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Urea nitrate catalyzed synthesis of 2-arylbenzothiazoles using the grindstone technique

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Abstract: An efficient, green and environmentally friendly grindstone method for the synthesis of 2-arylbenzothiazole derivatives in the presence of urea nitrate as the catalyst under solvent-free conditions was developed. All products were characterized by elemental analysis and spectral methods.

Keywords: 2-aminobenzenethiol; 2-arylbenzothiazole; green synthesis; grindstone technique; urea nitrate.

Introduction

Benzothiazole is a versatile pharmacophore, possessing a wide spectrum of biological activities [1–13]. Accordingly, efficient approaches to the synthesis of benzothiazole derivatives, including green chemistry, are of interest. The important characteristics of green chemistry are the recovery of the catalyst after the catalytic reaction and minimization of waste. In this report a green synthesis of 2-arylbenzothiazoles using fine grinding of substituted 2-aminobenzenethiol and substituted aldehyde using a mortar and pestle under solvent-free conditions in the presence of urea nitrate catalyst is described. Urea nitrate is easily prepared in the laboratory and has been used previously to catalyze various organic transformations including the imino Diels-Alder reaction [14], regioselective nitration [15, 16], aromatization of 1,4-dihydropyridines [17] and cleavage of oximes under microwave irradiation [18] among other transformations. **CAUTION:** *Urea nitrate is unstable and even at room temperature (rt) slowly releases nitric acid. As it is a powerful explosive* [19] *it must be handled with care* [20, 21]. *Urea nitrate can easily be neutralized by treatment with water.*

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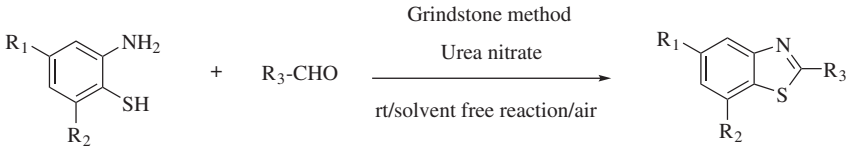
Results and discussion

In continuation of our research, an attempt was made to synthesize some derivatives of 2-arylbenzothiazole derivatives from 2-aminobenzenethiol under environmental benign conditions using urea nitrate as a catalyst via the grindstone method. The compounds **3a–f** were synthesized by performing organic transformations under solvent-free conditions. The reaction has previously been performed under different conditions (Table 1) using ZnO NPs [22], ZnO NPs (ball milling strategy) [23], tetrabutylammonium bromide (TBAB) [24], TiO_2 [25], glycerol [26], tungstophosphoric acid impregnated zirconium phosphate [27], sulfonated porous carbon (SPC) [28], calcined eggshell [29] and liquid-assisted hand grinding [30], among other methods. Most of the synthetic approaches reported in the literature are characterized by high yields and short reaction times but the catalysts used are impractical and hazardous solvents are used along with tedious isolation procedures. By contrast, the synthesis of urea nitrate is simple, economical and the products **3a–f** are obtained without using solvents and avoiding tedious isolation procedures. Bearing in mind the importance of urea nitrate as a catalyst, we made efforts to develop an environment friendly method using the grindstone technique. Our method involves grinding substituted 2-aminobenzenethiol and various aldehydes with a mortar and pestle using urea nitrate as a catalyst and the product is obtained in a few seconds, visualized by a dramatic color change. Excellent yields are obtained without a tedious purification process of column chromatography. The reaction is carried out at rt in the absence of any solvent with different substituted thiols **1** and aromatic aldehydes **2** in the presence of urea nitrate and produces compounds **3a–f** (Scheme 1). Compounds **3d**,**e** and **3f** have been synthesized previously using different methods [31, 32] but the yields and reaction times have not been satisfactory. In this work, these compounds were resynthesized using

Table 1 Comparative study of various catalysts.

Entry	Catalyst	Reaction condition	Time	Yield (%)
1	Urea nitrate (15 mol%)[a]	Grinding, solvent free, rt	30 s	98
2	ZnO NPs (5 mg) [22]	Solvent free or ethanol, rt	2–8 min	95
3	ZnO NPs [23]	Ball milling, 600 rpm, rt	30 min	87
4	Tetrabutylammonium bromide (TBAB) (15 mol%) [24]	Reflux at 60°C	30 min	90
5	TiO_2 P25 (0.1)/H_2O_2 [25]	Ambient-light conditions at 50°C	5 min	96
6	Glycerol (2 mL) [26]	Microwave irradiation at 100°C	4 min	92
7	Tungstophosphoric acid impregnated zirconium phosphate (5 mol%) [27]	Microwave irradiation at 100°C	15 min	95
8	Sulfonated porous carbon (SPC) (0.1 g) [28]	Microwave irradiation in water	6 min	93
9	Calcined egg shell [29]	Grinding, solvent free, rt	16 min	92

[a]Present work.



	R_1	R_2	R_3
3a	CH_3	CH_3	4-cyanophenyl
3b	CH_3	CH_3	3,4-dimethoxyphenyl
3c	CH_3	CH_3	2-furanyl
3d	H	H	3,4-dimethoxyphenyl
3e	H	H	4-ethoxyphenyl
3f	H	H	2-furanyl

Scheme 1

urea nitrate as a catalyst via the grinding procedure. It was found that the rate of reaction increased continuously with the increase in the catalyst concentration up to 15 mol%, which was found to be the optimal concentration. The optimum reaction time (grinding) was 30 s. The reaction was also attempted in the presence of HNO_3 and urea alone under otherwise similar conditions but the product was obtained in a lower yield along with a longer reaction time. The structures of all synthesized compounds were confirmed by analysis of IR and NMR spectra.

Conclusion

An efficient and green procedure for the synthesis of 2-arylbenzothiazoles from substituted 2-aminobenzenethiol was developed. The work is highly advantageous because of easy workup, solvent-free conditions, high yields, no waste generation and the ease of product isolation and purification.

Experimental

All chemicals were commercially procured from Sigma-Aldrich and Hi-Media and used without further purification. An agate mortar and pestle was used for the synthesis. Melting points were determined in open capillary tubes and are uncorrected. The IR spectra were recorded in KBr pellets on a Bruker FT-IR spectrometer. The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were scanned on a Bruker Avance II 400 spectrometer using tetramethylsilane (TMS) as an internal standard and $CDCl_3$ as a solvent. The mass spectra were recorded on a Waters Xevo G2-S QT spectrometer. The purity of synthesized compounds was checked by thin layer chromatography (TLC) using silica gel G as an adsorbent and eluting with hexanes/

ethyl acetate; visualization was accomplished by UV irradiation or exposure to iodine. The starting material 2-amino-4,6-dimethyl-benzenethiol was synthesized as previously reported [33].

Synthesis of urea nitrate catalyst

Urea (3 g) in a 100-mL beaker was treated dropwise by stirring with HNO_3 (10 mL). A clear solution was formed upon heating. The solution was cooled to rt and the resultant bright shiny crystals of urea nitrate were filtered, dried and stored in air tight vials. The catalyst is unstable in the presence of water.

General procedure for synthesis of 2-phenylbenzothiazoles 3a–f

An aromatic aldehyde (1 mol), *o*-aminothiophenol (1 mmol) and urea nitrate (15 mol%) were grounded together using a mortar and pestle at rt for few seconds giving rise to a dramatic color change as the reaction progressed. The resultant solid mass was treated with ice-cold water and the mixture was stirred for 30 min to remove urea. After filtration, the solid residue of **6a–f** was crystallized from ethanol.

4-(5,7-Dimethyl-benzothiazol-2-yl)-benzonitrile (3a) Yield 96%; dark yellow crystals; mp 212–215°C; IR: 3051 (C-H stretching, Ar), 2965 (C-H stretching, CH_3), 2213 (-CN, stretching) 1470 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 2.19 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 7.26–7.79 (m, 6H, Ar-H and BT-H); ^{13}C NMR: δ 20.3, 21.6, 115.9, 117.0, 124.4, 127.1, 127.5, 129.9, 132.3, 132.9, 134.5, 136.4, 137.3, 139.0, 153.1, 166.2; MS (EI): *m/z* 264.89 [M+]. Anal. Calcd for $C_{16}H_{12}N_2S$; C, 72.70; H, 4.58; N, 10.60. Found: C, 72.53; H, 4.52; N, 10.65.

2-(3,4-Dimethoxy-phenyl)-5,7-dimethyl-benzothiazole (3b) Yield 95%; red orange crystals; mp 174–177°C; IR: 3110 (C-H stretching, Ar), 2973 (C-H stretching, CH_3), 1452 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 2.26 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 6.95–7.87 (m, 5H, Ar-H and BT-H); ^{13}C NMR: δ 20.5, 21.8, 56.2, 57.4, 111.0, 112.2, 123.4, 128.8, 130.3, 131.5, 131.9, 138.5, 138.9, 148.3, 149.1, 152.6, 166.5; MS (EI): *m/z* 299.47 [M+]. Anal. Calcd for $C_{17}H_{17}NO_2S$; C, 68.20; H, 5.72; N, 4.68. Found: C, 65.30; H, 5.82; N, 4.71.

2-Furan-2-yl-5,7-dimethyl-benzothiazole (3c) Yield 98%; dark purple crystals; mp 182–185°C; I: 3085 (C–H stretching, Ar), 2943 (C-H stretching, CH_3), 1473 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 2.32 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.63 (dd, 1H, *J* = 3.4, 1.8 Hz), 7.08 (d, 2H, BT-H), 7.17 (dd, 1H, *J* = 3.4, 0.8 Hz), 7.87 (dd, 1H, *J* = 1.8, 0.8 Hz); ^{13}C NMR: δ 20.9, 21.4, 108.8, 112.3, 122.7, 129.7, 131.0, 137.0, 138.4, 144.1, 149.1, 151.1, 156.6; MS (EI): *m/z* 229.74 [M+]. Anal. Calcd for $C_{13}H_{11}NOS$; C, 68.09; H, 4.84; N, 6.11. Found: C, 68.11; H, 4.93; N, 6.23.

2-(3,4-Dimethoxy-phenyl)-benzothiazole (3d) Yield 98%; dark yellow crystals; mp 136–139°C; IR: 3120 (C-H stretching, Ar), 3053 (C-H stretching, CH_3), 1465 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 3.68 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.94–7.46 (m, 7H, Ar-H and BT-H); ^{13}C NMR: δ 56.1, 57.3, 111.6, 113.2, 122.4, 122.8, 124.9, 126.4, 128.4, 131.0, 134.1, 148.5, 149.1, 153.4, 163.5; MS (EI): *m/z* 271.82 [M+]. Anal. Calcd for $C_{15}H_{13}NO_2S$; C, 66.40; H, 4.83; N, 5.16. Found: C, 66.57; H, 4.93; N, 5.26.

2-(4-Ethoxy-phenyl)-benzothiazole (3e) Yield 95%; gray crystals; mp 117–120°C; IR: 3152 (C-H stretching, Ar), 3087 (C-H stretching, CH_3), 2925 (CH_2, C-H stretching), 1460 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 1.27 (t, 3H, CH_3, *J* = 7.0 Hz), 4.14 (q, 2H, CH_2, *J* = 7.0 Hz), 7.12–7.97 (m, 8H, Ar-H and BT-H); ^{13}C NMR: δ 14.7, 63.6, 114.5, 114.7, 122.7, 124.1, 125.2, 126.9, 127.3, 128.1, 128.5, 135.4, 154.3, 161.0, 167.1; MS (EI): *m/z* 255.68 [M+]. Anal. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.68; H, 5.19; N, 5.55.

2-Furan-2-yl-benzothiazole (3f) Yield 97%; dark purple crystals; mp 105–108°C; IR: 3080 (C-H stretching, Ar), 1458 cm^{-1} (aromatic C=C); ^{1}H NMR: δ 6.70 (1H, dd, *J* = 3.4, 1.8 Hz), 7.19 (1H, dd, *J* = 3.4, 0.9 Hz), 7.30–8.09 (m, 4H, BT-H), 7.98 (1H, dd, *J* = 1.8 Hz and 0.9 Hz); ^{13}C NMR: δ 108.8, 112.3, 122.6, 124.6, 124.8, 126.3, 133.8, 144.1, 149.1, 153.1, 156.6; MS (EI): *m/z* 201.59 [M+]. Anal. Calcd for $C_{11}H_7NOS$: C, 65.65; H, 3.51; N, 6.96. Found: C, 65.76; H, 3.58; N, 6.93.

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