Regioselectivity control in spirobifluorene mild nitration reaction: explaining the Crivello's reagent mechanism.

Dawod Yousif,‖,# Luca Vaghi,# Constantin G. Daniliuc,‡ Riccardo Po,† Antonio Papagni,#* Fabio Rizzo§,‖*

‖ Center for Soft Nanoscience (SoN), Westfälische Wilhelms-Universität Münster, Busso-Peus-Str. 10, 48149 Münster, Germany.

Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, via R. Cozzi 55, 20125 Milano, Italy

† Eni SpA—Renewables, New Energies and Material Science Research Center, "Istituto Guido Donegani", Via Fauser 4, 28100 Novara, Italy.

‡ Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstr. 36, 48149 Münster, Germany.

§ Istituto di Scienze e Tecnologie Chimiche "G. Natta" (SCITEC), Consiglio Nazionale delle Ricerche (CNR), via G. Fantoli 16/15, 20138 Milano, Italy.

Supporting Information Placeholder
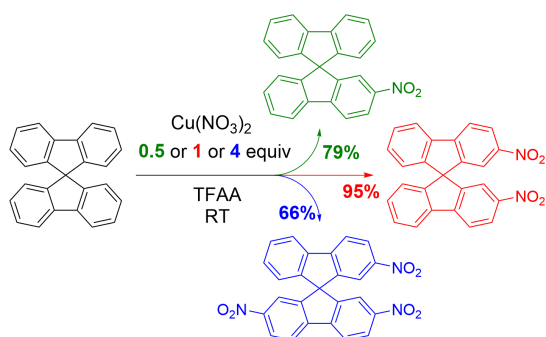
ABSTRACT: The regioselective nitration of 9,9'-spirobifluorene under mild conditions is reported for the first time by operating under Menke's and Crivello's conditions. The optimized protocol allows obtaining 2-nitro and 2,2'-dinitrospirobifluorene in yields of 79% and 95% and, for the first time, the 2,2',7-trinitro-9,9'-spirobifluorene with 66% yield. Besides, the role of dinitrate salt in Crivello's protocol has been now clarified, which opens novel scenarios in the preparation of functional materials.

Nitration of aromatic compounds is one of the most widely studied reactions and an immensely important industrial process,[1,2] due to the important role of nitroarenes as precursors of industrial products and functional materials.[2-5] Several reagents are available, the most common ones are mixtures of nitric and sulfuric acid, nitronium tetrafluoroborate[6] and acetyl nitrate.[7] However, nitrations are notoriously unselective, leading mixture of isomers. Moreover, they require harsh conditions, by means of an excess of highly corrosive mineral acids at high temperatures. Afterwards, the work-up with an aqueous washing step results in the production of acidic effluent, which is environmentally unfriendly and costly to treat.[8]

Crivello introduced the use of mixtures of ammonium nitrate and trifluoroacetic anhydride (TFAA) to nitrate a variety of aromatic compounds at room temperature in good yield.[9] Trifluoroacetyl nitrate seems to be the effective reactive nitrating agent that gives rise the nitronium ion upon heterolytic dissociation of the oxygen-nitrogen bond.[9,10] Despite of its efficacy, the method has been rarely applied to compounds with extended aromaticity, whereas metal nitrate mediated nitration of aromatic substrates is a current field of research.[11] It is worth to emphasize that Crivello tested several dinitrate salts as source of nitrating agent. The reported procedure involves the use of 1 equiv of nitrate salt regardless of the number of nitrate units, which seems to not significantly affect the mechanism. Among

the dinitrate salts, copper(II) nitrate results the best salt in terms of reaction time and yield.

9,9'-Spirobifluorene (Scheme 1) is a three-dimensional polyaromatic hydrocarbon compound receiving recently growing scientific and industrial interest.[12] Spirobifluorene-based functional materials found application in many technological fields, such as solar cells,[13] bioimaging,[14] microporous polymers,[15] and optoelectronics.[16] Particularly, spirobifluorene derivatives have been investigated as high energy host materials for phosphorescent OLEDs.[17] Moreover, the 9,9'-spirobifluorene can also be used as core of compounds showing peculiar optical properties, such as up-conversion[18] and chiroptics.[19] Spirobifluorene derivatives are generally synthesized by following two approaches, i.e., either by modifying the precursors[20] or by post modification of the spiro-core.[16] Due to the two fluorene units connected through a sp³-hybridized carbon, the functionalization mainly occurs at the 2,2',7,7' positions through electrophilic aromatic substitutions.[21] Particularly, the nitration[22] shows the formation of 2,2'-dinitrospirobifluorene **2** in fair yield (around 65%) under harsh conditions, with highly environmentally unfriendly and costly to treat waste. These conditions allow a very limited control of the regioselectivity. Indeed, even working under carefully controlled reaction conditions, the mono-substituted 2-nitrospirobifluorene **1** is recovered in very poor yield (11%)[22] (Scheme 1). Noteworthy, the formation of side products and the harsh conditions affect dramatically the reproducibility, as underlined by different yields reported in literature for **2** (from 39 to 65%).[15a,22] Additionally, the 2,2',7,7'-tetranitrospirobifluorene has been reported,[23] while there are no reports concerning the trinitro-derivative. Interestingly, alternative nitration conditions on spirobifluorene have not been explored so far, with the exception of the nitration of spirosilabifluorene under Menke conditions.[7,24] However, this substrate results more reactive towards electrophilic substitution.
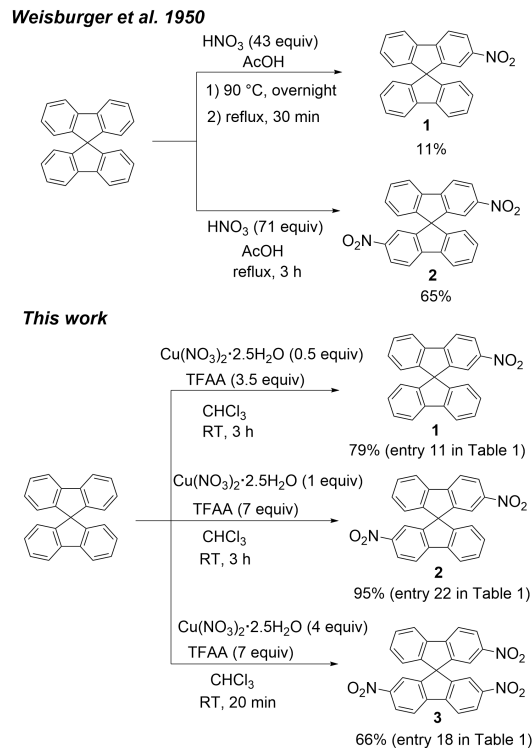
Willing to improve the nitration of spirobifluorene in terms of yields and environmental impact, we investigated the electrophilic substitution under mild conditions, i.e., by using Menke and Crivello conditions (Table 1 and S1). The presence of two independent fluorene units in one single compound contributed to a novel understanding of the mechanism originally described by Crivello.[9]

Menke's protocol involves the formation of acetyl nitrate as nitrating agent by reacting copper(II) nitrate in large excess of acetic anhydride (Ac$_2$O) at 40 °C.[7] By applying this procedure to 9,9'-spirobifluorene using 1 equiv of Cu(NO$_3$)$_2$·2.5H$_2$O (hemi-pentahydrate), after 3 h we isolated the mono- and dinitro-derivatives **1** and **2** in 21 and 59% yields respectively, without full conversion of the starting material (entry 1). Unexpectedly, by doubling the amount of salt and Ac$_2$O, the complete conversion of the substrate increases **2** up to 71% and we isolated for the first time the 2,2',7-trinitrospirobifluorene **3** in a significant 22% yield, without traces of compound **1**

(entry 2). However, the high amount of Ac$_2$O employed is far away from atom economy and environmentally friendly concepts.

Crivello's method fulfils these concepts. Nevertheless, the nitration of 9,9'-spirobifluorene using ammonium nitrate was totally unsuccessful. After 3 h we observed only a partial conversion of spirobifluorene together with several multi-nitrated products, indicating the lack of regioselectivity observed under Menke conditions (entries 3-4). This was in contrast with the excellent yield of the nitration of polyaromatic compounds (naphthalene and biphenyl) reported by Crivello (> 88%).[9] Based on these preliminary results and on the performance of copper(II) nitrate as source of nitrating agent reported by Crivello in comparison with other divalent nitrate salts, we carried out the reaction in chloroform at room temperature by replacing NH$_4$NO$_3$ with Cu(NO$_3$)$_2$·2.5H$_2$O, combined with a TFAA excess, resulting in the regioselective nitration of spirobifluorene (Scheme 1). First attempts were performed by using a molar ratio of 1:1:7 for spirobifluorene, Cu(NO$_3$)$_2$·2.5H$_2$O and TFAA, respectively (entry 5). After 3 h the desired 2,2'-dinitrospirobifluorene **2** was isolated in very good yield (79%) together with traces of **3** as side product (4%), indicating higher regioselectivity than the Menke approach. In accordance with Crivello, the reaction did not proceed by using Ac$_2$O instead of TFAA under the same molar ratio (entry 6).

Scheme 1. Nitration of 9,9'-spirobifluorene.

Weisburger et al. 1950

HNO$_3$ (43 equiv)
AcOH
1) 90 °C, overnight
2) reflux, 30 min
1
11%

HNO$_3$ (71 equiv)
AcOH
reflux, 3 h
2
65%

This work

Cu(NO$_3$)$_2$·2.5H$_2$O (0.5 equiv)
TFAA (3.5 equiv)
CHCl$_3$
RT, 3 h
1
79% (entry 11 in Table 1)

Cu(NO$_3$)$_2$·2.5H$_2$O (1 equiv)
TFAA (7 equiv)
CHCl$_3$
RT, 3 h
2
95% (entry 22 in Table 1)

Cu(NO$_3$)$_2$·2.5H$_2$O (4 equiv)
TFAA (7 equiv)
CHCl$_3$
RT, 20 min
3
66% (entry 18 in Table 1)

Nevertheless, the data were in contrast with Crivello's description. Indeed, Crivello used a constant of 1 equiv of nitrate source regardless of the number of nitrate groups of the salt to perform the mono-nitration. To

understand the mechanism of the nitration with cupric nitrate, we studied different parameters, i.e., reaction time, amounts of nitrate salt and TFAA, and solvent volume. Higher dilution induced lower reaction rates, as underlined by the reduced amount of **2** isolated after 3 h (entries 7 and 16). The amount of TFAA plays a fundamental role, as already mentioned by Crivello. A large excess of TFAA had a negative effect on the reaction in terms of time and yield (entry 8), whereas by reducing TFAA below the stoichiometric amount needed to remove all crystallization water from Cu(NO$_3$)$_2$·2.5H$_2$O, the nitration did not occur or gave only 2% of **1** (entry 9).

By halving the amount of salt, **1** was isolated in good yield, regardless of the amount of TFAA and reaction time (entries 10-11). In contrast, increasing copper(II) nitrate affected the formation of dinitro and trinitro derivatives. With 1 equiv of Cu(NO$_3$)$_2$·2.5H$_2$O the full conversion occurred already after 40 minutes with 72% of **1** and only 14% of **2** (entry 12), while higher amounts of **2** were obtained with 2-3 h (entries 13 and 5). A further enhancement of nitrate salt content speeded up the formation of **2**, and the time became a fundamental parameter (entries 15,17,18). Indeed, 2 equiv gave **2** in good yield already after 20 minutes with 26% of **1**, whereas longer reaction time increased the amount of **3** (entry 17). With a large excess of copper(II) nitrate (4 equiv), the 2,2',7-trinitrospirobifluorene **3** was isolated in 66% yield in 20 minutes (entry 18).

Interestingly, the formation of the tetranitro-derivative was not observed under our mild experimental conditions even in presence of large excess of cupric nitrate in 3 h.

These data suggest that the nitration process is regulated by i) the very different reactivity of the substrates (the starting material and the two nitro derivatives), and ii) the presence of at least two nitrating species.

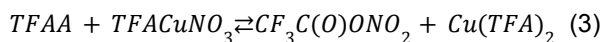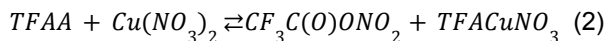**TABLE 1** Nitration of 9,9'-spirobifluorene (2 mmol) in chloroform at room temperature. (Isolated yields)

Entry	mol. nitrate salt[a]	mol. Anhydride[b]	Solvent mL	Time	% Spiro	% 1	% 2	% 3
1	1	32[c]	-[d]	3 h	2	21	59	-
2	2	64[c]	-[d]	3 h	-	-	71	22
3	1[e]	3.5	5	5 h		Mixture		
4	1[e]	7	5	3 h		Mixture		
5	1	7	5	3 h	-	-	79	4
6	1	7[c]	5	3 h		No reaction		
7	1	7	10	3 h	-	28	70	-
8	1	14	5	3 h	-	1	55	-
9	1	1	5	3 h	86	2	-	-
10	0.5	7	5	3 h	-	74	5	-
11	0.5	3.5	5	5 h	-	79	4	-
12	1	7	5	40 min	-	72	14	-
13	1	7	5	2 h	-	19	62	-
14	1	7	5	3 h		Mixture[f]		
15	2	7	5	20 min	-	25	70	-
16	2	7	10	20 min	7	80	6	-
17	1.5	7	5	3 h	-	-	41	40
18	4	7	5	20 min	-	-	30	66
19	0.5	7	5	3 h	7[g]		92	-
20	0.5	7	5	3 h			53[h]	40
21	1.25[i]	7	5	2.5 h	-	-	87	-
22	1.02[i]	7	5	3 h	-	-	95	-

a: Cu(NO$_3$)$_2$·2.5H$_2$O if not otherwise specified. b: TFAA if not otherwise specified. c: Ac$_2$O. d: at 40 °C. e: NH$_4$NO$_3$. f: substrate added after 5 minutes. g: compound **1** as starting material. h: compound **2** as starting material. i: portioning addition.

Crivello indicated the trifluoroacetyl nitrate as the nitrating agent (eq. *1*)

$$(CF_3CO)_2O + MNO_3 \rightleftarrows CF_3C(O)ONO_2 + CF_3C(O)OM$$
(1)
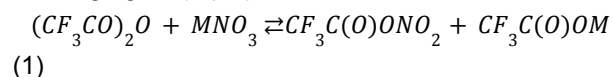
However, the use of dinitrate salt such as Cu(NO$_3$)$_2$ must also include the formation of a mixed salt, i.e., copper(II) trifluoroacetyl nitrate (TFACuNO$_3$), which can release a second nitronium ion upon further reaction with another TFAA unit (eq. *2* and *3*).

$$TFAA + Cu(NO_3)_2 \rightleftarrows CF_3C(O)ONO_2 + TFACuNO_3 \quad (2)$$

$$TFAA + TFACuNO_3 \rightleftarrows CF_3C(O)ONO_2 + Cu(TFA)_2 \quad (3)$$

Nevertheless, we cannot exclude the disproportionation of the mixed salt into cupric nitrate and cupric trifluoroacetate (eq. *4*), which restores the more reactive $Cu(NO_3)_2$.

$$TFACuNO_3 \rightleftarrows Cu(NO_3)_2 + Cu(TFA)_2 \quad (4)$$
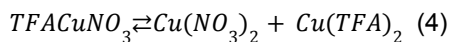
From our data, we hypothesized that the formation of trifluoroacetyl nitrate should be faster on $Cu(NO_3)_2$ (eq. *2*) and slower on $TFACuNO_3$ (eq. *3*), which could justify the conversion of the starting material into **1** as the first step, followed by the second nitration. In (*2*) and (*3*) TFAA plays a crucial role, and large quantities of TFAA speed up these equilibriums, increasing the nitration rate.

Unfortunately, it was not possible to isolate the intermediate species due to their high reactivity, as observed by Crivello. Nevertheless, we performed UV-Vis experiments to compare the absorption spectra of the commercially available $Cu(TFA)_2$ with the species forming during the reaction through time dependent absorption experiments (Figures S12-S13). Due to the high extinction coefficient, the region below 300 nm is saturated by the absorption of the organic ligand, while the d-d absorption band typical of copper alkanoates[25] is clearly visible in the red-NIR region. $Cu(TFA)_2$ maximum peak is at 780 nm, in good agreement with the literature.[26] $Cu(NO_3)_2$ shows no absorption in the infrared region. Interestingly, by adding TFAA a new band with maximum at 734 nm appears immediately, indicating the presence of a copper complex that cannot be identified as $Cu(TFA)_2$ due to the large different absorption band. Owing to the lack of other absorbing species in this region of the spectrum and the results of time dependent absorption experiments, we could assign the new absorption band to the mixed salt. However, the identification of this species is not sure, because change on the absorption band of copper complexes can also arise from modification of the coordination sphere.[27]

To understand the role of $TFACuNO_3$ and its evolution through the equilibrium (*2-4*), we performed the nitration firstly by mixing $Cu(NO_3)_2$ with TFAA to form the whole amount of trifluoroacetyl nitrate (from both eq. *2* and *3*), followed by the addition of 9,9'-spirobifluorene (entry 14). The obtained mixture of multi-nitrated products, like the outcome reached with NH_4NO_3, supports the hypothesis that the formation of $TFACuNO_3$ is the key to regulate the amount of nitronium ions in the mixture, thus preserving the regioselectivity.

The second important parameter for regioselectivity is the different reactivity of the substrates. The data suggest that the starting spirobifluorene is more reactive than **1**, and the formation of **2** begins when a reasonable quantity of **1** is formed. This was also confirmed by the increased amount of **2** with longer reaction time (entries 12 and 13). The slowly increase of **2** also supports the hypothesis that the second trifluoroacetyl nitrate generated from $TFACuNO_3$ (eq. *3*) occurs at slower rates than from $Cu(NO_3)_2$ (eq. *2*). Even if the equilibrium (eq. *4*) is active, the concentration of $Cu(NO_3)_2$ halves after the reaction with TFAA as well as the reactive mixed salt, and this does not justify the high chemoselectivity in mononitration with ½ mole of $Cu(NO_3)_2$ (entries 10 and 11). In contrast, this underlines the higher reactivity of spirobifluorene versus **1**.

Additionally, reacting **1** with ½ mole of $Cu(NO_3)_2$ gave the dinitro spirobifluorene **2** in high yield (92%, entry 19), while the same reaction performed on **2** produced a mixture of unreacted **2** (52%) and trinitrate-spirobifluorene **3** (40%, entry 20).

The lack of traces of tetranitrate-spirobifluorene by reacting 9,9'-spirobifluorene with an excess of $Cu(NO_3)_2$ for 3 h indicates the decreasing reactivity of substrate bearing larger number of nitro-groups. Furthermore, the reaction of a mixture of 9,9'-spirobifluorene and **1** (0.5 equiv each) with a defect of cupric nitrate (0.25 equiv) allowed recovering **1** as the main product with traces of unreacted spirobifluorene and of **2** (see Supporting Information), further confirming the scale of reactivity 9,9'-spirobifluorene ≫ **1** ≫ **2**.

Noteworthy, further optimization of the conditions allowed an enhancement of the yield of **2** up to 95% (entries 21-22). This outstanding outcome was reached with a slightly excess of nitrate salt (2%) and by portioning the addition of salt in small quantities every 30 minutes. This protocol allows controlling the release of nitronium ions and the complete conversion of 9,9'-spirobifluorene and **1** into **2**.

Summarising, the observed regioselectivity is the result of the following aspects in sequence: 1) generation of anhydrous $Cu(NO_3)_2$ (2.5 equiv of TFAA consumed); 2) fast generation of the first equivalent of trifluoroacetyl nitrate (1 equiv of TFAA consumed and 1 equiv. of mixed salt $TFACuNO_3$ formed), 3) higher reactivity of starting spirobifluorene in comparison of mono-nitrospirobifluorene; 4) slow generation of the second equivalent of trifluoroacetyl nitrate from the mixed salt and subsequent nitration of **1**.

To expand the scope of our protocol, we performed the nitration on other commercially available substrates, such as 2,2'-dibromo-9,9'-spirobifluorene and few fluorene derivatives (Scheme 2), due to their great importance in optoelectronics,[28] biology[29] and medicinal chemistry.[30] The 2,2'-dibromo-7,7'-dinitro-9,9'-spirobifluorene **4** was isolated with excellent yield (89%) by using 1 equiv of copper(II) nitrate, indicating high efficiency also over functionalized spirobifluorene. Starting from

9,9-dimethyl-9*H*-fluorene, the mononitrated 9,9-dimethyl-2-nitro-9*H*-fluorene **5** was obtained with an excellent yield (91%) by employing 0.5 equiv. of $Cu(NO_3)_2$, while the presence of one nitro group deactivates the substrate resulting in lower yield for 9,9-dimethyl-2,7-dinitro-9*H*-fluorene **6** (80%). Using 2-bromo-9,9-dimethylfluorene as substrate, the nitration proceeded more efficiently by giving the 2-bromo-9,9-dimethyl-7-nitro-9*H*-fluorene **7** in excellent yield (94%). Noteworthy, the yields of the three fluorene derivatives are higher than the values reported in literature, i.e., 75%,[31] 30%,[32] 73%,[33] for **5**, **6** and **7** respectively.

Scheme 2. Nitration of 2,2'-dibromo-9,9'-spirobifluorene, 9,9-dimethyl-9H-fluorene and 2-bromo-9,9-dimethylfluorene.
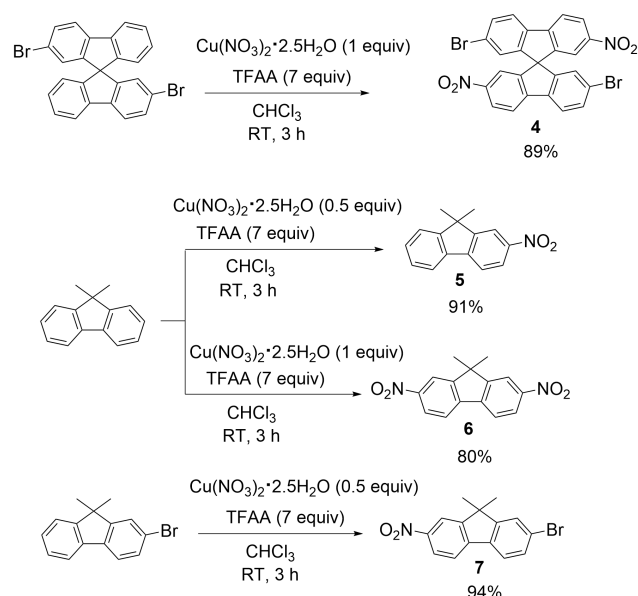
In conclusion, we developed an effective protocol for the nitration of spirobifluorene and fluorene at room temperature with high regioselectivity and an outstanding enhancement in yields compared to literature data. Although compounds **1**-**3** can be prepared under both Menke and Crivello conditions, we showed that the latter allows higher regioselectivity and yields. A possible explanation lies on the different reactivity of the acetyl nitrate and trifluoroacetyl nitrate as source of nitrating agent. Indeed, by considering the scale of reactivity of the involved substrates (9,9'-spirobifluorene ≫ **1** ≫ **2**), the amount of nitro derivatives recovered in 3 h is very different. Moreover, the amount of nitrate salt used under Menke conditions is definitively higher than under Crivello conditions, suggesting a lower efficiency as nitrating agent. The reported synthetic approach is expected to have a tremendous impact on the preparation of spirobifluorene- and fluorene-based functional materials thanks to the lower amount of nitrating agent compared to the classic nitration procedures (15 times less for the preparation of **2**.The new 2,7,2'-trinitrospirobifluorene paves the way to novel materials, for example in the field of microporous polyimides. Finally, the deepest understanding of the mechanism of divalent nitrate salt in Crivello method obtained by working on 9,9'-spirobifluorene will open novel scenarios for the nitration of polyaromatic hydrocarbon compounds.

AUTHOR INFORMATION

Corresponding Author

* **Antonio Papagni** - *Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, via R. Cozzi 55, 20125 Milano, Italy;* https://orcid.org/0000-0003-2744-3883

* **Fabio Rizzo** - *Center for Soft Nanoscience (SoN), Westfälische Wilhelms-Universität Münster, Busso-Peus-Str. 10, 48149 Münster, Germany; Istituto di Scienze e Tecnologie Chimiche "G. Natta" (SCITEC), Consiglio Nazionale delle Ricerche (CNR), via G. Fantoli 16/15, 20138 Milano, Italy*; https://orcid.org/0000-0003-4045-2653; Email: fabio.rizzo@cnr.it

Authors

Dawod Yousif - *Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, via R. Cozzi 55, 20125 Milano, Italy*

Luca Vaghi - *Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, via R. Cozzi 55, 20125 Milano, Italy;* https://orcid.org/0000-0001-5745-3826

Constantin G. Daniliuc – *Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstr. 36, 48149 Münster, Germany;* https://orcid.org/0000-0002-6709-3673

Riccardo Po - *Eni SpA-Renewables, New Energies and Material Science Research Center, "Istituto Guido Donegani", Via Fauser 4, 28100 Novara, Italy;* https://orcid.org/0000-0002-8374-195X

Acknowledgments

References

(1) (a) Yan, G.; Yang, M. Recent advances in the synthesis of aromatic nitro compounds. *Org. Biomol. Chem.* **2013**, *11*, 2554-2566; (b) Patra, S.; Mosiagin, I.; Giri, R.; Katayev, D. Organic Nitrating Reagents. *Synthesis* **2022**, *54*, 3432-3452.

(2) Olah, G. A.; Malhorta, R.; Narang, S. C. *Nitration – Methods and Mechanism*. VCH: New York, 1989.

(3) (a) Varghese, S.; Spierenburg, B.; Swartjies, A.; White, P.B.; Tinnemans, P.; Elemans, J. A. A. W.; Nolte, R. J. M. Direct Synthesis of Chiral Porphyrin Macrocyclic Receptors via Regioselective Nitration. *Org. Lett.* **2018**, *20*, 3719-3722. (b) Poronik, Y. M.; Sadowski, B.; Szychta, K.; Quina, F. H.; Vullev, V. I. Gryko, D. T. Revisiting the non-fluorescence of nitroaromatics: presumption versus reality. *J. Mater. Chem. C* **2022**, *10*, 2870-2904.

(4) Hughes, E. D.; Ingold, C. K.; Reed, R. I. Kinetics and Mechanism of Aromatic Nitration. Part II. Nitration by the Nitronium Ion, NO_2^+, derived from Nitric Acid. *J. Chem. Soc.* **1950**, 2400-2440.

(5) (a) Esteves, P. M.; Carneiro, J. W. M.; Cardoso, S. P.; Barbosa, A. G. H.; Laali, K. K.; Rasul, G.; Prakash, G. K. S.; Olah, G. A. Unified Mechanistic Concept of Electrophilic Aromatic Nitration: Convergence of Computational Results and Experimental Data. *J. Am. Chem. Soc.* **2003**, *125*, 4836-4849. (b) Queiroz, J. F.; Carneiro, J. W. M.; Sabino, A. A.; Sparrapan, R.; Eberlin, M. N.; Esteves, P. M. Electrophilic Aromatic Nitration: Understanding Its Mechanism and Substituent Effects. *J. Org. Chem.* **2006**, *71*, 6192-6203. (c) Peng, X.; Suzuki, H. Regioselective Double Kyodai Nitration of Toluene and Chlorobenzene over Zeolites. High Preference for the 2,4-Dinitro Isomer at the Second Nitration Stage. *Org. Lett.* **2001**, *3*, 3431-3434.

(6) (a) Olah, G.; Narang, S.; Olah, J.; Lammertsma, K. Recent aspects of nitration: New preparative methods and mechanistic studies (a review). *Proc. Nat. Acad. Sci. USA* **1982**, *79*, 4487–4494. (b) Zhang, M.-X.; Zuckerman, N. B.; Pagoria, P. F.; Steele, B. A.; Kuo, I.-F.; Imler, G. H.; Parrish, D. Mono- and Dinitro-BN-Naphthalenes: Formation and Characterization. *Molecules* **2021**, *26*, 4209.

(7) (a) Menke, J. B. Nitrieren mit Nitraten. *Rec. Trav. Chim.* **1925**, *44*, 141-149. (b) Laszlo, P.; Vandormael, J. Regioselective Nitration of Aromatic Hydrocarbons by Metallic Nitrates on the K10 Montmorillonite under Menke Conditions. *Chem. Lett.* **1988**, 1843-1846; (c) Delaude, L.; Laszlo, P.; Smith, K. Heightened Selectivity in Aromatic Nitrations and Chlorinations by the Use of Solid Supports and Catalysts. *Acc. Chem. Res.* **1993**, *26*, 607-613.

(8) *Chemistry of Waste Minimization*, J. H. Clark, Ed.; Chapman and Hall, London, 1995.

(9) (a) Crivello, J. V. Nitrations and Oxidations with Inorganic Nitrate Salts in Trifluoroacetic Anhydride. *J. Org. Chem.* **1981**, *46*, 3056-3060; (b) Crivello, J. V. Nitration of aromatic ring-containing compositions. US 3 715 323 A, 1973.

(10) Zelenov, V. P.; Bukalov, S. S.; Leites, L. A.; Aysin, R. R.; Subbotin, A. N.; Struchkova, M. I.; Fedyanin, I. V. Trifluoroacetyl nitrate. *Mendeleev Commun.* **2017**, *27*, 31-34.

(11) (a) Zhang, Y.; Dan, W.; Fang, X. Metal Nitrate Mediated Regioselective Nitration of BN-Substituted Arenes. *Organometallics* **2017**, *36*, 1677-1680. (b) Murai, M.; Nishinaka, N.; Kimura, M.; Takai, K. Regioselective Functionalization of 9,9-Dimethyl-9-silafluorenes by Borylation, Bromination, and Nitration. *J. Org. Chem.* **2019**, *84*, 5667-5676.

(12) example of recent review: (a) Poriel, C.; Rault-Berthelot, J. Pure Hydrocarbons: An Efficient Molecular Design Strategy for the Next Generation of Host Materials for Phosphorescent Organic Light-Emitting Diodes. *Acc. Mater. Res.* **2022**, *3*, 379-390. (b) Liu, S.; Xia, D.; Baumgarten, M. Rigidly Fused Spiro-Conjugated π-Systems. *ChemPlusChem* **2021**, *86*, 36-48.

(13) (a) Vaghi, L.; Rizzo, F. The Future of Spirobifluorene‑Based Molecules as Hole‑Transporting Materials for Solar Cells. *Sol. RRL* **2023**, 2201108. (b) Matsumoto, T.; Murakami, T.; Schlüter, F.; Murata, H.; Vohra, V.; Rizzo, F. Water-Soluble Organic Dyes as Efficient Anode Interlayer Materials for PEDOT:PSS-Free Inverted Bulk Heterojunction Solar Cells. *Sol. RRL* **2022**, *6*, 2100661. (b) Vaitukaityte, D.; Momblona, C.; Rakstys, K.; Sutanto, A. A.; Ding, B.; Igci, C.; Jankauskas, V.; Gruodis, A.; Malinauskas, T.; Asiri, A. M.; Dyson, P. J.; Getautis, V.; Nazeeruddin, M. K. Cut from the Same Cloth: Enamine-Derived Spirobifluorenes as Hole Transporters for Perovskite Solar Cells. *Chem. Mater.* **2021**, *33*, 6059-6067. (c) Bach, U.; Lupo, D.; Comte, P.; Moser, J. E.; Weissörtel, F.; Salbeck, J.; Spreitzer, H.; Grätzel, M. Solid-state dye-sensitized mesoporous TiO2 solar cells with high photon-to-electron conversion efficiencies. *Nature* **1998**, *395*, 583-585.

(14) Schlüter, F.; Riehemann, K.; Kehr, N. S.; Quici, S.; Daniliuc, C. G.; Rizzo, F. A highly fluorescent water soluble spirobifluorene dye with a large Stokes shift: Synthesis, characterization and bio-applications. *Chem. Commun.* **2018**, *54*, 642-645.

(15) (a) Weber, J.; Su, Q.; Antonietti, M.; Thomas, A. Exploring Polymers of Intrinsic Microporosity–Microporous, Soluble Polyamide and Polyimide. *Macromol. Rapid. Commun.* **2007**, *28*, 1871-1876. (b) Wen, P.; Kim, Y.; Chun, H.; Yang, S.-Y.; Lee, M.-H. Syntheses and characterizations of cardo polyimides based on new spirobifluorene diamine monomer. *Mater. Chem. Phys.* **2013**, *139*, 923-930.

(16) (a) Saragi, T. P. I.; Spehr, T.; Siebert, A.; Fuhrmann-Lieker, T.; Salbeck, J. Spiro Compounds for Organic Optoelectronics. *Chem. Rev.* **2007**, *107*, 1011-1065. (b) Poriel, C.; Sicard, L.; Rault-Berthelot, J. New generations of spirobifluorene regioisomers for organic electronics: tuning electronic properties with the substitution pattern. *Chem Commun.* **2019**, *55*, 14238-14254. (c) Qu, Y.-K.; Fan, J.; Liao, L.-S.; Jiang, Z.-Q. Spiro Compounds for Organic Light-Emitting Diodes. *Acc. Mater. Res.* **2021**, *2*, 1261-1271. (d) Wu, C.-L.;

Chen, C.-T.; Chen, C.-T. Synthesis and Characterization of Heteroatom-Bridged Bis-spirobifluorenes for the Application of Organic Light-Emitting Diodes. *Org. Lett.* **2014**, *16*, 2114-2117.

(17) (a) Wang, Y.; Yun, J. H.; Wang, L.; Lee, J. Y. High Triplet Energy Hosts for Blue Organic Light-Emitting Diodes. *Adv. Funct. Mater.* **2021**, *31*, 2008332. (b) Poriel, C.; Quinton, C.; Lucas, F.; Rault-Berthelot, J.; Jiang, Z.-Q.; Jeannin, O. Spirobifluorene Dimers: Understanding How The Molecular Assemblies Drive The Electronic Properties. *Adv. Funct. Mater.* **2021**, *31*, 2104980. (c) Kong, F.-C.; Zhang, Y.-L.; Quinton, C.; McIntosh, N.; Yang, S.; Rault-Berthelot, J.; Lucas, F.; Jeannin, O.; Cornil, J.; Jiang, Z.-Q.; Liao, L.-S.; Poriel, C. Pure Hydrocarbon Materials as Highly Efficient Host for White Phosphorescent Organic Light-Emitting Diodes: A New Molecular Design Approach. *Angew. Chem. Int. Ed.* **2022**, *61*, e202207.

(18) Vaghi, L.; Rizzo, F.; Pedrini, J.; Mauri, A.; Meinardi, F.; Cosentino, U.; Greco, C.; Monguzzi, A.; Papagni, A. Bypassing the statistical limit of singlet generation in sensitized upconversion using fluorinated conjugated systems. *Photochem. Photobiol. Chem.* **2022**, *21*, 913-921.

(19) (a) Ozcelik, A.; Aranda, D.; Pereira-Cameselle, R.; Talavaera, M.; Covelo, B.; Santoro, F.; Pena-Gallego, A.; Alonso-Gomez, J. L. ON/OFF Spiroconjugation through Peripheral Functionalization: Impact on the Reactivity and Chiroptical Properties of Spirobifluorenes. *ChemPlusChem* **2022**, *87*, e202100554. (b) Miki, K.; Noda, T.; Gon, M.; Tanaka, K.; Chujo, Y.; Mizuhata, Y.; Tokitoh, N.; Ohe, K. Near-Infrared Circularly Polarized Luminescence through Intramolecular Excimer Formation of Oligo(p-phenyleneethynylene)-Based Double Helicates. *Chem. Eur. J.* **2019**, *25*, 9211-9216. (c) Harada, N.; Ono, H.; Nishi-waki, T.; Uda, H. Synthesis, Circular Dichroism and Absolute Stereochemistry of Chiral Spiroaromatic Compounds. 9,9'-Spirobifluorene Derivatives. *Chem. Commun.* **1991**, 1753-1755.

(20) Chiang, C.-L.; Shu, C.-F.; Chen, C.-T. Improved Synthesis of 2,2'-Dibromo-9,9'-spirobifluorene and its 2,2'-Bisdonor-7,7'-biacceptor-Substituted Fluorescent Derivatives. *Org. Lett.* **2005**, *7*, 3717-3720.

(21) (a) Thiemann, F.; Piehler, T.; Haase, D.; Saak, W.; Lützen, A. Synthesis of Enantiomerically Pure Dissymmetric 2,2'-Disubstituted 9,9'-Spirobifluorenes. *Eur. J. Org. Chem.* **2005**, 1991-2001. (b) Cuntze, J.; Owens, L.; Alcazar, V.; Seiler, P.; Diederich, F. Molecular Clefts Derived from 9,9'-Spirobi[9H-fluorene] for Enantioselective Complexation of Pyranosides and Dicarboxylic Acids. *Helv. Chim. Acta* **1995**, *78*, 367-380. (c) Haas, G.; Prelog, V. Optisch aktive 9,9'-Spirobifluoren-Derivate. *Helv. Chim. Acta* **1969**, *52*, 1202-1218. (c) Haas, G.; Hulbert, P. B.; Klyne, W.; Prelog, V.; Snatzke, G. Chiroptische Eigenschaften und absolute Konfiguration von 9,9'-Spirobifluoren-Derivaten. *Helv. Chim. Acta* **1971**, *54*, 491-509.

(22) Weisburger, J. H.; Weisburger, E. K.; Ray, F. E. Some derivatives of 9,9'-Spirobifluorene. *J. Am. Chem. Soc.* **1950**, *72*, 4253-4255.

(23) (a) Pyka, I.; Ryvlin, D.; Waldvogel, S. R. Application of Rigidity-Controlled Supramolecular Affinity Materials for the Gravimetric Detection of Hazardous and Illicit Compounds. *ChemPlusChem* **2016**, *81*, 926-929. (b) Demers, E.; Maris, T.; Cabana, J.; Fournier, J.-H.; Wuest, J. D. Weakly Bonded Molecular Networks Built from Tetranitro- and Tetracyanospirobifluorenes. *Cryst. Growth Des.* **2005**, *5*, 1237-1245.

(24) Xiao, H.; Leng, B.; Tian, H. Hole transport triphenylamine–spirosilabifluorene alternating copolymer: synthesis and optical, electrochemical and electroluminescent properties. *Polymer* **2005**, *46*, 5707-5713.

(25) (a) Graddon, D. P. The absorption spectra of complex salts – IV Cupric Alkanoates. *J. Inrog. Nucl. Chem.* **1961**, *17*, 222-231. (b) Yamada, S.; Nakamura, H.; Tsuchida, R. Spectrochemical Study of Microscopic Crystals. XVI1. Structure of Cupric Formate, Acetate and Propionate. *Bull. Chem. Soc. Jpn.* **1957**, *30*, 953-957. (c) Kyuzou, M.; Mori, W.; Tanaka, J. Electronic structure and spectra of cupric acetate mono-hydrate revisited. *Inorg. Chim. Acta* **2010**, *363*, 930-934.

(26) Glebov, E. M.; Plyusnin, V. F.; Grivin, V. P.; Krupoder, S. A.; Liskovskaya, T. I.; Danilovich, V. S. Photochemistry of copper(II) polyfluorocarboxylates and copper(II) acetate as their hydrocarbon analogues. *J. Photochem. Photobiol. A* **2000**, *133*, 177-183.

(27) (a) Prenesti, E.; Daniele, P. G.; Berto, S. Toso, S. Spectrum–structure correlation for visible absorption spectra of copper(II) complexes showing axial co-ordination in aqueous solution. *Polyhedron* **2006**, *25*, 2815-2823. (b) Araki, T.; Sugahara, T.; Jiu, J.; Nagao, S.; Nogi, M.; Koga, H.; Uchida, H.; Shinozaki, K.; Suganuma, K. Cu Salt Ink Formulation for Printed Electronics using Photonic Sintering. *Langmuir* **2013**, *29*, 11192-11197. (c) Wasson, J. R.; Shyr, C.I; Trapp, C. The Spectral and Magnetic Properties of Copper(II) Cyanoacetate. *Inorg. Chem.* **1968**, *7*, 469-473.

(28) (a) Rizzo, F.; Cavazzini, M.; Righetto, S.; De Angelis, F.; Fantacci, S.; Quici, S. A Joint Experimental and Theoretical Investigation on Nonlinear Optical (NLO) Properties of a New Class of Push–Pull Spirobifluorene Compounds. *Eur. J. Org. Chem.* **2010**, *2010*, 4004-4016. (b) *Polyfluorenes*. Scherf, U. and Neher, D. Eds.; Springer, 2008.

(29) Zhang, H.; Fan, J.; Zhang, S.; Xu, W.; Wang, J.; Gao, P.; Peng, X. Fluorene-derived two-photon fluorescent probes for specific and simultaneous bioimaging of endoplasmic reticulum and lysosomes: group-effect and localization. *J. Mater. Chem. B* **2013**, *1*, 5450-5455.

(30) Bae, I. H.; Kim, H. S.; You, Y.; Chough, C.; Choe, W.; Seon, M. K.; Lee, S. G.; Keum, G.; Jang, S. K.; Kim, B. M. Novel benzidine and diaminofluorene prolinamide derivatives as potent hepatitis C virus NS5A inhibitors. *Eur. J. Med. Chem.* **2015**, *101*, 163-178.

(31) Shivani, Mishra, A.; Kumar, V.; Kaur, P.; Singh, K. Synthesis, linear and non-linear optical properties of "push-pull" chromophores based on 9,9-dimethyl-9H-fluoren-2-amine. *Dyes Pigm.* **2022**, *200*, 110160.

(32) Lee, S. Y.; Cho, Y. J.; Kwon, H. J.; Kim, B. O.; Kim, S. M. Novel compounds for organic electronic material and organic electroluminescent device using the same. WO 2011/126225 AI, 2011.

(33) Shaya, J.; Fontaine-Vive, F.; Michel, B. Y.; Burger, A. Rational Design of Push–Pull Fluorene Dyes: Synthesis and Structure–Photophysics Relationship. *Chem. Eur. J.* **2016**, *22*, 10627-10637.