The Reaction of Nitrosocarbonyl Compounds with 2,5-Disubstituted Furans. Synthesis of 1,4,2-Dioxazine and 1,4,2-Dioxazole Derivatives

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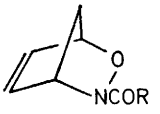
Oxidation of hydroxamic acids at room temperature in the presence of 2,5-dimethylfuran gives *cis*-1,4,2-dioxazolylbutenones (5), the structures of which have been confirmed by the synthesis of the dihydro-derivative (12) from the reaction of benzonitrile oxide with hexane-2,5-dione. If the oxidation is carried out at 0 °C good yields of the unstable furo[1,4,2]dioxazines (7), the formal products of the addition of the furan to the nitrosocarbonyl-arene or -alkane, can be isolated. Compounds (7) are the precursors to (5) and this isomerisation in the oxidation medium is essentially quantitative. It is probably catalysed by an unidentified component, since when pre-isolated (7) is heated the reaction is solvent-dependent and sometimes complex, the amounts of (5) formed being very variable. Nitrosocarbonylbenzene adds to the unsymmetrical compound 2-methyl-5-phenylfuran only at the 2,3-bond, giving the dioxazine (17) and thence the dioxazole (15) exclusively. Secondary amines add readily to the β-carbon of the enone group in (5) while tertiary amines, or more efficiently iodine, convert (5) into the *trans*-isomers (11).

The retro-reaction of (5c) at 80 °C to dimethylfuran and *p*-nitronitrosocarbonylbenzene has been demonstrated by trapping the latter, with 1,4-dimethyl-2,3-diphenylcyclopentadiene, as the adduct (21).

It is now clearly established that the oxidation of hydroxamic acids to nitrosocarbonyl-alkanes or -arenes in the presence of conjugated acyclic [1,2] or alicyclic [1,3-8] dienes leads to 6-membered heterocycles in which the nitrosocarbonyl function has formally behaved either as a



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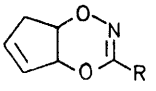

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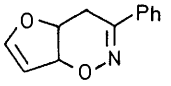

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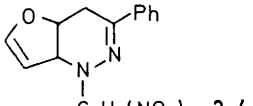


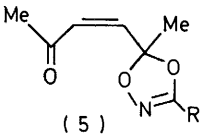
(4)

hetero-ene [1-3,6-8] or as a heterodiene.[5,8] In these roles, with *e.g.* cyclopentadiene, the products are respectively the 1,2-oxazine (1) or the 1,4,2-dioxazine (2). In some cases the latter arise only by isomerisation of the former through a [3,3] sigmatropic rearrangement.[5,8]

We have been studying the reactions of nitrosocarbonyl compounds with simple furans. In Diels–Alder reactions, furans are among the most useful and widely studied diene systems. Recent work with two hetero-diene systems, α-nitrosoalkenes [9-12] and α-azoalkenes,[9-11] has shown that adducts were formed in which the furan ring had behaved as the ene component; the 2,3-dihydrofurans (3) or (4) from furan and α-nitrosostyrene or α-2,4-dinitrophenylazostyrene were typical.[9] When hydroxamic acids were oxidised in the presence of furans, however, we found that entirely different products were isolated, containing not a 6- but a 5-membered heterocycle. Specifically 2,5-dimethylfuran gave the *cis*-1,4,2-dioxazolylbutenones (5). A preliminary account of this work has already been published, in which a conventional bridged adduct (6) was suggested as a likely precursor to (5).[13]

We now describe more fully our structural evidence for compounds (5): spectroscopic, degradative and, now, synthetic. We also show that the immediate precursor of (5) is probably not (6), but the very unstable 1,4,2-dioxazines (7), analogous to the furan adducts (3) and (4).

While a range of oxidising agents has been shown to be effective for the hydroxamic acids,[14] the most convenient in the dimethylfuran work were silver oxide or, more economically, lead dioxide;[13] any common aprotic solvent was suitable. Good to excellent yields of (5a—d) were obtained from the oxidation of benzo- (the most widely studied), *p*-bromobenzo-, *p*-nitrobenzo-, and pivalo-hydroxamic acids at room temperature. All were oils, except for (5c) which had m.p. 106.5—108.5 °C.



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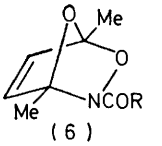
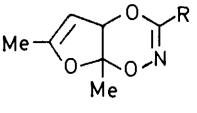


(6)

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



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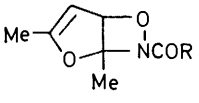
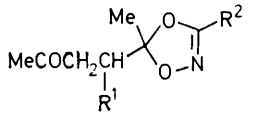


(8)

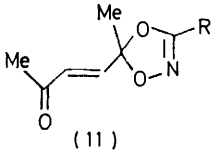
An occasional contaminant was identified as hex-3-ene-2,5-dione by its singlets in the ^1H n.m.r. spectrum of the reaction residues. It could be volatilised out in a stream of nitrogen. Another minor by-product, in yields of 0—20%, was characterised by two multiplets, each

integrating for 1 H, between δ 4.5 and 5.5, and two methyl singlets close together near δ 1.8. The subsequent identification of this compound as the dioxazine (7) and the significance of the variable yields will be discussed later.

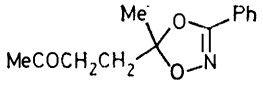
Analytical data for compounds (5) are given in Table 1. The i.r. bands (CCl_4) at 1 715 (enone, strong) and 1 625 cm^{-1} (C=N, weak [15,16]) in (5a), the u.v. bands (EtOH) at 234 (enone) and 264 nm (PhC=N–),[17,18] and the ^1H n.m.r. AB quartet at δ 5.96 and 6.10 (J 12 Hz) are fully consistent with the proposed structure. They do not



(9a) $R^1 = NMe_2$, R^2 = Ph
(9c) $R^1 = NMe_2$, $R^2 = p$-$NO_2C_6H_4$
(10) R^1 = morpholino, R^2 = Ph



(11)
a; R = Ph
b; R = p-BrC_6H_4
c; R = p-$NO_2C_6H_4$
d; R = Bu^t



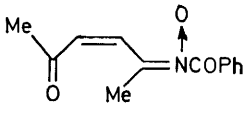
(12)

support any of the other 1 : 1 adducts which might have been expected, *e.g.* (6a) or (7a) or the oxazetidine (8a), the formal product of 2 + 2 cycloaddition for which precedent exists; [19] the products of regioisomeric fusion of (7a) and (8a) are likewise excluded.

The presence of an enone group is also confirmed by the chemical reactivity of the adducts. Michael addition of dimethylamine occurred rapidly to (5a) and (5c) to give the β-amino-ketones (9a) and (9c), whose ^1H n.m.r. spectra showed the presence of both diastereoisomers in each case (two separate singlets for each CMe and for NMe_2). The mixture (9c) gave a crystalline isomer, m.p. 110—111°C. Similarly (5a) gave a crystalline β-morpholino-ketone (10), m.p. 94.5—95.5 °C.

The tertiary amines triethylamine or pyridine caused the isomerisation of the double bond in (5a), presumably by reversible conjugate addition ($t_{\frac{1}{2}}$ 6.3 h when refluxed with 0.17 equiv. of pyridine in CCl_4). Iodine was much more efficient ($t_{\frac{1}{2}}$ 1.8 min with 0.14 equiv. of iodine). The *trans*-isomer (11a) was produced quantitatively in each case. The blue shift in the enone carbonyl absorption, to 1 710 cm^{-1} (CCl_4), and the greater coupling of the vinylic protons (16 Hz), clearly establish the relationship between (5a) and (11a) as *cis*- and *trans*-isomers. Compounds (5b—d) were similarly isomerised, the product (11c) being crystalline, m.p. 152.5—153.5 °C.

Catalytic reduction of the double bond in either (5a) or (11a) was complicated by competing hydrogenolysis of the N–O bond. A maximum yield of *ca.* 40% (n.m.r.) of the dihydro-derivative (12), m.p. 76—78 °C, was achieved by treatment of (5a) with *ca.* 1.5 equiv. of hydrogen over platinum in ethyl acetate. Complete



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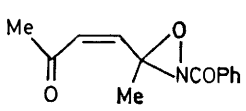


(14)

hydrogenation of (5a), or of an isolated sample of (12), gave quantitative yields of benzamide and hexane-2,5-dione, products which were also obtained by hydrogenation of the *trans*-isomer (11a).

The presence of an N–O bond in (5a) and (11a) is indicated by the ability to oxidise acidified KI, and by the formation of benzohydroxamic acid, along with hex-3-ene-2,5-dione in refluxing aqueous ethanol. In themselves these reactions do not prove the presence of the dioxazole ring; they might be equally expected of compounds (13) or (14).

TABLE 1

(*Z*)-4-(3-Substituted-5-methyl-1,4,2-dioxazol-5-yl)but-3-en-2-ones (5)

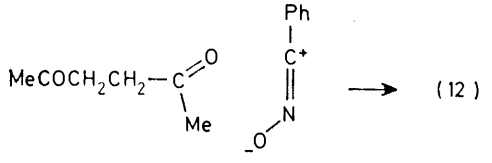
		$\nu_{max.}$		δ($CDCl_3$)							
		(CCl_4)	(cm^{-1})						Found (Required) (%)		
Compound	R	C=O	C=N	5-Me (s)	COMe (s)	Vinyl (ABq)	R	Formula	C	H	N
(5a)	Ph [a]	1 715	1 625	1.90	2.27	5.96, 6.10 (J 12 Hz)	7.3—7.6, 7.6—7.9 [d] *m*- + *p*-Ph, *o*-Ph	$C_{13}H_{13}NO_3$	67.5 (67.2)	5.6 (5.6)	6.1 (5.9)
(5b)	p-BrC_6H_4	1 706	1 618	1.90	2.27	5.86, 6.12 (J 12.5 Hz)	7.53 (aryl)	$C_{13}H_{12}BrNO_3$			4.5 (4.5)
(5c)	p-$NO_2C_6H_4$ [b]	1 716	1 621	1.96	2.31	5.95, 6.24 (J 13 Hz)	7.88, 8.03, 8.26, 8.41 (aryl)	$C_{13}H_{12}N_2O_5$	56.6 (56.5)	4.4 (4.4)	10.2 (10.1)
(5d)	CMe_3 [c]	1 712	1 630	1.77	2.30	5.84, 6.13 (J 12.5 Hz)	1.23 (s)	$C_{11}H_{17}NO_3$	63.1 (62.6)	8.4 (8.1)	6.9 (6.6)

[a] λ_{max}(EtOH) 234, 264 nm. [b] Recrystallised from acetone–iso-octane, m.p. 106.5—108.5. [c] Distilled; bath temperature 150 °C at 2 mmHg. [d] In CCl_4.

N-Acyl nitrones, like (13), have not been isolated. They are presumed to be highly unstable, since attempts to make them lead only to their rearrangement products, the oxime esters.[17] Moreover the hydrogenation of (13) could only afford hexanedione and benzamide by the creation of a C-to-O bond, an unlikely event under reducing conditions. *N*-Acyloxaziridines are known,[16,20] but their spectroscopic properties differ markedly from

those observed for the adduct. Thus for (14) i.r. and u.v. absorptions near 1 725 cm^{-1} and 245 nm respectively for the $^{-}NCOPh$ group would be expected.[16]

We decided to try to independently synthesise the dihydro-derivative (12) by the 1,3-dipolar mono-addition of benzonitrile oxide to hexane-2,5-dione (Scheme 1) [the mass spectrum of (5a) shows PhCNO as a dominant fragment in what is a cycloreversal of this sort of reaction [21]].



SCHEME 1

Base-generated nitrile oxides react with aldehydes and activated ketones, including α-diketones, to give dioxazoles [22] and with β-diketones at the enol carbon to give isoxazoles.[23] Simple ketones, which hexanedione would be expected to resemble, react only in the presence of boron trifluoride–ether.[18] With some modifications we successfully applied this to the synthesis of (12), the best yields (15—20%) being obtained when 2 equiv. of the catalyst were included before the addition of the benzonitrile oxide.

While the formation of compounds (5) is relatively insensitive to the nature of the hydroxamic acid used, we found that the nature of the substituents in the furan was critical to the success of the reaction.

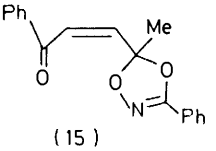
Thus neither tetramethylfuran nor 2,5-diphenylfuran was attacked by nitrosocarbonylbenzene or nitroso-carbonylisobutane, respectively.* Reaction occurred readily, however, with 2-methyl-5-phenylfuran which greatly clarified our understanding of the mechanism of the dioxazole formation.

Equimolar amounts of nitrosocarbonylbenzene and methylphenylfuran gave, as well as unchanged furan, a mixture of two isomers in the ratio 4 : 1. The latter crystallised and allowed the oily major isomer to be isolated and identified as the dioxazole (15), rather than the isomer (16). The singlet at δ 1.87 and the C=O i.r. absorption at 1 676 cm^{-1} must be assigned to the tertiary methyl and benzoyl groups of (15).

The minor isomer, m.p. 116.5—118.5 °C, † gave a sharp tertiary methyl singlet and a low-field AB quartet (C_6D_6) at 4.98 and 5.18 (J 2.5 Hz) in its n.m.r. spectrum. The i.r. spectrum (CCl_4) had a medium intensity band at 1 636 cm^{-1} and a weak one at 1 611 cm^{-1}. We attribute these to the enol ether double bond [24] and the Ph–C=N– group of the 2,3-dihydrofuran (17), a compound analogous to (3) and (4) observed in other furan reactions. The alternative isomeric dihydrofuran (18) can be rejected since there is no allylic coupling between the methyl group and the vinylic proton, which (18) would require.

Compound (17) is the precursor to (15), as suspected since enone stabilisation is released. The isomerisation was complete in 30 min in refluxing $CDCl_3$. Predictably, when the oxidation reaction with the methylphenyl-furan was carried out at 0 °C a much higher proportion of (17) (85%) was obtained.

We decided to re-investigate the dimethylfuran reactions at low temperature to see if analogous intermediates could be isolated. Such was the case when the benzohydroxamic acid oxidation was carried out at 0 °C. After 3 h there was a 63% yield of the isomeric mixture ‡ of (5a) and (7a) containing (^1H n.m.r.) 82% of the latter; oxidation for 6 h caused the proportion of (7a) to drop to 75%. Its n.m.r. peaks corresponded with those of the minor impurity noted earlier. Crystallisation of (7a) occurred readily, and though purification was difficult because of its great lability to heat and especially to traces of acid, a sample for analysis was



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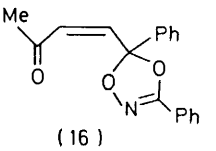

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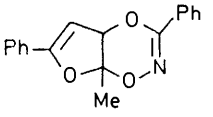

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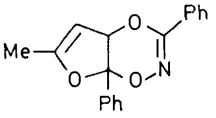


(18)

obtained. Its identity as (7a) follows securely from its i.r. bands at 1 662 (C=C, medium) and 1 611 cm^{-1} (C=N, weak) and, in its ^1H n.m.r. spectrum (CCl_4), two methyl peaks at δ 1.71 and 1.80, the latter weakly coupled to each of two hydrogen multiplets at δ 4.66 and 5.16. Irradiation at the δ 1.71 methyl peak converted the multiplets into a clean AB quartet [J 2.5 Hz; *cf.* compound (17)]. The existence of a homoallylic as well as an allylic coupling to the 5-methyl group in other 2,5-dimethyl-2,3-dihydrofuran derivatives has been reported previously; the $J_{3,4}$ values were comparable to that found here.[25]

Similarly, using low-temperature oxidation the dioxazines (7b—d) were isolated. These were all crystalline unstable solids; spectra and analytical data are given in Table 2, which also includes the yield at 0 °C as a percentage of the total adduct formation.

While it is clear that the dioxazines (17) and (7) are the

* Furan itself was very reactive in these oxidations, but the residues on work-up rapidly darkened and gave very complex spectra.

† If immersed in the m.p. apparatus at 114 °C. If it was heated slowly from a lower temperature the m.p. was lower. This behaviour reflects the thermal instability of the compound, and is also general for all of compounds (7).

‡ The low yields of these intermediates were in part due to incomplete oxidation, since the reaction time was necessarily shortened. Another contributing factor was that there was very little washing of the inorganic residues from the oxidising agent (Ag_2O or PbO_2), in order to minimise the work-up time for the intermediates.

respective precursors of (15) and (5) in the oxidation reactions, the isomerisation of *purified* samples of the dioxazines is not always straightforward. Thus (17) isomerised to (15) cleanly in $CDCl_3$ under reflux, but it reacted much more slowly in tetrachloroethylene at the same temperature giving 2-methyl-5-phenylfuran as well as (17) (*ca.* 45 : 55%). Similarly (7a) only gave (5a) in $CDCl_3$ or C_6D_6 at reflux, but in CCl_4 it reacted slowly to give (5a) and other intermediates (but no 2,5-dimethylfuran), which were converted into (5a) as the only product on prolonged reflux. Surprisingly the t-butyl adduct (7d) in CCl_4 or C_6D_6 gave no (5d), at least up to the half-life of (7d). Instead the spectrum showed that a complex reaction had occurred involving at least two products, one or both of which contained an NH group (this reaction has yet to be investigated further). However, from all of the oxidations if the reaction mixture was kept at room temperature long enough, or was allowed to warm up during evaporation of the solvent,* the dioxazole was the only product isolated. It is clear that in the oxidation reactions some or all of the isomerisation is being caused by the catalytic effect of one of the components. If this is a minor impurity it may account for the variable amounts of compounds (7) observed in the original oxidations. Traces of acid or base could be involved, since pure (7d) gives (5d) in almost quantitative yield in CCl_4 solution containing, for example, added pyridine or pivalic acid, despite its failure to give a significant yield of (7d) in their absence. Carboxylic acids, for example, are common by-products in hydroxamic acid oxidations.†

Our results now allow us to write (7), rather than (6),[13] as the precursor to (5a) (Scheme 2) which could arise concertedly, or go through the dipolar intermediate (19) invoked earlier.[13] In either case the reaction is catalysed, probably by acid or base.

Whether (6) itself is a very unstable precursor to (7), a rearrangement for which there is analogy,[5,8] is not possible to say. We regard it, however, as unlikely since both tetramethylfuran and 2,5-diphenylfuran were unreactive to nitrosocarbonyl compounds, though both are known participants as dienes in Diels–Alder reactions.[26-28] As ene components, in reaction with a nitrosocarbonyl compound as a heterodiene, they might be expected to be unreactive, the former through steric hindrance and the latter from electron deactivation of the 2,3-double bond.

SCHEME 2

TABLE 2

4a,7a-Dihydro-3-substituted-6,7-dimethylfuro[3,2-*e*]-1,4,2-dioxazines (7)

Compound	R	Isomeric yield [b] (%)	M.p.[a] (°C)	$\nu_{max.}$ (CCl_4) (cm^{-1}) C=C	C=N	δ($CDCl_3$) 7a-Me (s)	6-Me (d)[g]	4a-H (m)	5-H (m)	R	Formula	Found (Required) (%) C	H	N
(7a)	Ph	82	50.5—53 [e]	1 662	1 611	1.71	1.80	4.66 ($J_{4a,5H}$ 2.5 Hz)	5.16 [i]	7.2—7.5, 7.5—7.9 (*m*- + *p*-Ph, *o*-Ph)	$C_{13}H_{13}NO_3$	67.2 (67.5)	5.6 (5.6)	5.9 (6.1)
(7b)	*p*-BrC_6H_4	70	*c*, *f*	1 660	1 611	1.77 [h]		4.77	5.26	7.41, 7.56, 7.63, 7.78 (aryl)	$C_{13}H_{12}BrNO_3$	*f*		
(7c)	*p*-$NO_2C_6H_4$	65	*d*	1 660	1 621	1.81 [h]		4.81	5.29	7.88, 8.03, 8.14, 8.29 (aryl)	$C_{13}H_{12}N_2O_5$	*j*		
(7d)	CMe_3	80	50—52 [e]	1 661	1 619	1.67	1.81	4.64	5.01	1.13 (s)	$C_{11}H_{17}NO_3$	63.1 (62.6)	8.4 (8.1)	6.9 (6.6)

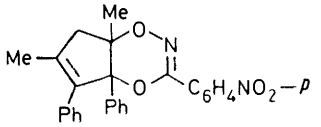
[a] The amount of (7) in the mixture of (5) and (7) after oxidation of the hydroxamic acid for 3 h at 0 °C. [b] Dependent on the rate and duration of heating. [c] From ether–pentane. [d] From acetone–iso-octane. [e] From pentane at −70 °C. [f] A sample of (7b) free of (5b) was not obtained. [g] The 6-Me contains a very small coupling. Irradiation at this resonance in (7a) showed the $J_{4a,5H}$ to be 2.5 Hz. [h] Overlapping singlet and doublet; these are distinguishable in CCl_4. [i] In CCl_4. [j] Too unstable for analysis.

* When pivalohydroxamic acid is oxidised in refluxing ethyl acetate for 2 h, pure (5d) is produced.

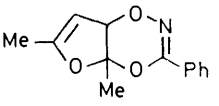
† The possible catalytic involvement of metal (Ag) or metal oxides (Ag_2O,PbO_2,PbO) must also be considered.

The reversibility of the reaction of *p*-nitronitrosocarbonylbenzene with dimethylfuran has been demonstrated.[13] When (5c) was refluxed in benzene with 2,5-dimethyl-3,4-diphenylcyclopentadiene, conversion into dimethylfuran and the dioxazine (20)[8] was complete after 12 h. The adduct (5a) reacted, though more slowly, to give the phenyl analogue of (20). When (7a) was refluxed with the diene in benzene the reaction was complete after 25 min, giving the isomer (5a) and

dimethylfuran (as well as the transfer adduct) in the ratio 4 : 1. Thus (7a) decomposes to dimethylfuran faster than does (5a). The *trans*-isomer (11c) was unreactive towards the diene, an expected result since its reversal to dimethylfuran would be unlikely.

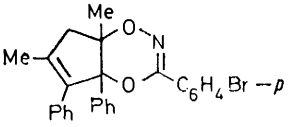


(20)

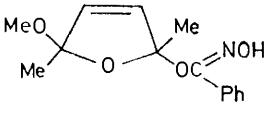


(21)

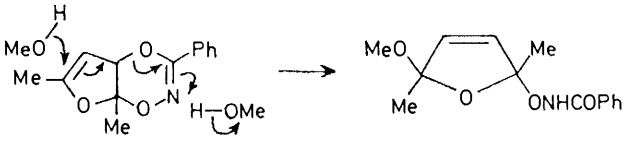
We have assumed throughout that the mode of regioisomeric fusion of the dioxazine ring to the 2,3-double bond in the furan is as shown in compounds (7) and (17). However, the spectroscopic properties of, for example, (7a) are just as easily reconcilable with structure (21), which would lead to (5a) by the same kind of electron shift shown in Scheme 2 for (7). This ambiguity contrasts with the strict requirement that the dioxazines from cyclopentadienes and nitrosocarbonyl compounds have the same mode of fusion as (7a) (carbonyl oxygen on allylic carbon), dictated by the [3,3] sigmatropic rearrangement of their bridged precursors.[8] This has recently been confirmed, along with the *cis*-stereochemistry, by the *X*-ray analysis of the bromo-compound (22).[29]



(22)



(24)



(7a) (23)

SCHEME 3

The preference for (7a) over (21) is here based on the reaction observed with methanol, part of a current study of the reactions of compounds (5) and (7) with nucleophiles. Rapid addition to (7a) occurs at room temperature to give quantitatively the *O*-2,5-dihydrofuranyl benzohydroxamate (23) (Scheme 3), whose stereochemistry is unconfirmed but is probably that shown [(5a) also gives (23) but requires reflux in methanol for 1 h. The addition is promoted by the leaving-group ability of the oxygen which releases amide resonance. The structure follows particularly from the i.r. spectrum (CCl_4) which has absorptions for NH between 3 300—3 400 and for amide C=O at 1 695 cm^{-1}. A similar addition to (21) would lead to the formation of the benzohydroximate (24), whose i.r. spectrum would be quite different.[30] While the ring-opening to (23) is convincing evidence for the structure of (7a), it of course provides no information on the stereochemistry at the ring junction.

EXPERIMENTAL

The following spectrometers were used: for i.r. a Beckman IR 10; for u.v. a Hitachi Perkin-Elmer RM-U6E; for ^1H n.m.r. a Varian T 60. Sodium sulphate was used to dry solutions in organic solvents.

(Z)-4-(3-*Substituted*-5-*methyl*-1,4,2-*dioxazol*-5-*yl*)*but*-3-*en*-2-*ones* (5).—The synthesis of (5a) is typical, but was suitably scaled down for (5b—d). The preparation of the hydroxamine acids required for (5b—d) has been described previously.[8]

PbO_2 (Fisher Scientific Co.; technical grade; 130 g, 0.54 mol) was added to ethyl acetate (here and in all other preparations pre-washed with aqueous sodium hydrogencarbonate and dried, 250 ml) containing 2,5-dimethylfuran (Aldrich Chemical Co.; 9.5 ml, 0.089 mol) and benzohydroxamic acid (10 g, 0.073 mol) and the whole was stirred at room temperature for 1 day. The suspension was filtered through a $\frac{1}{4}$-in layer of Celite and the filter cake washed thoroughly with ethyl acetate. The filtrates were taken to dryness using a rotary evaporator and a hot water bath to complete the isomerisation of any intermediate (7). The residue of (5a) (14 g, 83%) was a pale yellow oil.

The reaction could be completed more efficiently under reflux, there then being no traces of (7) in the final product. Thus a suspension of Ag_2O (1.3 g, 9.3 mmol) in ethyl acetate (10 ml) containing dimethylfuran (0.50 ml, 4.7 mmol) and pivalohydroxamic acid (0.50 g, 4.3 mmol) was refluxed for 2 h and filtered. The filtrate was washed with aqueous sodium hydrogencarbonate, dried, and evaporated to give pure (5d) as an oil.

In some preparations the ^1H n.m.r. spectrum of the residue showed the presence of small amounts of hex-3-ene-2,5-dione. This could be removed by blowing dry nitrogen over the product during a 12 to 24 h period.

Methylene chloride, chloroform, or carbon tetrachloride were suitable alternatives to ethyl acetate in any of the oxidation reactions.

The spectroscopic properties and elemental analyses of compounds (5) are given in Table 1.

Tertiary Amine Adducts of Compounds (5).—(a) *Dimethylamine and* (5a). The enone (5a) (100 mg, 0.43 mmol) and dimethylamine (19.5 mg, 0.43 mmol) in $CDCl_3$ (0.5 ml) were allowed to react in an n.m.r. tube. Reaction was complete within minutes, the spectrum showing peaks of comparable intensity for both diastereoisomeric adducts (9a). Those for the Me groups were at δ 1.58 and 1.60 (each 3 H, s, 5-Me), 1.95 and 2.10 (each 3 H, s, COMe), and 2.29 and 2.33 (each 6 H, s, NMe_2). Evaporation gave an oil which did not crystallise.

(b) *Dimethylamine and* (11a). The reaction in (a) was repeated on exactly half the scale, but using the *trans*-enone (11a) in place of (5a). The diastereoisomers (9a) were again obtained, the Me absorptions in the ^1H n.m.r. spectrum being identical to those above.

(c) *Morpholine and* (5a). Morpholine (144 mg, 1.65 mmol) and (5a) (0.362 g, 1.57 mmol) were dissolved in carbon tetrachloride (3 ml), a portion of the solution being monitored by ^1H n.m.r. spectroscopy. The reaction was fast ($t_{\frac{1}{2}}$ *ca.* 15 min); when complete the ratio of diastereoisomers was 1.3 : 1. Evaporation of the solution gave a residue which crystallised on addition of ether–hexane. The solid (120 mg) was the minor diastereoisomer. Re-

crystallisation from ether–iso-octane gave 4-(5-*methyl*-3-*phenyl*-1,4,2-*dioxazol*-5-*yl*)-4-*morpholinobutan*-2-*one* (10) as prisms, m.p. 94.5—95.5°: $\nu_{max.}$(CCl_4) 1 722 (C=O), 1 624 cm^{-1} (C=N, weak); δ($ClDCl_3$) 1.68 (3 H, s, 5-Me), 2.06 (3 H, s, COMe), 2.2—3.1 (6 H, m, morpholino 2- and 6-H_2 and butyl 3-H_2), 3.5—3.9 (5 H, m, morpholino 3- and 5-H_2 and butyl 4-H), 7.2—7.6 (3 H, m, *m*- + *p*-Ph), and 7.6—7.9 (2 H, m, *o*-Ph) (Found: C, 64.2; H, 7.1: N, 8.8. $C_{17}H_{22}N_2O_4$ requires C, 64.1; H, 7.0; N, 8.8%).

(d) *Dimethylamine and* (5c). The enone (5c) (1.0 g 3.6 mmol) was dissolved in ether (20 ml) kept at 0 °C and a slight excess of ethereal dimethylamine added. After being stirred for 2 h the solution was evaporated. The residual (quantitative) crystals consisted of approximately equal amounts of both diastereoisomers (^1H n.m.r.). Crystallisation from acetone–iso-octane gave one pure diastereoisomer of 4-*dimethylamino*-4-[5-*methyl*-3-(4-*nitrophenyl*)-1,4,2-*dioxazol*-5-*yl*]*butan*-2-*one* (9c), m.p. 110—111 °C; *m/e* 304 $(M - Me)^{+\cdot}$; $\nu_{max.}$ (CCl_4) 1 716 (C=O) and 1 620 cm^{-1} (C=N, weak); δ($CDCl_3$) 1.70 (3 H, s, 5-Me), 2.10 (3 H, s, COMe), 2.63 (2 H, d, CH_2,* *J* 6 Hz), 3.74 (1 H, t, CH, *J* 6 Hz), and 7.86, 8.01, 8.26, and 8.41 (4 H, q, aryl) (Found: C, 56.4; H, 6.0; N, 13.1. $C_{15}H_{19}N_3O_5$ requires C, 56.1; H, 6.0; N, 13.1%).

(E)-4-(3-*Substituted*-5-*methyl*-1,4,2-*dioxazol*-5-*yl*)*but*-3-*en*-2-*ones* (11).—The isomerisations were monitored by ^1H n.m.r. (solutions in carbon tetrachloride). For example when (5a) (1.1M) was refluxed with pyridine (0.19M), $t_{\frac{1}{2}}$ was 6.3 h; triethylamine was of comparable efficiency. Iodine was a powerful catalyst; thus when (5a) (0.54M) was kept at 35 °C with iodine (0.034M), $t_{\frac{1}{2}}$ was only 1.8 min.

On a preparative scale, (5a) (0.50 g, 2.2 mmol) was heated with iodine (6 mg, 0.024 mmol) in carbon tetrachloride (50 ml) for 5 h. The solution was washed with aqueous sodium thiosulphate, dried, and evaporated to give (11a) (0.39 g, 78%) as an oil whose ^1H n.m.r. spectrum showed it to be free of (5a) or other impurities. When pyridine was used for the isomerisations the final solution was washed with 0.1N-hydrochloric acid. Thus, the phenyl-substituted compound (11a), catalyst pyridine, triethylamine, or iodine, had $\nu_{max.}$ (CCl_4) 1 710, 1 690 cm^{-1} (C=O), 1 639, and 1 624 cm^{-1} (C=N, weak), δ(CCl_4) 1.80 (3 H, s, 5-Me), 2.21 (3 H, s, COMe), 6.30 and 6.55 (2 H, ABq, vinyl, *J* 16 Hz), 7.1—7.5 (3 H, m, *m*- + *p*-Ph), and 7.5—7.8 (2 H, m, *o*-Ph); the *p*-bromophenyl-substituted compound (11b), catalyst iodine, had $\nu_{max.}$ (CCl_4) 1 707, 1 686 (C=O), 1 640, and 1 621 cm^{-1} (C=N, weak), δ($CDCl_3$) 1.85 (3 H, s, 5-Me), 2.30 (3 H, s, COMe), 6.44, 6.68 (2 H, ABq, vinyl, *J* 16 Hz), and 7.61 (4 H, s, aryl); the *p-nitrophenyl-substituted compound* (11c), m.p. 152.5—153.5 °C (from acetone–iso-octane), catalyst triethylamine, had $\nu_{max.}$ (Nujol) 1 684 cm^{-1} (C=O), δ($CDCl_3$) 1.89 (3 H, s, 5-Me), 2.31 (3 H, s, COMe), 6.49 and 6.73 (2 H, ABq, vinyl, *J* 16 Hz), and 7.87, 8.02, 8.23, and 8.38 (4 H, q, aryl) (Found: C, 56.5; H, 4.5; N, 10.2. $C_{13}H_{12}N_2O_5$ requires C, 56.5; H, 4.4; N, 10.1%); and the *t-butyl-substituted compound* (11d), catalyst iodine, had $\nu_{max.}$ (CCl_4) 1 707, 1 687 (C=O), and 1 631 cm^{-1} (C=N, weak); δ($CDCl_3$) 1.24 (9 H, s, Bu^t), 1.71 (3 H, s, 5-Me), 2.31 (3 H, s, COMe), and 6.39 and 6.63 (2 H, ABq, vinyl, *J* 15.5 Hz) (Found: C, 62.9; H, 8.6; N, 6.9. $C_{11}H_{17}NO_3$ requires C, 62.6; H, 8.1; N, 6.6%).

4-(5-*Methyl*-3-*phenyl*-1,4,2-*dioxazol*-5-*yl*)*butan*-2-*one* (12).—(a) *By direct synthesis.* To a solution of α-chlorobenzaldoxime (2.0 g, 13 mmol) in dry ether (30 ml) at 0 °C was added triethylamine (1.3 g, 13 mmol). The hydrochloride, which formed immediately, was filtered off and washed with cold ether (10 ml).

To a stirred solution of hexane-2,5-dione (1.5 g, 13 mmol) in dry ether (10 ml) at 0 °C were added in rapid succession boron trifluoride–ether (3.6 g, 26 mmol) and then the above filtrate, immediately after preparation, containing the benzonitrile oxide. The solution was stirred for 20 min at 0 °C, refluxed for 1 h, poured into 1M-aqueous sodium carbonate (25 ml), and then shaken out, dried, and evaporated. The semi-crystalline residue was treated with a large volume of hexane and the crystals removed and identified as mainly diphenylfuroxan (benzonitrile oxide dimer). The syrup obtained from the hexane solution (1.7 g) contained 15% of the desired product (by ^1H n.m.r. analysis; values in several runs varied from 11 to 18%). Two such runs were combined and chromatographed on silica gel (40 g) from benzene with increasing amounts of ether, up to 10%. The main fraction containing (12) (0.7 g) was crystallised once from a large volume of hexane and then twice from ether–hexane to give the *dioxazole* as shining plates, m.p. 76.5—78 °C; *m/e* 233 $(M^{+\cdot})$; $\nu_{max.}$ (CCl_4) 1 725 (C=O) and 1 625 cm^{-1} (C=N, weak); δ($CDCl_3$) 1.64 (3 H, s, 5-Me), 2.14 (3 H, s, MeCO), 2.1—2.5 (2 H, m, CH_2), 2.5—2.9 (2 H, m, CH_2), 7.3—7.7 (3 H, m, *m*- + *p*-Ph), and 7.7—8.0 (2 H, m, *o*-Ph) (Found: C, 66.7; H, 6.5; N, 6.3. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%).

(b) *By hydrogenation of* (5a). A solution of (5a) (133 mg, 0.58 mmol) in ethyl acetate (10 ml) was hydrogenated at ambient temperature and pressure in the presence of PtO_2 (20 mg). After 1 equiv. of hydrogen had been consumed, starting material was still present (^1H n.m.r.), but this completely reacted when 1.5 equiv. of hydrogen was used. Work-up of the filtered solution gave a residue containing benzamide, (12), and hexane-2,5-dione, the latter two in a ratio of 2 : 3. The amide was precipitated by addition of carbon tetrachloride–hexane and its identity confirmed (mixed m.p.). The mother-liquor gave crude (12). The material so obtained from several runs was recrystallised as before, to give (12) identical with the product from (a).

(c) *By Hydrogenation of* (11a). The *trans*-isomer was hydrogenated as above. After 1 equiv. of hydrogen was consumed compound (12) was the major product, along with a small amount of the diketone; (11a) had completely reacted and is evidently more rapidly hydrogenated than the *cis*-isomer. Isolation of (12) was carried out as in (b).

Complete Hydrogenation of (5a).—A solution of (5a) (1 g) was exhaustively hydrogenated over Pd–charcoal (200 mg) in ethyl acetate (50 ml). Filtration and careful evaporation gave a residue of crystals and an oil. Addition of carbon tetrachloride gave insoluble benzamide, identified as in (b) above. The soluble oil was shown (^1H n.m.r.) to be almost pure hexane-2,5-dione. Removal of the solvent and extraction of the residue with cold pentane (10 ml) gave the pure diketone identical (i.r. and ^1H n.m.r. spectra) with an authentic sample (bis-*p*-nitrophenylhydrazone, m.p. and mixed m.p. 210—212 °C.

4a,7a-*Dihydro*-3-*substituted*-6,7a-*dimethylfuro*[3,2-e]-1,4,2-*dioxazines* (7).—The synthesis of (7a) is typical. A suspension of PbO_2 (10 g, 41.7 mmol) in ethyl acetate (50 ml) containing dimethylfuran (0.50 ml, 4.7 mmol) and benzohydroxamic acid (0.57 g, 4.2 mmol) was stirred at 0 °C for 3 h. After filtration through Celite, the residual

* These diastereotopic protons are evidently isochronous in $CDCl_3$.

lead oxides were washed with a little cold ethyl acetate, and the filtrate was evaporated without external heating. The residue was a semi-solid (0.61 g, 63%), a portion of which was analysed by ^{1}H n.m.r. spectroscopy as containing (7a) and (5a) in the ratio 4.5 : 1 [52% yield of (7a)]. Addition of pentane containing a few drops of ether gave *fairly* pure crystalline (7a). It was recrystallised by dissolving it in acetone at room temperature, adding pentane till crystallisation just began, filtering, and slowly cooling, finally to −70 °C. Ag_2O could be used in place of PbO_2 in the preparation of compounds (7). The percentage of (7) in the mixture of isomers, spectroscopic data, and elemental analyses of (7) are given in Table 2.

Isomerisation of Intermediates (7) *in Various Solvents.*—These reactions were carried out and monitored in n.m.r. tubes, using in general 20—50 mg of (7) in 0.4 ml of solution. Integration of the 4a- and 5-H of (7) *vs.* the vinylic peaks of (5) and/or the Me peaks in (7) *vs.* those in (5) enabled the extent of reaction to be determined. The solvents used, the temperature of the reaction (brackets), the half-life ($t_{\frac{1}{2}}$) of (7), and the products formed follow.

(a) *Compound* (7a). (i) $CDCl_3$ (refluxing $CHCl_3$); $t_{\frac{1}{2}}$ 6 min; (5a) only formed; (ii) CCl_4 (refluxing $CHCl_3$); $t_{\frac{1}{2}}$ *ca.* 1 h; (5a) and other products formed, but only (5a) after heating for 20 h; (iii) C_6D_6 (refluxing C_6H_6); $t_{\frac{1}{2}}$ 7 min; (5a) only formed.

(b) *Compound* (7b). The isomerisation was not investigated in detail; its stability was comparable with that of (7a).

(c) *Compound* (7c). (i) $CDCl_3$ (35 °C); $t_{\frac{1}{2}}$ 29 min; (5c) only formed; (ii) C_6D_6 (refluxing C_6H_6); $t_{\frac{1}{2}}$ 1.8 min; (5c) only formed.

(d) *Compound* (7d). (i) CCl_4 (refluxing $CHCl_3$); $t_{\frac{1}{2}}$ *ca.* 40 min; complex spectrum with no certain evidence of (5d), at least up to $t_{\frac{1}{2}}$; two products at least formed, one or both having NH or OH near δ 8.7 and 10.9; (ii) C_6D_6 (refluxing $CHCl_3$); $t_{\frac{1}{2}}$ *ca.* 40 min; as for (i). (iii) *Effect of pivalic acid.* 0.74M in (7d), 0.15M in acid, CCl_4 (refluxing $CHCl_3$); 35% complete in 40 min, complete in *ca.* 5 h; (5d) only formed except for a small amount of its *trans*-isomer (11d). (iv) *Effect of pyridine.* 0.6M in (7d), 0.3M in base, CCl_4 (refluxing $CHCl_3$); slow reaction complete in *ca.* 40 h, 85% yield of a 1 : 2 mixture of (5d) and (11d).

Confirmation of the N–O *Bond by Oxidation of Iodide.*—Addition if either isomer, (5a) or (11a) (*ca.* 20 mg) to a solution of KI (0.1 g) in 1 : 1 v/v ethanol–water (2 ml) containing 12N-HCl (0.1 ml) caused rapid liberation of iodine, which was not determined quantitatively. A blank reaction was run for comparison.

Cleavage of the Dioxazole Ring with Aqueous Ethanol.—(a) *Compound* (5a). The enone (5a) (50 mg, 0.22 mmol) was refluxed for 0.5 h in 1 : 1 v/v ethanol–water (5 ml). Most of the alcohol was removed under reduced pressure and the reaction mixture was then shaken with ether. The ethereal layer was dried and evaporated to give a mixture of *cis*- and *trans*-hex-3-ene-2,5-dione in the ratio *ca.* 4 : 5. Evaporation of the aqueous layer gave almost pure benzohydroxamic acid, identified by its i.r. spectrum (Nujol).

(b) *Compound* (11a). The experiment was repeated with the *trans*-isomer (11a) as in (a). After reflux for 0.5 h, reaction was only *ca.* 20% complete, a total of 5 h reflux being necessary. Work-up as in (a) gave, from the ethereal layer, the *cis*-ene-dione only,* and benzohydroxamic acid from the aqueous layer.

Oxidation of Benzohydroxamic Acid in the Presence of Tetramethylfuran and of 2,5-Diphenylfuran.—A solution of tetramethylfuran [27] (50 mg, 0.40 mmol) and benzohydroxamic acid (55 mg, 0.40 mmol) was stirred with a large excess of PbO_2 (500 mg) in ethyl acetate (5 ml) for 12 h. Evaporation gave a residue consisting largely of unchanged tetramethylfuran (^{1}H n.m.r.) and a small amount of material with a very complex absorption in the aliphatic region.

Similarly 2,5-diphenylfuran (Eastman, 0.22 g, 1 mmol) and pivalohydroxamic acid (0.3 g, 2.6 mmol) were stirred with PbO_2 (1.5 g, 6.3 mmol) in ethyl acetate (20 ml) for 6 h. Filtration and evaporation gave a residue devoid of any absorption in its ^{1}H n.m.r. spectrum ($CDCl_3$) in the vinylic or tertiary region, other than the singlet for the furan-ring hydrogens at δ 6.68.

3-(5-*Methyl*-3-*phenyl*-1,4,2-*dioxazol*-5-*yl*)*acrylophenone* (15).—The sodium salt of ethyl acetoacetate (from 26 g of ester, 0.20 mol), prepared in toluene (500 ml), and phenacyl bromide (49.8 g, 0.20 mol) were stirred together for 1 day and then water was added. Extraction with much water, drying, and evaporation gave ethyl α-phenacylacetoacetate (80%) as an oil of high purity (^{1}H n.m.r. spectrum). The ester (29 g, 0.12 mol) was refluxed for 6 h in 0.5N-Na_2CO_3 in methanol–water (1 : 1 v/v, 400 ml), and the solution was evaporated to a small volume and extracted with ether. The ethereal fractions were washed with water and dried to give 4-benzoylbutan-2-one (80%). The oily diketone (10.5 g, 0.060 mol) and zinc chloride (0.35 g) were heated for 3 h at 85 °C with acetic anhydride (8 g).[27] The dark solution was decomposed with an excess of aqueous sodium hydroxide and extracted with ether, from which the 2-methyl-5-phenylfuran (90%) was obtained by evaporation. Steam distillation and crystallisation (×2) from methanol gave rods, m.p. 37—38 °C (lit.,[31] 42 °C).

To a solution of 2-methyl-5-phenylfuran (1.00 g, 6.33 mmol) in ethyl acetate (50 ml) were added benzohydroxamic acid (0.96 g, 7.0 mmol), Ag_2O (2.32 g, 10.0 mmol), and sodium sulphate (3g), and the whole was stirred at room temperature for 24 g. Filtration and thorough washing of the precipitate gave a clear, slightly yellow solution, which was evaporated to a sticky, partially crystalline residue (1.53 g). The ^{1}H n.m.r. spectrum of a sample showed it to contain 2-methyl-5-phenylfuran (*ca.* 30%), compound (17), and compound (15), the latter two in the ratio 1 : 4 and in a total yield which was quantitative based on the furan consumed.

The solid material [compound (17)] was removed by the addition of hexane (100 ml), the soluble fraction being evaporated down and treated with fresh hexane (30 ml) which precipitated further slightly sticky solid material. The oil remaining after evaporation of the hexane mother-liquor was then shown to be free of (17) (^{1}H n.m.r.). Stirring for 12 h with pentane (50 ml) at room temperature removed all the methylphenylfuran. The pentane solution and several pentane washings were decanted off and the oily residue pumped *in vacuo* to give the pure *dioxazole* (15). It had $\nu_{max.}$ (CCl_4) 1 676 (C=O) and 1 621 cm^{-1} (C=N, weak); δ($CDCl_3$) 1.87 (3 H, s, 5-M3), 6.12 and 6.51 (2 H, ABq, vinyl, *J* 13 Hz), 6.9—7.5 (8 H, m, 3-Ph and *m*- + *p*-COPh), and 7.7—8.1 (2 H, m, *o*-COPh) (Found: C, 74.0; H, 5.5; N, 4.8. $C_{18}H_{15}NO_3$ requires C, 73.7; H, 5.2; N, 4.8%).

4a,7a-*Dihydro*-7a-*methyl*-3,6-*diphenylfuro*[3,2-e]-1,4,2-*dioxazine* (17).—The hexane-insoluble solid from the pre-

* We have no reasonable explanation yet of why the *cis*-enone (5a) gives a mixture of *cis*- and *trans*-ene-diones, while the *trans*-enone (11a) gives the *cis*-ene-dione and no *trans*.

paration of (15) was freed from traces of the latter by trituration with cold ether. Alternatively 2-methyl-5-phenylfuran (0.50 g, 3.17 mmol), benzohydroxamic acid (0.48 g, 3.50 mmol), Ag_2O (1.2 g, 4.9 mmol), and sodium sulphate (1 g) were stirred at 0 °C. After 4 h, reaction was *ca.* 70% complete (80% if left for 10 h), and of the isomeric products only *ca.* 15% was compound (15). Filtration and evaporation in the cold gave a solid residue which, on treatment with hexane containing a little ether, gave almost pure (17). Recrystallisation from benzene–ether–iso-octane gave the *dioxazine* as plates, m.p. 116.5—118.5 °C, if the capillary tube was immersed at 114 °C (heating from a lower temperature gave a lower m.p.), *m/e* 293 (M^+); $\nu_{max.}$(CCl_4) 1 636 (C=C, medium) and 1 611 cm^{-1} (C=N, weak); δ($CDCl_3$) 1.87 (3 H, s, 7a-Me), 5.46 (2 H, s, vinyl + tert.), 7.1—7.7 (8 H, m, Ph), and 7.7—8.1 (2 H, m, *o*-Ph); δ(C_6D_6) 1.58 (3 H, s, 7a-Me), 4.98 and 5.18 (2 H, ABq, vinyl + tert., *J* 2.5 Hz), 6.7—7.2 (6 H, m, *m*- + *p*-Ph), 7.2—7.5 (2 H, m, *o*-Ph), and 7.7—8.1 (2 H, m, *o*-Ph) (Found: C, 73.3; H, 5.3; N, 4.7. $C_{18}H_{15}NO_3$ requires C, 73.7; H, 5.2; N, 4.8%).

Isomerisation of (17).—(a) *In* $CDCl_3$. A solution of (17) (0.5M) in $CDCl_3$ in an n.m.r. tube was heated in refluxing $CHCl_3$. 75% Isomerisation occurred in 10 min and complete isomerisation in 30 min, (15) being the only product.

(b) *In tetrachloroethylene.* A similar solution was heated in this solvent at the same temperature. Isomerisation was much slower, with $t_{\frac{1}{2}}$ *ca.* 30 min. Peaks due to 2-methyl-5-phenylfuran developed as well as those of (15). After 3 h the solution contained 15—20% of (17); the products were (15) and the furan in the ratio *ca.* 5 : 4.

Trapping Experiments with 1,4-*Dimethyl*-2,3-*diphenylcyclopentadiene.*—(a) *Compound* (5c). (i) *N.m.r. analysis.* The reaction was monitored by ^1H n.m.r. spectroscopy using a solution of (5c) (138 mg, 0.50 mmol) and the diene (123 mg, 0.50 mmol) in C_6D_6 (0.5 ml) which was heated in refluxing benzene. The reaction was two-thirds complete in 4½ h and after 12 h the starting materials were undetectable, only peaks for 2,5-dimethylfuran and the adduct (20) [8] being observed.

(ii) *Identification of products.* In another experiment 0.50 mmol each of (5c) and the diene were heated neat in a sealed tube in refluxing benzene for 12 h. The contents were triturated with ether and the insoluble material (70 mg) was identified as (20) by crystallisation from acetone as prisms, m.p. 164.5—166 °C, undepressed on admixture with an authentic specimen.[8] The ethereal solution was shown to contain 2,5-dimethylfuran (comparative g.l.c. with a reference sample).

(b) *Compound* (11c). The *trans*-isomer (20 mg, 0.07 mmol) and the diene (30 mg, 0.14 mmol) were heated in C_6D_6 (0.3 ml) in refluxing benzene. After 18 h there was no trace of the formation of either dimethylfuran or (20). Slight decomposition of the diene (double-bond migration?) was observed.

(c) *Compound* (5a). A solution of (5a) (100 mg, 0.43 mmol) and the diene (106 mg, 0.43 mmol) was heated at reflux in C_6H_6 (0.5 ml) in an n.m.r. tube. The Me region of the spectrum was monitored. After 9½ h, only *ca.* 25% of starting material had reacted. A similar reaction in refluxing toluene was *ca.* one third complete after 2.5 h. The new peaks in the ^1H n.m.r. spectrum were due to dimethylfuran and the phenyl analogue of (20).

(d) *Compound* (7a). When a solution of (7a) (51 mg, 0.22 mmol) and the diene (55 mg, 0.22 mmol) was heated in C_6D_6 (0.4 ml), the isomerisation to (5a) was much faster than the formation of (20). After 25 min, (7a) had completely reacted, the spectrum showing (5a) and dimethylfuran [as well as peaks for the transfer product (20)] in the ratio *ca.* 4 : 1.

Addition of Methanol to form O-(5-*Methoxy*-2,5-*dimethyl*-2,5-*dihydro*-2-*furyl*)*benzohydroxamate* (23).—(a) *From* (7a). A solution of (7a) (30 mg, 0.13 mmol) and methanol (16 μl, 0.39 mmol) in $CDCl_3$ (0.4 ml) was monitored by ^1H n.m.r. Reaction was complete after *ca.* 4 h at room temperature. Some isomerisation to (5a) had occurred but the major product was (23), (ratio 1.8 : 1). When the reaction was repeated in methanol as solvent, the solution being evaporated to dryness within 10 min, the residue was essentially pure (23).

(b) *From* (5a). The n.m.r. experiment described in (a) was repeated using (5a) in place of (7a). After 4 h, only a trace (*ca.* 5%) of (23) was observed. In methanol as solvent, (5a) reacted only slowly at room temperature, reaction being only 50% complete after 24 h. The reaction was quantitative after refluxing for 1 h; this method was chosen for the preparation of (23). Addition of ether–hexane caused crystallisation of the adduct. Recrystallisation from ether–hexane gave the *hydroxamate* as prisms, m.p. 91—91.5 °C: $\nu_{max.}$ (CCl_4), 3 400, 3 310 (NH), and 1 695 cm^{-1} (C=O); δ($CDCl_3$) 1.56 (3 H, s, CMe), 1.69 (3 H, s, CMe), 3.41 (3 H, s, OMe), 6.09 (2 H, s, vinyl), 7.2—7.6 (3 H, m, *m*- + *p*-Ph), 7.6—8.1 (2 H, m, *o*-Ph), and 7—8.5 (1 H, broad, NH); δ(CS_2) includes 5.85 and 6.07 (2 H, ABq, vinyl, *J* 6 Hz) (Found: C, 64.0; H, 6.6; N, 5.3. $C_{14}H_{17}NO_4$ requires C, 63.9; H, 6.5; N, 5.3%).

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