

REACTIONS OF THE PYRROLIDINE DIENAMINE OF PUMMERER'S KETONE WITH
NITROSCARBONYLMETHANE

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Abstract - The pyrrolidine dienamine (2) of Pummerer's ketone (1) reacts with the dienophile nitrosocarbonylmethane to give a bridged oxazine (9). The structure (9), incorporating 2 mol equiv. of the nitroso compound with reductive loss of 1 oxygen atom, has been determined by X-ray methods. Other products were the hydroxamic acid (6) and the acetamidoenone (7).

Barton and his coworkers¹ proposed the constitution (1) for Pummerer's ketone, an oxidation product² of *p*-cresol, and, on structural and mechanistic grounds, formulated³ the oxidative coupling of phenols as a general biogenetic theory. This has withstood the test of numerous biosynthetic experiments and has formed the basis for the total synthesis of phenolic natural products following 'biomimetic' routes. Pummerer's ketone [the racemic form of (1)] has more recently been employed⁴ as a 'pharmacophoric synthon' for the synthesis of analogues of the morphine alkaloids. We selected the pyrrolidine dienamine (2)⁵ of Pummerer's ketone to extend our study⁶ of the Diels-Alder reactions of acylnitroso compounds (RCONO), a class of transient dienophiles formed by oxidation of hydroxamic acids (RCONHOH)⁷.

The ¹H nmr spectrum (100 MHz) of the dienamine (2), in deuteriochloroform at ambient temperature, showed broad, ill-defined signals for 1-, 2-, 4-, and 4a-H, in agreement with literature reports⁵. Confirmation that signal broadening arose from site exchange, presumably via the transformation (2) ⇌ (3), was obtained from variable temperature studies. At -60°C the spectrum showed a pair of AB quartets, δ 6.12 and 5.74 (J 10 Hz, 2- and 1-H), and δ 5.09 and 4.40 (J 6 Hz, 4a- and 4-H), as expected for the dienamine structure (2). With increasing temperature, the signals broadened and merged and at 60°C had coalesced to form a broad singlet, δ 5.34. The dienamine (2) reacted with nitrosocarbonylmethane (MeCONO) formed *in situ* from aceto-hydroxamic (MeCONHOH) under the usual conditions.⁶ Thus, acetohydroxamic acid (2 mol equiv.) was added slowly to the dienamine (2) and tetraethylammonium periodate (2 mol equiv.) in dichloromethane at 0°C. Chromatography of the reaction mixture gave, as a major crystalline product (28%), the oxazine (9), presumably derived from the enamine (8) by hydrolysis. Many structural features of this product (9) were revealed spectroscopically. However, the elemental composition implied the

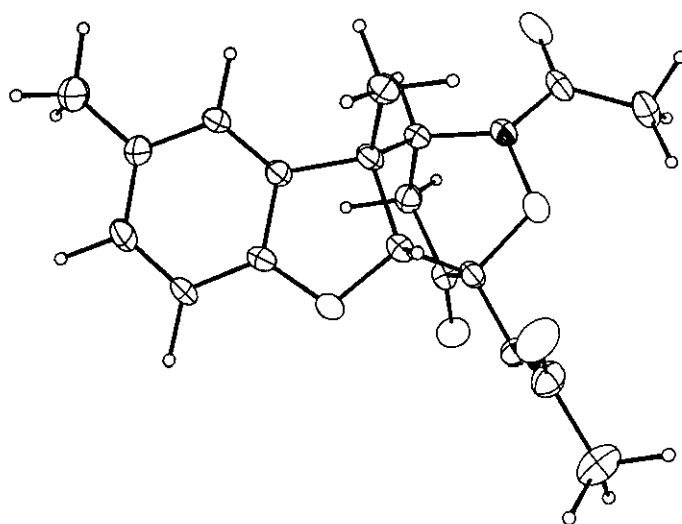
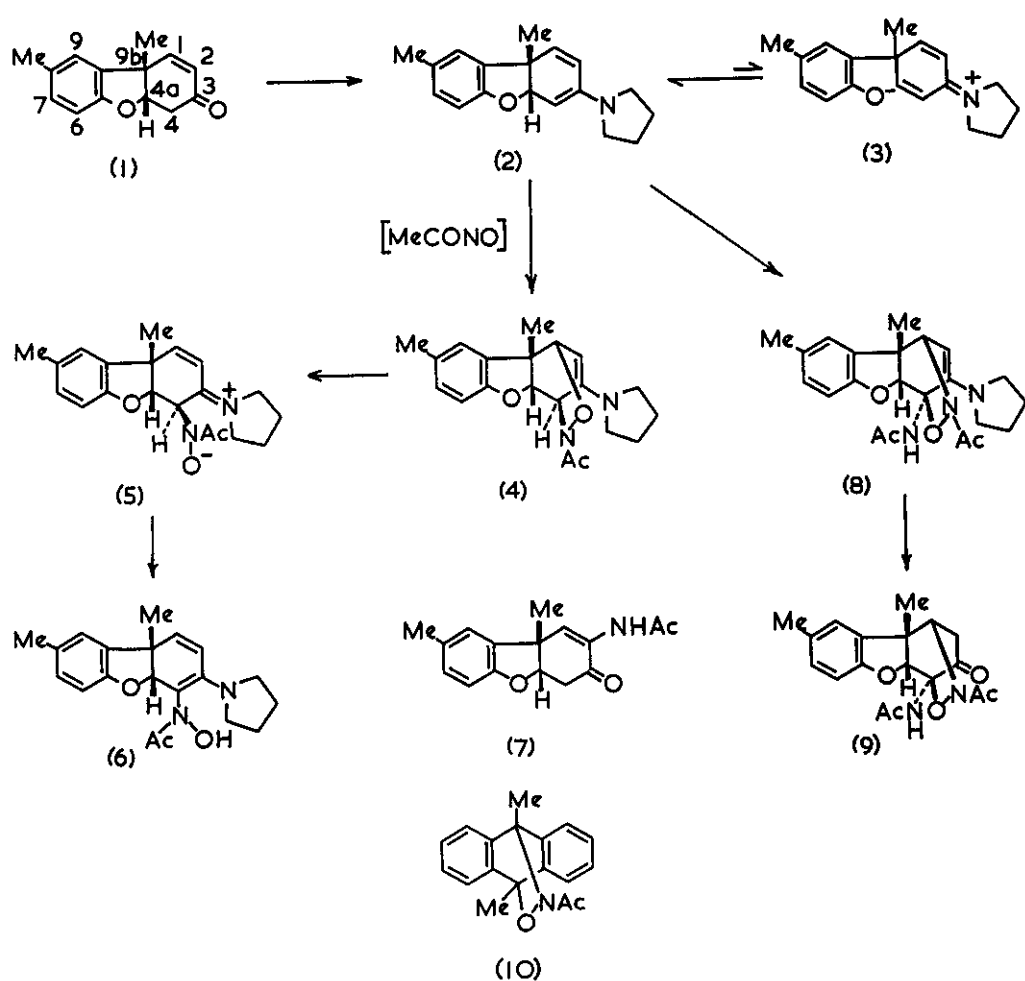


FIGURE : (9)

Compound (6): mp 166-168°C (from Et₂O-light petroleum); ν_{max} (CHCl₃) 3385, 1678, and 1486 cm⁻¹; δ_{H} (100 MHz; CDCl₃) 1.68 (7H, m, 9b-Me and pyrrolidinyl 3- and 4-CH₂), 2.14 (s, Ac), 2.28 (s, 8-Me), 2.2-3.0 (4H, m, pyrrolidinyl 2- and 5-CH₂), 5.93 (d, J 10.0 Hz, 2-H), 6.06 (d, J 1.8 Hz, 4a-H), 6.48 (dd, J 10.0 and 1.8 Hz, 1-H), 6.70 (d, J 8.4 Hz, 6-H), 7.00 (2H, m, 7- and 9-H), and 7.17 (br s, OH).
Compound (7): mp 167-168°C (from Et₂O-light petroleum); ν_{max} (CHCl₃) 3385, 1675, and 1510 cm⁻¹; δ_{H} (100 MHz; CDCl₃) 1.60 (s, 9b-Me), 2.04 (s, Ac), 2.30 (s, 8-Me), 2.86 (dd, J 17.7 and 3.7

PHYSICAL DATA FOR NEW COMPOUNDS

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reaction mechanisms, in particular the unaccounted loss of oxygen.
adduct (10). Experiments are in progress with other C-nitroso compounds in order to clarify the the usual conditions, either with acetoxyhydroxamic acid and tetraethylammonium periodate or with the products. However, this hydroxamic acid (6) was recovered in good yield after treatment, under Initially, the hydroxamic acid (6) was thought likely to be a precursor for the other two derivative. However, two products, (7) and (9), had again undergone reductive deoxygenation. opening and reclosure of the benzofuran ring in either a dieneamine [cf. (2) $\rightleftharpoons$ (3)] or enone⁹ Also, attachment of the acetyl group at C-2 rather than C-4 in the enone (7) may result from (4%). The hydroxamic acid (6) may arise from the reaction sequence (2) $\rightarrow$ (4) $\rightarrow$ (5) $\rightarrow$ (6). (14%), and 2 new crystalline products, the hydroxamic acid (6) (18%) and the acetamidone (9) Pummerer's ketone (1) (24%), presumably derived by hydrolysis of the dieneamine (2), the oxazine (9) equiv.) were heated in benzene at 60°C for 27 h. Chromatography of the reaction mixture gave of the 9,10-dimethylanthracene adduct (10)⁸. Thus, the dieneamine (2) and the adduct (10) (2 mol again treated with nitrosocarbonylmethane, this time released slowly by retro-Diels-Alder cleavage In order to clarify the mechanism of formation of the bridged oxazine (9), the dieneamine (2) was benzohydroxamic acid.
1750 cm⁻¹, was obtained from the dieneamine (2) and nitrosocarbonylmethane formed *in situ* from elucidated by X-ray crystallography (see Figure). A similar product (9; Ac = Bz), ν_{max} (CCl₄) carbonyl band with an unexpected high frequency, ν_{max} (CCl₄) 1750 cm⁻¹. The structure (9) was removal of 1 oxygen atom under oxidising conditions. Moreover, the ir spectrum showed a incorporation of 2 mol equivalents of nitrosocarbonylmethane with, remarkably, reductive

Hz, 4-H), 3.16 (dd, J 17.7 and 2.9 Hz, 4-H), 4.58 (ddd, J 3.7, 2.9, and 1.7 Hz, 4a-H), 6.68 (d, J 8.0 Hz, 6-H), 6.95 (br d, J 8.0 Hz, 7-H), 7.05 (br s, 9-H), 7.44 (d, J 1.6 Hz, 1-H), and 7.73 (br s, NH, exch. with D_2O).

Compound (9): mp 192-193°C (from CH_2Cl_2 -light petroleum); ν_{max} . (CCl_4) 3480, 1750, 1708, and 1665 cm^{-1} ; δ_H (200 MHz; $CDCl_3$) 1.65 (s, 9b-Me), 2.13 (s, ONAc), 2.15 (s, NHAc), 2.26 (s, 8-Me), 2.32 (dd, J 19.5 and 1.9 Hz, 2-H), 2.70 (dd, J 19.5 and 3.9 Hz, 2-H), 5.10 (m, 1-H), 5.98 (s, 4a-H), 6.63 (d, J 8.2 Hz, 6-H), 6.85 (br s, NH, exch. with D_2O), 6.90 (m, 9-H), and 6.95 (dm, J 8.2 Hz, 7-H); δ_C (50.4 MHz; $CDCl_3$) 20.2 (9b-Me), 20.75 (8-Me), 24.3 (COMe), 24.5 (COMe), 39.1 (C-2), 49.0 (C-9b), 54.2 (C-1), 83.5 (C-4a), 86.0 (C-4), 110.2 (C-6), 123.7 (C-9), 129.6 (C-8 or -9a), 130.5 (C-7), 131.9 (C-9a or -8), 156.3 (C-5a), 169.5 (COMe), 170.3 (COMe), and 197.45 (C-3); **crystal data:** $C_{18}H_{20}N_2O_5$, $M = 344.4$, triclinic, space group $P\bar{1}$, $a = 9.890(1)$, $b = 11.789(2)$, $c = 16.969(4)$ Å, $\alpha = 74.63(2)$, $\beta = 77.33(2)$, $\gamma = 74.74(1)^\circ$, $U = 1816.5$ Å³, $F(000) = 728$, $D_c = 1.26$ g cm^{-3} , $Z = 4$, $\mu(Mo-K\alpha) = 0.93$ cm^{-1} . 2428 Independent reflections ($I \geq 3.0\sigma_I$) were measured on an Enraf-Nonius CAD-4 automatic diffractometer. The structure was solved by MITHRIL¹⁰ using direct techniques and refined to a final R value of 0.087. There are two independent molecules in the asymmetric unit.

Compound (9; Ac = Bz): mp 186-188°C (from CH_2Cl_2 -light petroleum); ν_{max} . (CCl_4) 3385, 1750, 1688, and 1640 cm^{-1} ; δ_H (90 MHz; $CDCl_3$) 1.84 (s, 9b-Me), 2.28 (s, 8-Me), 2.42 (dd, J 19.5 and $ca.$ 2 Hz, 2-H), 2.94 (dd, J 19.5 and $ca.$ 4 Hz, 2-H), 5.28 (m, 1-H), 6.41 (s, 4a-H), 6.63 (d, J 8 Hz, 6-H), 6.98 (2H, m, 7- and 9-H), 7.45 (m, m - and p -Bz-H), and 7.86 (m, o -Bz-H).

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