Indian Journal of Chemistry
Vol. 61, July 2022, pp. 776-779

Application of diacetoxyiodobenzene in the desulfurization of arylthioureas

Sushma Singh[a,b], Poonam Devi[a], Rashmi Pundeer[a,c,] * & Vishwas Chaudhri[d,]*
[a]Department of Chemistry, Kurukshetra University, Thanesar, Kurukshetra-1361 19, Haryana, India
[b]Govt. College, Hisar- 125 001, Haryana, India
[c]Indira Gandhi University, Meerpur, Rewari- 122 502, Haryana, India
[d]J C Bose University of Science & Technology YMCA, Faridabad- 121 006, Haryana, India
*E-mail: vishwas_khurana@yahoo.co.in (VC)/ dr.rashmip@gmail.com (RP)

Received 31 December 2021; accepted (revised) 2 June 2022

In the present study, the utility of the hypervalent iodine(III) reagent, diacetoxyiodobenzene is extended for the efficient synthesis of variously substituted aryl cyanamides. The reaction presents efficient conversion of thioureas to cyanamides under the conditions of ambient temperature while stirring. This organoiodine(III) mediated method features easy isolation of the products and represents an excellent example illustrating thiophilic property of diacetoxyiodobenzene in the desulfurization of thioureas.

Keywords: Diacetoxyiodobenzene, Desulfurization, Thiophilicity, Aryl thiourea, Cyanamide

Unprecedented growth in the orbit of hypervalent iodine reagents is attributed to their low toxicity, ready availability, easy handling, selectivity under different conditions and tolerance to different functional groups. The reactivity of the iodine(III) reagents is similar to the heavy-metal based oxidants, including elements such as Pb(IV), Hg(II) and Tl(III), as well as transition metal catalysed processes. Hence, they provide suitable alternative to the toxic metal based reagents. The organoiodine(III) reagent, diacetoxyiodobenzene (DIB) is available commercially and has been used for the oxidation of alkynes, allenes, alkenes, enolizable ketones, electron rich aromatic compounds, alcohols, organic derivatives of nitrogen, phosphorus, sulphur, selenium, tellurium and other organic substrates.[1,2] Recently, the application of DIB has been demonstrated in the desulfurization of dithiocarbamate salts and in the regioselective N-acylation of 1, 3-disubstituted thioureas.[3] Thioureas are easily available starting materials to perform various organic transformations. Taking cues from this and in continuation of our work on exploring the synthetic potential of iodine(III) reagents, we sought to explore the thiophilicity of DIB in the desulfurization of arylthioureas.

Cyanamides are significant entities because of their valuable contributions in synthetic organic and medicinal chemistry. They have been proved to be (i) practicable precursors in the synthesis of N-alkyl or N-arylimides and heterocycles (ii) protective groups in the synthesis of secondary and tertiary amines containing heterocycles (iii) important mediators of biologically active compounds[4,5]. Because of the panoptic utility of cyanamides, there has been increasing interest in developing facile approaches for their synthesis. Most of the reported methods for their synthesis use cyano cation (CN^+) directly from highly toxic cyanogen bromide or indirectly from (CN^+) synthons which, in turn, are prepared from toxic cyanogen halides. Therefore, a non-metallic, non-toxic, eco-friendly, mild DIB-mediated strategy for the synthesis of cyanamides is of particular interest.

Experimental Details

General

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. The ^1H NMR spectra were recorded on Bruker 300 MHz instrument. Elemental analyses were carried out in Perkin-Elmer 2400 instrument. Most of the common chemicals were obtained from commercial suppliers. DIB used in present study was prepared according to literature procedure.[8,9]

General procedure for synthesis of aryl cyanamides, 2a-j

Aqueous ammonia (25%, 2 mL) was added to a stirred solution of phenylthiourea **1** (1 eq.) in acetonitrile

(5 mL). DIB (1 eq.) was added portion-wise over a period of 15 min. A light yellow precipitate of sulfur started to separate out during this period. After the complete addition of DIB, it was kept stirring for 15 min and conversion to the corresponding 1-phenylcyanamide was confirmed by TLC. The conversion of the 1-phenylthiourea to phenylcyanamide (**2a**) was observed within 10 min of the complete addition of DIB. The reaction mixture was allowed to stand, and the precipitated sulfur was filtered. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with water (25 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The oily liquid so obtained was characterized as cyanamide by spectral data.

Phenylcyanamide[5,10], **2a**: Yield: 80%; Oily liquid; IR (KBr)(ν, cm^{-1}): 3171, 2222, 1597, 1497, 1250, 748, 687; ^1H NMR (400 MHz, $CDCl_3$)(δ, ppm): 7.02-7.58 (m, 5H), 6.88 (br, s, 1H)

2-Methylphenylcyanamide[5], **2b**: Yield: 84%; m.p. 77-78°C; IR (KBr): 3052, 2270, 1549, 1498, 1198, 832, 752 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$)(δ, ppm): 2.19 (s, 1H, CH_3), 6.89-7.04 (m, 4H).

4-Methylphenylcyanamide[5,10], **2c**: Yield: 86%; IR(KBr): 3063, 2214, 1597, 1512, 1466, 1250, 810, 756 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$)(δ, ppm): 2.26 (s, 3H, CH_3), 6.90-7.14 (m, 4H)

2, 6-Dimethylphenyl cyanamide[5,10], **2d**: Yield: 54%; m.p. 143-146°C; IR(KBr): 3080, 2225, 1601, 1503, 1250, 1042, 876 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$)(δ, ppm): 2.12 (s, 6H, CH_3), 6.93-7.11 (m, 3H), 6.73 (br, s, 1H, NH)

4-Methoxyphenyl cyanamide[5], **2e**: Yield: 74%; m.p. 87-88°C; IR(KBr): 2924, 2854, 2222, 1605, 1504, 1458, 1296, 1234, 1173, 1026, 825 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$)(δ, ppm): 3.85 (s, 3H, OCH_3), 6.85-7.20 (m, 4H).

4-Chlorophenyl cyanamide[5,10], **2f**: Yield: 97%; m.p. 95-96°C; IR (KBr): 3152, 2222, 1620, 1511, 1461, 1302, 1065 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)(δ, ppm): 6.58 (br, s, 1H), 6.95-7.32 (m, 4H)

4-Bromophenylcyanamide[5], **2g**: Yield: 93%; m.p. 111-113°C; IR(KBr): 3148, 3063,2924, 2854, 2230, 1597, 1481,1250, 1072, 1011, 810 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$)(δ, ppm): 6.83 - 6.86 (d, J= 9 Hz, 2H), 7.42-7.45 (d, J= 9 Hz, 2H), 5.14 (br, s, 1H, NH)

3-Nitrophenylcyanamide[5], **2h**: Yield: 74%; m.p. 133-135°C; IR (KBr): 3145, 2928, 2238, 1624, 1365, 1266, 1082 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$+ DMSO) (δ, ppm): 7.41-7.85 (m, 4H)

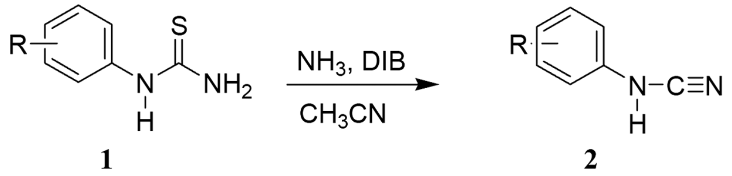
4-Nitrophenyl cyanamide[5], **2i**: Yield: 70%; m.p. 186-187°C; IR (KBr): 3217, 2152, 1589,1474, 1296, 1111, 841, 748, 625 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$+ DMSO) (δ, ppm): 7.52 - 7.87 (m, 4H)

4-carboxyethylphenylcyanamide[5], **2j**: Yield: 62%; m.p. 150-152°C; IR (KBr): 3156, 2901, 1729, 1578, 1378, 898 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.34 (t, 3H), 4.32 (q, 2H), 7.65 - 7.87 (m, 4H), 12.11 (br, s, 1H, COOH)

Results and Discussion

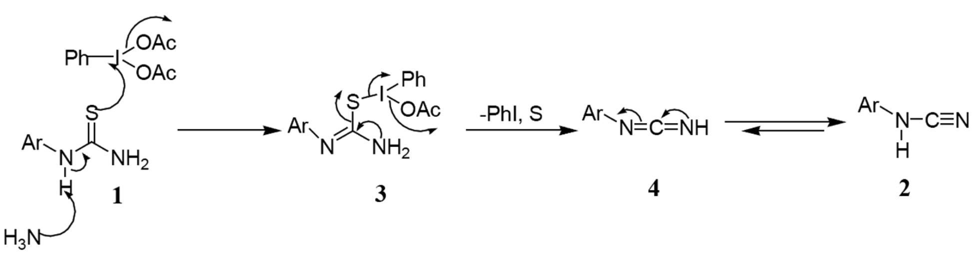
To start with, the reaction of 1-phenylthiourea **1a** (1 eq.) was carried out by taking 1.1 equivalents of DIB (1.1 eq.) in acetonitrile containing aqueous NH_3 (25%) at room temperature while stirring. The progress of the reaction was monitored by TLC. Yellow precipitates of sulphur were precipitated out and a single cyanamide product **2a** was obtained as oil in good yield. The product was characterized by IR and ^1H NMR data. IR spectrum of **1a** showed peaks at 2222 cm^{-1} and 3171 cm^{-1} for the stretching vibrations of the CN and NH group, respectively. The ^1H NMR displayed a characteristic broad singlet at δ 6.88 due to -NH- of cyanamide in addition to the required number of peaks in the aromatic region. Following the successful preparation of phenyl cyanamide from the corresponding thiourea, other aryl thioureas **1b-o** were also subjected to the DIB-mediated desulfurization to explore the substrate scope and limitations of this reaction. In all these cases, corresponding cyanamides were made successfully. DIB mediated synthesis of cyanamides from thioureas is shown in Scheme 1.

The reaction is believed to proceed *via* the formation of S-I complex **3** (from thiourea and DIB) triggered by ammonia followed by reductive elimination of iodobenzene and sulphur leading to the formation of carbodiimide intermediate **4** which is transformed into the stable cyanamide analogue. Precipitation of sulphur during the reaction also supports the mechanistic pathway. The mechanistic pathway for desulfurization of thioureas using DIB is shown in Scheme 2. Various arylthioureas, needed for the present study, can be prepared easily in high yields from corresponding amines following the literature procedure[6,7] (Table 1).



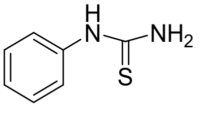
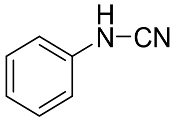
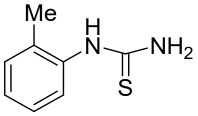
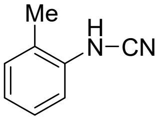
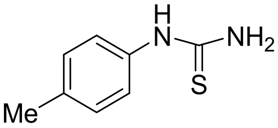
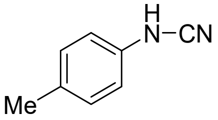
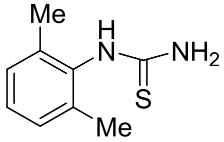
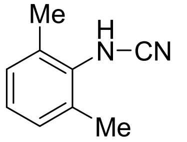
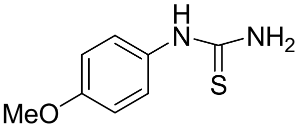
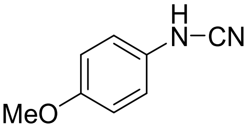
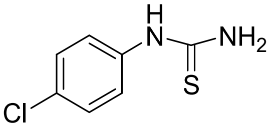
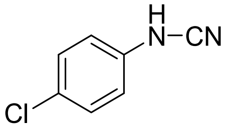
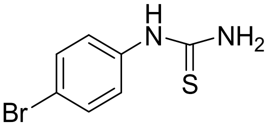
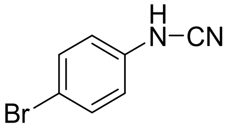
R = H; 2-CH_3; 4-CH_3; 2,6-diCH_3; 4-OCH_3; 4-Cl; 4-Br; 3-NO_2; 4-NO_2; 4-$CH_3CH_2CO_2$

Scheme 1 — DIB mediated synthesis of cyanamides from thioureas



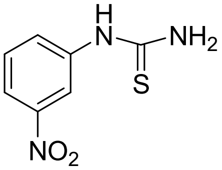
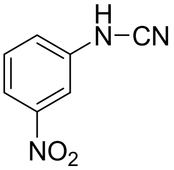
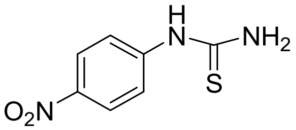
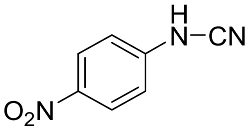
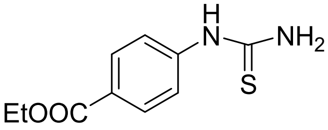
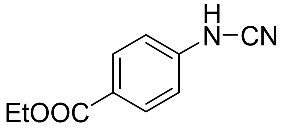
Scheme 2 — Mechanistic pathway for desulfurization of thioureas using DIB

Table 1 — Preparation of cyanamides 2 from arylthioureas 1 and DIB

S. No.	Substrate (1)	Product (2)	%Yield
2a	 1a		80
2b			84
2c			86
2d			54
2e			74
2f			97
2g			93

(*Contd.*)

Table 1 — Preparation of cyanamides 2 from arylthioureas 1 and DIB — (*Contd.*)

S. No.	Substrate (1)	Product (2)	%Yield
2h			74
2i			70
2j			62

Conclusion

Desulfurization ability of DIB is used for the smooth transformation of aryl thioureas to cyanamides under mild reaction conditions involving environmentally benign protocol. The method is compatible with both electron-releasing and electron-withdrawing groups on the aromatic ring giving their corresponding cyanamides. Easy isolation of the desired products makes the present approach a suitable alternative for the synthesis of various cyanamide compounds.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/58776.

Acknowledgements

The authors are thankful to the Department of Chemistry, Kurukshetra University, Kurukshetra, for providing research facilities.

References

1 (a) Zhdankin V V, *Hypervalent Iodine Chemistry: Preparation, Structure and Synthetic Applications of Polyvalent Iodine Compounds*, (John Wiley & Sons, Chichester) 2013; (b) Yoshimura A & Zhdankin V V, *Chem Rev*, 116 (2016) 3328.

2 (a) Prakash O, Moriarty R M, Chaudhri V, Pannu K & Pundeer R, *Indian J Heterocycl Chem,* 27 (2017) 327; (b) Prakash O, Kaur H, Sharma V, Bhardwaj V & Pundeer R, *Tetrahedron Lett,* 45 (2004) 9065; (c) Prakash O, Pundeer R & Kaur H, *Synthesis,* 45 (2003) 2768.

3 Singh C B, Ghosh H, Murru S & Patel B K, *J Org Chem,* 73 (2008) 2924.

4 (a) Larraufie M H, Maestri G, Malacria M, Ollivier C, Fensterbank L & Lacote E, *Synthesis,* 44 (2012) 1279; (b) Jihui L, Zhengzhang L, Yucang Z, Wenrong X & Shuying X, *Chin J Org Chem,* 37 (2017) 1903; (c) Mandapati U, Mandapati P, Pinapati S, Tamminana R & Rudraraju R, *SynthCommun,* 48 (2018) 500.

5 (a) Kluge A F, Lagu B R, Maiti P, Jaleel M, Webb M, Malhotra J, Mallat A & Srinivas P A, *Bioorg Med Chem Lett,* **28** (2018) 2655; (b) Prabhath M R R, Williams L, Bhat S V & Sharma P, *Molecules,* **22** (2017) 615; (c) Ayres J N, Ashford M W, Stöckl Y, Prudhomme V, Ling K B, Platts J A & Morrill L C, *Org Lett,* **19** (2017) 3835; (d) Škoch K, Císarová I & Štěpnicka P, *Chem-Eur J,* 24 (2018) 13788; (e) Kumar V, Kaushik M P & Mazumdar A, *Eur J Org Chem,* (2008) 1910; (f) Wong F F, Chen C Y & Yeh M Y, *Synlett,* (2006) 559; (g) Zhang G, Zhao Y & Ding C*, Org Biomol Chem,* 17 (2019) 7684.

6 Sigma-Aldrich Corporation, *Aldrich Chemistry - Handbook of fine chemicals*, (Sigma Aldrich, USA) 2008.

7 Dyson G M, George H J, *J Chem Soc,* 125 (1924) 1702.

8 Lucas H J & Kennedy E R, *Org Synth Coll*, 2 (1943) 351.

9 Furniss B S, Hannaford A J, Robergs V, Smith P W G, Tatchell A R, *Vogel's Text Book of Practical Organic Chemistry*, 5th edition, (Pearson Education, London) 1991.

10 Ghosh H, Yella R, Ali A R, Sahoo S K & Patel B K, *Tetrahedron Lett,* 50 *(*2009) 2407.