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Simple and convenient synthesis of 2-(Substituted-benzylsulfanyl)-1H-benzimidazoles

D.Shobha, M.Adharvana Chari, K.Mukkanti*

Dept. of Chemistry, Institute of Science and Technology, Jawaharlal Nehru Technological University, Hyderabad-500072, A.P., (INDIA)

E-mail : drmac_s@yahoo.com

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ABSTRACT

A simple and convenient procedure for the preparation of 2-(substituted – benzimidazoles by the reaction of 2-mercapto benzimidazole and benzyl bromides in methanol / sodium carbonate condition has been reported. This new method consistently has the advantage of excellent yields (87-95%) and short reaction time (3 h) at reflux temperature.

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KEYWORDS

2-Mercapto benzimidazole;
Benzyl bromides;
Sodium carbonate;
2-Benzylthiobenzimidazoles.

INTRODUCTION

Benzimidazoles and its derivaties are potentially biologically active compounds[1-5] some of them like thiobendazole, mebendazole and albendazole are widely used as anti-helimentic drugs[6]. Due to wide biological significance, we wish to synthesize 2-Benzylthiobenzi midazoles. 2-Benzylthiobenzimidazoles have been synthesized by the reaction of 2-mercapto benzimidaoles with alkyl or aryl halides in the presence of basses such as NaH/DMF[7], K_2CO_3/EtOH[5], NaOH/EtOH[8], NaOH[9], KOH[10]. 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-Benzylthiobenzimidazoles in terms of mild reaction conditions.

EXPERIMENTAL

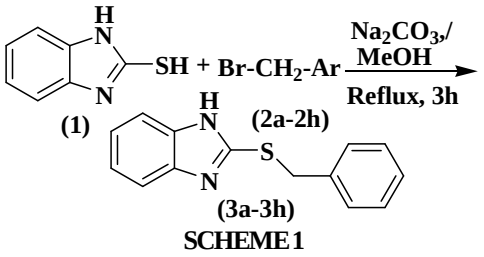
All chemicals were A.R.grade obtained from Qualigens, India. All the solvents were purified by standard techniques. Column chromatographic separations were carried out on silica gel 100-200 mesh size. I.R Spectra were scanned on FT/IR-4200 Type A, Spectrophotometer with Potassium bromide optics. NMR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

General procedure for the synthesis of 2-benzyl thiobenzimidazoles

A mixture of 2-mercaptobenzimidazole (1, 2 mmol), benzyl bromide (2a-2h, 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-3h)**. Entry 1-8 spectral data is in full agreement with the reported literature[11]. Some of the compounds spectral data is given below.

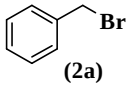
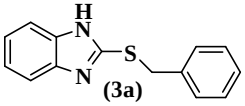
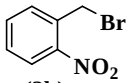
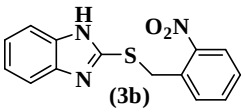
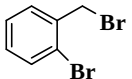
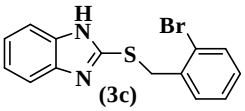
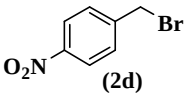
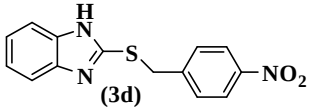
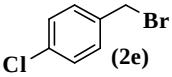
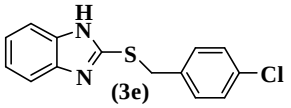
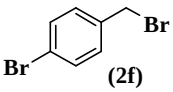
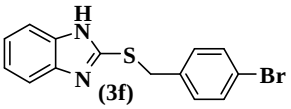
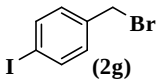
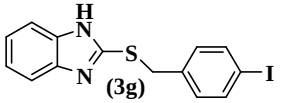
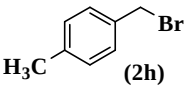
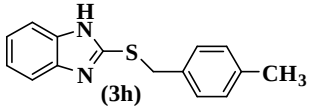
Entry 1 (3a): IR(KBr):ν_{max} 3069, 2963, 2811, 1619, 1513,1496, 1402, 1351, 1268, 1152, 1071, 1011, 980 cm^{-1}. ^1H NMR ($CDCl_3$+DMSO-d_6/TMS): δ 4.50 (S, 2H), 7.18-7.148 (m, 9H).

Entry 3 (3c):IR(KBr): ν_{max} 2736, 1632, 1509, 1402, 1268, 1228, 1044,1027,987 cm^{-1}. ^1H NMR ($CDCl_3$+DMSO-d_6/TMS): δ 4.69 (s, 2H), 7.08–7.20 (m, 4H), 7.43 (s, 3H), 7.49-7.55 (m, 1H).



SCHEME 1

TABLE 1

S.no.	Benzyl bromide	Product	Yield (%)[a]
1.	 (2a)	 (3a)	95
2.	 (2b)	 (3b)	92
3.	 (2c)	 (3c)	90
4.	 (2d)	 (3d)	92
5.	 (2e)	 (3e)	90
6.	 (2f)	 (3f)	88
7.	 (2g)	 (3g)	87
8.	 (2h)	 (3h)	90

[a]Yields refer to the Isolated yields

RESULTS AND DISCUSSION

Initially, we studied the synthesis of 2-benzylthio benzimidazoles (3a, Ar=Ph), using 2-mercapto benzimidazole **(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-benzylthiobenzimidazoles in 95% yield. The product was identified with spectral data and by comparision with the authentic sample[11].

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

All the products were characterised by I.R,^{1}H-NMR,L.C-Mass and analytical data. 2-Benzylthio benizimidazoles 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.

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