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UNUSUAL REACTION OF CYANOACETIC ACID ESTERS WITH *sym*-TRIAZINE MONOAZIDES

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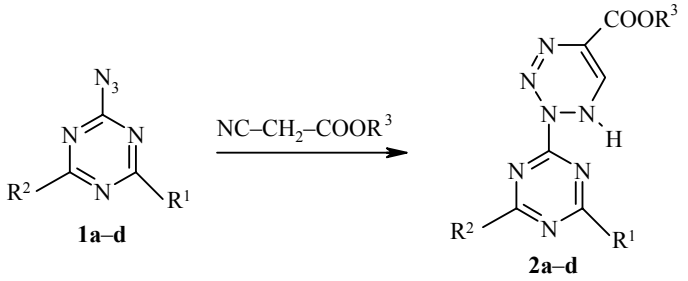
Continuing our studies on synthesis of derivatives in the *sym*-triazine series based on 2-azido-4,6-disubstituted 1,35-triazines [1-3] by reactions of compounds **1a-d** with methyl cyanoacetate and ethyl cyanoacetate, we obtained derivatives of a novel coupled heterocyclic system: 2-[1,3,5]triazin-2-yl-1,2-dihydro[1,2,3,4]tetrazine-5-carboxylic acid esters **2a-d**.



1a–d **2a–d**

a $R^1 = NH_2$, $R^2 = NEt_2$; **b** $R^1 = R^2 = NMe_2$; **c** R^1 = PhNMe, $R^2 = NMe_2$; **d** $R^1 = NH_2$, R^2 = piperidino; **a**, **b** R^3 = Me, **c**, **d** R^3 = Et

The IR spectra were recorded in nujol mulls of the samples on a Specord IR-75 spectrometer. The ^{1}H NMR spectra were recorded on a Bruker DRX-500 spectrometer (500 MHz) in DMSO-d_6, internal standard TMS. The mass spectra were taken on a Finnigan MAT INCOS50 (ionizing radiation energy, 70 eV). TLC was run on Silufol UV-250 plates in the system 1:1 acetone–hexane.

(4-Amino-6-diethylamino[1,3,5]triazin-2-yl)-1,2-dihydro[1,2,3,4]tetrazine-5-carboxylic Acid 2-Methyl Ester (2a). A solution of Na (0.16 g, 7.2 mmol) in methanol (5 ml) was added in small portions at room temperature with stirring to a solution containing 2-amino-4-(diethylamino)-6-azido-1,3,5-triazine (1 g, 4.8 mmol) and methyl cyanoacetate (0.48 g, 4.8 mmol) in absolute methanol (10 ml). Then the reaction mixture was stirred for another 30 min at the same temperature, and then it was boiled for 1 h and cooled down. The solvent was evaporated down to 2/3 volume, and then it was diluted with ice water (50 ml). Then it was acidified with 50% acetic acid to pH 7; the precipitate formed was separated, washed until the wash water tested neutral, and dried in air. The product was recrystallized from alcohol. Yield 1.25 g (85%); mp, 223-224°C.

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IR spectrum, ν, cm^{-1}: 1110, 1150 (C–O–C), 1600, 1640 (C=C, C=N), 1705 (C=O), 3300-3400 (N–H). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.05-1.15 (6H, t, *J* = 7.2, CH_3); 3.50-3.60 (4H, q, *J* = 7.2, $\underline{CH_2}CH_3$); 3.85 (3H, s, OCH_3); 6.75-7.03 (2H, br. s, NH_2); 8.50 (1H, s, CH); 15.10 (1H, s, NH). Mass spectrum (electron impact) (I_{rel}, %): 307 $[M]^+$ (47), 279 $[M - CO]^+$ (39), 250 $[279 - C_2H_5]^+$ (58), 208 $[250 - NC_2H_4]^+$ (18), 192 $[208 - NH_2]^+$ (35), 166 $[192 - CN]^+$ (20), 166 $[M - Φ^*]^+$ (15). Found, %: C 42.85; H 5.50; N 41.12. $C_{11}H_{17}N_9O_2$. Calculated, %: C 42.99; H 5.58; N 41.02.

Compound 2b was obtained similarly. TLC was used to check for completion of the reaction in each specific case (eluent, 1:1 acetone–hexane).

[4,6-bis(Dimethylamino)[1,3,5]triazin-2-yl]-1,2-dihydro[1,2,3,4]tetrazine-5-carboxyl Acid 2-Methyl Ester (2b). Yield 88%; mp >185°C (sublimes). IR spectrum, ν, cm^{-1}: 1100, 1190 (C–O–C), 1620, 1670 (C=C, C=N), 1700 (C=O), 3280-3350 (N–H). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.10 (12H, s, $N(CH_3)_2$); 3.90 (3H, s, OCH_3); 8.50-8.75 (1H, br. s, CH); 15.10 (1H, s, NH). Mass spectrum (electron impact), (I_{rel}, %): 307 $[M]^+$ (100), 279 $[M - CO]^+$ (90), 236 $[279 - CH_3NCH_2]^+$ (20), 193 $[236 - CH_3NCH_2]^+$ (50), 166 $[M - Φ]^+$ (25). Found, %: C 42.91; H 5.49; N 41.08. $C_{11}H_{17}N_9O_2$. Calculated, %: C 42.99; H 5.58; N 41.02.

(4-Dimethylamino-6-methylphenylamino[1,3,5]triazin-2-yl)-1,2-dihydro[1,2,3,4]tetrazine-5-carboxylic Acid 2-Ethyl Ester (2c). A solution of Na (0.13 g, 5.5 mmol) in methanol (5 ml) was added in small portions with stirring at room temperature to a solution containing 2-(dimethylamino)-4-(methylphenylamino)-6-azido-1,3,5-triazine (1 g, 3.7 mmol) and ethyl cyanoacetate (0.42 g, 3.7 mmol) in absolute ethanol (10 ml). Then the reaction mixture was stirred for another 40 min at the same temperature and then boiled for 1.5-2 h, and then cooled down. The solvent was evaporated down to 2/3 volume and diluted with ice water (50 ml). Then it was treated as in synthesis of compound **2a**. Yield 1.13 g (80%); mp 176-177°C. IR spectrum, ν, cm^{-1}: 1180, 1200 (C–O–C), 1630, 1650 (C=C, C=N), 1710 (C=O), 3350-3420 (N–H). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.15-1.31 (3H, t, *J* = 8.0, CH_3); 3.05 (6H, s, $N(CH_3)_2$); 3.45 (3H, s, NCH_3); 4.15-4.30 (2H, q, *J* = 8.0, $\underline{CH_2}CH_3$); 7.20-7.45 (5H, m, C_6H_5); 8.70-8.90 (1H, br. s, CH); 14.05-15.10 (1H, br. s, NH). Mass spectrum (electron impact), (I_{rel}, %): 383 $[M]^+$ (40), 355 $[M - CO]^+$ (35), 326 $[355 - C_2H_5]^+$ (10), 283 $[326 - OCNH]^+$ (50), 268 $[283 - CH_3]^+$ (30), 228 $[M - Φ]^+$ (20), 158 $[228 - N(CH_3)_2\text{-}CN]^+$ (80). Found, %: C 53.13; H 5.44; N 33.04. $C_{17}H_{21}N_9O_2$. Calculated, %: C 53.25; H 5.52; N 32.88.

Compound 2d was obtained similarly.

(4-Amino-6-piperidino[1,3,5]triazin-2-yl)-1,2-dihydro[1,2,3,4]tetrazine-5-carboxylic Acid 2-Ethyl Ester (2d). Yield 83%; mp >195°C (sublimes). IR spectrum, ν, cm^{-1}: 1080, 1150 (C–O–C), 1610, 1650 (C=C, C=N), 1710 (C=O), 3340-3400 (N–H). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.20-1.35 (3H, t, *J* = 7.7, CH_3); 1.49-1.65 (6H, m, CH_2-piperidyl); 3.60-3.80 (4H, m, NCH_2-piperidino); 4.25-4.40 (2H, q, *J* = 7.7, $\underline{CH_2}CH_3$); 6.75-7.05 (2H, br. s, NH_2); 8.55 (1H, s, CH); 15.05 (1H, s, NH). Mass spectrum (electron impact), (I_{rel}, %): 333 $[M]^+$ (60), 305 $[M - CO]^+$ (55), 276 $[305 - C_2H_5]^+$ (20), 233 $[276 - HNCO]^+$ (100), 178 $[M - Φ]^+$ (25), 150 $[1788 - CNH_2]^+$ (45), 84 $[piperidino]^+$ (23). Found, %: C 46.75; H 5.66; N 37.98. $C_{13}H_{19}N_9O_2$. Calculated, %: C 46.84; H 5.74; N 37.82.

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* Here and in the following, Φ means 5-methoxy(ethoxy)carbonyl-1,2-dihydro-1,2,3,4-tetrazin-2-yl.