SYNTHESIS OF N-CYANO-N-ALKOXYCARBONYL-ALKYLAMINO-*symm*-TRIAZINES AND THEIR SOLVOLYSIS

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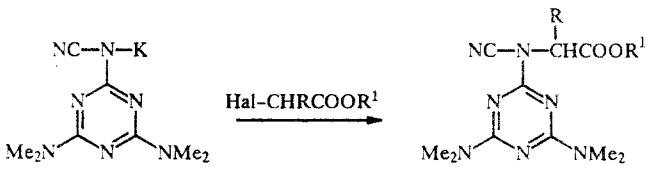
*The action of potassium salts of cyanoamino-*symm*-triazines on esters of chloroacetic and bromomalonic acids gave carbonylalkylamino-*symm*-triazines. The solvolysis of these esters proceeds with heterocyclization, leading to the formation of hydantoin derivatives.*

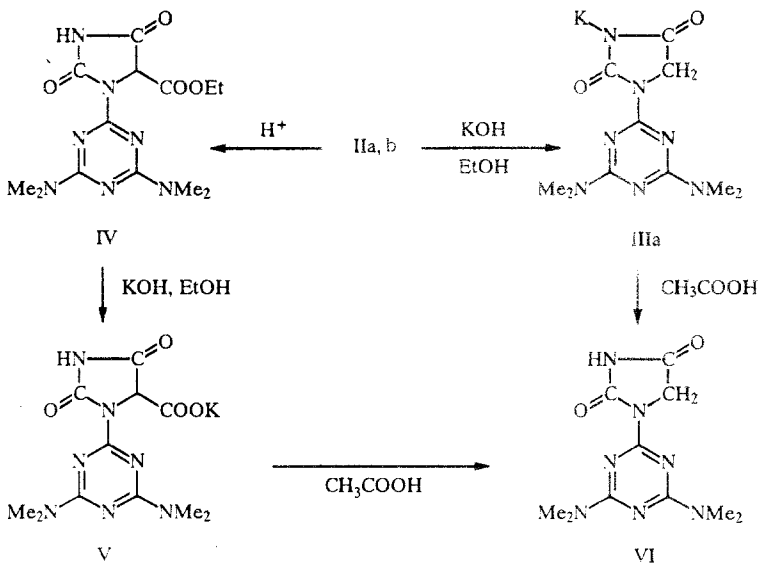
In a continuation of our study of the N-alkylation of cyanoamino-*symm*-triazines [1], we investigated the reaction of these compounds with α-haloacid esters in order to determine the applicability of N-cyano-N-alkoxycarbonylalkylamino-*symm*-triazines (IIa) and (IIb) obtained in this reaction for the synthesis of new heteryl-*symm*-triazines.



I IIa, b

IIa R = H, R^1 = Me; IIb R = COOEt, R^1 = Et; Hal = Cl, Br

Intramolecular heterocyclization occurs in the hydrolysis of IIa instead of the formation of the expected salt or amide of the acid. This heterocyclization leads to imidazolidinyl-*symm*-triazines (VI) through III.



IV IIIa V VI

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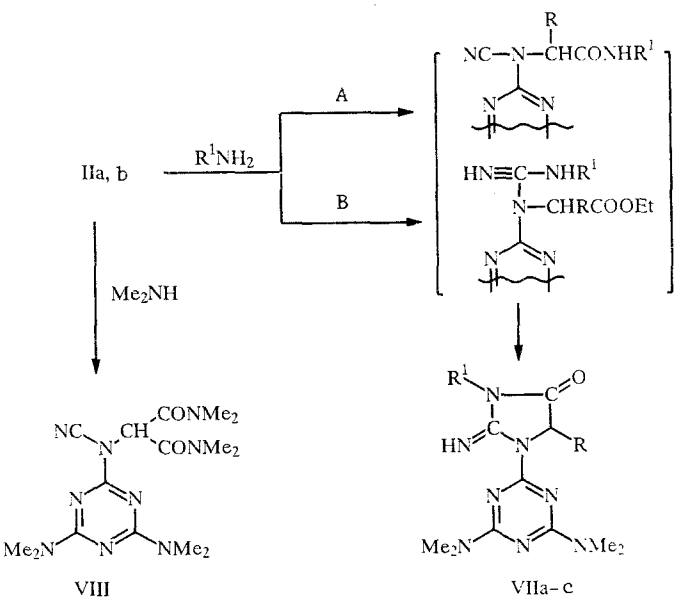
The action of ethanolic alkali on ethyl N-triazinyl-N-cyanoaminomalonate (IIb) also gave VI, while acid hydrolysis gave carboethoxy derivative IV, which is converted by the action of alkali into the corresponding salt V. The action of acid on salt V leads to decarboxylation and formation of VI.

In previous work [2], we have shown that cyanoamino-*symm*-triazines are readily converted in acid media into urea derivatives. On the other hand, these compounds are converted in alkaline media into iminoester derivatives [3]. This most probably occurs in the formation of VI.

The formation of N-cyano-N-carbamoylalkylamino-*symm*-triazines should have been expected in the ammonolysis and aminolysis of IIa and IIb but the products obtained were found to be imidazolidinyl-*symm*-triazines (VIIa) and (VIIb). The formation of VII may proceed at the site of the cyano group through a guanidine intermediate (pathway B) or by conversion of the starting ester into an amide (pathway A), which then undergoes intramolecular cyclization, elimination of alcohol, and formation of VIIa-VIIc.



The aminolysis of IIb by dimethylamine showed that this reaction proceeds exclusively at the site of the ester group to give VIII. This finding is evidence for the formation of VII through amides according to pathway A.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer for Vaseline mulls. The mass spectra were taken on an MKh-1303 mass spectrometer with direct sample inlet into the ionization chamber at 50 eV. The PMR spectra were taken on a Varian T-60 spectrometer. The thin-layer chromatography was carried out on Silufol UV-25 plates using 1:1 or 1:2 acetone—heptane as the eluent and development by 2% $AgNO_3$ + 0.4% BPS + 4% citric acid.

The elemental analysis data for C, H, and N corresponded to the calculated values.

2-N-Cyano-N-methoxycarbonylmethylamino-4,6-bis-dimethylamino-*symm*-triazine (IIa, $C_{11}H_{17}N_7O_2$). A mixture of 2.4 g (10 mmoles) potassium salt of N-cyanoamino-4,6-bis-dimethylamino-*symm*-triazine (Ia) and 1.08 g (10 mmoles) methyl chloroacetate was heated for 5-6 h in 8-10 ml dimethylformamide at 70°C. The flask contents were poured into ice water and the crystalline precipitate of IIa was filtered off. The yield of IIa was 2.2 g (80%), mp 147-148°C (from ethanol), R_f 0.54. Mass spectrum, *m/z* (%): 279 M^+. IR spectrum: 2240 (C≡N), 1520, 1600 (C=C, C=N), 1750 cm^{-1} (C=O). PMR spectrum in $CDCl_3$ + CD_3OD: 4.2 (3H, s, OCH_3), 4.38 ppm (2H, s, CH_2).

Diethyl Ester of N-Cyano-N-4,6-bis-dimethylamino-*symm*-triazinyl-2-aminomalonic Acid (IIb, $C_{15}H_{23}N_7O_4$). A sample of 2.4 g (10 mmoles) diethyl bromomalonate was added with stirring to 2.4 g (10 mmoles) potassium salt of 2-N-cyanoamino-4.6-bis-dimethylamino-*symm*-triazine in 8-10 ml dimethylformamide. The mixture was stirred for 6 h at 65-70°C and cooled. Then, 15-20 ml water was added and the crystalline precipitate of IIb was filtered off. The yield of IIb

was 3.5 g (96%), mp 139-140°C (from octane), R_f 0.48. IR spectrum: 2235 (C≡N), 1740 (CO), 1530, 1590 cm^{-1} (C=C, C=N). Mass spectrum, *m/z* (%): 365 (85) M^+, 320 (12), 292 (20), 221 (65), 166 (14). PMR spectrum in acetone-d_6: 1.28 (6H, t, CH_3CH_2), 3.09 and 3.12 (two 6H, s, $N(CH_3)_2$, 4.28 (4H, q, CH_2CH_3), 5.92 ppm (1H, s, CH).

2-(2′,4′-Dioxo-1′,3′-imidazolidin-1′-yl)-4,6-bis-dimethylamino-*symm*-triazine (VI, $C_{10}H_{15}N_7O_2$). A. A sample of 5 mmoles ester IIa or IIb was added with stirring to a solution of 0.34 g (5 mmoles) 84% KOH in 8-10 ml methanol. The mixture was heated for 6-7 h at 60°C. Methanol was distilled off. The residue was triturated with ether and filtered to give IIIa in 90% yield, mp 330-332°C (dec.). IR spectrum: 1510, 1580 (C=N), 1710-1740, 1780-1790 cm^{-1} (C=O). The salt obtained was dissolved in water and acidified by adding acetic acid to pH 6. The precipitate of VI was filtered off and washed with water. The yield of VI was 81%, mp 284-285°C (from dimethyl sulfoxide). IR spectrum 1720, 1780 (CO), 1150-1200 (hydantoin ring), 3330-3430 cm^{-1} (NH). PMR spectrum in DMSO-d_6: 3.1 (two 6H, s, $N(CH_3)_2$), 5.5 (1H, d, NH), 3.7 ppm (2H, s, CH_2). Mass spectrum, *m/z* (%): 266 (16), 265 (100) M^+, 250 (66), 236 (25), 222 (33), 207 (9), 179 (32), 151 (21).

B. A sample of V was dissolved in 10 ml water and acidified to pH 6. Product VI was obtained as a crystalline precipitate in 50% yield.

2-(2′,4′-Dioxo-5′-carboethoxycarbonyl-1′,3′-imidazolidin-1′-yl)-4,6-bis-dimethylamino-*symm*-triazine (IV, $C_{13}H_{19}N_7O_4$). A sample of 1.8 g (5 mmoles) diethyl ester of 4,6-bis-dimethylamino-*symm*-triazinyl-2-N-cyanoaminomalonic acid was dissolved in 9 ml 25% hydrochloric acid and left for 48 h at 20°C. The solution was neutralized by the addition of aqueous sodium bicarbonate and the precipitate of IV was filtered off. The yield of IV was 1.4 g (91%), mp 212-213°C (from ethanol), R_f 0.5. IR spectrum: 1660, 1720 (CO), 1510, 1580 (C=N), 1150-1200 cm^{-1} (hydantoin ring). Mass spectrum, *m/z* (%): 337 (80) M^+, 332 (30), 308 (6), 294 (12), 265 (100), 250 (40), 236 (8), 222 (20).

Potassium Salt of 2-(2′,4′-dioxo-5′-carboxy-1′,3′-imidazolidin-1′-yl)-4,6-bis-dimethylamino-*symm*-triazine (V, $C_{11}H_{13}N_7O_4K_2$). A sample of 0.13 g (2 mmoles) 84% KOH was dissolved in 3-4 ml methanol and 0.34 g (1 mmole) IV was added. The mixture was heated for 10-12 h at 70°C. Methanol was distilled off. The precipitate was triturated with ether and filtered off. The yield of V was 0.2 g (49%), mp 290-292°C. IR spectrum: 1650-1730 (C=O) cm^{-1}.

2-(2′-Imino-4′-oxo-5′-carbonamido-1′,3′-imidazolidin-1′-yl)-bis-dimethylamino-*symm*-triazines (VIIa)-(VIIc). A sample of 10 ml ice-cooled methanol was saturated with ammonia or methylamine and 5 mmoles IIa or IIb in 5 ml methanol was added to the solution obtained. The mixture was left for 96 h at 20°C. The crystalline precipitate of VIIa-VIIc was filtered off (dimethylformamide). The yield of VIIa ($C_{10}H_{16}N_8O$), R = R^1 = H, was 80%, mp 348-350°C (dec.), R_f 0.4. The yield of VIIb ($C_{11}H_{17}N_9O_2$), R = $CONH_2$, R^1 = H, was 98%, mp 252-255°C, R_f 0.35. Mass spectrum, *m/z* (%): 307 (100) M^+, 292 (42), 278 (16), 263 (80), 250 (22). The yield of VIIc ($C_{13}H_{21}N_9O_2$), R = $CONHCH_3$, R^1 = CH_3, was 80%, mp 274-276°C, R_f 0.63. Mass spectrum, *m/z*: 335 (100) M^+, 320 (6), 304 (18), 278 (82), 263 (16), 252 (10), 235 (6), 222 (12). IR spectrum: 1660 (C=O, C=N), 3360, 3210 (NH, NH_2), 1500, 1580 (C=N).

Dimethyldiamide of N-Cyano-N-4,6-bis-dimethylamino-*symm*-triazinyl-2-aminomalonic Acid (VIII, $C_{15}H_{25}N_9O_2$). A sample of 10 ml ice-cooled methanol was saturated with dimethylamine and added to a suspension of 1.82 g (5 mmoles) IIb in 5 ml methanol. The mixture was heated for 24 h in an ampule at 50°C. The precipitate formed was filtered off. The yield of VIII was 0.75 g (41.2%), mp 278-280°C (dec.) (from dimethyl sulfoxide). IR spectrum: 1670 (C=O), 2240 (C≡N), 1510, 1580 cm^{-1} (C=N). Mass spectrum, *m/z* (%): 363 M^+.

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