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Synthesis of 1,2,4-triazothiazine using the reaction of hydrazines using KF/CP NPs Condition

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Abstract: An efficient synthesis of 1,2,4-triazole via reaction between potassium thiocyanate, acid chlorides, arylhydrazines and activated acetylenic compounds in the presence of catalytic amounts of KF/CP NPs is described.

Keywords: Acid chloride; Arylhydrazine; Triazole; Potassium thiocyanate; Three-component reaction.

Introduction

1,2,4-Triazoles are of biological interest[1] and as a consequence, a number of synthetic methods have been developed to construct this ring system [2-4]. To date, there have been no viable one-pot convergent syntheses reported. However, annulation reactions of suitably substituted acyclic precursors represent an attractive alternative methodology, which may allow direct regioselective preparation of the target molecule. Recently, several new methods have been developed which illustrate the utility of the last approach [5-8]. Employing suitable catalyst increases the way to green chemistry. In the presence of nanocatalyst, some organic reactions have excellent yields and selectivity of product than to usual sized. Among heterogeneous catalysts, zeolites have been reported as a new class of promising support and catalysts for the development of environmentally friendly acidic catalysts. Due to its higher thermal and hydrothermal stability, zeolite has recently been garnering interest as a novel support. Recently, using potassium fluoride supported on zeolites such as clinoptilolite (CP) as new natural and cheap zeolite is very interesting. In this research investigation of antioxidant ability for some of the synthesized compounds is performed. Frequently compounds with antioxidant ability, eliminate the negative property of free radicals and utilize as transitional metals chelators. This result is due to their reducing properties and chemical structure. Also, these compounds could be avoid or decrease many sicknesses such as cardiovascular, inflammatory bowel syndrome, cancer, ageing, and alzheimer. As part of our current studies on the development of new routes in organic synthesis [9-12], we report an efficient synthesis of functionalized 1,2,4-triazoles, employing readily available starting materials. Thus, reaction of potassium isothiocyanate **1,** acid chlorides **2**, arylhydrazines **3** and activated acetylenic compounds in the presence of KF/CP NPs in water led to triazoles **5** in good yields (Scheme **1**).

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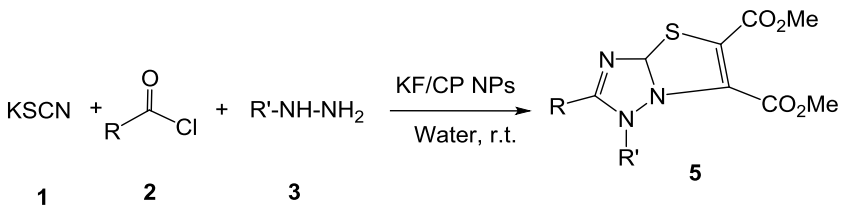
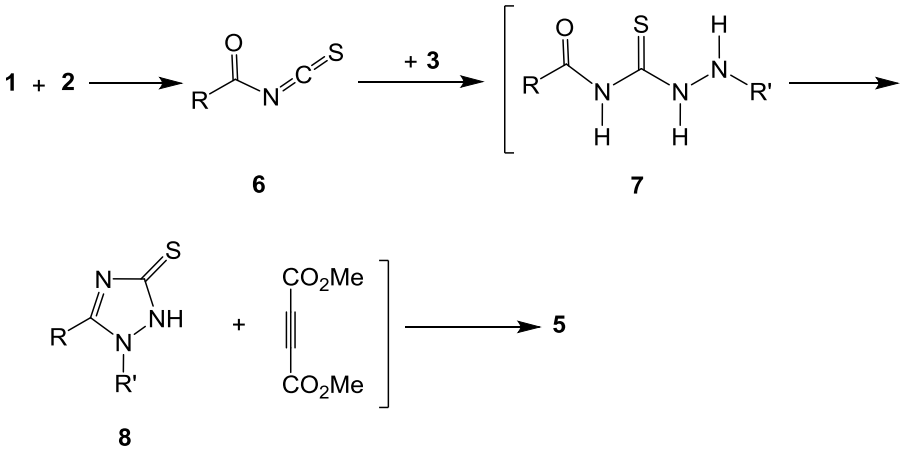


2, 3, 5	R	R'	Yield/ % of 5
a	Ph	Ph	75
b	*p*-NO_2-C_6H_4	Ph	70
c	*p*-Me-C_6H_4	Ph	65
d	Ph	2,4-$(NO_2)_2$-C_6H_3	58
e	*p*-Me-C_6H_4	2,4-$(NO_2)_2$-C_6H_3	63
f	*p*-Br-C_6H_4	2,4-$(NO_2)_2$-C_6H_3	73

Scheme 1: Synthesis of 1,2,4-triazoles

Structures of compounds **5a**–**f** were assigned by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. For example, the ^{1}H NMR spectrum of **5a** exhibited characteristic multipletes for the aromatic protons together with a singlet at δ = 14.26 ppm for NH groups. The ^{13}C NMR spectrum of **5a** showed the thiocarbonyl resonance at δ = 166.8 pm. The mass spectrum of **5a** displayed the molecular ion peak at *m*/*z* = 263. A tentative mechanism for this transformation is proposed in Scheme **2**. The reaction starts with formation of isothiocyanate **6** followed by addition of arylhydrazine **3** to generate **7**. Subsequent cyclization of intermediate **7** generates **8**, which is react with activated acetylenic compounds and converted into **5** by elimination of water.



Scheme 2: Proposed mechanism for the formation of **5**

In conclusion, the reaction of acid chlorides with ammonium isothiocyanate, arylhydrazines and activated acetylenic compounds in water led to 1, 2,4-triazoles in good yields. The present procedure has the advantage that the reaction is performed under neutral conditions, and the starting material can be used without any activation or modification.

Experimental

Ammonium isothiocyanate, acid chlorides, activated acetylenic compounds and arylhydrazines were obtained from Merck and were used without further purification. M.p.: Electrothermal-9100 apparatus; uncorrected. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra: Bruker DRX-500 AVANCE instrument; in DMSO at 500.1 and 125.7 MHz, respectively; δ in ppm, J in Hz. EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer, in *m/z*. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

General Procedure for the Preparation of Compounds 5.

A mixture of amonium isothiocyanate (2 mmol) and acid chloride (2 mmol) was warmed for five min. Then, arylhydrazine was added gently. The reaction mixture was stirred for 3 h at r.t. in water. After this DMAD (2 mmol) was added to mixture and mixed 1 h. The resulting precipitate was separated by filtration to afford compounds **5a-f**.

1,5-Diphenyl-1,2-dihydro-3H-1,2,4-triazole-3-thione (5a)

Cream powder, mp 255-257°, yield: (75%). IR (KBr): 3045, 1587, 1552, 1487, 1466, 1251. ^{1}H-NMR: 7.43 (1 H, *t*, ^3J = 7.4, CH), 7.52-7.57 (5 H, *m*, 5 CH), 7.99-8.00 (2 H, *m*, 2 CH), 8.02 (2 H, *d*, ^3J = 7.8, 2 CH), 14.26 (1 H, *s*, NH). ^{13}C-NMR: 123.8 (2 CH), 124.7 (C), 126.0 (2 CH), 127.7 (CH), 128.6 (2 CH), 129.1 (2 CH), 131.0 (CH), 137.7 (C), 149.2 (C), 166.3 (C=S).
EI-MS: 253 (M^+, 30); 167 (65); 149 (100); 146 (54), 104 (75), 77 (65); 45 (94). Anal. Calcd for $C_{14}H_{11}N_3S$ (253.32): C, 66.38; H, 4.38; N, 16.59; found: C, 65.82; H, 4.44; N, 16.39%.

5-(4-Nitropheny1)-1-phenyl-1,2-dihydro-3H-1,2,4-triazole-3-thione (5b)

Yellow powder, mp 276-278°, yield: (70%). IR (KBr): 3050, 1586, 1551, 1487, 1465, 1426, 1251. ^{1}H-NMR: 7.44 (1 H, *t*, ^3J = 7.4, CH), 7.54 (2 H, *t*, ^3J = 7.6, 2 CH), 8.00 (2 H, *d*, ^3J = 7.9, 2 CH), 8.22 (2 H, *d*, ^3J = 8.8, 2 CH), 8.36 (2 H, *d*, ^3J = 8.8, 2 CH),14.56 (1 H, *s*, NH). ^{13}C-NMR: 123.9 (2 CH), 124.2 (2 CH), 127.2 (2 CH), 128.0 (CH), 128.6 (2 CH), 130.6.1 (C), 137.5 (C), 147.6 (C), 148.5 (C), 166.9 (C=S). EI-MS: 298 (M^+, 15); 207 (100); 149 (54); 123 (64), 106 (78); 45 (44). Anal. Calcd for $C_{14}H_{10}N_4O_2S$ (298.31): C, 56.37; H, 3.38; N, 18.78; found: C, 55.88; H, 3.32; N, 18.90%.

5-(4-Methylpheny1)-1-phenyl-1,2-dihydro-3H-1,2,4-triazole-3-thione (5c)

Cream powder, mp 264-266°, yield: (65%). IR (KBr): 3030, 1591, 1514, 1489, 1463, 1344, 1248. ^{1}H-NMR: 2.40 (3 H, *s*, 3 CH), 7.29 (2 H, *d*, ^3J = 7.9, 2 CH), 7.41 (1 H, *t*, ^3J = 7.1, 1 CH), 7.51 (2 H, *t*, ^3J = 7.1, 2 CH), 7.75 (2 H, *d*, ^3J = 8.2, 2 CH), 8.05 (2 H, *d*, ^3J = 8.2, 2 CH), 14.60 (1 H, *s*, NH). ^{13}C-NMR: 20.9 (CH_3), 122.3 (C), 123.7 (2 CH), 125.9 (2 CH), 127.6 (C), 128.5 (2 CH), 129.6 (2 CH), 137.8 (C), 140.9 (C), 149.6 (C), 166.3 (C=S). EI-MS: 267 (M^+, 10); 106 (55); 176 (76); 149 (48); 117 (100); 91 (84), 92 (45) 45 (34). Anal. Calcd for $C_{15}H_{13}N_3S$ (267.35): C, 67.39; H, 4.90; N, 15.72; found: C, C, 67.22; H, 4.75; N, 5.81 %.

1-(2,4-Dinitrophenyl)-5-phenyl-1,2-dihydro-3H-1,2,4-triazole-3-thione (5d)

Yellow powder, mp 240-242°, yield: (58%). IR (KBr): 3043, 1582, 1554, 1398, 1466, 1251. ^{1}H-NMR: 7.45-7.55 (3 H, *m*, 3 CH), 7.61 (2 H, *t*, ^3J = 7.6, 2 CH), 8.28 (2 H, *d*, ^3J = 7.8, 2 CH), 9.08 (1 H, *s*, CH), 11.12 (1 H, *s*, NH). ^{13}C-NMR: 123.5 (CH), 127.3 (CH), 128.6 (2 CH), 129.0 (C), 130.3 (2 CH), 131.8 (CH), 134.4 (CH), 137.8 (C), 146.9 (C), 155.1 (C), 167.0 (C=S). EI-MS: 343 (M^+, 20); 240 (52); 196 (100); 176 (54); 167 (60); 103 (64), 45 (74). Anal. Calcd for $C_{14}H_9N_5O_4S$ (343.32): C, 48.98; H, 2.64; N, 20.40; found: C, 48.95; H, 2.63; N, 20.39%.

1-(2,4-Dinitrophenyl)-5-(4-methylphenyl)-1,2-dihydro-3H-1,2,4-triazole-3-thione (5e)

Yellow powder, mp 254-256°C, yield: (63%). IR (KBr): 3039, 1582, 1549, 1475, 1454, 1248. ^{1}H-NMR: 2.39 (3 H, *s*, Me), 7.30 (1 H, *d*, ^3J = 8.2, CH), 7.34 (2 H, *d*, ^3J = 8.2, 2 CH), 7.91 (2 H, *d*, ^3J = 8.2, 2 CH), 8.35 (1 H, *d*, ^3J = 8.2, CH), 8.89 (1 H, *s*, CH), 11.69 (1 H, *s*, NH). ^{13}C-NMR: 21.0 (Me), 116.1 (CH), 122.9 (CH), 128.7 (C), 128.9 (2 CH), 129.6 (2 CH), 129.9 (C), 130.0 (C), 134.2 (CH), 137.2 (C), 143.6 (C), 146.9 (C), 166.8 (C=S). EI-MS: 357 (M^+,

15); 240 (72); 177 (89); 161 (56); 117 (100); 176 (54); 45 (54). Anal. Calcd for $C_{15}H_{11}N_5O_4S$ (357.34): C, 50.42; H, 3.10; N, 19.60; found: C, 50.40; H, 3.10; N, 19.60%.

1-(2,4-Dinitrophenyl)-5-(4-bromophenyl)-1,2-dihydro-3H-1,2,4-triazole-3-thione (5f)

Yellow powder, mp 232-234°, yield: (73%). IR (KBr): 3041, 1579, 1547, 1480, 1454, 1250. ^{1}H-NMR: 7.32 (1 H, *d*, ^3J = 8.5, CH), 7.75 (2 H, *d*, ^3J = 8.3, 2 CH), 7.92 (2 H, *d*, ^3J = 8.3, 2 CH), 8.34 (1 H, *d*, ^3J = 8.5, CH), 8.91 (1 H, *s*, CH), 11.84 (1 H, *s*, NH). ^{13}C-NMR: 115.4 (CH), 124.7 (C), 127.2 (CH), 128.7 (C), 129.0 (C), 130.0 (2 CH), 131.4 (2 CH), 133.1 (C), 134.2 (CH), 152.7 (C), 157.8 (C), 168.4 (C=S). EI-MS: 422 (M^+, 10); 242 (100); 239 (45); 196 (86); 183 (68); 156 (65); 45 (58). Anal. Calcd for $C_{14}H_8N_5O_4S$ (422.21): C, 39.83; H, 1.91; N, 16.59; found: C, 39.80; H, 1.90; N, 16.60%.

References

[1] Borg, S.; Estenne-Bouhtou, G.; Luthman, K.; Csoregh, I.; Hessellink, W.; Hacksell, U. *J. Org. Chem*. **1995**, *60*, 3112.

[2] Garratt, P. J. In *Comprehensive Heterocyclic Chemistry II*; Storr, R. C., Ed.; Elsevier: Oxford, **1996**; Vol. 4, pp 127-163, 905-1006.

[3] Turnbull, K. In *Progress in Heterocyclic Chemistry;* Elsevier: Oxford, **1998**; Vol. 10, p 153.

[4] Balasubramanian, M.; Keay, J. G.; Scriven, E. F. V.; Shobana, N. *Heterocycles* **1994**, 37, 1951.

[5] Dunstan, A. R.; Weber, H.-P.; Rihs, G.; Widner, H.; Dziadulewicz, E. K. *Tetrahedron Lett.* **1998**, 39, 7983.

[6] Lee, C. H.; Lee, K.-J. *J. Heterocycl. Chem*. **2002**, 39, 845.

[7] Tarasova, O. A.; Klyba, L. V.; Vvedensky, V. Y.; Nedolya, N. A.; Trofimov, B. A.; Brandsma, L.;Verkruijsse, H. D. Eur. *J. Org. Chem*. **1998**, 253.

[8] Ong, C. W.; Chen, C. M.; Wang, L. F. *Tetrahedron Lett*. **1998**, 39, 9191.

[9] Yavari, I.; Sabbaghan, M.; Hossaini, Z. *Synlet.* **2006**, 2501.

[10] Yavari, I.; Djahaniani, H. *Tetrahedron Lett.* **2006**, *47*, 2953.

[11] Yavari, I.; Moradi, L. *Tetrahedron Lett.* **2006**, *47*, 1627.

[12] Yavari, I.; Hossaini, Z.; Sabbaghan, M. *Tetrahedron Lett.* **2006**, *47*, 6037.