Nano ZnO promoted synthesis of 1,3-oxazoline-2-thione derivatives

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The synthesis of 2-thioxo-1,3-oxazoles in the presence of zinc oxide nanoparticles (ZnO NPs, *ca* 21 nm) and under solvent-free conditions has been achieved through reaction of ammonium thiocyanate, acid chlorides, phenacyl bromide or its derivatives, and a catalytic amount of *N*-methylimidazole. The catalyst was recycled and reused six times with minor decrease in its catalytic activity. High yields, simple experimental procedure and short reaction times are advantages of this reaction.

Keywords: zinc oxide nanoparticles, 2-thioxo-1,3-oxazole, solvent-free conditions, *N*-methylimidazole

The value of nanosized materials has been described in several scientific and technological areas, including the catalytic activity of the metal oxide nanoparticles (NPs).[1,2] The high surface to volume ratio of metal oxide NPs is mainly responsible for their improved catalytic properties.[3] The catalytic influence of nanocrystalline zinc oxide is utilised in gas sensors and photo-catalysts. Currently, the application of this nanocatalyst in organic and inorganic reactions has emerged as a rapidly growing field.[4–7] A number of methods have been developed to synthesise 1,3-oxazolidine-2-thiones.[8-18] In this work, we combine **1**–**3** in the presence of *N*-methylimidazole and ZnO NPs to obtain the desired product **4** (Scheme 1).

Result and discussion

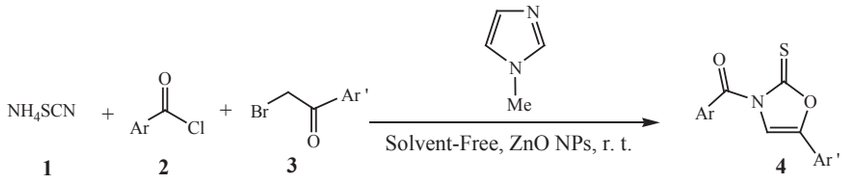
Reaction of phenacyl bromide (3) or its derivatives with acid chlorides (2) and ammonium thiocyanate (1) in the presence of *N*-methylimidazole (20 mol%) and ZnO NPs (10 mol%) lead to functionalised 2-thioxo-2,3-dihydro-1,3-oxazoles in good yield (Scheme 1).

This reaction does not occur without the ZnO NPs. Instead, a two-component reaction occurs between *N*-methyl imidazole and phenacyl bromide **3**. However, under similar conditions but without ZnO NPs, this reaction also occurs with ethyl bromopyruvate.[18] The structures for **4a**–**e** were assigned from their IR, ^{1}H NMR and ^{13}C NMR spectra. The ^{1}H NMR spectrum of **4a** exhibits characteristic signals for methine protons (δ = 7.27 ppm). The ^{13}C NMR spectra of the 1,3-oxazoline-2-thione ring system of **4a** showed signals in agreement with the proposed structure. A tentative mechanism for this transformation has been proposed (Scheme 2). The reaction may start with the formation of benzoyl isothiocyanate **5**, followed by the addition of *N*-methylimidazole and formation of 1 : 1 adduct **6**, which is subsequently attacked by phenacyl bromide to produce **7**. The latter undergoes the elimination of HBr followed by a cyclisation reaction, and loss of *N*-methylimidazole to generate **4**.

In conclusion, the reaction of phenacyl bromide or its derivatives with acid chlorides and ammonium thiocyanate in the presence of *N*-methylimidazole (20 mol%) and ZnO NPs (10 mol%) leads to functionalised 2-thioxo-2,3-dihydro-1,3-oxazoles in good yields. The solvent-free conditions and the simplicity of the procedure makes it an interesting alternative to the more complex multistep approaches. The present procedure has the advantage that not only is the reaction performed under neutral conditions, but also the reactants can be mixed without any prior activation or modification.

Experimental

All chemicals used in this work are purchased from Fluka (Buchs, Switzerland) and used without further purification. Melting points are measured on an Electrothermal 9100 apparatus. IR spectra are measured on a Shimadzu IR-460 spectrometer. ^{1}H, and ^{13}C NMR spectra are obtained using a Bruker DRX-400 Avance spectrometer at 400.1 and 125.8 MHz, respectively. Mass spectra were recorded on a Finnigan-MAT 8430 spectrometer operating at an ionisation potential



2, 3, 4	Ar	Ar'	Yied % of **4**
a	4-BrC_6H_4	4-$O_2NC_6H_4$	95
b	4-$O_2NC_6H_4$	4-BrC_6H_4	75
c	4-$O_2NC_6H_4$	4-$MeOC_6H_4$	70
d	4-$MeOC_6H_4$	4-BrC_6H_4	85
e	4-BrC_6H_4	4-$OMeC_6H_4$	83

Scheme 1 Reaction of ammonium thiocyanate, acid chloride and phenacyl bromide or its derivatives in the presence of ZnO NPs (10 mol%).

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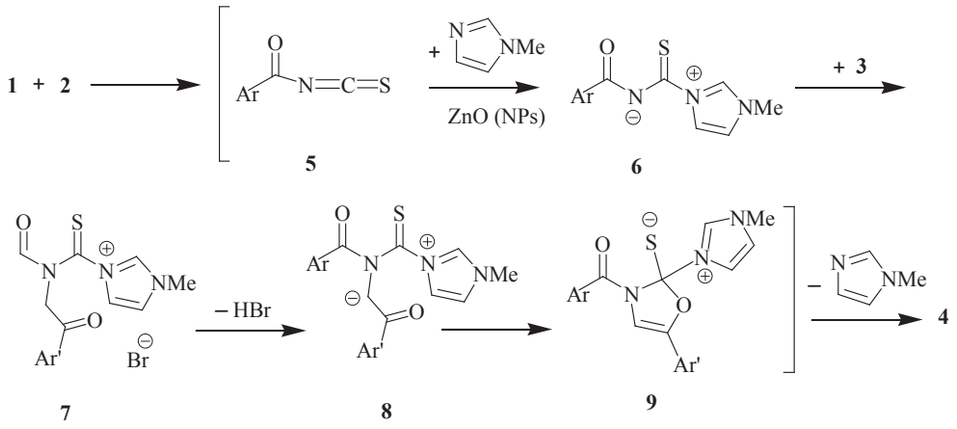

Scheme 2 Proposed mechanism for the formation of **4**.

of 70 eV. ^{1}H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$ using TMS as the internal standard.

Synthesis of compounds **4***; general procedure*

We first prepared ZnO NPs through a solid-state reaction method reported by Zhu and co-workers.[19,20] The ZnO NPs was used as a catalyst in the synthesis of functionalised 1,3-oxazoline-2-thiones derivatives. A magnetically stirred mixture of **1** (0.15 g, 2 mmol) and acid chloride **2** (2 mmol) was warmed at about 70 °C in a water bath for 20 min. Phenacyl bromide **3** or its derivatives (2 mmol) is added gently and the mixture is allowed to cool to room temperature. *N*-methylimidazole (0.032 g, 20 mol%) and ZnO NPs (10 mol%) were added. The reaction mixture was stirred for 12 h and extracted by Et_2O (2 × 5 mL) to afford the pure title compounds.

(4-Bromophenyl)[5-(4-nitrophenyl)-2-thioxo-1,3-oxazol-3(2H)-yl]methanone (**4a**): Pale yellow powder; 0.59 g; yield 95%; m.p. 132–134 °C. IR (KBr) (ν_{max}/cm^{-1}): 1728, 1576, 1453, 1369 and 1293 cm^{-1}. ^{1}H NMR: δ 7.27 (1 H, s, CH); 7.20–7.66 (6 H, *m*, 6 CH); 7.87 (2 H, *d*, ^{3}J = 7.4 Hz, 2CH) ppm. ^{13}C NMR: δ 95.4 (CH), 124.5 (C), 127.7 (2 CH); 127.9 (2 CH); 128.5 (2 CH); 130.5 (2 CH); 135.1 (C); 147.6 (C); 151.0 (2C); 161.9 (C=O); 163.8 (C=S) ppm. MS, *m/z* (%): 405 (M^{+}, 15), 181 (100), 150 (87), 127 (64), 77 (95). Anal. calcd for $C_{16}H_9BrN_2O_4S$ (405.22): C, 47.43; H, 2.24; N, 6.91; found: C, 47.52; H, 2.32; N, 6.98%.

(4-Nitrophenyl)[5-(4-bromophenyl)-2-thioxo-1,3-oxazol-3(2H)-yl]methanone (**4b**): Yellow crystals; yield 75%; m.p. 131–133 °C. IR (KBr): 1723, 1631, 1552, 1440 and 1373 cm^{-1}. ^{1}H NMR: δ 7.02 (1 H, s, CH); 7.45–8.58 (8 H, *m*, 8 CH) ppm. ^{13}C NMR: δ 119.8 (CH), 124.9 (C), 127.7 (2 CH); 127.9 (2 CH); 128.4 (2 CH); 130.8 (2 CH); 143.4 (C); 149.4 (C); 151.8 (2C); 160.1 (C=O); 164.6 (C=S) ppm. MS, *m/z* (%): 405 (M^{+}, 10), 181 (88), 150 (86), 127 (58), 77 (100). Anal. calcd for $C_{16}H_9BrN_2O_4S$ (405.22): C, 47.43; H, 2.24; N, 6.91; found: C, 47.54; H, 2.35; N, 7.00%.

(4-Nitrophenyl)[5-(4-methoxyphenyl)-2-thioxo-1,3-oxazol-3(2H)-yl]methanone (**4c**): Yellow crystals; yield 70%; m.p. 157–159 °C. IR (KBr): 1730, 1591, 1548, 1513 and 1432 cm^{-1}. ^{1}H NMR: δ 4.09 (3 H, s, MeO), 6.62 (1 H, s, CH), 7.48–8.06 (8 H, m,8 CH) ppm. ^{13}C NMR: δ 53.6 (MeO), 110.0 (CH); 115.5 (2 CH); 127.9 (C); 128.1 (2 CH), 129.5 (2 CH); 130.8 (C), 134.6 (2 CH); 145.6 (C); 154.9 (2 C); 159.5 (C=O); 167.8 (C=S). MS, *m/z* (%): 356 (M^{+}, 10), 249 (78), 151 (100), 107 (88), 31 (100). Anal. calcd for $C_{17}H_{12}BrN_2O_5S$ (356.35): C, 57.30; H, 3.39; N, 7.86; found: C, 57.43; H, 3.45; N, 7.96%.

(4-Methoxyphenyl)[5-(4-bromophenyl)-2-thioxo-1,3-oxazol-3(2H)-yl]methanone (**4d**): Yellow powder; yield 85%; m.p. 162–164 °C. IR (KBr): 1723, 1548, 1500, 1460 and 1372 cm^{-1}. ^{1}H NMR: δ 4.07 (3 H, s, MeO), 7.03 (1 H, s, CH), 7.29–8.52 (8 H, m,8 CH) ppm. ^{13}C NMR: δ 53.3 (MeO), 111.6 (CH); 118.3 (2 CH); 123.0 (C); 124.6 (2 CH), 127.7 (2 CH); 128.6 (C), 129.3 (2 CH); 143.4 (C); 151.8 (2 C); 160.1 (C=O); 164.6 (C=S). Anal. calcd for $C_{17}H_{12}BrNO_3S$ (390.25): C, 52.32; H, 3.10; N, 3.59; found: C, 52.40; H, 3.22; N, 3.67%.

(4-Bromophenyl)[5-(4-methoxyphenyl)-2-thioxo-1,3-oxazol-3(2H)-yl]methanone (**4e**): Pale yellow powder; yield 83%; m.p. 163–165 °C. IR (KBr): 1734, 1672, 1514, 1449 and 1263 cm^{-1}. ^{1}H NMR: δ 3.88 (3 H, s, MeO), 5.21 (1 H, s, CH), 6.81–7.69 (8 H, m,8 CH) ppm. ^{13}C NMR: δ 53.2 (MeO), 114.0 (3 CH); 121.3 (2 CH); 124.6 (C), 126.9 (2 CH); 129.3 (2 CH), 130.9 (C), 142.7 (C); 145.4 (C), 149.2 (C); 160.7 (C=O); 165.9 (C=S). Anal. calcd for $C_{17}H_{12}BrNO_3S$ (390.25): C, 52.32; H, 3.10; N, 3.59; found: C, 52.40; H, 3.20; N, 3.68%.

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