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NOVEL SYNTHESIS OF THE 2-BENZAZEPINE SYSTEM

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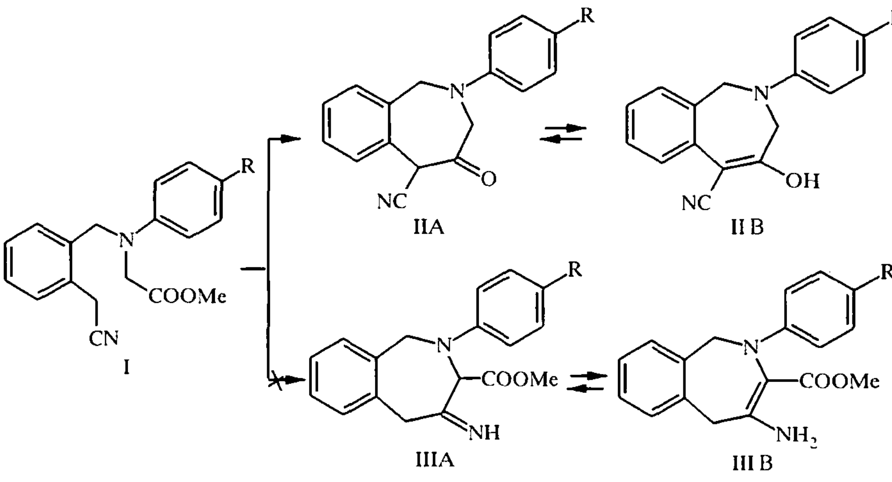
Several substances that include the 2-benzazepine moiety possess useful properties [1]. Therefore, it seems timely to develop new syntheses of functionally substituted 2-benzazepines. The present work proposes a new method for constructing the 2-benzazepine system based on intramolecular acylation of the acetonitrile methylene group in methyl N-(2-cyanomethylbenzyl)-N-arylglycines I.



I, II, III R = H (a), Me (b), Br (c)

The starting materials are prepared in high yield by alkylation of N-arylglycines methyl esters with *o*-bromomethylphenylacetonitrile in *iso*-propanol in the presence of NaOAc upon heating for 8-10 h.

Compound Ia; mp 107°C (propan-2-ol). PMR spectrum ($CDCl_3$): 7.1-7.6 (6H, m, Ar–H); 6.6-7.0 (3H, m, Ar–H); 4.60 (2H, s, $COCH_2N$); 3.98 (2H, s, Ar–CH_2–N); 3.76 (2H, s, CH_2CN); 3.68 ppm (3H, s, OCH_3). Found, %: C 73.26; H 6.04; N 9.72. $C_{18}H_{18}N_2O_2$. Calculated, %: C 73.45; H 6.16; N 9.52.

Compound Ib; mp 112°C (propan-2-ol). PMR spectrum ($CDCl_3$): 7.25-7.50 (4H, m, Ar–H); 7.07 (2H, d, Ar–H); 6.69 (2H, d, Ar–H); 4.56 (2H, s, $COCH_2N$); 3.93 (2H, s, Ar–CH_2–N); 3.77 (2H, s, CH_2CN); 3.66 (3H, s, OCH_3); 2.25 ppm (3H, s, Ar–CH_3). Found, %: C 73.87; H 6.39; N 9.31. $C_{19}H_{20}N_2O_2$. Calculated, %: C 74.00; H 6.54; N 9.08.

Compound Ic; mp 96°C (propan-2-ol). PMR spectrum ($CDCl_3$): 7.2-7.6 (6H, m, Ar–H); 6.62 (2H, d, Ar–H), 4.57 (2H, s, $COCH_2N$); 3.96 (2H, s, ArCH_2–N); 3.72 (2H, s, CH_2CN); 3.69 ppm (3H, s, OCH_3). Found, %: C 57.79; H 4.52; N 7.62; Br 21.67. $C_{18}H_{17}BrN_2O_2$. Calculated, %: C 57.92; H 4.59; N 7.51; Br 21.41. IR spectra of Ia-c (KBr): 2240 (C≡N), 1745 (C=O), 1200 cm^{-1} (C–O).

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The esters I were cyclized by heating in methanol containing sodium methoxide for 1-1.5 h with subsequent treatment with water and acidification of the reaction mixture with acetic acid. The cyclization could lead to two tautomers: the ketone (A) and the enol (B). The IR spectra exhibit strong bands near 2200 (C≡N), 3160 (br., OH), and 1610 cm^{-1} (C=C). This suggests that these compounds in the solid state are 2-aryl-4-hydroxy-2,3-dihydro-1H-2-benzazepine-5-carbonitriles (IIB). Obviously they also exist in this form in DMSO-d_6 solution. Thus, the PMR spectra recorded in this solvent contain two two-proton singlets in the range 4.47-4.52 and 4.56-4.60 ppm ($C\underline{H}_2$–N–CH_2), a one-proton broad singlet at 11.56-11.63 ppm (O–H) that disappears in D_2O, and a complicated multiplet of aromatic protons (and a singlet near 2.10 ppm for IIb).

Compound IIa; mp 163°C (propan-2-ol). PMR spectrum (DMSO-d_6): 11.6 (1H, s, OH); 6.5-7.5 (9H, m, Ar–H); 4.60 (2H, s, N–CH_2); 4.51 (2H, s, N–CH_2). Found, %: C 78.09; H 5.51; N 10.86. $C_{17}H_{14}N_2O$. Calculated, %: 77.84; H 5.38; N 10.68.

Compound IIb; mp 145°C (propan-2-ol). PMR spectrum (DMSO-d_6): 11.6 (1H, s, OH); 7.0-7.5 (4H, m, $C_{(6-9)}$–H); 6.91 (2H, d, $C_{(3')}$–H, $C_{(5')}$–H); 6.64 (2H, d, $C_{(2')}$–H, $C_{(6')}$–H); 4.57 (2H, s, N–CH_2); 4.47 (2H, s, N–CH_2), 2.10 (3H, s, Ar–CH_3). Found, %: C 78.11; H 5.76; N 10.24. $C_{18}H_{16}N_2O$. Calculated, %: C 78.24; H 5.84; N 10.14.

Compound IIc; mp 163°C (propan-2-ol). PMR spectrum (DMSO-d_6): 11.6 (1H, s, OH); 7.0-7.5 (6H, m, Ar–H); 6.72 (2H, d, $C_{(2')}$–H, $C_{(6')}$–H); 4.59 (2H, s, N–CH_2); 4.52 (2H, s, N–CH_2). Found, %: C 59.72; H 3.81; N 8.35; Br 23.54. $C_{17}H_{13}BrN_2O$. Calculated, %: C 59.84; H 3.84; N 8.21; Br 23.42.

The spectral data of the synthesized compounds also rule out consideration of them as products III of the alternative cyclization involving the nitrile of the cyanomethyl and the methylene of the glycine, no matter which of the two theoretically possible tautomers they might be, the imine A or the enamine B.

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REFERENCE

1. S. Kasparek, *Adv. Heterocycl. Chem.*, **17**, 45 (1974).