INTRODUCTION

Thioethers are very useful building blocks for the synthesis of various organosulfur compounds. They have various applications in organic synthesis, in bioorganic, medicinal and heterocyclic chemistry [1-3]. Thioethers can also act as safety-catch linker in peptide chemistry [4] and as useful heteroatomic functional groups in organic synthesis such as chiral sulfoxides that can be applied as auxiliaries in asymmetric synthesis [5]. Moreover, thioethers have been employed as sulfur-based ligands in transition metal complexes [6,7]. In this respect, a few number of synthetic methods for the preparation of thioether derivatives by the reaction of trialkylphosphites [8-11] in the presence of catalysts in organic solvents was reported. In continuation of our research concerning benzimidazoles [12-14], we report now the facile S-alkylation of 2-mercaptobenzimidazole derivatives with trialkylphosphite.

EXPERIMENTAL

All compounds were characterized by their \(^1\)H NMR and \(^{13}\)C NMR spectra as well as by microanalysis or HRMS spectra. NMR spectra were recorded on Bruker ARX 200 (200 MHz for \(^1\)H and 50.3 MHz for \(^{13}\)C) spectrometer (\(\delta\) ppm/TMS, J-Hz); for \(^{13}\)C NMR, the multiplicities were determined through DEPT. Mass spectra were recorded on a Varian MAT 311 spectrometer. Melting points were measured using a Köfler apparatus and were uncorrected. Column chromatography was carried out by use of silica gel 60 Merck (230-400 Mesh).

Reaction of \(o\)-phenylenediamines (1a-c) with carbon disulfide: \(o\)-Phenylenediamines (0.065 mol) was treated with carbon disulphide (0.095 mol) in alcohol (100 mL) for 3 h in the presence of sodium hydroxide (5 g). The carbon disulphide and alcohol were removed under reduced pressure and the residue was crystallized from aqueous alcohol (charcoal). The obtained solid was recrystallized in ethanol.

2-Mercaptobenzimidazole (2a): Yield = 81%; m.p. = 302 °C. \(^1\)H NMR (DMSO-d6): 7.10 (m, 2Har); 7.27 (m, 2Har); 12.42 (s, NH). \(^{13}\)C NMR (DMSO-d6): 119.43 (CH); 126.36 (CH); 138.82 (C); 167.12 (C). HRMS, \(m/z\): 150(M), calcd. for C6H6N2S: 150.02395, found: 150.0239.

5-Chloro-2-mercaptobenzimidazole (2c): Yield = 72%; m.p. = 290 °C. \(^1\)H NMR (DMSO-d6): 6.81 (d, \(J_{AB} = 7.9\) Hz, 1Har); 7.03 (q, \(J_{AX} = 7.9\) Hz, 1Har); 7.25 (d, \(J_{BX} = 7.9\) Hz, 1Har); 11.83 (s, NH). \(^{13}\)C NMR (DMSO-d6): 101.34 (CH); 109.64 (CH); 137.45 (C); 141.94 (C); 146.14 (C); 167.54 (C). HRMS, \(m/z\): 183(M), calcd. for C6H5ClN2S: 183.9962, found: 183.996.

Synthesis of 2-S-alkylbenzimidazoles: In a double walls flask, phosphorus oxychloride (0.095 mol) was added for 1 h

Improved Method of S-Alkylation of 2-Mercaptobenzimidazole Derivatives with Trialkylphosphite

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A new method of S-alkylation of 2-mercaptobenzimidazole derivatives has been developed by the condensation of these heterocycles with trialkylphosphite in the presence of phosphorus oxychloride giving the corresponding 2-S-alkylbenzimidazoles. The structure of the obtained products has been established by spectroscopic data.

Keywords: 2-Mercaptobenzimidazole, 2-S-alkylbenzimidazoles, Trialkylphosphite, Phosphorus oxychloride, S-alkylation.
Some papers have reported the alkylation of heteroatoms by triethyl phosphate as 1,2-dihydro-4H-3,1-benzothiazine-2,4-diones with N-substituted benzylamines and trialkyl phosphites lead to the mixture of the S-alkylation and phosphonate products which was recrystallized from ethanol.

2-S-Methylbenzimidazole (3a): Yield = 76%; m.p. = 198 °C. \(^1\)H NMR (DMSO-d_6): 2.79 (s, CH_3); 7.60 (d, J = 2.0 Hz, 1H); 8.09 (q, J = 3 Hz, 2H); 12.19 (s, NH). \(^1\)C NMR (DMSO-d_6): 12.53 (s, CH_3); 27.23 (CH_2); 113.59 (CH); 8.1 Hz, 1Har); 7.56 (d, J = 7.2 Hz, CH_3); 3.49 (s, CH_3); 6.91 (m, 4Har); 12.53 (s, CH_3); 113.59 (CH); 125.14 (CH); 133.78 (C); 142.03 (C); 155.63 (C). HRMS, m/z: 209(M), calcd. for C_9H_9N_3O_2S: 223.042, found: 223.041.

2-S-Ethyl-5-chlorobenzimidazole (3e): m.p. = 198 °C. \(^1\)H NMR (DMSO-d_6): 2.79 (s, CH_3); 7.60 (d, J = 2.0 Hz, 1H); 8.09 (q, J = 3 Hz, 2H); 12.19 (s, NH). \(^1\)C NMR (DMSO-d_6): 12.53 (s, CH_3); 27.23 (CH_2); 113.59 (CH); 8.1 Hz, 1Har); 7.56 (d, J = 7.2 Hz, CH_3); 3.49 (s, CH_3); 6.91 (m, 4Har); 12.53 (s, CH_3); 113.59 (CH); 125.14 (CH); 133.78 (C); 142.03 (C); 155.63 (C). HRMS, m/z: 209(M), calcd. for C_9H_9N_3O_2S: 223.042, found: 223.041.

2-S-Methyl-5-nitrobenzimidazole (3b): Yield = 65%; m.p. = 190 °C. \(^1\)H NMR (DMSO-d_6): 2.79 (s, CH_3); 7.60 (d, J = 2.0 Hz, 1H); 8.09 (q, J = 3 Hz, 2H); 12.19 (s, NH). \(^1\)C NMR (DMSO-d_6): 12.53 (s, CH_3); 27.23 (CH_2); 113.59 (CH); 8.1 Hz, 1Har); 7.56 (d, J = 7.2 Hz, CH_3); 3.49 (s, CH_3); 6.91 (m, 4Har); 12.53 (s, CH_3); 113.59 (CH); 125.14 (CH); 133.78 (C); 142.03 (C); 155.63 (C). HRMS, m/z: 209(M), calcd. for C_9H_9N_3O_2S: 223.042, found: 223.041.

2-S-Ethylbenzimidazole (3c): Yield = 83%; m.p. = 170 °C. \(^1\)H NMR (DMSO-d_6): 1.36 (t, J = 7.2 Hz, CH_3); 3.49 (q, J = 7.2 Hz, CH_3); 7.31 (m, 2Har); 7.66 (m, 2Har); 5.35 (s, NH). \(^1\)C NMR (DMSO-d_6): 12.53 (s, CH_3); 113.59 (CH); 125.14 (CH); 133.78 (C); 142.03 (C); 155.63 (C). HRMS, m/z: 178(M), calcd. for C_9H_7N_2S: 178.057, found: 178.057.

2-S-Ethyl-5-nitrobenzimidazole (3d): Yield = 65%; m.p. = 190 °C. \(^1\)H NMR (DMSO-d_6): 1.36 (t, J = 7.2 Hz, CH_3); 3.49 (q, J = 7.2 Hz, CH_3); 7.60 (d, J = 8.7 Hz, 1Har); 8.07 (q, J = 2.0 Hz, 1H); 12.53 (s, CH_3); 113.59 (CH); 8.1 Hz, 1Har); 7.56 (d, J = 7.2 Hz, CH_3); 3.49 (s, CH_3); 6.91 (m, 4Har); 12.53 (s, CH_3); 113.59 (CH); 125.14 (CH); 133.78 (C); 142.03 (C); 155.63 (C). HRMS, m/z: 178(M), calcd. for C_9H_7N_2S: 178.057, found: 178.057.

2-S-Ethyl-5-chlorobenzimidazole (3e): Yield = 59%; m.p. = 208 °C. \(^1\)H NMR (DMSO-d_6): 1.36 (t, J = 7.2 Hz, CH_3); 3.49 (q, J = 7.2 Hz, CH_3); 7.11 (d, J = 8.1 Hz, 1Har); 7.47 (q, J = 2.0 Hz, 1H); 12.73 (s, NH). \(^1\)C NMR (DMSO-d_6): 12.53 (s, CH_3); 110.65 (CH); 117.51 (CH); 121.44 (CH); 125.72 (C); 135.20 (C); 143.67 (C); 152.06 (C). HRMS, m/z: 212(M), calcd. for C_9H_9N_2S: 212.01750, found: 212.0175.

**RESULTS AND DISCUSSION**

Some papers have reported the alkylation of heteroatoms by triethyl phosphate as 1,2-dihydro-4H-3,1-benzothiazine-2,4-diones with N-substituted benzylamines and trialkyl phosphites lead to the mixture of the S-alkylation and phosphonate products with yield of 20%.

2-Mercaptobenzimidazoles are interesting starting compounds because of their chemical reactivity and biological activities. 2-Mercaptobenzimidazoles have been prepared by condensation of o-phenylenediamines with carbon disulphide in basic alcoholic solution [15,16] (Scheme-I). The structure of the new compounds 2(a-c) was confirmed by spectroscopic data (NMR, mass).

2-Mercaptobenzimidazoles 2(a-c) were treated with triethyl phosphate and a catalytic amount of POCl_3 in xylene (Scheme-II). The structure of the new compounds 3(a-f) was determined by NMR spectroscopy and mass spectrometry. NMR spectra showed the presence of an S-bound ethyl group which confirms the structure of the products 3(a-f).

Considering our thioether products 3(a-f) we assume that the nucleophilic sulfur of the one-thiol tautomer of compounds 2(a-c) attacks triethylphosphate at the electrophilic methylene carbon of the ethoxide residue (Scheme-III).

**Conclusion**

In this work, we describe a new and selective method of S-alkylation of 2-mercaptobenzimidazole derivatives by trialkyl phosphites. The pure target S-alkylbenzimidazoles were obtained in moderate to high yields (59-83%). Since benzimidazole derivatives are of versatile importance as drugs (e.g., proton pump inhibitors, anthelmints, fungicides) and dye components the described synthetic method will add significantly to the development of new functional S-alkylbenzimidazoles in future.
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