1,4,2-Dioxazole Synthesis by the Reaction of Nitrosocarbonyl Compounds with 2,5-Dimethylfuran

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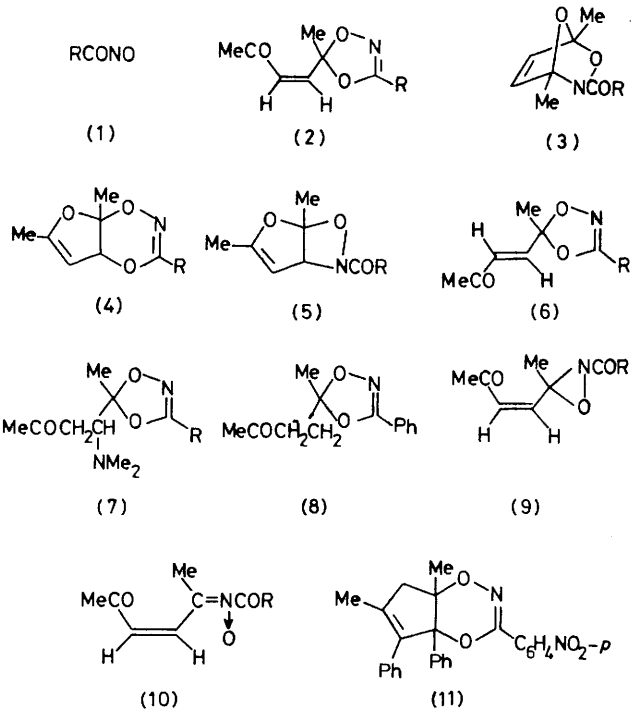
Summary Oxidation of hydroxamic acids in the presence of 2,5-dimethylfuran gives excellent yields of the 3-substituted-5-methyl-5-(*cis*-3-oxobutenyl)-1,4,2-dioxazoles (**2**); the reaction is reversible and probably occurs by way of an initially formed Diels–Alder adduct.

NITROSOCARBONYL compounds (**1**), the intermediates in hydroxamic acid oxidations,[1] react with dienes to give 3,6-dihydro-1,2-oxazines, the normal Diels–Alder adducts (4+2 addition),[1] and 5,6-dihydro-1,4,2-dioxazines;[2,3] the latter arise either through isomerisation of the oxazines,[2] or perhaps by direct cycloaddition (2+4), competitive with the formation of the oxazines.[3]

We report that yet another heterocyclic system can be obtained from nitrosocarbonyl compounds and dienes, namely 3-substituted-5-methyl-5-(*cis*-3-oxobutenyl)-1,4,2-dioxazoles (**2**) by reaction with 2,5-dimethylfuran.

Treatment of a suspension of benzohydroxamic acid and silver oxide in ethyl acetate containing an excess of dimethylfuran at room temperature for 12 h gave a nearly quantitative yield of an oil, to which we assign the structure (**2a**) on the basis of its spectra and chemical reactions. These readily exclude all the plausible bicyclic adducts with dimethylfuran, namely the oxazine (**3**) (4+2 addition), the dioxazine (**4**) (2+4), the oxazetidine (**5**) (2+2), and likewise the regioisomers of (**4**) and (**5**).

The ^{1}H n.m.r. spectrum (CCl_4) of the oil showed, as well as phenyl absorption, two vinylic Hs as an AB quartet at τ 3·90 and 4·04 (J 12 Hz, *cis*-alkene), and two Me singlets at 7·73 (COMe) and 8·10 (tertiary Me); the i.r. spectrum (CCl_4) had CO absorption at 1715 (*cis*-enone) and a weak



a; R = Ph
b; R = Bu^t
c; R = *p*-BrC_6H_4
d; R = *p*-$NO_2C_6H_4$

band at 1625 cm^{-1} (C=N[4]), while the u.v. spectrum (EtOH) had two bands at 234 (enone) and 264 nm (PhC=N-[5,6]). In the mass spectrum the two dominant peaks were at *m/e* 231 (M^{+}) and 119 ($PhCNO^{+}$); the latter fragment can be viewed as arising from a retro 1,3-dipolar cycloaddition.[7]

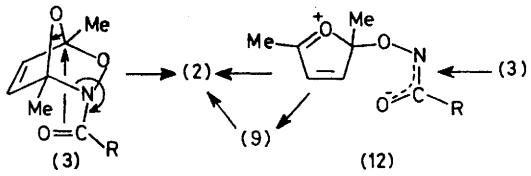
The reaction with dimethylfuran is quite general. From the appropriate hydroxamic acids the dioxazoles (**2b—d**) were prepared. The t-butyl derivative (**2b**) and the *p*-bromophenyl derivative (**2c**) were oils; the *p*-nitrophenyl derivative (**2d**) was crystalline, m.p. 106·5—108·5 °C.

The *cis*-compound (**2a**) could be isomerised quantitatively to the oily *trans*-isomer (**6a**) by refluxing it with pyridine or triethylamine as catalyst in benzene or chloroform: M^{+} 231; ν(CCl_4) 1710 and 1690 cm^{-1}; the ^1H n.m.r. spectrum (CCl_4) included a vinylic AB quartet at τ 3·32 and 3·42 (*J* 16 Hz, *trans*-alkene) and very slight Me shifts from those of (**2a**). Similarly (**2b—d**) could be isomerised; the *trans*-isomer (**6d**) was crystalline, m.p. 152·5—153·5 °C.

The mechanism of isomerisation of (**2**) to (**6**) probably involves reversible Michael addition of the tertiary amine to the double bond. Dimethylamine adds smoothly to either (**2**) or (**6**) to give a diastereomeric mixture of the stable amino ketones (**7**). Crystallisation of the mixture obtained from the *p*-nitro compound (**2d**) gave one isomer of (**7d**), m.p. 110—111 °C: *m/e* 304 $(M-Me)^{+}$; ν(Nujol) 1718 cm^{-1} (C=O); τ($CDCl_3$) included Me singlets at 7·62 (6H, NMe_2), 7·90 (3H, COMe), and 8·30 (3H, tertiary Me).

Catalytic hydrogenation ($Pt-H_2$, ethyl acetate) of either (**2a**) or (**6a**) gave the dihydro derivative (**8**), m.p. 76—78 °C (M^{+} 233), isolable only in low yield, and shown to be the precursor to the final and quantitative hydrogenolysis products, hexane-2,5-dione and benzamide; the spectra of the dihydro derivative were in full accord with the assigned structure. Hydrogenolysis also occurred on reduction of (**2a**) with $LiAlH_4$, the products including benzylamine as expected.[5]

The above reactions of (**2**) confirm the presence of the enone group. Other reactions support the presence of the N–O bond in the heterocyclic ring. Thus treatment of (**2a**) or (**6a**) in boiling aq. EtOH, or in dioxan containing a trace of HCl, gave hex-3-ene-2,5-dione and benzohydroxamic acid; similar treatment of (**8**) gave hexane-2,5-dione and the hydroxamic acid. Compounds (**2a**), (**6a**), and (**8**) liberated I_2 from acidified KI.



SCHEME

Two other *cis*-enone structures, which are reconcilable with much of the data described, are the oxaziridine (**9**) and the nitrone (**10**). We discount the former since it would be expected to have an i.r. absorption near 1725 cm^{-1} and a u.v. absorption near 246 nm for its *N*-benzoyl group, and to isomerise to the dioxazole on heating;[8] the behaviour on heating is quite different (see below). We were not able to find any literature record of an *N*-acylnitrone, but structure (**10**) can be readily rejected since the observed formation of hexane-2,5-dione in the reaction with $Pt-H_2$ would require the creation of a C to O bond under reducing conditions.

The most reasonable mechanism for the formation of (**2**) is by way of the Diels–Alder adduct (**3**) (Scheme). Isomerisation of (**3**) to (**2**) may occur directly (arrows), or by way of oxygen-assisted ring opening to the dipolar structure (**12**), which closes to (**2**) (O to C bond formation). An alternative closure to (**9**) is possible, either from (**12**) (N to C), or directly from (**3**) (4 centre reaction), followed by isomerisation of (**9**) to (**2**),† but this seems unlikely since more forcing conditions are usually needed for this ring expansion.[8] Thus 3,3-pentamethylene-2-benzoyloxaziridine[8] was unchanged after treatment with silver oxide in ethyl acetate for 12 h.

The reaction is reversible. When (**2d**) was refluxed with 1,4-dimethyl-2,3-diphenylcyclopentadiene in benzene, intermolecular transfer of (**1d**) took place giving 2,5-dimethylfuran and the known[3] adduct (**11**). The *trans*-isomer (**6d**) by contrast, and predictably, was unreactive when similarly treated.

We thank the National Research Council of Canada for financial support.

(*Received*, 31*st May* 1977; *Com.* 535.)

† In the pathways suggested the O in the original dimethylfuran becomes the O in the enone CO and the N–O bond is kept intact. In alternative electron shifts the nitroso O becomes the O in the enone and an N–O bond is broken and re-formed. No distinction between these is possible on the evidence at present.

[1] G. W. Kirby and J. G. Sweeny, *J.C.S. Chem. Comm.*, 1973, 704.
[2] G. W. Kirby and J. W. M. Mackinnon, *J.C.S. Chem. Comm.*, 1977, 23.
[3] D. Mackay, K. N. Watson, and L. H. Dao, preceding communication.
[4] H. Nohira, K. Inoue, H. Hattori, T. Okawa, and T. Mukaiyama, *Bull. Chem. Soc. Japan*, 1967, **40**, 664.
[5] O. Exner, *Coll. Czech. Chem. Comm.*, 1956, **21**, 1500.
[6] S. Morrochi, A. Ricca, and L. Velo, *Tetrahedron Letters*, 1967, 331.
[7] A. Selva, A. Citterio, E. Pella, and R. Tonani, *Org. Mass Spectrom.*, 1974, **9**, 1017.
[8] E. Schmitz and S. Schramm, *Chem. Ber.*, 1967, **100**, 2593.