Chemistry of Heterocyclic Compounds, Vol. 41, No. 7, 2005

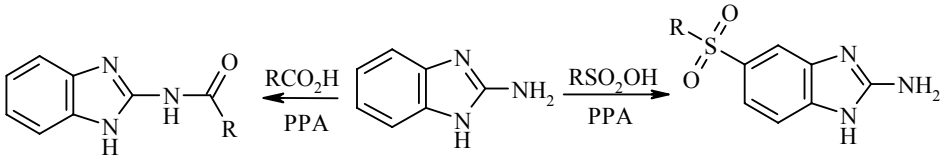
SYNTHESIS OF 5(6)-ARENESULFONYL DERIVATIVES OF 2-AMINOBENZIMIDAZOLE IN POLYPHOSPHORIC ACID

E. B. Mel'nikova[1], M. M. El'chaninov[1], and B. S. Lukyanov[2]

Keywords: 2-aminobenzimidazole, arenesulfonic acid, polyphosphoric acid, protonation.

Despite the explosive growth of 2-aminobenzimidazole chemistry, some of its substitution reactions have been insufficiently studied.

An indirect method was described earlier for obtaining 2-arenesulfonyl aminobenzimidazoles by heating *o*-phenylenediamine with arenesulfonyl guanidines [1]. Then it was found that 2-aminobenzimidazoles react with arenesulfonyl chlorides at the NH group of the imidazole ring [2]. We attempted to synthesize 2-arenesulfonyl aminobenzimidazoles by using arenesulfonic acids (TsOH, $PhSO_2OH$) in polyphosphoric acid (PPA) at 160-180°C. However, the reaction unexpectedly occurred at the benzene ring, and we obtained 5(6)-arenesulfonyl derivatives **2,3** in high yields (76-82%). Under analogous conditions, using sulfuric acid we synthesized 5(6)-sulfonic acid **4**. We also established that reaction of 2-aminobenzimidazole under the same conditions with carboxylic acids ($MeCO_2H$, $PhCO_2H$) leads exclusively to 2-acylamino derivatives **5, 6**.



5, **6** **1** **2–4**

2, **6** R = Ph, **3** R = *p*-MeC_6H_4, **4** R = OH, **5** R = Me

Such regioselective orientation of the reaction allows us to hypothesize that in the first case, double protonation of compound **1** occurs with strong acids, deactivating the amino group, while the latter reacts as a base when treated with weaker carboxylic acids.

Thus for the first time we have demonstrated the possibility of reaction of 2-aminobenzimidazole with arenesulfonic acids at the benzene ring.

The ^{1}H NMR spectra were recorded in DMSO-d_6 (400 MHz), internal standard TMS.

2-Amino-5(6)-benzenesulfonylbenzimidazole (2). A solution of 2-aminobenzimidazole (1.33 g, 10 mmol) in polyphosphoric acid (PPA) (20 g) was heated at 160-180°C until completely homogenized, and then sodium benzenesulfonate (1.8 g, 10 mmol) was added. The mixture was heated at that temperature for another 30 min with vigorous stirring and then was poured into water (100 ml) and neutralized with an ammonia

[1] South Russian State Technical University, Novocherkassk 346428; e-mail: fkoh@novoch.ru.
[2] Scientific Research Institute of Physical and Organic Chemistry, Rostov State University, Rostov-on-Don 344090, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 1105-1107, July, 2005. Original article submitted March 13, 2005.

 0009-3122/05/4107-0938©2005 Springer Science+Business Media, Inc.

solution, and then the precipitate was filtered out. To purify the precipitate, it was dissolved in a 10% aqueous solution of sodium hydroxide, boiled with activated charcoal, and neutralized with hydrochloric acid to pH 8; compound **3** precipitated as cream-colored flakes. Yield 2.07 g (76%); mp 239-241°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.45 (2H, s, NH_2); 7.14 (1H, d, *J* = 8.3, H-7); 7.40 (1H, d, *J* = 8.3, H-6); 7.52 (1H, s, H-4); 7.64 (3H, m, H-3,4,5 arom.); 7.82 (2H, d, *J* = 6.8, H-2,6 arom.); 10.92 (1H, br. s, NH). Found, %: C 56.85; H 4.19; N 15.60. $C_{13}H_{11}N_3O_2S$. Calculated, %: C 57.13; H 4.06; N 15.37.

2-Amino-5(6)-tosylbenzimidazole (3) was obtained as for compound **2**, from compound **1** (1.33 g, 10 mmol) and *p*-toluenesulfonic acid (1.72 g, 10 mmol). Yield 2.35 g (82%); mp 259-261°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.36 (3H, s, CH_3); 6.48 (2H, s, NH_2); 7.15 (1H, d, *J* = 8.3, H-7); 7.30 (2H, d, *J* =8.7, H-3,4 arom.); 7.38 (1H, d, *J* = 8.3, H-6); 7.57 (1H, s, H-4); 7.72 (2H, d, *J* = 8.7, H-2,5 arom.); 10.94 (1H, br. s, NH). Found, %: C 58.87; H 4.69; N 14.35. $C_{14}H_{13}N_3O_2S$. Calculated, %: C 58.52; H 4.56; N 14.62.

2-Amino-5(6)-sulfonylbenzimidazole Hydrosulfate (4) was obtained as for compound **2**, from compound **1** (1.33 g, 10 mmol) and sulfuric acid (*d* 1.84) (1.47 g, 15 mmol), but the sulfonic acid was separated in a different way. The reaction mass was poured into water (100 ml). Upon cooling with ice, colorless crystals of compound **4** precipitated, which were crystallized from water. Yield 1.96 g (63%); mp >350°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.25 (1H, d, *J* = 8.2, H-7); 7.48 (1H, d, *J* = 8.2, H-6); 7.58 (1H, s, H-4); 8.40 (2H, s, NH_2); 12.38 (2H, br. s, NH). Found, %: N 13.88. $C_7H_9N_3O_7S_2$. Calculated, %: N 13.50.

2-Acetylaminobenzimidazole (5) was obtained as for compound **2**, from compound **1** (1.33 g, 10 mmol) and acetic acid (1.2 g, 20 mmol) at 140°C. The crude reaction product was crystallized from 2-propanol. Yield 1.52 g (87%); mp 310-311°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.15 (3H, s, CH_3); 7.00 (2H, m, H-6,7); 7.40 (2H, m, H-4,5); 11.78 (1H, br. s, NH); 11.48 (1H, br. s, NH). Found, %: C 62.02; H 4.97. $C_9H_9N_3O$. Calculated, %: C 61.70; H 5.18.

2-Benzoylaminobenzimidazole (6) was obtained as for compound **5**, from compound **1** (1.33 g, 10 mmol) and benzoic acid (2.44 g, 20 mmol) at 160-180°C. Yield 1.82 g (77%); mp 287-288°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.03 (2H, dd, *J* = 6.4, H-6,7); 7.40 (2H, dd, *J* = 6.4, H-4,5); 7.52 (3H, m, H-3,4,5 arom.); 8.18 (2H, d, *J* = 6.8, H-2,6 arom.); 12.12 (2H, br. s, NH). Found, %: C 71.13; H 4.32. $C_{14}H_{11}N_3O$. Calculated, %: C 70.87; H 4.67.

This work was carried out with the financial support of grant 04-03-32485 of the Russian Foundation for Basic Research.

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