Sphalerite: A natural catalyst for an efficient synthesis of 2-aminobenzothiazolomethyl naphthol derivatives under solvent-free conditions

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Abstract
An efficient method is described for the synthesis of 2-aminobenzothiazolomethyl naphthol derivatives by one-pot three-component reaction of substituted aromatic aldehydes, 2-naphthol and 2-amino-benzothiazole using sphalerite (ZnS) as a natural catalyst under solvent free conditions with good yield. All the synthesized products have been characterized by Melting point of the product, TLC, UV-visible, FTIR, ^{1}H NMR, ^{13}C NMR and mass spectral studies. The short reaction duration, high yield of the product, ease of work-up, no need of chromatography and no use of hazardous solvents make the method advantageous.

Keywords
Sphalerite, solvent-free, 2-Aminobenzothiazolomethyl naphthols, green catalyst

Introduction

Multi-component synthesis (MCS) is special type of organic synthesis in which designing of new drugs is based on the development of hybrid molecules by combining different pharmacophore fragments into a single structure, which may lead to compounds with interesting biological profile. As pathogenic bacteria continuously evolve the mechanism of resistance to currently used antibacterials, the discovery of novel and potent antibacterial drugs is the best way to overcome bacterial resistance and develop effective therapies[1]. Condensed heterocyclic systems are of considerable interest not only because of their potential biological activities, but also because of their versatility as synthones in organic transformations[2]. The literature survey has revealed that 2-amino benzothiazole and the compounds containing this moiety exhibit excellent biological activity[3-11]. 2-Amino-benzothiazolomethyl naphthol derivatives[12] have been reported by Shaabani et al., with drawbacks such as long reaction time and large quantity of catalyst at 90 ^{o}C. Kumar[13,14] et al. have also synthesized the target compounds with drawbacks like higher temperature, no recyclability of catalyst, larger mol% of catalyst, and comparatively long reaction time. However, Sphalerite was reported as a catalyst in C-H bond activation reactions[15]. Some other catalysts, such as trichloroisocyanuric acid[16], heteropolyacids[17], $NaHSO_4.H_2O$[18] and ionic liquid[19], have been used for the synthesis of 2-aminobenzothiazolomethyl naphthol derivatives, but these reported methods have suffered with one or more drawbacks like long duration, harsh reaction conditions, reusability of catalyst, hazardous solvent, ultrasonication conditions, etc. Although the ultrasonication technology has been shown feasible on a small scale, the commercialization of sonolysis is still a challenge due to its high energy requirement which makes ultrasonication an uneconomical technique[20].

Therefore, there is need to develop economically benign method to remove these drawbacks. In this way, multi-component reaction which exploits a catalyst under solvent-free conditions could reveal an ideal methodology, provided that the catalyst shows high catalytic activity under solvent-free conditions. Continuing our interest on multi-component synthesis[21-24] in the present communication, a rapid, efficient, environmentally benign and step economic synthesis of 2-aminobenzothiazolomethyl naphthol derivatives has been reported using Sphalerite as a catalyst.

Materials and methods

Experimental section

The ^{1}H and ^{13}C NMR spectra are recorded on BRUKER AVANCE II 400 NMR spectrometer using TMS as an internal standard at 20-25 ^{o}C; data for ^{1}H NMR are reported in chemical shift (ppm), IR spectra were recorded by SHIMADZU PRESTIGE 21, IR spectrometer of sample dispersed in KBr pellet is reported in terms of frequency of absorption (cm^{-1}). Mass spectra are recorder using an ion trap mass spectrometer (Model 6310 Agilent). Merck's pre-coated TLC plates were used. Melting points were determined in open capillaries and were uncorrected. 2-Naphthol and substituted aldehydes were purchased from Himedia Laboratory Pvt. Ltd., Mumbai, India and used as received, 2-amino benzothiazole was purchased from Sigma Aldrich.

One-pot three-component reaction

A 100 mL, three-necked, round bottom flask equipped with a thermometer and water condenser was charged Sphalerite as a catalyst. Substituted aromatic aldehydes (1 mmol), 2-naphthol (1 mmol), and 2-amino benzothiazole (1 mmol) were added in the above solution and resulting mixture was stirred at about 80-85 ^{o}C. The reaction was monitored by TLC. After completion of the reaction, the mixture was removed from the round bottom flask and recrystallized by ethanol 5 ml. No column chromatography was required for the purification of the targeted product.

Analytical data of some representative compounds

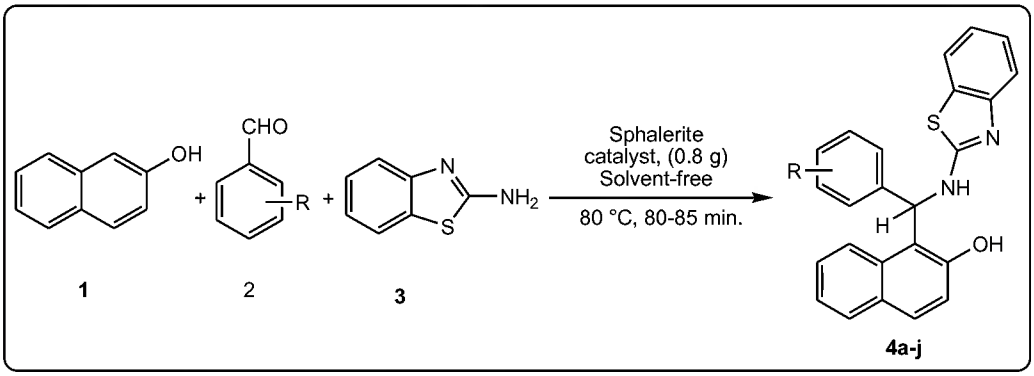
*1-(Benzo[d]thiazol-2-ylamino)(phenyl)methyl)naphthalene-2-ol (**4a**)*

White powder, mp 202-203 ^{o}C, IR (KBr) (υ_{max}, cm^{-1}): 3509, 3382, 1596, 1545, 1512, 1446 cm^{-1}; ^{1}H NMR (DMSO-d^{6}, 400 MHz): d = 6.96-7.93 (16H, m, 15H arom and 1H-CH), 8.67 (1H, s, NH), 10.11 (1H, s, OH); ^{13}C NMR (DMSO-d^{6}, 100 MHz): d = 53.36, 118.02, 118.57, 118.81, 120.49, 120.84, 122.27, 123.58, 125.23, 126.04, 127.83, 128.34, 128.56, 129.28, 130.59, 132.12, 142.25, 151.96, 153.19, 166.33; EIMS m/z 383.3 $C_{24}H_{18}N_{2}OS$ (calcd. 382.11).

Results and Discussion

2-aminobenzothiazolomethyl naphthol derivatives have been synthesized by one-pot three-component reaction of substituted aromatic aldehydes, 2-amino benzothiazole, and 2-naphthol using sphalerite as natural catalyst under solvent free conditions at 80 ^{o}C for about 80-85 min., (Scheme 1).

All the synthesized 2-aminobenzothiazolo-phenylmethyl-2-naphthol derivatives were characterized by m.p., FTIR, ^{1}H NMR, ^{13}C NMR, and mass spectral studies. FTIR spectra of all derivatives show peaks between 3200 and 3600 cm^{-1} due to N-H stretching, peak between 2864 and 2916 cm^{-1} due to C-Hstr of benzene ring, peak between 1500 and 1600 cm^{-1} may arise due to C=C str. A peak around 1400 and 1200 cm^{-1} can be assigned to N-H ben and C-N str, respectively.



Scheme 1. Synthesis of 2-aminobenzothiazolomethyl naphthol derivatives under solvent-free conditions

^{1}H NMR of compound 4a showed the multiplet between 6.96 and 7.93 ppm due to 16 hydrogen of which 15 hydrogen of aromatic rings and one aliphatic hydrogen of -CH. Singlet at 8.67 and 10.11 ppm arise due to hydrogen attached with nitrogen and hydroxyl group. Likewise, derivatives 4e, 4f,

and 4g show the singlet at 10.34 ppm for hydroxyl, singlet at 3.69 ppm due to methoxy and another singlet at 2.23 ppm for methyl substituent, respectively. In contrast, the ^{13}C NMR spectra of 2-aminobenzothiazolo-phenylmethyl-2-naphthol derivatives (4a and 4d) only consist of 20 peaks instead of 24 peaks. This was, however, expected as the chemical environment for (14, 10), (13, 11), (20, 23), and (21, 22). Derivatives 4f and 4g showed the corresponding peak for methoxy and methyl substitution at 67.47 and 20.60, respectively. Mass spectra of product 4a show the $[M+H]^+$ molecular ion peak at 383.3 and other fragments peak at 151 and 212 for corresponding fragments which are shown in the Fig. 2. This supports the probable structure of product 4a. All other derivatives exhibit the corresponding molecular ion and fragment peaks in mass spectra.

In order to study the best catalyst under similar conditions different catalysts were used and concluded that the best catalyst was sphalerite (Table 1). In order to evaluate the effect of catalyst loading, one-pot three component reaction of 2-amino benzothiazole, benzaldehyde and 2-naphthol was carried out using viz. 0.20 g, 0.40 g, 0.60 g, 0.80 g, 0.85 g, 0.90 g and 0.95 g sphalerite catalyst was used and found that 0.80 g catalyst was optimum catalyst for the above reaction, yield (93%) table 2 entry 4. There is no change in the yield of the higher quantity of the catalyst loading. Higher quantity of the catalyst neither increases the yield nor reduces the conversion time.

Table 1. Optimization of reaction catalyst[a]

Entry	Catalyst	Time (min.)	Yield (%)[c]
1	Sphalerite	80	93
2	$SnCl_2.2H_2O$	90	76
3	$NiNO_3.6H_2O$	90	81
4	Al_2O_3	95	86
5	$SrCl_2.6H_2O$	90	86
6	$CeCl_3.7H_2O$	90	85
7	$Cr(NO_3)_2.9H_2O$	95	81
8	$ZnCl_2$	95	84
9	$CuCl_2$	95	87

[a]*Reactions Conditions*: Benzaldehyde (1 mmol), 2-naphthol (1 mmol), and 2-amino-benzothiazole (1 mmol), Sphalerite (8 mg) catalyst, solvent-free for 90 min at 80 ^oC.
[c]Isolated yields.

Table 2. Effect of catalyst loading[a]

Entry	Catalyst Amount (g)	Yield (%)[b]
1	0.20	68
2	0.40	75
3	0.60	89
4	0.80	93
5	0.85	93
6	0.90	93
7	0.95	93

[a]*Reactions Conditions*: Benzaldehyde (1 mmol), 2-naphthol (1 mmol), and 2-amino-benzothiazole (1 mmol), sphalerite (0.8 g) catalyst, solvent-free for 90 min at 80 ^oC.
[b]Catalyst in mg.
[c]Isolated yields.

After the optimization of reaction catalyst and amount of catalyst loading, the best optimum temperature was also studied for this the above reaction was carried out at different temperature under similar conditions and observed that at 80 ^oC temperature give the high yield (93%) of the targeted product (Fig. 1). Further increasing the temperature did not show any significant effect on the yield and reaction time. So 80 ^oC was found to be the optimum temperature for the reaction.

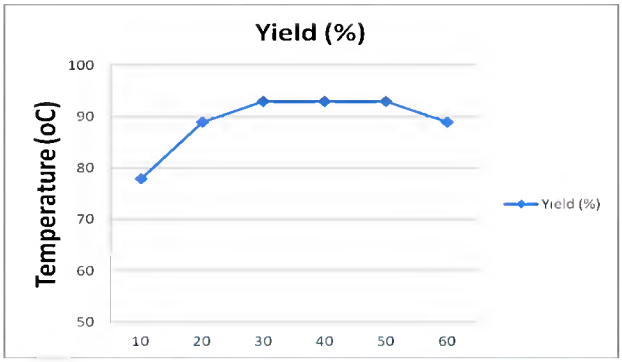


Figure 1. Effect of temperature on product yield

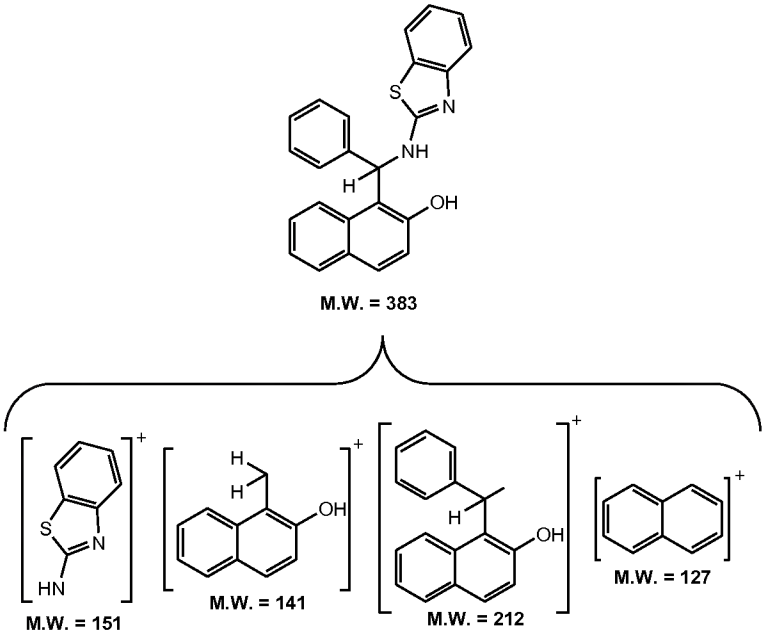


Figure 2. Fragmented ions of 1-(benzo[*d*]thiazol-2-ylamino)(phenyl)methyl)naphthalene-2-ol (**4a**)

Table 3. Synthesis of 2-aminobenzothiazolomethyl naphthol derivatives[a]

Entry	Compound	R	Time (min.)	Yield (%)[b]	R_f value[c]
1	**4a**	-H	80	93	0.67
2	**4b**	-$N(CH_3)_2$	80	91	0.63
3	**4c**	-3-OH	80	92	0.69
4	**4d**	-4-OH-3-OCH_3	85	91	0.57
5	**4e**	-2-OH	85	88	0.73
6	**4f**	-4-OCH_3	80	91	0.45
7	**4g**	-4-CH_3	85	89	0.65
8	**4h**	-4-Cl	80	87	0.59
9	**4i**	-3-NO_2	80	92	0.74
10	**4j**	-3-OH	80	90	0.54

[a]*Reactions Conditions*: Substituted aromatic aldehyde (1 mmol), 2-naphthol (1 mmol), and 2-amino-benzothiazole (1 mmol), sphalerite (0.8 g) catalyst, solvent-free for 80-85 min at 80 ^{o}C.

[b]Isolated yields.

[c]Rf values were determined in ethanol/carbon tetrachloride (70:30) ratio.

Advantage of this catalyst system over the other system is that catalyst is natural, easily available, cheap, non-toxic and no use of hazardous solvents, which is a critical issue from environment point of view. Low cost of the catalyst and no use of metal salts and solvent reduces the cost of production. Thus, considering the overall effects of reaction time, temperature, and catalyst loading, further scope of this system was tried. Results are summarized in Table 3 which shows that reaction performed efficiently and the yields of the synthesized products are good.

Conclusions

In conclusion, a rapid and environmentally benign method for the synthesis of 2-aminobenzothiazolo-phenylmethyl-2-naphthol derivatives has been developed using chitosamine hydrochloride as a non-toxic and green catalyst under solvent free conditions. The structure of the synthesized 2-aminobenzothiazolo-phenylmethyl-2-naphthol derivatives has been confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectra studies. The short reaction duration and ease of work-up make are the method advantageous.

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