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SYNTHESIS OF MESOIONIC 1,2,4-TRIAZOLO[4,3-*a*]PYRIMIDIN-5-ONES AND SUBSITUTED FORMAMIDINES FROM DIETHYL (5-1-R-1H-1,2,4-TRIAZOL -3-YL)AMINOMETHYLENEMALONATES

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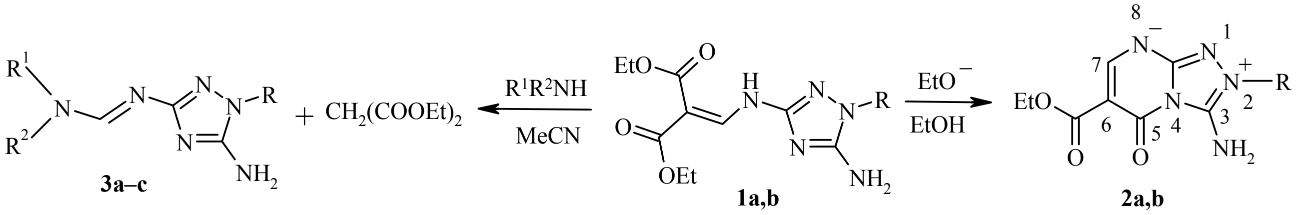
Hetaryl-substituted aminomethylenemalonates obtained by the condensation of aminoazoles with 2-alkoxymethylenemalonates are commonly used for the synthesis of biologically active azolopyrimidines [1, 2]. However, cyclization of hetaryl-substituted aminomethylenemalonates to give azolopyrimidines often proceeds only at high temperature or under upon microwave activation [1] or by using special reagents [2]. In the present work, we found that brief heating of diethyl aminomethylenemalonates **1a** and **1b** in ethanol in the presence of sodium ethylate leads to the formation of mesoionic 1,2,4-triazolo[4,3-*a*]pyrimidin-5-ones **2a** or **2b** in high yield. This reaction does not occur upon heating aminomethylenemalonates **1a** or **1b** with tertiary aliphatic amines in ethanol at reflux. However, heating esters **1** with primary or secondary amines in ethanol or acetonitrile at reflux leads to nucleophilic substitution of the malonate ester and formation of amidines **3a-c** in high yield.



1a, **2a**, **3 a**, **b** R = Ph; **1b**, **2b**, **3c** R = Bn; **3 a**, **c** $R^1R^2 = (CH_2CH_2)_2O$; **b** R^1 = Bn, R^2 = H

The structures of products **2** and **3** were confirmed by elemental analysis, mass spectrometry, ^1H–^1H NOESY, ^1H–^{13}C HMBC, and HSQC correlation spectra. The ^1H and ^{13}C NMR spectra of pyrimidones **2a** and **2b** are similar to the spectra of other mesoionic 2-substituted 3-amino-2H-1,2,4-triazolo[4,3-*a*]pyrimidin-5-ones [3]. The structure of amidines **3** was also unequivocally indicated by the X-ray diffraction structural analysis of **3a**.

The ^1H and ^{13}C NMR spectra were taken on a Bruker Avance 600 spectrometer at 600 and 150 MHz, respectively, in DMSO-d_6 with TMS as the internal standard. The electron impact mass spectra were taken on a Finnigan MAT Incos 50 mass spectrometer with direct sample inlet into the ion source and 70 eV ionization energy.

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3-Amino-6-ethoxycarbonyl-5-oxo-2-phenyl-5H-1,2,4-triazolo[4,3-*a*]pyrimidin-2-ium-8-ide (2a). Diester **1a** (0.69 g, 2 mmol) was added to a solution of sodium (0.14 g, 6 mmol) in anhydrous ethanol (5 ml). The mixture obtained was heated at reflux for 20 min, neutralized by adding acetic acid, and cooled. The precipitate formed was filtered off to give 0.54 g (90%) compound **2a**; mp 275-276°C (acetic acid–ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (3H, t, *J* = 7.1, CH_3); 4.14 (2H, q, *J* = 7.1, CH_2); 7.54-7.63 (5H, m, C_6H_5); 8.50 (1H, s, CH); 8.60 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 14.45 ($OCH_3\underline{C}H_3$), 58.98 ($O\underline{C}H_2CH_3$), 95.12 (C-6), 125.16, 129.62, 129.77, 134.40 (C_6H_5), 145.07 (C-3), 152.04 (C-8a), 157.60 (C-5), 162.72 (C-7), 164.90 ($\underline{C}O_2Et$). Mass spectrum, *m/z* (I_{rel}, %): 299 $[M]^+$ (8), 253 (100), 186 (27), 119 (16), 91 (29), 77 (78). Found, %: C 55.86; H 4.76; N 23.11. $C_{14}H_{13}N_5O_3$. Calculated, %: C 56.18; H 4.38; N 23.40.

3-Amino-2-benzyl-6-ethoxycarbonyl-5-oxo-5H-1,2,4-triazolo[4,3-*a*]pyrimidin-2-ium-8-ide (2b) was obtained in 78% yield (0.49 g) analogously to compound **2a**; mp 209-210°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, t, *J* = 7.2, CH_3); 4.12 (2H, q, *J* = 7.2, CH_2); 5.23 (2H, s, $C\underline{H}_2C_6H_5$); 7.32-7.38 (5H, m, C_6H_5); 8.43 (1H, s, CH); 8.71 (2H, s, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 313 $[M]^+$ (4), 91 (100), 65 (20). Found, %: C 57.18; H 5.01; N 22.08. $C_{15}H_{15}N_5O_3$. Calculated, %: C 57.50; H 4.83; N 22.35.

N^3-[(*E*)-Morpholin-4-ylmethylidene]-1-phenyl-1H-1,2,4-triazole-3,5-diamine (3a). A mixture of diester **1a** (0.69 g, 2 mmol), morpholine (0.37 g, 4.2 mmol), and acetonitrile (5 ml) was heated at reflux for 5 h and then cooled. The precipitate formed was filtered off to give 0.46 g (84%) compound **3a**; mp 208-208.5°C (acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.42-3.61 (8H, m, $4CH_2$); 6.21 (2H, s, NH_2); 7.25-7.53 (5H, m, C_6H_5); 8.26 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 42.52, 48.58, 65.44, 66.57, 121.68, 125.75, 129.16, 137.71, 153.59 (C-5 triazole), 155.03 (N–CH=N), 163.52 (C-3 triazole). Mass spectrum, *m/z* (I_{rel}, %): 272 $[M]^+$ (100), 241 (25), 186 (17), 175 (17), 77 (27). Found, %: C 57.35; H 5.94; N 30.88. $C_{13}H_{16}N_6O$. Calculated, %: C 57.34; H 5.92; N 30.86.

N'-(5-Amino-1-phenyl-1H-1,2,4-triazol-3-yl)-N-benzylimidoformamide (3b) was obtained in 80% yield (0.47 g) analogously from compound **1a** and benzylamine; mp 181-182°C (acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.47 (2H, d, *J* = 5.7, CH_2); 6.25 (2H, s, NH_2); 7.23-7.52 (10H, m, $2C_6H_5$); 7.81 (1H, m, NH); 8.37 (1H, d, *J* = 3.9, CH). ^{13}C NMR spectrum, δ, ppm: 43.44 (CH_2), 121.64, 125.68, 126.76, 127.35, 128.23, 129.14, 137.76, 139.05 (arom.), 153.36 (N–CH=N), 153.55 (C-5 triazole), 163.99 (C-3 triazole). Mass spectrum, *m/z* (I_{rel}, %): 292 $[M]^+$ (8), 175 (49), 133 (35), 119 (32), 106 (35), 91 (100), 77 (81). Found, %: C 65.48; H 5.50; N 29.02. $C_{16}H_{16}N_6$. Calculated, %: C 65.74; H 5.52; N 28.75.

1-Benzyl-N^3-[(*E*)-morpholin-4-ylmethylidene]-1H-1,2,4-triazole-3,5-diamine (3c) was obtained in 74% yield (0.42 g) from compound **2a** and morpholine; mp 206-208°C (acetonitrile). ^{1}H NMR spectrum, δ, ppm: 3.38-3.57 (8H, m, $4CH_2$); 4.97 (2H, s, $C\underline{H}_2C_6H_5$); 6.17 (2H, s, NH_2); 7.17-7.32 (5H, m, C_6H_5); 8.17 (1H, s, CH). Mass spectrum, *m/z* (I_{rel}, %): 286 $[M]^+$ (17), 125 (92), 91 (99), 65 (34), 54 (100). Found, %: C 58.49; H 6.51; N 29.37. $C_{14}H_{18}N_6O$. Calculated, %: C 58.73; H 6.34; N 29.35.

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