Synthesis and characterisation of 1,2,3-triazoles derivatives; a potential heterocycle by using Ni-Ferrite Nanoparticles

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Abstract:

A simple, ecofriendly and efficient novel route has been devised for the synthesis of substituted triazoles by reacting active methylene compounds with azide using transition metal-based nanoparticles. Some of the striking features of the present protocol over existing routes are environmentally benign synthesis, milder reaction conditions, excellent yields, high selectivity, short reaction times, use of green energy source, less waste generation and recycling of the catalyst. The structures of the synthesized products were confirmed by different spectral techniques like IR, ^{1}H NMR and ^{13}C NMR.

Keywords: Cyclisation, Hetero-annulation. Nano catalyst, Sustainability, Transition metal.

Introduction:

Azoles are a large class of five membered ring heterocyclic compounds containing at least one nitrogen atom in their structure **(1)**. The construction of this type of molecule has received great attention due to the wide spectrum of biological activities that have been attributed to structurally distinct azoles and azines **(2-4)**. Fluconazole, itraconazole, voriconazole, Atorvastatin, Cimetidine, Losartan and posaconazole are antifungal agents commercially available that contain a heterocyclic nucleus **(5-9)**. Celecoxi-b is a non-steroidal anti-inflammatory and analgesic agent of the azole class **(10)**. Transition metal-based nanoparticles are playing a pivotal role in most heterogeneous catalytic reactions that are steeply growing with the development of a colloidal synthetic protocol that enables fine control of size, shape, morphology and composition of metal nanoparticles at an atomic level **(11-14)**.

Experimental

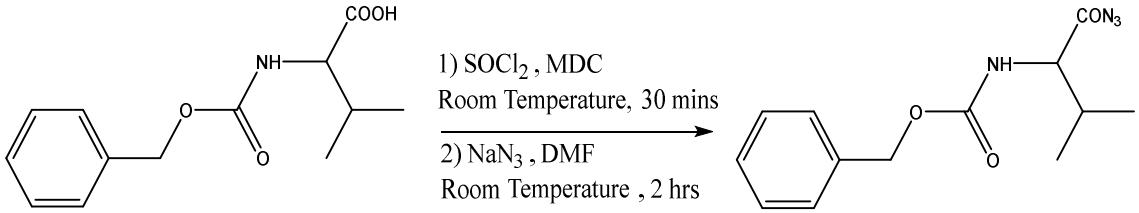
Melting points of all synthesized compounds were determined in open capillary tubes on an electro thermal apparatus and are uncorrected. The progress of reaction was monitored by thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV light as visualizing agent. Proton NMR spectra were recorded on Varian 600 MHz NMR spectrophotometer using $CDCl_3$/DMSO-d_6 as solvent and TMS as an internal standard (chemical shifts in δ ppm).

Synthesis of (1-Azidocarbonyl-2-methyl-propyl)-carbamic acid benzyl ester (2)

In a 100 ml round bottom flask, mixture of thionyl chloride (6g, 0.075 mol) and compound **1** (12.5 g, 0.05 mol) in dichloromethane (25mL) was transferred. The solution was further stirred for 3-4 hrs. The progress of reaction was monitored by TLC (by making methyl ester of acid chloride). Upon completion of reaction, solvent was removed under reduce pressure, obtained crude product Acyl Chloride was used as such for next step. Acyl Chloride product and sodium azide (0.015mol) in dry dimethylformamide (40mL) was stirred at 20°C for 5-6hrs. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was poured into ice cold water (500 mL). The product thus obtained, was filtered, washed with cold water followed by ether to get **2.**

Yield: 78%, m.p.: 268-270 °C

Reaction Scheme 1



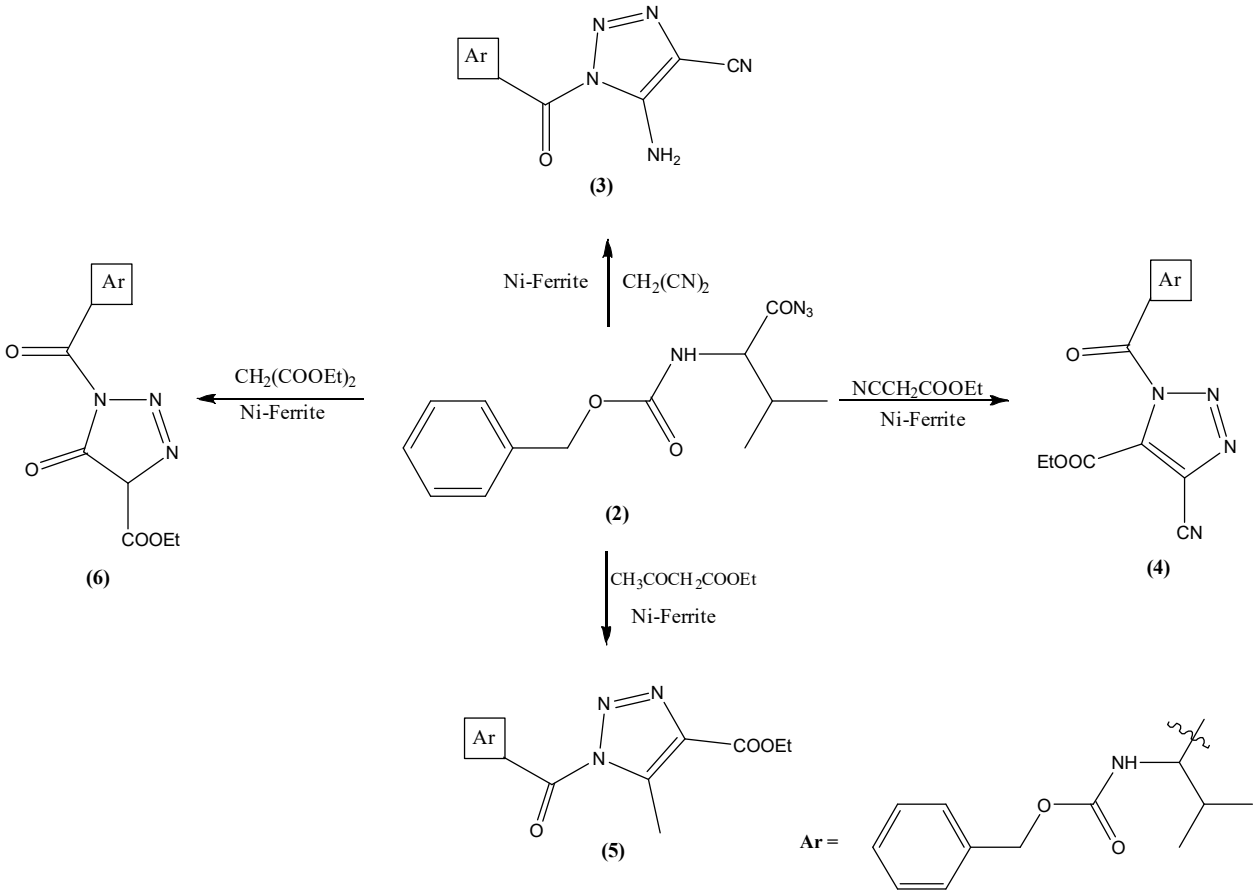
(1) **(2)**

Synthesis of [1-(5-Amino-4-cyano-[1, 2, 3] triazole-1-carbonyl)-2-methyl-propyl]-carbamic acid benzyl ester (98-101)

Cold solution of compound **2** (1.38g, 0.02mol) was added to active methylene compound (0.02mol) in presence of Nickel Ferrite Nanoparticles, reaction was stirred at room temperature in absolute alcohol, the progress of reaction was monitored by TLC. The product

obtained was poured onto crushed ice; solid thus obtained was collected by filtration and recrystallized to obtain compound **3-6**.

Reaction Scheme 2:



Physical data of compounds **3-6** is given in **table 1**

Compounds	Molecular formula	Molecular weight	M.P. (°C)	% Yield
3	$C_{16}H_{18}N_6O_3$	342	290-92	82
4	$C_{19}H_{21}N_5O_5$	399	296-98	83
5	$C_{19}H_{24}N_4O_5$	388	>300	79
6	$C_{18}H_{22}N_4O_6$	390	>300	78

Spectral Characteristic data of 1-(2-Benzyloxycarbonylamino-3-methyl-1-oxo-but-1-yl)-4-amino-5-cyano-3H-[1, 2, 3] triazole (Compound 3)

IR (cm^{-1}): 3320(NH), 2156(CN), 1680(CO).
^{1}H NMR (δ ppm): 1.1 (d, 6H, 2 x CH_3), 2.6 (m, 1H, CH), 4.0(s, 2H, NH_2), 4.4 (d, 1H, CH), 5.34 (s, 2H, OCH_2), 6.1 (s, 1H, NH), 7.19- 7.28 (m, 5H, Ar-H)
^{13}C NMR (δ ppm): 16.6 (2 x CH_3), 28 (CH), 59.6(CH), 69.6(CH_2), 118.2(CN), 127.3-140.2(ArC, C=C), 160.5(C=O), 178.02(C=O).

Spectral Characteristic data of 1-(2-Benzyloxycarbonylamino-3-methyl-1-oxo-but-1-yl)-5-cyano-3H-[1, 2, 3] triazole-4-carboxylic acid ethyl ester (Compound 4)

IR (cm^{-1}): 3330(NH), 2150(CN),1683(CO).
^{1}H NMR (δ ppm): 1.2 (d, 6H, 2 x CH_3), 1.3 (t, 3H, CH_3), 2.7 (m, 1H, CH), 3.5(q, 2H, CH_2), 4.4 (d, 1H, CH), 5.35 (s, 2H, OCH_2), 6.1 (s, 1H, NH), 7.19- 7.28 (m, 5H, Ar-H)
^{13}C NMR (δ ppm): 13.6(CH_3), 16.6(2 x CH_3), 28.3(CH), 58.6(CH_2), 59.6(CH), 69.6(CH_2), 118.2(CN), 128.3-141.5(ArC, C=C), 161.8(C=O), 171.5(C=O), 179.5(C=O).

Spectral Characteristic data of 1-(2-Benzyloxycarbonylamino-3-methyl-1-oxo-but-1-yl)-5-methyl-1H-[1, 2, 3] triazole-4-carboxylic acid ethyl ester (Compound 5)

IR (cm^{-1}): 3323(NH), 2154(CN), 1676(CO).
^{1}H NMR (δ ppm): 1.1 (d, 6H, 2 x CH_3), 1.4 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.6 (m, 1H, CH), 3.7 (q, 2H, OCH_2), 4.4 (d, 1H, CH), 5.35 (s, 2H, OCH_2), 6.2 (s, 1H, NH), 7.21- 7.45 (m, 5H, Ar-H)
^{13}C NMR (δ ppm): 13.4(CH_3), 16.6(2 x CH_3), 28.3(CH), 44.6(CH_3), 58.1(CH), 59.6(CH_2), 69.6(CH_2), 128.3-141.5(ArC, C=C), 162.7(C=O), 175.4(C=O), 176.2(C=O).

Spectral Characteristic data of 1-(2-Benzyloxycarbonylamino-3-methyl-1-oxo-but-1-yl)-5-oxo-4, 5-dihydro-1H-[1, 2, 3] triazole-4-carboxylic acid ethyl ester (Compound 6)

IR (cm^{-1}): 3323(NH), 2148(CN), 1682(CON).

^{1}H NMR (δ ppm): 1.1 (s, 6H, 2 x CH_3), 1.4(t, 3H, CH_3), 2.6 (m, 1H, CH), 3.5(q, 2H, OCH_2), 4.2 (s, 1H, CH), 4.3 (d, 1H, CH), 5.45 (s, 2H, OCH_2), 6.1 (s, 1H, NH), 7.19- 7.28 (m, 5H, Ar-H)

^{13}C NMR (δ ppm): 13.5(CH_3), 16.6 (2 x CH_3), 29.5 (CH), 60.4(CH), 62.3(CH), 70.2(CH_2), 75.2(CH_2), 127.3-140.2(ArC, C=C), 161.5(C=O), 170.5(C=O), 175.5(C=O), 178.3(C=O).

CONCLUSION

Triazoles were prepared in good yield by using Nano catalyzed route. Use of Nickel Ferrite nano catalyst was found to be very effective w.r.t reaction time and high atom economy. Magnetic nanoparticles facilitate easy separation and recycling, promoting sustainable organic synthesis practices.

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