

Scientific paper

A Novel One-pot Synthesis of Isothiocyanates and Cyanamides from Dithiocarbamate Salts Using Environmentally Benign Reagent Tetrapropylammonium Tribromide

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Abstract

A highly efficient and simple protocol for the synthesis of isothiocyanates and cyanamides from their respective amines in the presence of a mild, efficient, and non-toxic reagent tetrapropylammonium tribromide is described. High environmental acceptability of the reagents, cost effectiveness and high yields are the important attributes of this methodology.

Keywords: TPATB, desulfurization, oxidation, isothiocyanates, sodium bicarbonate, cyanamide.

1. Introduction

Isothiocyanates are one of the most important synthetic intermediates for the preparation of both sulphur and nitrogen containing organic compounds especially for heterocycles.¹ The isothiocyanate functionality is frequently encountered in natural products, including sesquiterpenes.² Additionally, synthetic isothiocyanates have proven to have some biological activity, such as anti-proliferative³ and enzyme inhibitory for the HIV virus.⁴ Numerous methods for the preparation of isothiocyanates have been reported, starting from amines,⁵ dithiocarbamates,⁶ organic halides,⁷ olefins⁸ and aldoximes.⁹ Among the literature methods, the most widely used procedure is the synthesis by the decomposition of dithiocarbamates using heavy metals,¹⁰ thiophosgene, iodine, ethylchlorocarbamate and claycop.¹¹ Although many synthetic methods for the preparation of isothiocyanates have been reported to date,^{12–32} most methods suffer from the employment of highly toxic reagents. Thus, there is still need for a commercially viable and environmentally acceptable protocol for the synthesis of isothiocyanates. We describe herein a modified, environmentally benign and cost-effective met-

hod for the synthesis of isothiocyanates via TPATB-mediated decomposition of dithiocarbamate salt in the presence of sodium bicarbonate in water/ethyl acetate biphasic solvent system at room temperature (Scheme 1).

Similarly, in continuation of our work we have synthesised cyanamides from the dithiocarbamate salt. Cyanamides have attracted considerable attention as a class of versatile organic molecules. They have a wide range of uses in organic synthetic chemistry³³ and coordination chemistry³⁴ as they can be used as building blocks for the construction of not only diverse N-containing compounds but also as metal ligands with their unique reactivity and structure of the cyanamide unit. Additionally, it has been found that some cyanamide based compounds show a diversity of interesting bioactivities, inhibition of spontaneous myogenic, and peptide activator activities.³⁵ It has also been proved that cyanamide is a natural product present in higher plants even though its distribution is limited.³⁶ The broad applications of cyanamides have resulted in the development of several methods for their synthesis over the years. The most common among these is the reaction of cyanogens chloride or bromide with amines or with imide salts.³⁷ However, this method involves the use of po-

tassium or sodium cyanide and bromine for the preparation of cyanogen halide (which is again highly toxic), making the protocol environmentally unacceptable. Literature reports on various other methods for the preparation of cyanamide using different synthetic strategies, such as cyanation of amines using CN^+ equivalents as synthons,^{38–44} Tiemann rearrangement of amidoximes,⁴⁵ coupling reactions involving Pd isocyanides, allyl carbonates and trimethylsilyl azide,⁴⁶ and sodium bis(trimethylsilyl)amide as deoxygenating or desulfurizing agents.⁴⁷ Yet another method for the preparation of cyanamides involves the reaction of hypervalent iodine(V) species with *N,N'*-disubstituted glycolamide.⁴⁸ However, all the procedures reported so far seem to have certain environmental concerns as they involve direct or indirect use of toxic and corrosive reagents, strong alkaline conditions, expensive reagents and catalysts, high reaction temperatures and tedious purification procedures. We have been interested to an extent in the synthesis of isothiocyanates and cyanamides, therefore, in this context we develop an alternative method involving the use of alkyl or aryl dithiocarbamate using tetrapropylammonium tribromide as a double desulfurizing agent.

2. Experimental

2.1. General Procedure for the Synthesis of Phenyl Isothiocyanate

To a stirred and ice cooled suspension of phenyl dithiocarbamate salt (Table 1, compound **1**) (540 mg, 2 mmol) in ethylacetate (5 mL), and water (5 mL) was added NaHCO_3 (336 mg, 4 mmol). To this was added TPATB (0.852 g, 2 mmol) pinch wise over a period of 10–15 minutes to yield phenylisothiocyanate (Table 1, compound **1a**). During this period, precipitation of elemental sulfur was observed. Completion of the reaction was confirmed by TLC. Ethyl acetate (10 mL) was further added to the reaction mixture. The organic layer was washed with water (2–5 mL), dried over anhydrous Na_2SO_4 , concentrated under reduced pressure and purified over a short column of silica gel while eluting it with hexane–ethyl acetate (97:3) to give the pure product (Table 1, compound **1a**) (216 mg, 80%).

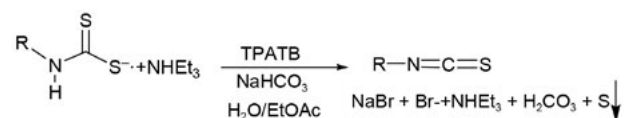
2.2. General Procedure for the Synthesis of Phenylcyanamide

To a stirred and ice cooled suspension of dithiocarbamate (Table 2, compound **1**) (540 mg, 2 mmol) in ethyl acetate (5 mL), was added NaHCO_3 (336 mg, 4 mmol). To this was then added TPATB (0.852 g, 2 mmol) pinch wise over a period of 10–15 minutes to yield phenylisothiocyanate. During this period precipitation of elemental sulfur was observed. After complete addition of TPATB, 25%

aqueous NH_3 (2.5 mL) was added drop wise to the stirred reaction mixture to give 1-phenylthiourea. After stirring for 10 minutes at room temperature, the excess of NH_3 was removed in a rotary evaporator whereby the solvent ethyl acetate was also simultaneously removed leaving behind the aqueous layer. To the crude reaction mixture was then further added ethyl acetate (5 mL) and NaHCO_3 (336 mg, 4 mmol). To the resultant solution, TPATB (0.852 g, 2 mmol) was added in small pinches, during which further precipitation of elemental sulfur was observed. The conversion of 1-phenylthiourea to phenylcyanamide (Table 2, compound **1b**) was observed within 5 minutes of the complete addition of TPATB. Completion of the reaction was confirmed by TLC. The precipitated sulfur was filtered, washed with ethyl acetate (2×5 mL). The organic layer was washed with water (2×5 mL) and dried over anhydrous Na_2SO_4 , concentrated under reduced pressure and purified over a short column of silica gel eluting it with hexane–ethyl acetate (97:3) to give the pure product (Table 2, compound **1b**) (188 mg, 80%) as an oily liquid.

3. Results and Discussion

The dithiocarbamic acid salt is readily converted into the corresponding isothiocyanate (Table 1, compound **1a**), simply by treating it with TPATB in the presence of sodium bicarbonate in water/ethyl acetate biphasic medium in good to excellent yields in shorter time (15 minutes) as shown in Scheme 1.

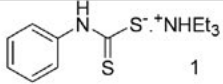
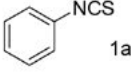
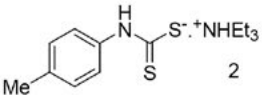
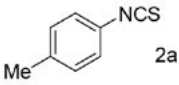
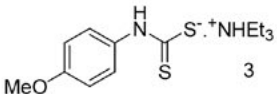
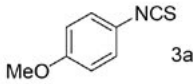
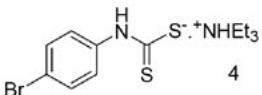
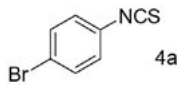
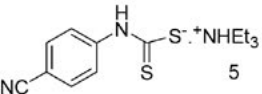
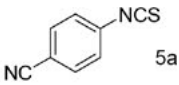
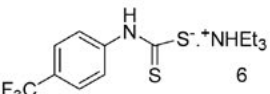
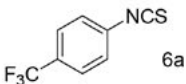
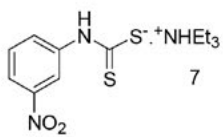
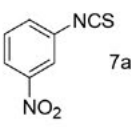
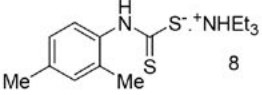
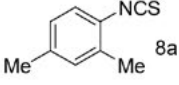
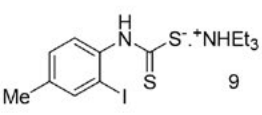
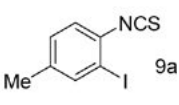
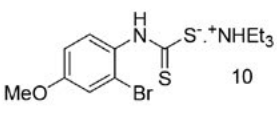
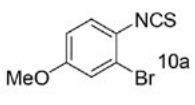
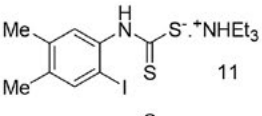
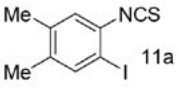
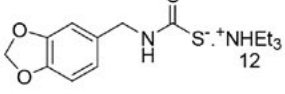
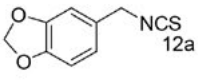
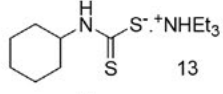
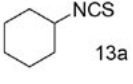
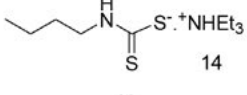
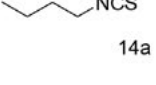
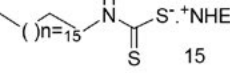
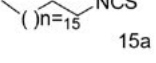


Scheme 1. Preparation of isothiocyanate from dithiocarbamate salt

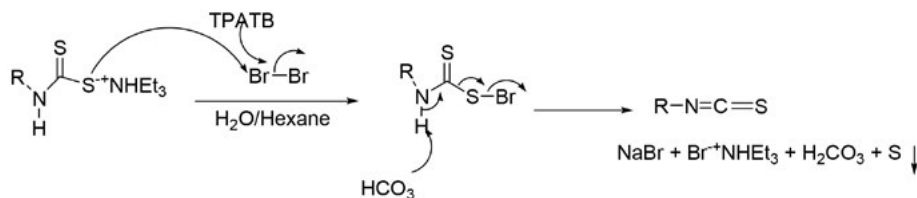
The use of water/ethyl acetate biphasic solvent system has several potential advantages. In addition to the benign character of both water and ethyl acetate, the coexistence of water with ethyl acetate helps in extracting the isothiocyanate to the organic layer leaving behind the impurities in the aqueous layer which in turn facilitates an easy workup. TPATB is soluble in ethyl acetate and on stirring dissolves, thus getting delivered to the water-ethyl acetate interphase for desulfurization. Moreover, the water phase dissolves the base sodium bicarbonate and retains the dithiocarbamic acid salt in aqueous layer. The use of sodium bicarbonate over organic bases offers a mild and effective green approach towards the synthesis of isothiocyanates. The mechanism of the present transformation is given below in Scheme 2.⁴⁸

Thus, the method provides an ecologically and economically viable process for the preparation of isothiocyanates. The preparation of isothiocyanates was performed

Table I. Preparation of Isothiocyanates from Dithiocarbamate Salt and TPATB^a

Substrate	Product ^b	Yield (%) ^c
 1	 1a	80
 2	 2a	92
 3	 3a	81
 4	 4a	92
 5	 5a	92
 6	 6a	90
 7	 7a	77
 8	 8a	90
 9	 9a	85
 10	 10a	80
 11	 11a	92
 12	 12a	86
 13	 13a	90
 14	 14a	85
 15	 15a	88

^a Reactions were monitored by TLC; ^b Confirmed by IR, ¹HNMR and ¹³CNMR; ^c Isolated yield.



Scheme 2. Mechanism of the formation of isothiocyanate from dithiocarbamate salt

on freshly prepared dithiocarbamate salts synthesized from a variety of structurally different alkyl and aryl amines. The results are summarized in Table 1. Substrates containing activating substituents (Table 1, compounds 2–3) gave the expected products efficiently as also did substrates containing deactivating substituents (Table 1, compounds 4–7). Trisubstituted substrates (Table 1, compounds 8–10) as well as highly hindered substrates (Table 1, compound 11) gave the corresponding isothiocyanates in high yields. Benzylic substrate (Table 1, compound 12) and aliphatic substrates (Table 1, compounds 13–15) also gave their expected products (Table 1, compound 12a) and (Table 1, compounds 13a–15a) respectively in excellent yields.

Similarly, for the synthesis of cyanamides the methodology was based on: (i) formation of isothiocyanate from alkyl/aryl dithiocarbamate salt by desulfurization with TPATB in the presence of triethylamine as the base in ethyl acetate solvent, (ii) treating the *in situ* generated isothiocyanate with aqueous NH_3 to afford alkyl/aryl thioamides and (iii) further oxidative desulfurization of thioamides to cyanamide with TPATB in the presence of triethylamine (Scheme 2). The mechanism of the present transformation is given below.⁴⁹ Based on these findings, we thus report herein a practical, environmentally benign, high yielding and one pot preparation of cyanamides from dithiocarbamate salts using cheap and non-toxic reagent TPATB (Scheme 3) in an innocuous solvent ethyl acetate.

Implementing this one pot method, a wide variety of aromatic and aliphatic cyanamides have been prepared from their parent dithiocarbamate salts. Phenyl cyanamide (Table 2, compound 1b) was obtained in excellent yield from its dithiocarbamate (Table 2, compound 1). Monosubstituted substrates bearing deactivating substituents (Table 2, compounds 2–6) readily underwent this reaction to produce the desired cyanamides (Table 2, compounds 2b–6b) in high yields. The method worked smoothly for substrates with electron donating substituents such as (Table 2, compounds 7–8) to afford the corre-

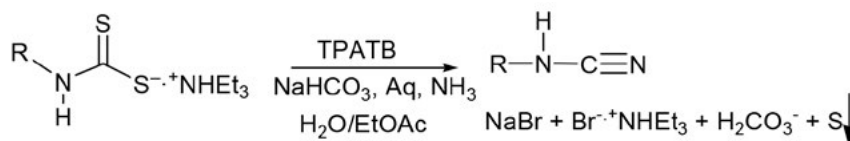
sponding cyanamides (Table 2, compounds 7b–8b) in high yields. A noteworthy aspect is that the present methodology can be applied to substrates containing sensitive substituents such as keto functionality (Table 2, compound 9b) as well as trisubstituted ones (Table 2, compound 10b). Cyclic and open chain aliphatic cyanamides (Table 2, compounds 11b–12b) were obtained from their corresponding dithiocarbamate salts (Table 2, compounds 11–12) under the same reaction conditions. We further investigated the efficacy of this method towards benzylic dithiocarbamate (Table 2, compounds 13–14) and dithiocarbamate salt of homoveratryl amine (Table 2, compound 15) which underwent the reaction smoothly to yield their respective corresponding cyanamide products (Table 2, compounds 13b–14b) and (Table 2, compound 15a) in good yields under the similar reaction conditions.

4. Spectroscopic and Analytical Data

1-Isothiocyanato-benzene (1a). Oily; ^1H NMR (400 MHz, CDCl_3) δ 7.21–7.37 (m, 5H, ArH). ^{13}C NMR (100 MHz, CDCl_3) δ 125.8, 127.4, 129.6, 131.3, 135.3. IR (KBr) 3064, 2164, 2063, 1591, 1489, 1474, 1451, 1070, 927, 905, 749, 684 cm^{-1} . Anal. Calcd for $\text{C}_7\text{H}_5\text{NS}$ (135.19): C, 62.19; H, 3.73; N, 10.36; S, 23.72. Found: C, 62.22; H, 3.71; N, 10.35; S, 23.73.

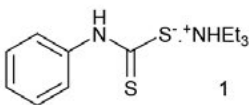
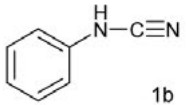
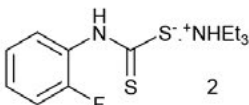
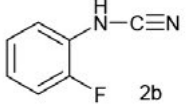
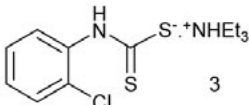
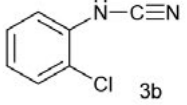
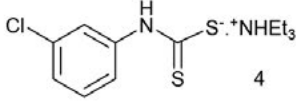
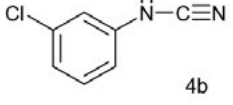
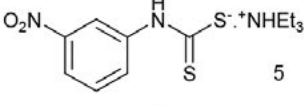
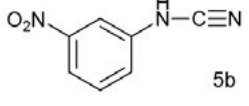
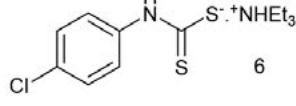
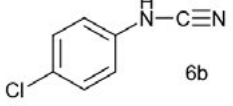
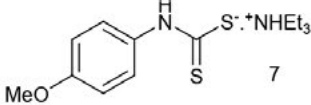
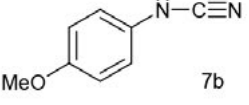
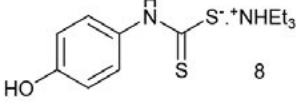
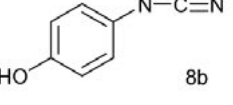
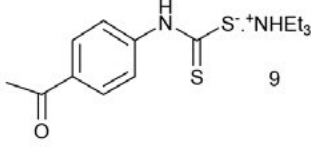
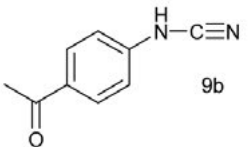
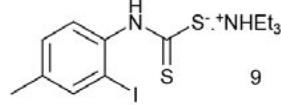
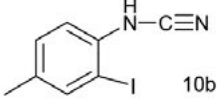
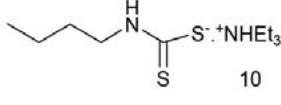
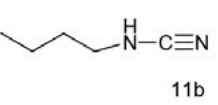
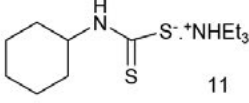
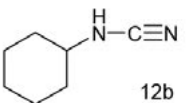
1-Isothiocyanato-4-methyl-benzene (2a). Oily; ^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 3H, CH_3), 7.06–7.13 (m, 4H, ArH). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 125.4, 128.2, 130.1, 134.4, 137.4. IR (KBr) 2920, 2094, 1503, 929, 812, 790, 497 cm^{-1} . Anal. Calcd for $\text{C}_8\text{H}_7\text{NS}$ (149.15): C, 64.36; H, 4.73; N, 9.39; S, 21.51. Found: C, 64.32; H, 4.75; N, 9.41; S, 21.56.

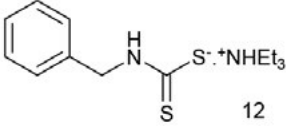
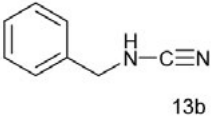
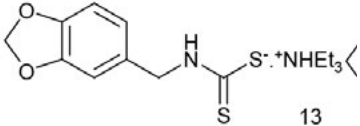
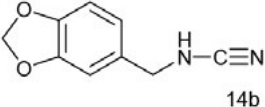
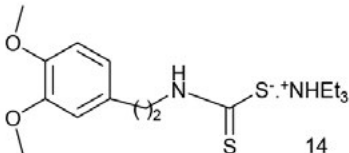
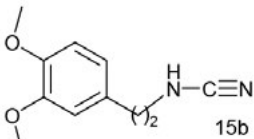
1-Isothiocyanato-4-methoxy-benzene (3a). Oily; ^1H NMR (400 MHz, CDCl_3) δ 3.80 (s, 3H, CH_3), 6.85 (d, 2H, $J = 8.8$ Hz, ArH), 7.16 (d, 2H, $J = 8.8$ Hz, ArH). ^{13}C NMR



Scheme 3. Mechanism for the formation of cyanamide

Table 2. Preparation of cyanamides from dithiocarbamates and TPATB^a

Substrate	Product ^b	Yield (%) ^c
 1	 1b	72
 2	 2b	70
 3	 3b	70
 4	 4b	75
 5	 5b	71
 6	 6b	77
 7	 7b	70
 8	 8b	68
 9	 9b	65
 9	 10b	78
 10	 11b	60
 11	 12b	62

Substrate	Product ^b	Yield (%) ^c
 12	 13b	64
 13	 14b	67
 14	 15b	66

^a Reactions were monitored by TLC; ^b Confirmed by IR, ¹H NMR and ¹³C NMR; ^c isolated yield

(100 MHz, CDCl₃) δ 55.4, 114.6, 123.2, 126.8, 133.7, 158.4. IR (KBr) 3000, 2956, 2835, 2170, 2098, 1580, 1599, 1503, 1459, 1440, 1292, 1251, 1179, 1166, 1028, 927, 824, 614, 513 cm⁻¹. Anal. Calcd for C₈H₇NOS (165.22): C, 58.16; H, 4.27; N, 8.48; S, 19.40. Found: C, 58.08; H, 4.23; N, 8.34; S, 19.34.

1-Bromo-4-isothiocyano-benzene (4a). White solid, m.p. 58 °C (lit.^{1a} 58 °C), ¹H NMR (400 MHz, CDCl₃) δ 7.09 (d, 2H, *J* = 8.8 Hz, *ArH*), 7.47 (d, 2H, *J* = 8.8 Hz, *ArH*). ¹³C NMR (100 MHz, CDCl₃) δ 120.8, 127.2, 130.5, 132.8, 136.9. IR (KBr) 3074, 2925, 2171, 2071, 1578, 1478, 1474, 1399, 1067, 1011, 923, 818, 490, 438 cm⁻¹. Anal. Calcd for C₇H₄BrNS (214.03): C, 39.24; H, 1.88; N, 6.54; S, 14.99. Found: C, 39.21; H, 1.93; N, 6.50; S, 15.04.

4-Isothiocyano-benzonitrile (5a). White solid; m.p. 119–120 °C (lit.²¹ 121 °C), ¹H NMR (CDCl₃, 400 MHz) δ 7.31 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 110.6, 117.9, 126.5, 133.6, 135.9, 139.4; IR (KBr) 3435, 2197, 2124, 2104, 1591, 1492, 1277, 933, 836, 544 cm⁻¹. Anal. Calcd for C₈H₄N₂S (166.13): C, 59.95; H, 2.51; N, 17.49; S, 20.03. Found: C, 59.98; H, 2.49; N, 17.45; S, 19.98.

1-Isothiocyano-4-trifluoromethyl-benzene (6a). White solid; m.p. 43 °C (lit.²² bp 205–207 °C); ¹H NMR (CDCl₃, 400 MHz) δ 7.32 (d, *J* = 8.4 Hz, 2H, *ArH*), 7.61 (d, *J* = 8.4 Hz, 2H, *ArH*); ¹³C NMR (CDCl₃, 100 MHz) δ 122.4, 125.1, 126.1, 126.9, 127.0, 129.0, 129.4, 135.15, 138.4; IR (KBr) 3427, 2081, 1613, 1413, 1325, 1137, 1106, 1066, 839, 590 cm⁻¹. Anal. Calcd for C₈H₄F₃NS (203.12): C, 47.26; H, 1.98; N, 6.89; S, 15.79. Found: C, 47.22; H, 1.96; N, 6.91; S, 15.75.

1-Isothiocyano-3-nitro-benzene (7a). Oily; ¹H NMR (400 MHz, CDCl₃) δ 7.54 (s, 2H, *ArH*), 8.06 (s, 1H, *ArH*),

8.11–8.14 (m, 1H, *ArH*). ¹³C NMR (100 MHz, CDCl₃) δ 120.7, 121.9, 130.6, 131.6, 133.3, 139.6, 148.8. IR (KBr) 3091, 3074, 2227, 2161, 2106, 1526, 1470, 1348, 1302, 892, 809, 736, 665 cm⁻¹. Anal. Calcd for C₇H₄N₂O₂S (180.13): C, 46.63; H, 2.23; N, 15.55; S, 17.81. Found: C, 46.65; H 2.26; N, 15.51; S, 17.78.

1-Isothiocyano-2,4-dimethyl-benzene (8a). Oily; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (s, 3H, CH₃), 2.33 (s, 3H, CH₃), 6.96 (d, 1H, *J* = 9.2 Hz, *ArH*), 7.01 (s, 1H, *ArH*), 7.07 (d, 1H, *J* = 8.0 Hz, *ArH*). ¹³C NMR (100 MHz, CDCl₃) δ 18.2, 21.1, 125.6, 127.4, 131.2, 134.6, 137.4. IR (KBr) 2920, 2131, 2085, 1490, 1455, 1379, 1229, 1036, 947, 901, 875, 812 cm⁻¹. Anal. Calcd for C₉H₉NS (163.17): C, 66.19; H, 5.55; N, 8.58; S, 19.66. Found: C, 66.15; H, 5.52; N, 8.63; S, 19.64.

2-Iodo-1-isothiocyano-4-methylbenzene (9a). White solid; m.p. 62–65 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (s, 3H, CH₃), 7.13 (m, 2H, *ArH*), 7.62 (s, 1H, *ArH*). ¹³C NMR (100 MHz, CDCl₃) δ 20.9, 94.2, 126.7, 130.1, 132.3, 136.1, 139.1, 139.9. IR (KBr) 2916, 2134, 1633, 1474, 1042, 929, 811 cm⁻¹.

2-Bromo-1-isothiocyano-4-methoxy-benzene (10a). White solid; m.p. 77 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.80 (s, 3H, CH₃), 6.82 (m, 1H, *ArH*), 7.11 (m, 1H, *ArH*), 7.18 (d, 1H, *J* = 8.0 Hz, *ArH*); ¹³C NMR (100 MHz, CDCl₃) δ 56.0, 114.4, 118.5, 121.6, 124.1, 127.7, 136.7, 158.8; IR (KBr) 2972, 2125, 1594, 1560, 1483, 1296, 1263, 1220, 1039, 807, 617 cm⁻¹. Anal. Calcd for C₈H₆BrNOS (244.05): C, 39.33; H, 2.47; N, 5.73; S, 3.14. Found: C, 39.29; H, 2.52; N, 5.70; S, 3.11.

1-Iodo-2-isothiocyano-4,5-dimethyl-benzene (11a). White solid; m.p. 54 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.18

(s, 3H, CH_3), 2.22 (s, 3H, CH_3), 6.99 (s, 1H, ArH), 7.30 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 19.5, 117.2, 124.1, 127.8, 129.3, 133.8, 137.4, 137.9; IR (KBr) 2922, 2853, 2192, 2118, 1472, 1372, 1273, 1076, 1048, 933, 882, 824, 708 cm^{-1} . Anal. Calcd for C_9H_8INS : C, 37.39; H, 2.79; N, 4.84; S, 11.09. Found: C, 37.42; H, 2.81; N, 4.81; S, 11.06. MS (AP^+) Calcd for C_9H_8INS : 288.94. Found: 288.97 (M^+).

5-(Isothiocyanatomethyl)benzo[d][1,3]dioxole (12a).

Reddish oil. 1H NMR (400 MHz, $CDCl_3$) δ 4.59 (s, 2H, CH_2), 5.98 (s, 2H, CH_2), 6.74–6.80 (m, 3H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.7, 101.5, 107.7, 108.6, 120.7, 128.0, 132.1, 147.8, 148.2. IR (KBr) 2895, 2087, 1503, 1445, 1369, 1322, 1251, 1101, 1028, 924 cm^{-1} .

Isothiocyanato-cyclohexane (13a). 1H NMR (400 MHz, $CDCl_3$) δ 1.28–1.96 (m, 10H, CH_2), 3.67 (m, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0, 24.9, 33.0, 55.2, 129.6. IR (KBr) 2937, 2858, 2175, 2102, 2060, 1450, 1361, 1320, 986, 891, 720, 702 cm^{-1} . Anal. Calcd for $C_7H_{11}NS$ (141.23): C, 59.53; H, 7.85; N, 9.92; S, 22.70. Found: C, 59.50; H, 7.81; N, 9.88; S, 22.74.

1-Isothiocyanato-*n*-butane (14a). Oily liquid. 1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, $J = 7.4$ Hz, 3H, CH_3), 1.37–1.47 (m, 2H, CH_2), 1.61–1.69 (m, 2H, CH_2), 3.42 (t, $J = 6.6$ Hz, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 19.7, 31.9, 44.7, 129.4. IR (KBr) 2925, 2088, 1597, 1401, 1218, 1116, 753 cm^{-1} .

1-Isothiocyanato-octadecane (15a). Gummy, 1H NMR ($CDCl_3$, 400 MHz) δ 0.879 (t, $J = 6.8$ Hz, 3H, CH_3), 1.25 (m, 28H, CH_2), 1.71–1.72 (m, 4H, CH_2), 3.50 (t, $J = 6.4$ Hz, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.3, 22.8, 26.7, 29.0, 29.5, 29.7, 29.8, 30.1, 32.1, 45.2; IR (KBr) 2923, 2853, 2185, 2096, 1463, 1455, 1346, 721 cm^{-1} . Anal. Calcd for $C_{19}H_{37}NS$: C, 73.24; H, 11.97; N, 4.50; S, 10.29. Found: C, 73.27; H, 12.01; N, 4.48; S, 10.25. MS (ES^-) Calcd for $C_{19}H_{37}NS$: 311.26. Found: 311.19 (M^+).

Phenyl cyanamide (1b). Gummy; 1H NMR ($CDCl_3$, 400 MHz) δ 7.02–7.07 (m, 3H, ArH), 7.28–7.33 (m, 2H, ArH), 7.64 (brs, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.2, 115.5, 123.6, 129.8, 137.4. IR (KBr) 3175, 2919, 2227, 1600, 1501, 1249, 748, 689 cm^{-1} . Anal. Calcd for $C_7H_6N_2$ (118.13): C, 71.17; H, 5.12; N, 23.71. Found: C, 71.27; H, 5.09; N, 23.67.

2-Fluorophenyl cyanamide (2b). White solid; m.p. 95 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 6.87 (brs, 1H, NH), 6.90–7.45 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.9, 115.7, 115.9, 116.8, 124.1, 124.1, 125.09, 125.12, 125.6, 125.8, 150.1, 152.5. IR (KBr) 3068, 2037, 1606, 1587, 1495, 1265, 1212, 1104, 941, 808, 752 cm^{-1} . Anal. Calcd for $C_7H_5FN_2$ (136.13): C, 61.76; H, 3.70; N, 20.58. Found: C, 61.80; H, 3.73; N, 23.53.

2-Chlorophenyl cyanamide (3b). White solid; m.p. 101–103 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 6.56 (brs, 1H, NH), 7.05 (m, 1H, ArH), 7.31 (m, 2H, ArH), 7.35 (m, 1H, ArH). ^{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} . Anal. Calcd for $C_7H_5ClN_2$ (152.58): C, 55.10; H, 3.30; N, 18.36. Found: C, 55.11; H, 3.32; N, 18.29.

3-Chlorophenyl cyanamide (4b). White solid; m.p. 93–95 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 6.92 (m, 1H, ArH), 7.03 (m, 2H, ArH), 7.26 (t, $J = 8.0$ Hz, 1H, ArH). ^{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} . Anal. Calcd for $C_7H_5ClN_2$ (152.58): C, 55.10; H, 3.30; N, 18.36. Found: C, 55.10; H, 3.29; N, 18.29. MS (ESI): 152 (M^+).

3-Nitrophenyl cyanamide (5b). Yellow solid; m.p. 133–135 °C; 1H NMR ($CDCl_3$ + DMSO, 400 MHz) δ 7.38 (d, $J = 8.4$ Hz, 1H, ArH), 7.52 (t, $J = 8.4$ Hz, 1H, ArH), 7.85 (m, 2H, ArH). ^{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} . Anal. Calcd for $C_7H_5N_3O_2$ (163.14): C, 51.54; H, 3.09; N, 25.76. Found: C, 51.58; H, 3.12; N, 25.71; MS (ESI): 163 (M^+).

4-Chlorophenyl cyanamide (6b). White solid; m.p. 95 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 6.91 (d, $J = 8.0$ Hz, 2H, ArH), 7.28 (d, $J = 8.0$ Hz, 2H, ArH). ^{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} . Anal. Calcd for $C_7H_5ClN_2$ (152.58): C, 55.10; H, 3.30; N, 18.36. Found: C, 55.09; H, 3.33; N, 18.32.

4-Methoxyphenyl cyanamide (7b). White solid; m.p. 86–89 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 3.78 (s, 3H, CH_3), 6.87 (d, $J = 8.8$ Hz, 2H, ArH), 6.95 (d, $J = 8.8$ Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 112.8, 115.2, 117.0, 130.6, 156.1. IR (KBr) 3180, 2926, 2218, 1456, 1295, 1238, 1105, 1037, 826 cm^{-1} . Anal. Calcd for $C_7H_8N_2O$ (148.17): C, 64.85; H, 5.44; N, 18.91. Found: C, 64.91; H, 5.40; N, 18.93.

4-Hydroxyphenyl cyanamide (8b). White solid; m.p. 259–261 °C; 1H NMR ($CDCl_3$ + DMSO, 400 MHz) δ 5.67 (brs, 1H, NH), 6.77 (d, $J = 8.8$ Hz, 2H, ArH), 6.83 (d, $J = 8.8$ Hz, 2H, ArH), 8.98 (brs, 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} . Anal. Calcd for $C_7H_6N_2O$ (134.14): C, 62.68; H, 4.51; N, 20.88. Found: C, 62.72; H, 4.55; N, 20.83.

4-Acetylphenyl cyanamide (9b). White solid; m.p. 153–157 °C; 1H NMR ($CDCl_3$ + DMSO, 400 MHz) δ 2.56 (s,

3H, CH₃), 7.08 (d, *J* = 8.8 Hz, 2H, ArH), 7.91 (d, *J* = 8.8 Hz, 2H, ArH). ¹³C NMR (100 MHz, CDCl₃ + 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. Anal. Calcd for C₉H₈N₂O (160.18): C, 67.49; H, 5.03; N, 17.48. Found: C, 67.53; H, 5.08; N, 17.44. MS (ESI): 160 (M⁺).

2-Iodo-4-methylphenyl cyanamide (10b). White solid; m.p. 144 °C; ¹H NMR (CDCl₃, 400 MHz) δ 2.29 (s, 3H, CH₃), 6.17 (brs, 1H, NH), 7.17 (dd, *J* = 8.2 Hz, 2H, ArH), 7.56 (s, 1H, ArH). ¹³C NMR (100 MHz, CDCl₃) δ 20.4, 84.2, 110.7, 115.4, 130.9, 135.4, 139.6. IR (KBr) 3229, 2919, 2217, 1603, 1573, 1502, 1420, 1383, 1283, 1032, 866, 805 cm⁻¹. Anal. Calcd for C₈H₈N₂ (258.06): C, 37.23; H, 2.73; N, 10.86. Found: C, 37.27; H, 2.75; N, 10.84.

***n*-Butyl cyanamide (11b).** Gummy; ¹H NMR (CDCl₃, 400 MHz) δ 0.94 (t, *J* = 7.6 Hz, 3H, CH₃), 1.40 (m, 2H, CH₂), 1.58 (m, 2H, CH₂), 3.06 (m, 2H, CH₂), 4.61 (brs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 13.6, 19.5, 31.7, 45.7, 117.2. IR (KBr) 3207, 2961, 2875, 2221, 1614, 1463, 1373, 1171 cm⁻¹. Anal. Calcd for C₅H₁₀N₂ (98.15): C, 61.19; H, 10.27; N, 28.54. Found: C, 61.22; H, 10.23; N, 28.48.

Cyclohexyl cyanamide (12b). Gummy; ¹H NMR (CDCl₃, 400 MHz) δ 1.31 (m, 5H, CH₂), 1.61 (m, 1H, CH₂), 1.78 (m, 2H, CH₂), 1.95 (m, 2H, CH₂), 3.09 (m, 1H, CH₂), 3.91 (brs, 1H, NH). ¹³C NMR (100 MHz, CDCl₃) δ 24.3, 25.1, 32.6, 54.3, 115.9. IR (KBr) 3196, 2933, 2857, 2217, 1453, 1367, 1167 cm⁻¹. Anal. Calcd for C₇H₁₂N₂ (124.19): C, 67.70; H, 9.74; N, 22.56. Found: C, 67.67; H, 9.70; N, 22.50.

Benzyl cyanamide (13b). Gummy; ¹H NMR (CDCl₃, 400 MHz) δ 4.11 (d, *J* = 5.2 Hz, 2H, CH₂ CH₂), 4.66 (brs, 1H, NH), 7.27–7.37 (m, 5H, ArH). ¹³C NMR (100 MHz, CDCl₃) δ 49.9, 116.7, 127.9, 128.4, 128.9, 136.4. IR (KBr) 3207, 2925, 2220, 1455, 1359, 1155, 1014 cm⁻¹. Anal. Calcd for C₈H₈N₂ (132.17): 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 (14b). White solid; m.p. 82–84 °C; ¹H NMR (CDCl₃, 400 MHz) δ 4.05 (d, *J* = 5.2 Hz, 2H, CH₂), 4.57 (brs, 1H, NH), 5.94 (s, 2H, OCH₂), 6.77 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) 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. Anal. Calcd for C₉H₈N₂O₂ (176.18): C, 61.36; H, 4.58; N, 15.90. Found: C, 61.41; H, 4.61; N, 15.85.

3,4-Dimethoxyphenylethyl cyanamide (15b). Gummy; ¹H NMR (CDCl₃, 400 MHz) δ 2.84 (t, 2H, CH₂), 3.28 (q, *J* = 7.2 Hz, 2H, CH₂), 3.83 (s, 3H, CH₃), 3.84 (s, 3H, CH₃), 4.37 (brs, 1H, NH), 6.76 (m, 3H, ArH). ¹³C NMR (100 MHz, CDCl₃) δ 35.5, 47.5, 55.92, 55.95, 111.4, 111.9, 116.5, 120.9, 130.0, 147.8, 148.9. IR (KBr) 3274, 2937, 2219, 1592,

1517, 1464, 1262, 1236, 1156, 1142, 1026, 913 cm⁻¹. Anal. Calcd for C₁₁H₁₄N₂O₂ (206.24): C, 64.06; H, 6.84; N, 13.58. Found: C, 64.12; H, 6.80; N, 13.54.

5. Conclusion

In conclusion, we have developed a general, economical and environmentally benign method for the preparation of isothiocyanates and cyanamides from their corresponding dithiocarbamic acid salts. The use of non-toxic and eco-friendly reagents and solvents without the formation of any side products makes this methodology potentially useful. The yield could in fact be considered as very good if not excellent.

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Povzetek

Opisujemo zelo učinkovit in enostaven pristop k sintezi izotiocianatov in cianamidov iz ustreznih aminov ob prisotnosti blagega, učinkovitega in nestrupenega reagenta tetrapropilamonijevega tribromida. Dobra okoljska sprejemljivost, stroškovna učinkovitost in visoki izkoristki so glavne odlike te metodologije.