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HETEROCYCLIZATION OF ETHYL ESTERS OF 2-CHLORO-3-SUBSTITUTED AMINOACRYLIC ACIDS WITH *o*-PHENYLENEDIAMINE

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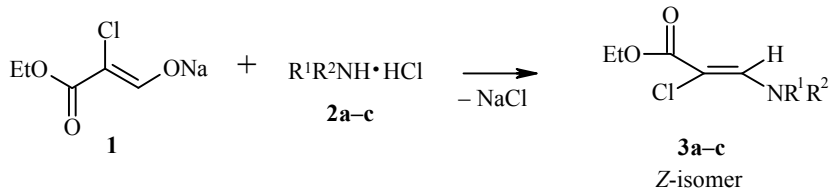
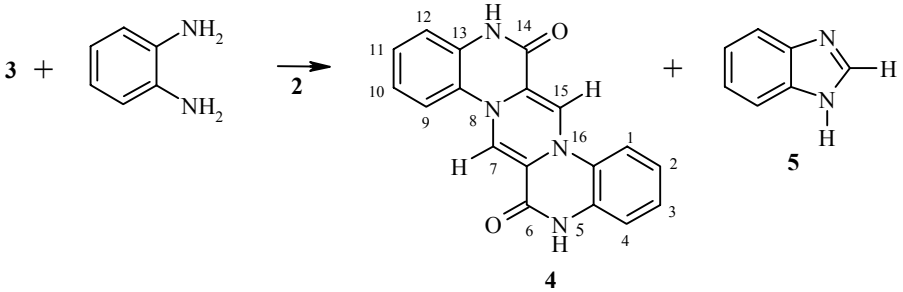
The heterocyclization of carbonyl-substituted chloroenamines with bifunctional nucleophilic reagents features participation of the enamine carbon atoms. It is interesting that the carbonyl group is not altered in this process [1, 2]. We have shown that the reaction of carboethoxychloroenamines **3** with *o*-phenylenediamine takes an unusual course, in which all three electrophilic sites are involved, leading to condensed heterocycle **4**. Enamines **3a-c** were obtained by the reaction of enolate **1** with the corresponding amine hydrochloride salts **2** in chloroform at room temperature. The ^{1}H and ^{13}C NMR spectra show that enamines **3** are obtained as a single isomer. The X-ray diffraction structural analysis data for analogous enamines [3] suggest that enamines **3** have *Z*-configuration.



2, 3 a $R^1 = H$, $R^2 = Me$, **b** $R^1 = H$, $R^2 = Ph$, **c** $R^1 + R^2 = –(CH_2)_2O(CH_2)_2–$

Heterocyclization of enamines **3** with *o*-phenilenediamine proceeds when boiling reaction mixture in the polar solvents. The yield of desired products is only 10-25%. The highest yield is obtained using the morpholino-substituted enamine **3c**. Benzimidazole and other substances which failed to be isolated individually were formed alongside with heterocycle **4** in the reaction course.



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Ethyl Ester of 2-Chloro-3-methylaminoacrylic Acid (3a). A mixture of enolate **1** (17.25 g, 0.1 mol) and methylamine hydrochloride **2a** (0.1 mol) in chloroform (100 ml) was stirred at room temperature for 8 h. The NaCl precipitate was filtered off and the solvent was removed from the filtrate. Distillation of the residue gave enamine **3a** in 80% yield; bp 63-65°C (0.09 mm Hg). ^{1}H NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 1.15 (3H, t, Me); 2.88 (3H, d, Me); 4.05 (2H, q, OCH_2); 6.68 (1H, br. d, NH); 8.05 (1H, d, N=CH). IR spectrum, ν, cm^{-1}: 1710 (C=O), 3260 (NH). Found, %: Cl 21.65; N 8.54. $C_6H_{10}ClNO_2$. Calculated, %: Cl 21.71; N 8.56.

Ethyl Ester of 2-Chloro-3-phenylaminoacrylic Acid (3b) was obtained analogously in 87% yield; mp 91°C (acetonitrile). ^{1}H NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 1.32 (3H, t, Me); 4.30 (2H, q, OCH_2); 7.10 (5H, m, Ph); 8.15 (1H, d, N=CH). Found, %: Cl 15.70; N 6.19. $C_{11}H_{12}ClNO_2$. Calculated, %: Cl 15.74; N 6.21.

Ethyl Ester of 2-Chloro-3-morpholinoacrylic Acid (3c) was obtained analogously in 85% yield; mp 86°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 (3H, t, Me); 3.60 (8H, d, –$(CH_2CH_2)_2O$–); 4.05 (2H, q, OCH_2); 7.00 (1H, s, N=CH). Found, %: Cl 14.08; N 5.54. $C_{10}H_{14}ClNO_2$. Calculated, %: Cl 14.12; N 5.57.

5,6,13,14-Tetrahydroquinoxalino[1,2,4,5]pyrazino[1,2-*a*]quinoxaline-6,14-dione (4). A mixture of corresponding enamine **3a-c** (0.005 mol) and *o*-phenylenediamine (0.5 g, 0.005 mol) in propan-2-ol (30 ml) was heated at reflux for 48 h. The resultant red precipitate was filtered off, washed with acetone, and dried in vacuum. ^{1}H NMR spectrum, δ, ppm: 6.91 (2H, s, =CH–N); 7.23 (4H, m, Ar); 7.72 (4H, m, Ar); 11.93 (2H, s, NH). ^{13}C NMR spectrum, δ, ppm: 88.25 (d, =CHN), 115.10, 120.81, 123.01, 124.91, 128.29 (Ar); 14.78 (=C–N), 155.45 (C=O). IR spectrum, ν, cm^{-1}: 1630 (C=N), 1690 (C=O). Found, %: C 68.01; H 3.75; N 17.56. $C_{18}H_{12}N_4O_2$. Calculated, %: C 68.35; H 3.79; N 17.72. After removal of the solvent, an additional amount of benzimidazole was obtained in 40% yield; mp 169°C (170.5°C [4]).

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