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LETTERS TO THE EDITOR

N-Substituted Imines of Hexafluoroacetone and Methyl Trifluoropyruvate in Cyclocondensation with 2-Aminobenzimidazole

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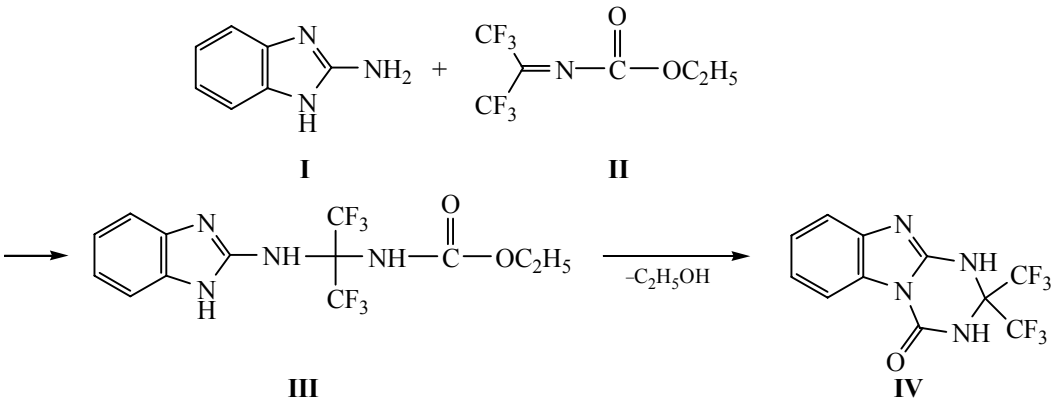
Cyclocondensation of *N*-substituted imines of hexafluoroacetone and methyl trifluoropyruvate with 1,3-binucleophiles (e.g., 2-aminopyridines [1, 2], 2-aminothiazolines [1, 3], 2-aminothiazoles [1], amidines [4], *N*-substituted ureas [5, 6]) afforded trifluoromethyl-containing five- and six-membered heterocycles.

The present report concerns the cyclocondensation of ethoxycarbonylimine of hexafluoroacetone **II** and methyl trifluoropyruvate acylimines **Va–Vd** with 2-aminobenzodiazole **I**, 1,3-binucleophile containing the guanidine moiety. Imines **II** and **Va–Vd** reacted with 2-aminobenzodiazole **I** under heating. The reaction proceeds through initial addition of binucleophile to the highly electrophilic C=N bond and subsequent heterocyclization with ethanol or methanol release. Reaction of hexafluoroacetone ethoxycarbonylimine **II** with 2-aminobenzodiazole **I** afforded ethyl [1-(1*H*-benzimidazol-2-yl)amino-2,2,2-trifluoro-1-trifluoromethylethyl]carbamate **III**. The latter was heated in DMF at 90°C for 2 h to give 2,2-bis(trifluoromethyl)-2,3-dihydro-1*H*-benzo[4,5]imidazo[1,2-*a*][1,3,5]triazin-4-one **IV** in 74% yield (Scheme 1).

The cyclocondensation of methyl trifluoropyruvate acylimines **Va–Vd** with 2-aminobenzodiazole **I** was carried out without isolating adducts by heating an equimolar mixture of reactants in DMF at 90°C for 2 h. The reaction products were *N*-(2-trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)amides **Va–Vd**.

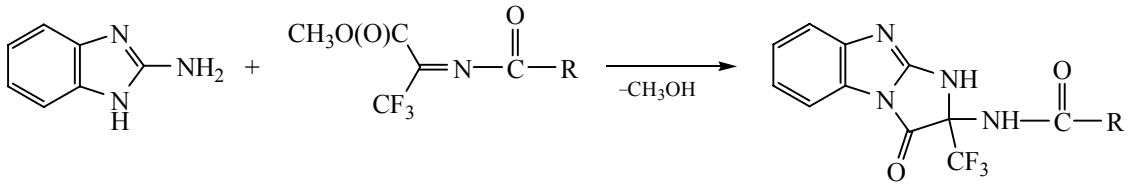
The synthesized 2,2-bis(trifluoromethyl)-2,3-dihydro-1*H*-benzo[4,5]imidazo[1,2-*a*][1,3,5]triazin-4-one **IV** and *N*-(2-trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)amides **VIa–VId** are colorless crystalline substances. Their NMR spectra

Scheme 1.



I **II** **III** **IV**

Scheme 2.



I **Va–Vd** **VIa–VId**

V, VI: R = *i*-C_3H_7 (**a**), 3-CH_3-C_6H_4 (**b**), 2-F-C_6H_4 (**c**), 4-F-C_6H_4 (**d**).

contained characteristic signals. The signal of CF_3-group in the ^{19}F NMR spectrum of **IV** appears at –2.16 ppm; in the case of compounds **VIa–VId** this signal lies in the range of 1.83–2.66 ppm (Scheme 2).

Hence the cyclocondensation of 2-amino-benzoimidazole with *N*-substituted imines of hexafluoroacetone and methyl trifluoropyruvate resulted in trifluoromethyl-containing benzo[4,5]imidazo[1,2-*a*]-[1,3,5]triazin-4-one and 2,3-dihydro-1*H*-imidazo-[1,2-*a*]benzimidazol-2-ylamides.

Ethyl [1-(1*H*-benzimidazol-2-yl)amino-2,2,2-trifluoro-1-trifluoromethylethyl]carbamate (III). To a suspension of 5 mmol of compound **I** in 10 mL of benzene was added 5 mmol of **II** while stirring at 20°C. The reaction mixture was stirred for 1 h at 50°C, then cooled, and evaporated. The residue was recrystallized from hexane. Yield 1.6 g, 86%, mp > 300°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.06 t (3H, Me, *J* 7.1 Hz), 3.94 q (2H, CH_2O, *J* 7.2 Hz), 6.78–6.91 m (2H, CH_{Ar}), 6.97–7.12 m (2H, CH_{Ar}), 6.38 (1H, NH), 8.36 (1H, NH), 10.44 (1H, NH). ^{19}F NMR spectrum (DMSO-d_6): δ_F 3.68 ppm. Found, %: C 42.38; H 3.49; N 15.31. $C_{13}H_{12}F_6N_4O_2$. Calculated, %: C 42.17; H 3.27; N 15.13.

2,2-Bis(trifluoromethyl)-2,3-dihydro-1*H*-benzo-[4,5]imidazo[1,2-*a*][1,3,5]triazin-4-one (IV). A solution of 5 mmol of compound **III** in 10 mL of DMF was heated for 2 h at 90°C, then cooled, and poured into 50 mL of water. The precipitate was recrystallized from 50% EtOH. Yield 1.2 g, 74%, mp 304–306°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 6.90–7.18 m (3H, CH_{Ar}), 7.70 d (1H, CH_{Ar}, *J* 7.7 Hz), 9.92 s (1H, NH), 11.81 (1H, NH). ^{19}F NMR spectrum (DMSO-d_6): δ_F –2.16 ppm. Found, %: C 40.58; H 1.66; N 17.51. $C_{11}H_6F_6N_4O$. Calculated, %: C 40.76; H 1.87; N 17.28.

***N*-(2-Trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)isobutyramide (VIa)** was prepared similarly. Yield 1.2 g, 76%, mp 264–266°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.77 d (3H, Me, *J* 7.1 Hz), 0.90 d (3H, Me, *J* 7.1 Hz), 2.59 m (1H, CH), 7.06–7.19 m (3H, CH_{Ar}), 7.43 t (1H, CH_{Ar}, *J* 5.9), 10.11 s (1H, NH), 12.74 br.s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6): δ_F 1.83 ppm. Found, %: C 51.73; H 3.84; N 17.31. $C_{17}H_{13}F_3N_4O_2$. Calculated, %: C 51.55; H 4.02; N 17.17.

3-Methyl-*N*-(2-trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)benzamide (VIb) was obtained similarly. Yield 72%, mp 251–253°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.07 s (3H, Me), 7.12–7.27 m (1H, CH_{Ar}), 7.30–7.38 m (1H, CH_{Ar}), 7.43–7.53 m (6H, CH_{Ar}), 10.75 s (1H, NH), 13.04 br.s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6): δ_F 2.20 ppm. Found, %: C 57.62; H 3.32; N 15.18. $C_{18}H_{13}F_3N_4O_2$. Calculated, %: C 57.76; H 3.50; N 14.97.

***N*-(2-Trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)-2-fluorobenzamide (VIc)** was prepared similarly. Yield 69%, mp 230–232°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 6.86–7.15 m (5H, CH_{Ar}), 7.19–7.42 m (3H, CH_{Ar}), 10.59 s (1H, NH), 12.85 br.s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 2.12 (3F, CF_3), from –35.53 to –35.60 m (1F, CF_{Ar}). Found, %: C 53.72; H 2.42; N 14.60. $C_{17}H_{10}F_4N_4O_2$. Calculated, %: C 53.98; H 2.66; N 14.81.

***N*-(2-Trifluoromethyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazol-2-yl)-4-fluorobenzamide (VId)** was prepared similarly. Yield 72 %, mp 269–271°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.08–7.20 m (2H, CH_{Ar}), 7.22–7.37 m (3H, CH_{Ar}), 7.41–7.49 m (1H, CH_{Ar}), 7.82–7.98 m (1H, CH_{Ar}), 10.54 s (1H, NH), 12.74 br.s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 2.66 s (3F, CF_3), from –28.76 to –29.06 m (1F, CF_{Ar}). Found, %: C 53.70; H 2.41; N 14.64. $C_{17}H_{10}F_4N_4O_2$. Calculated, %: C 53.98; H 2.66; N 14.81.

^1H and ^{19}F NMR spectra were recorded on a Bruker DPX 200 spectrometer at 200.13 and 188.29 MHz,

respectively, internal reference TMS or external reference CF_3COOH. Melting points were determined in glass capillaries. Hexafluoroacetone ethoxycarbonylimine **II** and *N*-substituted imines of methyl trifluoropyruvate **Va–Vd** were prepared by procedure in [7]. 2-Aminobenzimidazole **I** (Aldrich) was used without further purification.

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