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2-AMINO-3-AROYL-1-(2-BENZIMIDAZOLYL)-INDOLIZINES IN THE SYNTHESIS OF NEW HETEROCYCLIC SYSTEMS

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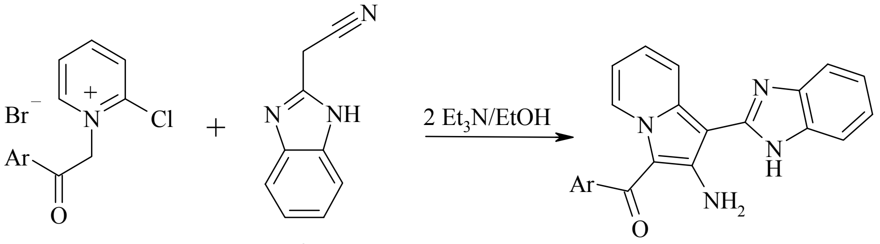
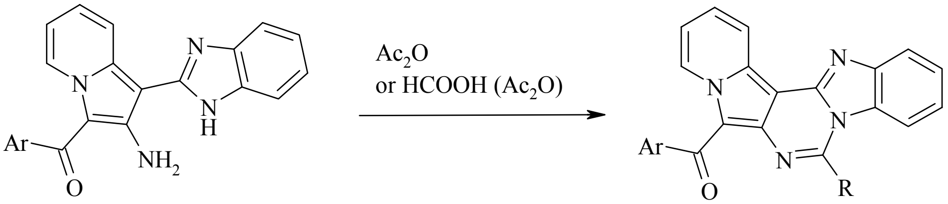
In a previously developed method [1] we obtained 1-(2-benzimidazolyl)indolizines **3a,b** from the salts **1a**,**b** and 2-benzimidazolylacetonitrile (**2**).



1a,b **2** **3a,b**

3 a Ar = Ph, **b** Ar = 4-MeOC$_6$H$_4$

On boiling the imidazolines **3a,b** in acetic anhydride or formic acid, with the addition acetic anhydride as water removing medium [2, 3] we obtained the new heterocyclic systems indolizino[2′,1′:4,5]pyrimido-[1,6-*a*]benzimidazoles **4a-c** [4].



3a,b **4a–c**

4 a Ar = Ph, R = Me, **b** Ar = 4-MeOC$_6$H$_4$, R = Me, **c** Ar = 4-MeOC$_6$H$_4$, R = H

In the IR and ^{1}H NMR spectra of compounds **4a-c** the signals of the amino and imino groups, which are sharply visible in the spectra of compounds **3a,b,** are extinguished. The protons H-8 and H-10 of compounds **3a,b and 4a-c** respectively are moved to weak field in the ^{1}H NMR spectra which probably indicates non-bonding interactions with the nitrogen atom of the imidazole ring.

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^{1}H NMR spectra of DMSO-d$_6$ solutions with TMS as internal standard were recorded with a Bruker DPX 200 (200 MHz) instrument, while IR spectra of nujol mulls were recorded on an IKS-40 spectrometer. Mass spectra were recorded on a Varian 1200 L (70 eV) instrument. Purity of substances were tested by TLC on Silufol UV-254 plates with 3:5 acetone–hexane eluent and developed with iodine vapor.

Indolizines **3a,b** were prepared by method [1].

2-Amino-1-(2-benzimidazolyl)-3-benzoylindolizine (3a). Yield 30%; mp 249-250°C. IR spectrum, ν, cm^{-1}: 3488 (NH), 3308, 3166, 3132 (NH$_2$), 1696 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.97 (1H, s, NH); 9.57 (1H, d, *J* = 7.4, H-5); 8.12 (1H, d, *J* = 8.8, H-8); 7.37-7.58 (8H, m, H$_{arom}$); 7.06-7.11 (2H, m, H$_{arom}$); 6.85 (1H, t, *J* = 7.4, H-6); 6.39 (2H, br. s, NH$_2$). Mass spectrum (EI), *m/z* ($I_{rel,}$%): 352 [M]$^+$ (100). Found, %: C 74.89; H 4.51; N 16.00. $C_{22}H_{16}N_4O$. Calculated, %: C 74.97; H 4.58; N 15.91.

2-Amino-1-(2-benzimidazolyl)-3-(4-methoxy)benzoylindolizine (3b). Yield 85%; mp. 235-237°C. IR spectrum, ν, cm^{-1}: 3446 (NH), 3300, 3174, 3104 (NH$_2$), 1682 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.95 (1H, s, NH); 9.47 (1H, d, *J* = 6.9, H-5); 8.11 (1H, d, *J* = 8.8, H-8); 7.60 (2H, d, *J* = 8.6, H-2'$_{arom,}$6'$_{arom}$); 7.38-7.48 (3H, m, H$_{arom}$); 7.02-7.11 (4H, m, H$_{arom}$); 6.82 (1H, t, *J* = 6.9, H-6); 6.45 (2H, br. s, NH$_2$); 3.89 (3H, s, CH$_3$O). Mass spectrum (EI), *m/z* (I_{rel}, %): 3.82 [M$^+$] (100). Found, %: C 72.31; H 4.67; N 14.75. $C_{23}H_{18}N_4O_2$. Calculated, %: C 72.22; H 4.75; N 14.66.

Preparation of Compounds 4a,b (General Method). The corresponding compound **3** (0.001 mmol) was boiled in acetic anhydride (10 ml) for 3h. After 15-25 min a yellow precipitate began to separate from the boiling acetic anhydride. After cooling the reaction mixture, the precipitate was filtered off, washed consecutively with acetic acid (2×5 ml) and ethanol (2×10 ml) and dried with hexane.

1-Benzoyl-3-methylindolizino[2',1':4,5]pyrimido[1,6-*a*]benzimidazole (4a). Yield 95%; mp 298°C. IR spectrum, ν, cm^{-1}: 1662 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.08 (1H, d, *J* = 6.8, H-13); 8.55 (1H, d, *J* = 8.5, H-10); 8.05 (1H, d, *J* = 7.1, H-5); 7.78-7.89 (4H, m, H$_{arom}$); 7.40-7.63 (6H, m, H$_{arom}$); 2.84 (3H, s, CH$_3$). Mass spectrum (EI), *m/z (*I_{rel}, %): 376 [M]$^+$ (100). Found, %: C 76.49; H 4.36; N 14.80. $C_{24}H_{16}N_4O$. Calculated, %: C 76.57; H 4.29; N 14.89.

1-(4-Methoxybenzoyl)-3-methylindolizino[2',1':4,5]pyrimido[1,6-*a*]benzimidazole (4b). Yield 94%; mp 294-295°C. IR spectrum, ν, cm^{-1}: 1684 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.83 (1H, d, *J* = 6.5, H-13); 8.38 (1H, d, *J* =8.3, H-10); 7.89-7.94 (3H, m, H$_{arom}$); 7.82 (1H, d, *J* = 7.8, H-8); 7.63 (1H, t, *J* = 6.5, H-12); 7.48 (1H, t, *J* = 8.3, H-11); 7.31 (2H, m, H-6,7); 7.05 (2H, d, *J* = 8.7, H-3'$_{arom}$, 5'$_{arom}$); 3.90 (3H, s, CH$_3$O); 2.79 (3H, s, CH$_3$). Mass spectrum (EI), *m/z* (I_{rel}, %): 406 [M]$^+$ (100). Found, %: C 73.94; H 4.38; N 13.85. $C_{25}H_{18}N_4O_2$. Calculated, %: C 73.86; H 4.47; N 13.79.

1-(4-Methoxybenzoyl)indolizino[2',1':4,5]pyrimido[1,6-*a*]benzimidazole (4c). Indolizine **3b** (0.38 g, 0.001 mmol) was boiled in formic acid (8 ml) and acetic anhydride (2 ml) for 2 h.. On the following day the precipitate was filtered off, washed sequentially with acetic acid (5 ml) and ethanol (2×10 ml), and dried with hexane. Yield 57%; mp 284°C. IR spectrum, ν, cm^{-1}: 1668 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.90 (1H, d, *J* = 7.1, H-13); 9.59 (1H, s, H-3); 8.58 (1H, d*, J* = 8.3, H-10); 8.25 (1H, d, *J* = 8.1, H-5); 7.78-7.89 (4H, m, H$_{arom}$); 7.41-7.52 (3H, m, H$_{arom}$); 7.06 (2H, d, *J* = 8.8, H-3'$_{arom}$, 5'$_{arom}$). Mass spectrum (EI), *m/z* (I_{rel},%): 392 [M]$^+$ (100). Found, %: C 73.51; H 4.20; N 14.23. $C_{24}H_{16}N_4O_2$. Calculated, %: C 73.44; H 4.11; N 14.29.

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