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Novel Synthesis of 2-Arylbenzothiazoles Mediated by Ceric Ammonium Nitrate (CAN): A Rebuttal

Vijay Nair* and Anu Augustine

Organic Chemistry Division, Regional Research Laboratory (CSIR), Trivandrum, India

gvn@csrrltrd.ren.nic.in; vijaynair_2001@yahoo.com

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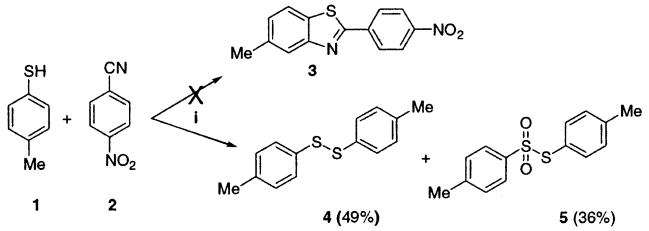
ABSTRACT

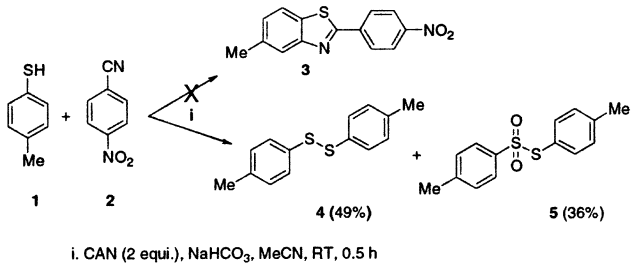


The reported synthesis of 2-arylbenzothiazoles mediated by ceric ammonium nitrate (CAN) is irreproducible; the only products formed in this reaction are bis-(*p*-tolyl) disulfide and *p*-tolyl *p*-toluenethiosulfonate.

In a recent paper published in this journal,[1] the author claimed a synthesis of the title compounds by the purported reaction of benzenethiols and benzonitriles mediated by ceric ammonium nitrate (CAN). Although no mechanistic postulates were given, it may be surmised that the author visualizes the formation of a benzenesulfenyl radical from the thiol by CAN oxidation followed by its addition to benzonitrile, generating a thioiminyl radical and the addition of the latter to the phenyl ring, and rearomatization to deliver the product. CAN, like a whole range of oxidants, is known to oxidize thiol to sulfenyl radical, which invariably leads to disulfide and/or further oxidation products such as sulfoxides, sulfones, etc. (vide infra).[2] Thus we reinvestigated the report, and our results are presented herein.

In our studies, a solution of CAN in dry acetonitrile was treated with a mixture of 4-methyl thiophenol and 4-nitrobenzonitrile precisely under the conditions given in Tale's paper.[1] Two products were formed in this reaction, and spectroscopic analysis revealed them to be the bis(*p*-tolyl) disulfide **4**[3] (49%) and *p*-tolyl *p*-toluenethiosulfonate **5**[4] (36%). It may be emphasized that not even a trace of the benzothiazole **3** was observed in this reaction (Scheme 1).

Scheme 1



As expected, a blank reaction, in which 4-methyl thiophenol was treated with CAN under the same reaction conditions, led to the products **4** and **5** in the same ratio.

(1) Tale, R. H. *Org. Lett.* **2002**, *4*, 1641.
(2) (a) Ho, T. L. *Synthesis* **1972**, 561. (b) Ho, T. L. *Synthesis* **1973**, 347. (c) Molander, G. A. *Chem. Rev.* **1992**, 92, 29.
(3) (a) Meshram, H. M. *Org. Prep. Proced. Int.* **1993**, *25*, 232. (b) Zhong, P. Guo, M.-P. *Synth. Commun.* **2001**, *31*, 1825.
(4) (a) Buckman, J. D.; Bellas, M.; Kim, H. K.; Field, L. J. *J. Org. Chem.* **1967**, *32*, 1626. (b) Barton, D. H. R.; Jaszberenyi, J. C.; Theodorakis, E. A. *Tetrahedron* **1991**, *47*, 9167. (c) Palumbo, G.; Caputo, R. *Synthesis* **1981**, 888.

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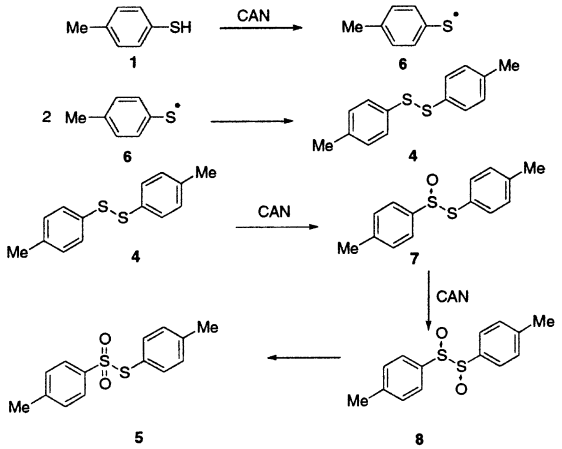
Similar results were obtained when we repeated the experiment with benzonitrile and 2,4-dimethoxy benzonitrile. In these cases also, no participation of the nitrile was observed; both nitriles were quantitatively recovered after the reaction.

The products were characterized by the usual spectroscopic methods and by comparing the data with those of authentic samples.[5] The IR spectrum of **4** showed absorptions at 2920, 1634, 1600, 1465, 1398, and 795 cm^{-1}. In the ^1H NMR spectrum, the signal corresponding to the methyl protons appeared as a singlet at δ 2.32 (s, 6H, Me) and the aromatic protons appeared as doublets at δ 7.37 (d, 4H, ArH, $J = 8.3$ Hz) and 7.10 (d, 4H, ArH, $J = 8.3$ Hz). In the ^{13}C NMR spectrum, the methyl carbons appeared as a singlet at δ 21.04. In the IR spectrum of **5**, the stretching corresponding to the S−O bond appeared at 1330 and 1142 cm^{-1}. In the ^1H NMR spectrum, the methyl protons appeared as singlets at δ 2.42 and 2.38 and the aromatic protons appeared as doublets at δ 7.56 (d, 2H, ArH, $J = 8.2$ Hz), 7.42 (d, 2H, ArH, $J = 8.1$ Hz), 7.29 (d, 2H, ArH, $J = 8.0$ Hz), and 7.18 (d, 2H, ArH, $J = 7.9$ Hz). In the ^{13}C NMR spectrum, the methyl carbons resonated at δ 21.61 and 21.44. In the mass spectrum, the peak observed at 278 corresponds to the molecular ion $[M]^{\cdot+}$.

Interestingly, when we conducted the same experiment with only 1 equiv of CAN instead of 2 equiv, the disulfide was formed exclusively in 91% yield.

A mechanistic rationale for this reaction as shown in Scheme 2 can be given. The initial event would be the

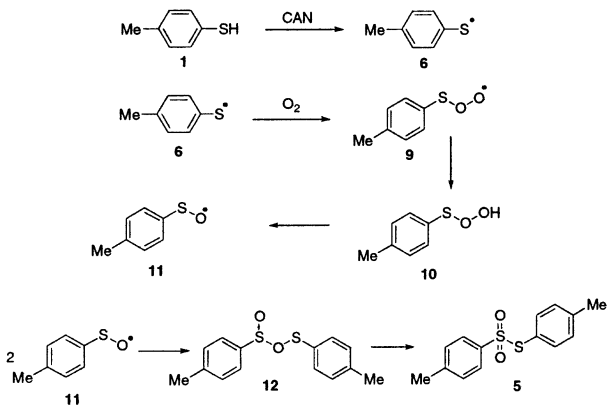
Scheme 2



oxidation of the thiocresol to the radical **6**, which undergoes dimerization resulting in the formation of the disulfide **4**. It is known that CAN promotes selective oxidation of diaryl sulfides to sulfoxides in excellent yields.[2] The thiosulfinate **7** formed by the oxidation of disulfide **4** with CAN gets further oxidized to the disulfoxide **8** which undergoes rearrangement leading to the formation of **5**.[6]

An alternative mechanism for the formation of **5** can invoke the formation of the sulfinyl radical **11**, which in turn is derived by the trapping of the thiyl radical **6** with oxygen, and subsequent transformations. The sulfinyl radical **11** undergoes coupling reaction to deliver thiosulfonate **5** presumably through the sulfenyl sulfinate **12**[7] (Scheme 3).

Scheme 3



It may be emphasized that we have conducted the experiment several times precisely under the reported conditions and found that our results as outlined above are consistently reproducible.

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(5) **Typical Experimental Procedure and Data of 4 and 5.** To a mixture of *p*-thiocresol (248 mg, 2 mmol) and $NaHCO_3$ (500 mg) in anhydrous MeCN (15 mL) was added dropwise a solution of CAN (2.192 g, 2 equiv) in the same solvent at room temperature with stirring. After 30 min, the reaction mixture was washed with water and extracted with chloroform (3 × 15 mL). After the mixture was dried over anhydrous Na_2SO_4, the solvent was removed and the crude product, when subjected to column chromatography, afforded the products **4** (60 mg, 49%) and **5** (50 mg, 36%) as crystalline solids. Data of **4**. Mp: 44−46 °C. IR (KBr) ν_{max}: 2920, 1634, 1600, 1465, 1398, 795 cm^{-1}. ^1H NMR (300 MHz; 3:1 v/v $CDCl_3$−CCl_4): δ 7.37 (d, 4H, ArH, $J = 8.3$ Hz), 7.10 (d, 4H, ArH, $J = 8.3$ Hz), 2.32 (s, 6 H, Me). ^{13}C NMR (75 MHz; 3:1 v/v $CDCl_3$−CCl_4): δ 137.33, 134.18, 129.77, 128.77, 21.04. Data of **5**. Mp: 74−75 °C. IR (KBr) ν_{max}: 2915, 1593, 1485, 1330, 1142, 818 cm^{-1}. ^1H NMR (300 MHz; 3:1 v/v $CDCl_3$−CCl_4): δ 7.56 (d, 2H, ArH, $J = 8.2$ Hz), 7.42 (d, 2H, ArH, $J = 8.1$ Hz), 7.29 (d, 2H, ArH, $J = 8.0$ Hz), 7.18 (d, 2H, ArH, $J = 7.9$ Hz) 2.42 (s, 3 H, Me), 2.38 (s, 3 H, Me). ^{13}C NMR (75 MHz; 3:1 v/v $CDCl_3$−CCl_4): δ 144.37, 141.85, 140.87, 136.49, 130.14, 129.31, 127.66, 124.93, 21.61, 21.44. HRMS: calcd for $C_{14}H_{14}O_2S_2$, 278.0435; found 278.0424. Anal. Calcd for $C_{14}H_{14}O_2S_2$: C, 60.40; H, 5.07; S, 23.04. Found: C, 60.68; H, 5.02; S, 23.18.

(6) (a) Freeman, F. *Chem. Rev.* **1984**, *64*, 117. (b) Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 8998. (c) Gu, D.; Harpp, D. N. *Tetrahedron Lett.* **1993**, *34*, 67.

(7) Kice, J. L. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, Chapter 2. (b) Mizuno, H.; Matsuda, M.; Iino, M. *J. Org. Chem.* **1981**, *46*, 520.