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Short Note

(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)(5-bromo-1-hydroxy-1*H*-indol-3-yl)methanone †

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† In memory of Prof. Dr. Alan Roy Katritzky.

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Abstract: The title compound was easily prepared by a nitrosoarene-alkyne cycloaddition reaction carried out in toluene at 80 °C. The product is a highly functionalized compound that can be further derivatized through various functional group interconversion procedures.

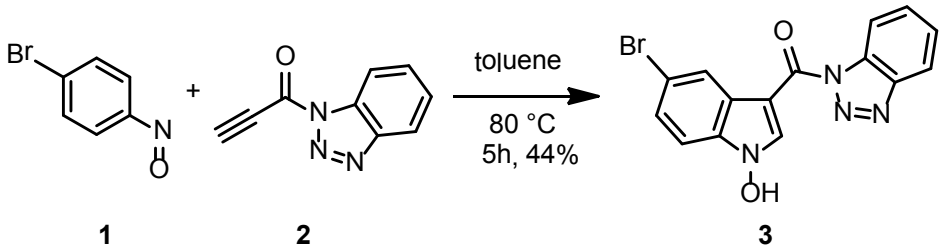
Keywords: indoles; alkynones; nitrosoarenes; annulation

Indoles are one of the most important and widespread classes of heterocycles in nature and many indole derivatives have been widely studied as bioactive compounds [1–3]. In the last decade, some members of our research team developed an indole synthesis via the cycloaddition of nitro- and nitrosoaromatics with alkynes [4–6]. By this method, indoles and *N*-hydroxyindoles were prepared in moderate to good yields. A direct one-pot alkylation was introduced affording excellent yields of *N*-alkoxyindoles [7,8]. A drawback of this protocol was the use of an excess of aromatic alkyne (12 or 30 fold), which helped to minimize the formation of side products like anilines, azobenzenes and azoxybenzenes. A stoichiometric alkyne/nitrosoarene molar ratio of 1/1 was used for the first time in the reaction with ethynylpyrimidine derivatives, in which the *N*-hydroxyindole product precipitates from the reaction mixture. In this latter case the indolization was employed to afford natural occurring compounds as meridianins, marine alkaloids from *Aplidium meridianum*, widely studied as kinase

inhibitors [9]. This synthetic procedure was then studied by Ragaini and Srivastava who developed catalytic processes mediated by transition metal complexes using the respectively nitroarenes [10,11] and *C*-nitrosoaromatics [12,13].

Other conjugated alkynones were tested to check the validity and the generality of the synthetic protocol. An interesting ynone that can be potentially used in many derivatization procedures is 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one **2** (Scheme 1) [14]. To our delight the 1:1 reaction between this alkynone and 4-bromonitrosobenzene **1** in hot toluene produced the corresponding *N*-hydroxyindole **3**, which precipitates during the reaction, enabling its simple isolation.

Scheme 1. Synthesis of (1*H*-Benzo[*d*][1,2,3]triazol-1-yl)(5-bromo-1-hydroxy-1*H*-indol-3-yl)methanone.



As shown by Katritzky and others the chemistry of benzotriazoles (Bt) provides a powerful tool in organic synthesis. The benzotriazole unit was studied as a leaving group, proton activator, cation stabilizer, and anion and radical precursor as reviewed by Katritzky and Rachwal [15,16]. Kindu and coworkers developed a straightforward procedure to obtain molecules having the alkaloid skeleton starting from benzotriazolyl adducts connected to an indole fragment [17]. The title compound is thus a good candidate to be further functionalized to many different indole alkaloid products. The potential value of this transformation is currently under investigation.

Experimental

1H-Benzo[d][1,2,3]triazol-1-yl)(5-bromo-1-hydroxy-1H-indol-3-yl)methanone

A mixture of 4-bromonitrosobenzene **1** (223 mg, 1.20 mmol) and 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one **2** (205 mg, 1.20 mmol), in toluene (15 mL) was stirred at 80 °C for 5 h under an inert atmosphere. Precipitation of the desired product was observed during the reaction. After cooling to r.t. the title compound **3** was isolated by filtration (188 mg, yield = 44%), collected as a grey solid and characterized without further purification.

Grey Solid, Mp. 194–196 °C.

FT-IR (KBr disk, cm^{-1}): 1691, 1444, 1357, 1290, 1105, 1034, 791, 755.

^{1}H-NMR (400 MHz; DMSO-d_6): δ (ppm) 12.70 (s, 1 H); 8.90 (s; 1H); 8.51 (d; 1H, J = 1.7 Hz); 8.38 (d; 1H, J = 8.3 Hz); 8.27 (d, 1H, J = 8.3 Hz); 7.80 (t; 1H, J = 8.3 Hz); 7.63-7.60 (m; 2H); 7.55 (dd, 1H, J = 1.7 Hz, J = 8.7 Hz).

^{13}C-NMR (100 MHz; DMSO-d_6): δ (ppm) 160.2; 145.1; 135.5; 132.4; 131.8; 130.6; 126.8; 126.4; 125.9; 123.3; 120.0; 116.2; 114.5; 112.2; 100.1.

MS (CI$^+$): *m/z* = 359 $[MH]^+$, 357 $[MH]^+$.

Anal. calcd. for $C_{15}H_9BrN_4O_2$, C, 50.44; H, 2.54; N, 15.69; Found: C, 50.56; H, 2.48; N, 15.32.

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Author Contributions

All the authors discussed and equally contributed to the design of the research. FT and LV performed the research and analyzed the data. AP wrote the paper. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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