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An efficient synthesis of 2-(Substituted–benzylsulfanyl)-benzothiazoles

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ABSTRACT

A simple and convenient procedure for the preparation of 2-(substituted–benzylsulfanyl)-benzothiazoles by the reaction of 2-mercaptobenzothiazole and and benzyl bromides in methanol /Na_2CO_3 condition has been reported. This new method consistently has the advantage of excellent yields (84-94%) and short reaction time (3 h) at reflux temperature.

KEYWORDS

2-Mercaptobenzothiazole;
Benzylbromides;
Sodium carbonate;
2-(Substituted-benzylsulfanyl)-benzothiazoles.

INTRODUCTION

Benzothiazoles and its derivaties are potentially biologically active compounds[1-4]. Due to wide biological significance, we wish to synthesize 2-(substituted–benzylsulfanyl)-benzothiazoles.2-(substituted–benzylsulfanyl)-benzothiazoles have been synthesized by the reaction of 2-mercaptobenzothiazole with benzyl halides in the presence of basses such as sodium in ethanol[5], CsF-Celite[6]. Dibenzyl carbonate in the presence catalytic amounts of DABCO[7], NaOH[8]. Many of these processes suffer from one or more limitations, such as long reaction times, occurrence of several side reactions, drastic reaction conditions, low yields, and tedious work-up procedure. Therefore, the search continues for a better reagent for the synthesis of 2-(substituted–benzylsulfanyl)-benzothiazoles in terms of mild reaction conditions. Now, we wish to report the synthesis of 2-(substituted–benzylsulfanyl)-benzothiazoles.

EXPERIMENTAL

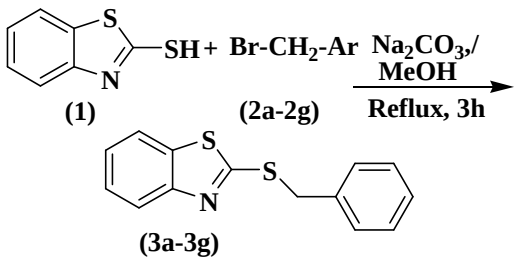
All chemicals were A.R.grade obtained from Qualigens, India. All the solvents were purified by standard techniques. Column chromatographic separations were carried out on silica gel 100-200 mesh size. I.R Spectra were scanned on FT/IR-4200 Type A, Spectrophotometer with Potassium bromide optics. NMR spectra were recorded on a 300 MHz and Mass spectra were recorded on a LC-MS.

General procedure for the synthesis of 2-(substituted–benzylsulfanyl)-benzothiazoles

A mixture of 2-mercaptobenzothiazole (1, 2 mmol), benzyl bromide (2a-2g, 2 mmol) and finely grounded anhydrous sodium carbonate (5 mmol) in methanol was stirred at reflux temperature for appropriate time (TABLE 1). The completion of reaction was monitored by TLC. After completion of reaction, evaporate the solvent and add 20 ml of ethyl acetate and water. The organic layer was concentrated and the crude product was purified by silica gel column chromatography using ethyl acetate – n-hexane (1:9) as eluent to afford the desired products **(3a-3g)**. Entry 1-7 spectral data is in full agreement with the reported literature[9]. Some of the compounds spectral data is given below.

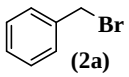
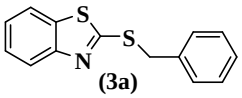
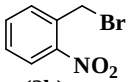
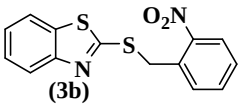
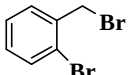
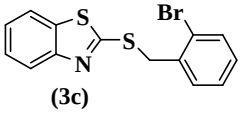
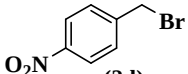
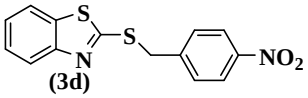
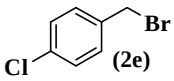
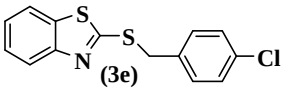
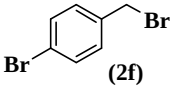
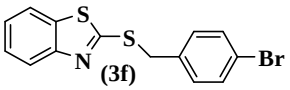
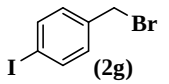
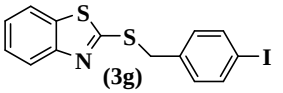
Entry 1 (3a)

White solid; m.p. 38-40^{0}C; IR(KBr): ν_{max} 3092, 3045,



SCHEME 1

TABLE 1: Synthesis of 2-(Substituted –benzylsulfanyl)-benzothiazoles

S.no.	Benzyl bromide	Product	Yield (%)[a]
1.	 (2a)	 (3a)	94
2.	 (2b)	 (3b)	93
3.	 (2c)	 (3c)	91
4.	 (2d)	 (3d)	92
5.	 (2e)	 (3e)	90
6.	 (2f)	 (3f)	88
7.	 (2g)	 (3g)	84

[a]Yields refer to the isolated yields

2920, 1495, 1454, 1309, 1240, 1124, 1070, 1019, 998 cm^{-1}; ^1H NMR ($CDCl_3$ /TMS): δ 4.62 (s, 2H), 7.24-7.34 (m, 4H), 7.40-7.46 (m, 3H), 7.80 (d, J=8.0Hz,1H), 7.90 (d, J=8.0Hz,1H); ms: m/z = 259; Anal. Calcd.for $C_{14}H_{11}NS_2$: C, 65.33; H, 4.30; N, 5.44. Found: C, 65.26; H,4.27; N, 5.35.

Entry 3 (3c)

Yellow solid; m.p. 40-42^{0}C; IR(KBr): ν_{max} 3065, 1558, 1455, 1427, 1309, 1262, 1026, 994 cm^{-1}; ^1H NMR ($CDCl_3$ /TMS): δ 4.72 (s, 2H), 7.12 (t, J=7.6Hz, 1H), 7.21 -7.30 (m, 2H), 7.42 (t, J=7.6Hz, 1H), 7.60 (dd, J=11.5 and 8.0Hz, 2H), 7.72 (t, J=8.0Hz, 1H), 7.90 (d, J=8.0Hz, 1H); ms: m/z=337; Anal. Calcd. for $C_{14}H_{10}BrNS_2$: C, 50.28; H, 3.10; N,4.15. Found: C, 50.20; H, 3.05, N, 4.05.

RESULTS AND DISCUSSION

Initially, we studied the synthesis of 2-(substituted–benzylsulfanyl)-benzothiazoles (3a,Ar=Ph), using 2-mercaptobenzothiazole(1) and benzyl bromide **(2a)** at reflux temperature in methnol in the presence of anhydrous sodium carbonate as base for 3 hours to get the 2-(substituted-benzylsulfanyl)-benzothiazoles in 94% yield. The product was identified with spectral data and by comparision with the authentic sample[9].

Similarily 2-mercaptobenzimidazoles was reacted with other substituted benzyl bromides **(2b-2g)** under similar conditions to give the corresponding 2-benzylthiobenzimidazoles **(3b-3g)** in excellent yields(TABLE 1).

All the products were characterised by I.R, ^1H-NMR, L.C-Mass and analytical data. 2-(substituted–benzylsulfanyl)-benzothiazoles are important class of heterocycles, and this methodology may find useful applications in the synthesis of drug intermediates and other bio active compounds. It is noteworthy which the survival of a variety of sensitive groups, worked well without formation of any side products under the reaction conditions.

CONCULSION

We have reported a convenient and useful methodology for the synthesis of 2-(substituted –benzylsulfanyl)-benzothiazoles in excellent yields. The advantage of this methodology is the use of very mild reaction conditions, which can tolerate various functional groups that can be used for further synthetic manipulations. Further, commericial availiability of large number of benzyl bromides or easy methods of their preparation makes this reaction a more attractive choice.

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