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NOTE

Syntheses of Biologically Active Bisbenzimidazolylesulphone Derivatives

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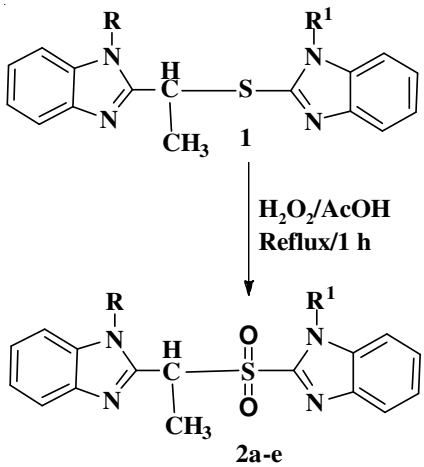
2-(1-Chloroethyl)-1*H*-benzimidazole on condensation with 2-mercaptobenzimidazole in methanol using triethylamine as a base under reflux for 3 h yielded 2-((1-(1*H*-benzimidazol-2-yl)ethyl)thio)-1*H*-benzimidazole which on alkylation using two equivalent of alkylating agent under phase transfer catalyst conditions give N,N'-dialkylbisbenzimidazole sulphides. Upon oxidation with H_2O_2 in acetic acid under reflux for 2 h gave N,N'-dialkylbisbenzimidazole sulphones which are analogues of prazoles.

Keywords: Benzimidazole, 2-Mercatpobenzimidazole, 2-Chloromethyl benzimidazole.

Benzimidazole group of substances has found to be a practical applications in several fields [1-5]. The interest in benzimidazole chemistry has been revived somewhat by the discovery of 5,6-dimethyl bnzimidazole moiety is part of the chemical structure of vitamin B_{12}. A large number of patents describe benzimidazole derivatives of use in textile industry [6-9] such as foaming or softening agents. 2-Mercapto benzimidazole and several benzimidazoles have been found to be use in the photographic industry and also antioxidant for rubber. The derivatives of benzimidazole acts as crucial role in medical field having pharmacological activities. Benzimidazolyl sulfones are most common structures in valuable such as pharmaceuticals and polymeric sciences. Sulfonylchlorides or sulfoanhydrides are general substrates employed in the Friedel-Crafts sulfonylation [10,11].

Melting points were determined in open capillaries in sulfuric acid bath and are uncorrected. Thin-layer chromatography (TLC) performed on precoated with silica gel glass plates GF-254. IR spectra were recorded on Jasca FT-IR 5300. ^{1}H NMR were recorded in $CDCl_3$/DMSO-d_6 using Varian 400 MHz instrument and Mass spectra were recorded on an Agilent LC-MS instrument giving only M^+ values in Q+1 mode.

Preparation of compounds 2a-e from 1: A mixture of compound **1** (5 mM), H_2O_2 (10 mM) and Acetic acid (20 mL) were refluxed for 2 h. At the end of this period, the reaction mixture was poured into ice-cold water. The separated solid was filtered, washed with water (2 × 10 mL) and dried to obtain crude compound **2**, which on recrystallization from a suitable solvent gave pure **2a-e** (**Scheme-I**). The physical data of all the compounds (**2a-e**) are given in Table-1.



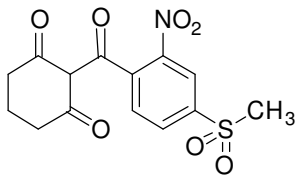
2a, R = R^1 = H, **2b**, R = R^1 = CH_3, **2c**, R = R^1 = C_2H_5, **2d**, R = R^1 = $PhCH_2$, **2e**, R = R^1 = *n*-Bu

Scheme-I: Synthesis of bisbenzimidazolyl sulphones

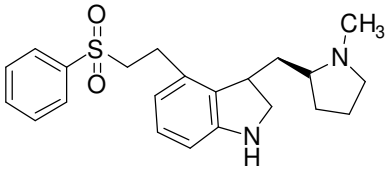
TABLE-1
PHYSICAL DATA OF THE SYNTHESIZED COMPOUNDS **2a-e**

S. No.	Substrate	Alkylating agnet	Product	Yield (%)	m.p. (°C)
1	1	–	**2a**	76	> 250
2	1	DMS	**2b**	72	> 250
3	1	DES	**2c**	74	> 250
4	1	$PhCH_2Cl$	**2d**	76	> 250
5	1	*n*-BuBr	**2e**	66	> 250

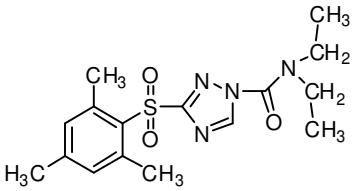
2-((1-(1*H*-Benzimidazol-2-yl)ethyl)sulfonyl)-1*H*-benzimidazole (2a): IR (KBr): No diagnostic peak in IR region



Mestrione (Herbicide)



Eletriptan (treatment of migraine)



Cafenstrole (Herbicide)

3500-3000 cm^{-1}, indicating absence of -NH group, 1336 (SO_2); ^1H NMR (400 MHz, DMSO-d_6/TMS): 1.72 (d, 3H, -$CHCH_3$), δ 3.76 (s, 3H, -NCH_3 of –$CHCH_3$Bz), 3.74 (s, 3H, -NCH_3 of -SBz), 3.89 (q, 1H, -$CHCH_3$), 6.76-7.59 (complex, m, 8H, aryl protons); MS (CI): *m/z* 323 [M^++1].

2-((1-(1-Methylbenzimidazol-2-yl)ethyl)sulfonyl)-1-methylbenzimidazole (2b): IR (KBr): No diagnostic peak in IR region 3500-3000 cm^{-1}, indicating absence of -NH group, 1336 (SO_2); ^1H NMR (400 MHz, DMSO-d_6/TMS): 1.72 (d, 3H, -$CHCH_3$), δ 3.76 (s, 3H, -NCH_3 of –$CHCH_3$Bz), 3.74 (s, 3H, -NCH_3 of -SBz), 3.89 (q, 1H, -$CHCH_3$), 6.76-7.59 (complex, m, 8H, aryl protons); MS (CI): *m/z* 323 [M^++1].

2-((1-(1-Ethylbenzimidazol-2-yl)ethyl)sulfonyl)-1-ethylbenzimidazole (2c): IR (KBr): No diagnostic peak in IR region 3500-3000 cm^{-1}, indicating absence of -NH group, 1342 (SO_2); ^1H NMR (400 MHz, DMSO-d_6/TMS): δ 1.28 (m, 2H, -NCH_2 of ethyl of-$CHCH_3$Bz), 1.59 (m, 2H, -NCH_2 of ethyl of -SBz), 1.68 (d, 3H, -$CHCH_3$), 3.77 (t, 3H, -CH_3 of ethyl of -$CHCH_3$Bz), 3.83 (m, 1H, -$CHCH_3$), 3.86 (s, 3H, -CH_3 of ethyl of -SBz), 6.58-7.63 (complex, m, 8H, aryl protons); MS (CI): *m/z* 351 [M^++1].

2-((1-(1-Benzylbenzimidazol-2-yl)ethyl)sulfonyl)-1-benzylbenzimidazole (2d): IR (KBr): No diagnostic peak in IR region 3500-3000 cm^{-1}, indicating absence of -NH group, 1336 (SO_2); ^1H NMR (400 MHz, DMSO-d_6/TMS): δ 1.72 (d, 3H, -$CHCH_3$), 3.89 (m, 1H, -$CHCH_3$), 4.69 (s, 2H, -NCH_2 of benzyl of-$CHCH_3$Bz), 5.25 (s, 2H, NCH_2 of benzyl of -SBz), 7.27-8.36 (complex, m, 18H, 10 aromatic benzyl + 8H aryl protons); MS (CI): *m/z* 475 [M^++1].

2-((1-(1-(*n*-Butyl)benzimidazol-2-yl)ethyl)sulfonyl)-1-(*n*-butyl)benzimidazole (2e): IR (KBr): No diagnostic peak in IR region 3500-3000 cm^{-1}, indicating absence of -NH group, 1338 (SO_2); ^1H NMR (400 MHz, DMSO-d_6/TMS): δ 1.26 (t, 2H, -NCH_2 of butyl of –$CHCH_3$Bz), 1.65 (m, 2H, -NCH_2CH_2 of butyl of-$CHCH_3$Bz), 1.70 (d, 3H, -$CHCH_3$), 2.54 (m, 2H, -$NCH_2CH_2CH_2$ of butyl of-$CHCH_3$Bz), 3.72 (t, 3H, -$NCH_2CH_2CH_2CH_3$ of butyl of-$CHCH_3$Bz), 1.45 (t, 2H, -NCH_2 of butyl of SBz), 1.79 (m, 2H, -NCH_2CH_2 of butyl of-SBz), 2.68 (m, 2H, -$NCH_2CH_2CH_2$ of butyl of-SBz), 3.85 (t, 3H, -$NCH_2CH_2CH_2CH_3$ of butyl of-SBz), 6.68-7.68 (complex, m, 8H, aryl protons), 3.92 (m, 1H, -$CHCH_3$); MS (CI): *m/z* 407 [M^++1].

2-(1-Chloroethyl)-1*H*-benzimidazole on condensation with 2-mercaptobenzimidazole in methanol using triethylamine (TEA) as a base under reflux for 3 h gave 2-((1-(1*H*-benzimidazol-2-yl)ethyl)thio)-1*H*-benzimidazole. This on methylation using two equivalent of dimethylsulphate in dimethylformamide (DMF) as a solvent and K_2CO_3 as a base using tetrabutylammonium bromide (TBAB) as phase transfer catalyst at room temperature for 3 h gave previously reported [12] N,N'- dimethylbisbenzimidazolesulphide. Using this strategy, the reactions of N,N'-dimethylbisbenzimidazolesulphide was also performed with two equivalents of each of diethyl sulphate, benzyl chloride and *n*-butyl bromide to obtain previously reported [12] N,N'-diethylbisbenzimidazolesulphide, N,N'-dibenzylbisbenzimidazolesulphide and N,N'- dibutylbisbenzimidazolesulphide respectively. N,N'-Dialkylbisbenzimidazole sulphides (**1**) was treated with hydrogen peroxide in acetic acid under reflux for 2 h gave N,N'-dialkylbisbenzimidazole sulphones (**2**). The structures of **2** have been established on the basis of IR, ^1H NMR and LC-MS (Q+1) spectral data.

Conclusion

In this work, a mild and simple method for the synthesis of a variety of substituted bisbenzimidazole sulphones have been developed. All the compounds having biologically active compounds especially which are analogues to pyrazoles.

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