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LETTERS TO THE EDITOR

SYNTHESIS OF [1,2,3]TRIAZOLO-[4',5':4,5]PYRIMIDO[1,6-*a*]BENZIMIDAZOLE, A NEW HETEROCYCLIC SYSTEM

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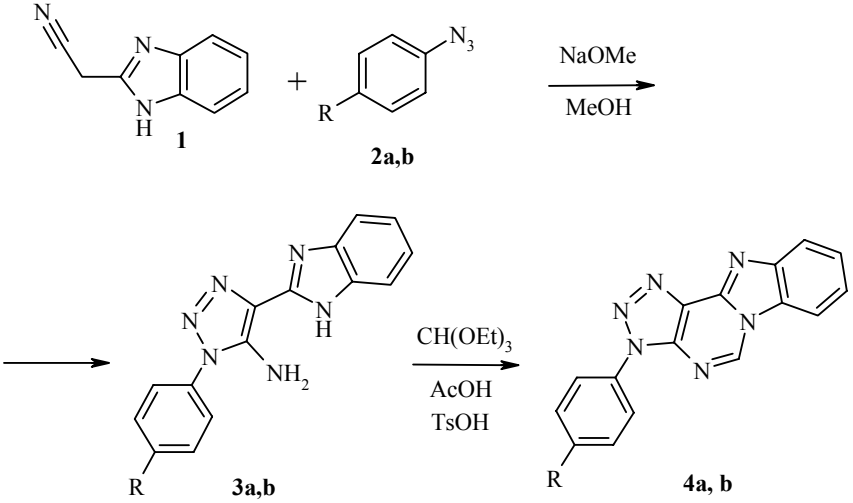
Benzimidazole derivatives are used in medicine as antiulcer, antihypertonic, antivirus, antifungal, antineoplastic, antihistaminic, and anthelmintic agents [1-3]. Biological activity is also found for imidazo[1,2-*a*]pyrimidine [4-9] and triazolo[4,5-*d*]pyrimidine [10-16]. In the present work, we propose a convenient method for the synthesis of a new polynuclear system, namely, [1,2,3]triazolo[4',5':4,5]pyrimido-[1,6-*a*]benzimidazole, in which the above-mentioned fragments are combined.

Derivatives of 1H-1,2,3-triazole are formed upon the cycloaddition of aryl azides to CH-acids [17]. However, the reactions of azides with nitriles possessing an active methylene group have not been studied sufficiently.



a R = Br, **b** R = NO_2

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We assumed that 1H-benzimidazol-2-ylacetonitrile **1** would react as readily as the analog, 1,3-benzotriazol-2-ylacetonitrile, for which the reaction time is 1-2 min and the yield of triazoles is more than 80%.

However, our experiments showed that the yields of **3a** and **3b** in the reaction of nitrile **1** with aryl azides are lower (52 and 68%). The reaction time was longer and an additional equivalent of base was required. This discrepancy may be a result of stabilization of the carbanion of **1** due to possible charge delocalization involving the nitrogen atom in the 1H-benzimidazole system and competing reactions.

The existence of two nucleophilic sites in amines **3** (NH_2 and NH) may be exploited to form a new ring. We have found that closure to form a pyrimidine ring proceeds rather readily upon the reaction of aminotriazoles **3a** and **3b** with ethyl orthoformate. Benzimidazoles **4a** and **4b** are obtained in good yields despite the low reactivity of the amino group deactivated by the electron-withdrawing effect of the triazole ring. Analogous 1-aryl-4-(thiazolyl)- and 1-aryl-4-(benzthiazolyl)-1H-1,2,3-triazol-5-ylamines and methyl 5-amino-1-aryl-1H-1,2,3-triazole-4-carboxylates do not react with ethyl orthoformate in acetic acid. In the case of formation of benzimidazoles **4a** and **4b**, the reaction probably starts with attack of ethyl orthoformate at the nitrogen atom in the benzimidazole fragment. Subsequent reaction of the resultant adduct with the amino group in the thiazole ring leads to the formation of an aromatic system.

Thus, our approach permits the synthesis of representatives of a new heterocyclic system, namely, [1,2,3]triazolo[4',5':4,5]pyrimido[1,6-*a*]benzimidazoles by variation of the substituents in azides **2**, 1H-benzimidazole, and the orthoester.

The ^{1}H NMR spectra were taken on a Varian Unity +400 spectrometer at 400 MHz in DMSO-d_6 with TMS as the internal standard. The mass spectra were taken on an Agilent 1100LC/MSD unit with chemical ionization.

4-(1H-Benzimidazol-2-yl)-1-(4-bromophenyl)-1H-1,2,3-triazol-5-ylamine (3a). 1H-Benzimidazol-2-ylacetonitrile **1** (1.57 g, 0.01 mol) and aryl azide **2a** (0.01 mol) were added with vigorous stirring to a solution of sodium methylate prepared from sodium (0.5 g) and methanol (20 ml). The mixture was stirred at room temperature until a precipitate formed. The precipitate was filtered off and recrystallized from ethanol–DMF to give **3a** in 52% yield; mp 237-238°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.71 (2H, s, NH_2); 7.10-7.13 (2H, m, H_{Bim}-6,5); 7.44-7.47 (1H, m, H_{Bim}-4); 7.54-7.56 (1H, m, H_{Bim}-7); 7.67 (2H, d, J = 8.8, H_{Ar}-3,5); 7.77 (2H, d, J = 8.8, H_{Ar}-2,6); 12.83 (1H, s, H_{Bim}-1). Mass spectrum, *m/z*: 356 $[M+H]^+$. Found, %: C 50.64; H 3.22; N 23.48. $C_{15}H_{11}BrN_6$. Calculated, %: C 50.72; H 3.12; N 23.65.

4-(1H-Benzimidazol-2-yl)-1-(4-nitrophenyl)-1H-1,2,3-triazol-5-ylamine (3b) was synthesized analogously in 68% yield using 4-nitrophenyl azide **2b**; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.99 (2H, s, NH_2); 7.10-7.17 (2H, m, H_{Bim}-6,5); 7.50-7.55 (2H, m, H_{Bim}-4,7); 8.05 (2H, d, J = 8.8, H_{Ar}-2,6); 8.46 (2H, d, J = 8.8, H_{Ar}-3,5). Mass spectrum: 322 $[M+H]^+$. Found, %: C 55.89; H 3.56; N 30.47. $C_{15}H_{11}N_7O_2$. Calculated, %: C 56.07; H 3.45; N 30.52.

3-(4-Bromophenyl)-3H-[1,2,3]triazolo[4',5':4,5]pyrimido[1,6-*a*]benzimidazole (4a). Acetic acid (40 ml) and toluenesulfonic acid (0.2 g) were added with stirring to a suspension of compound **3** (50 mmol) in ethyl orthoformate (25 ml) and heated for 4 h at 95-100°C. A precipitate formed. The mixture was cooled to room temperature. The precipitate and recrystallized from ethanol–DMF to give **4a** in 80% yield; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.54 (1H, t, J = 8.0, H_{Bim}-9); 7.62 (1H, t, J = 8.0, H_{Bim}-8); 7.89 (2H, d, J = 8.8, H_{Ar}-3,5); 7.95 (1H, d, J = 8.0, H_{Bim}-7); 8.17 (2H, d, J = 8.8, H_{Ar}-2,6); 8.45 (1H, d, J = 8.0, H_{Bim}-10); 10.03 (1H, s, H_{Py}-5), Mass spectrum, *m/z*: 366 $[M+H]^+$. Found, %: C 52.47; H 2.40; N 23.13. $C_{16}H_9BrN_6$. Calculated, %: C 52.62; H 2.48; N 23.01.

3-(4-Nitrophenyl)-3H-[1,2,3]triazolo[4',5':4,5]pyrimido[1,6-*a*]benzimidazole (4b) was synthesized analogously in 88% yield; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.58 (1H, t, J = 8.0, H_{Bim}-9); 7.65 (1H, t, J = 8.0, H_{Bim}-8); 7.99 (1H, d, J = 8.0, H_{Bim}-7); 8.49 (1H, d, J = 8.0, H_{Bim}-10); 8.58 (4H, br. s, C_6H_4), 10.07 (1H, s, H_{Py}-5). Mass spectrum: 332 $[M+H]^+$. Found, %: C 57.90; H 2.53; N 29.47. $C_{16}H_9N_7O_2$. Calculated, %: C 58.01; H 2.74; N 29.60.

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