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A Remarkable Rearrangement During Reaction Between Triazolopyridinium Ylides and Dimethyl Acetylenedicarboxylate

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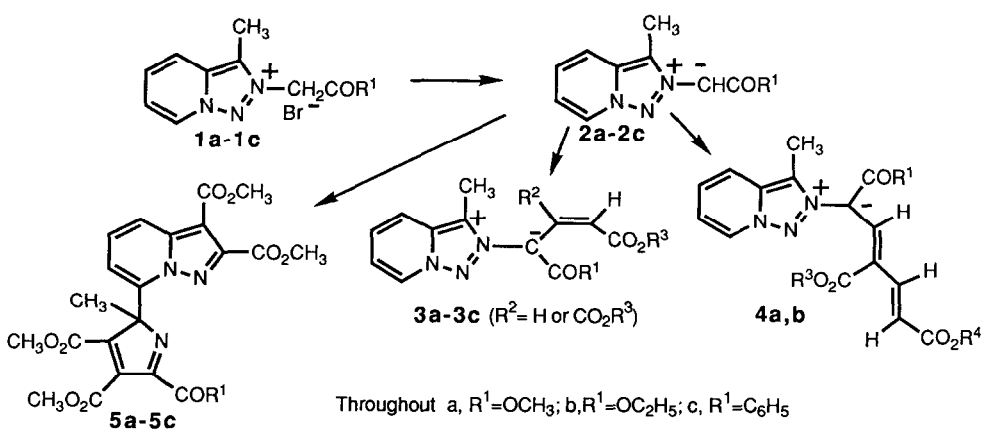
Key Words
Triazolopyridinium ylides; cycloaddition; pyrazolo[1,5-*a*]pyridines; X-ray structure.

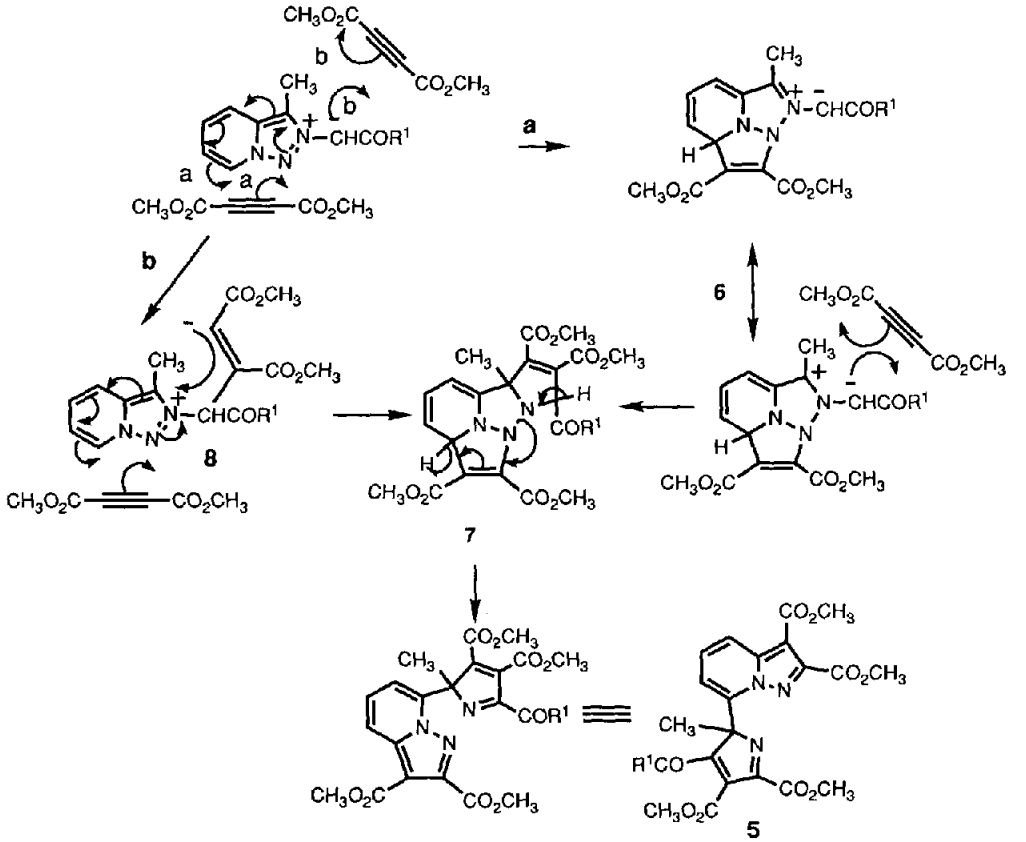
Abstract. *The ylides from 2-acylmethyltriazolopyridinium salts (**1**) react with dimethyl acetylenedicarboxylate in toluene solution to give the 7-pyrroleninylpyrazolo[1,5-a]pyridines (**5**).*

We have reported elsewhere[1] that the 2-acylmethyltriazolopyridinium salts(**1**) readily form ylides (**2**) when treated in acetonitrile solution with potassium carbonate, and that these ylides react with acetylenic esters to give further novel ylides (**3**) and (**4**). A change of solvent to toluene, and the use of a mixture of potassium carbonate and triethylamine as base,[2] produced with dimethyl acetylenedicarboxylate (DMAD) completely different products, shown below to be pyrazolo[1,5-*a*]pyridines (**5**)



Throughout a, R^1=OCH_3; b,R^1=OC_2H_5; c, R^1=C_6H_5

The new compounds were colourless (the ylides were yellow or orange) and showed in their ^1H N.M.R. spectra only three signals in the aromatic region (for compounds (**5a**) and (**5b**); compound (**5c**) showed eight protons). The three "pyridine" protons were similar to those of the 4,5, and 6 positions in triazolopyridines. Microanalysis showed that the compounds (**5**) were formed from 1 molecule of ylide and 2 of DMAD with the loss of two hydrogen atoms, and four ester methyl signals are seen in the N.M.R. spectra. The other point of note is that the methyl signal, originally at δ2.8 in the ^1H spectrum and at δ9.3 in the ^{13}C spectrum, is now at δ2.04 and 21.3 respectively, indicating a change from sp^2 to sp^3 in the carbon to which the methyl group is attached. A signal in the ^{13}C N.M.R. spectrum at δ83 also indicates a quaternary carbon with heavy deshielding substitution. The structure of compound (**5c**) was established by an X-ray diffraction study, and is shown in Figure 1. We have frequently observed reactions of triazolopyridines in which the bond between N1 and the bridgehead nitrogen is broken but a cleavage of the N1-N2 bond is quite unknown, and we can find no precedent in the literature.



SCHEME

There are two possible mechanisms for the reaction, shown in the SCHEME (routes a and b). We believe that the change to a non-polar solvent allows successful competition by concerted $[8_{\pi}+2_{\pi}]$ cycloaddition giving a diazacyclazine (**6**)(SCHEME - route a) with the alternative attack at the ylidic carbon which with subsequent proton shift, leads to the ylides (**3**) and (**4**). The diazacyclazine provides a 1,3-dipole for reaction with a further molecule of DMAD. Cyclisation is followed by fission of the N1-N2 bond.to give the pyrrolenine. The alternative (route b) is that the ylide (**8**), lacking a rapid proton transfer route, instead cyclizes, in turn triggering the addition of the second molecule of DMAD, to give intermediate (**7**). An oxidation is required, possibly with concomitant reduction of a molecule of DMAD. In the crystal structure the original triazolopyridine ring structure is clearly seen, supporting a mechanism where the N1-N2 bond is cleaved at a late stage in the reaction.

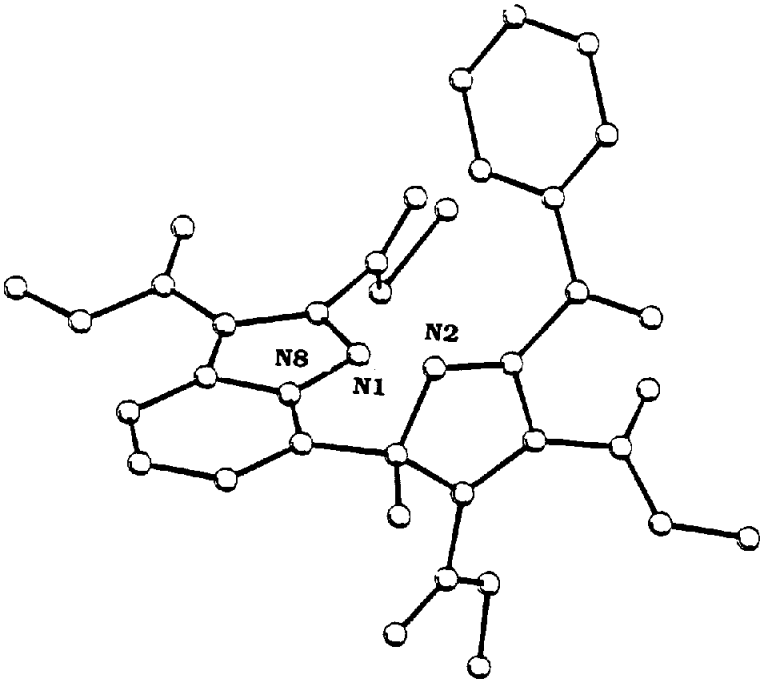


Figure 1. X-ray structure of compound (**5c**), showing original triazolopyridine nitrogen atoms.

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1. B.Abarca, R. Ballesteros, F. Mojarrad, M.R. Metni, S. Garcia-Granda, E.Perez- Careño,and G.Jones, *Tetrahedron*, accepted for publication

2. In a typical experiment, the salt (**1c**) (4.5 mmol) and anhydrous potassium carbonate (0.5 g) were suspended in toluene (20 ml) and vigorously stirred, while triethylamine (0.45 ml) was added, at room temperature. The solution turned yellow and formation of the ylide was complete after 3h. Dimethyl acetylenedicarboxylate (10.5 mmol) was added, when a red colour was observed. Stirring overnight was followed by filtration, evaporation, and chromatography of the residue on silica, eluting with hexane/ethyl acetate (9:1). The compound (**5c**) thus obtained crystallised from ethanol, m.p. 130-131°C (73%). (Found: C, 61.2; H, 4.3; N, 7.85. $C_{27}H_{23}N_3O_9$ requires C, 60.8; H, 4.3; N, 7.85%). $\delta(^1H)$ 8.25 (1H, dd, J = 8.8 and 1.5 Hz, H4), 8.14 (2H, d, J = 8.6 Hz, H2', 6'), 7.61-7.52 (2H, m), 7.46 - 7.38 (3H, m), 3.92 (3H, s), 3.80 (3H, s), 3.66 (3H, s), 2.1 (3H, s). $\delta(^{13}C)$ 22.42 (q), 51.73 (q), 52.51 (q), 52.58 (q), 52.76 (q), 83.07 (s), 102.78 (s), 115.47 (d), 120.21 (d), 127.74 (d), 128.62 (d), 130.66 (d), 134.37 (s), 134.63 (s), 137.17 (s), 137.78 (s), 142.32 (s), 146.58 (s), 158.42 (s), 161.2 (s), 162.65 (s), 163.09 (s), 170.19 (s), 189.24 (s).

Compound **5a** (82% yield) had m.p. 137-138°C (ethanol) (Found: C, 48.8; H, 4.0; N, 7.4. $C_{22}H_{21}N_3O_{10}.3H_2O$ requires C, 48.8; H, 3.9; N, 7.75%). $\delta(^1H)$ 8.2 (1H, dd, J = 8.8 and 1.5 Hz H4), 7.51 (1H, dd, J = 8.8 and 7.4 Hz, H5), 7.42 (1H, dd, J = 7.4 and 1.5 Hz, H6), 3.97 (3H, s), 3.96 (3H, s), 3.93 (3H, s), 3.89 (3H, s), 3.66 (3H, s), 2.04 (3H, s). $\delta(^{13}C)$, 21.33 (q), 51.53 (q), 52.36 (q), 52.48 (q), 52.78 (q), 53.18 (q), 82.38 (s), 102.72 (s), 115.31 (d), 120.23 (d), 127.69 (d), 136.83 (s), 138.0 (s), 142.42 (s), 146.35 (s), 158.09 (s), 160.86 (s), 161.28 (s), 162.9 (s), 163.2 (s), 163.55 (s), 164.32 (s). Compound **5b** (65% yield) had m.p. 132-134°C (ethanol). (Found: C, 55.1; H, 4.4; N, 8.15. $C_{23}H_{23}N_3O_{10}$ requires C, 55.1; H, 4.6; N, 8.4%). $\delta(^1H)$ 8.19 (2H, d, J = 8.6 and 1.3 Hz, H4), 7.45 (1H, dd, J = 8.6 and 8.8 Hz, H5), 7.32 (1H,dd, J = 8.8 and 1.3 Hz, H6), 4.2 (2H, q, OCH_2), 3.95 (3H, s), 3.91 (3H, s), 3.88 (3H, s), 3.65 (3H, s), 2.03 (3H, s), 1.37 (3H, t). $\delta(^{13}C)$ 13.82 (q), 21.35 (q), 51.54 (q), 52.35 (q), 52.47 (q), 52.72 (q), 62.68 (t), 82.35 (s), 102.63 (s), 115.29 (d), 120.15 (d), 127.83 (d), 136.86 (s), 138.09 (s), 142.35 (s), 146.26 (s), 157.84 (s), 160.8 (s), 160.84 (s), 162.83 (s), 163.25 (s), 163.56 (s), 164.55 (s). All spectra were performed on solutions in $CDCl_3$. Off resonance multiplicities are given for ^{13}C spectra, thus (q).

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