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Synthesis of thiazolanes in the presence of ZnO-NPs as efficient catalyst

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Abstract: In this research, thiazolane derivatives are obtained in good to excellent yields by using a multicomponent reaction of activated acetylens, primary amines and carbon disulfide in the presence of catalytic amount of ZnO-NPs under solvent-free conditions.

Keywords: 1,3-Thiazolane, Activated acetylens, Primary amines, Solvent-free, Arylisothiocyanate.

Introduction

Multicomponent reactions (MCRs), with three or more reactants join in a one-pot procedure to afford a single product [1-3]. They are economically and environmentally useful because multi-step synthesis produce large amounts of trash frequently because of complex isolation actions frequently involving comfortable, toxic, and hazardous solvents after each step [4-7]. MCRs are absolutely suited for combinatorial library synthesis and increased utilize in the finding procedure for new drugs and agrochemicals [8]. They supply a dominant tool toward the one-pot synthesis of diverse and complex compounds as well as small and drug-like heterocycles [9]. Green chemistry move towards hold out significant potential not only for reduction of byproducts, waste produced, and lowering of energy but also in the expansion of new methodologies toward before exclusive materials, using existing technologies [10]. Between existing part of chemistry, medicinal and pharmaceutical chemistry are possibly developed for greening [11].

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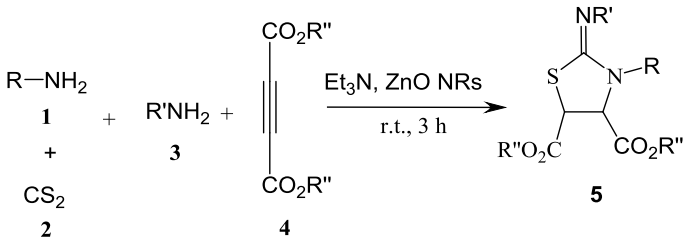
Hence, we investigated a simple three-component reaction between activated acetylenic compounds, primary amines, carbondisulfide and primary amins that are produced isothiocyanates *in situ* in the presence of ZnO-NPs as cartalyst solvent-free conditions at room temperature which afforded 1,3-thiazolane derivatives **5** in good isolated yield**s** (Scheme **1**).

Results and discussion

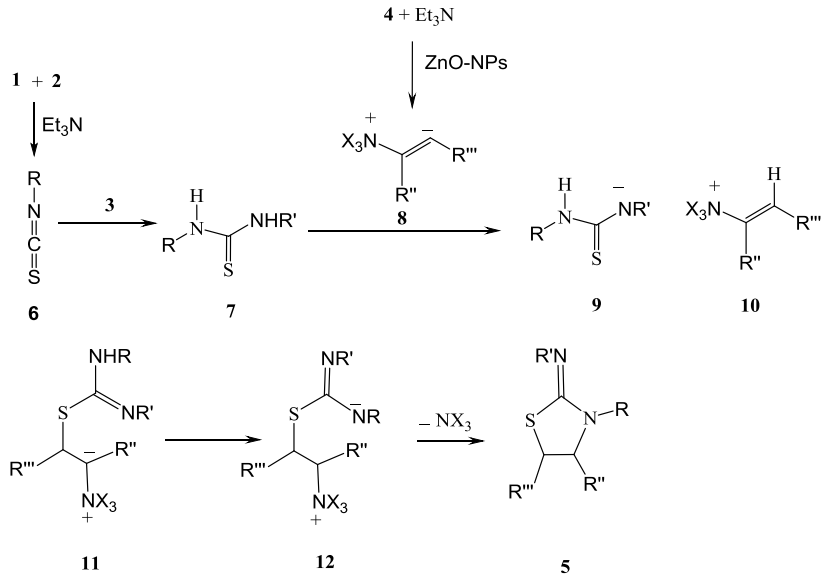
The ^{1}H NMR spectrum of **5a** displayed signals for vicinal methine protons at δ = 4.78 and 4.92, which appeared as two set of doublets with $^{3}J_{HH}$ values of 12.4 Hz. The methoxy groups showed two separate singlet at δ = 3.78 and 3.85. Observation of $^{3}J_{HH}$ = 12.4 Hz for the vicinal methine protons in **5a** indicates the dominance of anti arrangement. The carbonyl groups resonances in the ^{13}C NMR spectra of **5a** are appeared at 172.5 (C=O), 173.7 (C=O) ppm. Also the mass spectra of **5a** displayed the molecular ion peak in the appropriate m/z values. A proposed mechanism for the formation of compound **5** is shown in Scheme **2**. Apparently, the zwitterionic intermediate **8** which formed from the reaction of Et_3N in the presence of

ZnO-NPs and electron deficient acetylenic ester **4** is protonated by the intermediate **5** that was generated in situ from the reaction of primary amine **2** and carbondisulfide 2 that are produced isothiocyanate **6**, produce intermediates **9** and **10**. Nucleophilic attack of the conjugate base **9** on intermediate **10** leads to adduct **11** which undergo proton shifts to afford new zwitterionic **12**. Finally, intramolecular cyclization of **12** with elimination of Et_3N and ZnO-NPs produces compound **5**.



5	R	R'	R"	R"'	Yield (%) of **5**
a	Ph	Me	Me	Me	78
b	4-MeO-C_6H_4	Et	Me	Me	85
c	4-MeO-C_6H_4	n-Bu	Et	Et	80
d	4-Me-C_6H_4	^{t}Bu	Et	Et	80
e	4-Br-C_6H_4	Me	Me	Me	82

Scheme 1: Reaction of activated acetylenes, isothiocyanates and primary amins



Scheme 2: Proposed mechanism for the formation of **4**.

The morphologies of the products were examined by SEM. Fig. **1** shows the typical SEM image of the samples obtained by the reflux method. ZnO nanoparticles were obtained from the reaction between Zn(AcO)2.2H2O and NaOH by reflux method without adding template. As shown in this Fig., when only Zn^{+2} was used (without any template), ZnO nanoparticles were formed.

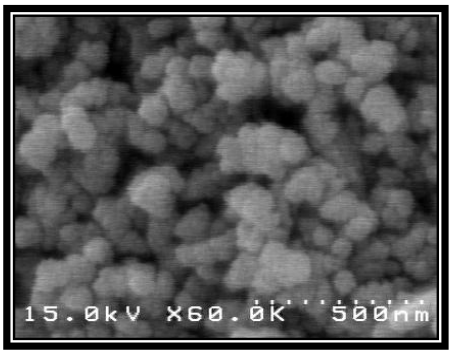


Figure 1. SEM image of NP-ZnO

In XRD image, all the main peaks in the model corresponded to the wurtzite structure of ZnO, which can be indexed on the basis of JCPDS file No. 36-1451. No other characteristic peaks of the impurities are detected, showing the high purity of the catalysis. We see that all samples display highest relative intensities for the (1 0 1) peak revealing a preferred orientation of their corresponding products. While, comparing with other peaks, the samples show different relative intensities of the (0 0 2) peak. The average crystal sizes for NP-ZnO is about 30 nm.

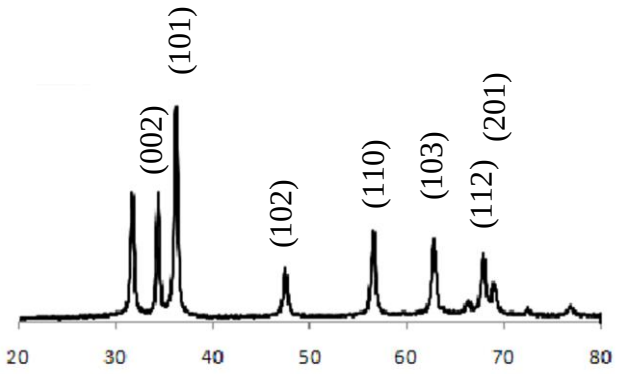


Figure 2. XRD spectra of NP-ZnO.

The catalyst can be resolved five times without significant loss of activity by filtering. The reusability of the catalyst was checked for the synthesis of compound **4a**. The catalyst was separate after each run and washed thoroughly with ethylacetate; it was then dried at room temperature for 24 h and used for the next catalytic cycle.

Conclusion

In conclusion, we found that the reaction of activated acetylenic compounds with isothiocyanates that are produced from ythe reaction of primary amines and carbondisulfide and primary amines in the presence of catalytic amount of ZnO-NPs leads to a facile synthesis of some functionalized thiazolanes under solvent-free conditions without using any catalyst.

Experimental

All chemicals used in this work were prepared from Fluka (Buchs, Switzerland) and were used without further purification. Electrothermal 9100 apparatus is employed for measuring of melting points of products. Elemental analyses for C, H, and N were performed with Heraeus CHN–O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MAT 8430 spectrometer operating at an ionization potential of 70 eV. Measurement of IR spectra was performed by Shimadzu IR-460 spectrometer. ^{1}H, and ^{13}C NMR spectra were evaluated with a BRUKER DRX-500 AVANCE spectrometer at 500.1 and 125.8 MHz, respectively. ^{1}H, and ^{13}C, spectra were obtained for solutions in $CDCl_3$ using TMS as internal standard or 85% H_3PO_4 as external standard.

General Procedure for the Preparation of nanoparticle ZnO

Sodium hydroxid (0.44 g) was disolved in distilled water (75 mL) at room temprature, zinc acetate dihydrate (0.6 g) was added to the mixture and the solution was refluxed for 1.5 h at 80 ◦C. The solution was then cooled at room temperature, the precipitate was assembled by filtration and washed with distilled water and ethanol (96%) several times. NP-ZnO was dried in the air at room temprature during 24 h.

General procedure for preparation of compounds 5

To a magnetically stirred mixture of activated acetylenes **4** (2 mmol) and ZnO Nps (0.02g) was added mixture of primary amines **1,** carbondisulfide **2** and primary amines **3** (2 mmol) at room temperature. The reaction mixture was then stirred. After completion of the reaction [TLC (AcOEt/hexane 1:7) monitoring], 15 mL H_2O was poured into the reaction mixture. The

solid residue was filtered and washed by cold diethyl ether to afforded pure compounds **5**.

Dimethyl 2-(methylimino)-3-phenyl-1,3-thiazolane-4,5-dicarboxylate (5a):

Yellow powder, m.p. 156-158°C, yield: 0.46 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 1745, 1738, 1698, 1657, 1574, 1467, 1382, 1215 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2O_4S$ (308.35): C, 54.53; H, 5.23; N, 9.08. Found: C, 54.62; H, 5.34; N, 9.23%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.83 (3 H, s, NMe), 3.78 (3 H, s, MeO), 3.85 (3 H, s, MeO), 4.78 (1 H, d, ^3J = 12.4, CH), 4.92 (1 H, d, ^3J = 12.4, CH), 7.23 (1 H, t, ^3J = 7.4, CH), 7.35 (2 H, d, ^3J = 7.6, 2 CH), 7.54 (2 H, t, ^3J = 7.6, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 34.6 (NMe), 42.7 (CH), 51.6 (MeO), 52.4 (MeO), 58.4 (CH), 122.8 (CH), 128.3 (2 CH), 129.6 (2 CH), 139.8 (C), 163.4 (C=N), 172.5 (C=O), 173.7 (C=O) ppm. MS, *m/z* (%): 308 (M$^+$, 15), 277 (86), 77 (64), 31 (100).

Dimethyl 2-(ethylimino)-3-(4-methoxyphenyl)-1,3-thiazolane-4,5-dicarboxylate (5b):

Pale yellow powder, m.p. 168-170 °C, yield: 0.59 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1742, 1736, 1686, 1632, 1525, 1487, 1325, 1219 cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_2O_5S$ (352.41): C, 54.53; H, 5.72; N, 7.95. Found: C, 54.64; H, 5.80; N, 8.10%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.24 (3H, t, ^3J = 7.3, CH_3), 3.27 (2 H, q, ^3J = 7.3, CH_2), 3.70 (3 H, s, MeO), 3.76 (3 H, s, MeO), 3.87 (3 H, s, MeO), 4.75 (1 H, d, ^3J = 12.2, CH), 4.87 (1 H, d, ^3J = 12.2, CH), 7.14 (2 H, d, ^3J = 7.8, 2 CH), 7.28 (2 H, d, ^3J = 7.6, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.2 (CH_3), 41.5 (CH_2), 43.7 (CH), 51.5 (MeO), 52.6 (MeO), 55.4 (MeO), 59.3 (CH), 111.2 (2 CH), 130.3 (2 CH), 134.8 (C), 154.2 (C), 160.7 (C=N), 171.8 (C=O), 172.6 (C=O) ppm. MS, *m/z* (%): 352 (M$^+$, 10), 321 (64), 108 (96), 31 (100).

Diethyl 2-(buthylimino)-3-(4-methoxyphenyl)-1,3-thiazolane-4,5-dicarboxylate (5c):

White powder, m.p. 162-164 °C, yield: 0.70 g (83%). IR (KBr) (ν_{max}/cm^{-1}): 1740, 1738, 1687, 1645, 1438, 1357, 1256 cm^{-1}. Anal. Calcd for $C_{20}H_{28}N_2O_5S$ (408.51): C, 58.80; H, 6.91; N, 6.86. Found: C, 58.92; H, 6.98; N, 6.90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.19 (3H, t, ^3J = 7.2, CH_3), 1.22 (3H, t, ^3J = 7.4, CH_3), 1.28 (3H, t, ^3J = 7.3, CH_3), 1.68 (2 H, q, ^3J = 7.3, CH_2), 1.78 (2 H, m, CH_2), 2.83 (2 H, t, ^3J = 6.8, NCH_2), 3.75 (3 H, s, MeO), 4.12 (2 H, q, ^3J = 7.3, CH_2O), 4.23 (2 H, q, ^3J = 7.3, CH_2O), 4.62 (1 H, d, ^3J = 11.7, CH), 5.02 (1 H, d, ^3J = 11.7, CH), 7.12 (2 H, d, ^3J = 7.6, 2 CH), 7.32 (2 H, d, ^3J = 7.6, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.3 (CH_3), 13.8 (CH_3), 14.3 (CH_3), 21.4 (CH_2), 32.5 (CH_2), 43.6 (CH), 54.8 (MeO), 59.5 (CH), 61.2 (CH_2O), 62.0 (CH_2O), 62.7 (NCH_2), 114.5 (2 CH), 130.8 (2 CH), 135.4 (C), 156.7 (C), 161.2 (C=N), 172.3 (C=O), 174.2 (C=O) ppm. MS, *m/z* (%): 408 (M$^+$, 8), 363 (84), 108 (68), 45 (100).

Diethyl 2-(tert-butylimino)-3-(4-methylphenyl)-1,3-thiazolane-4,5-dicarboxylate (5d):

Yellow powder, m.p. 164-166 °C, yield: 0.59 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 1736, 1732, 1694, 1587, 1467, 1346, 1238 cm^{-1}. Anal. Calcd for $C_{20}H_{28}N_2O_4S$ (392.51): C, 61.20; H, 7.19; N, 7.14. Found: C, 61.32; H, 7.25; N, 7.22%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (3H, t, ^3J = 7.4, CH_3), 1.32 (3H, t, ^3J = 7.4, CH_3), 1.35 (9H, s, Me_3C), 2.28 (3 H, s, CH_3), 4.15 (2 H, q, ^3J = 7.4, CH_2O), 4.28 (2 H, q, ^3J = 7.4, CH_2O), 4.73 (1 H, d, ^3J = 11.5, CH), 4.96 (1 H, d, ^3J = 11.5, CH), 7.24 (2 H, d, ^3J = 7.5, 2 CH), 7.36 (2 H, d, ^3J = 7.6, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.8 (CH_3), 14.2 (CH_3), 22.4 (CH_3), 28.7 (Me_3C), 44.3 (CH), 48.7 (Me_3C), 58.7 (CH), 61.4 (CH_2O), 62.3 (CH_2O), 129.4 (2 CH), 130.2 (C), 131.4 (2 CH), 140.7 (C), 160.4 (C=N), 172.5 (C=O), 175.3 (C=O) ppm. MS, *m/z* (%): 392 (M$^+$, 20), 377 (84), 91 (84), 45 (100).

Dimethyl 2-(methylimino)-3-(4-bromophenyl)-1,3-thiazolane-4,5-dicarboxylate (5e):

Yellow crystals, m.p. 183-185 °C, yield: 0.62 g (80%). IR (KBr) (ν_{max}/cm^{-1}): 1737, 1732, 1695, 1587, 1485, 1436, 1342, 1225 cm^{-1}. Anal. Calcd for $C_{14}H_{15}BrN_2O_4S$ (387.25): C, 43.42; H, 3.90; N, 7.23. Found: C, 43.53; H, 3.95; N,7.32%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.12 (3H, s, NMe), 3.75 (3 H, s, MeO), 3.82 (3 H, s, MeO), 4.83 (1 H, d, ^3J = 11.8, CH), 4.92 (1 H, d, ^3J = 11.8, CH), 7.10 (2 H, d, ^3J = 7.8, 2 CH), 7.54 (2 H, d, ^3J = 7.8, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 34.5 (NCH_3), 44.2 (CH), 51.2 (MeO), 51.8 (MeO), 60.3 (CH), 116.7 (C), 129.7 (2 CH), 132.6 (2 CH), 139.4 (C), 162.3 (C=N), 172.4 (C=O), 173.8 (C=O) ppm. MS, *m/z* (%): 387 (M$^+$, 15), 356 (78), 156 (64), 31 (100).

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