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BENZAZOLES

5*. SYNTHESIS AND ARYLSULFONYLATION OF 1-HYDROXYMETHYLBENZIMIDAZOLE

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1-Hydroxymethylbenzimidazole was synthesized by the reaction of benzimidazole with formaldehyde. Arylsulfonylation of the former in the presence of triethylamine occurred anomalously with deformylation to give 1-arylsulfonylbenzimidazoles in place of the expected 1-arylsulfonyloxymethyl-benzimidazoles.

Keywords: 1-arylsulfonylbenzimidazoles, 1-hydroxymethylbenzimidazole, arylsulfonylation, hydroxy-methylation, deformylation.

The increased interest in benzimidazole derivatives is explained by their high biological activity and a broad spectrum of effects [2-7]. In this series, pharmacologically active substances were discovered [2-4] as well as fungicides, herbicides, and plant growth regulators [5-7].

We have previously studied the interaction of 2-alkylbenzimidazoles with arylsulfonyl chlorides to give 1-arylsulfonylbenzimidazoles [8]. The present work is devoted to the synthesis and arylsulfonylation of 1-hydroxymethylbenzimidazole.

1-Hydroxymethylbenzimidazole (**2**) was synthesized by the reaction of benzimidazole (**1**) with formaldehyde. The reaction of compound **2** with arylsulfonyl chlorides **3a-j** in the presence of triethylamine gave the 1-arylsulfonylbenzimidazoles **5a-j** instead of the expected 1-arylsulfonyloxymethylbenzimidazoles **4a-j**.

Compounds **5a-j** may be formed by two routes (A, B). In route A, the starting compound **2** underwent deformylation to give compound **1** which reacted with the arylsulfonyl chlorides **3a-j** to produce compounds **5a-j**. To test the possibility of this decomposition we have studied the behavior of compound **2** in the absence of arylsulfonyl chlorides. However, in all cases, compound **2** was recovered unchanged. This shows that the reaction of compound **2** with arylsulfonyl chlorides by route A does not occur and the reaction evidently goes *via* route B.

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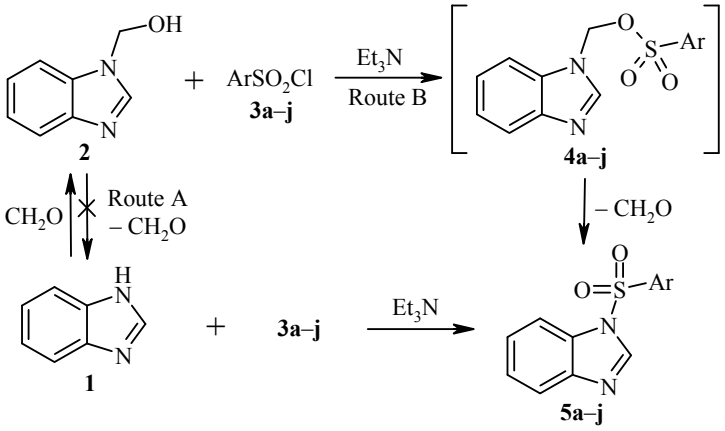

3–**5** **a** Ar = Ph, **b** Ar = 4-MeC_6H_4, **c** Ar = 4-$MeOC_6H_4$, **d** Ar = 4-(*t*-Bu)C_6H_4, **e** Ar = 4-ClC_6H_4, **f** Ar = 3-$O_2NC_6H_4$, **g** Ar = 4-$MeCONHC_6H_4$, **h** Ar = 2,4-$Me_2C_6H_3$, **i** Ar = 3,4-$Me_2C_6H_3$, **j** Ar = 2,4,6-$Me_3C_6H_2$

It should be noted that in the reaction of 3-hydroxymethylbenzoxazolin-2-ones with 3,4,5-trimethoxybenzoyl chloroanhydride, acylation occurs "normally", i.e., at the hydroxyl group [9]. Therefore it can be proposed that in the case of compounds **4a-j** a O→N rearrangement with simultaneous splitting off the formyl group is possible. This anomalous behavior of compound **2** requires further investigation.

Compounds **5a-j** were also prepared by counter synthesis from compound **1** and the arylsulfonyl chlorides in the presence of triethylamine.

The structures of the synthesized compounds **5a-j** were confirmed by IR, ^{1}H NMR, and mass spectroscopy and counter synthesis. The Table 1 contains the yields of compounds **5a-g,i,j** obtained *via* method B, their physicochemical properties, and literature data for these substances prepared by other methods [8, 10-14].

TABLE 1. Physicochemical Characteristics of Compounds **5a-g,i,j**, synthesized by method B.

Compound	Empirical formula	Found, N % / Calculated, N %	Mp*, °C	Yield, %
5a	$C_{13}H_{10}N_2O_2S$	11.03 / 10.85	104-106 (105-106 [10-12])	53
5b	$C_{14}H_{12}N_2O_2S$	10.02 / 10.29	86-88 (86-88 [8, 11])	62
5c	$C_{14}H_{12}N_2O_3S$	10.01 / 9.72	92-94 (92-94 [8])	54
5d	$C_{17}H_{18}N_2O_2S$	9.13 / 8.91	127-128 (127-128 [8])	53
5e	$C_{13}H_9ClN_2O_2S$	9.73 / 9.57	126-128 (125-127 [8])	63
5f	$C_{13}H_9N_3O_4S$	14.09 / 13.85	158-160 (159-160 [13, 14])	72
5g	$C_{15}H_{13}N_3O_3S$	13.61 / 13.32	200-202 (196-198 [14])	56
5i	$C_{15}H_{14}N_2O_2S$	9.68 / 9.78	115-117 (115-117 [8])	51
5j	$C_{16}H_{16}N_2O_2S$	8.98 / 9.33	117-119 (120-122 [8])	61

* Recrystallization solvents: ethanol (compounds **5a-f,i,j**), 40% aqueous ethanol (compound **5g).**

Thus, arylsulfonylation of 1-hydroxymethylbenzimidazole was accompanied by deformylation, leading to the formation of 1-arylsulfonylbenzimidazoles in place of the expected 1-arylsulfonyloxymethyl-benzimidazoles.

EXPERIMENTAL

IR spectra of nujol mulls were recorded with a Perkin-Elmer 2000 spectrometer. ^{1}H NMR spectra were recorded with a Unity +400 (400 MHz) spectrometer with TMS as internal standard. Mass spectra were recorded with a Kratos MS 30 instrument with direct injection of the sample into the ion source (ionization energy 70 eV). The progress of reactions and the purity of the synthesized compounds were monitored by TLC on Silufol UV-254 plates with 10:1 benzene–acetone eluent and development with 1 g $KMnO_4$ in 4 ml H_2SO_4 and 96 ml H_2O.

1-Hydroxymethylbenzimidazole (2). 33% Formaldehyde (1.5 ml, 15 mmol) was added to a solution of compound **1** (1.18 g, 10 mmol) in ethanol (20 ml) and heated at 75-85°C on a water bath for 2 h, the solvent was evaporated, and the residue was recrystallized from benzene. Yield 1.15 g (78%); mp 144-146°C. ^{1}H NMR spectrum (CD_3OD), δ, ppm (*J*, Hz): 7.99 (1H, s, H-2); 7.54 (2H, m H-4,5); 7.21 (2H, m, H-6,7), 4.61 (2H, s, CH_2), 4.23 (1H, br. s, OH). Found, %: C 65.06; H 5.58; N 19.12. $C_8H_8N_2O$. Calculated, %: C 64.85; H 5.44; N 18.91.

1-Arylsulfonylbenzimidazoles 5a-j (General Method). Synthesis from compound **2**. A solution of compound **2** (1.48 g, 10 mmol) and triethylamine (1.11 g, 11 mmol) in acetone (30 ml) was added dropwise to a solution of arylsulfonyl chloride **3a-j** (11 mmol) in acetone (20 ml). The reaction mixture was stirred at room temperature for 4 h, the acetone was then evaporated and water (50 ml) was added to the residue. The obtained precipitation of the product **5a-j** was filtered off and recrystallized from the corresponding solvent (Table 1).

Compounds **5a-j** were also obtained by an analogous method from benzimidazole (**1**) (1.18 g, 10 mmol) [8].

Mixed samples of compounds **5a-j** obtained from compounds **1** and **2** showed no depression of the melting points.

1-(2',4'-Dimethylbenzenesulfonyl)benzimidazole (5h). Yield 1,86 g (65%); mp 66-68°C. IR spectrum, ν, cm^{-1}: 1365 (SO_2 asym), 1168 (SO_2 sym). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.35 (1H, s, H-2); 7.94 (1H, d, $J_{4,5}$ = 8.1, H-4); 7.66 (1H, m, H-5); 7.46 (1H, m, H-6); 7.21 (2H, m, H-5',6'); 7.06 (1H, dd, $J_{7,6}$ = 8.1, $J_{7,5}$ = 1.9, H-7); 6.92 (1H, s, H-3'); 2.33 (3H, s, 2'-CH_3); 2.19 (3H, s, 4'-CH_3). Mass spectrum, *m/z* (I_{rel}, %): 286 $[M]^+$ (61), 169 (100), 117 (43). Found, %: N 10.06. $C_{15}H_{14}N_2O_2S$. Calculated, %: N 9.78.

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