Nickel mediated tandem reaction towards the synthesis of cyanamides

[1]Dr. Nagalakshmi Vedula, [2] Srinivasa Rao Gundumolu, [3]Dr. Mohan Seelam

[1, 2] *Department of chemistry, Ch. S. D. St. Theresa's college for women, Eluru-534003, Andhra Pradesh, India,*
[3]*Dept. of Chemistry, Bapatla Engineering College, Bapatla-522102, Andhra Pradesh, India.*

Abstract: The synthesis of cyanamides from isothiocyanates through tandem reaction using nickel catalyst has been demonstrated. Aromatic cyanamides were constructed from isothiocyanates through addition/desulfurization. Cheap nickel sulfate was used for the synthesis of various cyanamides. In addition, nickel catalyst was found to be desulfurization reagent that has not been previously reported. The final products have been obtained from starting precursors in good to high yield.

Index Terms **–** nickel catalyst, cyanamides, desulfurization, tandem reaction.

I. INTRODUCTION

Cyanamides are very strong intermediates in the synthesis of biologically, medicinally and pharmaceutically important heterocyclic compounds. [1, 2] In recent decades, cyanamides (RR1N – CN) have been used as herbicides in the synthesis of N-alkyl or N-aryl imides [3, 4]. Cyanamides have also been used as a protective form of secondary amines in organic synthesis [5]. Additionally, cyanamides are used as a protected form of secondary amines.

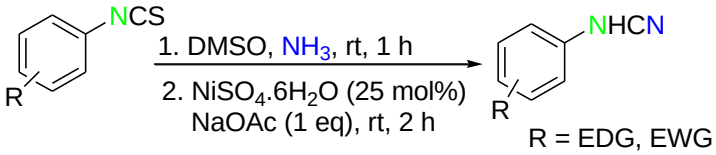
The preparation of cyanamides was achieved by the gas cyanogen chloride or cyanogen reaction amine bromide or salt imide[6,7]. Additionally cyanamides were built from different starting points precursors include urea, thiores, [8] amidoximes, [9] chemical isocyanides and azide trimethylsilyl,[10] and N, N-replacing glycyclamide[11]. Wong and coauthors have a one-pot reaction designed for the production of isocyanate cyanamides and isothiocyanates with deoxygenating or desulphurizing agent, such as bis- sodium (Trimethylsilyl) amide [12, 13]. Patel and the co-authors recently synthesis recorded of thiocarbamate cyanamides salts [14] with the hypervalent reagent iodine (III). Nonetheless, most of the reports were extremely caustic, damaging, and effective reagents. Except the disadvantages listed above, some of the reactions called for high temperature and cyan cation (CN+) that is derived from toxic cyanide halides,[7] while some other reactions may yield low yields and demand cumbersome methods of purification[14]. To overcoming the aforementioned drawbacks, an efficient Method required. In this regard, we wish to demonstrate synthesis of aryl / alkyl cyanamides isothiocyanates by cheap addition / desulfurization, available readily, and air-stable nickel as a catalyst conditions for mild reaction.

II. MATERIALS AND METHODS

2.1. General information: CS_2, $NiCl_2.6H_2O$, $NiSO_4.6H_2O$, $Ni(NO_3)_2.6H_2O$, Et_3N, pyridine, sodium bicarbonate and ammonia were purchased from Aldrich and used without further purification. The solvents were purchased and dried according to standard procedure prior to use. ^1H NMR (400 MHz) spectra were recorded with a Varian 400 spectrometer. Infrared (IR) spectra recorded on a Perkin Elmer Spectrum one FT-IR spectrometer. Elemental analyses were recorded with Perkin Elmer CHNS analyzer. VKSI medico centrifuge machine was used for our experimental procedure for the synthesis of cyanamides and some substituted phenyl tetrazolamines. Aryl/alkyl isothiocyanates have prepared by our reported procedure.

2.2. General procedure for the synthesis of phenyl cyanamide (2a): To a stirred solution of DMSO (4-5 ml), phenyl isothiocyanate (2 mmol, 270 mg) was added in slowly and followed by Ammonia (2 ml) was added at room temperature. The whole reaction mixture stirred for one hour at room temperature. Thiourea formation was monitored by TLC. To this, $NiSO_4.6H_2O$ (25 mol%, 121 mg) was added slowly followed by sodium acetate (2 mmol (1 eq), 164 mg) was added slowly for 10 min and stirred for 2 h at room temperature. During this time black colors precipitate (NiS) was observed. And it was removed by centrifugation. The clear solution was concentrated by using rotary evaporator and the crude mixture was purified by silica gel (60-120 mesh) column chromatography using 10 % ethylacetate in hexane as eluent to obtain a phenyl cyanamide as a target product, which was characterized by ^1H NMR, ^{13}C NMR and IR spectroscopy analysis.

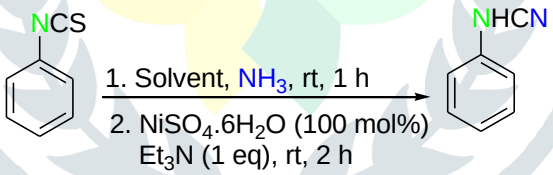
Aryl/alkyl cyanamides could be obtained from the reaction between isothiocyanates and ammonia using $NiSO_4.6H_2O$ as catalyst and NaOAc as base in the presence of DMSO solvent under mild reaction conditions. Both aryl and alkyl isothiocyanates could give their respective target products in moderate to good yields.



III. RESULTS AND DISCUSSIONS

The optimization of the reaction was checked with phenyl isothiocyanates as model substrate. Initially, various solvents were checked for this reaction (Table.1). Among them DMSO could show better activity (Table.1, entry 2) than other solvents. The solvents like H_2O, THF and toluene couldn't give target product (Table.1, entries 4-6). DMF solvent could give target product in 75% (Table1, entry 1) yield and CH_3CN gave target product in moderate yield (Table.1, entry 3). Later, we have also examined the reaction in the presence of combination of solvents (Table.1, entries 7-8). Unfortunately no combination of solvent could give target product in good yield. Later, various bases were examined for this reaction (Table.2). Both organic and in-organic bases could show similar effect. The organic base pyridine couldn't give target product. The control experiment is confirmed that no target could observe in the absence of solvent (Table.1, entry 9) and base (Table .2, entry 7) and the starting material is recovered intact. Different nickel sources were tested. All nickel sources could show similar effect (Table.3, entries 1-3). Less amount of catalyst such as 50 mol% and 25 mol% were checked and they could give complete conversion (Table.3, entries 4-5). But unfortunately the reaction could give target product in moderate yield in the presence of 10 mol% catalysts (Table.3, entry 6). No reaction could observe in the absence of catalyst (Table.3, entry 7).

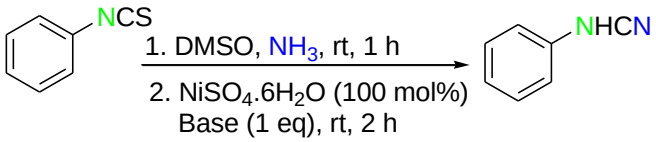
Table.1 Solvent optimization for the preparation of cyanamide [a]



Entry	Solvent	Yield (%)
1	DMF	75
2	DMSO	95
3	CH_3CN	45
4	H_2O	ND
5	THF	ND
6	Toluene	ND
7	DMF/H_2O (1:1)	50
8	DMF/H_2O (1:2)	20
9	-	ND

[a] Conversion was confirmed by TLC

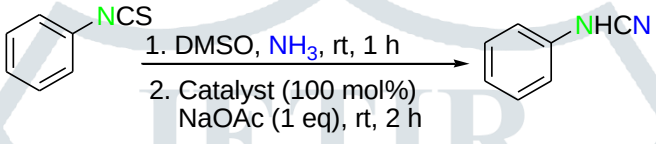
Table.2 Base optimization for the synthesis of cyanamide [a]



Entry	Base	Yield (%)[a]
1	Et_3N	95
2	Pyridine	ND
3	NaOAc	95
4	$NaHCO_3$	95
5	Na_2HPO_4	95
6	NaOH	95
7	-	ND

[a]Conversion was confirmed by TLC

Table.3 Catalyst optimization for the construction of cyanamide [a]

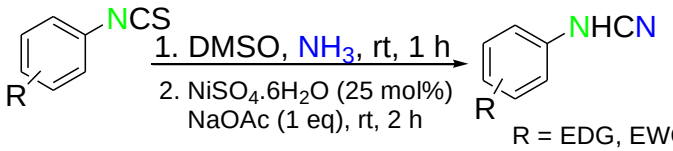


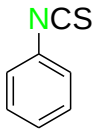
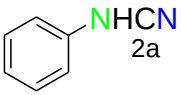
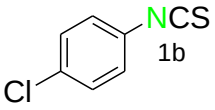
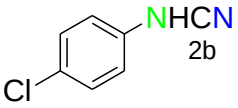
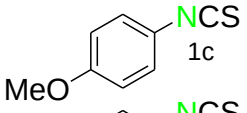
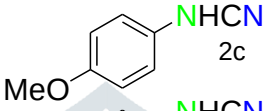
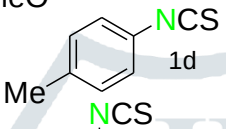
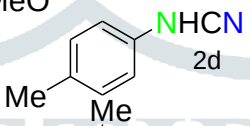
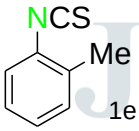
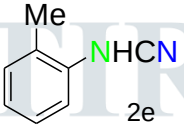
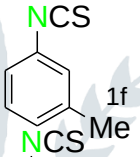
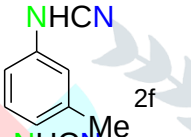
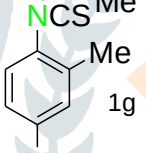
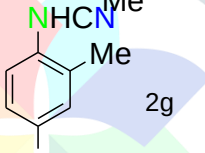
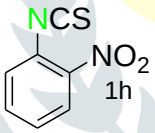
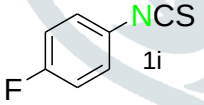
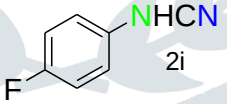
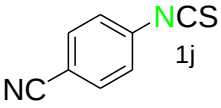
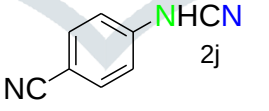
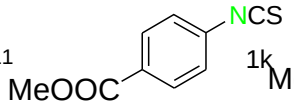
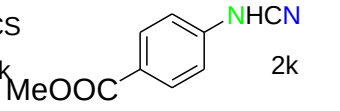
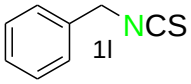
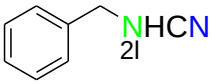
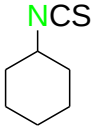
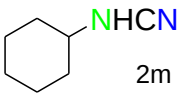
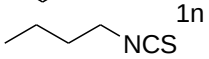
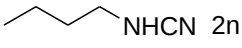
Entry	Catalyst	Conversion (%)[a]
1	$NiCl_2.6H_2O$	95
2	$NiSO_4.6H_2O$	95
3	$Ni(NO_3)_2.6H_2O$	95
4[b]	$NiSO_4.6H_2O$	95
5[c]	$NiSO_4.6H_2O$	95
6[d]	$NiSO_4.6H_2O$	50
7	-	ND

[a]Conversion was confirmed by TLC

Having the optimal conditions in our hand, we explored the substrate scope (Table.4). The substrates having both electron donating and electron withdrawing substituents on the aryl rings could give their respective target product in moderate to high yield. The phenyl ring having electron donating groups such as 4-methoxy, 4-methyl could give their respective aromatic cyanamides (2c, 2d) in 94-97% yield. The unsubstituted phenyl ring also gave target product in excellent yield (2a). The phenyl ring having weak electron withdrawing groups such as 4-chloro and 4-fluoro substituents gave their target products in 82% and 75% yields, respectively (2b and 2g). Aryl ring bearing other strong electron withdrawing substituent's nitrile and nitro couldn't give target products under optimized reaction conditions. But, very interestingly the reactions could give target product in moderate yield at higher temp 70 °C with strong base K_2CO_3 (2f and 2j). Ortho methyl group on aryl ring could give their respective target product in 70% yield (2e). Di-Me substituent on aryl ring gave final product in 80% yield (2g). Finally we have also studied about aliphatic isothiocyanates. The aliphatic substrates readily underwent the reaction to produce the target products in 83-88% yields (2l-2m).

Table.4 Substrate scope for the synthesis of aryl/alkyl cyanamides[a]

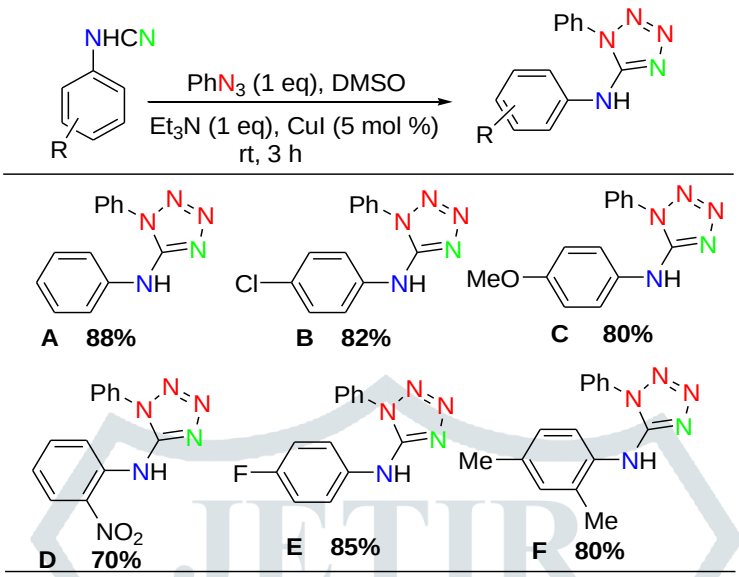


Entry	Substrate	Product	Isolated yield (%)[b]
1	 1a	 2a	95
2	 1b	 2b	82
3	 1c	 2c	97
4	 1d	 2d	94
5	 1e	 2e	70
6	 1f	 2f	78
7	 1g	 2g	85
8	 1h	 2h	40[c]
9	 1i	 2i	75
10	 1j	 2j	72[c]
11	 1k	 2k	42[c]
12	 1l	 2l	88
13	 1m	 2m	83
14	 1n	 2n	85

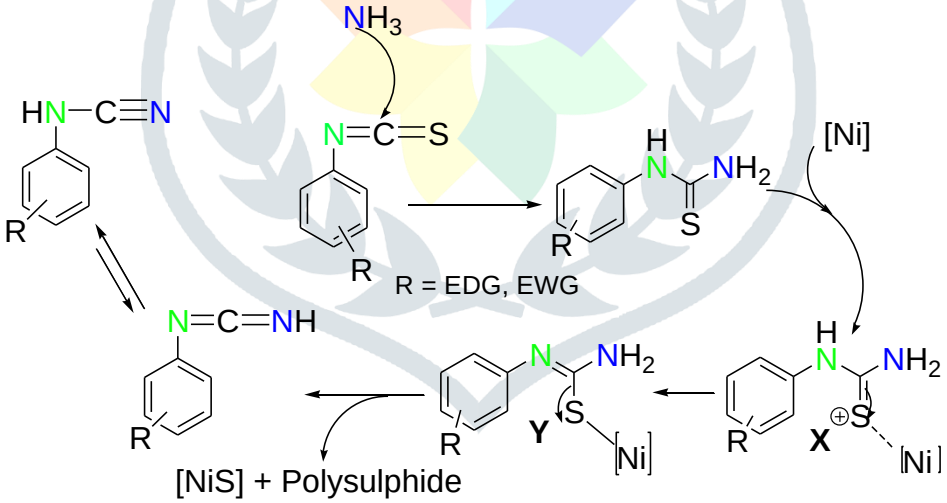
[a] Reaction conditions: Phenyl isothiocyanate (1 mmol), DMSO (2 ml), Aq NH3 (2 ml), rt, 1 h, then, $NiSO_4.6H_2O$ (25 mol %), NaOAc (1 eq), rt, 2 h. [b] Isolated yield. [c] Temp 70 °C and K_2CO_3 was used.

We extended of our work we made some substituted phenyl tetrazolamines using the click reaction under below shown reaction conditions (**Table.5**). The click reaction of cyanamides 2a, 2b, 2c, 2f, 2g and 2h with phenyl azide gave their respective target products **A-F** in moderate to good yield.

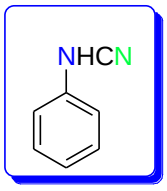
Table.5 Synthesis of phenyl tetrazolamines



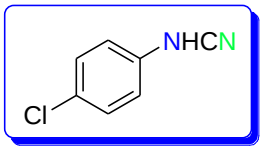
Mechanism: We proposed the mechanism of formation of aryl/alkyl cyanamides from isothiocyanantes in the above scheme. Isothiocyanate reacts with ammonia in the presence of solvent to give thiourea. Then, nickel co-ordinates to sulfur in thiourea to give intermediate **X**. Desulfurization of **X** afforded target product aryl/alkyl cyanamides via intermediate **Y** along with by product NiS and poly sulfide (the extra sulfur might have converted into sulfide) using base.



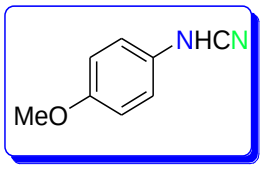
Proposed mechanism for the syntheses of cyanamides



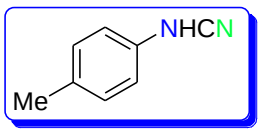
Phenylcyanamide (**2a**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.29-7.25 (m, 3H), 5.81 (1H, br. s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 130.6, 130.1, 128.9, 114.3; FT-IR (KBr) 3350, 3064, 2222, 1693, 1489, 1250, 1070, 909 cm^{-1}. Anal. Calcd. for $C_7H_6N_2$: C, 71.17; H, 5.12; N, 23.71. Found: C, 71.28; H, 5.09; N, 23.62.



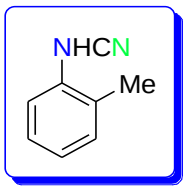
4-Chlorophenylcyanamide (**2b**): yield 82%; Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.8, 2H), 6.97-6.93 (m, 2H), 5.51 (1H, br. s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 134.5, 130.6, 129.1, 117.1; FT-IR (KBr) 3399, 3076, 2214, 1670, 1505, 1250, 1114, 1023, 959, 817 cm^{-1}. Anal. Calcd. for $C_7H_5ClN_2$: C, 55.10; H, 3.30; Cl, 23.24; N, 18.36. Found: C, 55.25; H, 3.28; N, 18.30.



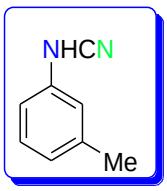
4-Methoxyphenylcyanamide(**2c**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 9.6 Hz, 2H), 5.81 (br s, 1NH), 3.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 138.6, 131.9, 127.8, 121.7, 55.4; FT-IR (KBr) 3357, 3076, 2899, 2236, 1587, 1253, 1212, 1104, 1055, 941, 808 cm^{-1}. Anal. Calcd. for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91; O, 10.80. Found: C, 64.99; H, 5.42; N, 18.85.



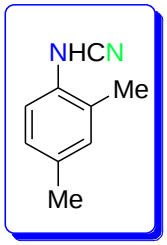
4-Methylphenylcyanamide(**2d**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.17 (m, 2H), 7.01 (d, *J* = 9.6 Hz, 2H), 5.23 (1H, br. s, 1NH), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 132.4, 128.5, 124.6, 120.0, 21.3; FT-IR (KBr) 3378, 3097, 2896, 2835, 2200, 1601, 1580, 1503, 1252, 1179, 1028, 927 cm^{-1}. Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.79; H, 6.09; N, 21.12.



***o*-Tolylcyanamide** (**2e**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.21 (m, 1H), 7.17-7.12 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.09 (br s, 1NH), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 139.6, 137.8, 134.5, 130.9, 129.9, 117.0, 20.6; FT-IR (KBr) 3412, 3074, 2867, 2223, 1690, 1435, 1379, 1229, 1125, 1036, 941, 875 cm^{-1}. Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.80; H, 6.02; N, 21.12.



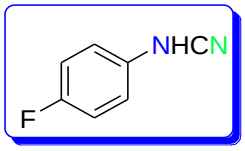
***m*-Tolylcyanamide** (**2f**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.22 (d, *J* = 8.8, 1H), 6.97-6.93 (m, 2H), 5.43 (1H, br. s, 1NH); 2.31 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 131.6, 131.3, 130.4, 120.3, 120.0, 115.4, 24.1; FT-IR (KBr) 3423, 3048, 2899, 2217, 1656, 1588, 1490, 1409, 1288, 1261, 1123, 1078, 823. Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.80; H, 6.02; N, 21.12.



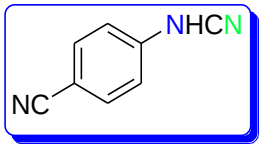
2,4-Dimethylphenylcyanamide (**2g**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.61 (1H, br. s, 1NH); 2.30 (s, 3H, CH_3); 2.26 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6,

137.8, 134.5, 130.9, 129.9, 119.9, 113.9, 20.6, 18.2; FT-IR (KBr) 3368, 3077, 2888, 2863, 2212, 1635, 1599, 1513, 1491, 1287, 1215, 1027, 823 cm^{-1}. Anal. Calcd. for $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16. Found: C, 74.02; H, 6.88; N, 19.09.

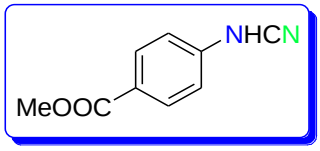
2-Nitrophenylcyanamide (**2h**): Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.5; yield 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 9.2 Hz, 2 H), 7.65 (d, *J* = 8.8 Hz, 2 H), 6.23 (1H, br. s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 141.6, 136.7, 134.0, 132.1, 120.9, 115.1; FT-IR (KBr) 3375, 3065, 2215, 1656, 1564, 1490, 1379, 1229, 1125, 1036, 941, 832 cm^{-1}. Anal. Calcd. for $C_7H_5N_3O_2$: C, 39.73; H, 3.33; N, 10.30. Found: C, 39.88; H, 3.30; N, 10.23.



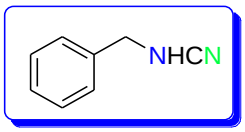
4-Fluorophenylcyanamide (**2i**): Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.6; yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 6.39 (br s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 136.5, 126.2, 120.3, 114.9; FT-IR (KBr) 3359, 3056, 2217, 1654, 1554, 1394, 1279, 1140, 939, 822 cm^{-1}. Anal. Calcd. for $C_7H_5FN_2$: C, 61.76; H, 3.70; F, 13.96; N, 20.58. Found: C, 61.92; H, 3.67; N, 13.89.



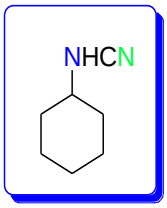
4-(Cyanoamino)benzonitrile(**2j**): Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.5; yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.34-7.31 (m, 2H), 5.29 (1H, br. s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 132.7, 128.1, 120.0, 115.6, 115.0; FT-IR (KBr) 3355, 3100, 2256, 2217, 1667, 1526, 1348, 1277, 1078, 973, 892 cm^{-1}. Anal. Calcd. for $C_8H_5N_3$: C, 67.12; H, 3.52; N, 29.35. Found: C, 67.20; H, 3.50; N, 29.29.



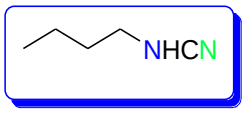
Methyl-4-(cyanoamino)benzoate (**2k**): Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.5; yield 42%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 9.6 Hz, 1H), 7.38-7.33 (m, 2H), 5.91 (br s, 1NH), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 142.8, 134.4, 130.5, 130.0, 121.7, 54.8; FT-IR (KBr) 3415, 3082, 2896, 2234, 1749, 1675, 1607, 1524, 1459, 1345, 1261, 1145, 1099, 870 cm^{-1}. Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90; O, 18.16. Found: C, 61.50; H, 4.56; N, 15.84.



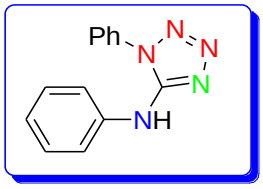
Benzylcyanamide (**2l**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.30-7.27 (m, 3H), 5.61 (1H, br. s, 1NH), 4.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 137.9, 130.3, 128.6, 118.0, 45.0; FT-IR (KBr) 3412, 3066, 2898, 2196, 1632, 1583, 1491, 1287, 1146, 1027, 826 cm^{-1}. Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.78; H, 6.08; N, 21.14.



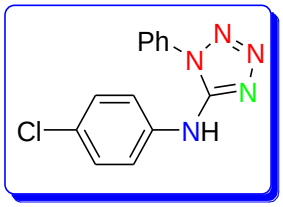
Cyclohexylcyanamide(2m): yield 83%; Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (1H, br. s, 1NH), 4.13-4.10 (m, 1H), 2.16-2.02 (m, 2H), 1.94-1.75 (m, 5H), 1.46-1.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.5, 48.5, 30.8, 25.2, 19.2;FT-IR (KBr) 3363, 3086, 2912, 2873, 2207, 1651, 1532, 1491, 1287, 1146, 1027, 828 cm^{-1}. Anal. Calcd. for $C_7H_{12}N_2$: C, 67.70; H, 9.74; N, 22.56. Found: C, 67.80; H, 9.71; N, 22.49.



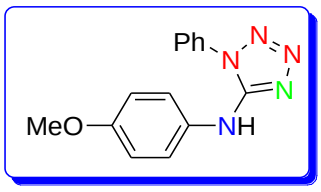
Butylcyanamide (**2n**): Analytical TLC on silica gel, 1:19 ethyl acetate/hexane R_f = 0.8; yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (1H, br. s, 1NH), 3.92 (t, *J* = 5.6 Hz, 2H) 1.73-1.60 (m, 2H), 1.35-1.21 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.4, 40.9, 30.8, 19.1, 14.2; FT-IR (KBr) 3423, 3097, 2911, 2883, 2205, 1631, 1567, 1491, 1287, 1027, 808 cm^{-1}. Anal. Calcd. for $C_5H_{10}N_2$: C, 61.19; H, 10.27; N, 28.54. Found: C, 61.30; H, 10.24; N, 28.46.



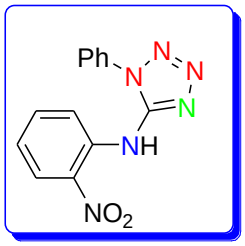
***N*,1-Diphenyl-1*H*-tetrazol-5-amine (A)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.41 (m, 7H), 6.85 (d, *J* = 8.8 Hz, 3H), 6.02 (br s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 132.8, 131.6, 129.2, 128.5, 128.1, 121.5, 120.9, 117.6; FT-IR (KBr) 3426, 3097, 1645, 1631, 1567, 1512, 1491, 1287, 1250, 1146, 1027, 896 cm^{-1}. Anal. Calcd. for $C_{13}H_{11}N_5$: C, 65.81; H, 4.67; N, 29.52. Found: C, 65.90; H, 4.65; N, 29.45.



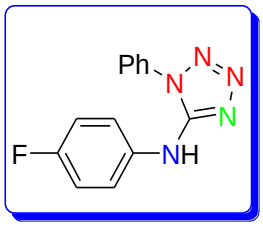
***N*-(4-Chlorophenyl)-1-phenyl-1*H*-tetrazol-5-amine (B)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.48 (m, 4H), 7.25 (d, *J* = 6.8 Hz, 3H), 7.16 (d, *J* = 8.8 Hz, 2H), 5.96 (br s, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 137.0, 132.3, 128.3, 128.1, 127.8, 127.0, 124.7, 118.1; FT-IR (KBr) 3420, 3090, 1645, 1601, 1590, 1489, 1125, 1036, 941, 854, 788, 612 cm^{-1}. Anal. Calcd. for $C_{13}H_{10}ClN_5$: C, 57.47; H, 3.71; Cl, 13.05; N, 25.78. Found: C, 57.62; H, 3.69; N, 25.72.



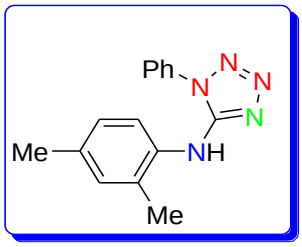
***N*-(4-Methoxyphenyl)-1-phenyl-1*H*-tetrazol-5-amine (C)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 2H), 7.54-7.47 (m, 5H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.02 (br s, 1NH), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 142.9, 133.7, 132.6, 129.7, 129.5, 129.3, 126.1, 121.4, 55.0; FT-IR (KBr) 3426, 3082, 2900, 1657, 1612, 1586, 1514, 1448, 1325, 1216, 1145, 1099, 829 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}N_5O$: C, 62.91; H, 4.90; N, 26.20; O, 5.99. Found: C, 63.05; H, 4.88; N, 26.14.



***N*-(2-Nitrophenyl)-1-phenyl-1*H*-tetrazol-5-amine (D)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (br s, 1NH), 8.09-8.06 (m, 2H), 8.05-7.76 (m, 2H), 7.74 (d, *J* = 2Hz, 2H), 7.05 (d, *J* = 7.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 146.3, 143.8, 141.8, 137.3, 129.6, 127.1, 125.6, 121.0, 120.7, 118.0; FT-IR (KBr) 3417, 3087, 1667, 1654, 1612, 1567, 1521, 1458, 1394, 1332, 1265, 1104, 1080, 941 cm^{-1}. Anal. Calcd. for $C_{13}H_{10}N_6O_2$: C, 55.32; H, 3.57; N, 29.77; O, 11.34. Found: C, 55.49; H, 3.53; N, 29.70.



***N*-(4-Fluorophenyl)-1-phenyl-1*H*-tetrazol-5-amine (E)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.33 (m, 7H), 7.12 (d, *J* = 8 Hz, 2H), 5.98 (br s, 1H, 1NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 142.1, 134.7, 133.0, 128.6, 128.5, 120.6, 119.3, 114.3,114.0; FT-IR (KBr) 3389, 3088, 1693, 1612, 1543, 1489, 1421, 1400, 1239, 1121, 1070, 927, cm^{-1}. Anal. Calcd. for $C_{13}H_{10}FN_5$: C, 61.17; H, 3.95; F, 7.44; N, 27.44. Found: C, 61.32; H, 3.93; N, 27.37.



***N*-(2,4-Dimethylphenyl)-1-phenyl-1*H*-tetrazol-5-amine (F)**: Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.7; yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.27 (m, 5H), 7.09 (s, 1H), 6.84 (d, *J* = 7.2 Hz, 2H), 5.90 (br s, 1H, 1NH), 2.47 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 135.3, 134.8, 134.1, 133.2, 131.4, 130.0, 129.9, 127.1, 125.5, 121.4, 21.0, 20.9; FT-IR (KBr) 3424, 3054, 2896, 2855, 1651, 1602, 1580, 1503, 1358, 1252, 1179, 1056, 1028, 898 cm^{-1}. Anal. Calcd. for $C_8H_6Br_2N_2O$: C, 31.41; H, 1.98; N, 9.16; Found: C, 31.55; H, 1.96; N, 9.10.

IV. Acknowledgment

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