Reversible Cyclisation of *ortho*-Blocked *N*-Arylnitroso-imines

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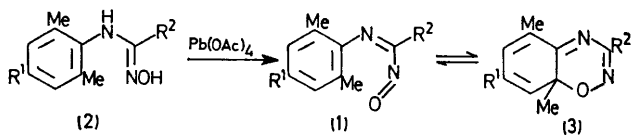
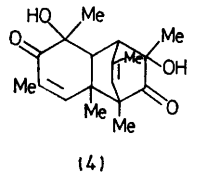
Summary *N*-Aryl-*C*-nitroso-imines (**1**), in which the *ortho* positions of the *N*-aryl substituent are occupied by methyl groups, undergo rapid but reversible ring-closure to the 1,2,4-oxadiazines (**3**); the nitroso-imines can be intercepted in a Diels–Alder reaction with thebaine, whereas the tautomers (**3**) slowly dimerise.

WE have reported that *N*-arylnitroso-imines are generated by the oxidation of the corresponding amidoximes, and that, in the absence of a trapping agent, they undergo very rapid and irreversible ring-closure to 1,2,4-benzoxadiazines.[1] In the hope of increasing the lifetime of the transient nitroso-imines, the *ortho* positions of the *N*-aryl substituent were blocked with methyl groups; the nitroso-imines (**1**) have therefore been generated from the corresponding amidoximes.

The *N*-mesitylnitroso-imine (**1a**) was generated by oxidation of the amidoxime (**2a**), m.p. 162—164 °C, with lead tetra-acetate in dichloromethane at −78 °C. A red solution was obtained; the colour faded when the temperature of the solution was allowed to rise above −20 °C, and a yellow oil was isolated in quantitative yield. The 1,2,4-oxadiazine structure (**3a**) was assigned to the product on the basis of its ^{1}H n.m.r. spectrum, which showed signals for the



a; R^1 = Me, R^2 = CO_2Et
b; R^1 = Me, R^2 = COPh
c; R^1 = Me, R^2 = p-Me·C_6H_4
d; R^1 = H, R^2 = CO_2Et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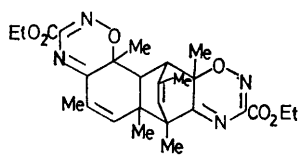
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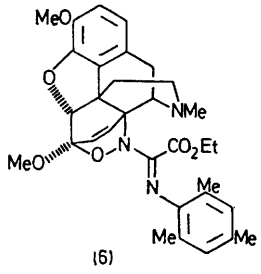
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ring methyl groups at δ 1·09, 1·95, and 2·19, and for the ring hydrogen atoms at δ 5·93 and 6·40. The u.v. spectrum contained a long wavelength absorption at 390 nm (ε 510). When the oil was allowed to remain at room temperature for several days, a colourless crystalline dimer, m.p. 161—162 °C, was isolated (40%). Cyclohexa-2,4-dienones readily form dimers by Diels–Alder addition;[2] comparison of the 100 MHz ^{1}H n.m.r. spectrum of the known[3] dimer (**4**) of 6-hydroxy-2,4,6-trimethyl cyclohexa-2,4-dienone with that of the dimer obtained from the oxadiazine (**3a**) showed that the two dimers were closely similar in structure. In particular, the adjacent methine hydrogens of (**4**) (δ 2·81 and 3·15) have a very small coupling constant (< 1 Hz) because, as models show, the C–H bonds are nearly orthogonal; similarly, the methine hydrogens of the dimer of (**3a**), which occur at δ 2·61 and 3·51, show no discernible coupling. On this basis, the structure (**5**) is assigned to the dimer of (**3a**); this mode of dimerisation is the one normally observed with cyclohexa-2,4-dienone derivatives.[2]

When the oxidation of the amidoxime (**2a**) was carried out at −78 °C in the presence of thebaine, a red colour was not observed in the solution, and a 1:1 adduct, (**6**), of thebaine and the nitroso-imine (**1a**), m.p. 92—96 °C, was isolated (84%). The presence of a mesityl group in (**6**) is indicated by a signal at δ 6·77 (2H) corresponding to that expected for the ring hydrogen atoms; the three methyl groups appear as separate signals at δ 1·98, 2·11, and 2·20, presumably because of restricted rotation of the substituent. The oxadiazine (**3a**) and thebaine gave the same adduct (**6**) (70%) after 24 h in dichloromethane at room temperature; this indicates that closure of the nitroso-imine to the oxadiazine is reversible, although the equilibrium strongly favours the oxadiazine.

Sodium borohydride in methanol–tetrahydrofuran at −10 °C very rapidly reduced the oxadiazine (**3a**) to the amidoxime (**2a**) in high yield (80%); this could result from nucleophilic addition to the diene-imine followed by ring opening, or possibly by reduction of the nitroso-imine tautomer. The oxadiazine (**3a**) did not react with phosphorus trichloride, but was degraded to a complex mixture of products by trifluoroacetic acid or by irradiation. 4-Phenyl-1,2,4-triazoline-3,5-dione gave a Diels–Alder adduct (70%; m.p. 149 °C) with (**3a**) at room temperature.

An analogous series of reactions was observed with the nitroso-imines (**1b**), (**1c**), and (**1d**): in each case the nitroso-imine cyclises to the 1,2,4-oxadiazine (**3**).

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[1] T. L. Gilchrist, M. E. Peek, and C. W. Rees, preceding communication.
[2] A. J. Waring, in 'Advances in Alicyclic Chemistry,' eds. H. Hart and G. J. Karabatos, Academic Press, New York, 1966, Vol. 1., p. 129.
[3] E. Adler, J. Dahlen, and G. Westin, *Acta Chem. Scand.*, 1960, **14**, 1580.