Synthesis of Butenolides from α-(Phenylthio)-ketones and -esters: Crystal Structure of an Intermediate β-Phenylthio-γ-lactone [1]

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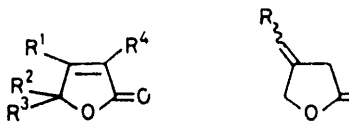
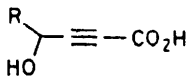
Alkylation of α-(phenylthio)-ketones or -esters with iodoacetate anion gives 1,4-dicarbonyl compounds which are reduced stereoselectively to β-phenylthio-γ-butyrolactones. Oxidation to sulphoxides and thermolysis provides a general synthesis of β- and γ-substituted $\Delta^{\alpha\beta}$-butenolides. Treatment of 5,5-dimethyl-4-oxo-3-(phenylthio)-hexanoic acid with $NaBH_4$ gives a single γ-lactone whose PhS and Bu^t groups are shown to be *cis* by an *X*-ray crystal structure determination.

Δ^2-Butenolides [furan-2(5*H*)-ones] (1) occur as natural products,[2,3] and are versatile synthetic intermediates, since *e.g.* they react readily as Michael acceptors [4] and can be reduced to furans.[5,6] There is a variety of methods available for preparing butenolides, including oxidation of furans,[7] isomerisation of ylidene-γ-butyrolactones (2),[8] partial reduction of maleic anhydrides,[9] and partial hydrogenation of the acids (3).[4,10] Recently some interesting syntheses based on carbonylation reactions (CO + zero-valent transition metal) have been reported.[11]

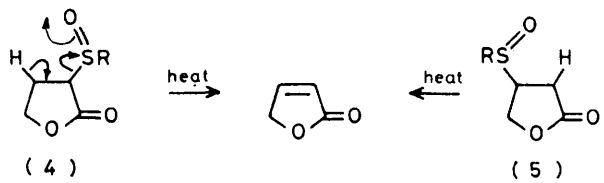


(1) (2)



(3)

A number of useful butenolide syntheses are based on organosulphur chemistry. These all have as their final step the thermal *syn*-elimination of an alkylsulphenic acid [12] from an alkylsulphinyl-substituted γ-lactone, and can be divided into those in which the sulphur substituent is α to carbonyl (4), and those in which it is β (5). The first route has the advantage that the sulphur substituent can be introduced by direct sulphenylation (followed by oxidation).[13,14] It can be made connective at both the α- and β-positions by alkylation (Scheme 1).[15,16] The most general version, involving the alkylation of dianions (6) with epoxides,[15] has recently been employed in a synthesis of the antibiotic lepiochlorin (7).[17] The main disadvantage of the α-alkylsulphinyl-γ-lactone route is that if an α-alkyl substituent is present, elimination can also occur into this side-chain to give an α-ylidene lactone [*e.g.* equation (1) [13]].



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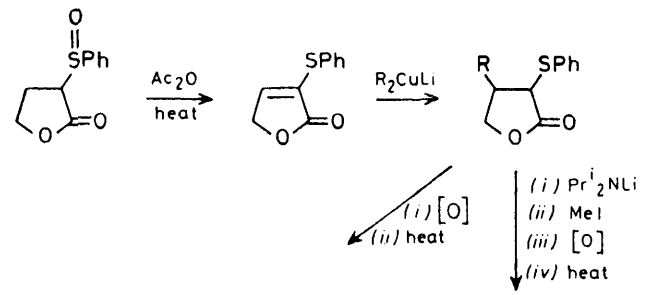
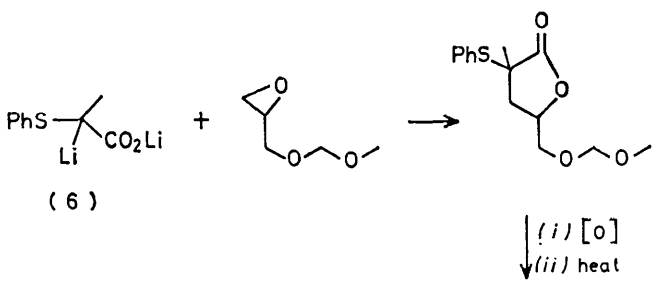
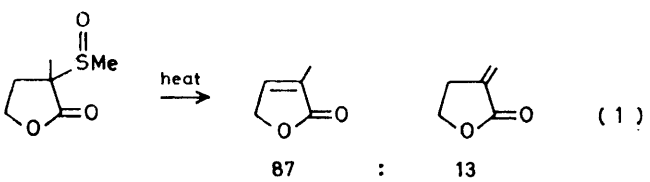


Scheme 1



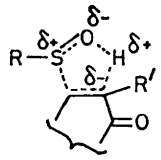
(6) (7)



87 : 13 (1)

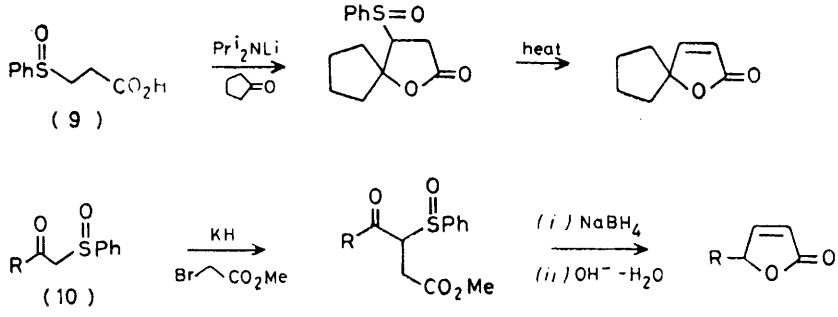
Thermal elimination of sulphenic acids from β-alkylsulphinyl carbonyl compounds is completely regio-

selective and occurs at a low temperature because of the acidity of the α-protons (8).[1,18-22] This reaction forms the basis of several attractive new syntheses of αβ-unsaturated carbonyl compounds in general,[19] and of a

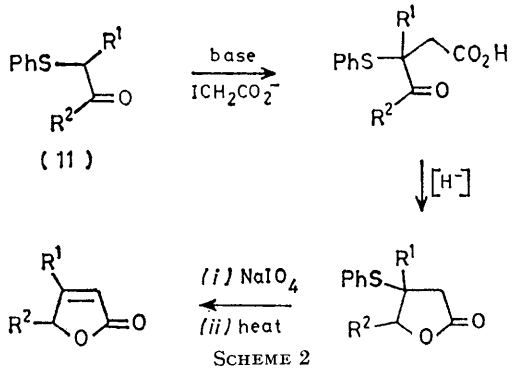


(8)

method for the α-hydroxylation of butenolides.[20] It was also used in butenolide synthesis by Uda and co-workers [21] [starting from (9), a synthetic equivalent of $^{-}CH{=}CHCO_2H$], and Bartlett [22] who employed (10) as a



specific enolate equivalent (for $RCOCH_2^{-}$). We have recently reported briefly [1] on the use of α-(phenylthio)-ketones as specific enolate equivalents for $R^2COC^{-}HR^1$ in the preparation of 1,4-dicarbonyl compounds and now present our full results on butenolide synthesis according to the strategy outlined in Scheme 2.



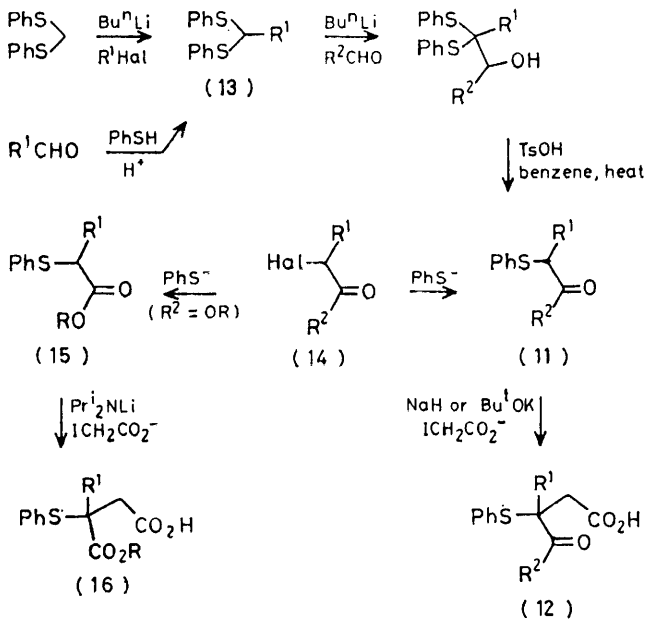
SCHEME 2

RESULTS AND DISCUSSION

Alkylation of α-(Phenylthio)-ketones and -esters with Sodium Iodoacetate.—α-(Phenylthio)ketones are specific enolate equivalents,[23] because enolate anions are formed from them, and alkylation occurs, preferentially on the phenylthio (PhS) side [*e.g.* (11) ⟶ (12)].[24,25] It is clearly a requirement that compounds (11) themselves must be available regiochemically pure, as they are by our regiospecific synthesis from bis(phenylthio)acetals (13).[26] Alternatively, α-halogenoketones (14), if available, can be treated with sodium thiophenoxide;[27] this latter is also the simplest route to α-(phenylthio)esters (15).

Our initial attempts to react the anions of α-(phenylthio)ketones with methyl iodoacetate gave only moderate yields of adducts (see Table 1), possibly because of transmetallation or radical reactions; however, the use of sodium iodoacetate (ICH_2CO_2Na) as the alkylating agent gave much better results. The enolates of α-(phenylthio)ketones (11) were generated by sodium hydride (NaH) in dry tetrahydrofuran (THF) at room temperature [24] and treated with 1 equiv. of a suspension of ICH_2CO_2Na in THF to give the γ-keto-acids (12) in high yield, along with a little recovered (11). Potassium t-butoxide was also used as the base (in THF at 0 °C), but this resulted in the recovery of larger amounts of (11) (Table 1).

Metallation of α-(phenylthio)esters (15) with NaH requires dimethylformamide as co-solvent;[28] the sodium enolates thus formed did not react with ICH_2CO_2Na.



Changing the enolate counter ion to lithium (Pr^i_2NLi, THF, 0 °C) proved successful, although considerable amounts of (15) were recovered in addition to the succinic half-esters (16) (Table 1). We also investigated

TABLE 1

Formation of butenolides from α-(phenylthio)-ketones and -esters

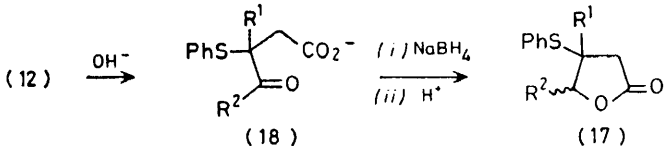
Compound	R^1	R^2	R^3	Ion [d]	Products: Acid (12) [a,b]	Butanolide (17) [a,c]	Butenolide (25) [a]
					(12)	(17)	(25)
(11a)	Me	Me		Na	81 (85)	99 (3 : 2)	77
				K	58 (89)		
(11b)	H	Me		Na	74 (82)	98 (3 : 1)	83
				Na [e]	40 (48)		
(11c)	H	Bu^t		K	54 (91)	98 (1 : 0)	75
(11d)	H	Ph		K	38 (77)		
(11e)	Me	Ph		K	15 (52)	84 (4 : 1)	70
(11f)	Et	Me		Na [e]	52 (60)	98 (3 : 2) [f]	78
						(23)	
(11g)	H	Me	Me			90	81
(11h)	Me	Me	Pr			52	78

	R^1	R	Products: Half-ester (16)	Butanolide (22)	Butenolide (25)
(15j)	H	Me	41 (80)	58	
(15k)	Pr^i	Me	51 (89)	62	77
(15l)	Me	Et	60 (76)	63	81
(15m)	Et	Et	44 (88)	90	81

[a] Isolated yields (%). [b] Values in parentheses refer to yields based on recovered (11) or (15). [c] Diastereoisomer ratio in parentheses. [d] Enolate counterion of (11). [e] By alkylation (NaH–THF) of (11) with ICH_2CO_2Me. Product is (12) methyl ester. [f] Using $Zn[BH_4]_2$ in Et_2O.

alkylation of the aldehyde (11; R^1 = Et, R^2 = H) with ICH_2CO_2Na (NaH, THF). This reaction gave (12; R^1 = Et, R^2 = H) as part of a mixture which was not separated but reduced with sodium borohydride to give the γ-lactone (22m) in only 26% overall yield.

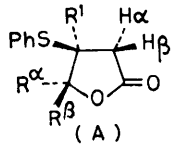
Reduction of the γ-Dicarbonyl Compounds (12) *and* (16) *to the γ-Lactones* (17), (22), *and* (23).—On treatment with sodium borohydride in alkaline aqueous ethanol, the γ-keto-acids (12) underwent reduction at the ketone group, and acidic work-up gave the β-phenylthio-γ-lactones (17) in very good yields (Table 1). Unequal mixtures of diastereoisomers of (17) resulted in all cases except when R^2 was t-butyl, the lactone (17c) being a single isomer (98% yield). *X*-Ray crystallographic analysis shows that this isomer has the PhS and t-butyl groups *cis* (see below).



We were able to assign the diastereoisomeric pairs of some of the other lactones (17) by consideration of the shifts (Δδ) on changing the n.m.r. solvent from $CDCl_3$ to C_6D_6 (Table 2). For (17c) the Δδ values for protons on the side of the ring *trans* to the PhS and t-butyl groups are almost twice as high as for that *cis* to these two groups and for the t-butyl group itself. This indicates that the side of the ring *trans* to these two large groups is the more highly solvated, as might be expected. This pattern is followed for the major diastereoisomer of (17b), although the Δδ values are somewhat smaller, and

TABLE 2

Solvent shift values (Δδ) for the lactones (17)



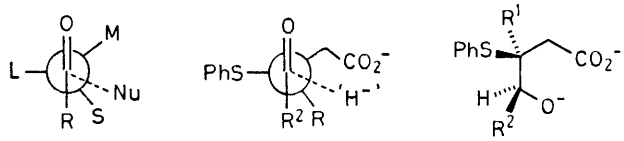
(A)

Compound	R^1	Rα	Rβ	a	Δδ [= $\delta_{CDCl_3} - \delta_{C_6D_6}$] R^1	Rα	Hα	Rβ	Hβ
(17c)	H	H	t-Bu	100	1.24	1.18	1.19	0.73	0.78
(17b)	H	H	Me	75	0.73	0.68	0.61	0.36	0.32
	H	Me	H	25	0.48	0.40	0.44	0.37	0.31
(17a)	Me	H	Me	60	0.51	0.61	0.58	0.31	0.31
	Me	Me	H	40	not measured				

[a] Proportion of diastereoisomer obtained (%).

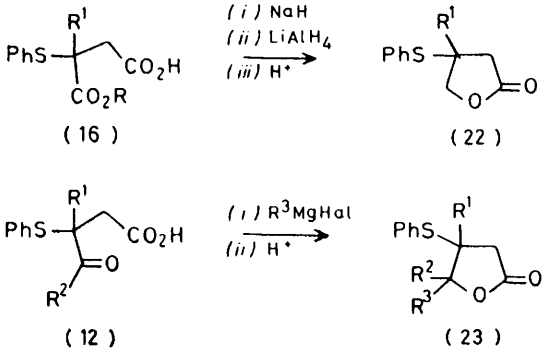
thus we have assigned this as the *cis*-isomer. In the minor diastereoisomer [*trans*-(17b)], the Δδ values are almost constant, indicating a more equal solvation of the sides of the ring. For (17a) it was only possible to achieve a partial separation of the major diastereoisomer by chromatography; the Δδ values for this follow those for the major diastereoisomer of (17b), and we therefore tentatively assign it as the *cis*-isomer.

The high stereoselectivity shown in the reduction of (12) to (17) is somewhat surprising, since the PhS and $CH_2CO_2^-$ groups of (18) might seem to be similar in size. We believe that the best explanation of these results is given by Felkin's [29] model of asymmetric induction in additions to ketones, as refined by the theoretical work of Anh and Eisenstein.[30] According to these workers, the preferred transition state is (19). Felkin *et al.* noted [29] that polar substituents on the α-carbon had a greater preference for position L, *anti* to the incoming nucleophile, than would be expected from the actual



steric bulk; this phenomenon was interpreted by Anh and Eisenstein in frontier-orbital [30] terms, with the 'largest' substituent being that with the lowest energy σ* (C_α-substituent) orbital. In our compounds (18), the lowest σ* orbital is clearly that of C_α–SPh, and we can thus assign [in (19)] L = SPh, M = $CH_2CO_2^-$ and S = R^1, giving a preferred transition state (20) which leads to the *cis*-products (21). In accordance with Felkin's model, the stereoselectivity increases with increasing size of R^2 (from 75 : 25 for R^2 = Me to 100 : 0 for R^2 = Bu^t when R^1 = H, and from 60 : 40 for R^2 = Me to 80 : 20 for R^2 = Ph when R^1 = Me), but decreases when R^1 is enlarged from H to Me or Et (75 : 25 to 60 : 40 for R^2 = Me) because of the increased *gauche* interaction between R^1 and the nucleophile in conformation (20). We have observed similar stereoselectivities in the reduction of α-(diphenylphosphinoyl)ketones.[32]

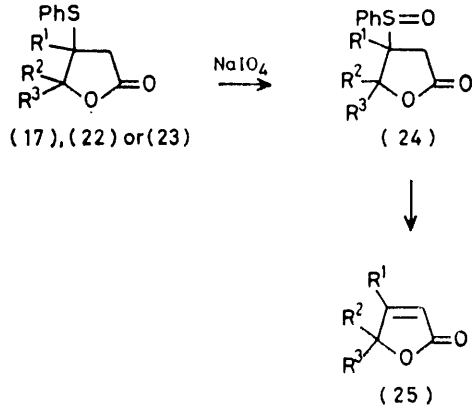
The succinic half-esters (16) were reduced (as their sodium salts) with lithium aluminium hydride in THF to give the γ-lactones (22). It was also possible to obtain 5,5-dialkyldihydrofuranones (23) by treatment of (12)



(16) (22) (12) (23)

with Grignard reagents. With (12; R^1 = H, R^2 = Me) and MeMgI, this reaction gave a 90% yield of lactone, but in a more sterically demanding case [(12; R^1 = R^2 = Me) and PrMgBr] some attack at sulphur occurred, the lactone being produced in 52% yield along with some phenyl propyl sulphide.

Conversion of β-Phenylthio-γ-lactones to Butenolides.—The final stage of our butenolide synthesis was achieved



(17), (22) or (23) (24) (25)

simply by periodate oxidation [33] of the β-phenylthio-γ-lactones to the corresponding sulphoxides (24), and thermolysis of these to give butenolides (25) by *syn*-elimination of phenylsulphenic acid. Indeed, when the lactone had a substituent at the β-position (24; $R^1 \neq$ H), elimination occurred spontaneously in the oxidation reaction mixture and butenolides (25; $R^1 \neq$ H) were isolated directly. The sulphoxides (24b) and (24g) were briefly refluxed in toluene to cause elimination. In all cases the elimination of phenylsulphenic acid occurred regiospecifically towards the carbonyl group and the butenolides were obtained in 70—83% yields after preparative layer chromatography.

Thus we have shown that α-(phenylthio)-ketones and -esters can be converted into butenolides (25) *via* β-phenylthio-γ-lactones [(17), (22), or (23)]; we have also found that these latter compounds can be converted into γ-(phenylthio)acrylic esters; [1] this and related reactions will be described separately.

Crystal Structure Determination of (4R*,5R*)-4,5-*Dihydro-4-(phenylthio)-5-t-butylfuran-2-(3H)-one* (17c).—*Crystal data.* $C_{14}H_{18}O_2S$, M = 250.4. Orthorhombic, space group $P2_12_12_1$, a = 11.122(2), b = 12.366(2), c = 10.072(2) Å, U = 1 385.3(3) Å^3, Z = 4, D_c = 1.200 g cm^{-3}, μ = 18.7 cm^{-1}.

Data collection. Intensities were collected on a Syntex $P2_1$ four-circle diffractometer equipped with a graphite monochromator using Ni-filtered Cu-K_α radiation (λ = 1.5418 Å). 1 372 Symmetry-independent reflexions with $2\theta \leqslant 130°$ were measured in the θ—2θ scan mode. The raw data were corrected for background and for Lorentz and polarisation factors, but not for absorption. 1 274 Reflexions had $|F| > 3\sigma_F$ and were treated as observed.

Structure solution and refinement. The structure was solved with SHELX-76. Starting with the position of the sulphur atom obtained with Patterson techniques, three successive Fourier maps yielded all the non-hydrogen atoms. Isotropic refinement with unit weights reduced R to 0.120, which dropped to 0.091 with anisotropic temperature factors. At this stage most of the hydrogen atoms were located by a difference electron-density map. Weights $w = (\sigma_F^2 + 0.0005F^2)^{-1}$ were introduced and further refinement with fixed hydrogen

TABLE 3

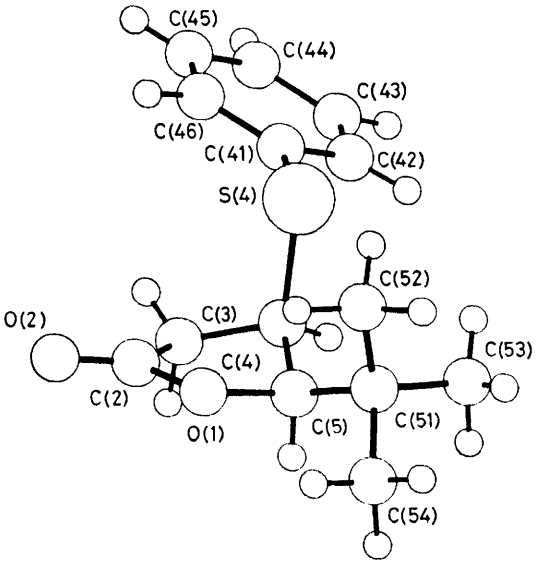
Atomic co-ordinates (× 10^4) *

	x/a	*y/b*	*z/c*
O(1)	3 139(2)	6 420(2)	1 496(3)
C(2)	3 992(3)	5 639(3)	1 433(4)
O(2)	4 846(3)	5 660(3)	2 148(3)
C(3)	3 663(3)	4 841(3)	381(4)
C(4)	2 312(3)	4 991(3)	245(3)
S(4)	1 531(1)	4 131(1)	1 441(1)
C(41)	1 861(3)	2 846(3)	724(4)
C(42)	1 295(3)	2 532(3)	−439(4)
C(43)	1 527(4)	1 540(3)	−982(4)
C(44)	2 320(5)	842(4)	−362(6)
C(45)	2 864(5)	1 139(4)	794(6)
C(46)	2 648(4)	2 149(3)	1 327(5)
C(5)	2 221(3)	6 211(3)	501(4)
C(51)	1 055(4)	6 785(3)	885(4)
C(52)	667(5)	6 540(5)	2 307(6)
C(53)	104(5)	6 442(5)	−147(7)
C(54)	1 289(6)	7 999(4)	764(6)
H(3)	3 950(32)	4 123(33)	584(36)
H′(3)	4 139(31)	5 143(29)	−374(35)
H(4)	1 992(29)	4 778(26)	−692(36)
H(42)	710(33)	3 015(30)	−817(34)
H(43)	1 101(38)	1 369(32)	−1 770(44)
H(44)	2 503(42)	285(32)	−612(52)
H(45)	3 398(41)	683(37)	1 221(44)
H(46)	3 141(37)	2 336(32)	2 047(40)
H(5)	2 579(32)	6 596(27)	−239(35)
H(52)	1 369(43)	6 671(35)	2 913(41)
H′(52)	416(37)	5 754(37)	2 379(44)
H″(52)	−120(45)	6 918(35)	2 348(41)
H(53)	−128(43)	5 669(38)	−39(42)
H′(53)	−418(46)	6 817(42)	19(47)
H″(53)	429(43)	6 736(41)	−993(41)
H(54)	566(40)	8 393(37)	1 053(38)
H′(54)	1 878(39)	8 222(34)	1 451(44)
H″(54)	1 643(39)	8 213(34)	−298(43)

* Hydrogen atoms are given the same numbers as the carbon atoms to which they are bound; several hydrogen atoms attached to the same carbon atom are distinguished by means of primes and double primes.

temperature factors gave the positions of the remaining H atoms and finally converged at an R^1 of 0.044. None of the positional parameters (Table 3) shifted more than 0.1σ in the last cycle. Observed and calculated structure factors and anisotropic thermal parameters are deposited as Supplementary Publication No. SUP 23117 (10 pp.).*

Description of the structure. A picture of the molecule is shown in the Figure. Bond lengths (Table 4) and bond



Molecular structure of the lactone (17c)

angles (Table 5) within the lactone ring compare well with similar structures.[34] The two substituents at C(4) and C(5) are *cis* with respect to each other. The five-membered ring possesses an 'envelope' conformation with O(1), C(2), C(3), and C(5) in the plane ($\sigma = 0.004$ Å) and C(4) 0.58 Å above it. The C(4)–S(4) bond is nearly

TABLE 4

Bond lengths (Å)

O(1)–C(2)	1.355(5)	C(41)–C(46)	1.370(6)
O(1)–C(5)	1.454(5)	C(42)–C(43)	1.368(7)
C(2)–O(2)	1.192(5)	C(43)–C(44)	1.383(8)
C(2)–C(3)	1.494(6)	C(44)–C(45)	1.363(8)
C(3)–C(4)	1.519(7)	C(45)–C(46)	1.381(7)
C(4)–S(4)	1.827(5)	C(5)–C(51)	1.528(7)
C(4)–C(5)	1.533(7)	C(51)–C(52)	1.526(8)
S(4)–C(41)	1.784(6)	C(51)–C(53)	1.542(9)
C(41)–C(42)	1.385(6)	C(51)–C(54)	1.528(8)

perpendicular to the 'envelope' and *trans*-diaxial to C(5)–H(5). This conformation is also found with other 4,5-disubstituted γ-lactone rings [34,35] and it seems that for electronic reasons C(4) enjoys the most freedom to move out of the ring plane. The phenyl ring ($\sigma = 0.007$ Å) forms an angle of 18° with the lactone 'envelope'. The six substituents at C(5)–C(51) and the nine hydrogen atoms of the t-butyl group assume the preferred staggered arrangement. Although the phenyl ring and the methyl group closest to it [C(52)] are pointing away from each other, the steric interaction between the two bulky substituents causes the bond angles C(4)–C(5)–C(51) and C(5)–C(4)–S(4) to be rather large for sp^3 carbon atoms.

* For details see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1980, Index issue.

TABLE 5

Bond angles (°)

C(2)–O(1)–C(5)	109.4(4)	C(42)–C(43)–C(44)	120.0(5)
O(1)–C(2)–O(2)	121.0(4)	C(43)–C(44)–C(45)	120.1(5)
O(1)–C(2)–C(3)	109.4(4)	C(44)–C(45)–C(46)	119.9(5)
O(2)–C(2)–C(3)	129.6(5)	C(41)–C(46)–C(45)	120.5(5)
C(2)–C(3)–C(4)	103.0(4)	O(1)–C(5)–C(4)	104.1(4)
C(3)–C(4)–S(4)	109.9(4)	O(1)–C(5)–C(51)	109.8(4)
C(3)–C(4)–C(5)	99.8(4)	C(4)–C(5)–C(51)	123.8(4)
S(4)–C(4)–C(5)	115.5(4)	C(5)–C(51)–C(52)	112.6(4)
C(4)–S(4)–C(41)	98.8(3)	C(5)–C(51)–C(53)	106.4(5)
S(4)–C(41)–C(42)	119.9(4)	C(52)–C(51)–C(53)	112.6(6)
S(4)–C(41)–C(46)	120.8(4)	C(5)–C(51)–C(54)	107.0(5)
C(42)–C(41)–C(46)	119.3(5)	C(52)–C(51)–C(54)	108.5(5)
C(41)–C(42)–C(43)	120.2(5)	C(53)–C(51)–C(54)	109.5(5)

EXPERIMENTAL

I.r. spectra were taken on a Perkin-Elmer 257 or 297, n.m.r. spectra on a Varian HA100D, EM390, EM360A, or a Hitachi Perkin-Elmer R24A, mass spectra on an A.E.I. MS30, and high-resolution mass spectra on an A.E.I. MS902 or MS30 machine. N.m.r. peaks marked with an asterisk are due to diastereotopic groups of protons. Melting and boiling points are uncorrected. T.l.c. was run on silica gel GF254, using the following eluting systems: (A) acetone (30%)–light petroleum (b.p. 60—80 °C); (B) ether (20%)–light petroleum (b.p. 30—40 °C); (C) ether (50%)–light petroleum (b.p. 30—40 °C); (D) acetic acid (1%)–ether. Sodium iodoacetate was prepared as a suspension in dry THF by the reaction of iodoacetic acid with a slight excess of petrol-washed sodium hydride. Potassium iodoacetate was prepared similarly using potassium t-butoxide.

3-Methyl-4-oxo-3-(phenylthio)pentanoic Acid (12a) *by the Sodium Hydride method.*—3-(Phenylthio)butan-2-one (11a) [36] (2.65 g) was added dropwise under nitrogen to petrol-washed sodium hydride (0.42 g) in dry THF (70 ml), followed after 1 h by a slight excess of sodium iodoacetate in dry THF (20 ml). The mixture was stirred at room temperature for 4 h, water added, the THF layer separated, and the basic aqueous layer extracted with chloroform (2 × 30 ml). The combined organic fractions were dried (Na_2SO_4) and evaporated to give recovered (11a) (0.15 g). The aqueous layer from the reaction was acidified with hydrochloric acid and extracted with chloroform (3 × 20 ml), and the extracts dried (Na_2SO_4) and evaporated to give an orange solid which was recrystallised from carbon tetrachloride to give microscopic colourless needles of the *keto-acid* [2.83 g, 81%, 85% based on recovered (11a)], m.p. 105—106 °C, R_F(D) 0.72; $\nu_{max.}$ (CH_3CN) 3 700—2 800 (CO_2H), 1 737 (acid C=O), and 1 703 cm^{-1} (ketone C=O); δ (CD_3CN) 8.8 (1 H, v br, CO_2H), 7.38 (5 H, s, Ph), 2.87 and 2.65 (2 H, AB q, J_{AB} 17 Hz, CH^*_2CO), 2.31 (3 H, s, COMe), and 1.55 (3 H, s, MeCS); *m/e* 238 (M^+, 14%), 195 (100), 177 (36), 149 (57), 110 (27), and 109 (25) (Found: C, 60.5; H, 5.8; S, 13.1. $C_{12}H_{14}O_3S$ requires C, 60.5; H, 5.9; S, 13.5%). Similarly prepared was *4-oxo-3-(phenylthio)pentanoic acid* (12b) from (phenylthio)acetone (11b) [27] in 74% yield [82% based on recovered (11b)], m.p. 140.5—141 °C, R_F(D) 0.70; $\nu_{max.}$ (CH_3CN) 3 680—2 740 (CO_2H), 1 736 (acid C=O), and 1 712 cm^{-1} (ketone C=O); δ (CD_3CN) 7.3—7.6 (5 H, m, Ph), 4.06 (1 H, dd, J 6.5 Hz, SC*H*CH^*_2), 2.70 and 2.76 (2 H, ABX system,

J_{AB} 17, J_{AX} 6.5, J_{BX} 8.5 Hz, CHC*H*$^*_2$CO), and 2.28 (3 H, s, COMe); *m/e* 224 (M^+, 22%), 181 (34), 135 (28), 110 (100), and 59 (27) (Found: C, 58.9; H, 5.5; S, 14.2. $C_{11}H_{12}O_3S$ requires C, 58.9; H, 5.4; S, 14.3%).

Methyl 4-Oxo-3-(phenylthio)pentanoate [(12b) *Methyl Ester*].—Under nitrogen, (phenylthio)acetone (11b) [27] (1.32 g) was added dropwise to petrol-washed sodium hydride (0.19 g) in dry THF (20 ml), followed after 10 min by methyl iodoacetate (1.60 g). The mixture was stirred for 30 h, ammonium chloride and sodium thiosulphate solutions added, the THF layer separated, and the aqueous layer extracted with chloroform (2 × 20 ml). The combined organic fractions were dried (Na_2SO_4) and evaporated to give an oil which was passed down a column of silica with dichloromethane as eluant to give (11b) (0.19 g) and then the *keto-ester* (0.98 g, 52%), R_F(A) 0.30; $\nu_{max.}$ (film) 1 734 (ester C=O), and 1 709 cm^{-1} (ketone C=O); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 4.03 (1 H, dd, *J* 5.5, 8.5 Hz, SC*H*CH*$^*_2$), 3.77 (3 H, s, CO_2Me), 2.71 and 2.85 (2 H, ABX system, J_{AB} 17, J_{BX} 8.5, J_{AX} 5.5 Hz, CHC*H*$^*_2$CO), and 2.36 (3 H, s, COMe); *m/e* 238 (M^+, 71%), 207 (25), 195 (100), 153 (76), and 109 (88) (Found: M^+, 238.0658. $C_{12}H_{14}O_3S$ requires *M*, 238.0663). Similarly prepared was *methyl 3-ethyl-4-oxo-3-(phenylthio)pentanoate* [(12f) methyl ester] from 3-(phenylthio)pentan-2-one (11f) [28] in 40% yield [48% based on recovered (11f)], R_F(A) 0.30; $\nu_{max.}$ (film) 1 735 (ester C=O), and 1 700 cm^{-1} (ketone C=O); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 3.62 (3 H, s, CO_2Me), 2.70 and 2.74 (2 H, AB q, J_{AB} 17 Hz, CH*$^*_2$CO), 2.37 (3 H, s, COMe), 2.00 (2 H, 10 lines, *J* 7.5 Hz, MeC*H*$^*_2$ [ABqq, J_{AB} 15, $J_{AX} = J_{BX}$ 7.5 Hz, Δ_{AB} *ca.* 0.2 p.p.m.]), and 1.04 (3 H, t, *J* 7.5 Hz, *Me*CH_2); *m/e* 266 (M^+, 13%), 295 (10), 223 (100), 191 (48), 163 (100), and 110 (35). The *semicarbazone* [37] had m.p. 149—151 °C (from methanol–water) (Found: C, 55.5; H, 6.6; N, 12.9; S, 9.9. $C_{15}H_{21}N_3O_3S$ requires C, 55.7; H, 6.6; N, 13.0; S, 9.9%).

5,5-Dimethyl-4-oxo-3-(phenylthio)hexanoic Acid (12c) *by the Potassium t-Butoxide Method.*—α-(Phenylthio)pinacolone (11c) [28] (4.6 g) was added dropwise in dry THF (40 ml) to potassium t-butoxide (1.1 equiv.) in dry THF (50 ml) at 0 °C under nitrogen. After 0.5 h, this yellow enolate solution was added dropwise to a suspension of potassium iodoacetate in dry THF (80 ml), and stirring at 0 °C continued for 24 h. The mixture was worked-up as for (12a) above to give the *keto-acid* [2.9 g, 54%, 91% based on recovered (11c)] as colourless prisms, m.p. 77—78 °C (from light petroleum (b.p. 60—80 °C)–ether), R_F(D) 0.80; $\nu_{max.}$ (Nujol) 3 300—2 600 (OH) and 1 705—1 700 cm^{-1} (C=O × 2); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 4.36 (1 H, dd, *J* 5, 10 Hz, SC*H*CH*$^*_2$), 2.66 and 3.02 (2 H, ABX system, J_{AB} 17.5, J_{AX} 10, J_{BX} 5 Hz, CHC*H*$^*_2$CO), and 1.28 (9 H, s, CMe_3); *m/e* 266 (M^+, 45%), 182 (55), 181 (100), and 163 (50) (Found: C, 62.9; H, 6.8; S, 12.0. $C_{14}H_{18}O_3S$ requires C, 63.1; H, 6.8; S, 12.0%). Similarly prepared were (12a) in 58% yield, *4-oxo-4-phenyl-3-(phenylthio)butanoic acid* (12d) from 1-phenyl-2-(phenylthio)ethane (11d) [36] in 38% yield [with 58% (11d) recovered], as colourless needles, m.p. 94—95 °C [from light petroleum (b.p. 40—60 °C)–ether], R_F(D) 0.6; $\nu_{max.}$ (Nujol) 3 600—3 200 (OH), 1 710 (CO_2H), and 1 680 cm^{-1} (PhC=O); δ ($CDCl_3$) 7.91 (2 H dd, *J* 2, 7 Hz, Ar-*H ortho* to CO), 7.1—7.5 (8 H, m, Ar-H), 4.82 (1 H, dd, *J* 6, 9 Hz, SC*H*CH*$^*_2$), and 2.83 and 3.15 (2 H, ABX system, J_{AB} 18, J_{AX} 9, J_{BX} 6 Hz, CHC*H*$^*_2$CO); *m/e* 286 (M^+, 100%), 181 (70), and 163 (35) (Found: M^+, 286.0634. $C_{16}H_{14}O_3S$ requires *M*, 286.0663), and *3-methyl-4-oxo-4-phenyl-3-(phenylthio)butanoic acid* (12e) from 1-phenyl-2-(phenylthio)-propan-1-one (11e) [26] in 15% yield [with 71% (11e) recovered], as colourless needles, m.p. 137—138 °C [from light petroleum (b.p. 60—80 °C)–ether], R_F(D) 0.82; $\nu_{max.}$ (Nujol) 3 200—2 600 (OH), 1 705 (CO_2H), and 1 670 cm^{-1} (COPh); δ 8.02—8.18 (2 H, m, Ar-*H ortho* to CO), 7.2—7.6 (8 H, m, Ar-H), 2.68 and 3.22 (2 H, ABq, *J* 17 Hz, CH*$^*_2$CO), and 1.71 (3 H, s, Me); *m/e* 300 (M^+, 8%), 195 (100), and 177 (30) (Found: M^+, 300.0722. $C_{17}H_{16}O_3S$ requires *M*, 300.0820).

Methyl 3-Methyl-2-(phenylthio)butanoate (15k).—Prepared from methyl 3-methyl-2-bromobutanoate as previously described for (15m),[28] the *ester* (89%) had b.p. 70—92 °C at 0.05 mmHg; R_F (B) 0.52; $\nu_{max.}$ (film) 1 735 cm^{-1} (C=O); 7.1—7.5 (5 H, m, Ph), 3.57 (3 H, s, CO_2Me), 3.43 (1 H, d, *J* 9 Hz, CHC*H*CO), 1.9—2.3 (1 H, m, CHC*H*Me_2), 1.08 and 0.98 (each 3 H, d, *J* 6.5 Hz, CH*Me*$^*_2$); *m/e* 224 (M^+, 70%), 165 (100) and 110 (45) (Found: M^+, 224.0882. $C_{12}H_{16}O_2S$ requires *M*, 224.0871).

1-Methyl Hydrogen 2-(Phenylthio)succinate (16j).—Methyl 2-(phenylthio)acetate (15j) [38] (1.82 g) in dry THF (10 ml) was added to a stirred, cooled (0 °C) solution of lithium di-isopropylamide [from n-BuLi (6.5 ml of a 1.55M solution in hexane) and di-isopropylamine (1.01 g) in dry THF (20 ml)] under a nitrogen atmosphere. After 0.5 h this solution was added to a suspension of potassium iodoacetate (2.5 g) in dry THF (25 ml). The mixture was stirred at 0 °C for 24 h and worked up as for (12a) above to give recovered (15j) (0.89 g, 49%) and the *succinic half-ester* (0.98 g, 41%), an oil, R_F (D) 0.51; $\nu_{max.}$ (film) 3 300—2 600 (OH), 1 740 (CO_2Me), and 1 710 cm^{-1} (CO_2H); δ ($CDCl_3$) 7.1—7.5 (5 H, m, Ph), 3.98 (1 H, dd, *J* 6, 9 Hz, SC*H*CH*$^*_2$), 3.68 (3 H, s, CO_2Me), and 2.73 and 3.01 (2 H, ABX system, J_{AB} 17, J_{AX} 9, J_{BX} 6 Hz, CHC*H*$^*_2$CO); *m/e* 240 (M^+, 100%), 194 (40), 181 (35), 180 (50), 135 (60), and 109 (55) (Found: M^+, 240.0462. $C_{11}H_{12}O_4S$ requires *M*, 240.0457). Similarly prepared were *1-methyl hydrogen 2-isopropyl-2-(phenylthio)succinate* (16k) from the ester (15k) in 51% yield [with 43% (15k) recovered], as colourless prisms, m.p. 70—71 °C [from light petroleum (b.p. 40—60 °C)], R_F(D) 0.63; $\nu_{max.}$ (Nujol) 3 200—2 500 (OH), 1 750 (CO_2Me), and 1 710 cm^{-1} (CO_2H); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 3.70 (3 H, s, CO_2Me), 2.71 and 3.01 (2 H, ABq, J_{AB} 16.5 Hz, CH*$^*_2$CO), 2.22 (1 H, septet, *J* 6.5 Hz, C*H*Me), and 1.12 (6 H, d, *J* 6.5 Hz, Me_2CH); *m/e* 282 (M^+, 50%), 223 (20), 110 (100), and 109 (50) (Found: C, 59.5; H, 6.5; S, 11.4. $C_{14}H_{18}O_4S$ requires C, 59.5; H, 6.5; S, 11.4%); *1-methyl hydrogen 2-methyl-2-(phenylthio)succinate* (16l) from ethyl α-(phenylthio)propionate (15l) [38] in 60% yield (with 21% recovered starting ester), as colourless plates from ether–light petroleum (b.p. 40—60 °C), m.p. 94—95 °C, R_F(D) 0.55; $\nu_{max.}$ (Nujol) 3 500—2 700 (OH) and 1 735—1 710 (C=O × 2) cm^{-1}; δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 4.09 (2 H, q, *J* 7 Hz, OCH_2Me), 2.65 and 3.13 (2 H, AB q, J_{AB} 17 Hz, CH*$^*_2$CO), 1.58 (3 H, s, MeCS), and 1.14 (3 H, t, *J* 7 Hz, *Me*CH_2); *m/e* 268 (M^+, 60%), 195 (100), 177 (50), and 110 (50) (Found: C, 58.1; H, 6.0; S, 11.9. $C_{13}H_{16}O_4S$ requires C, 58.2; H, 6.0; S, 11.9%); and *1-ethyl hydrogen 2-ethyl-2-(phenylthio)succinate* (16m) from ethyl α-(phenylthio)butyrate (15m) [28] in 44% yield [with 50% recovered (15m)], as colourless plates, m.p. 65—66 °C [from light petroleum (b.p. 40—60 °C)], R_F(D) 0.80; $\nu_{max.}$ (film) 3 700—2 700 (OH), and 1 715 cm^{-1} (C=O); δ ($CDCl_3$) 10.94 (1 H, br s, CO_2H), 7.2—7.6 (5 H, m, Ph), 4.10 (2 H, q, *J* 7 Hz, OCH_2Me), 2.81 and 2.91 (2 H, AB q, J_{AB} 16.5 Hz, CH*$^*_2$CO), 1.7—2.2 (2 H, m, MeCH_2CS), and 1.05

and 1.17 (each 3 H, t, *J* 7 Hz, *Me*CH_2); *m/e* 282 (M^+, 45%), 209 (42), 191 (31), 163 (48), and 110 (100) (Found: M^+, 282.0925. $C_{14}H_{18}O_4S$ requires *M*, 282.0925).

2-(*Phenylthio*)*butanal* (11; R^1 = Et, R^2 = H)—At −70° in a nitrogen atmosphere, di-isobutylaluminium hydride [39] (5.5 ml of a 1.4M solution in hexane, 1 equiv.) was added dropwise to a solution of the ester (15m) (1.71 g) in dry light petroleum (b.p. 60—80 °C) (60 ml). After 30 min, hydrochloric acid (3M) was added, the organic layer separated, and the aqueous layer extracted with light petroleum (2 × 20 ml). The combined organic fractions were dried (Na_2SO_4) and evaporated to give the pure aldehyde [40] (1.39 g, quantitative), R_F(A) 0.52; $\nu_{max.}$ (film) 2 820, 2 715 (H–CO), and 1 716 cm^{-1} (C=O); δ ($CDCl_3$) 9.35 (1 H, d, *J* 4 Hz, CHC*H*O), 7.1—7.5 (5 H, m, Ph), 3.42 (1 H, dt, *J* 4, 7.5 Hz, CH_2CH-CHO), 1.76 (2 H, 10 lines, *J ca.* 7.5 Hz, MeC*H*$^*_2$CH), and 1.06 (3 H, t, *J* 7.5 Hz, *Me*CH_2).

4-(*Phenylthio*)-5-*t-butyl*-4,5-*dihydrofuran*-2(3H)-*one* (17c).—The keto-acid (12c) (2.66 g) was dissolved in ethanol (20 ml) and water (20 ml) containing potassium hydroxide (0.56 g) and stirred vigorously whilst sodium borohydride (0.20 g) was added. After 3 h the solution was carefully acidified with dilute aqueous hydrochloric acid, then left stirring at room temperature for 4 h. The solution was partitioned between ether and water, the combined organic extracts (200 ml) were washed with water (2 × 30 ml), aqueous sodium hydrogencarbonate solution (2 × 30 ml), and brine (2 × 20 ml), and dried ($MgSO_4$). Solvent removal *in vacuo* gave a white solid whose n.m.r. indicated only one diastereoisomer. The product was recrystallised from light petroleum (b.p. 40—60 °C) to give the *lactone* (2.44 g, 98%) as needles, m.p. 58—58.5 °C, R_F(C) 0.4; $\nu_{max.}$ (Nujol) 1 795 cm^{-1} (C=O); δ 7.2—7.5 (5 H, m, Ph), 4.31 (1 H, d, *J* 5 Hz CHC*H*–O), 4.02 (1 H, ddd, *J* 6, 5, 2.5 Hz, PhSC*H*), 2.57 and 2.79 (2 H, ABX system, J_{AB} 17.5, J_{AX} 6, J_{BX} 2.5 Hz, CHC*H*$^*_2$CO), and 1.18 (9 H, s, CMe_3); *m/e* 250 (M^+, 40%), 140 (100), and 110 (20) (Found: C, 67.2; H, 7.3; S, 13.0. $C_{14}H_{18}O_2S$ requires C, 67.2; H, 7.3; S, 12.8%).

Similarly prepared was 5-*methyl*-4-(*phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (17b) from the keto-acid (12b), as a mixture of diastereoisomers (98%) which were separated by preparative t.l.c. The *major isomer* (72%) was isolated as colourless prisms, m.p. 42—43 °C (from ethanol at −20 °C), R_F(C) 0.30; $\nu_{max.}$ (Nujol) 1 780 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 4.83 (1 H, quintet, *J* 6.5 Hz, CH–O), 4.06 (1 H, dt, *J* 7.5, 6.5 Hz, PhSC*H*), 2.57 and 2.86 (2 H, ABX system, J_{AB} 17, J_{BX} 7.5, J_{BX} 6.5 Hz, CHC*H*$^*_2$CO), and 1.46 (3 H, d, *J* 6.5 Hz, *Me*CH); the *minor isomer* (24%) was an oil, R_F(C) 0.4); $\nu_{max.}$ (film) 1 784 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 4.43 (1 H, quintet, *J* 6.5 Hz, CH–O), 3.48 (1 H, ddd, *J* 8, 7.5, 6.5 Hz, PhSC*H*), 2.50 and 2.93 (2 H, ABX system, J_{AB} 18, J_{AX} 7.5, J_{BX} 8 Hz, CHC*H*$^*_2$CO), and 1.38 (3 H, d, *J* 6.5 Hz, *Me*CH); the mixture had *m/e* 208 (M^+, 49%), 136 (100), 135 (44), and 110 (23) (Found: M^+, 208.0554. $C_{11}H_{12}O_2S$ requires *M*, 208.0557). Also prepared in this way were 4,5-*dimethyl*-4-(*phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (17a) from the keto-acid (12a) in 99% yield, as a mixture of diastereoisomers M and N (3 : 2), R_F(C) 0.24 (M) and 0.28 (N); $\nu_{max.}$ (film) 1 773 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 4.46^M and 4.48^N (1 H, each q, *J* 6.5 Hz, MeC*H*–O), 2.37 and 2.63^M, 2.44 and 2.70^N (2 H, each AB q, J^M_{AB} 17.5 Hz, J^N_{AB} 17 Hz, CH$^*_2$CO), 1.31^N and 1.54^M (3 H, each d, *J* 6.5 Hz, *Me*CH), 1.33^N and 1.44^M (3 H, each s, MeCS); *m/e* 222 (M^+, 46%), 113 (100), 110 (61), and 43 (54) (Found: C, 64.6; H, 6.2; S, 14.1. $C_{12}H_{14}O_2S$ requires C, 64.8; H, 6.4; S, 14.4%); and 4-*methyl*-5-*phenyl*-4-(*phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (17e) from the keto-acid (12e) in 84% yield as a mixture of diastereoisomers M and N (4 : 1), R_F(C) 0.35 (M and 0.50 (N); $\nu_{max.}$ (film) 1 790 cm^{-1} (C=O); δ 7.1—7.6 (10 H, m, Ph), 5.36^M and 5.42^N (1 H, each s, HC–O), 2.47 and 2.79^M, 2.50 and 2.84^N (2 H, each AB q, J_{AB} 17.5 Hz, CH$^*_2$CO), and 1.56 (3 H, s, MeCS); *m/e* 177 (M^+ − $PhCH_2O$, 20%), 109 (100), and 105 (70).

4-*Ethyl*-5-*methyl*-4-(*phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (17f).—Under nitrogen, zinc borohydride [41] (6 ml of a 1N solution in ether, 5 equiv.) was added to the keto-ester [(12f) methyl ester] (0.32 g) in dry ether (30 ml). After 20 h, ammonium chloride solution was added, the organic layer separated, and the aqueous layer extracted with ether (3 × 15 ml). The organic fractions were dried ($MgSO_4$) and evaporated to give the pure *lactone* (0.28 g, 98%), a mixture of diastereoisomers M and N (3 : 2), R_F(A) 0.27; $\nu_{max.}$ (film) 1 772 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 4.54 (1 H, q, *J* 6.5 Hz, MeC*H*–O), 2.47 and 2.63^M, 2.52 and 2.56^N (2 H, each AB q, J^M_{AB} 17.5 Hz, J^N_{AB} 16.5 Hz, CH$^*_2$CO), 1.1—1.5 (2 H, m, C*H*$^*_2$Me), 1.27^N and 1.55^M (3 H, each d, *J* 6.5 Hz, *Me*CH–O), 1.10^M and 1.17^N (3 H, each t, *J* 7.5 Hz, *Me*CH_2); *m/e* 236 (M^+, 10%), 208 (20), 193 (20), 127 (25), 110 (50), 99 (53), and 59 (100) (Found: C, 66.4; H, 6.9; S, 13.3. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8; S, 13.6%).

4-(*Phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (22j).—The half-ester (16j) (0.96 g, 4 mmol) in dry THF (5 ml) was added slowly to a vigorously stirred suspension of sodium hydride (220 mg, 80% in oil, excess) in dry THF (20 ml) under a nitrogen atmosphere. After 0.5 h, lithium aluminium hydride (80 mg, 2 mmol) was added portionwise with vigorous stirring and the suspension left stirring for 0.5 h, then carefully acidified using dilute aqueous hydrochloric acid and again left stirring for 3 h. The solution was partitioned between ether and water, and the combined organic extracts washed with water (2 × 15 ml), aqueous sodium hydrogencarbonate (2 × 15 ml), and brine (2 × 10 ml), and dried ($MgSO_4$). Solvent evaporation *in vacuo* followed by column chromatography eluting with ether–light petroleum (b.p. 40—60 °C), gave the lactone [20] as a colourless oil (0.51 g, 58%), R_F(C) 0.35; $\nu_{max.}$ (film) 1 785 cm^{-1} (C=O); δ 7.2—7.5 (5 H, m, Ph), 4.16 and 4.52 (2 H, ABX system, J_{AB} 9, J_{AX} 5, J_{BX} 6 Hz, SCHC*H*$^*_2$O), 3.85—4.15 (1 H, m, PhSC*H*), 2.46 and 2.89 (2 H, ABX system, J_{AB} 18, J_{AX} 8, J_{BX} 6 Hz, CHC*H*$^*_2$CO). Similarly prepared were 4-*isopropyl*-4-(*phenylthio*)-4,5-*dihydrofuran*-2(3H)-*one* (22k) from the half-ester (16k) in 62% yield, colourless prisms, m.p. 59—59.5 °C [from ether–light petroleum (b.p. 30—40 °C)], R_F(C) 0.35; $\nu_{max.}$ (Nujol) 1 785 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 4.24 and 4.39 (2 H, AB q, J_{AB} 9.5 Hz, CH$^*_2$–O), 2.65 (2 H, s, CH_2CO), 2.03 (1 H, septet, *J* 7 Hz, Me_2CH), 1.13 and 1.15 (each 3 H, d, *J* 7 Hz, *Me*$^*_2$-CH); *m/e* 236 (M^+, 32%), 127 (47), and 110 (100) (Found: C, 66.0; H, 6.75; S, 12.8. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8; S, 13.6%); and 4-*methyl*-4-(*phenylthio*)4,5-*dihydrofuran*-2(3H)-*one* (22l) from the half-ester (16l) in 63% yield, colourless prisms, m.p. 80—81 °C [from ether–light petroleum (b.p. 30—40 °C)], R_F(B) 0.15; $\nu_{max.}$ (Nujol) 1 778 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 4.09 and 4.34 (2 H, ABq, J_{AB} 10 Hz, CH$^*_2$–O), 2.49 and 2.75 (2 H, AB q, J_{AB} 17.5 Hz, CH$^*_2$CO), and 1.53 (3 H, s, Me); *m/e* 208 (M^+, 25%), 110 (100), 109 (39), and 99 (30) (Found: C, 6.32; H, 5.85; S, 14.5. $C_{11}H_{12}O_2S$ requires C, 63.4; H, 5.8; S, 15.4%).

4-Ethyl-4-(phenylthio)-4,5-dihydrofuran-2(3H)-one (22m).—(a) *From the aldehyde* (11; R^1 = Et, R^2 = H). The aldehyde (0.73 g) was added dropwise to petrol-washed sodium hydride (0.15 g) in dry THF (20 ml), followed after 0.5 h by sodium iodoacetate (slight excess) [39] in dry THF (20 ml). After 4 h, all the aldehyde had reacted (by t.l.c.) so the mixture was worked up as for (12a) above. The acidic extract (0.81 g) was a mixture of at least four products (t.l.c., eluting with Et_2O–1% AcOH). It was reduced with sodium borohydride as for (17c) above to give the *lactone* (0.23 g, 26% after preparative t.l.c.). It had R_F(A) 0.26; $\nu_{max.}$ (film) 1 778 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 4.08 and 4.26 (2 H, AB q, J_{AB} 10 Hz, CH^*_2–O), 2.52 and 2.58 (2 H, AB q, J_{AB} 17.5 Hz, CH^*_2CO), 1.72 (2 H, q, J 7.5 Hz, CH_2Me), and 1.12 (3 H, t, J 7.5 Hz, *Me*CH_2); *m/e* 222 (M^+, 56%), 113 (62), 110 (100), and 109 (15) (Found: C, 65.0; H, 6.6; S, 14.5. $C_{12}H_{24}O_2S$ requires C, 64.8; H, 6.4; S, 14.4%).

(b) *By reduction of the ester* (16m). Under nitrogen, the ester (0.17 g) was added to an excess of petrol-washed sodium hydride in dry THF (20 ml). After 10 min, lithium aluminium hydride (15 mg) was added to this suspension of the sodium salt of (16m) with vigorous stirring. After a further 20 min, the mixture was acidified with hydrochloric acid (3M), and stirring continued overnight. The THF layer was separated and the aqueous layer extracted with chloroform (3 × 10 ml). The extracts were dried (Na_2SO_4), evaporated, and subjected to preparative t.l.c. to give the lactone (0.12 g 90%).

5,5-Dimethyl-4-(phenylthio)-4,5-dihydrofuran-2(3H)-one (23g).—To the keto-acid (12b) (0.27 g) in dry ether (30 ml) was added methylmagnesium iodide (2 equiv.) in dry ether (10 ml) and the mixture was stirred overnight. Hydrochloric acid (3M) was then added, it was stirred for 1 h, the ether layer was separated, and the aqueous layer extracted with chloroform (3 × 10 ml). The combined organic fractions were dried (Na_2SO_4), evaporated, and subjected to preparative t.l.c. to give the *lactone* (0.26 g, 90%), R_F(A) 0.26; $\nu_{max.}$ (film) 1 771 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.5 (5 H, m, Ph), 3.71 (1 H, dd, J 8, 10.5 Hz, SC*H*CH^*_2), 2.68 and 2.88 (2 H, ABX system, J_{AB} 17.5, J_{AX} 10.5, J_{BX} 8 Hz, $CHCH^*_2CO$), and 1.42 and 1.46 (each 3 H, s, CMe^*_2); *m/e* 222 (M^+, 34%), 136 (100), and 135 (36) (Found: C, 65.0; H, 6.6; S, 14.2. $C_{12}H_{14}O_2S$ requires C, 64.8; H, 6.4; S, 14.4%).

4,5-Dimethyl-4-phenylthio-5-propyl-4,5-dihydrofuran-2(3H)-one (23h).—The keto-acid (12a) (0.43 g) in dry ether (15 ml) was treated with propylmagnesium bromide (2 equiv.) in dry ether (10 ml). After 3 h, hydrochloric acid was added, and after a further 1 h the ether layer was separated and the aqueous layer extracted with chloroform (2 × 10 ml). The combined organic fractions were dried (Na_2SO_4), evaporated, and subjected to preparative t.l.c. to give phenyl propyl sulphide [42] (0.05 g, 15%), R_F(A) 0.65; δ ($CDCl_3$) 7.0—7.5 (5 H, m, Ph), 2.84 (2 H, t, J 7 Hz, SCH_2CH_2), 1.66 (2 H, sextet, J 7 Hz, CH_2CH_2Me), and 1.00 (3 H, t, J 7 Hz, *Me*CH_2); and the *lactone* (23h) (0.25 g, 52%), R_F(A) 0.29; $\nu_{max.}$ (film) 1 770 cm^{-1} (C=O); δ ($CDCl_3$) 7.2—7.6 (5 H, m, Ph), 2.2—3.1 (2 H, m, CH^*_2CO), 1.2—2.1 (4 H, m, CH_2CH_2Me), 1.37 (6 H, s, Me), and 1.01 (3 H, t, J 7 Hz, *Me*CH_2); *m/e* 264 (M^+, 9%), 155 (23), 150 (100), 110 (58), 59 (28), and 41 (37) (Found: M^+, 264.1181. $C_{15}H_{20}O_2S$ requires M, 264.1183).

5-Methylfuran-2(5H)-one (25b).—The lactone (17b) (56 mg), sodium metaperiodate [33] (65 mg), methanol (5 ml), and water (2 ml) were stirred for 24 h. Water was added, and the mixture extracted with chloroform (3 × 10 ml). Drying (Na_2SO_4) and evaporation of the extracts gave the sulphoxide (24; R = R^2 = H, R^1 = Me) (60 mg), R_F(A) 0.15; $\nu_{max.}$ (film) 1 770 (C=O) and 1 040 cm^{-1} (S=O), which was heated to 110 °C in deuteriotoluene (0.5 ml) in an n.m.r. tube for 1.5 h. The resulting mixture was subjected to preparative t.l.c. to give β-angelicalactone [3,43] (22 mg, 83%), R_F(A) 0.19; δ ($CDCl_3$) 7.42 (1 H, dd, J 1.5, 5.5 Hz, CHC*H*=CHCO), 6.09 (1 H, dd, J 2, 5.5 Hz, CHCH=C*H*CO), 5.12 (1 H, ddq, J 1.5, 2, 6.5 Hz, MeC*H*CH=CHCO), and 1.46 (3 H, d, J 6.5 Hz, *Me*CH); *m/e* 98 (M^+, 92%), 83 (63), 69 (24), 55 (100), 54 (30), and 43 (92). Similarly prepared was 5,5-dimethylfuran-2-(5*H*)-one (25g) [44] from the lactone (23g) in 81% yield, R_F(A) 0.22; $\nu_{max.}$ (film) 1 746 (C=O) and 1 638 cm^{-1} (C=C); δ ($CDCl_3$) 7.36 (1 H, d, J 5.5 Hz, *HC*=CHCO), 5.97 (1 H, d, J 5.5 Hz, HC=C*H*CO), and 1.49 (6 H, s, Me_2C); *m/e* 112 (M^+, 13%), 97 (100), 55 (35), and 43 (75).

4,5-Dimethylfuran-2(5H)-one (25a).—The lactone (17a) (75 mg), sodium periodate [33] (100 mg), methanol (5 ml), and water (2 ml) were stirred for 24 h. The resulting mixture was yellow (iodine was liberated). Sodium thiosulphate solution was added, the mixture extracted with chloroform (3 × 10 ml), and the extracts dried, evaporated, and subjected to preparative t.l.c. (sulphoxide elimination had occurred spontaneously) to give the butenolide [6,45] (29 mg, 77%), R_F(A) 0.20; $\nu_{max.}$ (film) 1 750 (C=O), and 1 643 cm^{-1} (C=C); δ ($CDCl_3$) 5.77 (1 H, nm, C=CHCO), 4.89 (1 H, br q, J 6.5 Hz, MeC*H*), 2.06 (3 H, d, J 1 Hz, *Me*C=CH), and 1.43 (3 H, d, J 6.5 Hz, *Me*CH); *m/e* 112 (M^+, 25%), 97 (22), 83 (10), and 69 (100). Also prepared in this way were *5-t-butylfuran-2(5H)-one* (25c) from the lactone (17c) in 75% yield, a colourless oil, R_F(C) 0.25; $\nu_{max.}$ (film) 1 790, 1 760 (C=O), and 1 680 cm^{-1} (C=C); δ 7.48 (1 H, dd, J 1.5, 6 Hz, CHC*H*=CHCO), 6.14 (1 H, dd, J 2.5, 6 Hz, CHCH=C*H*CO), 4.73 (1 H, dd, J 1.5, 2.5 Hz, O–C*H*CH=CHCO), and 1.02 (9 H, s, Me_3C); *m/e* 140 (M^+, 5%) (Found: M^+, 140.0838. $C_8H_{12}O_2$ requires M, 140.0838): 4-methyl-5-phenylfuran-2(5*H*)-one (25e) [46] from the lactone (17e) in 70% yield, R_F(B) 0.15; δ ($CDCl_3$) 6.9—7.2 (5 H, m, Ph), 5.49 and 5.13 (each 1 H, br s, O–C*H*CMe=C*H*CO), and 1.33 (3 H, br s, Me); 4-ethyl-5-methylfuran-2(5*H*)-one (25f) [6] from the lactone (17f) in 78% yield, R_F(A) 0.22; $\nu_{max.}$ (film) 1 748 (C=O) and 1 640 cm^{-1} (C=C); δ ($CDCl_3$) 5.77 (1 H, q, J 1.5 Hz, C=CHCO), 4.94 (1 H, dq, J 1.5, 7 Hz, MeC*H*), 2.2—2.5 (2 H, m, $MeCH^*_2$-C=C), 1.44 (3 H, d, J 7 Hz, *Me*CH), and 1.23 (3 H, t, J 7.5 Hz, *Me*CH_2); *m/e* 126 (M^+, 19%), 83 (100), and 55 (32): *4,5-dimethyl-5-propylfuran-2(5H)-one* (25h) from the lactone (23h) in 78% yield, a colourless oil, R_F(A) 0.25; $\nu_{max.}$ (film) 1 746 (C=O) and 1 645 cm^{-1} (C=C); δ ($CDCl_3$) 5.71 (1 H, q, J 1.5 Hz, MeC=C*H*CO), 1.98 (3 H, d, J 1.5 Hz, *Me*C=CH), 1.0—1.9 (4 H, m, CH_2), 1.42 (3 H, s, MeC–O), and 0.8—1.0 (3 H, m, *Me*CH_2CH_2); *m/e* 154 (M^+, 1%), 112 (25), 111 (100), and 43 (57): 4-(1-methylethyl)furan-2(5*H*)-one (25k) [47] from the lactone (22k) in 77% yield, R_F(C) 0.22; $\nu_{max.}$ (film) 1 790, 1 750 (C=O), and 1 640 cm^{-1} (C=C); δ ($CDCl_3$) 5.79 (1 H, q, J 1.5 Hz, C=CHCO), 4.80 (2 H, d, J 1.5 Hz, OCH_2), 2.73 (1 H, br septet, J 7 Hz, Me_2CH), and 1.24 (6 H, d, J 7 Hz, Me_2CH); *m/e* 126 (M^+, 45%), 113 (55), 110 (80), and 97 (85): 4-methylfuran-2(5*H*)-one (25l) [6,48] from the lactone (22l) in 81% yield, R_F(C) 0.20; $\nu_{max.}$ (film) 1 785, 1 750 (C=O), and 1 645 cm^{-1} (C=C); δ ($CDCl_3$) 5.8 (1 H, nm, C=CHCO), 4.71 (2 H, d, J 1.5 Hz, OCH_2), and 2.12 (3 H, d, J 1 Hz, *Me*C=CH); *m/e* 98 (M^+, 40%), 85 (50), and 69 (100); and 4-ethylfuran-2(5*H*)-one (25m) from the lactone

(22m) in 81% yield, as fine colourless needles, m.p. 34—35 °C (from pentane) (lit.,[49] 33 °C, lit.,[6] 36 °C), R_F(A) 0.20; $\nu_{max.}$ (film) 1 777, 1 738 (C=O), and 1 636 cm^{-1} (C=C); δ ($CDCl_3$) 5.82 (1 H, quintet, *J* 1 Hz, C=CHCO), 4.75 (2 H, d, *J* 1 Hz, OCH_2), 2.44 (2 H, dq, *J* 1, 7.5 Hz, $MeCH_2C$=CH), and 1.14 (3 H, t, *J* 7.5 Hz, $MeCH_2$); *m/e* 112 (M^+, 18%), 83 (100), and 55 (35).

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