Synthesis of [1,2,4]Triazolo[1,5-*a*]pyrimidinium-2-olates and Structure Elucidation of their 1 : 2 Adducts with Dimethyl Acetylenedicarboxylate

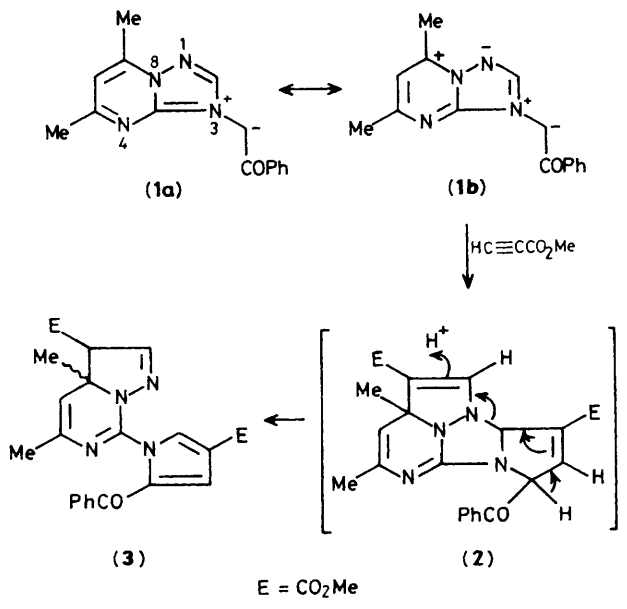
Hugh Marley,[a] Kevin J. McCullough,[b] Peter N. Preston,[b] and Stanley H. B. Wright[a]

[a] *Merck Sharp and Dohme Research Laboratories, Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU, U.K.*
[b] *Department of Chemistry, Heriot-Watt University, Riccarton, Currie, Edinburgh, EH14 4AS, U.K.*

The synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidinium betaines (**5**) are described and the structure of their 1 : 2 adducts (**8**) with dimethyl acetylenedicarboxylate determined.

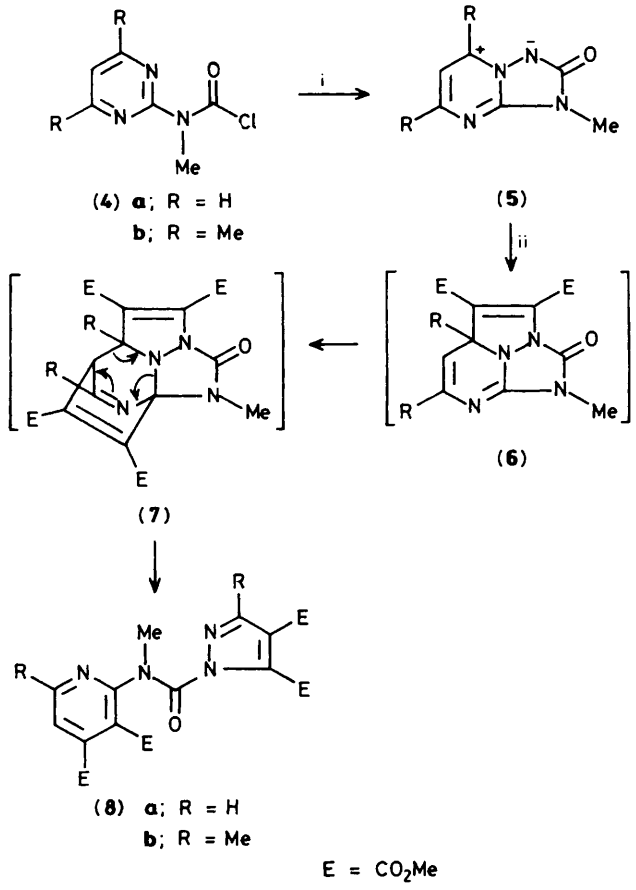
1,3-Dipolar cycloaddition reactions of heteroaromatic betaines with acetylene dipolarophilies are well documented,[1–3] but only recently have such reactions of a 1,2,4-triazole heteroaromatic betaine been reported.[4] Hori *et al.*[4] described the transformation of a triazolo[1,5-*a*]pyrimidine ylide (**1**) with methyl propiolate into a pyrazolo[1,5-*c*]-pyrimidine (**3**). This result was rationalised by invoking the generation of an 'ylide induced ylide' (**1b**) followed by a double 1,3-dipolar cycloaddition reaction [(**1**) → (**2**) → (**3**)]. We now report a novel cycloaddition reaction of a [1,2,4]triazolo[1,5-*a*]pyrimidine heteroaromatic betaine leading to cleavage of both the pyrimidine and triazole rings.

3-Methyl-[1,2,4]triazolo[1,5-*a*]pyrimidinium-2-olates (**5a,b**)† were prepared from 2-methylaminopyrimidines *via* carbamoyl chlorides (**4**)‡ by modification of a known route[5] to



† Satisfactory analytical and spectroscopic data were obtained for new compounds (**4a,b**), (**5a,b**), and (**8a,b**).

‡ Compound (**4a**), b.p. 120 °C, 0.4 torr (Kugelrohr) was prepared (70%) from 2-methylaminopyrimidine, $COCl_2$, PhMe, C_5H_5N, 40 °C, 0.5 h. Compound (**4b**), b.p. 100 °C, 0.2 Torr (Kugelrohr) was prepared (88%) from 2-methylamino-4,6-dimethylpyrimidine in similar fashion but with exclusion of pyridine in the reactants.



Reagents: i, Me_3SiN_3, PhMe; ii, DMAD (3.5 mol equiv.), xylene.

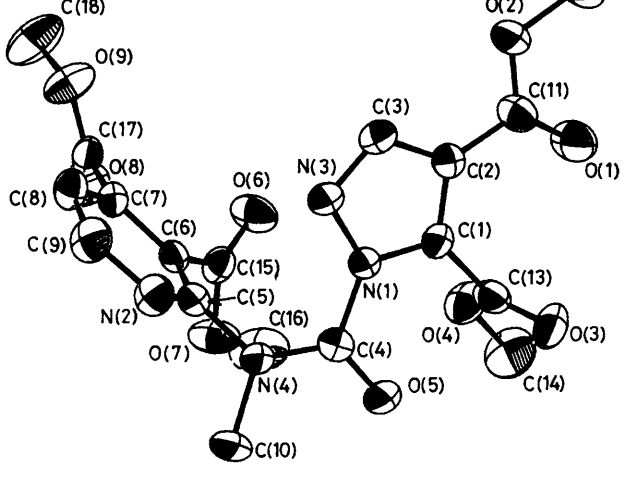


Figure 1. *X*-Ray crystal structure (ORTEP) of (**8a**).

similar pyridinium compounds. Reaction of betaines (**5a**)§ and (**5b**)§ with dimethyl acetylenedicarboxylate (DMAD) (3.5 mol equiv., xylene, reflux) gave crystalline compounds (**8a**) [m.p. 152—153 °C, 62%, yield] and (**8b**) [m.p. 145—146 °C, 65% yield]. Spectroscopic and analytical data¶ were consistent with 1:2 adducts [*e.g.* (**8a**), *m/z* 434, $C_{18}H_{18}N_4O_9$ and (**8b**), *m/z* 462, $C_{20}H_{22}N_4O_9$] but definitive structural assignment was not possible. However, single crystal *X*-ray analysis unambiguously identified the adduct from betaine (**5a**) as that depicted in structural formula (**8a**) and Figure 1 (ORTEP);‖ by analogy, betaine (**5b**) gives rise to adduct (**8b**).

In the present work it is likely that an initial 1,3-dipolar cycloaddition of the azomethine imine (**5**) is followed by a hetero Diels–Alder reaction [(**6**) → (**7**)] with ensuing fragmentation to the pyridine derivatives (**8**). As observed with the ylide (**1**),[4] cycloadditions of betaines (**5**) with DMAD involve [1,7]-annulation and not the anticipated [1,3-*a*]-annulation as would be expected by analogy with monocyclic mesoionic systems.[6,7] There is, therefore, encouragement to extend this type of transformation to heteroaromatic betaines related to (**5**) with a view to the synthesis of unusually-substituted heterocycles.

Received, 19th August 1986; Com. 1197

References

1 '1,3-Dipolar Cycloaddition Chemistry,' ed. A. Padwa, John Wiley, Inc., New York, 1984.
2 W. D. Ollis and C. A. Ramsden, *Adv. Heterocycl. Chem.*, 1976, **19**, 1.
3 W. D. Ollis, S. P. Stanforth, and C. A. Ramsden, *Tetrahedron*, 1985, **41**, 2239.
4 M. Hori, T. Kataoka, H. Shimuzu, E. Imai, K. Tanaka, K. Kimura, and Y. Hashimoto, *Tetrahedron Lett.*, 1986, **27**, 717.
5 G. Palazzo and L. Baiocchi, *Ann. Chim. (Rome)*, 1966, **56**, 1020.
6 S. Nakazawa, T. Kiyosawa, K. Hirakawa, and H. Kato, *Chem. Commun.*, 1974, 621.
7 W. Lwowski, S. Kanemasa, R. A. Murray, V. T. Ramakrishna, T. K. Thirwengadam, K. Yoshida, and A. Subbaraj, *J. Org. Chem.*, 1986, **51**, 1719.

§ Compounds (**5a**) [tan, m.p. 246 °C (decomp.), 59%] and (**5b**) [yellow, m.p. 244 °C (decomp.), 62%] were prepared from appropriate pyrimidine (**4**), Me_3SiN_3, PhMe, reflux, 18 h. *Spectral data: e.g.* for (**5b**): i.r. $\nu_{max.}$ ($CHCl_3$) 1680 cm^{-1}; ^1H n.m.r. (CD_3OD) δ 2.94 (s, 3H, 5-Me), 2.98 (d, 3H, *J* 0.5 Hz, 7-Me), 3.50 (s, 3H, N-Me), 7.13 (q, 1H, *J* 0.5 Hz, H-6); *m/z* 178 (100%) [$M^{\cdot+}$], 136 (43), 107 (32).

¶ *Spectral data* for (**8a**): i.r. $\nu_{max.}$ (Nujol) 1757, 1740, 1725, and 1710 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 3.53 (s, 3H, NMe), 3.80 (s, 3H, CO_2Me), 3.88 (s, 3H, CO_2Me), 3.92 (s, 3H, CO_2Me), 4.03 (s, 3H, CO_2Me), 7.57 (s, 1H, Ar-H), 7.73 (d, 1H, *J* 5.0 Hz, Ar-H), 8.89 (d, 1H, *J* 5.0 Hz, Ar-H); *m/z* 434 (1%) [$M^{\cdot+}$], 403 (6), 375 (100) [$M^{\cdot+} - CO_2Me$].

‖ *Crystal data* for (**8a**), $C_{18}H_{18}N_4O_9$, *M* = 434.3, monoclinic, *a* = 11.167(5), *b* = 7.5333(18), *c* = 24.272(6) Å, β = 96.20(3)°, *U* = 2029.9 Å^3, space group $P2_1/c$ (No. 14), *Z* = 4, D_m = 1.46(1) g cm^{-3} (flotation in CCl_4–hexane), D_c = 1.421 g cm^{-3}, μ(Cu-K_α) = 9.51 cm^{-1}, *F*(000) = 904, m.p. 152—153 °C (thick, colourless plates from ethyl acetate–hexane), crystal dimensions 0.58 × 0.43 × 0.40 mm. The intensity data were collected on a CAD-4 diffractometer (Cu-K_α radiation, λ = 1.54180 Å, ω=2θ scans) and corrected for Lorentz, polarisation, and absorption effects. Out of 4311 unique data measured ($3 < \theta < 69°$), 2639 had $I > 2\sigma(I)$. The structure was solved by direct methods (SHELX 84) and refined (SHELX 76) by full-matrix least squares methods (all non-hydrogen atoms anisotropic). All methyl groups were treated as idealised rigid groups (d_{C-H} 1.080 Å). At convergence, *R* and R_w {$W = 1/[\sigma^2(F) + 0.0764F^2]$} were 0.056 and 0.088 respectively. The bond distances and angles were generally close to expected values with e.s.d.s in the ranges 0.003—0.004 Å and 0.1—0.3 Å respectively. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.