J. Chem. Sci. Vol. 125, No. 1, January 2013, pp. 153–157.

Nano indium oxide as a recyclable catalyst for the synthesis of arylaminotetrazoles

SIAVASH BAHARI* and MEHDI AHMADI SABEGH

Department of Chemistry, Ahar Branch, Islamic Azad University, Ahar, 5451116714, Iran
e-mail: siavashbahari89@gmail.com; s-bahari@iau-ahar.ac.ir

MS received 18 February 2012; revised 17 May 2012; accepted 18 June 2012

Abstract. Nano indium oxide is an effective heterogeneous catalyst for the reaction between aryl cyanamides and sodium azide to synthesize the arylaminotetrazoles in good yields. This method has advantages of high yields, simple methodology, short reaction times and easy work-up. The catalyst can be recovered and reused in good yields.

Keywords. Arylaminotetrazole; aryl cyanamides; nano indium oxide; reusable catalyst.

1. Introduction

Despite the scarcity of tetrazoles in natural systems, the chemistry of this heterocycle has gained increasing attention since the early 1980s. Tetrazoles have a wide range of applications as lipophilic spacers and carboxylic acid surrogates in pharmaceuticals, as special explosives and information recording systems in materials, as ligands in coordination chemistry and as precursors to a variety of nitrogen-containing compounds.[1–8]

The conventional method of synthesizing tetrazoles is by addition of azide ions to organic nitriles or cyanamides.[9–14] Earlier reported methods for the synthesis of arylaminotetrazoles suffer from drawbacks such as poor yield, long reaction times, harsh reaction conditions; difficulty of obtaining and/or starting materials preparation, tedious work-up, the use of expensive and toxic metal reagents, and the *in situ*-generated hydrazoic acid, which is highly toxic and explosive.[15–19] On the other hand, in most cases only the 1-aryl-5-amino-1*H*-tetrazoles were obtained.

Nasrollahzadeh and co-workers have shown that cyanamides may be converted to arylaminotetrazoles using $FeCl_3$–SiO_2 as a heterogeneous catalyst which often result in a mixture of isomers 5-arylamino-1*H*-tetrazoles (isomer **A**) and 1-aryl-5-amino-1*H*-tetrazoles (isomer **B**) (scheme 1).[20]

Several syntheses of arylaminotetrazoles have been reported through the [2+3] cycloaddition of cyanamides using NaN_3 in the presence of catalysts such as natrolite zeolite (local zeolite)[21] and $ZnCl_2$.[22] The development of a catalytic synthetic method for tetrazoles still remains an active research area.

In recent years there has been a tremendous interest in various chemical transformations performed under the heterogeneous catalysis. Among heterogeneous catalysts, metal nanoparticles have been used widely as efficient catalysts in organic reactions due to their high catalytic activity, ease of handling, reusability, and benign character.[23–28] Indium (III) compounds are mild and water-tolerant Lewis acids and show high regio-, stereo-, and chemoselectivity.[29–33] However, until now the use of nano In_2O_3 as a catalyst is limited in organic synthesis.[34]

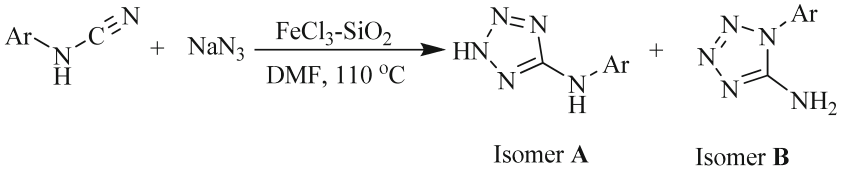
Here, we describe an efficient method for the preparation of arylaminotetrazoles using nano In_2O_3 as a heterogeneous catalyst (scheme 2).

2. Experimental

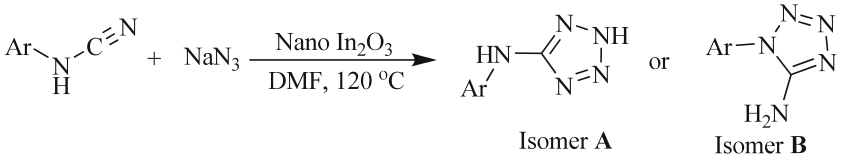
2.1 *General*

All reagents were purchased from Merck and Aldrich chemical companies and used without further purification. Products were characterized by FT-IR, ^{1}H NMR and ^{13}C NMR, elemental analysis (CHN), and melting points. ^{1}H NMR spectra were recorded on Bruker Avance DRX 250, 300 and 500 MHz instruments. NMR spectra were recorded in $CDCl_3$, DMSO-d_6 and acetone-d_6. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) as internal standard. J values are given in Hz. ^{13}C NMR spectra were recorded at 125 and 75 MHz. FT-IR (KBr) spectra

*For correspondence



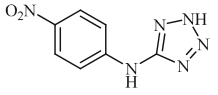
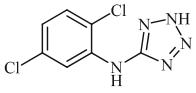
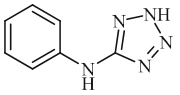
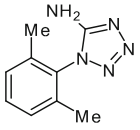
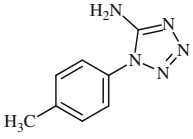
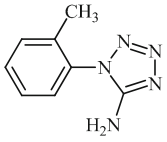
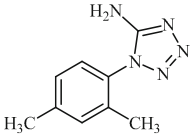
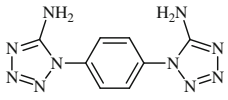
Scheme 1. Synthesis of arylaminotetrazoles by the $FeCl_3$–SiO_2.



Scheme 2. Synthesis of arylaminotetrazoles by the nano In_2O_3.

were recorded on PerkinElmer 781 spectrophotometers. Melting points were obtained on a Reichert 7905 hot-stage microscope or an Electrothermal IA9000 capillary apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed on silica gel polygram SIL G/UV 254 plates.

Table 1. Synthesis of arylaminotetrazoles (**3**) via secondary aryl cyanamides (**1**) catalysed by nano In_2O_3.

Entry	Ar	Product	**3** (**A** or **B**)	Time (min)	Yield[a]%	m.p.(°) [lit. mp[ref]]
1	4-NO_2-C_6H_4		**3a** (**A**)	110	81	218–220 [218–220[21]]
2	2,5-$(Cl)_2$-C_6H_3		**3b** (**A**)	110	80	272–274 [273–274[21]]
3	C_6H_5		**3c** (**A**)	100	82	214–215 [215–217[21]]
4	2,6-$(Me)_2$-C_6H_3		**3d** (**B**)	60	86	148–150 [147–149[22b]]
5	4-Me-C_6H_4		**3e** (**B**)	60	80	177–178 [175.5–177[16]]
6	2-Me-C_6H_4		**3f** (**B**)	60	84	191–192 [191–192[21]]
7	2,4-$(Me)_2$-C_6H_3		**3g** (**B**)	60	83	199–201 [199–201[21]]
8	1,4-C_6H_4		**3h** (**B**)	55	84	220–221 [220–221[14c]]

[a]Yield refers to pure isolated products

2.2 *General procedure for the synthesis of arylaminotetrazoles*

Nano In_2O_3 (0.1 g) was added to a mixture of cyanamides (**1a–h**) (2 mmol), NaN_3 (0.2 g, 3 mmol) in distilled dimethylformamide (5 mL) and stirred at 120°C for the appropriate time (table 1). After completion of the reaction (as monitored by TLC), the catalyst was centrifuged, washed with ethyl acetate and the centrifugate was treated with ethyl acetate (35 mL) and 5 N HCl (20 mL). The resultant organic layer was separated and the aqueous layer was again extracted with ethyl acetate (20 mL). The combined organic layers were washed with water, concentrated, and washed with ethanol to give different arylaminotetrazoles. The physical data (mp, IR, NMR) of known compounds were found to be identical to those reported in the literature.[21,22]

5-Arylamino-1*H*-tetrazoles isomers (**A**) contain two NH bonds (NH of the amine attached to the aryl group (NH^A) and NH of the tetrazole ring (NH^T)) and 1-aryl-5-amino-1*H*-tetrazoles isomers (**B**) contain a NH_2 bond. The disappearance of one strong and sharp absorption band (CN stretching band) and the appearance of a NH stretching band in the IR spectra provided clear evidence for the formation of arylaminotetrazoles. ^{13}C NMR spectra displayed signals at δ = 154–157.5 ppm, indicative of C5 in the tetrazole ring.[21,22]

2.2a *1-(2,6-Dimethylphenyl)-5-amino-1H-tetrazole* (**3d**): M.P. 148–150°; FT-IR (KBr): 3441, 3383, 3351, 2952, 2921, 1697, 1651, 1604, 1583, 1558, 1526, 1486, 1442, 1247, 1228, 1194, 1168, 1032, 987, 938, 780 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6, δ / ppm): 1.92 (6H, s), 6.67 (2H, s), 7.30 (d, J = 7.7 Hz, 2H), 7.42 (t, J = 7.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): 16.8, 125.2, 128.3, 135.9, 136.0, 155.2; Anal. Calcd for $C_9H_{11}N_5$: C, 57.12; H, 5.86; N, 37.02. Found: C, 57.19; H, 5.91; N, 37.09.

3. Results and discussion

The cyanamides were prepared according to the literature.[14b] The general synthetic method is depicted in scheme 1. Arylaminotetrazoles were obtained from the reaction of cyanamides with sodium azide in the presence of nano In_2O_3 as an efficient heterogeneous catalyst at 120° for the appropriate time in good yields (table 1).

To show the advantages of nano In_2O_3, its reaction was compared with $FeCl_3$–SiO_2, glacial HOAc, $ZnCl_2$ and Natrolite zeolite in the synthesis of 5-(2,5-dichlorophenyl)amino-1*H*-tetrazole (**3c**). As shown in table 2, nano In_2O_3 is an effective catalyst since the products are regiospecific, whereas with $FeCl_3$–SiO_2 and glacial HOAc, a mixture of isomers will be produced. $ZnCl_2$[22] is homogeneous which cannot be separated from the reaction mixture, while nano In_2O_3 is heterogeneous and can easily be recovered and reused. Natrolite zeolite[21] is a good catalyst, but there are difficulties in the preparation and availability of catalyst. Not many organic solvents are suitable for the cycloaddition reactions which usually need high temperatures (sometimes as high as 130°), and so DMF is a most commonly used solvent for this purpose.[2,20,21] The optimum amount of nano In_2O_3 was found to be 0.1 g in the presence of cyanamide (2 mmol) and sodium azide (3 mmol) in DMF (6 mL). We have also examined a variety of structurally divergent phenylcyanamide possessing a wide range of functional groups to understand the scope and generality of nano In_2O_3-promoted

Table 2. Comparison of nano In_2O_3 activity with other reagents in the synthesis of arylaminotetrazoles.

Entry	Catalyst	Solvent	Time (min)	Yield[a]%	Product (**A** or **B**)
1	$FeCl_3$-SiO_2 (0.1 g)	DMF[b]	120	76	**A**+**B**
2	Glacial HOAc (3 mL)	Glacial HOAc[c]	30 h[d]	72	**A**+**B**
3	$ZnCl_2$ (0.4 g)	H_2O[e]	15 h	84	**A**
4	Natrolite zeolite (0.1 g)	H_2O[e]	9 h	49	**A**
5	Natrolite zeolite (0.1 g)	DMF[f]	95	81	**A**
6	Nano In_2O_3 (0.05 g)	DMF	120	69	**A**
7	Nano In_2O_3 (0.07 g)	DMF	120	73	**A**
8	Nano In_2O_3 (0.10 g)	DMF	120	80	**A**
9	Nano In_2O_3 (0.10 g)	DMSO	120	80	**A**
10	Nano In_2O_3 (0.15 g)	DMF	120	81	**A**

[a]Isolated yield. [b]Under thermal conditions at 110°. [c]Glacial acetic acid as both solvent and proton source. [d]Room temperature. [e]Under reflux conditions. [f]Under thermal conditions at 110–115°

cycloaddition reaction to form arylaminotetrazoles and the results are summarized in table 1.

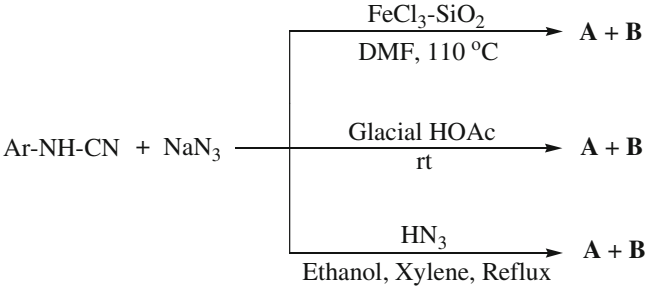
The products were completely regiospecific. This observation is in contrast with those reports that the other reagents will often produce a mixture of isomers (scheme 3).

As shown in table 1, cyanamides having methyl as an electron releasing group (entries 4–7) were completed at 120° after 60 min, while the species bearing the electron withdrawing groups NO_2 or Cl (entries 1–2) require higher reaction times.

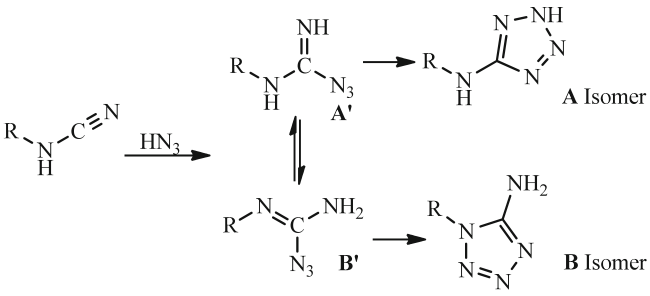
The influences of various substituents in different *ortho*, *meta* or *para* positions on the type of products were examined. Generally, when the substituent on the aryl ring of **1** is electron-releasing, formation of 1-aryl-5-amino-1*H*-tetrazoles (**B**) is favoured via the guanidine azide intermediate **B′** (table 1, entries 4, 5, 6 and 7), while with electron-withdrawing substituents the product is shifted toward the formation of 5-arylamino-1*H*-tetrazoles (**A**) via the guanidine azide intermediate **A′** (table 1, entries 1 and 2). In the earlier research carried out, the nature of the substituent did not have any effect.[15–17,35–37] In the previously reported methods, substituents as different in their electrical effects as the methyl group and the *p*-nitrophenyl group permit the formation of the same type of compound (isomer **B**).[17] No clear explanation was given by the previous workers about the isolation or detection of other isomers, although Stolle and Heintz reported the isolation of 5-anilinotetrazole in low yield from the reaction of phenylthiourea with lead oxide and sodium azide.[38] In other words, in the synthesis of aminotetrazoles from cyanamides, only the 1-aryl-5-amino-1*H*-tetrazole (**B**) or a mixture of isomers (**A** + **B**) was obtained (scheme 4).[13,20]

Due to the presence of two CN groups, **1 h** (table 1, entry 8) interestingly afforded the double-addition product.

4-Nitrophenylcyanamide interestingly gave 5-(4-nitrophenyl)amino-1*H*-tetrazole (isomer **A**), while with



Scheme 3. Synthesis of arylaminotetrazoles under different conditions.



Scheme 4. Synthesis of arylaminotetrazoles by the hydrazoic acid.

HN_3, $FeCl_3$-SiO_2 and glacial HOAc, 1-(4-nitrophenyl)-5-amino-1*H*-tetrazole (isomer **B**) or a mixture of isomers (**A** + **B**) was obtained.

The mechanism of the catalysis may originate from the nitrile group coordinating with the surface of the solid acid. The solid acid is supposed to activate the nitriles and enhance their reactivity with sodium azide. However, further experiments are necessary to gain a clearer insight into these reactions.

The catalyst recycling is an important step as it reduces the cost of the process. Nano In_2O_3 was recovered quantitatively by simple centrifugation and reused for three cycles with consistent activity. This reusability demonstrates the high stability and turnover of nano In_2O_3 under operating conditions.

4. Conclusion

We have developed a simple and efficient method for the synthesis of arylaminotetrazoles by treatment of cyanamides with sodium azide in the presence of nano In_2O_3 as an effective heterogeneous catalyst. The significant advantages of this methodology are high yields, elimination of dangerous and harmful hydrazoic acid, a simple work-up procedure, and easy preparation and handling of the catalyst. The catalyst can be recovered by filtration and reused.

Acknowledgements

We are thankful to the Islamic Azad University, Ahar Branch for partial financial support to carry out this research work.

References

1. Bulter R N 1996 In: *Comprehensive heterocyclic chemistry II*; A R Katritzky, C W Ress and E F V Scriven (eds) New York: Pergamon **4** 621
2. Herr R 2002 *J. Bioorg. Med. Chem.* **10** 3379
3. Holland G F and Pereira J N 1967 *J. Med. Chem.* **10** 149

4. Figdor S K and Schach von Wittenau M 1967 *J. Med. Chem.* **10** 1158
5. Rhonnstad P and Wensbo D 2002 *Tetrahedron Lett.* **43** 3137
6. Klapötke T M, Stierstorfer J and Weber B 2009 *Inorg. Chim. Acta* **362** 2311
7. John E O, Kirchmeier R L and Shreeve J M 1989 *Inorg. Chem.* **28** 4629
8. Modarresi-Alam A R, Khamooshi F, Rostamizadeh M, Keykha H, Nasrollahzadeh M, Bijanzadeh H R and Kleinpeter E 2007 *J. Mol. Struc.* **841** 61
9. Kadaba P K 1973 *Synthesis* **71**
10. Wittenberger S J 1994 *Org. Prep. Proc. Int.* **26** 499
11. Curran D P, Hadida S and Kim S Y, 1999 *Tetrahedron* **55** 8997
12. Huff B E and Staszak M A 1993 *Tetrahedron Lett.* **34** 8011
13. Modarresi-Alam A R and Nasrollahzadeh M 2009 *Turk. J. Chem.* **33** 267
14. (a) Nasrollahzadeh M, Bayat Y, Habibi D and Moshaee S 2009 *Tetrahedron Lett.* **50** 4435; (b) Habibi D and Nasrollahzadeh M 2012 *Monatsh Chem.* **143** 925; (c) Habibi D, Nasrollahzadeh M, Bayat Y 2011 *Synth. Commun.* **41** 2135; (d) Habibi D, Nasrollahzadeh M, Kamali T A 2011 *Green Chem.* **13** 3499; (e) Habibi D and Nasrollahzadeh M 2012 *Synth. Commun.* **42** 2023
15. Finnegan W G, Henry R A and Lieber E 1953 *J. Org. Chem.* **18** 779
16. Henry R A, Finnegan W G and Lieber E 1954 *J. Am. Chem. Soc.* **76** 88
17. Garbrecht W L and Herbst R M 1953 *J. Org. Chem.* **18** 1014
18. M S Congreve 1996 *Synlett.* 359
19. Vorobiev A N, Gaponik P N, Petrov P T, Vestsi Nats. Akad. Navuk Belarusi, Ser. Khim. Navuk; 2003, No. 2, 50, 2004 *Chem. Abstr.* **140** 16784g
20. Habibi D and Nasrollahzadeh M 2010 *Synth. Commun.* **40** 3159
21. Nasrollahzadeh M, Habibi D, Shahkarami Z and Bayat Y 2009 *Tetrahedron* **51** 10715
22. (a) Habibi D, Nasrollahzadeh M, Faraji A R and Bayat Y 2010 *Tetrahedron* **66** 3866; (b) Habibi D, Nasrollahzadeh M, Sahebekhtiari H and Sajadi S M 2012 *Synlett* **23** 2795
23. (a) Mohammadi B, Hosseini Jamkarani S M, Kamali T A, Nasrollahzadeh M, Mohajeri A 2010 *Turk. J. Chem.* **34** 613; (b) Modarresi-Alam A R, Nasrollahzadeh M, Khamooshi F 2007 *Arkivoc* **xvi** 234; (c) Modarresi-Alam A R, Khamooshi F, Nasrollahzadeh M, Amirazizi H A 2007 *Tetrahedron* **63** 8723; (d) Modarresi-Alam A R, Nasrollahzadeh M, Khamooshi F 2008 *Sci. Iran*. **15** 452; (e) Modarresi-Alam A R, Khamooshi F, Nasrollahzadeh M, Amirazizi H A 2008 *Tetrahedron* **64** 4656; (f) Habibi D, Heydari S and Nasrollahzadeh M 2012 *J. Chem. Res*. **36** 573; (g) Habibi D, Nasrollahzadeh M, Mehrabi L and Mostafaee S 2012 *Monatsh fur Chem*. doi:10.1007/s00706-012-0871-9; (h) Habibi D, Nabavi H, Nasrollahzadeh M 2013 *J. Chem.* Article ID 645313; (i) Bahari S, Mohammadi-Aghdam B, Molaei R, Gharibi Z 2012 *Can. J. Chem*. **90** 784; (j) Bahari S, Mohammadi-Aghdam B, Sajadi S M, Zeidali F 2012 *Bull. Korean Chem. Soc*. **33** 2251
24. (a) Astruc D, Lu F and Aranzaes J R 2005 *Angew. Chem., Int. Ed.* **44** 7852; (b) Polshettiwar V, Baruwati B and Varma R S 2009, *Green Chem.* **11** 127
25. Adak L, Chattopadhyay K and Ranu B C 2009 *J. Org. Chem.* **74** 3982
26. Dey R, Chattopadhyay K and Ranu B C 2008 *J. Org. Chem.* **73** 9461
27. Jammi S, Sakthivel S, Rout T, Mandal S, Mitra R, Saha P and Punniyamurthy T 2009 *J. Org. Chem.* **74** 1971
28. Zhang W, Zhang X, Tian Y, Yue Y, Guo Y and Wang Z 2011 *J. Org. Chem.* **76** 4741
29. Ghosh R and Maiti S 2007 *J. Mol. Catal. A: Chem.* **264** 1
30. Nair V, Ros S, Jayan C N and Pillai B S 2004 *Tetrahedron* **60** 1959
31. Kundu D, Majee A and Hajra A 2009 *Tetrahedron Lett.* **50** 2668
32. Ranu B C, Dey S S and Hajra A 2002 *Tetrahedron* **58** 2529
33. Ranu B C, Hajra A and Jana U 2002 *Tetrahedron Lett.* **41** 531
34. Reddy V P, Kumar A V, Swapna K and Rao K R 2009 *Org. Lett.* **11** 1697
35. Henry R A, Finneganand W G and Lieber E 1955 *J. Am. Chem. Soc.* **77** 2264
36. Garbrecht W L and Herbst R M 1953 *J. Org. Chem.* **18** 1003
37. Garbrecht W L and Herbst R M 1953 *J. Org. Chem.* **18** 1022
38. Stolle R and Heintz K 1937 *J. Prakt. Chem.* **147** 286