

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

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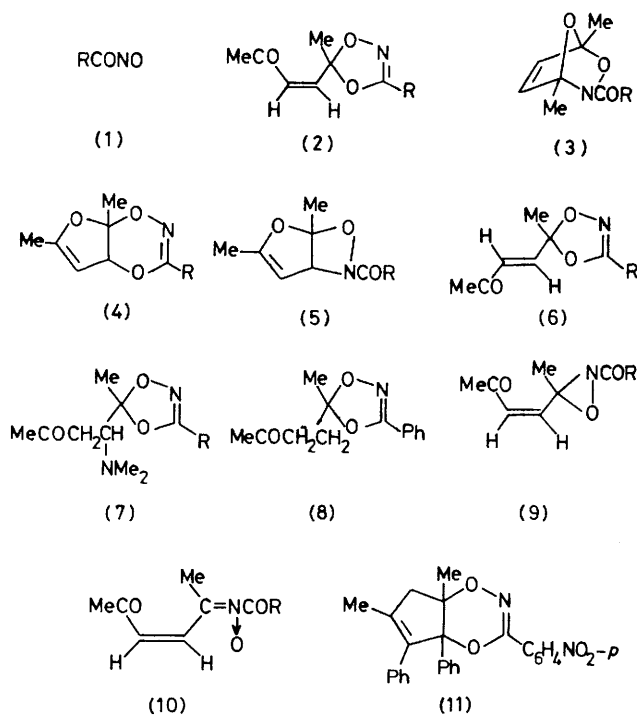
**Summary** Oxidation of hydroxamic acids in the presence of 2,5-dimethylfuran gives excellent yields of the 3-substituted-5-methyl-5-(*cis*-3-oxobutenyl)-1,4,2-dioxazoles (2); the reaction is reversible and probably occurs by way of an initially formed Diels-Alder adduct.

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

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 <sup>1</sup>H n.m.r. spectrum (CCl<sub>4</sub>) of the oil showed, as well as phenyl absorption, two vinylic Hs as an AB quartet at  $\tau$  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<sub>4</sub>) had CO absorption at 1715 (*cis*-enone) and a weak



a; R = Ph  
b; R = Bu<sup>t</sup>  
c; R = *p*-BrC<sub>6</sub>H<sub>4</sub>  
d; R = *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>

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

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.  $106.5\text{--}108.5^\circ\text{C}$ .

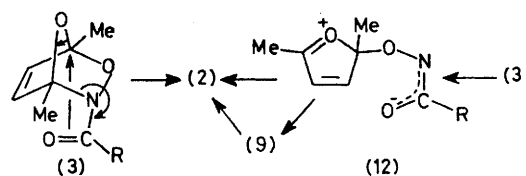
The *cis*-compound (**2a**) could be isomerised quantitatively to the oily *trans*-isomer (**6a**) by refluxing it with pyridine or triethylamine as catalyst in benzene or chloroform:  $M^+$  231;  $\nu(\text{CCl}_4)$  1710 and  $1690\text{ cm}^{-1}$ ; the  $^1\text{H}$  n.m.r. spectrum ( $\text{CCl}_4$ ) included a vinylic AB quartet at  $\tau$  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.  $152.5\text{--}153.5^\circ\text{C}$ .

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.  $110\text{--}111^\circ\text{C}$ ;  $m/e$  304 ( $M-\text{Me}$ )<sup>+</sup>;  $\nu(\text{Nujol})$   $1718\text{ cm}^{-1}$  ( $\text{C}=\text{O}$ );  $\tau(\text{CDCl}_3)$  included Me singlets at 7.62 (6H,  $\text{NMe}_2$ ), 7.90 (3H,  $\text{COMe}$ ), and 8.30 (3H, tertiary Me).

Catalytic hydrogenation ( $\text{Pt-H}_2$ , ethyl acetate) of either (**2a**) or (**6a**) gave the dihydro derivative (**8**), m.p.  $76\text{--}78^\circ\text{C}$  ( $M^+$  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  $\text{LiAlH}_4$ , the products including benzylamine as expected.<sup>5</sup>

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  $\text{I}_2$  from acidified KI.

† 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.



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  $1725\text{ cm}^{-1}$  and a u.v. absorption near 246 nm for its *N*-benzoyl group, and to isomerise to the dioxazole on heating;<sup>8</sup> 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  $\text{Pt-H}_2$  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**),<sup>†</sup> but this seems unlikely since more forcing conditions are usually needed for this ring expansion.<sup>8</sup> Thus 3,3-pentamethylene-2-benzoyloxaziridine<sup>8</sup> 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<sup>3</sup> adduct (**11**). The *trans*-isomer (**6d**) by contrast, and predictably, was unreactive when similarly treated.

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