794mg (2.42 mmol) of N-(3-aminopropyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide and 50 ml of DMF were added to a round bottom flask. After 710mg (2.42mmol) of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (1.50g, yield:99%). **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, DMSO) δ 11.54 (s, 1H), 9.64 (s, 2H), 8.76 (t, J = 5.6 Hz, 1H), 8.14 (d, J = 7.6 Hz, 2H), 7.92 (d, J = 3.9 Hz, 1H), 7.86 (d, J = 4.0 Hz, 1H), 7.71 (t, J = 7.5 Hz, 2H), 7.67 – 7.61 (m, 1H), 5.95 – 5.82 (m, J = 12.8, 6.8 Hz, 2H), 5.81 – 5.69 (m, J = 12.5 Hz, 2H), 3.30 – 3.23 (m, 2H), 3.19 – 3.09 (m, J = 6.1 Hz, 2H), 3.09 – 3.02 (m, J = 12.3, 6.4 Hz, 2H), 3.02 – 2.93 (m, 2H), 2.10 (d, J = 2.3 Hz, 3H), 1.70 – 1.58 (m, 2H), 1.51 – 1.40 (m, 2H), 1.40 – 1.33 (m, J = 6.4 Hz, 2H), 1.27 (s, 2H) **FTIR-ATR** (cm^{-1}): 3311, 3217, 3043, 2936, 2858, 1701, 1652, 1624, 1560, 1526, 1499, 1464, 1439, 1389, 1331, 1310, 1253, 1209, 1182, 1138, 1105, 1071, 1007, 965, 943, 799, 761, 743, 701, 677, 663, 636, 602, 570, 564 **TGA analysis**: 180 °C

Synthesis of N-(3-(3-butylthioureido)propyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide

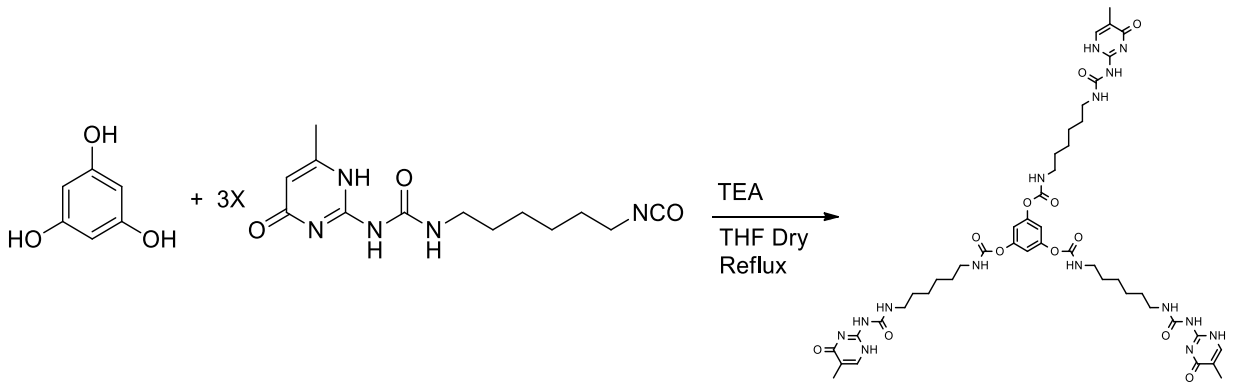


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
N-(3-aminopropyl)-5-(2-phenyl-2H-tetrazol-5-yl)thiophene-2-carboxamide	328.39	0.334	1.02	1		
1-isothiocyanatobutane	115.20	0.117	1.02	1	0.12	0.955

Solvent: DMF

334mg (1.02mmol) of N-(3-aminopropyl)-4-(2-phenyl-2H-tetrazol-5-yl)benzamide and 30 ml of DMF were added to a round bottom flask. After 117mg (1.02mmol) of 1-isothiocyanatobutane were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (235mg, yield:52%). **Physical aspect**: Solid, pink powder **^{1}HNMR** (400 MHz, DMSO) δ 8.82 – 8.72 (m, 2H), 8.14 (d, J = 7.5 Hz, 2H), 7.93 (d, J = 3.8 Hz, 1H), 7.87 (d, J = 3.8 Hz, 1H), 7.71 (t, J = 7.5 Hz, 2H), 7.69 – 7.62 (m, J = 7.4 Hz, 1H), 7.51 – 7.35 (m, 2H), 3.56 – 3.40 (m, 6H), 1.84 – 1.68 (m, J = 6.1 Hz, 2H), 1.44 (dd, J = 18.9, 11.3 Hz, 2H), 1.36 – 1.22 (m, J = 14.7, 7.6 Hz, 2H), 0.88 (t, J = 7.3 Hz, 3H) **FTIR-ATR** (cm^{-1}): 3311, 3258, 3074, 2955, 2932, 2865, 2324, 2196, 2112, 1694, 1636, 1618, 1597, 1551, 1498, 1466, 1431, 1422, 1380, 1357, 1325, 1311, 1285, 1256, 1227, 1189, 1128, 1072, 1007, 963, 944, 915, 885, 867, 821, 757, 744, 700, 677, 648, 571 **TGA analysis**: 180 °C

Synthesis of benzene-1,3,5-triyl tris((6-(3-(5-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)hexyl)carbamate) (compound 6)

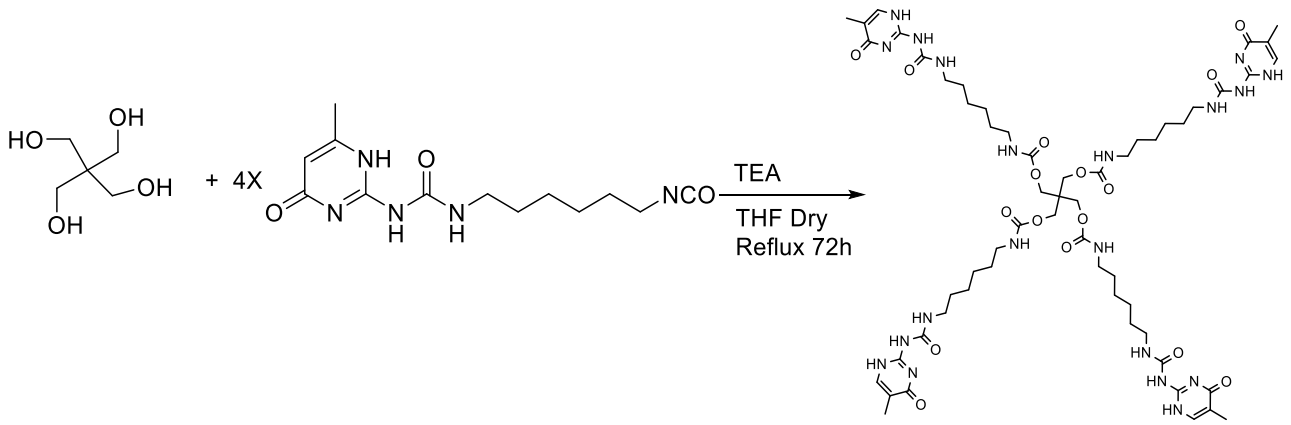


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
phloroglucinol	126.11	0.100	0.79	1		
1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea	293.32	0.698	2.38	3		
TEA	101.19	0.240	2.38	3	0.33	0.728

Solvent: Dry THF

100mg (0.79 mmol) of phloroglucinol and 20 ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. Afterwards 240mg (2.38 mmol) of TEA were added and, after 10 min. 698mg (2.38 mmol) of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea. The reaction mixture was heated at reflux under magnetic stirring for 72 hours. The mixture was allowed to cool down, then the precipitate was filtered over a filter funnel and washed with H_2O and DCM to give the pure product (685mg, yield:86%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$ + TFA) δ 11.43 (s, 3H), 8.19 (s, 3H), 6.96 – 6.45 (m, J = 65.3 Hz, 6H), 6.33 – 6.00 (m, J = 5.8 Hz, 3H), 3.40 – 3.19 (m, J = 37.6, 6.5 Hz, 12H), 2.52 – 2.37 (m, J = 9.1 Hz, 9H), 1.72 – 1.52 (m, 12H), 1.48 – 1.31 (m, 12H) **FTIR-ATR** (cm^{-1}): 3224, 3155, 3028, 2970, 2935, 2858, 1737, 1699, 1662, 1581, 1521, 1452, 1411, 1378, 1305, 1253, 1233, 1218, 1139, 1094, 1018, 937, 877, 799, 767, 742, 662, 602, 565 **MALDI mass**: 1006.08 m/z

Synthesis of Tetrakis(methyl [6-({[(5-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)amino]carbonyl}amino)hexyl]carbamate)methane (compound 7)

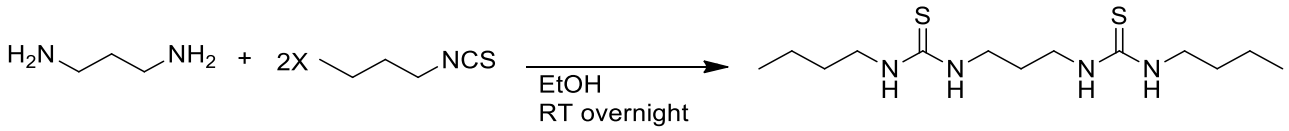


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
pentaerythritol	136.15	0.074	0.55	1		
1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea	293.32	0.709	2.40	4.4		
TEA	101.19	0.223	2.20	4	0.31	0.728

Solvent: Dry THF

74mg (0.55 mmol) of pentaerythritol and 20 ml of Dry THF were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. Afterwards 223mg (2.20 mmol) of TEA were added and, after 10 min. 709mg (2.40 mmol) of 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea. The reaction mixture was heated at reflux under magnetic stirring for 72 hours. The mixture was allowed to cool down, then the precipitate was filtered over a filter funnel and washed with H_2O and DCM to give the pure product (526mg, yield:73%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, $CDCl_3$ + TFA) δ 7.06 – 6.50 (m, 12H), 6.18 (d, J = 28.3 Hz, 4H), 4.59 – 3.61 (m, J = 146.4, 124.2 Hz, 8H), 3.53 – 2.91 (m, J = 52.2, 45.5 Hz, 16H), 2.41 (d, J = 36.1 Hz, 12H), 1.96 – 1.00 (m, J = 95.6, 67.3 Hz, 32H) **FTIR-ATR** (cm^{-1}): 3223, 3143, 3034, 2933, 2856, 1698, 1663, 1577, 1522, 1460, 1440, 1411, 1379, 1358, 1310,1253, 1176, 1140, 1044, 1021, 937, 873, 811, 767, 740, 601, 567 **MALDI mass**: 1309.43 m/z

Synthesis of 1,1'-(propane-1,3-diyl)bis(3-butylthiourea) (compound 8)

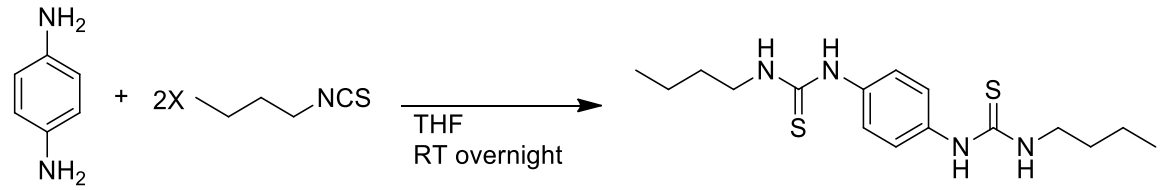


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
propane-1,3-diamine	74.12	1.00	13.5	1		
1-isothiocyanatobutane	115.20	3.11	27.0	2	3.25	0.955

Solvent: EtOH

1.00g (13.5 mmol) of propane-1,3-diamine and 30 ml of EtOH were added to a round bottom flask. After 3.11g (27.0 mmol) of 1-isothiocyanatobutane were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (4g, yield:97%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 7.37 (s, 4H), 1.73 – 1.61 (m, 2H), 151 – 1.39 (m, 4H), 1.28 (dd, J = 14.9, 7.4 Hz, 4H), 0.88 (t, J = 7.3 Hz, 6H) **FTIR-ATR** (cm^{-1}): 3218, 3095, 3019, 2958, 2929, 2862, 1676, 1548, 1519, 1466, 1448, 1411, 1363, 1320, 1275, 1251, 1214, 1200, 1152, 1111, 1063, 1016, 981, 931, 904, 870, 771, 730, 642, 570

Synthesis of 1,1'-(1,4-phenylene)bis(3-butylthiourea) (compound 9)

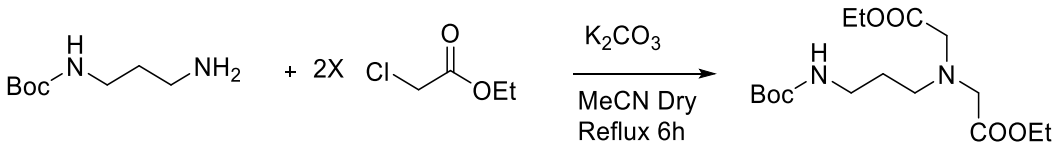


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
benzene-1,4-diamine	108.14	1.00	9.25	1		
1-isothiocyanatobutane	115.20	2.13	18.50	2	2.23	0.955

Solvent: THF

1.00g (9.25 mmol) of benzene-1,4-diamine and 50 ml of THF were added to a round bottom flask. After 2.13g (18.50 mmol) of 1-isothiocyanatobutane were added. The reaction mixture was stirred overnight. Water was added and the solid formed was filtered and washed several times with cyclohexane to give the pure product (2.70g, yield:86%). **Physical aspect**: Solid, white powder **^{1}HNMR** (400 MHz, DMSO) δ 9.40 (s, 4H), 7.66 (s, 4H), 6.90 (d, J = 8.5 Hz, 2H), 6.57 (d, J = 8.5 Hz, 2H), 3.52 – 3.38 (m, J = 23.3, 6.4 Hz, 4H), 1.59 – 1.41 (m, 4H), 1.38 – 1.22 (m, 4H), 0.98 – 0.80 (m, 6H) **FTIR-ATR** (cm^{-1}): 3253, 3170, 3107, 3001, 2957, 2932, 2871, 1890, 1674, 1630, 1537, 1516, 1501, 1466, 1424, 1392, 1362, 1320, 1291, 1260, 1238, 1222, 1195, 1151, 1103, 1082, 1060, 1013, 937, 907, 855, 799, 784, 733, 647, 611, 567, 551

Synthesis of diethyl 2,2'-((3-((tert-butoxycarbonyl)amino)propyl)azanediyl)diacetate

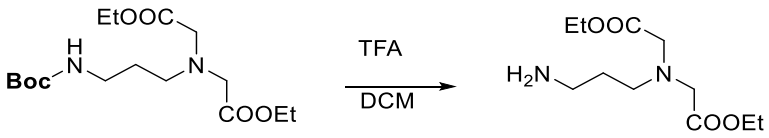


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
tert-butyl (3-aminopropyl)carbamate	174.24	5.00	29.00	1		
ethyl 2-chloroacetate	122.55	7.03	58.00	2	6.10	1.145
potassium carbonate	138.21	12.29	89.00	3.1		

Solvent: Dry acetonitrile

5.00g (29.00 mmol) of tert-butyl (3-aminopropyl)carbamate and 20ml of dry acetonitrile were added to a round bottom flask equipped with a water condenser, under nitrogen atmosphere. Then 12.29g (89.00 mmol) of potassium carbonate were added and, after 10 min., 7.03 (58.00 mmol) of ethyl 2-chloroacetate were added dropwise in 1h. The reaction mixture was heated at reflux, stirring for 6 hours. The mixture was allowed to cool down, the was extracted with ethyl acetate (2X 20ml), washing with brine (2X 20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the pure product (10.23g, yield:98%). **Physical aspect**: Pale yellow liquid **^{1}HNMR** (400 MHz, $CDCl_3$) δ 4.18 (dt, J = 7.1, 5.9 Hz, 4H), 3.51 (s, 4H), 3.24 (d, J = 5.7 Hz, 2H), 2.76 (t, J = 6.5 Hz, 2H), 1.70 – 1.58 (m, 2H), 1.45 (s, 9H), 1.29 (t, J = 7.1 Hz, 6H)

Synthesis of diethyl 2,2'-((3-aminopropyl)azanediyl)diacetate

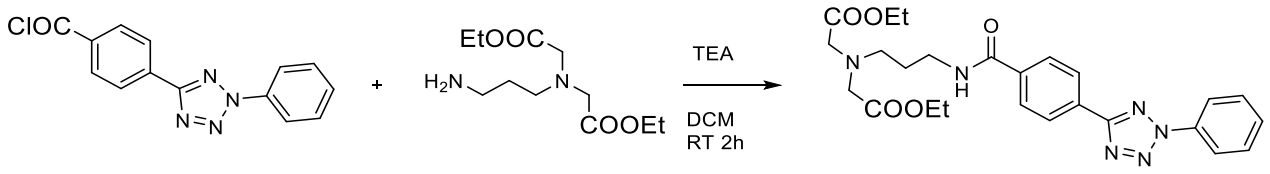


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
diethyl 2,2'-((3-((tert-butoxycarbonyl)amino)propyl)azanediyl)diacetate	356.42	1.00	2.68	1		
TFA	114.02	3.05	26.80	10	2.05	1.49

Solvent: DCM

1.00g (2.68 mmol) of diethyl 2,2'-((3-((tert-butoxycarbonyl)amino)propyl)azanediyl)diacetate and 10 ml of DCM were added to a round bottom flask. Afterwards 3.05g (26.80 mmol) of TFA were added. The reaction mixture was stirred overnight. The mixture was quenched with $NaCO_3$ in order to neutralize the excess of TFA (until pH=7), then was extracted with DCM (2X 20ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the pure product (640mg, yield:97%). **Physical aspect**: Liquid, yellow oil **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.50 (s, 2H), 4.21 (dd, J = 14.2, 7.1 Hz, 4H), 3.49 (s, 4H), 3.27 (s, 2H), 2.85 (s, 2H), 1.93 (s, 2H), 1.29 (t, J = 6.9 Hz, 6H)

Synthesis of diethyl 2,2'-((3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)azanediyl)diacetate

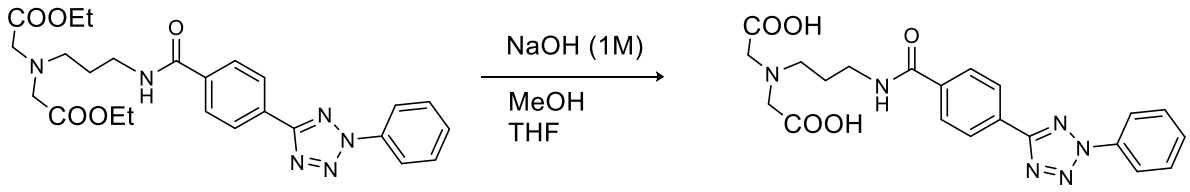


Reagent	M.W. (g/mol)	Weight (g)	mmol	eq	V(ml)	D(g/ml)
4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride	284.71	0.742	2.61	1		
diethyl 2,2'-((3-aminopropyl)azanediyl)diacetate	174.24	0.642	2.61	1		
TEA	101.19	0.264	2.61	1	0.10	0.728

Solvent: DCM

742mg (2.61mmol) of 4-(2-phenyl-2H-tetrazol-5-yl)benzoyl chloride and 30 ml of DCM were added to a round bottom flask. After 264mg (2.61mmol) of TEA were added and, after 10 min. 642mg (2.61mmol) of diethyl 2,2'-((3-aminopropyl)azanediyl)diacetate were added. The reaction mixture was stirred for 2 hours. The mixture was extracted with DCM (2X 20ml), washing with NaOH (1M) (2X10ml) and brine (2X 10ml). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (DCM/EtOAc 4:1→3:2) to give the pure product (340mg, yield:30%). **Physical aspect**: Liquid, red oil **^{1}HNMR** (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.4 Hz, 2H), 8.23 (d, J = 7.6 Hz, 2H), 8.13 (d, J = 8.4 Hz, 2H), 7.61 (t, J = 7.6 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 4.19 (dd, J = 14.1, 7.0 Hz, 4H), 3.77 – 3.64 (m, J = 5.6 Hz, 2H), 3.64 – 3.50 (m, J = 14.7 Hz, 4H), 2.95 – 2.83 (m, 2H), 1.87 – 1.75 (m, 2H), 1.28 (t, J = 7.1 Hz, 6H)

Synthesis of 2,2'-((3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)azanediyl)diacetic acid (compound 10)



Reagent	M.W. (g/mol)	Weight (g)	mmol	eq
diethyl 2,2'-((3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)azanediyl)diacetate	494.54	0.340	0.69	1
NaOH (1M)	39.99	0.100	2.5	1

Solvent: THF/MeOH

340mg (0.69 mmol) of diethyl 2,2'-((3-(4-(2-phenyl-2H-tetrazol-5-yl)benzamido)propyl)azanediyl)diacetate was dissolve in 5ml of a mixture of THF/MeOH (1:1). Then NaOH (1M) was added and the reaction stirred at room temperature overnight. Then HCl was added until the formation of a precipitate, which was filtered and washed with DCM to give the pure product (242mg, yield:80%). **Physical aspect**: Solid, orange powder **^{1}HNMR** (400 MHz, DMSO) δ 8.73 (s, 1H), 8.27 (d, J = 7.7 Hz, 2H), 8.19 (d, J = 7.5 Hz, 2H), 8.07 (d, J = 7.6 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H), 7.68 – 7.62 (m, J = 7.3 Hz, 1H), 3.83 – 3.63 (m, 4H), 3.64 – 3.45 (m, J = 5.5 Hz, 2H), 3.05 – 2.89 (m, 2H), 1.90 – 1.69 (m, 2H) **TGA analysis**: 180 °C