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Novel and Improved Method for the Synthesis of 2-mercaptobenzimidazole Derivatives

A. EL KIHEL[1]*, H. AIT SIR[1], S. JEBBARI[1], M. AHBALA[1], S. GUESMI[2] and P. BAUCHAT[3]

[1]Laboratoire de chimie bioorganique, Faculté des Sciences, BP20, 24000, El Jadida, Maroc.
[2]Laboratoire de Chimie de Coordination et d'Analytique, Faculté des Sciences, BP20, 24000, El Jadida, Maroc.
[3]Université de Rennes1, Sciences Chimiques de Rennes U.M.R.6226, ICMV, Campus de Beaulieu, Avenue Général Leclerc, 35042, Rennes, France
*Corresponding author E-mail: abdellatifelkihel@gmail.com

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ABSTRACT

2-mercaptobenzimidazole derivatives were synthesized by reaction of o-phenylenediamines with N-aminorhodanine. This reaction represent a new synthesis of 2-mercaptobenzazole. The structure of the obtained products was established by spectroscopic data.

Keywords: 2-mercaptobenzimidazole, o-phenylenediamines, N-aminorhodanine.

INTRODUCTION

Thiols are very useful building blocks for the synthesis of various organosulfur compounds: they have several applications in organic synthesis, in bioorganic, medicinal and heterocyclic chemistry[1]. Also, in addition to that, thiols can act as safety-catch linker in peptide chemistry[2]. Morever, thiols have been employed as sulfur-based ligands in transition metal complexes[3, 4]. In this respect, a number of synthetic methods for the preparation of thiol derivatives by the reaction of o-phenylendiamine with carbon disulphide[5, 9], thiourea[10, 11], O-isopropylxanthic acid potassium salt[12], 5-phenyl-1,3,4-oxadiazole-2(3H)-thione derivatives and N-phenylisothiocyanate[13], thiocyanic acid ammoniac salt[14]. In continuation of our research concerning benzimidazoles[15, 19]. The condensation of o-phenylenediamine with N-aminorhodanine was carried out.

Experimental section

General Procedure

O-phenylenediamines (0.065 mol) was heated with N-aminorhodanine (0.065 mol) in xylene (50 ml) for 5 hours. The obtained residue was filtered and was crystallized from aqueous alcohol (charcoal). The obtained solid was recrystallized in ethanol.

2-mercaptobenzimidazole 3a

Yield = 87 %; mp>250°C.1HNMR (DMSO-d6): 7.10 (m, 2Har); 7.27 (m, 2Har); 12.42 (s,NH).13CNMR (DMSO-d6): 119.43 (CH); 126.36 (CH); 138.82 (C); 167.12 (C=S). HRMS, m/z: 150(M), calcd for $C_7H_6N_2S$: 150.02517, found: 150.0251.

2-mercapto-5-nitrobenzimidazole 3b

Yield = 81 %; mp>250°C.1HNMR (DMSO-d6): 7.12 (d, JAB= 8.3Hz, 1Har); 7.29 (q, JBX=2.1Hz, JAB= 8.3Hz, 1Har); 7.46 (d, JBX= 2.1Hz, 1Har); 12.03 (s, NH).13CNMR (DMSO-d6):108.24 (CH); 113.46 (CH); 125.70 (CH); 137.45 (C); 141.94 (C); 148.01 (C); 167.54 (C=S).HRMS, m/z: 195(M), calcd for $C_7H_5N_3O_2S$: 195.01025, found: 195.0102.

2-mercapto-5-methylbenzimidazole 3c

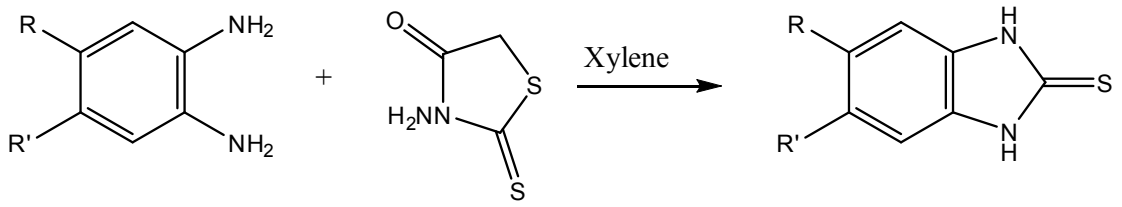
Yield = 83 %; mp>250°C. ^{1}HNMR (DMSO-d_6): 2.21(s, CH_3); 6.43 (d, JAB= 8.3Hz, 1Har); 6.83 (q, JBX=1.7Hz, JAB= 8.3Hz, 1Har); 7.05 (d, JBX= 1.7Hz, 1Har); 12.03 (s, NH). ^{13}CNMR (DMSO-d_6): 21.31 (CH_3); 109.50 (CH); 109.99 (CH); 123.49 (CH); 130.69 (C); 131.92 (C); 132.95 (C); 168.12 (C=S). HRMS, m/z: 164(M), calcd for $C_9H_8N_2S$: 164.04082, found: 164.0408.

5-chloro-2-mercaptobenzimidazole 3d

Yield = 79 %; mp>250°C. 1HNMR (DMSO-d6): 6.81 (d, JAB= 7.9Hz, 1Har); 7.03 (q, JBX=1.9Hz, JAB= 7.9Hz, 1Har); 7.25 (d, JBX= 1.9Hz, 1Har); 11.83 (s, NH).13CNMR (DMSO-d6):101.34 (CH); 109.64 (CH); 123.71 (CH); 135.54 (C); 140.84 (C); 146.14 (C); 165.24 (C=S). HRMS, m/z: 183(M), calcd for $C_7H_5ClN_2S$: 183.9962, found: 183.996.

5,6-dichloro-2-mercaptobenzimidazole 3e

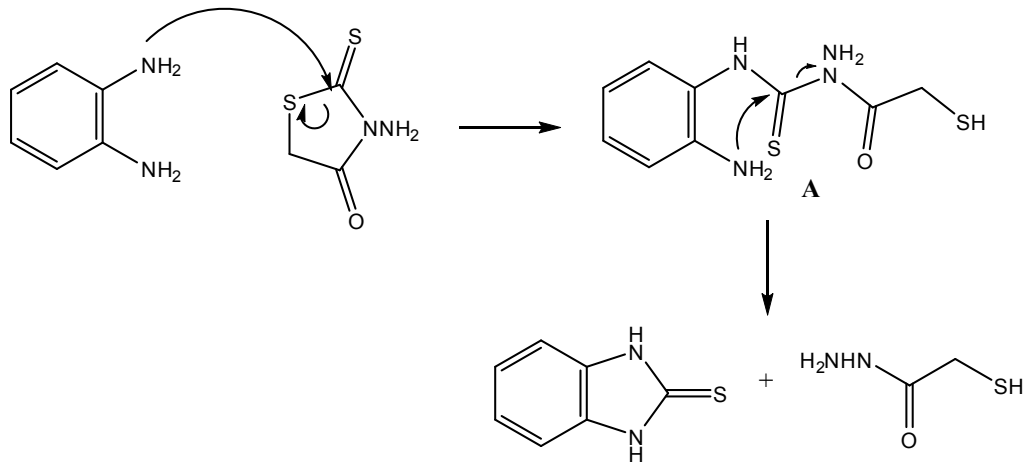
Yield = 75 %; mp>250°C. ^{1}HNMR (DMSO-d_6): 7.79 (s, 1Har); 11.82 (s, NH). ^{13}CNMR (DMSO-d_6): 128.60 (CH); 127.25 (C); 135.49 (C); 168.30 (C=S). HRMS, m/z: 217(M), calcd for $C_7H_4N_2S$: 217.94722, found: 217.9472.



1a-f
R=H, CH_3, Cl, NO_2
R'= H, CH_3, CL

2a-f
R=H, CH_3, Cl, NO_2
R'= H, CH_3, CL

Scheme 1: The reaction of 2-mercaptobenzimidazoles synthesis



Scheme 2: Proposed formation mechanism of the product

5,6-dimethyl-2-mercaptobenzimidazole 3f

Yield = 80 %; mp>250°C. ^{1}HNMR (DMSO-d_6): 2.32(s, CH_3); 7.02 (s, 1Har); 12.63 (s, NH). ^{13}CNMR (DMSO-d_6): 20.43 (CH_3); 111.00 (CH); 131.25 (C); 131.59 (C); 168.00 (C=S). HRMS, m/z: 178(M), calcd for $C_9H_{10}N_3S$: 178.05647, found: 178.0564.

RESULTS AND DISCUSSION

In this work, we report a novel method for synthesis of 2-mercaptobenzimidazole derivatives. 2- Mercaptobenzimidazoles are interesting starting compounds because of their chemical reactivity and biological activities. A mixture of o-phenylenediamines 1(a-g) and N-aminorhodanine in xylene was heated during 8 hours. (Scheme 1). The structure of the products 2(a-g) has been determined by NMR and mass data. 1HNMR spectra showed the presence of the signal of NH and the signal of the C=S was observed in 13CNMR spectra which confirms the structure of the products 2(a-g).

A possible mechanism for the formation of the 2-mercaptobenzimidazole (2a-g) is shown in scheme 2. The key step is at the intermediate A, in which the cyclization goes to the C=S group not to C=O group in order to lead to the benzotriazepine product. In the reaction, the only 2-mercaptobenzimidazole product was obtained (Scheme 2)

CONCLUSION

In this work, we developed a novel and improved method for 2-mercaptobenzimidazole derivatives by the condensation of o-phenylenediamines with N-aminorhodanine

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