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The dipolar cycloaddition of methyl acrylate to 1,5,6-trimethyl-3-oxidopyrazinium

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5,6-Dimethylpyrazin-2-one reacts with iodomethane to give a quaternary salt, deprotonation of which liberates a 3-oxidopyrazinium which undergoes a 1,3-dipolar cycloaddition with methyl acrylate to form methyl 5,8-dimethyl-4-methylene-2-oxo-3,8-diazabicyclo[3.2.1]octane-6-*exo*-carboxylate, $C_{11}H_{16}N_2O_3$, as the major product.

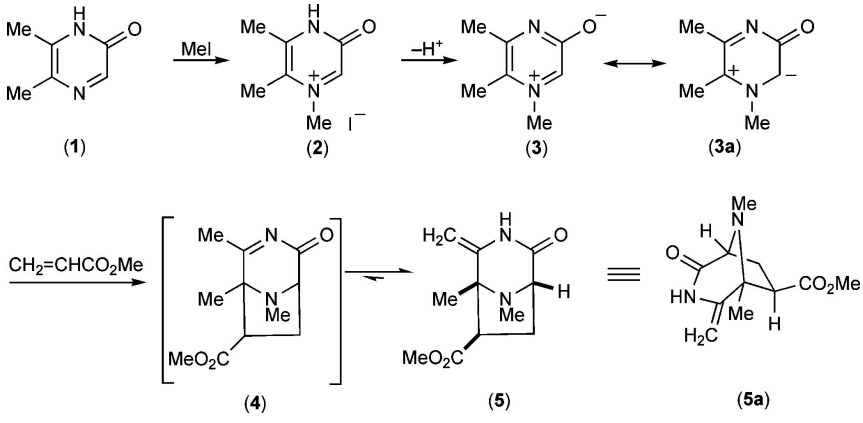
Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.031
wR factor = 0.089
Data-to-parameter ratio = 8.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

We have been investigating the 1,3-dipolar cycloaddition chemistry of 3-oxidopyraziniums (Kiss *et al.*, 1987; Allway *et al.*, 1990; Yates *et al.*, 1995). These reactions efficiently produce bridged bicyclic systems, *viz*. 3,8-diazabicyclo[3.2.1]octanes, which comprise key structural components of such biologically active natural products as anticancer quinocarcin (Takahashi & Tomita 1983; Tomita *et al.*, 1983; Hirayama & Shirahata, 1983) and antibiotic lemonomycin (He *et al.*, 2000). Our studies were initially inspired by the series of benchmark papers by Katritzky and co-workers [for reviews, see Dennis *et al.* (1976) and Katritzky & Dennis (1989)] on the cycloadditions of 3-oxidopyridiniums. In neither Katritzky's extensive studies nor our own on 3-oxidopyraziniums had the possible influence of a substituent on the 1,3-dipole at one (or both) of the future ring-junction positions been assessed. This report describes our first study to remedy this omission, in which the reactivity of 1,5,6-trimethyl-3-oxidopyrazinium, (3) (see scheme; synthesis of 1,5,6-trimethyl-3-oxidopyrazinium and its reaction with methyl acrylate), was assessed.



5,6-Dimethylpyrazin-2-one, (1) (Jones, 1949; Karmas & Spoerri, 1952), was reacted with iodomethane to produce the methiodide (2), treatment of which with triethylamine allowed the generation of the zwitterion (3), *in situ* and in the presence of methyl acrylate. The reactivity and regioselectivity of such 3-oxidodiaziniums is easily understood in terms of a resonance contributor [(3a) in this case]. The immediate products of the

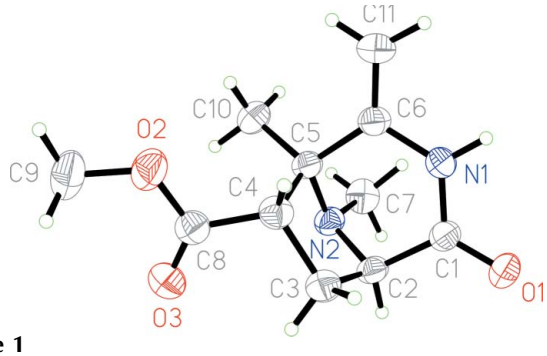


Figure 1
Plot of (4), with displacement ellipsoids drawn at the 50% probability level.

cycloadditions [(4) in this case] are not isolated, but tautomerize to the enamide structure [(5) in this case], (5a) showing better the bicyclic nature of the product. A mixture of two isomeric products was formed from which the major isomer was isolated, crystalline, allowing an X-ray analysis to show that it was the *exo*-ester (4) (Fig. 1). Thus, the additional oxidopyrazinium-6-methyl, appearing at the ring junction (C-5) in the cycloadduct, did not affect the efficiency or stereoselectivity of the cycloaddition, compared with the comparable reaction of 1,5-dimethyl-3-oxidopyrazinium which also gave a 6-*exo*-ester as the major product (Yates *et al.*, 1995).

Experimental

5,6-Dimethylpyrazin-2-one (Jones, 1949; Karmas & Spoerri, 1952) (800 mg, 6.5 mmol) and iodomethane (2 ml, 32.5 mmol, 5 equivalents) were heated under reflux in MeCN (150 ml) under nitrogen for 24 h. The solvent was evaporated under vacuum and the residue extracted with CH_2Cl_2. Insoluble material was removed by filtration and the solution evaporated, leaving 3,4-dihydro-1,5,6-trimethyl-3-oxopyrazinium iodide as a dark-brown crystalline solid (1.12 g, 66%; m.p. >523 K); ^{1}H NMR (D_2O, 300 MHz, δ, p.p.m.)): 8.20 (1H, *s*, C2—H), 4.15 (3H, *s*, NMe), 2.50 and 2.45 (2 × *s*, 2 × 3H, 2 × CMe). Analysis found: C 32.31, H 4.02, N 10.39%; $C_7H_{11}N_2O$ requires: C 31.60, H 4.17, N 10.53%

A solution of 3,4-dihydro-1,5,6-trimethyl-3-oxopyrazinium iodide (1.5 g, 5.6 mmol), Et_3N (1.6 ml, 11.2 mmol, 2 equivalents), and methyl acrylate (1.52 ml, 16.8 mmol, 3 equivalents) in dry MeCN (100 ml) was heated under reflux for 2 h. Solvents were removed from the resulting orange solution under vacuum, H_2O (30 ml) was added and the product extracted into CH_2Cl_2 (3 × 30 ml). The combined dried extract was evaporated leaving a brown oil (0.88 g, 70%) from which, by careful chromatography over silica, eluting with *n*-hexane–EtOAc (1:1), the major (thin-layer chromatography) adduct was obtained as colourless plates (330 mg, 26%; m.p. 383–388 K).

Crystal data

$C_{11}H_{16}N_2O_3$
M_r = 224.26
Monoclinic, $P2_1/c$
a = 9.818 (10) Å
b = 7.89 (2) Å
c = 14.80 (3) Å
β = 102.23 (8)°
V = 1120 (4) Å^3
Z = 4
D_x = 1.330 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 17414 reflections
θ = 2.1–25.0°
μ = 0.10 mm^{-1}
T = 293 (2) K
Plate, colourless
0.3 × 0.2 × 0.1 mm

Data collection

Rigaku R-AXIS II diffractometer
φ scans
Absorption correction: none
17414 measured reflections
1767 independent reflections
1516 reflections with $I > 2\sigma(I)$
R_{int} = 0.037
θ_{max} = 25.0°
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 9$
$l = -17 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.089
S = 1.03
1767 reflections
210 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0555P)^2 + 0.1608P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.037 (6)

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^{i}	0.913 (18)	2.082 (19)	2.980 (6)	167.6 (15)

Symmetry code: (i) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.

H atoms were found by difference Fourier methods and refined isotropically, with refined C—H distances in the range 0.932 (15)–1.041 (19) Å and an N—H distance of 0.913 (18) Å.

Data collection: *MSC Diffractometer Control Software* (Molecular Structure Corporation, 1992); cell refinement: *DENZO* (Otwinowski & Minor, 1987); data reduction: *DENZO*; program(s) used to solve structure: *SAPI91* (Fan, 1991); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2001); software used to prepare material for publication: *TEXSAN* (Molecular Structure Corporation, 1995).

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