tetrahydrofuran was stirred at room temperature for 1 h and then poured into 50 mL of 1% hydrochloric acid solution. The mixture was extracted with 30 mL of methylene chloride, and the aqueous solution was saturated with sodium chloride and reextracted with methylene chloride. The combined extracts were dried and evaporated. Purification of the residue as above yielded 92 mg (92%) of crystalline ketone **12g**.

1-(Benzenesulfonyl)-3-(α-hydroxyprenyl)indole (18j). A mixture of 380 mg (10.0 mmol) of lithium aluminum hydride and 1.36 g (4.0 mmol) of ketone **18i** in 30 mL of dry tetrahydrofuran was stirred at 0 °C for 1 h. Ethyl acetate, 5 mL, was added dropwise, and the mixture was allowed to warm to room temperature. It then was poured into 30 mL of water and extracted with methylene chloride. The extract was dried (K_2CO_3) and evaporated. Crystallization of the residual, yellow oil from 4:1 ethanol–hexane gave 1.13 g (83%) of colorless, crystalline alcohol **18j**: mp 111–112 °C; UV λ_{max} 249 nm (ε 12900), 276 (5500), 283 (5100); IR (CH_2Cl_2) OH 3580 (m), 3430 (br w), C=C 1605 (w), 1580 (w), SO_2 1365 (s), 1170 (s) cm^{-1}; ^1H NMR δ 1.77, 1.80 (s, 3 each, methyls), 5.51 (dm, 1, J = 9 Hz, olefinic H), 5.64 (d, 1, J = 9 Hz, OCH), 7.1–8.0 (m, 9, Ar Hs), 7.51 (s, 1, indole α-H); MS, m/e (rel intensity) 341 (M^+, 2), 182 (base), 167 (79). Anal. Calcd for $C_{19}H_{19}O_3NS$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.56; H, 5.55; N, 4.11.

Evaporation of the mother liquor from the above crystallization, chromatography of the residue, and elution with 4:1 hexane–ethyl acetate gave 82 mg (6%) of colorless crystalline ketone **18k**: mp 99–100 °C (hexane–ether); UV λ_{max} 217 nm (ε 24200), 265 (9100), 273 (10200), 285 (11000); IR (CH_2Cl_2) C=O 1655 (s), C=C 1600 (m), 1580 (w), 1530 (s), SO_2 1370 (s), 1165 (s) cm^{-1}; ^1H NMR δ 1.02 (d, 6, J = 7 Hz, methyls), 2.32 (m, 1, CH), 2.76 (d, 2, J = 7 Hz, CH_2 Hs), 7.3–8.4 (m, 9, Ar Hs), 8.21 (s, 1, indole α-H); MS, m/e (rel intensity) 341 (M^+, 57), 299 (56), 284 (base), 200 (76), 141 (54), 77 (41). Anal. Calcd for $C_{19}H_{19}O_3NS$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.56; H, 5.51; N, 3.90.

β-Dehydroprenylindole (3). A solution of 1.37 g (4.0 mmol) of alcohol **18j** and 8.40 g (150 mmol) of potassium hydroxide in 50 mL of a 4:1 ethanol–water mixture was heated at 50–54 °C for 2 h. It then was poured into 100 mL of water and extracted with ether. The extract was washed with brine, dried (K_2CO_3), and evaporated. Rapid chromatography of the solid residue, 710 mg, on neutral alumina (activity III) and elution with 2:1 hexane–ethyl acetate afforded 600 mg (82%) of pale yellow, powdery β-dehydroprenylindole (**3**): mp 129–130 °C (lit.[36] mp 130–132 °C); UV, IR, and ^1H NMR spectrally identical with an authentic sample.[41]

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(41) Kindly supplied by Drs. K.-F. Cheng and Y.-C. Kong.

Michael Adducts of a Half-Blocked Enedione as Sources of 3-Substituted 2,5-Diketones and 2,5-Dialkylfurans

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The dioxazolylbutenones **2a**, formed by isomerization of the Diels–Alder adducts of 2,5-dimethylfuran with (nitrosocarbonyl)benzene [2 + 4], are efficient Michael acceptors of a wide variety of carbon and heteroatom nucleophiles. The resulting adducts **5** function as half-blocked 1,4-diones. They can be converted into the corresponding diketones **10** by hot aqueous EtOH or Pd–H_2 or into the 3-substituted 2,5-dimethylfurans **19** by BF_3, either directly or by way of **10**. Hydroperoxide anion adds conjugatively to **2a** to give the epoxide **23**, but 1,2-addition is competitive and is followed by dioxazole ring opening to give a peroxy compound regarded as **21**. The [2 + 4] cycloaddition of 2,5-dialkylfurans and nitrosocarbonyl compounds is general, but 2-methylfuran appears to add (although in poor yield) in the opposite [4 + 2] mode, the adduct spontaneously isomerizing to the mono-*O*-benzoyloximino enedione **32**.

The nitrosocarbonyl group was first established as the oxidation intermediate from a hydroxamic acid in 1973.[1] Its dienophilic behavior at its nitroso end has been successfully exploited by a number of workers,[1-5] but its ability to act as an enophile in Diels–Alder reactions has also been recognized.[6-8]

We have shown that both (nitrosocarbonyl)alkanes and -arenes react as hetero dienes with 2,5-dimethylfuran to

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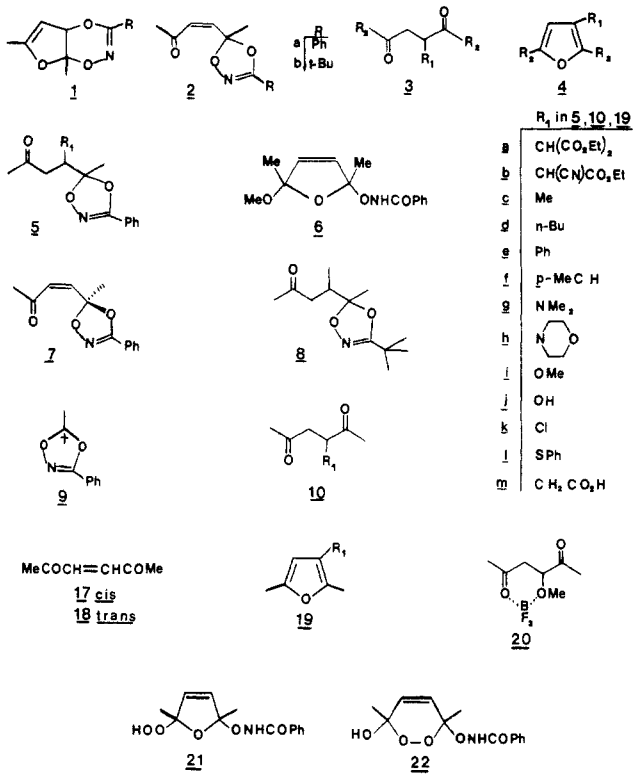
0022-3263/86/1951-2351$01.50/0

Chart I



give the unstable dioxazines **1** (Chart I), and we believe that this addition occurs directly, as the primary reaction. Though **1** is formally the product of cycloaddition of the nitroso group as the dienophile to the furan, followed by a [3,3]sigmatropic rearrangement, we could find no evidence that **1** was formed in this way.[8] Low-temperature isolation of **1** was possible, but normal workup conditions caused their isomerization in high yield to the *cis*-dioxazolylbutenones **2**.[7,8]

We wish to describe here the use of **2** and related dioxazoles as excellent precursors to internally monosubstituted 1,4-diketones **3** and thence to 3-substituted 2,5-dialkylfurans **4**.

Syntheses of 1,4-diones have been last reviewed in 1976,[9,10] and methods employed since then cover the same basic range of reaction types. These include the following: (i) addition of nitroalkanes to enones (1,4),[11] of 1-(2-methyl-2,3-dioxolan-2-yl)-2-nitroethane to aldehydes (1,2),[12] or silyl enol ethers to nitroalkenes,[13] followed in each case by an appropriate hydrolysis and oxidation; (ii) addition of lithium alkoxyvinylcuprates to enones;[14] (iii) addition of acyl anion equivalents to enones[15-17], especially the cyanide or thiazolium ion catalyzed reaction of aldehydes and enones, developed by Stetter;[15] (iv) addition of oxiranes to the lithium salt of ketimines, followed by oxidation;[18] (v) aldol condensation of methyl ketones with α-hydrazono aldehydes followed by hydrolysis and hydrogenation;[19] (vi) acylation of the anions of γ-sulfonyl ketals, followed by desulfonation and deketalization;[20] (vii) the Paal synthesis using α-halo ketones and β-keto esters, exemplified by the synthesis of furoguaiacidin diethyl ester;[21] (viii) bis addition of aldehydes to acetylene and hydrogenation and oxidation of the resulting yne diols;[22] (ix) γ-selective oxygen insertion in γ,δ-enones catalyzed by $PdCl_2/CuCl_2$;[23] (x) from furan derivatives, either directly by hydrolytic ring opening of furans[24] or 3*H*-2-furanones[25] or by oxidation of the γ-hydroxy ketones obtained through 4,5-dihydro-2-furanyl cations when α-cyclopropyl ketones are treated with acid;[26] (xi) oxidative cleavage of tertiary cyclobutanols;[27] (xii) photoaddition of 1 mol of an aldehyde to an enone[28] or of 2 mol to an alkyne;[29] (xiii) radical processes involving coupling of α-keto radicals with acetonyl radicals derived from a 2-propenyl percarbonate[30] or the addition of acyl radicals derived from aldehydes to 3-buten-2-one ketal;[31] (xiv) and a number of oxidative couplings of ketones at the α-position, methods which are capable only of yielding symmetrical 1,4-diketones.[18]

Discussion

Michael Additions to Enones 2. Possessing as they do a very electropositive β-carbon, the enones **2** are highly reactive.

Amost all the reactions were carried out on the (nitrosocarbonyl)benzene adducts **2a**, to give the β-substituted ketones **5**, and they proceded smoothly with a wide range of nucleophiles. The products, which in principle consist of two diastereomers, were isolated by a suitable aqueous workup and were usually purified by silica gel chromatography. Analytical data including ^1H NMR assignments are given in Table I and ^{13}C NMR assignments in Table II.

The stabilized anions from diethyl malonate and ethyl cyanoacetate reacted over 12 h at room temperature to give excellent yields of **5a** and **5b**. Cuprates were used to introduce alkyl and aryl nucleophiles. The sulfur complex Me_2SCuLi was more successful (51% after chromatography) than Me_2CuLi (25%) in the synthesis of the methyl

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Table I. ^{1}H NMR[a] and IR[b] Assignments and Elemental Analyses for 4-R_1-4-(3-Phenyl-5-methyl-1,4,2-dioxazol-5-yl)-2-butanones 5

compd	R_1	C_5H_3	C_1H_3	C_3H_2	C_4H	meta + para Ph H	ortho Ph H	R_1	IR, C=N C=O	calcd / found C	calcd / found H	calcd / found N
5a	$CH(CO_2Et)_2$	1.61	2.20	2.60–3.90[c,d]		7.33–7.48	7.61–7.80	1.20, t, 3 H (7.2); 1.23, t, 3 H (7.2); 4.16, q, 2 H; 4.17, q, 2 H[c]	1620 1710	61.37 61.42	6.44 6.63	3.58 3.47
5b	$CHCNCO_2Et$[e]	1.70	2.30	2.83–3.06	3.29–3.86	7.27–7.33	7.33–7.97	1.30, t, 3 H (7.0); 4.27, q, 2 H; 3.95–4.15, CHCN		62.78 63.03	5.85 5.96	8.13 7.92
5c[f]	CH_3	1.59	2.15	2.20–2.95[d]		7.27–7.49	7.72–7.81	1.10, d, 3 H (6.3)	1615 1710	68.00 67.81	6.93 7.09	5.66 5.56
5d[f,g]	*n*-Bu	1.58	2.12 2.18	2.28–2.78[d]		7.41–7.50	7.75, d (7.8)	0.83–1.51, 9 H	1615 1710	70.56 70.67	8.01 8.19	4.84 4.79
5e[g]	Ph	1.44	2.01	2.94, dd (9.4, 17.1) 3.13, dd (4.3, 17.1)	3.77, dd (4.3, 9.4)		7.80, d (7.3)	7.16–7.53, 8 H[h]	1625 1726	73.77 73.69	6.19 6.22	4.53 4.82
5f[g]	*p*-$CH_3C_6H_4$	1.44	2.03	2.91, dd (9.4, 16.9) 3.11, dd (4.2, 16.9)	3.72, dd (4.2, 9.4)	7.44–7.53	7.80, d (7.3)	2.32, s, 3 H; 7.14, d, meta Ar H; 7.27, d, ortho Ar H	1612 1710	74.28 74.27	6.55 6.70	4.33 4.41
5g[f,g]	$N(CH_3)_2$	1.65 1.67	2.06 2.20	2.57–2.72	3.59–3.72	7.40–7.51	7.73, d (7.3) 7.79, d, (6.8)	2.33, s, 6 H; 2.37, s 6 H	ref 8		ref 8	
5i[f]	OCH_3	1.64 1.66	2.20	2.68–2.77	3.96–4.15	7.28–7.49	7.73–7.85	3.53, s, 3 H; 3.55, s, 3 H	1628 1719	63.87 63.84	6.51 6.57	5.32 5.54
5j[f]	OH	1.67 1.69	2.18 2.20	2.71–2.79	4.23–4.43	7.29–7.58	7.73–7.85	3.52, d (3.3); 3.64, d (4.9)	1610 1704	62.64 62.75	6.07 6.12	5.62 5.81
5k[f]	Cl	1.80	2.19	2.93–3.02	4.45–4.65	7.36–7.46	7.50–7.82		1610 1705		*i*	
5l[g,j]	SPh	1.81	2.18	2.76, dd (9.8, 17.5) 2.93, dd (3.4, 17.5)	4.09, dd (3.4, 9.8)		7.59, d (7.7)	7.2–7.42, 8 H	1620 1715	66.84 66.84	5.61 5.72	4.10 4.16
5l[g,k]	SPh	1.76	2.18	2.79, dd (9.2, 17.5) 2.96, dd (4.2, 17.5)	4.02, dd (4.2, 9.2)	7.39–7.50	7.71, d (7.4)	7.55, d, 2 H (7.6); 7.23–7.31, 3 H				

[a] δ Values in $CDCl_3$. Couplings in Hz shown in parentheses. [b] Nujol (solid) or film. In cm^{-1}. [c] C_3H_2 region contains CH of malonate. [d] C_3H_2, C_4H signals not resolved. [e] Crystalline diastereomer from a mixture of diastereomers. [f] Unseparated diastereomeric mixture; where two absorptions are quoted it is not known which of these belongs to which diastereomer. [g] Obtained on a 400-MHz spectrometer; all others on an 80-MHz spectrometer. [h] Includes meta + para H of ring Ph. [i] Too unstable for analysis to be done. [j] Crystalline diastereomer, mp 100–101 °C. [k] The second diastereomer was very enriched in the mother liquor from the crystallization making the assignments possible.

Table II. ^{13}C NMR Assignments[a] for 4-R_1-4-(3-Phenyl-5-methyl-1,4,2-dioxazol-5-yl)-2-butanones 5

compd	R_1	CH_3C–O	C_1	C_3	C_4	OCO	Ph C_1	Ph C_4	Ph C_3	Ph C_2	CN	CO	R_1
5a	$CH(CO_2Et)_2$	22.3	29.8	40.9	50.7	117.2	123.0	126.7	128.7	131.6	158.3	205.4	13.9 (CH_3, CH_3); 50.2 (CH); 61.5 (CH_2); 61.8 (CH_2); 168.1 (CO)
5c	CH_3[b]	20.9	30.4	44.8	36.6	118.6	123.3	126.6	128.6	131.3	158.0	206.6	14.9
		21.4			36.9								
5d	n-Bu[b]	21.4	29.9	43.5	41.5	118.8	123.3	126.6	128.6	131.3	159.9	207.0	13.9 (CH_3); 21.4 (CH_2); 22.9 (CH_2)
5e	Ph[c]	23.1	30.4	43.7	48.6	118.1	123.1	126.6	128.7	131.4	158.2	205.7	127.4, 128.5, 129.0, 138.7
		22.8	30.6			117.9							
5f	p-$CH_3C_6H_4$	23.0	30.4	43.7	48.2	118.2	123.2	126.7	128.7	131.5	158.3	206.0	21.1 (CH_3); 128.9, 129.2, 135.6, 137.0 (Ar)
5g	$N(CH_3)_2$[b]	22.5	30.3	42.0	64.9	118.9	123.3	126.7	128.7	131.4	157.6	206.6	35.8
		22.7	30.5								158.5	206.7	36.3
5i	OCH_3[b]	19.0	30.7	44.0	78.9	116.8	123.0	126.6	128.7	131.5	158.1	205.2	60.2
		19.6		44.2		116.9						205.3	
5j	OH[b]	19.4	30.7	43.8	70.2	116.4	122.8	126.6	128.5	131.4	158.2	207.2	
		20.0		44.1								207.6	
5k	Cl[b]	19.8	30.5	45.4	56.8	115.6	122.5	126.8	128.8	131.8	158.4	203.0	
		21.6		46.0	57.4	115.9							
5l	SPh[d]	20.7	30.7	43.6	50.2	118.0	122.8	126.7	128.4	131.4	158.2	204.1	127.5, 128.1, 130.0, 132.3
5l	SPh[e]	22.7	29.7	43.6	50.8	118.1	123.5	126.8	128.6	131.5	158.2	204.8	127.6, 129.0, 131.5, 132.3

[a, b] Values in $CDCl_3$. [b] Unseparated diastereomeric mixture; where two absorptions are quoted it is not known which of these belongs to which diastereomer. [c] One diastereomer only formed in the reaction; its assignments are shown in the first row. A second diastereomer was formed on reflux in aqueous EtOH; its assignments that differ are shown in the second row. [d] Crystalline diastereomer, mp 100–101 °C. [e] The second diastereomer was very enriched in the mother liquor from the crystallization, making the assignments possible.

derivative **5c**; variation in the stoichiometry to $Me_5Cu_3Li_2$[33] did not improve the yield. The *n*-butyl derivative **5d** was isolated in a poor yield, but the crude reaction product was found to contain as its major ingredient the *n*-butyl diketone (70%), though breakdown of the adducts was not in general a problem during workup. Lithium diphenyl- and di-*p*-tolylcuprates gave high yields of the arylated ketones **5e** and **5f**.

Heteroatom nucleophiles (N, O, Cl, S) were captured with great efficiency (85–100%). The products **5g** and **5h** from dimethylamine and morpholine have been described previously.[8] While methanol itself ketalized **2a** to the 2,5-dihydrofuranyl hydroxamate **6**,[8] in the presence of methoxide ion it added conjugatively to give the ether **5i**. Addition of water to give the ketol **5j** was achieved with 0.1 M NaOH in dioxane. Though the isolated yield was about 65%, it is likely that the conversion was higher but that the reaction conditions caused some hydrolysis to the water-soluble hydroxy dione.[34] Jensen has shown that in the base-catalyzed hydration of β-substituted enones the equilibrium ratio of aldol to enone is high.[35]

Hydrogen chloride gave a nearly quantitative yield of **5k**, which was rather unstable but could be stored in ethereal solution at −10 °C. We have not yet investigated the chemistry of this presumably very reactive substance. Addition of sulfur was exemplified by the formation of **5l** from lithium thiophenoxide.

With the exception of the malonate **5a** and the aryl adducts **5e** and **5f** the products from **2a** were in general a mixture of diastereomers in comparable amounts (1:1 to 3:2). These were detectable by the occurrence of double resonances for nuclei in either the ^1H (usually the CH_3 groups) or more commonly the ^{13}C (from one to five nuclei) NMR spectra. Single signals were observed for all resonances in the malonate and aryl adducts **5a,e,f**, which are not due to fortuitous coincidence in diastereomers. This was proven for **5e** by its subsequent reaction in aqueous ethanol (see below), which was accompanied by rapid epimerization, the spectra then having three additional ^{13}C resonances and a new methyl ^1H singlet (not due to the product diketone); the malonate **5a** showed similar behavior. The formation of only one diastereomer of the *p*-tolyl adduct **5f** is inferred from the fact that the same set of single resonances (^{13}C) was observed both in the crude chromatographed material and in the fraction obtained from it after recrystallization.

Clearly small nucleophiles show little diastereoselectivity, while larger ones (aryl, malonate) are highly selective. Very bulky nucleophiles are unreactive toward addition, since lithium di-*tert*-butylcuprate caused degradation of **2a**, while with the β-naphthyl cuprate the enone was recovered. Despite the great electrophilicity of the β-carbon in **2** the adjacent quaternary carbon does put steric limitations on its reactivity.

To determine the stereochemical preference of the addition in the case of the arylation reactions, an X-ray structure determination was done on the crystalline *p*-tolyl adduct **5f** (Figure 1), mp 83–83.5 °C, the first example of such an analysis on a dioxazole system. Bond lengths and angles are given in Table III.

Arguments to account for the stereoselectivity in the attack on the enone **2a** can only be speculative, though we may assume that lithium coordination with the heteroat-

(33) Clive, D. L. J.; Farina, V.; Beaulieu, P. *J. Chem. Soc., Chem. Commun.* **1981**, 643.

(34) There was no evidence in the product that retro-aldol condensation had taken place.

(35) Jensen, J. L.; Hashtroudi, H. *J. Org. Chem.* **1976**, *41*, 3299.

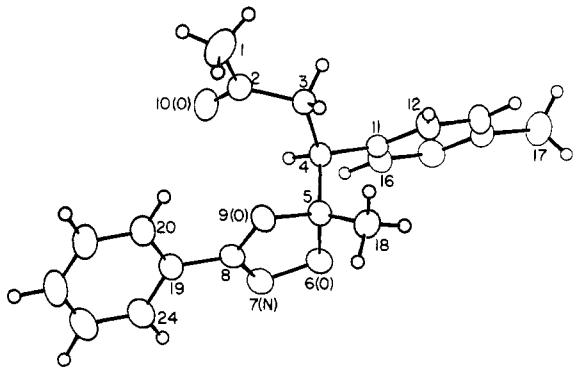


Figure 1. ORTEP diagram of *p*-tolyl derivative **5f**.

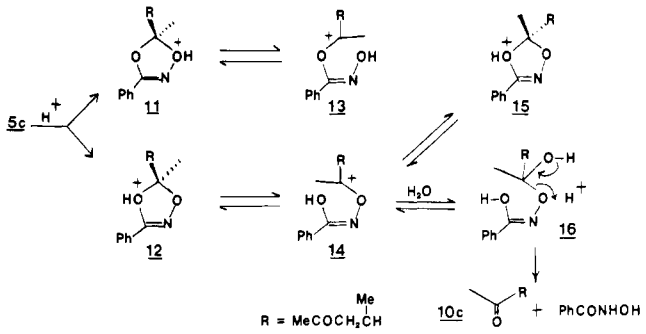
Table III. Bond Lengths and Angles of the *p*-Tolyl Compound 5f

	Bond Lengths, Å		
C(1)–C(2)	1.497 (4)	C(2)–C(3)	1.507 (2)
C(2)–O(10)	1.209 (2)	C(3)–C(4)	1.535 (2)
C(4)–C(5)	1.540 (2)	C(4)–C(11)	1.514 (2)
C(5)–O(6)	1.442 (2)	C(5)–O(9)	1.448 (2)
C(5)–C(18)	1.504 (3)	O(6)–N(7)	1.428 (2)
N(7)–C(8)	1.275 (2)	C(8)–O(9)	1.355 (2)
C(8)–C(19)	1.460 (2)	C(11)–C(12)	1.384 (2)
C(12)–C(13)	1.386 (3)	C(13)–C(14)	1.380 (3)
C(14)–C(15)	1.372 (3)	C(14)–C(17)	1.509 (3)
C(15)–C(16)	1.385 (3)	C(16)–C(11)	1.383 (2)
C(19)–C(20)	1.384 (3)	C(20)–C(21)	1.384 (3)
C(21)–C(22)	1.374 (4)	C(22)–C(23)	1.378 (4)
C(23)–C(24)	1.376 (3)	C(24)–C(19)	1.385 (3)
C(1)–H(1A)	0.96 (3)	C(1)–H(1B)	0.95 (3)
C(1)–H(1C)	0.99 (4)	C(3)–H(3A)	1.02 (2)
C(3)–H(3B)	0.97 (2)	C(4)–H(4)	1.00 (2)
C(12)–H(12)	1.00 (2)	C(13)–H(13)	0.98 (2)
C(15)–H(15)	0.95 (2)	C(16)–H(16)	0.97 (2)
C(17)–H(17A)	0.93 (3)	C(17)–H(17B)	0.90 (4)
C(17)–H(17C)	0.94 (3)	C(18)–H(18A)	1.00 (2)
C(18)–H(18B)	1.00 (2)	C(18)–H(18C)	0.97 (2)
C(20)–H(20)	1.00 (2)	C(21)–H(21)	1.00 (2)
C(22)–H(22)	0.99 (2)	C(23)–H(23)	1.02 (2)
C(24)–H(24)	0.98 (2)		
	Bond Angles, deg		
C(1)–C(2)–C(3)	115.8 (1)	C(1)–C(2)–O(10)	121.8 (1)
C(3)–C(2)–O(10)	122.45 (9)	C(2)–C(3)–C(4)	114.41 (9)
C(3)–C(4)–C(5)	111.22 (9)	C(3)–C(4)–C(11)	114.07 (9)
C(5)–C(4)–C(11)	111.80 (8)	C(4)–C(5)–O(6)	108.72 (8)
C(4)–C(5)–O(9)	107.98 (7)	C(4)–C(5)–C(18)	117.8 (1)
O(6)–C(5)–O(9)	103.18 (6)	O(6)–C(5)–C(18)	109.28 (9)
O(9)–C(5)–C(18)	108.89 (9)	C(5)–O(6)–N(7)	107.57 (9)
O(6)–N(7)–C(8)	105.79 (9)	N(7)–C(8)–O(9)	116.08 (8)
N(7)–C(8)–C(19)	125.46 (9)	O(9)–C(8)–C(19)	118.41 (8)
C(5)–O(9)–C(8)	105.2 (1)	C(4)–C(11)–C(12)	123.0 (1)
C(4)–C(11)–C(16)	119.9 (1)	C(16)–C(11)–C(12)	117.1 (1)
C(11)–C(12)–C(13)	121.1 (1)	C(12)–C(13)–C(14)	121.4 (1)
C(13)–C(14)–C(15)	117.6 (1)	C(13)–C(14)–C(17)	121.1 (1)
C(15)–C(14)–C(17)	121.3 (1)	C(14)–C(15)–C(16)	121.2 (1)
C(15)–C(16)–C(11)	121.6 (1)	C(8)–C(19)–C(20)	120.2 (1)
C(8)–C(19)–C(24)	120.1 (1)	C(24)–C(19)–C(20)	119.6 (1)
C(19)–C(20)–C(21)	119.9 (1)	C(20)–C(21)–C(22)	120.1 (1)
C(21)–C(22)–C(23)	120.2 (1)	C(22)–C(23)–C(24)	120.0 (1)
C(23)–C(24)–C(19)	120.2 (1)		

oms is important in the cuprate reactions. Whatever the mechanism the relative stereochemistry depicted in the enantiomer of the tolyl derivative **5f** in Figure 1, 4*S*, 5*S* is achieved by delivery of the tolyl group on the top (i.e., the *si*, *re*) face of the C_3 to C_4 double bond in the enantiomer **7** of the enone.

High selectivity even by small nucleophiles can be readily achieved by the use of a bulkier substituent on the dioxazole ring. Thus the adduct **2b**, from (nitrosocarbonyl)isobutane,[8] with lithium dimethylcuprate gave the β-methyl ketone **8**, whose ^{13}C NMR spectrum showed

Scheme I



single resonances for all atoms. We assume, though without additional evidence, that **8** has the same relative configuration as **7**.

The mass spectra of the adducts **5** showed in general, as well as the parent ion, a peak at *m/e* 231 indicative of the retro-Michael reaction and at *m/e* 162 which must be attributed to the aromatically stabilized 1,4,2-dioxazolium cation **9**.[36]

γ-Diketone Preparation. Just as **2** is in principle a half-blocked *cis*-enedione, so is the adduct **5** a half-blocked internally monosubstituted γ-diketone. Whether **5** exists as a single diastereomer or a mixture, release of the keto group gives racemic diketone.

The adduct could be hydrolyzed to the diketones **10** under neutral conditions (the other product is presumably the hydroxamic acid), by refluxing them in 1:1 aqueous EtOH, typically for 6–8 h. Failures were noted in the case of **5g** and **5i**, containing electron-withdrawing substituents. Steric effects may also be inhibitory, since the *tert*-butyl adduct **8** was stable to the hydrolysis conditions.

As noted above epimerization at the tertiary carbon precedes solvolysis, isolation of the product from diastereomerically pure **5a** or **5e** after a 0.5-h reflux showing approximately equal amounts of the two isomers. Similarly a 3:2 mixture of **5c**, as isolated from the cuprate reaction on **2a**, equilibrated to a 1:1 mixture.

Protonation of one diastereomer of **5c** on either O_1 or O_4 of the dioxazole ring gives **11** or **12** (Scheme I) which can open to the hydroximic acid derived cations **13** and **14**, respectively. As shown for **14** (and similarly for **13**) the cation must recyclize to the epimers **12** or **15** faster than it is quenched by water to give the ketal derivative **16** and thence the diketone **10c** and benzohydroxamic acid, to account for the observed epimerization.

The involvement of O-protonated species like **12** and **14** would also be in keeping with the resistance of the β-dimethylamino and β-methoxy ketones **5g** and **5i** to solvolysis, since such cations would be destablized by the very electrophilic adjacent carbon atom.

The diketones **10g,i,j** could, however, be made from **5g,i,j** by hydrogenolysis with palladium–charcoal. This deblocking technique, previously used in the proof of structure of the dihydro derivative of **2a**,[8] appears to be quite general. Analytical data and ^1H NMR absorptions of the diketones **10** are given in Table IV.

Compound **10j** is Henze's ketol,[37] and was identical with an independently synthesized sample;[38] it has been implicated in the biological conversion of fat to liver glycogen.[39]

(36) Selva, A.; Citterio, A.; Pella, E.; Tonani, R. *Org. Mass. Spectrom.* **1974**, *9*, 1017.
(37) Henze, M. *Z. Physiol. Chem.* **1930**, *189*, 121. Henze, M.; Müller, R. *Z. Physiol. Chem.* **1930**, *193*, 88.
(38) Schechter, M. S.; Green, N.; LaForge, F. B. *J. Am. Chem. Soc.* **1949**, *71*, 3165.

Table IV. ^{1}H NMR Assignments[a] and Elemental Analyses for 3-R_1-2,5-Hexanediones 10

compd	R_1	CH_3	C_4H_2	C_3H	R_1	calcd C	calcd H	found C	found H
10a	$CH(CO_2Et)_2$	2.15, 2.30	2.79-3.78[b,c]		1.25, t, 3 H (7.2); 1.26, t, 3 H (7.2); 4.17, q, 4 H[b]	57.34	7.40	57.41	7.29
10d	*n*-Bu	2.13, 2.23	2.32-3.05[c]		0.81-1.71, m, 9 H	70.55	10.66	70.58	10.85
10e[d]	Ph	2.11, 2.15	2.55, dd (4.1, 17.8); 3.44, dd (10.0, 17.8)	4.22, dd (4.1, 10.0)	7.14-7.41, m, 5 H	75.76	7.42	75.64	7.70
10g	$N(CH_3)_2$	2.24, 2.27	2.33-3.09	3.80, dd (3.5, 9.6)	2.24, br, 6 H	61.12	9.62	61.28	9.63
10i[d]	OCH_3	2.21, 2.25	2.78-2.80	4.06, dd (5.3, 6.5)	3.43	58.32	8.39	58.39	8.27
10j	OH	2.22, 2.27	2.92, 4 d	4.34, dd	3.73	ref 37			
10l	SPh	2.11, 2.33	2.71, dd (4.7, 18.0); 3.14, dd (9.4, 18.0)	4.07, dd (4.7, 9.4)	7.27-7.46, m, 5 H	64.84	6.35	64.97	6.59

[a] δ Values in $CDCl_3$. Couplings in Hz shown in parentheses. [b] C_4H_2 region includes CH of malonate group. [c] C_4H_2, C_3H signals not resolved. [d] Obtained on a 400-MHz spectrometer; all others on an 80-MHz spectrometer.

Table V. ^{1}H NMR Assignments[a] and Elemental Analyses for 3-R_1-2,5-Dimethylfurans 19

compd	R_1	CH_3	C_4H	R_1	calcd C	calcd H	found C	found H
19a	$CH(CO_2Et)_2$	2.22, 2.22	6.06	1.27, t, 6 H (7.2); 4.21, q, 2 H; 4.40, q, 2 H	61.41	7.14	61.39	7.11
19d	*n*-Bu	2.15, 2.20	5.75	0.90-1.50, m, 9 H	78.90	10.59	78.91	10.55
19e	Ph	2.27, 2.40	6.15	7.20-7.80, m, 5 H	83.69	7.02	83.59	7.00
19f	*p*-$CH_3C_6H_4$	2.25, 2.33	6.06	2.36, s, 3 H; 7.07-7.31, m, 5 H	83.83	7.58	83.88	7.62
19l	SPh	2.27, 2.30	5.95	7.05-7.47, m, 5 H	70.55	5.92	70.51	6.12

[a] δ Values in $CDCl_3$ at 80 MHz. Couplings in Hz shown in parentheses.

In principle the diketones described above might be prepared by the Michael addition to the unblocked counterpart of **2**, *cis*-3-hexen-2,5-dione (**17**) or its trans isomer (**18**). Both, like **2**, are obtained from 2,5-dimethylfuran,[40] but in poorer yields. The patent literature in fact contains a number of references to the successful addition of sulfur anions to the ene diones.[41] While diethyl malonate anion readily added to **18** to give **10a**, methoxide ion caused its complete destruction. Lithium diphenylcuprate gave 2% of **10e** with **17**, while the di-*n*-butylcuprate gave no **10d** with either **17** or **18**. The ene diones are thus much more limited in scope as Michael acceptors than **2**.

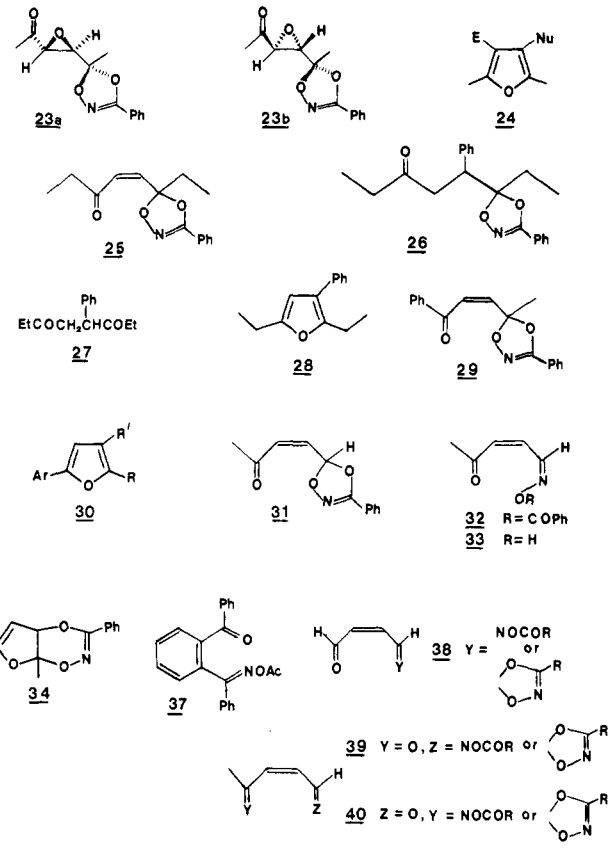
Furan Syntheses. The conversion of the diketones into the furans was expected to be routinely possible by acid-catalyzed dehydration. This was confirmed for the diketo malonate **10a** in the presence of boron trifluoride etherate, the rapid reaction to **19a** being followed in $CDCl_3$ by ^{1}H NMR spectroscopy. The precursor to **10a**, the adduct **5a**, could itself be converted into **19a** with BF_3 in ether or chloroform.

The overall reaction was examined in more detail for the phenyl adduct **5e** in $CDCl_3$ at 0 °C. With 1.5 equiv of BF_3 rapid formation of an intermediate was observed which decayed slowly to **19e**. The peaks of the intermediate were coincident with those of the diketone **10e**, a product possible only if cleavage of the dioxazole to benzonitrile oxide had occurred or if adventitious water was present, in which case the coproduct would have been benzohydroxamic acid. This point was not examined further, but an aqueous quench at an early stage of the reaction did give a mixture of the diketone and the furan.

Using 1.5–3 equiv of BF_3 in ether or chloroform, we were able to convert the adduct **5** into the furans in excellent yields (See Table V for analytical data and ^{1}H NMR absorptions). An exception was the *n*-butyl adduct **5d** where only a 40% yield of the furan was obtained even with 12 equiv of BF_3 (the diketone was found as well[42]); an authentic sample of this volatile furan was made by the Wolff–Kishner reduction of the 3-butyryl ketone. Other failures were with the dimethylamino, methoxy, and hydroxy adducts **5g**, **5i**, and **5j**, which were unreactive or decomposed. Even if cleavage of these to the diketones had occurred, the ensuing cyclization to the furans in the case of **19g** and **19i**, both known compounds,[43,44] would have failed, since the diketones (prepared by the hydrogenolysis route) were shown to be inert even to a large excess of BF_3. Their resistance to cyclization may be due to preferential complexation by boron to the β-heteroatom and the ketonic oxygen, e.g., as in **20** (from **10i**), from which cyclization is not possible. Similar complexation of oxygen

(39) Stöhr, R.; Henze, M. *Z. Physiol. Chem.* **1932**, *206*, 1.
(40) Levisalles, J. *Bull. Soc. Chim. Fr.* **1957**, 997.
(41) Evers, W. J.; Heinsohn, H. H., Jr.; Mayers, B. J. U.S. Patent 3836563, 1974; 3910966, 1975; 3922288, 1973; 3996287, 1976. Evers, W. J.; Heinsohn, H. H., Jr.; Mayers, B. J.; Karoll, E. A. U.S. Patent 3917869, 1973. Evers, W. J.; Mayers, B. J. U.S. Patent 3931270, 1976.
(42) With BF_3 formation of the diketone is obviously more efficient than its cyclization. We did not try to improve the cyclization yields by using other catalysts.
(43) Thorstad, O.; Undheim, K.; Lantz, R.; Hornfeldt, A. B. *Acta Chem. Scand., Ser. B* **1975**, *29*, 652.
(44) Eugster, C. H.; Allner, K.; Rosenkranz, R. E. *Chimica* **1961**, *15*, 516.

Chart II



atoms from both the alcohol and the acid is said to occur in BF_3-catalyzed esterification.[45]

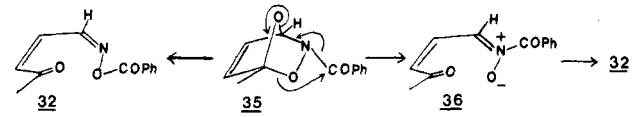
The furylmalonate **19a** was converted into the known[46] furylacetic acid **19m** by hydrolysis.

Epoxide of 2a. Epoxidation was best achieved (60% before workup) by using 0.2 M Na_2CO_3 in 30% H_2O_2 with *tert*-butyl alcohol as cosolvent at 45 °C, a wide range of other conditions being less effective.

A minor ether insoluble crystalline product, mp 122.5–123 °C (12%), was identified as either the hydroperoxy ether **21** or the hydroxy peroxide **22**, of a single but undetermined stereochemistry (unique resonances for all ^1H and ^{13}C nuclei). Nonequivalent methyl, vinyl, and methine signals, two exchangeable protons (NMR), NH/OH and CO absorptions (IR), and a positive peroxide test all demanded these choices. The hydroperoxide **21** was preferred since the vinyl coupling of 5.7 Hz was more reconcilable with a five- than a six-membered ring,[47] and its formation parallels the ketalization reaction of **2a** to **6** with methanol, 1,2-Addition of hydroperoxide anion to an enone is normally reversible and is disfavored over 1,4-addition, which is the rate-determining step;[48] here cyclization competes successfully with the retro-1,2-addition.

The NMR spectra (^1H and ^{13}C) of the oily epoxide were those of an equal mixture of two diastereomers. The two coupling constants for the methine protons, 1.9 and 2.1 Hz, showed them to be trans in both epoxides, and an enantiomer of each is shown in **23a** and **23b** (Chart II). *Cis* epoxides have methine coupling constants in the range of 4 Hz.[49] Regardless of the starting stereochemistry of the

Scheme II



enone, trans epoxides are predicted in this reaction procedure.[50]

The chemistry of the epoxide **23** remains to be explored. Lithium dimethylcuprate (2 equiv) gave the β-hydroxy ketone **5j**, the product of reductive cleavage, and not the α-methylated derivative observed with simple epoxides or epoxy esters.[51] Szajewski's modification applied to **23** (Me_2CuLi; E^+; $-H_2O$) should lead to the α-substituted enone,[52] which after a Michael addition (Nu^-; H^+) and BF_3 treatment could open up a route to furans **24**, substituted in the β-positions with groups originating as an electrophile and a nucleophile.

Reactions of (Nitrosocarbonyl)benzene with Other Furans. As expected oxidation of benzohydroxamic acid (PbO_2, in ethyl acetate) in the presence of 2,5-diethylfuran[53] gave the 4-octen-3-one derivative **25**, from which the phenyl derivative **26** was efficiently obtained with the cuprate. Conversion of **26** into 4-phenyloctane-3,6-dione (**27**) by hydrolysis and of either of these into the furan **28** proceeded in good yields, though more slowly than with the dimethylfuran derived products.

We previously showed that 2-methyl-5-phenylfuran gave exclusively the enone **29** with (nitrosocarbonyl)benzene.[8] It follows predictably that 2-alkyl-5-arylfurans can be converted by the appropriate sequence (PhCONHOH, oxidation; R^-; H^+; BF_3) into regioisomerically pure furans of the general structure **30**.

There was little evidence of reaction of furan itself when benzohydroxamic acid was oxidized in the presence of an excess of it. With 2-methylfuran a considerable amount of dibenzamide was produced, and there was a 27% yield of a 1:1 adduct, mp 73–75 °C, of (nitrosocarbonyl)benzene and the furan. An acetyl methyl absorption in the NMR spectra (^1H, ^{13}C) and an IR band at 1685 cm^{-1} were reconcilable with structure **31**, but a ^{13}C absorption at 163.7 ppm and the absence of any near 113 ppm (cf. C_5 in the dioxazole rings of **2a** or **2b**) made **31** untenable. The only reasonable structure is 1-(benzoyloximino)-2-penten-4-one (**32**), to which we assign the cis,cis configuration, with certainty at least at the alkene group (vinylic H, J = 11.6 Hz[8]).

Attempts to chromatograph the ester **32** caused partial cleavage to the oxime **33** on silica gel, and complete cleavage on basic alumina. The oxime could be reconverted into the same ester by using benzoyl chloride in pyridine, and it was synthesized by monooximation of *cis*-1-oxo-2-penten-4-one.[54] This synthetic oxime had different spectra than those of the oxime described by Severin et al.[55] and was presumably a stereoisomer, but it gave the same benzoate as the methylfuran reaction.

The diminishing sequence of reactivity toward (nitrosocarbonyl)benzene from dimethylfuran (very reactive) to

(45) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; Wiley: New York, 1980; Chapter 9, p 301.
(46) Blanchette, J. A.; Brown, E. V. *J. Am. Chem. Soc.* **1952**, *74*, 2098.
(47) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 275.
(48) Bunton, C. A.; Minkoff, G. J. *J. Chem. Soc.* **1949**, 665.
(49) Lehn, J. M.; Riehl, J. J. *Mol. Phys.* **1964**, *8*, 33.
(50) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: New York, 1972; Chapter 6, p 308.
(51) Herr, R. W.; Wieland, D. M.; Johnson, C. R. *J. Am. Chem. Soc.* **1970**, *92*, 3813.
(52) Szajewski, R. P. *J. Org. Chem.* **1978**, *43*, 1819.
(53) Fetizon, M.; Baranger, P. *C. R. Hebd. Seances Acad. Sci.* **1953**, *236*, 499.
(54) Hirsch, J. A.; Szur, A. J. *J. Heterocycl. Chem.* **1972**, *9*, 523.
(55) Severin, T.; Adhikary, P.; Brautigam, I. *Chem. Ber.* **1976**, *109*, 1179.

furan (unreactive) suggests that the addition to the methylfuran might have occurred on the substituted side to give **34** as the initial product. It is not, however, easy to see how this would lead to the oxime **32**. More plausibly a mechanistic switch may occur in the sequence of furans so that methylfuran reacts conventionally, as the diene, to give **35**, a mode of addition consistent with the polarity of the two components. The isomerization of **35** to **32** (Scheme II) might occur in one step (arrows) or in two, e.g., by way of the presumably very unstable[56,57] *N*-acyl nitrone **36**. The formation of **32** is completely analogous to that of the *O*-acetyl oxime **37** when acetohydroxamic acid is oxidized in the presence of diphenylisobenzofuran, which can only be expected to act as a diene.[3]

It is reasonable to suppose that the direction of addition (4 + 2 or 2 + 4) is likely to be just as sensitive to electronic effects in the nitrosocarbonyl compound as in the furan. A wide range of hydroxamic acids, RCONHOH, is available, from those with very electron-releasing R groups as in *N*-hydroxyureas (e.g., R = NMe_2) or urethanes (e.g., R = OMe) to those with very electron-withdrawing R groups (e.g., R = CF_3, EtOCO). Appropriate combinations of these with furan or 2-methylfuran are potential sources of half-blocked malealdehyde **38** or either of the half-blocked oxopentenones **39** or **40**. If both the latter are available the aldehyde and ketone functions can be utilized separately in whichever order is desired. Compounds like **38–40** are valuable starting points in organic synthesis.

Experimental Section

IR spectra were obtained on a Beckman IR 10 or Acculab 10 spectrometer, samples being used as liquid films or Nujol mulls. The ^1H and ^{13}C NMR spectra were run on a Bruker WP-80 or WH-400 spectrometer, in $CDCl_3$ with tetramethylsilane as internal standard. Low- and high-resolution mass spectra were obtained respectively on Varian MAT CHT and VG-7070 F spectrometers. Gas–liquid chromatography was performed on a Hewlett-Packard 5840 A gas chromatograph with a glass column (1.8 m × 2.0 mm i.d.) packed with 5% OV 275 on Chromosorb W AW-DMCS (80/100 mesh). For quantitative work naphthalene was used as an internal standard.

Unless otherwise stated column chromatography was done on silica gel (Merck, 70–270 mesh), elution being achieved with a methylene chloride to ethyl acetate sequence.

Solvents used in alkyllithium and cuprate work were distilled from sodium/benzophenone under dry N_2. All organometallic operations were done in a dry Ar atmosphere.

Organic solutions from aqueous extractions were dried with $MgSO_4$.

Microanalyses were done by Guelph Chemical Laboratories, Guelph, Ontario.

(*Z*)-4-(3-R-5-Methyl-1,4,2-dioxazol-5-yl)-3-buten-2-ones 2a (R = Ph) and 2b (R = CMe_3)[8]: ^{13}C NMR [**2a**] δ 24.4 (ring Me), 30.7 (CO*Me*), 113.4 (OCO), 122.9, 126.6, 128.6, 131.5 (PhC_1, C_4, C_3, C_2), 132.2, 131.5 (CH=CH), 158.0 (C=N), 200.6 (C=O), [**2b**] 24.4 (ring Me), 27.1 (C*Me*$_3$), 30.7 (CO*Me*), 31.1 (*C*Me_3), 112.6 (OCO), 132.2, 135.3 (CH=CH), 166.3 (C=N), 200.6 (C=O).

4-R$_1$-4-(3-Phenyl-5-methyl-1,4,2-dioxazol-5-yl)-2-butanones (5). See Table I for IR, ^1H NMR, and elemental analyses data and Table II for ^{13}C NMR data.

5a, R$_1$ = CH(CO$_2$Et)$_2$. Diethyl malonate (3.0 mL, 20 mmol) and sodium methoxide (1.2 g, 22 mmol) were stirred together in ether (100 mL) for 2.5 h. The enone **2a** (3.8 g, 16.4 mmol) was added dropwise in ether (10 mL; this was the method throughout when the enone was added to aprotic solutions) to the stirred anion suspension, and stirring was continued for 23 h. The whole was acidified with 1 M acetic acid, water was added, and the ether layer was shaken out and dried. Evaporation gave the β-keto malonate (6.0 g, 94%) as a slightly red oil, directly pure.

5b, R$_1$ = CHCN(CO$_2$Et). The enone (0.50 g, 2.2 mmol) was reacted with the sodium salt of ethyl cyanoacetate (from 0.27 g, 2.4 mmol) under the same conditions as described for **5a**. The ^1H NMR spectrum of the residual oil showed it to be a mixture of about 70% of product and 30% of starting material, which were separated by column chromatography, with the product crystallizing.

5c, R$_1$ = Me. Method A. 1.4 M solution of MeLi in ether (2.4 mL, 3.4 mmol) was injected into a suspension of Me_2SCuBr (0.41 g, 2.0 mmol) in ether (100 mL) at 0 °C, and the whole was stirred for 5 min. The enone (0.133 g, 0.57 mmol) was added with stirring, and after 2.5 h the reaction mixture was poured into an excess of 0.5 M HCl at 0 °C. The ether layer was isolated, washed with aqueous Na_2CO_3, dried, and evaporated to a residue, which was chromatographed. The methylated ketone was obtained as an oil (0.072 g, 51%).

Method B. A 1.4 M MeLi solution (3.0 mL, 4.2 mmol) was introduced into a suspension of CuBr (0.25 g, 1.7 mmol), followed by the enone (0.16 g, 0.71 mmol). The procedure and workup were exactly as in A except that the reaction mixture was quenched with aqueous NH_4Cl rather than HCl. Chromatography gave the product (0.035 g, 25%) as before.

Method C. In accordance with Clive's method,[33] the cuprate of 5:3 stoichiometry was prepared from CuBr (0.72 g, 5 mmol) and MeLi (5.9 mL, 1.4 M solution, 8.3 mmol). The enone (0.39 g, 1.7 mmol) was added, and workup as in B led to the methyl adduct (0.034 g, 24%) after chromatography.

5d, R$_1$ = *n*-Bu. The cuprate was prepared at 0 °C by stirring a mixture of CuBr (0.29 g, 2.0 mmol) and 1.6 M solution of *n*-BuLi (2.5 mL, 4.0 mmol) in ether (100 mL) for 10 min. The solution was cooled to −78 °C, the enone (0.366 g, 1.58 mmol) was added, and the whole was stirred for 5 h. After an aqueous NH_4Cl quench the crude product was shown by ^1H NMR spectroscopy to consist mainly of the diketone **10d**, but chromatography (neutral Al_2O_3) gave a pure fraction of **5d** as a colorless oil (0.050 g, 11%).

5e, R$_1$ = Ph. The phenyl cuprate was prepared similarly, from PhLi (3.41 mL of 1.9 M solution, 6.5 mmol) and CuBr (0.465 g, 3.24 mmol) in ether (100 mL), and the enone (0.693 g, 3.00 mmol) was added to it at 0 °C. After 8 h of stirring and an aqueous NH_4Cl workup the ether soluble material was chromatographed. Biphenyl was eluted with hexane and the phenyl adduct, as a light yellow oil (0.797 g, 86%), with ethyl acetate.

5f, R$_1$ = *p*-MeC$_6$H$_4$. Following Gilman's procedure,[58] a solution of $(p\text{-}MeC_6H_4)_2CuLi$ in ether (100 mL) was prepared from *p*-bromotoluene (1.88 g, 11.0 mmol), Li (0.16 g, 23 mmol), and CuI (0.106 g, 5.5 mmol). To the lime-colored solution at 0 °C was added the enone (1.01 g, 4.37 mmol), and the whole was stirred for 7 h and then poured into cold aqueous NH_4Cl. Ether (200 mL) was added, the ether layer was worked up, and the soluble residue was chromatographed as described for the phenyl adduct. The tolyl derivative crystallized (1.21 g, 86%) and was recrystallized from ether–hexane as needles, mp 83–83.5 °C. A crystal was used for X-ray analysis (see below).

5g, R$_1$ = NMe$_2$, and 5h, R$_1$ = Morpholino. The syntheses have been described.[8]

5i, R$_1$ = OMe. To a solution of the enone (0.130 g, 0.56 mmol) in MeOH (3 mL) was added a solution of NaOMe in MeOH (10 mL, 0.1 M, 1.0 mmol). After 16 h at room temperature the solvent was removed in a stream of N_2, and an ether–water workup gave the β-methoxy ketone as a colorless oil (0.133 g, 90%) from the ethereal layer.

5j, R$_1$ = OH. The enone (1.00 g, 4.33 mmol) was stirred for 24 h in 0.1 M NaOH in aqueous dioxane (1:1, 20 mL). The wine-colored solution was neutralized with acetic acid, its volume was reduced to about half under reduced pressure, ether (50 mL) was added, and the whole was shaken out with several small portions of water. Evaporation of the dried ether layer gave the hydroxy ketone as a viscous oil (0.70 g, 65%) in high purity.

5k, R$_1$ = Cl. Hydrogen chloride was bubbled into a solution of the enone (1.32 g, 5.72 mmol) in ether (60 mL) at 0 °C for 20 min. Water was carefully added, and the organic phase was

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separated and then washed thoroughly with water. Drying and evaporation gave the chloro ketone as a pale yellow oil (1.39 g, 91%), which darkened slowly even at 0 °C but could be stored in solution in either or chloroform at 0 °C for months with little deterioration.

5l, R_1 = SPh. An ethereal solution of 1.6 M *n*-BuLi (1.02 mL, 1.63 mmol) was introduced into a solution of thiophenol (0.17 mL, 1.63 mmol) in ether (10 mL) which was then stirred for 2 min. The enone (0.378 g, 1.63 mmol) was added, and stirring was continued for another 10 min. After an aqueous NH_4Cl–ether workup a red oil was obtained, which was purified by chromatography on basic Al_2O_3 (SiO_2 destroyed it), giving the pure thioether (0.478 g, 86%). Crystallization from ether–hexane gave one diastereomer of mp 100–101 °C.

Tables I and II show ^1H and ^{13}C NMR assignments for both diastereomers of **5** except in the case of **5a,e,f**, where only one was produced. In the case of **5a** and **5e** the second was obtained by epimerization in refluxing aqueous EtOH; the absorptions of the second isomer of **5a** are not recorded in the tables. In principle four diastereomers of **5b** can be formed. The ^1H NMR data refer to one crystalline isomer; the spectrum of the total mixture was complex.

Unless crystalline, all samples submitted for elemental analysis were given a separate chromatographic purification.

Attempted Addition of Lithium Di-*tert*-butyl- and Dinaphthylcuprates. The *tert*-butyl complex was generated from an ethereal solution of 2.2 M *t*-BuLi (2.3 mL, 4.83 mmol) and CuBr (0.346 g, 2.41 mmol) in ether (70 mL) at 0 °C. The enone (0.446 g, 1.93 mmol) was added, and the solution was immediately cooled to −78 °C and stirred for 11.5 h. When the black solution was worked up no recognizable products were observed in the ^1H NMR spectrum.

The Grignard reagent from 2-bromonaphthalene (1.36 g, 6.57 mmol) and magnesium (0.159 g, 6.54 mmol) in ether (50 mL) was added to ether (80 mL) containing the enone (0.724 g, 3.13 mmol) and CuI (0.603 g, 3.17 mmol) at 0 °C. After being stirred for 7 h, the solution was worked up as usual. As well as unreacted enone, a crystalline solid mp 186–188 °C was isolated whose ^1H NMR spectrum and mass spectrum (M^+ = 254) indicated it to be 2,2′-binaphthyl.

4-(3-*tert*-Butyl-5-methyl-1,4,2-dioxazol-5-yl)-2-pentanone (8). A solution of 1.4 M MeLi (7.04 mL, 9.50 mmol) was introduced into a suspension of CuBr (0.704 g, 4.91 mmol) in ether (150 mL), which was then stirred for 15 min. The enone **2b** (0.669 g, 3.17 mmol) was added and the reaction mixture stirred for 2.5 h. Following an aqueous NH_4Cl workup the ethereal layer gave a residue, which was extracted with several portions of cold hexane. Evaporation of the hexane gave the adduct (0.317 g, 44%): IR 1713 (C=O), 1625 cm^{-1} (C=N); ^1H NMR δ 1.02 (C_4Me, d, J = 6.6 Hz), 1.24 (CMe_3, s), 1.45 (ring Me, s), 2.15 (COMe, s), 2.62–4.11 (3 H, C_3 and C_4, m, ABC system); ^{13}C NMR 4.8 (C_4Me), 21.1 (ring Me), 27.1 (*CMe*$_3$), 30.3 (*COMe*), 31.2 (*CMe*$_3$), 36.7 (C_4), 44.9 (C_3), 117.3 (OCO), 166.1 (C=N), 206.7 ppm (C=O); M^+ 227. Anal. Calcd for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.43; H, 9.28; N, 6.36.

The γ-Diketones 10 (See Table IV). (i) Deblocking of the Dioxazole Ring by Aqueous EtOH. The adduct **5** was refluxed in 1:1 aqueous EtOH until thin-layer chromatography showed that the reaction was complete. The solution was evaporated until most of the alcohol had been removed and then extracted with ether. The ether solution was washed with aqueous Na_2CO_3, dried, and evaporated, the product at that point being of high purity. Analytical samples were finally purified by chromatography. Details follow thus: weight, number of moles of adduct **5**; total volume of solvents; time of reflux (though minimum times were not always determined); weight of diketone **10** (yield).

3-(Dicarbethoxymethyl)hexane-2,5-dione (10a): 0.485 g, 1.24 mmol; 18 mL; 12 h; 0.280 g (83%).

4-Acetyloctan-2-one (10d): 0.439 g, already partially deblocked (see synthesis of **5d** above) and obtained from 0.513 g of enone **2a** (2.22 mmol); 16 mL; 8 h; 0.279 g (74%, based on the two reactions from the enone).

3-Phenylhexane-2,5-dione (10e): 0.084 g, 0.271 mmol; 14 mL; 8.5 h; 0.046 g (89%).

3-(Phenylthio)hexane-2,5-dione (10l): 0.452 g, 1.33 mmol; 16 mL; 20 h; 0.283 g (96%).

The dimethylamino, methoxy, and hydroxy compounds **10g**, **10i**, and **10j**, and the *tert*-butyldioxazolyl ketone **8** were all inert to refluxing aqueous EtOH.

(ii) Hydrogenolysis of the Dioxazole Ring. The compound **5** was added to ethyl acetate containing 5% Pd on charcoal, and hydrogenation was carried out at room temperature and pressure. When reaction was complete (thin-layer chromatography) the mixture was filtered through Celite and the solvent evaporated. Insoluble benzamide was removed by extracting the residue with cold ether or repeated treatment with pentane or hexane. Analytical samples were further purified by chromatography. Details follow thus: weight, number of moles of **5**; volume of ethyl acetate; weight of Pd/C; time of hydrogenation; weight of diketone **10** (yield); method of isolation.

3-(Dicarbethoxymethyl)hexane-2,5-dione (10a): 0.100 g, 0.256 mmol; 10 mL; 0.50 g; 4 h; 0.063 g (90%); extracted with ether–hexane.

3-(*N*,*N*-Dimethylamino)hexane-2,5-dione (10g): 0.723 g, 2.62 mmol; 50 mL; 0.134 g; 17 h; 0.205 g (50%); extracted with cold ether.

3-Methoxyhexane-2,5-dione (10i): 0.652 g, 4.53 mmol; 20 mL; 0.137 g; 27 h; 0.303 g (85%); extracted repeatedly with pentane.

3-Hydroxyhexane-2,5-dione, Henze's Ketol[37] (10j): 0.168 g, 0.68 mmol; 10 mL; 0.080 g; 24 h; 0.077 g (87%); this volatile product was estimated by careful evaporation, addition of MeOH (27.5 μL, 0.68 mmol) and $CDCl_3$ (1 mL), and integration of the Me peaks in the ^1H NMR spectrum). An authentic sample was prepared from methylglyoxal.[38]

Synthesis of 10a from *trans*-3-Hexene-2,5-dione (18). The *trans*-enedione (0.224 g, 2.00 mmol) and sodium hydride–mineral oil (50% dispersion, 0.096 g, 2.00 mmol) were allowed to react in ether (50 mL), and diethyl malonate (0.320 g, 2.00 mmol) was added. After being stirred for 12 h, water was added and the mixture neutralized with acetic acid. The ether soluble residue was washed with very small portions of hexane to remove the mineral oil, leaving the adduct **10a** as an oil (0.176 g, 32%).

Attempted Addition of MeO^- to *trans*-Enedione 18. A solution of the enedione (0.050 g, 0.45 mmol) in 0.10 M NaOMe in MeOH (3.0 mL) was kept at room temperature for 24 h and then neutralized with acetic acid and extracted with ether. The ether layer on workup gave a residue with a very complex ^1H NMR spectrum.

Reaction of Ph_2CuLi with *cis*-Enedione 17. This *cis*-enedione (0.50 g, 4.5 mmol) was injected neat into a solution of the cuprate at 0 °C, prepared from 2.4 M PhLi (4.7 mL, 11.3 mmol) and CuBr (0.81 g, 5.65 mmol) in ether (100 mL). After 30 min the solution was subjected to the usual aqueous NH_4Cl workup. The ^1H NMR spectrum was very complex, but GLC showed that about 1% of the phenyl adduct **10e** had been produced.

Attempted Reaction of *n*-Bu_2CuLi with Enediones 17 and 18. The cuprate from 2.6 M *n*-BuLi (2.58 mL, 6.70 mmol) and CuBr (0.480 g, 3.35 mmol) was reacted at 0 °C for 30 min with both the *cis*- and the *trans*-enediones **17** and **18** (0.300 g, 2.67 mmol) in ether (50 mL) in separate experiments. After the standard workup examination of the ether-soluble material both by ^1H NMR spectroscopy and by GLC showed no trace of 4-acetyloctan-2-one (**10d**).

The Furans 19 (See Table V). General Method of Cyclization of the Adducts 5 Using BF_3·OEt_2. The adduct **5** was dissolved in $CHCl_3$ and the BF_3·OEt_2 injected into the solution. When cyclization was complete (TLC) aqueous Na_2CO_3 was added and the whole was shaken. Evaporation of the organic layer gave the furan in high purity. Details follow thus: weight, number of moles **5**; volume, number of moles of BF_3·OEt_2; volume of $CHCl_3$; reaction time; weight of furan (yield).

3-(Dicarbethoxymethyl)-2,5-dimethylfuran (19a): 4.30 g, 11.0 mmol; 2.06 mL, 16.3 mmol; 50 mL; 3 h; 2.96 g (99%).

3-Butyl-2,5-dimethylfuran (19d): 0.079 g, 0.27 mmol; 0.42 mL, 3.31 mmol; 0.50 mL ether; 1 h; 0.017 g, estimated by GLC (40%). Unreacted diketone **10d** was observed in the chromatogram at a longer retention time.

3-Phenyl-2,5-dimethylfuran (19e): 0.144 g, 0.47 mmol; 0.09 mL, 0.71 mmol; 20 mL; 30 min; 0.079 g (99%).

3-*p*-Tolyl-2,5-dimethylfuran (19f): 0.443 g, 1.37 mmol; 0.26 mL, 2.05 mmol; 25 mL; 20 min; 0.250 g (98%).

3-(Phenylthio)-2,5-dimethylfuran (19l): 0.086 g of the crystalline diastereomer, mp 100–101 °C, 0.25 mmol; 0.065 mL, 0.502 mmol; 15 mL; 30 min; 0.034 g (66%).

Attempted Formation of Furans 19g,i–k. The dimethylamino (**5g**), methoxy, (**5i**), hydroxy (**5j**), and chloro (**5k**) adducts were also subjected to the BF_3·OEt_2 treatment in solution, typically 1 mmol of each being reacted with 1.5 mmol of the catalyst. There was no evidence of cyclization, the solutions darkening and finally developing complex ^1H NMR spectra.

The Furans 19. Control Reactions Using ^1H NMR Spectroscopy. (i) The Dicarbethoxy Derivative 19a. In separate experiments the diketone **10a** and the adduct **5a** (0.2 mmol in each case) in $CDCl_3$ (0.5 mL) in an NMR tube were treated with BF_3·OEt_2 (38 μL, 0.3 mmol) and monitored immediately in the proton probe of the spectrometer. In each case clean and rapid formation of the furan **19a** was evident.

(ii) The Phenyl Derivative 19e. The experiment was repeated on the same scale using the adduct **5e** in $CDCl_3$ cooled to 0 °C, adding the catalyst, and immediately inserting the tube into the probe which was kept at 0 °C. The spectrum was run at rapid intervals, single pulses being used. The intermediate diketone **10e** reached a maximum in about 50 s and slowly decayed to product, while disappearance of **5e** was complete in about 70 s. Apart from the benzohydroxamic acid derived peaks all others were accounted for by **5e**, **10e**, and **19e** at all times.

In another identical run the solution was quenched with aqueous NH_4Cl when the peaks due to **5e** had disappeared. Workup gave the diketone, confirmed by the identity of its ^1H NMR spectrum, its R_f value, and its GLC retention time with those of an authentic sample.

Hydrolysis of 19a to 2,5-Dimethyl-3-furylacetic Acid (19m). The diester **19a** (1.50 g, 5.9 mmol) was refluxed for 12 h in a MeOH–H_2O solution (3:1, 50 mL) saturated with Na_2CO_3. The solution was then acidified, evaporated to a small volume, and shaken out with ether and water. The yellow oil from the ether layer was redissolved in ether and extracted with aqueous Na_2CO_3. Acidification and ether extraction gave the acid **19m** (0.81 g, 88%), whose NMR spectrum indicated it to be pure but which resisted all efforts to crystallize it from a variety of solvents. Amp of 94–95 °C was reported for this compound:[46] ^1H NMR δ 2.16, 2.20 (2 Me s), 3.30 (CH_2, s), 5.85 (C_4H, s), 11.30 (CO_2H, br).

Alternative Synthesis of 3-Butyl-2,5-dimethylfuran (19d). BF_3·OEt_2 (9.2 mL, 73 mmol) was introduced over 1 min into a mixture of butyric anhydride (13.3 g, 84 mmol) and 2,5-dimethylfuran (7.7 mL, 73 mmol) under N_2. After 45 min of stirring the whole was extracted with ether and aqueous Na_2CO_3 and the ketone purified by distillation, bp 122–123 °C (23 mm) (10.5 g, 87%).

To 3-butyryl-2,5-dimethylfuran (4.22 g, 25.4 mmol) in diethylene glycol (21 mL) containing dissolved KOH (3.7 g, 66 mmol) was added anhydrous hydrazine (1.72 mL, 54 mmol). Heat was applied, gently at first, and then the solution was refluxed for 5.5 h. Distillation of all fractions up to 240 °C, ether–water extraction of these fractions, and fractionation of the ether soluble material gave **19d** as a colorless liquid, bp 180–182 °C (725 mm) (2.33 g, 60%).

Epoxidation of Enone 2a. To a solution of the enone **2a** (0.75 g, 3.2 mmol) in *t*-BuOH (4 mL) and 30% H_2O_2 (1.8 mL, 16 mmol) was added Na_2CO_3 (0.13 g, 1.2 mmol), and the mixture was stirred at 45–47 °C for 2 h. After cooling and the addition of water, the whole was thoroughly extracted with CH_2Cl_2, and the dried organic phase was evaporated. Addition of ether gave an insoluble crystalline product, mp 122.5–123 °C (0.096 g, 12%), considered to be *cis*- or *trans*-5-hydroperoxy-2,5-dimethyl-2,5-dihydro-2-furyl benzohydroxamate (**21**); it gave a positive peroxide test: IR 3230, 3200–3150 (NH, OH), 1610 cm^{-1} (C=O): ^1H NMR δ 1.54, 1.73 (2 Me s) 6.09, 6.18 (2 vinyl H, AB q, J = 5.8 Hz), 7.4–7.6 (3 H, m, meta + para H on Ph), 7.8 (2 H, d, ortho H on Ph), 10.7–(1 H, b), 12.2 (1 H, b); ^{13}C NMR 22.8, 22.9 (2 Me), 94.6 (C_2, C_5), 128.3, 129.3, 132.4, 132.8 (Ph), 200.7 ppm (CO). Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 59.07; H, 5.74; N, 5.27.

The ether soluble material was chromatographed with ether–hexane (1:3) to give the epoxide as a pale yellow oil (0.334 g, 42%) as an approximately equal mixture of the trans diastereomers **23a,b**: ^1H NMR δ 1.75 (2 ring Me s, coincident), 2.08, 2.09 (2 COMe s), 3.46, 3.49 (methine H's, one diastereomer, 2 d, J = 2.1 Hz), 3.59, 3.61 (methine H's, other diastereomer, 2 d, J = 1.9 Hz), 7.39–7.51 (meta + para H on Ph, m), 7.74–7.77 (ortho H on Ph, m); ^{13}C NMR 20.3, 20.8 (epoxide ring Me), 24.5 (2 CO*Me*), 57.8, 57.9 (4 methine C's), 112.2, 112.3 (2 OCO), 122.5, 126.8, 128.8, 131.7 (Ph C_1, C_4, C_3, C_2, single resonances only observed), 158.4, 158.7 (2 C=N), 203.4 ppm (2 C=O); M^+ 247. Anal. Calcd for $C_{13}H_{17}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 62.96; H, 5.35; N, 5.93.

(*Z*)-1-(3-Phenyl-5-ethyl-1,4,2-dioxazol-5-yl)-1-penten-3-one (25). A solution of 2,5-diethylfuran[53] (4.3 g, 34.7 mmol) and benzohydroxamic acid (6.0 g, 43.8 mmol) in ethyl acetate (100 mL) was stirred with PbO_2 (58 g, 242 mmol) for 24 h. The suspension was filtered through a Celite bed and the filtrate evaporated to give crude **25**. Chromatography with ether–hexane (1:3) gave the pure pentenone as a pale yellow oil (4.94 g, 55%): IR 1690 (C=O), 1615 cm^{-1} (C=N); ^1H NMR δ 1.05 (Me, t, J = 7.4 Hz), 1.08 (Me, t, J = 7.2 Hz), 2.19 (ring CH_2, q), 2.54 (COCH_2Me, q), 5.86, 6.18 (vinyl H's, 2 d, J = 12.6 Hz), 7.38–7.49 (meta + para H on Ph, m), 7.74 (ortho H on Ph); ^{13}C NMR 6.9 (Me), 7.5 (Me), 30.9 (ring CH_2), 36.6 (COCH_2), 115.6 (OCO), 123.2, 126.8, 128.6, 131.4 (Ph C_1, C_4, C_3, C_2), 131.4, 132.4 (vinyl C's), 158.1 (C=N), 203.8 ppm (C=O); M^+ 259. Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.46; H, 6.38; N, 5.47.

1-Phenyl-1-(3-phenyl-5-ethyl-1,4,2-dioxazol-5-yl)-3-pentanone (26). The phenyl cuprate was prepared from PhLi (2.83 mL of 2.4 M solution, 6.80 mmol) and CuBr (0.488 g, 3.40 mmol), the enone **25** was added (0.705 g, 2.72 mmol), and the whole was stirred for 7 h. Following the usual workup the crude product was chromatographed with 3% ether in hexane to give the β-phenyl ketone **26** as an oil (0.788 g, 86%): IR 1710 (C=O), 1620 cm^{-1} (C=N); ^1H NMR (400 MHz) δ 0.88 (Me, t), 0.90 (Me, t), 1.71 (ring CH_2, m), 2.25 (COCH_2Me, m), 2.91 (C_2H, dd, J = 9.4, 16.7 Hz), 3.09 (C_2H, dd, J = 4.2, 16.7 Hz), 3.81 (C_1H, J = 4.2, 9.4 Hz), 7.16–7.50 (C_1Ph, meta + para H on Ph, 8 H), 7.81 (ortho H on Ph); ^{13}C NMR 6.5 (Me), 7.6 (Me), 29.5 (ring CH_2), 36.5 (C_4), 42.6 (C_2), 47.9 (C_1), 115.5 (OCO), 123.2, 126.6, 128.7, 131.4 (ring Ph C_1, C_4, C_3, C_2), 128.5, 129.2, 127.4, 139.0 (C_1 Ph C's), 158.7 (C=N), 208.5 ppm (C=O); M^+ 337. Anal. Calcd for $C_{22}H_{25}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.80; H, 6.88; N, 4.35.

4-Phenyl-3,6-octanedione (27). The adduct **26** (0.195 g, 0.58 mmol) was refluxed for 40 h in 1:1 aqueous EtOH (16 mL). Evaporation of the alcohol followed by extraction with ether and aqueous Na_2CO_3 gave the diketone **27** as an oil (0.119 g, 94%): IR 1703 cm^{-1} (C=O); ^1H NMR δ 0.97 (Me, t, J = 7.2 Hz), 1.03 (Me, t, J = 7.3 Hz), 2.25–2.70 (C_2 and C_5 methylene, 4 H, m), 3.26, 3.39, 3.48, 3.61 (C_5 methylene, 2 H, AB or ABX), 4.24 (C_4H, X of ABX, J_{AX} + J_{BX} = 14.1 Hz), 7.25–7.70 (Ph).

3-Phenyl-2,5-diethylfuran (28). (i) From 26. The phenyl adduct **26** (0.142 g, 0.42 mmol) in $CHCl_3$ (0.5 mL) was treated with BF_3·OEt_2 (0.16 mL, 1.26 mmol) and after 30 min the whole was shaken out with ether and aqueous Na_2CO_3. The ether layer gave the furan as an oil (0.083 g, 76%).

(ii) From 27. The diketone **27** (0.229 g, 1.05 mmol) was treated in exactly the same way by using the proportions of catalyst and solvent described in i to give the furan **28** (0.166 g, 79%): ^1H NMR δ 1.26 (Me, t, J = 7.5 Hz), 1.28 (Me, t, J = 7.5 Hz), 2.65 (CH_2, q, J = 7.5 Hz), 2.77 (CH_2, q, J = 7.5 Hz), 6.10 (C_4H, s), 7.24–7.40 (Ph); M^+ 200. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.20. Found: C, 83.74; H, 8.17.

1-(*O*-Benzoyloximino)-2-penten-4-one (32). 2-Methylfuran[59] (1.6 mL, 14.6 mmol) and benzohydroxamic acid (2.0 g, 14.6 mmol) in ethyl acetate (40 mL) were stirred for 14 h with PbO_2 (27.8 g, 116 mmol). Filtration and evaporatin gave a dark brown oil. The product from a total of three such runs was treated with cold ether, which gave pale yellow crystals (2.16 g) considered to be dibenzamide. The soluble fraction was crude product (2.57 g, 27%). It was dissolved in ether and hexane was added until the cloudiness just appeared. The solution on keeping for 12 h at 0 °C gave the pale yellow crystalline oxime ester **32**, mp 73–75 °C, which was evidently a single diastereomer: IR 1750 (ester CO), 1685 cm^{-1} (ketone CO); ^1H NMR (the couplings here were confirmed by 2D ^1H NMR spectroscopy) δ 2.33 (Me, s), 6.62 (C_3H,

(59) From the Huang-Minlon reduction of furfural.

d, J = 11.6 Hz), 6.73 (C_2H, d of d, J = 10.1, 11.6 Hz), 7.26-8.12 (Ph), 9.35 (C_1H, d of d, J = 0.8, 10.1 Hz); ^{13}C NMR 31.6 (Me), 128.7, 130.0 (Ph C), 132.6, 133.7 (Ph C, C_2 and C_3, overlapping), 154.3 (C=N), 163.7 (ester CO), 198.1 ppm (keto CO); EIMS gave no parent ion, but CIMS gave $(M + 1)^+$ at 218. Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10, N, 6.45. Found: C, 66.31; H, 5.23; N, 6.69.

When attempts were made to purify the ester **32** on a silica column a low yield of it was eluted. It was followed by the more polar hydrolysis product, the oxime **33** (see below). When a basic alumina column was used cleavage to **33** was complete, no **32** being eluted.

The oxime **33** from the column (0.033 g, 0.29 mmol) was dissolved in $CDCl_3$ (0.5 mL) in an NMR tube, and pyridine (0.24 mL, 0.29 mmol) and benzoyl chloride (0.041 g, 0.29 mmol) were added. The ^1H spectrum, run within 30 s, showed the reaction to be already complete. The solution was worked up with ether and aqueous $NaHCO_3$, the ethereal solution giving the ester **32** identical with the material from the benzohydroxamic acid oxidation.

Synthesis of 1-Oximino-2-penten-4-one (33). To a solution of NaOH (0.094 g, 2.35 mmol) and hydroxylamine hydrochloride (0.18 g, 2.57 mmol) in water (3 mL) was added *cis*-1-oxo-2-penten-4-one[54] (0.230 g, 2.34 mmol). After being stirred for 5 min, the solution was saturated with NaCl and extracted with methylene chloride, giving the product (0.054 g, 11%) as an oil from the organic phase: ^1H NMR δ 2.33 (Me, s), 6.25-6.70 (C_2H, C_3H, m), 8.85 (C_1H, m), 10.1 (OH, br s).

When the oxime was benzoylated with benzoyl chloride and pyridine and the mixture worked up, all as described above, the benzoate was identical with the product of the benzohydroxamic acid oxidation.

X-ray Analysis of 5f. Crystals of **5f**, $C_{20}H_{21}NO_3$, M_r 323.40, are triclinic, space group $P\bar{1}$ with a = 6.101 (1) Å, b = 10.652 (1) Å, c = 14.552 (2) Å, α = 106.69 (1)°, β = 101.22 (1)°, γ = 100.20 (1)°, V = 860.8 (2) Å^3, Z = 2, ρ_c = 1.248 g cm^{-3}, $F(000)$ = 344, λ = 0.71069 Å, μ (Mo Kα) = 0.905 cm^{-1}. Intensity data were collected on a crystal of dimensions ≈0.4 mm^3 by using θ-2θ scans (3.2° < 2θ ≤ 45°) with a variable scan speed of 2.93-29.30° min^{-1} and a scan width of 0.95° below Kα_1, to 0.95° above Kα_2 on a Syntex $P2_1$ diffractometer. From a total of 2273 independent reflections measured, 1874 had intensities $I \leq 3\sigma(I)$ and were used in the structure refinement. Two standard reflections (128, 050), monitored after every 100 measurements, showed only minor fluctuations. The data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods (MULTAN80) and refined by full-matrix least-squares methods. After two cycles of anisotropic refinement, all hydrogen atoms were located from a difference Fourier synthesis. The final R and R_w values were 0.031 and 0.034, respectively ($R = \sum||F_o| - |F_c||/\sum|F_o|$, $R_w = [\sum_w||F_o| - |F_c||^2/\sum_w|F_o|^2]^{1/2}$). An empirical weighting scheme of the form $w^{-1} = 2.94 - 0.078|F_o| + 0.007|F_o|^2$ was employed in the final cycles to give constant error in the various ranges of F_{obsd}. A final difference map was featureless with maximum residuals of 0.14 e Å^{-3}. Scattering factors were taken from the "International Tables for X-ray Crystallography",[60] and for hydrogen, the data of Stewart et al.[61] were used. Computer programs used have been described elsewhere.[62] Bond lengths and angles of **5f** are shown in Table III.

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Registry No. (±)-**2b**, 100909-74-8; (±)-**2b**, 100910-05-2; (±)-**5a** (isomer 1), 100909-75-9; (±)-**5a** (isomer 2), 100910-06-3; **5b**, 100909-76-0; (±)-**5c** (isomer 1), 100909-77-1; (±)-**5c** (isomer 2), 100910-07-4; (±)-**5d** (isomer 1), 100909-78-2; (±)-**5d** (isomer 2), 100910-08-5; (±)-**5e** (isomer 1), 100909-79-3; (±)-**5e** (isomer 2), 100910-09-6; (±)-**5f**, 100909-80-6; (±)-**5g** (isomer 1), 100927-99-9; (±)-**5g** (isomer 2), 100910-10-9; (±)-**5i** (isomer 1), 100909-81-7; (±)-**5i** (isomer 2), 100910-11-0; (±)-**5j** (isomer 1), 100909-82-8; (±)-**5j** (isomer 2), 100910-12-1; (±)-**5k** (isomer 1), 100909-83-9; (±)-**5k** (isomer 2), 100910-13-2; (±)-**5l** (isomer 1), 100909-84-0; (±)-**5l** (isomer 2), 100910-14-3; **8**, 100909-85-1; (±)-**10a**, 100909-86-2; (±)-**10d**, 100909-87-3; (±)-**10e**, 100910-15-4; (±)-**10l**, 100909-88-4; (±)-**10g**, 100909-89-5; (±)-**10i**, 100909-90-8; (±)-**10j**, 66296-80-8; **17**, 17559-81-8; **18**, 820-69-9; **19a**, 100909-91-9; **19d**, 100909-92-0; **19e**, 19842-57-0; **19f**, 100909-93-1; **19l**, 100909-94-2; **19m**, 100909-95-3; (±)-**21** (isomer 1), 100909-96-4; (±)-**21** (isomer 2), 100909-97-5; (±)-**23a**, 100909-98-6; (±)-**23b**, 100992-07-2; (±)**25**, 100909-99-7; **26**, 100910-00-7; (±)-**27**, 100910-01-8; **28**, 100910-02-9; **32**, 100910-03-0; **33**, 100910-04-1; butyric anhydride, 106-31-0; 3-butyryl-2,5-dimethylfuran, 82873-11-8; *cis*-1-oxo-2-penten-4-one, 34218-22-9; diethyl malonate, 105-53-3; ethyl cyanoacetate, 105-56-6; *p*-bromotoluene, 106-38-7; 2,5-dimethylfuran, 625-86-5; 2,5-diethylfuran, 10504-06-0; benzohydroxamic acid, 495-18-1; 2-methylfuran, 534-22-5.

Supplementary Material Available: Tables of atomic coordinates and isotropic thermal parameters for non-hydrogen and hydrogen atoms, anisotropic thermal parameters, and structure factors (14 pages). Ordering information is given on any current masthead page.

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Low Valent Titanium Induced Cross-Coupling of Chiral α,β-Unsaturated Ketones with Acetone[1]

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The cross-coupling of chiral (*R*)-(−)-(4-methylcyclohexylidene)acetone and (*R*)-(−)-(4-methylcyclohexylidene)acetophenone with acetone, on a Ti(0) surface, leads, inter alia, to the corresponding chiral (*R*)-(−)-(4-methylcyclohexylidene)-2-substituted-3-methyl-2-butene. By contrast, due to steric acceleration, chiral (*S*)-(+)-(2,2,4,6,6-pentamethylcyclohexylidene)acetone, (*S*)-(+)-(4-(dimethyl-*tert*-butylsiloxy)-2,2,6,6-tetramethylcyclohexylidene)acetone, and (*S*)-(+)-(4-(dimethyl-*tert*-butylsiloxy)-2,2,6,6-tetramethylcyclohexylidene)acetophenone yield only achiral cross-coupled products with acetone on a Ti(0) surface.

Ti(0) surfaces have been prepared by reduction of $TiCl_3$ or $TiCl_4$ with metals[2-7] such as magnesium, zinc, zinc-copper couple, alkali metals (Li, Na, K), and metal hydrides ($LiAlH_4$). The surfaces have been used in the pi-

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