Thermal Rearrangement of Ethyl 5-Nitro-4-phenyl-2-oxa-3-azabicyclo[3.1.0]hex-3-ene-1-carboxylate into a Quinoxaline System

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The title compound **2** is found to undergo thermal isomerization into the quinoxaline derivative **3**, as shown by a crystal structure determination of the latter; a mechanistic rationale for this unusual rearrangement is suggested.

Thermal ring opening of 1,6,6-trimethyl-4-phenyl-2-oxa-3-azabicyclo[3.1.0.]hex-3-ene has been previously reported to lead to fragmentation products together with a minor amount of an isomeric azirine.[1] After the first 1,5-difunctionalized derivative of the same bicyclic ring **2** became recently available by 1,3-dipolar cycloaddition of diazomethane on the activated C(4)–C(5) double bond of the nitroisoxazole **1** followed by loss of nitrogen,[2] we decided to explore its reactivity.

Surprisingly, prolonged heating of this compound in the solid state (60 °C, 70 h) gave rise mainly to the 1,2-dihydro-2-oxoquinoxaline 4-oxide **3**, that was isolated as a pure product in 55% yield.

Treatment of **3** with diazomethane molar ratio (1:3) afforded a complex mixture containing the methyl derivatives **4** and **5** as the predominant components; these products,

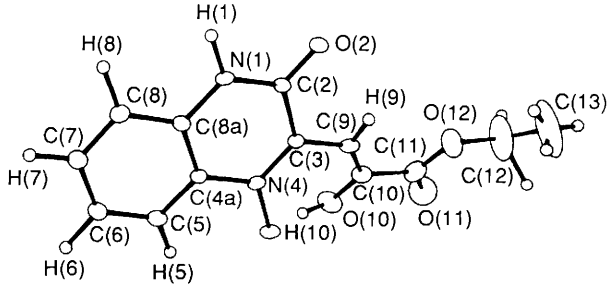
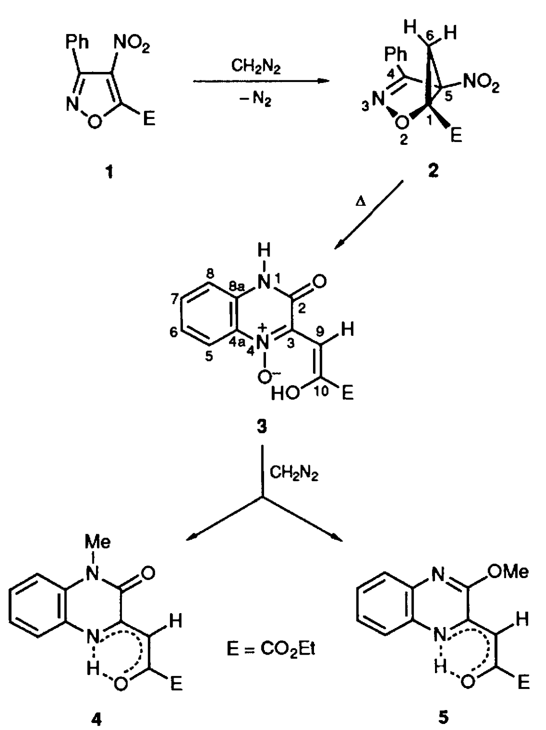


Fig. 1 ORTEP drawing of **3**; selected bond lengths (Å): N(1)–C(2) 1.342(6), C(2)–O(2) 1.230(6), C(2)–C(3) 1.476(6), C(3)–N(4) 1.346(6), N(4)–O(4) 1.331(5), N(4)–C(4a) 1.403(6), C(4a)–C(8a) 1.393(6), C(3)–C(9) 1.423(7), C(9)–C(10) 1.334(8), C(10)–O(10) 1.316(8)



Scheme 1

arising from a concomitant deoxygenation process, were separated by flash-column chromatography.

Although the spectral data for **3**† clearly indicate the conversion of the phenyl and NO_2 groups of the starting isoxazoline **2** into a benzo-condensed and a *N*-oxide moiety, respectively, the framework of the reaction product, reported in Fig. 1, was unambiguously determined by a single crystal X-ray analysis.‡

The isomerization of compound **2** into **3** does not appear to be straightforward. A plausible mechanistic pattern probably involves in the primary step the N–O isoxazoline breaking, assisted by a Beckmann-type migration of the phenyl group, with formation of the keteneimine **7** through the intermediate **6** or by a concerted ring opening of the cyclopropane moiety of **2**; addition of a trace of water to **7** can then give rise to the nitroamide **8** which, in turn, evolves into the final product **3** by cyclization and elimination of the catalyst.§

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References

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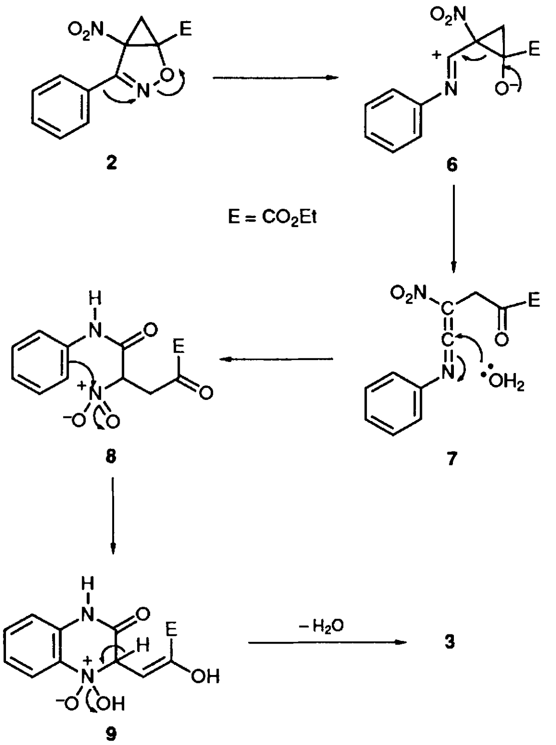

Scheme 2

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† *Physical and spectroscopic data:* for **3**: m.p. 205–206 °C; IR(KBr) ν 3250–2500 (broad structured band, NH and OH), 1732 (CO_2Et), 1673 (CONH), 1280 cm^{-1} (N^+–O^-); ^1H NMR ([$^2H_6$]DMSO, 200 MHz) δ 1.28 (t, *J* 7.1 Hz, 3H, CH_3CH_2O), 4.26 (q, *J* 7.1 Hz, 2H, CH_3CH_2O), 7.05 (s, 1H, H-9), 7.36–7.44 (m, 2H, Ar-2H), 7.61–7.70 (m, 1H, Ar-1H), 8.12–8.17 (m, 1H, Ar-1H), 12.97 (br, s, 1H, NH/OH), 13.43 (s, 1H, OH/NH); ^{13}C NMR ([$^2H_6$]DMSO, 50 MHz) δ 14.0 (q, CH_3CH_2O, 61.83 (t, CH_3CH_2O), 96.20 (d, C-9), 116.66(d), 119.41(d), 124.78(d), 129.35(s), 131.05(s), 132.10(d) (aromatic Cs), 140.38 (s, C-3), 153.65 (s, 2-CO/C-10), 157.29 (s, C-10/2-CO), 163.20 (s, CO_2Et); MS(EI, 70 eV) *m/z* 276 (M^+) (8%), 260 [$(M\text{–}O)^+$] (34%), 203 [$(M\text{–}CO_2Et)^+$] (51%), 187 {[$(M\text{–}O)\text{–}CO_2Et]^+$}/{[$(M\text{–}CO_2Et)\text{–}O]^+$} (100%).

The other new compounds **4** and **5** also gave satisfactory elemental analyses and spectral data.

‡ *Crystal data* for **3**: $C_{13}H_{12}N_2O_5$, orange crystals (from acetone), *M* = 276.3, triclinic, space group $P\bar{1}$, a = 6.885(1), b = 7.942(1), c = 12.138(1) Å, α = 76.48(1), β = 84.16(1), γ = 74.38(1)°, V = 621.0(1) Å^3, Z = 2, $F(000)$ = 288, μ = 1.08 cm^{-1}, D_c = 1.48 g cm^{-3}, graphite monochromated (Mo-Kα) radiation (λ = 0.7107 Å). 1976 Reflections were collected on an Enraf-Nonius CAD4 automatic diffractometer in the range $5 \leq 2\theta \leq 50°$. 1457 Unique reflections with $I > 3\sigma(I)$ were used in the structure determination and refinement. The structure was solved by using direct methods and successive Fourier syntheses; then it was refined by using the full-matrix least squares SHELX76 program[3] to R = 0.073 and R_w = 0.057, where $w = 1/\sigma^2 (F_0)$. Anisotropic thermal parameters were used for all the non-hydrogen atoms; the hydrogen atoms were refined isotropically. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

§ A rigorous exclusion of air moisture was not ensured in our experiments.