



An efficient synthesis of cyanamide from amine promoted by a hypervalent iodine(III) reagent

Harisadhan Ghosh, Ramesh Yella, Abdur Rezzak Ali, Santosh K. Sahoo, Bhisma K. Patel *

Department of Chemistry, Indian Institute of Technology Guwahati 781 039, Assam, India

ARTICLE INFO

Article history:

Received 26 January 2009

Revised 21 February 2009

Accepted 4 March 2009

Available online 9 March 2009

ABSTRACT

In a one-pot strategy we have achieved an efficient method for the synthesis of organic cyanamides starting from dithiocarbamic acid salts/amines. In this strategy the in situ generated alkyl or aryl isothiocyanates, obtained by the desulfurization of dithiocarbamic acid salts with diacetoxyiodobenzene (DIB) react with aqueous ammonia forming alkyl or aryl thiourea which on subsequent oxidative desulfurization with DIB led to the formation of corresponding cyanamide in good yields. Mild reaction conditions, shorter reaction time, an environmentally benign protocol, and easy isolation of the desired product make the present methodology a suitable alternative for the preparation of various organic cyanamides.

© 2009 Elsevier Ltd. All rights reserved.

Due to its unique reactivity, cyanamide is an important functional group in synthetic organic chemistry. Cyanamides are useful precursors in the synthesis of pharmaceutically important heterocycles¹ and *N*-alkyl or *N*-aryl imides.² Due to the easy removal of the cyano group from cyanamide,³ they often serve as a useful protecting groups in the synthesis of secondary and tertiary amines containing heterocycles.³ Cyanamides are also important intermediates for the synthesis of many biologically active compounds, such as minoxidil⁴ and herbicides.⁵

The most frequently adopted method for the synthesis of cyanamides is the cyanation of amine using cyanogen halides,⁶ or its synthon (CN⁺). The reagents capable of delivering electrophilic cyanogens (CN⁺) are 2-chlorobenzyl thiocyanate,⁷ 1-cyanoimidazole,⁸ 2-cyanopyridazin-3-(2*H*)-ones,⁹ 1-cyanobenzotriazole and metal cyanide,¹⁰ tosylcyanide,¹¹ thiocyanogen,¹² and cyanogen azide.¹³ In an alternative approach, cyanamides are obtained from ureas and thioureas.¹⁴ The other less commonly adopted method is the Tiemann rearrangement of amidoximes.¹⁵ Recently, they were prepared from organic isocyanides and trimethylsilyl azide via a Si–N bond cleavage catalyzed by $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2$,¹⁶ and in one pot by reacting isocyanate or isothiocyanate with sodium bis(trimethylsilyl)amide as deoxygenating or desulfurizing agent in THF at room temperature.¹⁷ In yet another method, cyanamides were prepared from *N,N'*-disubstituted glycylamide using a penta-valent iodine reagent in the presence of tetraethylammonium bromide at ambient temperature.¹⁸

Most of the reported methods use cyano cation (CN⁺) directly from highly toxic cyanogen bromide or indirectly from (CN⁺) synthons which, in turn, are prepared from toxic cyanogen halides. An other reported method uses extremely alkaline conditions, toxic

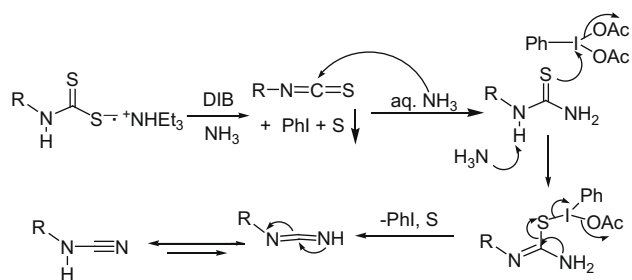
and expensive reagents, high reaction temperatures giving low yields, and involving tedious purification procedures. Due to ready availability, low toxicity, and easy handling, the use of hypervalent iodine reagents is of current interest.¹⁹ Hypervalent iodine(III) has a mild oxidizing ability similar to mercury, lead, and thallium-based reagents and hence is a suitable alternative to toxic, heavy metal-based reagents.²⁰ Recently we have exploited the thiophilic nature of DIB in the regioselective *N*-acylation of thiourea to *N*-acyl urea.²¹ Further, the desulfurization ability of DIB has been used for the preparation of isothiocyanate from the corresponding dithiocarbamate salt.²² The in situ generated isothiocyanates on reaction with various bis-nucleophiles gave different heterocycles.²² Taking cues from this work, we have reasoned that isothiocyanate can be obtained from dithiocarbamic acid salt and DIB in the presence of aqueous ammonia without using triethylamine. The in situ generated isothiocyanate will react further with ammonia giving alkyl or aryl thiourea, which, on oxidative desulfurization with DIB and ammonia, would form organic cyanamide. All these processes can be performed in one pot. Herein, we report a high yielding 'one-pot' preparation of cyanamides from dithiocarbamate salts using the non-metallic, non-toxic, eco-friendly hypervalent iodine(III) reagent diacetoxyiodobenzene (DIB).

Various dithiocarbamate salts can be prepared easily in high yields from amines following the literature procedure.^{11,23} When a freshly prepared salt of dithiocarbamate salt **1** (2 equiv) in acetonitrile (5 mL) was treated with aqueous ammonia (25%) (2 mL) and DIB (2 equiv) under ice-cooled conditions, 1-phenylthiourea was obtained. When DIB (2 equiv) was added to this reaction mixture, phenylcyanamide (**1a**) was isolated in 85% yield.²⁴ A plausible mechanism for the transformation of dithiocarbamic acid salt **1** to cyanamide **1a** is shown in Scheme 1.

The mechanism for the formation of isothiocyanate is expected to be similar to the one recently proposed by us.²² The in situ gen-

* Corresponding author. Tel.: +91 61 582307; fax: +91 61 690762.

E-mail address: patel@iitg.ernet.in (Bhisma K. Patel).



Scheme 1. Proposed mechanism for the formation of cyanamide.

erated isothiocyanate on reaction with NH_3 would give 1-phenylthiourea. The 1-phenylthiourea on oxidative desulfurization leads to the formation of a carbodiimide intermediate which is converted to its stable cyanamide analogue (**1a**).

The precipitation of elemental sulfur supports the mechanism proposed. The formation of isothiocyanate was confirmed by recording the IR spectra of the crude reaction mixture, which shows a strong peak at 2063 cm^{-1} characteristic of isothiocyanate. Further, when isolated 1-phenylthiourea in acetonitrile was treated with DIB in aqueous ammonia, it gave cyanamide (**1a**) confirming the intermediacy of phenylisothiocyanate and 1-phenylthiourea in the reaction mixture. It may be mentioned here that the reaction of 1-phenylthiourea with DIB in the absence of any base is reported to give 1,2,4-thiadiazole.²⁵

Irrespective of the mechanism involved, the success of the method depends on the strong thiophilic nature of the DIB. Employing this one-pot strategy, we have successfully prepared a series of cyanamides (Table 1) from both aliphatic and aromatic amines. Aromatic amines containing various substituents in the phenyl ring (**1–7**) gave corresponding cyanamides (**1a–7a**) in good yields. Benzylic amines **8** and **9** gave a satisfactory yield of corresponding cyanamides **8a** and **9a** respectively. This method was also extremely successful in the preparation of cyclohexyl (**10a**), cyclopropyl (**11a**), and *n*-butyl (**12a**) cyanamides starting from their parent amine/dithiocarbamate salt.

This method is compatible with a number of other functional groups such as $-\text{OH}$, $-\text{NO}_2$, and $-\text{COR}$ as was tested in substrates **13**, **14**, and **15** giving their corresponding cyanamides **13a**, **14a**, and **15a**, respectively, (Table 2). The stability of other functional groups containing substrates such as alkenes **16** and esters **17** were also found to be compatible in the second stage of the reaction giving, respectively, products **16a** and **17a**.

It was difficult to get suitable thiocarbamate salts having these functionalities. Hence, their compatibility was tested from isothiocyanates **16** and **17** having these functionalities. It is heartening to know that both these functionalities survived under the reaction condition giving cyanamides **16a** and **17a**, respectively, in good yields. However in the case of **16a** and **17a**, 0.5 mL of aq NH_3 was used per mmol of the substrate instead of 1 mL of the aq NH_3 used when the reaction started from thiocarbamate salt.

In an attempt to synthesize cyanamide of secondary amines such as pyrrolidine, no traces of cyanamide could be detected. Rather, it underwent oxidative dimerization. This is possible because of the inability of the secondary amine to form isothiocyanate, thereby further supporting our mechanism. Thus, by this method, cyanamide of a secondary amine cannot be prepared and this is perhaps the only drawback of the method.

In conclusion, hypervalent iodine reagent DIB serves as an efficient desulfurizing agent for the conversion of dithiocarbamic acid salts to cyanamides. Organic cyanamide in the past was prepared by an arduous method involving toxic and expensive reagents. Although the isolated yield looks moderate considering three steps

Table 1
Preparation of cyanamide from dithiocarbamate salt and DIB^a

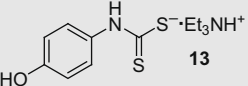
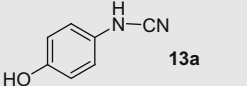
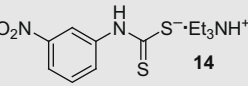
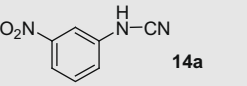
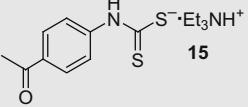
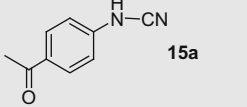
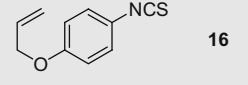
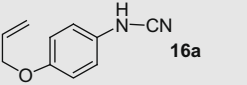
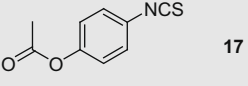
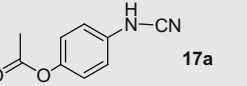
Substrate	Product ^b	Yield ^c (%)
		85
		72
		65
		78
		68
		71
		60
		76
		78
		77
		63
		67

^a Reactions were monitored by TLC.

^b Confirmed by IR, ^1H , and ^{13}C NMR.³¹

^c Isolated yield.

Table 2Preparation of cyanamide from dithiocarbamate salt and DIB^a

Substrate	Product ^b	Yield ^c (%)
		72
		65
		83
		76
		83

^a Reactions were monitored by TLC.^b Confirmed by IR, ¹H, and ¹³C NMR.³¹^c Isolated yield.

in one pot, the yields are, in fact, good to excellent. Thus, this is perhaps the most efficient method reported so far for the preparation of organic cyanamides.

Acknowledgments

B.K.P. acknowledges support of this research from DST New Delhi (SR/S1/OC-15/2006) and CSIR 01(2270)/08/EMR-II. H.G. thanks the CSIR for fellowships. Thanks are due to CIF IIT Guwahati for NMR spectra.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.03.017.

References and notes

- (a) Sandler, S. R.; Karo, W.. In *Organic Functional Group Preparations*; Academic: New York, 1972; Vol. 3; (b) Sandler, S. R.; Karo, W.. In *Organic Functional Group Preparations*; Academic: New York, 1972; Vol. 2; (c) Nickon, A.; Fieser, L. F. *J. Am. Chem. Soc.* **1952**, 74, 5566; (d) Jia, Q.; Cai, T.; Haug, M.; Li, H.; Xian, M.; Poulos, T. L.; Wang, P. G. *J. Med. Chem.* **2003**, 46, 2271; (e) Cai, T.; Xian, M.; Wang, P. G. *Bioorg. Med. Chem. Lett.* **2002**, 12, 1507; (f) Kumar, V.; Kaushik, M. P.; Mazumdar, A. *Eur. J. Org. Chem.* **2008**, 1910; (g) Saneyoshi, M.; Tokuzen, R.; Maeda, M.; Fukuoka, F. *Chem. Pharm. Bull.* **1968**, 16, 505; (h) Gilman, A. G.; Goodman, L. S.; Rall, T. W.; Murad, F. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 7th ed.; Pergamon Press: New York, 1990; (i) La Mattina, J. L. *J. Heterocycl. Chem.* **1983**, 20, 533.
- Stephens, R. W.; Domeier, L. A.; Todd, M. G.; Nelson, V. A. *Tetrahedron Lett.* **1992**, 33, 733.
- (a) Donetti, A.; Omodei-Sale, A.; Mantegani, A.; Zugna, E. *Tetrahedron Lett.* **1969**, 39, 3327; (b) Pala, G.; Mantegani, A.; Zugna, E. *Tetrahedron* **1970**, 26, 1275; (c) Currie, A. C.; Newbold, G. T.; Spring, F. S. *J. Chem. Soc.* **1961**, 4693.
- McCall, J. M.; Tenbrink, R. E.; Ursprung, J. J. *J. Org. Chem.* **1975**, 40, 3304.

- (a) Hu, L. Y.; Guo, J.; Magar, S.; Fischer, J. B.; Burkehowie, K. J.; Durant, G. J. *J. Med. Chem.* **1997**, 40, 4281; (b) Robinson, J. R.; Brown, W. H. *Can. J. Chem.* **1951**, 29, 1069.
- (a) Van Barun, J. *Ber. Dtsch. Chem. Ges.* **1900**, 33, 1468; (b) Kaupp, G.; Schmeyers, J.; Boy, J. *Chem. Eur. J.* **1998**, 4, 2467.
- Wheland, R. C.; Martin, E. L. *J. Org. Chem.* **1975**, 40, 3101.
- Wu, Y.-Q.; Limburg, D. C.; Wilkinson, D. E.; Hamilton, G. S. *Org. Lett.* **2000**, 2, 795.
- Kim, J.-J.; Kweon, D.-H.; Cho, S.-D.; Kim, H.-K.; Jung, E.-Y.; Lee, S.-G.; Falck, J. R.; Yoon, Y.-J. *Tetrahedron* **2005**, 61, 5889.
- Hughes, T. V.; Hammond, S. D.; Cava, M. P. *J. Org. Chem.* **1998**, 63, 401.
- (a) Davis, W. A.; Cava, M. P. *J. Org. Chem.* **1983**, 48, 2774; (b) Kahne, D.; Collum, D. *Tetrahedron Lett.* **1981**, 22, 5011.
- Boltz, K. H.; Dell, H. D. *Justus Liebigs Ann. Chem.* **1967**, 709, 63.
- Hermes, M. E.; Marsh, F. D. *J. Org. Chem.* **1972**, 37, 2969.
- (a) Takahiro, S.; Toshihiro, I.; Kenya, K.; Katsuro, M. *Tetrahedron Lett.* **1973**, 14, 2121; (b) Mai, K.; Patil, G. *Synth. Commun.* **1986**, 16, 1823; (c) Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Chem. Lett.* **1985**, 603; (d) Sato, R.; Itoh, K.; Itoh, K.; Nishina, H.; Goto, T.; Saito, M. *Chem. Lett.* **1984**, 1913.
- Bakunov, S. A.; Rukavishnikov, A. V.; Tkachev, A. V. *Synthesis* **2000**, 1148.
- Kamijo, S.; Jin, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2002**, 41, 1780.
- (a) Wong, F. F.; Chen, C.-Y.; Yeh, M.-Y. *Synlett* **2006**, 559; (b) Chen, C.-Y.; Wong, F. F.; Huang, J.-J.; Lin, S.-K.; Yeh, M.-Y. *Tetrahedron Lett.* **2008**, 49, 6505.
- Chaudhuri, K. H.; Mahajan, U. S.; Bhalerao, D. S.; Akamanchi, K. G. *Synlett* **2007**, 2815.
- (a) Wirth, T.; Ochiai, M.; Zhdankin, V. V.; Koser, G. F.; Tohma, H.; Kita, Y. *Topics in Current Chemistry: Hypervalent Iodine Chemistry-Modern Developments in Organic Synthesis*; Springer: Berlin, 2002; (b) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, 1997; (c) Zhdankin, V. V.; Stang, P. *Chem. Rev.* **1996**, 96, 1123; (d) Varvoglis, A. *Tetrahedron* **1997**, 53, 1179; (e) Zhdankin, V. V.; Stang, P. *Chem. Rev.* **2002**, 102, 2523; (f) Zhdankin, V. V.; Stang, P. *Chem. Rev.* **2008**, 108, 5299.
- (a) Kitamura, T.; Fujiwara, Y. *Org. Prep. Proc. Int.* **1997**, 29, 409; (b) Wirth, T. *Angew. Chem., Int. Ed.* **2005**, 44, 3656; (c) Wirth, T. *J. Org. Chem.* **2005**, 70, 2893; (d) Ochiai, M. In *Chemistry of Hypervalent Compounds*; Akiba, K., Ed.; VCH: New York, 1999; pp 359–387. Chapter 13.
- Singh, C. B.; Ghosh, H.; Murru, S.; Patel, B. K. *J. Org. Chem.* **2008**, 73, 2924.
- Ghosh, H.; Yella, R.; Nath, J.; Patel, B. K. *Eur. J. Org. Chem.* **2008**, 6189.
- (a) Emami, S.; Foroumadi, A. *Chin. J. Chem.* **2006**, 24, 791; (b) Sattigeri, V. J.; Soni, A.; Singhal, S.; Khan, S.; Pandya, M.; Bhateja, P.; Mathur, T.; Rattan, A.; Khanna, J. M.; Mehta, A. *Arkivoc* **2005**, ii, 46.
- General procedure for preparation of phenyl cyanamide (1a) from dithiocarbamate salt (1):** Aqueous ammonia (25%, 2 mL) was added to a stirred and ice-cooled suspension of dithiocarbamate **1** (540 mg, 2 mmol) in acetonitrile (5 mL). DIB (644 mg, 2 mmol) 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-phenylthiourea was confirmed by TLC. To the reaction mixture DIB (644 mg, 2 mmol) was added portion-wise over a period of 15 min during which further precipitation of elemental sulfur was observed. The conversion of the 1-phenylthiourea to phenylcyanamide (**1a**) 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 Na₂SO₄, concentrated under reduced pressure, and purified through a short column of silica gel to give the pure product **1a**⁹ (201 mg, 85%). Oily Liquid: ¹H NMR (400 MHz, CDCl₃): δ 7.02–7.07 (m, 3H), 7.28–7.33 (m, 2H), 7.64 (br s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 112.2, 115.5, 123.6, 129.8, 137.4. IR (KBr): 3175, 2919, 2227, 1600, 1501, 1249, 748, 689 cm⁻¹. C₇H₆N₂ (118.13): calcd C, 71.17; H, 5.12; N, 23.71. Found: C, 71.27; H, 5.09; N, 23.67.
- Mamaeva, E. A.; Bakibaev, A. A. *Tetrahedron* **2003**, 59, 7521.
- Singh, G. R.; Mehra, S. C. *Asian J. Chem.* **2006**, 18, 3132.
- Bunnett, J. F.; Hrutford, B. F. *J. Am. Chem. Soc.* **1961**, 83, 1691–1697.
- Niwa, R.; Kamada, H.; Shitara, E.; Horiuchi, J.; Kibushi, N.; Kato, T. *Chem. Pharm. Bull.* **1996**, 44, 2314.
- Lee, Y.; Martasek, P.; Roman, L. J.; Silverman, R. B. *Bioorg. Med. Chem. Lett.* **2000**, 10, 2771.
- Jacobsen, G. B.; Westernberg, G.; Markides, K. E.; Laangstoem, B. J. *Am. Chem. Soc.* **1996**, 118, 6868.
- Spectral data of compounds:** *p*-Tolyl cyanamide **2a**:^{1f} Gummy: ¹H NMR (400 MHz, CDCl₃): δ 2.28 (s, 3H, CH₃), 6.91 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 20.7, 112.4, 115.5, 130.3, 133.2, 134.9. IR (KBr): 3165, 2950, 2228, 1620, 1515, 1249 cm⁻¹. C₈H₈N₂ (132.17): calcd C, 72.70; H, 6.10; N, 21.20. Found: C, 72.73; H, 6.08; N, 21.15. 2-Methoxyphenyl cyanamide **3a**:²⁶ Gummy: ¹H NMR (400 MHz, CDCl₃): δ 3.87 (s, 3H, OCH₃), 6.88 (m, 1H), 6.95–7.05 (m, 2H), 7.18 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 55.9, 110.8, 111.0, 114.9, 121.5, 123.8, 126.8, 146.9. IR (KBr): 3219, 2939, 2839, 2224, 1603, 1509, 1454, 1259, 1026 cm⁻¹. C₈H₈N₂O (148.17): calcd C, 64.85; H, 5.44; N, 18.91. Found: C, 64.81; H, 5.40; N, 18.88. 2,4-Dimethylphenyl cyanamide **4a**: mp 115–119 °C. ¹H NMR (400 MHz, CDCl₃): δ 2.18 (s, 3H, CH₃), 2.26 (s, 3H, CH₃), 6.74 (br s, 1H, NH), 6.93 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 17.3, 20.7, 112.8, 115.7, 124.7, 127.9, 131.8, 133.2, 133.3. IR (KBr): 3186, 2915, 2233, 1599, 1512, 1433, 1271, 1031 cm⁻¹. C₉H₁₀N₂ (146.19): calcd C, 73.94; H, 6.89; N, 19.16. Found: C,

73.87; H, 6.86; N, 19.14. MS (ESI): 146 (M^+). 2-Chloro-phenyl cyanamide **5a**:²⁷ mp 101–103 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.56 (br s, 1H), 7.05 (m, 1H), 7.31 (m, 2H), 7.35 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 110.0, 116.2, 120.4, 124.5, 128.6, 129.9, 134.3. IR (KBr): 3163, 2921, 2243, 1598, 1500, 1426, 1295, 1049 cm^{-1} . $\text{C}_7\text{H}_5\text{ClN}_2$ (152.58): calcd C, 55.10; H, 3.30; N, 18.36. Found: C, 55.11; H, 3.32; N, 18.29. 3-Chloro-phenyl cyanamide **6a**:^{17a} mp 93–95 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.92 (m, 1H), 7.03 (m, 2H), 7.26 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 111.1, 113.8, 115.9, 124.0, 130.9, 135.7, 138.7. IR (KBr): 3154, 2910, 2237, 1602, 1513, 1423, 1256 cm^{-1} . $\text{C}_7\text{H}_5\text{ClN}_2$ (152.58): calcd C, 55.10; H, 3.30; N, 18.36. Found: C, 55.10; H, 3.29; N, 18.29. MS (ESI): 152 (M^+). 4-Chloro-phenyl cyanamide **7a**:²⁶ mp 95 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.91 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 111.4, 116.9, 128.9, 129.9, 136.2. IR (KBr): 3166, 2954, 2234, 1600, 1494, 1251, 1091 cm^{-1} . $\text{C}_7\text{H}_5\text{ClN}_2$ (152.58): calcd C, 55.10; H, 3.30; N, 18.36. Found: C, 55.09; H, 3.33; N, 18.32. Benzyl cyanamide **8a**:⁹ Gummy. ^1H NMR (400 MHz, CDCl_3): δ 4.11 (d, J = 5.2 Hz, 2H, CH_2), 4.66 (br s, 1H), 7.27–7.37 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ 49.9, 116.7, 127.9, 128.4, 128.9, 136.4. IR (KBr): 3207, 2925, 2220, 1455, 1359, 1155, 1014 cm^{-1} . $\text{C}_8\text{H}_8\text{N}_2$ (132.17): calcd C, 72.70; H, 6.10; N, 21.19. Found: C, 72.66; H, 6.13; N, 21.11. Benzo[1,3]dioxol-5-ylmethyl-cyanamide **9a**:²⁸ mp 82–84 °C. ^1H NMR (400 MHz, CDCl_3): δ 4.05 (d, J = 5.2 Hz, 2H, CH_2), 4.57 (br s, 1H), 5.94 (s, 2H, OCH_2), 6.77 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 49.9, 101.4, 108.46, 108.54, 116.5, 121.7, 130.1, 147.8, 148.2. IR (KBr): 3233, 2952, 2897, 2220, 1500, 1445, 1038, 925, 809 cm^{-1} . $\text{C}_9\text{H}_8\text{N}_2\text{O}_2$ (176.18): calcd C, 61.36; H, 4.58; N, 15.90. Found: C, 61.41; H, 4.61; N, 15.85. Cyclohexyl-cyanamide **10a**:⁹ Gummy. ^1H NMR (400 MHz, CDCl_3): δ 1.31 (m, 5H), 1.61 (m, 1H), 1.78 (m, 2H), 1.95 (m, 2H), 3.09 (m, 1H), 3.91 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 24.3, 25.1, 32.6, 54.3, 115.9. IR (KBr): 3196, 2933, 2857, 2217, 1453, 1367, 1167 cm^{-1} . $\text{C}_7\text{H}_{12}\text{N}_2$ (124.19): calcd C, 67.70; H, 9.74; N, 22.56. Found: C, 67.67; H, 9.70; N, 22.50. Cyclopropyl-cyanamide **11a**:²⁹ Gummy. ^1H NMR (400 MHz, CDCl_3): δ 0.71 (m, 4H, $2 \times \text{CH}_2$), 2.71 (m, 1H, CH), 5.10 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 7.1, 26.9, 116.3. IR (KBr): 3206, 2224, 1571, 1471, 1358, 1238, 1014 cm^{-1} . $\text{C}_4\text{H}_6\text{N}_2$ (88.11): calcd C, 58.52; H, 7.37; N, 34.12. Found: C, 58.49; H, 7.40; N, 34.06. *n*-Butyl-cyanamide **12a**:⁹

Gummy. ^1H NMR (400 MHz, CDCl_3): δ 0.94 (t, J = 7.6 Hz, 3H, CH_3), 1.40 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 3.06 (m, 2H, CH_2), 4.61 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.6, 19.5, 31.7, 45.7, 117.2. IR (KBr): 3207, 2961, 2875, 2221, 1614, 1463, 1373, 1171 cm^{-1} . $\text{C}_5\text{H}_{10}\text{N}_2$ (98.15): calcd C, 61.19; H, 10.27; N, 28.54. Found: C, 61.22; H, 10.23; N, 28.48. 4-Hydroxy-phenyl cyanamide **13a**:⁹ mp 259–261 °C. ^1H NMR (400 MHz, CDCl_3 + DMSO): δ 5.67 (br s, 1H), 6.77 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 8.98 (br s, 1H, OH). ^{13}C NMR (100 MHz, CDCl_3 + DMSO): δ 112.8, 115.6, 115.8, 129.5, 152.2. IR (KBr): 3213, 2992, 2230, 1613, 1519, 1444, 1258, 1224 cm^{-1} . $\text{C}_7\text{H}_6\text{N}_2\text{O}$ (134.14): calcd C, 62.68; H, 4.51; N, 20.88. Found: C, 62.72; H, 4.55; N, 20.83. 3-Nitro-phenyl cyanamide **14a**:^{17a} Yellow Solid. Mp 133–135 °C. ^1H NMR (400 MHz, CDCl_3 + DMSO): δ 7.38 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 8.4 Hz, 1H), 7.85 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3 + DMSO): δ 109.6, 110.7, 116.8, 120.8, 130.1, 139.9, 148.4. IR (KBr): 3147, 2919, 2241, 1621, 1531, 1354, 1260, 1071, 937, 871 cm^{-1} . $\text{C}_7\text{H}_5\text{N}_3\text{O}_2$ (163.14): calcd C, 51.54; H, 3.09; N, 25.76. Found: C, 51.58; H, 3.12; N, 25.71. MS (ESI): 163 (M^+). 4-Acetyl-phenylcyanamide **15a**:³⁰ mp 153–157 °C. ^1H NMR (400 MHz, CDCl_3 + DMSO): δ 2.56 (s, 3H, CH_3), 7.08 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3 + DMSO): δ 25.9, 110.9, 114.5, 129.8, 131.2, 142.9, 196.2. IR (KBr): 3188, 2966, 2228, 1666, 1599, 1585, 1411, 1362, 1278, 1176, 962 cm^{-1} . $\text{C}_9\text{H}_8\text{N}_2\text{O}$ (160.18): calcd C, 67.49; H, 5.03; N, 17.48. Found: C, 67.53; H, 5.08; N, 17.44. MS (ESI): 160 (M^+). 4-(Allyloxy)-phenyl cyanamide **16a**: mp 66–70 °C. ^1H NMR (400 MHz, CDCl_3): δ 4.49 (d, J = 4.4 Hz, 2H), 5.29 (d, J = 10.8 Hz, 1H), 5.40 (d, J = 17.2 Hz, 1H), 6.02 (m, 1H), 6.87 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 69.5, 112.4, 116.1, 116.9, 118.1, 130.7, 133.2, 155.0. IR (KBr): 3148, 3079, 2954, 2887, 2214, 1510, 1240, 1172, 1108, 1014, 994 cm^{-1} . $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}$ (174.20): calcd C, 68.95; H, 5.79; N, 16.08. Found: C, 68.91; H, 5.77; N, 16.00. MS (ESI): 174 (M^+). 4-Cyanamide-phenylacetate **17a**: mp 95–97 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.32 (s, 3H), 6.93 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 7.08 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 111.5, 116.5, 122.9, 135.4, 146.4, 170.7. IR (KBr): 3168, 3100, 2974, 2233, 1754, 1610, 1512, 1374, 1226, 1202, 1164, 1014 cm^{-1} . $\text{C}_9\text{H}_8\text{N}_2\text{O}_2$ (176.18): calcd C, 61.36; H, 4.58; N, 15.90. Found: C, 61.40; H, 4.61; N, 15.8.