

C-MORPHOLINO- OR PIPERIDINO- γ -TRIAZOLES FROM 1,1-ENEDIAMINES AND ETHYL AZIDOFORMATE

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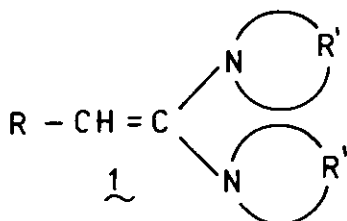
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Abstract - Ethyl azidoformate adds instantaneously to 1,1-enediamines at low temperature and the expected triazolines undergo easily a rare elimination of N-ethoxycarbonylamines to give C-morpholino- or piperidino- γ -triazoles in yields ranging from 50 to 70%.

While involved in the study of ethoxycarbonylnitrene (EtOCON) with nucleophilic alkenes¹, we enlarged our interest to 1,3-dipolar cycloaddition of ethyl azidoformate (EtOCON₃) toward compounds such as ketene silyl acetals² and 1,1-enediamines (N,N-acetals)³.

Bulk work has been done in the field of 1,3-dipolar addition of azides on enamines mainly by Fusco, Bianchetti, Pocar and their group⁴ and many other authors⁵ while few examples have been reported concerning enediamines^{6,7}. The presence of an additional donor group in conjugation with the double bond makes this class of compounds worth of interest.

In this communication we focus the attention on the relatively novel behaviour of triazolines obtained by 1,3-dipolar addition of ethyl azidoformate on enediamines 1. Actually triazolines 2 have been not isolated from the reaction performed at low temperature between ethyl azidoformate and enediamines 1. Enediamines are much more reactive than enamines⁴ or ketene silyl acetals² and usually EtOCON₃ is quantitatively consumed in few minutes at -15 °C. 1,3-Cycloaddition of azides with electron rich alkenes are considered to be LUMO controlled reactions and should be accelerated by substituents which raise the dipolarophile HOMO⁵.

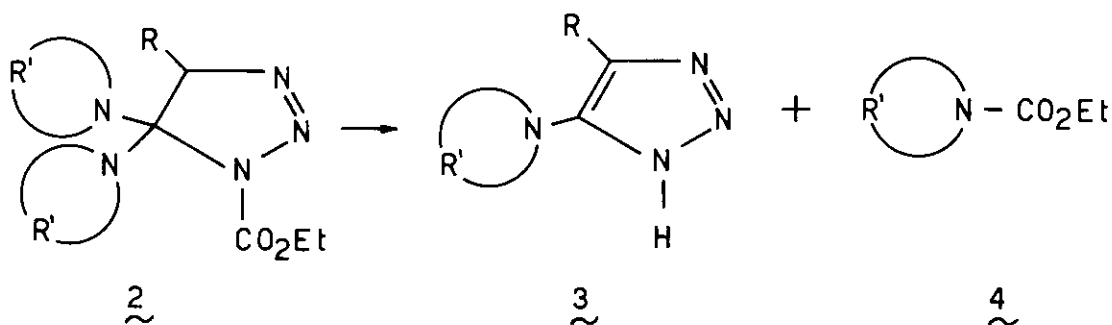


- a R = CH₃ , R' = -CH₂(CH₂)₃CH₂-
b R = CH₃ , R' = -(CH₂)₂-O-(CH₂)₂-
c R = H , R' = -(CH₂)₂-O-(CH₂)₂-

Inspection of the crude reaction mixtures by ir and ^1H nmr spectroscopy shows signals attributable to the carbonyl group (1735 cm^{-1})⁸ and to the methyl group (doublet at $\delta\ 1.5$)⁶ of the triazolines 2a and 2b.

These compounds do not survive, at room temperature, a period of time exceeding 15 h.

Silica gel column chromatography of the crude reaction mixtures allowed the isolation of two main products: the triazoles 3 (a, 65%; b, 49%; and c, 25% yield, respectively) and the N-ethoxycarbonyl derivatives of the secondary amines used in the preparation of the enediamines, 4 (a, 70%; b, 68%; and c, 50% yield). The structure of 5-morpholino- or 5-piperidino-1H-1,2,3-triazole has been tentatively indicated as the most probable tautomer^{9,10}, although the annular tautomerism depends largely from several factors¹¹.



This reaction recalls the reaction observed by Fusco on triazolines derived from enamines¹⁰ but in that case the N-acyl derivative of the secondary amine, generated by mild heating, has been not isolated. The reaction observed might be due to a displacement of the ethoxycarbonyl group by attack of the secondary amine formed in a first elimination step. On the other hand triazolines obtained by aryl azide addition to enediamines may be isolated and the usual amine elimination^{5,6}, involving the proton on carbon 4, requires a separate treatment with acids or silica gel chromatography.

EXPERIMENTAL

Gc analyses were performed on a Carlo Erba 4100 gas chromatograph with a column of 3% SP 2250 (2 m x 2 mm) on 100/120 Supelcoport. Mass spectra were obtained on a Kratos MS 80 spectrometer at an ionization potential of 70 eV. High-resolution mass spectra (hrms) were obtained on a Kratos MS 80 spectrometer (15000 resolution). ^1H nmr spectra were recorded on a Bruker WP-80 SY spectrometer and on a Varian XL-300 spectrometer with CHCl_3 as an internal standard. ^{13}C nmr spectra were obtained on a Varian XL-300 spectrometer with CDCl_3 as an internal standard.

Infrared spectra (ir) were obtained on a Perkin-Elmer 257 infracord instrument. Melting points were taken on a Kofler apparatus. EtOCON_3^{12} and 1,1-enediamines¹³ were prepared by standard procedures.

1,1-Dipiperidinopropene (1a): ir (CCl_4) 1645 cm^{-1} ; ^1H nmr (CDCl_3) δ 3.6 (q, 1H, CH=C), 2.9 (m, 4H, CH_2N), 2.7 (m, 4H, CH_2N), 1.6 (d, 3H, CH_3), 1.5 (m, 12H, CH_2); mass spectrum, m/z (relative intensity) 208 (M^+ , 100), 126 (10), 125 (64), 124 (41), 110 (48), 97 (18), 96 (20), 84 (16), 82 (20), 56 (16), 41 (14); hrms, M^+ , 208.1931, calcd for $\text{C}_{13}\text{H}_{24}\text{N}_2$, 208.1939.

1,1-Dimorpholinopropene (1b): ir (CCl_4) 1640 cm^{-1} ; ^1H nmr (CDCl_3) δ 3.8 (q, 1H, CH=C), 3.0 (t, 8H, CH_2O), 2.7 (t, 8H, CH_2N), 1.6 (d, 3H, CH_3); mass spectrum, m/z (relative intensity) 212 (M^+ , 6), 170 (6), 115 (53), 100 (31), 98 (34), 88 (22), 87 (56), 86 (100), 72 (17), 70 (31), 57 (73), 56 (32); hrms, M^+ , 212.1525, calcd for $\text{C}_{11}\text{H}_{20}\text{N}_2\text{O}_2$, 212.1525.

1,1-Dimorpholinoethylene (1c): ir (CCl_4) 1630 cm^{-1} ; ^1H nmr (CDCl_3) δ 3.4 (t, 8H, CH_2O), 3.0 (s, 2H, $\text{CH}_2=\text{C}$), 2.6 (t, 8H, CH_2N); mass spectrum, m/z (relative intensity) 198 (M^+ , 100), 153 (13), 135 (41), 115 (13), 114 (92), 113 (31), 112 (36), 99 (10), 87 (23), 86 (72), 85 (13); hrms, M^+ , 198.1365, calcd for $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2$, 198.1368.

Reaction of EtOCON_3 with 1,1-Enediamines.

EtOCON_3 (1 mol) was added at -15°C to 1,1-enediamine (1 mol). The reaction occurred immediately. The crude mixture was chromatographed on silica gel with a mixture of ethyl ether and ethyl acetate (70:30).

With 1,1-dipiperidinopropene (1a) as starting material two products were collected: $3a$ (65%) and $4a^{14}$ (70%).

$3a$: mp $108-109^\circ\text{C}$; ir (CCl_4) 3470 cm^{-1} ; ^1H nmr (CDCl_3) δ 11.5 (br, 1H, NH), 3.1 (m, 4H, CH_2N), 2.3 (s, 3H, CH_3), 1.7 (m, 6H, CH_2); ^{13}C nmr (CDCl_3) δ 154.6 (CH_3CC), 132.8 (CH_3CC), 51.1 (αCH_2), 25.7 (βCH_2), 24.1 (γCH_2), 11.1 (CH_3); mass spectrum, m/z (relative intensity) 166 (M^+ , 100), 165 (85), 125 (22), 110 (27), 84 (12); hrms, M^+ , 166.1207, calcd for $\text{C}_8\text{H}_{14}\text{N}_4$, 166.1218.

With 1,1-dimorpholinopropene (1b) as starting material two products were obtained: $3b$ (49%) and $4b^{15}$ (68%).

$3b$: mp $121-122^\circ\text{C}$; ir (CHCl_3) 3480 cm^{-1} ; ^1H nmr (CDCl_3) δ 12.5 (br, 1H, NH), 3.8 (t, 4H, CH_2O), 3.1 (t, 4H, CH_2N), 2.3 (s, 3H, CH_3); ^{13}C nmr (CDCl_3) δ 153.7 (CH_3CC), 132.6 (CH_3CC), 66.7 (CH_2O), 50.1 (CH_2N), 11.0 (CH_3); mass spectrum, m/z (relative intensity) 168 (M^+ , 100), 153 (12), 137 (10), 111 (12), 110 (78); hrms, M^+ , 168.1012, calcd for $\text{C}_7\text{H}_{12}\text{N}_4\text{O}$, 168.1011.

With 1,1-dimorpholinoethylene (1c) as starting material two products were collected: $3c$ (25%) and $4c^{15}$ (50%).

$3c$: mp $89-90.5^\circ\text{C}$; ir (CHCl_3) 3480 cm^{-1} ; ^1H nmr (CDCl_3) δ 11.6 (br, 1H, NH), 7.2

(s, 1H, CH), 3.8 (t, 4H, CH₂O), 3.2 (t, 4H, CH₂N); ¹³C nmr (CDCl₃) δ 157.0 (HCC), 127.0 (HCC), 66.3 (CH₂O), 48.7 (CH₂N); mass spectrum, m/z (relative intensity) 154 (M⁺, 96), 139 (9), 123 (9), 96 (100), 69 (13); hrms, M⁺, 154.0854, calcd for C₆H₁₀N₄O, 154.0854.

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