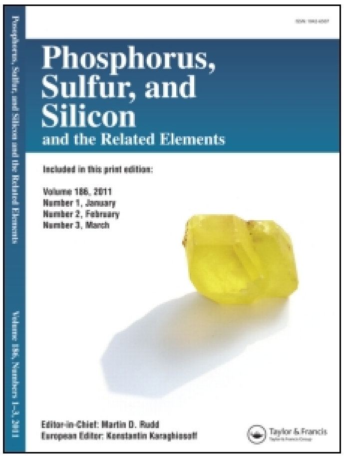

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF 3-METHYLENE-1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES AND 1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES NOVEL FORMATION AND CRYSTAL STRUCTURE OF 3-[(4-HYDROXY-4-THIANYL)METHYL] - 1-OXA-8-THIASPIRO[4.5]DECAN-2-ONE

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To cite this Article Satyamurthy, Nagichettiar , Berlin, K. Darrell , Powell, Douglas R. and Van Der Helm, Dick(1984) 'SYNTHESIS OF 3-METHYLENE-1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES AND 1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES NOVEL FORMATION AND CRYSTAL STRUCTURE OF 3-[(4-HYDROXY-4-THIANYL)METHYL] - 1-OXA-8-THIASPIRO[4.5]DECAN-2-ONE', Phosphorus, Sulfur, and Silicon and the Related Elements, 19: 2, 137 — 153

To link to this Article: DOI: 10.1080/03086648408077573

URL: http://dx.doi.org/10.1080/03086648408077573

Phosphorus and Sulfur, 1984, Vol. 19, pp. 137–153
0308-664X/84/1902-0137/$18.50/0

SYNTHESIS OF 3-METHYLENE-1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES AND 1-OXA-8-HETERASPIRO[4.5]DECAN-2-ONES. NOVEL FORMATION AND CRYSTAL STRUCTURE OF 3-[(4-HYDROXY-4-THIANYL)METHYL]-1-OXA-8-THIASPIRO[4.5]DECAN-2-ONE

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(*Received July 14, 1983*)

A series of new 3-methylene-1-oxa-8-heteraspiro[4.5]decan-2-ones have been prepared as the first members of the family. Reaction of 1-oxa-6-heteraspiro[2.5]octanes with diethyl malonate, followed by hydrolysis, gave 3-carboxy-1-oxa-8-heteraspiro[4.5]decan-2-ones. The carboxy lactone, upon treatment with diethylamine and formaldehyde followed by sodium acetate and acetic acid, produced α-methyleneheteraspiro lactones in good yields and in high purity. Moreover, the carboxy lactones could be decarboxylated smoothly to give 1-oxa-8-heteraspiro[4.5]decan-2-ones in good yields. The present method appears to be superior to the widely used Reformatsky reaction since only low yields of the required lactones could be obtained when applied in the work reported herein.

An investigation of dilithiated acetic acid as a co-reactant with spiro epoxides of heteracyclohexyl systems was undertaken but rather than the expected γ-lactones, unusual γ-hydroxylactones were obtained. Apparently, the anionic behavior of the dilithiated acetic acid caused the condensation to occur. All lactone systems were characterized via IR, ^{1}H NMR and ^{13}C NMR analysis and mass spectral data.

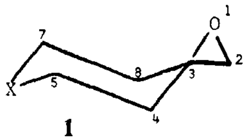
A single crystal analysis by X-ray diffraction of 3-[(4-hydroxy-4-thianyl)methyl]-1-oxa-8-thiaspiro[4.5]decane-2-one [space group $P2_12_12_1$, $Z = 4$, $a = 5.916(2)$, $b = 11.585(3)$, $c = 21.986(5)$ A, $T = 138$ K] was completed. Least-squares refinement converged to $R = 0.045$ for 1319 diffractometer data. Both thiacyclohexyl rings are in the chair conformation and have C—O bonds which are axial. The sulfur ring with the hydroxyl group is orientationally disordered. This is the first example of such a fused heterocycle in which a structure of the crystal has been reported.

INTRODUCTION

Enormous interest in α-methylenelactones is apparent from the current literature.[1,2] Several α-methylene-γ-butyrolactones have shown potential antitumor activity[3] and a structure-activity relationship has been reported.[4] Although emphasis to date has been on the isolation of natural occurring α-methylene-γ-butyrolactones rather than simple systems,[5] the natural products have exhibited high toxicity in clinical use. It has been suggested that the complexity of the structures in terms of multifunctional character and stereochemistry may account for the toxicity.[4a,6] On the other hand, several simple systems have shown good activity,[3,7] but a search of the literature did not reveal many examples of a six-membered heterocycle containing such a lactone unit in spite of the obvious fact that the hydrophilic properties might be enhanced over a carbocycle analog. We report herein the first members containing a spiro lactone unit bonded to a six-membered heterocycle which contains either O, $NCH_2C_6H_5$, S or $C_6H_5P(S)$ in the ring.

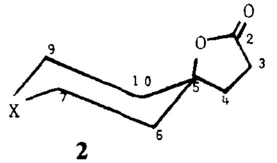
RESULTS AND DISCUSSION

A number of approaches to the title lactones were considered initially. Since epoxides **1a**,[8] **1b**[8] and **1c**[9] were known, treatment with diethyl malonate, followed by



1

a. X = NCH_2Ph
b. X = S
c. X = $(CH_3)_3CCH$
d. X = P(S)Ph
e. X = O



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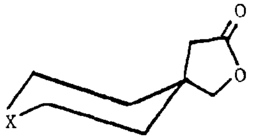
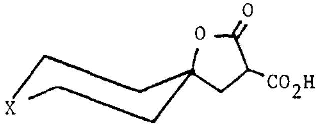


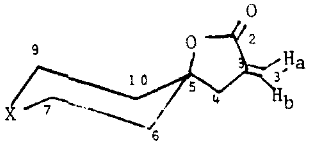
3

hydrolysis and decarboxylation,[10-12] should give lactones **2** and **3**. However, attack of the malonate anion at a hindered spiro carbon[13,14] may be difficult with the result being attack on the more vulnerable methylene carbon of **1a**–**1c**. Indeed only one isomer **2a**–**c** (IR and NMR data in Tables I and III) was found in our reaction mixtures. It was possible to prepare **2c** via the use of a Meyer's reagent but the yield was less (see Experimental). Lactones **2a** and **2c** appear to be biased and probably have an axial C(5)—O bond. Presumably, **2b** is a mobile system. In view of previous findings on simple carbocyclic systems,[10] we present that members of **4** are the immediate precursors of **2**. Conversion of crude **4a** to **5a** was initially attempted with



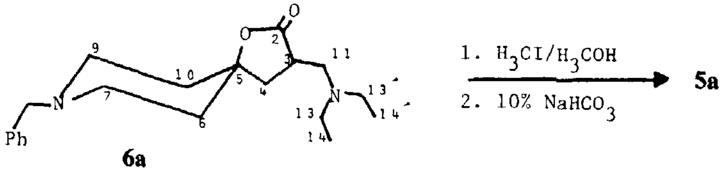
4

a. X = NCH_2Ph
b. X = S
c. X = $(CH_3)_3CCH$
d. X = P(S)Ph
e. X = O



5

diethylamine and formaldehyde.[14,15] However, only amino lactone **6a** resulted,[16] but it was possible to obtain **5a** by a modified procedure.[11b]



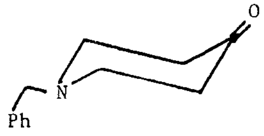
6a

Because this overall method was somewhat time consuming and the yield was modest, it was found that members of **4** could be treated as shown[17] to give all members of **5** in good yields. Again, in **5a**, **5c** and **5d** it is presumed the C—O bond

$$\mathbf{4} \xrightarrow[2.\ H_3CCO_2Na/H_3CCO_2H]{1.\ Et_2NH/H_2C{=}O} \mathbf{5}$$

is axial since a preference of this kind is known in biased system **5c** prepared and reported earlier[18] and confirmed by X-ray analysis.

Although the Reformatsky reagent has been employed in our laboratory[18,19] to prepare α-methylene-γ-butyrolactones,[18,19] low yields were encountered presumably because of competitive alkylation of the heteroatom by residual haloester. However, it has been observed[20–22] that the Reformatsky reagent in ether/benzene could be used in a manner reminiscent of a Grignard reagent in a frequently very fast reaction with ketones. Using the Reformatsky reagent prepared from ethyl α-bromomethylacrylate and activated zinc[23] in ether, addition occurred to 1-benzyl-4-piperidone (**7**) or 1-phenyl-4-phosphorinanone 1-sulfide (**8**) in THF to give **5a** and **5d** but in relatively modest yields. Since the two products were identical in all respects to those obtained previously, via the synthesis from diethyl malonate, the structures were confirmed. The benzyl bromide derivative of **5a**, namely **9**, furnished supporting analytical evidence for **5a** since no previous members of the families have been reported.



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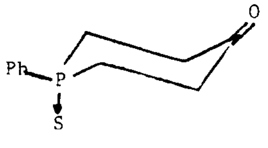

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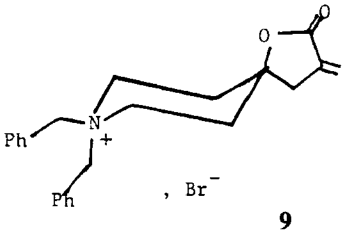

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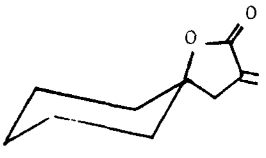
Infrared analysis of **5a–e** and **9** had $\lambda_{C=O}$ at 1660–1670 cm^{-1}. The ^{1}H NMR spectra were complex and relatively uninformative (Table I). In contrast, ^{13}C NMR analysis had resonances for C(5) of the lactone rings in **5a–e** and **9** at 80.8, 80.6, 82.2, 80.9 (J_{PC} = 5.27 Hz), 79.8 and 78.1 ppm, respectively, suggesting possibly the C(5)—O bond is in a preferred axial arrangement.[18] Of course, **5b** is mobile[24] and **5e** is likely to be also but a preference for C(5)—O to be axial is not unreasonable since that has been observed for the mobile carbocyclic system **10**.[25]



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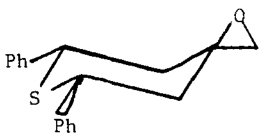

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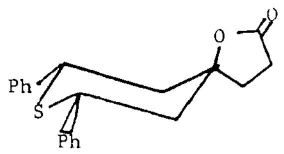

12

It is noteworthy that C(5) in lactones **2a–c** has ^{13}C signals at 83.3, 83.8, and 84.6 ppm, respectively. Very probably these systems have a preferred C(5)—O axial bond

TABLE I

IR, ^{1}H NMR data for lactones, γ-hydroxylactones, and α-methylene-γ-lactones

Compd.	IR[a], cm^{-1}				^{1}H NMR[b]
	$\nu_{(C=O)}$	$\nu_{(C-OH)}$	ν_{OH}	$\nu_{C=C}$	
2a	1770				1.56–2.14 [m, 6 H, H(4), H(6), H(10)], 2.26–2.80 [m, 6 H, H(3), H(7), H(9)], 3.49 [s, 2 H, $C\underline{H}_2C_6H_5$], 7.12–7.44 [m, 5 H, Ar$\underline{H}$]
2b	1770				1.70–3.14 [m, 12 H, H(3), H(4), H(6), H(7), H(9), H(10)], 0.86 [s, 9 H, $C(C\underline{H}_3)_3$],
2c	1765				0.96–2.10 [m, 11 H, H(4), H(6), H(7), H(8), H(9), H(10)], 2.44–2.70 [t, 2 H, H(3), J = 8.0 Hz]
5a	1765			1670	1.62–1.96 [m, 4 H, H(6), H(10)], 2.40–2.66 [t, 4 H, H(7), H(9), J = 6.0 Hz], 2.68–2.80 [t, 2 H, H(4)],[c] 3.52 [s, 2 H, $C\underline{H}_2C_6H_5$], 5.56–5.68 [t, 1 H, $H_b(3')$],[d] 6.16–6.28 [5, 1 H, $H_a(3')$],[d] 7.28 [s, 5 H, Ar$\underline{H}$]
5b[e]	1755			1662	1.72–3.20 [m, 8 H, H(6), H(7), H(9), H(10)], 2.66–2.78 [t, 2 H, H(4)],[c] 5.60–5.72 [t, 1 H, $H_b(3')$],[d] 6.20–6.32 [t, 1 H, $H_a(3')$][d]
5c[f]	1755			1662	0.88 [s, 9 H, $C(C\underline{H}_3)_3$], 1.02–2.0 [m, 9 H, H(6), H(7), H(8), H(9), H(10)], 2.66–2.72 [t, 2 H, H(4)],[c] 5.56–5.64 [t, 1 H, $H_b(3')$],[d] 6.10–1.20 [t, 1 H, $H_a(3')$][d]
5d	1750			1662	1.58–2.80 [m, 8 H, H(6), H(7), H(9), H(10)], 2.80–2.92 [t, 2 H, H(4)],[c] 5.68–5.80 [t, 1 H, $H_b(3')$],[d] 6.28–6.40 [t, 1 H, $H_a(3')$],[d] 7.24–8.18 [m, 5 H, Ar$\underline{H}$]
5e	1760			1665	1.74–1.94 [t, 4 H, H(6), H(10)], 2.74–2.86 [5, 2 H, H(4)],[c] 3.60–4.00 [m, 4 H, H(7), H(9)], 5.63–5.74 [t, 1 H, $H_b(3')$],[d] 6.21–6.32 [t, 1 H, $H_a(3')$][d]
9[h]	1760			1660	1.96–2.30 [m, 4 H, H(6), H(10)], 2.90–3.02 [t, 2 H, H(4)],[c] 3.26–3.60 [m, 4 H, H(7), H(9)], 4.48 [s, 2 H, $(C\underline{H}_2C_6H_5)_a$], 4.94 [s, 2 H, $(C\underline{H}_2C_6H_5)_e$], 5.72–5.82 [t, 1 H, $H_b(3')$],[d] 6.12–6.24 [t, 1 H, $H_a(3')$][d] 7.30–7.76 [m, 10 H, Ar$\underline{H}$]
12	1770				2.00–2.40 [m, 6 H, H(4), H(6), H(10)], 2.50–2.78 [m, 2 H, H(3)], 4.34–4.64 [dd, 2 H, H(7), H(9), J = 3.0 and 11.0 Hz], 7.14–7.52 [m, 10 H, Ar$\underline{H}$]
13a	1745	1110	3510		1.40–2.80 [m, 22 H, H(3), H(4), H(6), H(7), H(9), H(10), H(11), H(6′), H(7′), H(9′), H(10′), O$\underline{H}$], 3.52 (s, 4 H, 2, $C\underline{H}_2C_6H_5$), 7.25 (s, 10 H, Ar$\underline{H}$)
13b	1750	1170	3450		1.32–3.40 [m, 22 H, H(3), H(4), H(6), H(7), H(9), H(10), H(11), H(6′), H(7′), H(9′), H(10′), O$\underline{H}$]
13c	1735	1130	3500		0.86 [s, 18 H, 2 $C(C\underline{H}_3)_3$], 1.18–2.48 [m, 24 H, H(3), H(4), H(6), H(7), H(8), H(9), H(10), H(11), H(6′), H(7′), H(8′), H(9′), H(10′), O$\underline{H}$]

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[a] Spectrum recorded on a KBr pellet unless otherwise noted.

[b] ppm from Me_4Si in $DCCl_3$, unless otherwise noted.

[c] Three-line pattern resulting from X_2 portion of AMX_2 where $J_{AX} = J_{MX} = 2.5$ Hz.

[d] A or M portion of AMX_2 pattern where $J_{AM} < J_{AX}$; $J_{MX} = 2.5$ Hz.

[e] Reference 24.

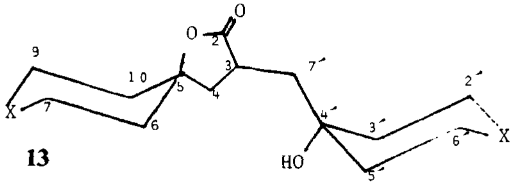
[f] Reference 25.

[g] Spectrum recorded as a thin film.

[h] ppm from TMS in D_3COD.

also although **2b** is mobile as indicated previously.[24] Another observation pertinent to the stereochemical analysis of members of **2a–c** and members of **5a–e** is the relative constancy of ^{13}C resonances for C(4) in the former [27.8 to 28.0 ppm) and in the latter [39.2 to 40.6 ppm). This also seems to support our contention of a high population in solution of the conformers with a C(5)—C(4) equatorial bond in these lactones.

One other technique was examined for the preparation of members of **2**. Since steroidal epoxides are known to react with lithiated carboxylic acids (prepared via treatment of the acids with excess lithium diisopropylamide) in dry THF to give spiro lactones,[26] such an approach seemed logical for **2**. Initially, the method involved reaction of dilithiated acetic acid with *trans*-5,7-diphenyl-1-oxa-6-thiaspiro[2.5]octane (**11**)[8] and did give a low yield of **12**. Reactions conditions were critical and the original procedure had to be modified.



13

a. X = NCH_2Ph
b. X = S
c. X = $(CH_3)_3CCH$

When **1a–c** was treated as indicated, a novel, condensation procedure ensued. Characterization of products **13** included analysis of IR and NMR data (Tables I and II) as well as mass spectral patterns. All three members of **13a–c** had a strong band near 1750 cm^{-1} [C=O][27] and at 3500 cm^{-1} [O—H stretch]. Bands of medium intensity occurred at 1100–1170 cm^{-1}, characteristic of a tertiary alcohol group.[28] ^{1}H NMR spectra of **13a–c** were complex (Table I) but ^{13}C NMR spectra (Table II) proved informative. Signals for C(2) in **13a–c** were *deshielded* by 4.02, 3.67 and 4.29

TABLE II

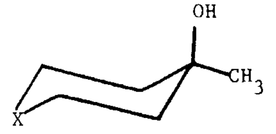
^{13}C Chemical shifts for the γ-hydroxylactones[a]

Compd.	C(2)	C(3)	C(4)	C(5) C(5′)	C(6)[b] C(10)	C(7)[b] C(9)	C(8)[b] C(8′)	C(11)	C(6′)[b] C(10′)	C(7′)[b] C(9′)	Other
13a	179.57	43.80	36.69	82.45 68.22	35.56 35.51	49.14 49.08		41.73	37.87 37.48	49.61 49.42	$\underline{C}H_2C_6H_5(8)$, 62.71;[b] $\underline{C}H_2C_6H_5(8')$, 62.90;[b] $\underline{Ar}$, 137.95, 128.92, 128.79, 127.99, 127.95, 126.83, 126.78
13b	179.32	44.41	34.90	82.76 68.60	37.99 37.05	24.07		42.69	39.53 39.13	24.77 24.57	
13c	180.10	45.34	36.79	83.72 69.57	35.90	22.41 22.35	47.27 47.86	43.33	38.49 37.69	23.49 22.79	$C(\underline{C}H_3)_3$, 27.52; $\underline{C}(CH_3)_3$,32.38

[a] In $DCCl_3$ from TMS.
[b] Assignments of upper and lower lines may be reversed.

ppm, respectively, compared with that found for C(2) in lactones **2a–c**. This downfield shift may be due to a β-effect of the substituent at C(3) such as found for the carbonyl carbon atom in 2-substituted cyclopentanones.[29] A downfield shift of 10–11 ppm was noted for C(3) in **13a–c**, apparently as the result of substitution. A β-deshielding effect of 6–8 ppm was found for C(4) resonances whereas a γ-*shielding* effect ($\approx$ 1 ppm) was observed for C(5) in **13a–c** as compared to **2a–c**.

^{13}C NMR shifts for C(4′) in **13a–c** are 68.2, 68.6 and 69.5 ppm (Table II), respectively, while in model systems **14a–c** the values for corresponding carbons

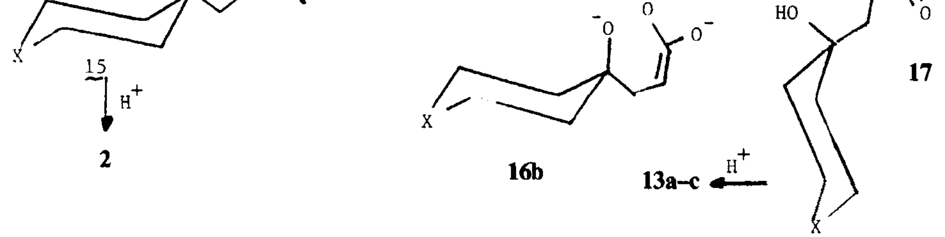


14

a. X = NCH_2Ph
b. X = S
c. X = $(CH_3)_3CCH$

[C(4)] were 67.5, 67.7 and 68.7 ppm (Table IV), respectively.[8] Thus, we assume C(4′)—O in **13a, c** and C(4)—O in **14a, c** are axial in biased systems while the counterparts in **13b** and **14b** may have a preferred axial arrangement but the system is probably mobile. The slightly increased deshielding of C(4′) in **13a–c** may be a result of the influence of the large equatorial substituent. We note also that signals for C(7, 9) in **13a, c** occurred near the frequency for that found in **2a, c**. This seems to support the hypothesis that the C(4′)—O bond is axial in both systems.

Formation of γ-hydroxylactones **13a–c** appears defensible via consideration of the removal of a proton from the alpha carbon of the probable intermediate **15**. Reaction of trianion **16a** (or more likely the enolate form **16b**) with epoxides **1a–c**



should logically give **17**, the precursor of **13a–c**. Lactonization surely occurs during acidification of the reaction mixture. Generation of the trianion **16** seems reasonable,[26] but this is the first report of such in this type of heterocycle.[30]

In view of the rarity of structures such as **13**, an X-ray diffraction analysis was performed on **13b**, 3-[(4-hydroxy-4-thianyl)methyl]-1-oxa-8-thiaspiro[4.5]decan-2-

TABLE III

^{13}C Chemical shifts for model lactones and α-methylene-γ-lactones[a]

Compd.	C(2)	C(3)	C(3′)	C(4)	C(5)	C(6) C(10)	C(7) C(9)	C(8)	Other
2a	175.55	32.25		27.89	83.34	36.07	49.20		$\underline{C}H_2C_6H_5$, 62.44; Ar—$\underline{C}$: 137.79, 128.31, 127.58, 126.38
2b	175.65	33.59		28.05	83.81	37.88	24.72		
2c	175.81	33.44		28.00	84.65	36.85	22.61	46.51	$C(\underline{C}H_3)_3$, 26.96; $\underline{C}(CH_3)_3$, 31.77
5a	169.07	134.73	122.09	39.22	80.80	36.95	49.31		$\underline{C}H_2C_6H_5$, 62.56; Ar—$\underline{C}$: 137.97, 128.66, 127.90, 126.73
5b[b]	168.64	134.11	122.55	40.09	80.65	38.06	24.28		
5c[c]	169.44	135.54	121.54	40.56	82.20	37.99	22.90	46.86	$C(\underline{C}H_3)_3$, 27.48; $\underline{C}(CH_3)_3$, 32.30
5d[d,e]	168.87	133.92	123.52	40.63 (1.26)	80.91 (5.27)	32.64 (5.13)	27.32 (51.49)		Ar—C: C(α), 131.02 (79.52); C(β), 130.53 (10.38); $C(\overline{\gamma})$, 128.59, (12.41); C(δ), 131.90 (2.96)
5e	168.98	134.43	122.73	39.77	79.87	37.52	63.99		
9[f]	169.66	131.67	124.07	39.37	78.14	31.78	52.99		$(\underline{C}H_2C_6H_5)_a$, 62.18; $(\underline{C}H_2C_6H_5)_e$, 67.35; Ar—$\underline{C}$: 135.14, $134.\overline{55}$, 134.11, 130.33, 130.09, $128.3\overline{3}$, 127.70
12	175.64	34.89		28.04	85.50	44.18	44.88		Ar—$\underline{C}$:140.27, 128.57, 127.58, 127.29

[a] In $DCCl_3$ from Me_4Si unless otherwise stated.
[b] Reference 18.
[c] Reference 25.
[d] J_{PC} in parentheses are in Hertz.
[e] ^{31}P NMR shift (ppm from 85% H_3PO_4 in $DCCl_3$), 32.39.
[f] ppm from Me_4Si in H_3COD.

TABLE IV

^{13}C NMR shifts for the model alcohols[a,b]

Compd.	C(2), C(6)	C(3), C(5)	C(4)	Other
14a	49.64	38.52	67.52	$\underline{C}H_3$, 29.33; $\underline{C}H_2C_6H_5$; 62.91, Ar—$\underline{C}$, 137.94, 128.98, 127.89, 126.70
14b	24.31	39.51	67.79	$\underline{C}H_3$, 30.29
14c[c]	C(1), 68.72; C(2, 6), 39.25; C(3, 5), 22.61; C(4), 47.62; $C(\underline{C}H_3)_3$, 27.57; $\underline{C}(CH_3)_3$, 32.30			

[a] In $DCCl_3$ from $(CH_3)_4Si$.

[b] Reference 8.

[c] These data are presented separately since the numbering of the ring carbons differs from the numbering scheme for the heterocyclics.

one. A stereoview of **13b** is displayed in Figure 1.[31] The numbering scheme, bond distances, and angles are shown in Figure 2. Selected torsion angles are given in Table V. The molecule contains a lactone ring bound to two thiacyclohexyl rings. Both sulfur rings have chair conformations. Atom C(5) forms a spiro junction between the lactone ring and one sulfur ring with O(1) of the lactone bound axially. A methylene bridge joins the lactone ring and the other sulfur ring. A hydroxyl group is bound axially to the sulfur ring at the methylene juncture. In the crystal structure this latter sulfur ring is disordered. The disorder was resolved by placing the ring and hydroxyl atoms in two orientations with an occupancy ratio of 4 : 1.

The C—S distances of the ordered ring, 1.806(6) Å, are equal and only somewhat shorter than the 1.817(5) Å given by Sutton[32] as the mean for a paraffinic C—S distance. Although the average of the torsion angles in the six-membered ring [56.7(6)°] is slightly larger than that reported for cyclohexane (55.9°)[33], the two

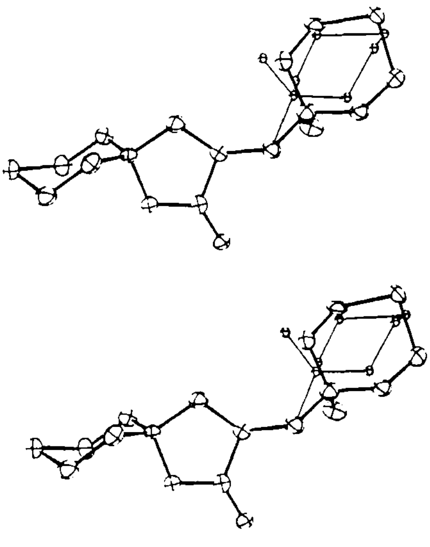


FIGURE 1 A stereoview of **13b**.

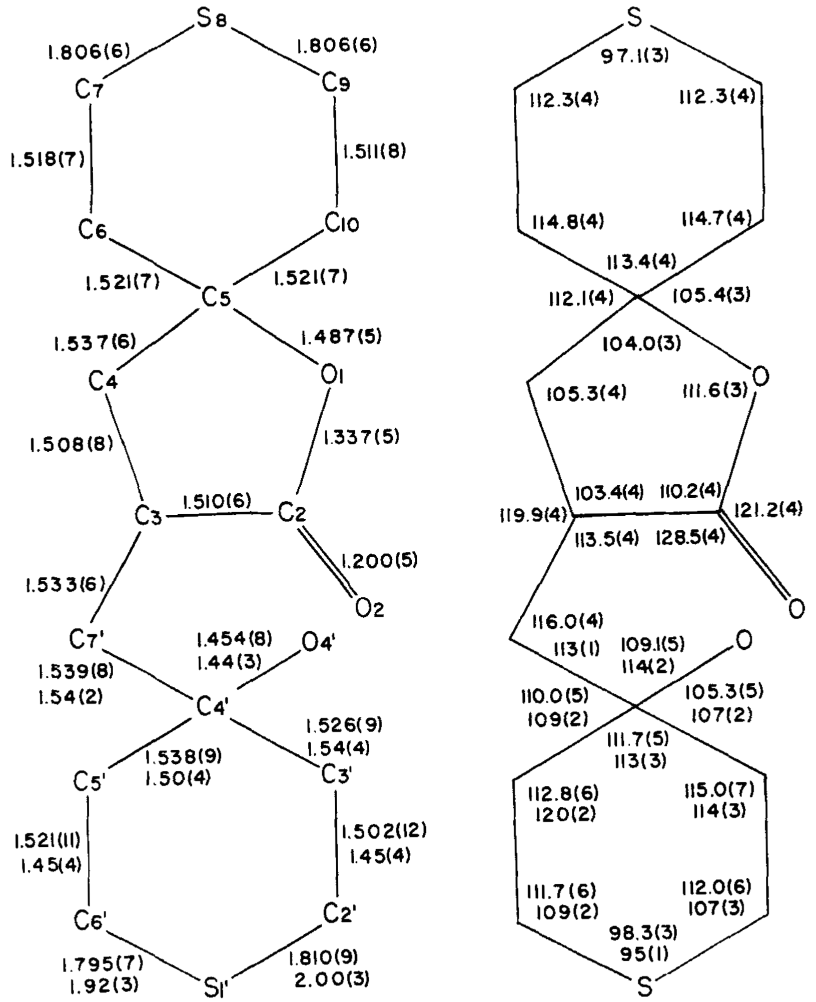


FIGURE 2 Bond distances and angles. Where two values are given, the upper value is for the 80% orientation and the lower value is for the 20% orientation. Other angles are O(1)—C(5)—C(6) 18.9(4)°, C(4)—C(5)—C(10), 113.1(4)°, C(3')—C(4')—C(7') 111.6(5)° and 106(2)°, O(4')—C(4')—C(5') 109.0(6) and 109(2)°. Standard deviations for last digit in parentheses.

torsion angles at the spiro junction of the sulfur ring [−53.5(6)° and 53.9(6)°] indicate a flattening of the ring at this point. This flattening is probably due to steric interactions between the lone pair of electrons on O(1) and the axial hydrogens on C(7) and C(9).

The torsion angles in the lactone ring indicate a twist (C_2) type of geometry with the twist axis running approximately through atom O(1) and bisecting the C(3)—C(4) bond. The bond distances in the lactone have values close to those reported for similar lactone rings.[34–36] Averages compiled from the literature are O(1)—C(2) 1.348, C(2)—O(2) 1.200, C(2)—C(3) 1.515, C(3)—C(4) 1.515, C(4)—C(5) 1.530, and C(5)—O(1) 1.468 Å. The two bonds to O(1) show the greatest differences, −0.011 Å

TABLE V

Selected torsion angles (°) for **13b**

				100,80%	20%
O(1)	C(2)	C(3)	C(4)	21.2(5)	
C(2)	C(3)	C(4)	C(5)	−22.7(5)	
C(3)	C(4)	C(5)	O(1)	17.3(5)	
C(4)	C(5)	O(1)	C(2)	−4.4(5)	
C(5)	O(1)	C(2)	C(3)	−10.6(5)	
C(5)	C(6)	C(7)	S(8)	59.5(5)	
C(6)	C(7)	S(8)	C(9)	−56.2(4)	
C(7)	S(8)	C(9)	C(10)	56.6(4)	
S(8)	C(9)	C(10)	C(5)	−60.2(5)	
C(9)	C(10)	C(5)	C(6)	53.9(6)	
C(10)	C(5)	C(6)	C(7)	−53.5(6)	
S(1′)	C(2′)	C(3′)	C(4′)	−59.6(9)	−66(4)
C(2′)	C(3′)	C(4′)	C(5′)	57.5(9)	61(4)
C(3′)	C(4′)	C(5′)	C(6′)	−58.4(9)	−58(3)
C(4′)	C(5′)	C(6′)	S(1′)	62.7(8)	60(3)
C(5′)	C(6′)	S(1′)	C(2′)	−56.3(6)	−54(2)
C(6′)	S(1′)	C(2′)	C(3′)	54.5(7)	59(2)

Standard deviation for last digit in parentheses.

to C(2) and 0.019 Å to C(5). The other differences are all less than 0.008 Å. The bond angles in the lactone ring show the same trends as those found in similar lactone rings.

The two orientations of the disordered sulfur ring are related by a simple rotation through an axis which runs close to the C(7′) and S(1′) positions. A comparison of the bond distances for the 80% occupied ring with those in the spiro-fused sulfur ring reveals no differences greater than 3σ. The bond angles and torsion angles suggest more puckering in the disordered sulfur ring than in the ordered ring. Because several atoms in the 20% orientation are near atom sites of the 80% orientation, the bond distances and angles for the 20% ring are of dubious quality. It is interesting to note that no intermolecular contacts were found which would prohibit the disordered model, although several contacts were of the order of the sum of the van der Waals radii. Molecular packing in the crystal structure is aided by the formation of a weak intermolecular hydrogen bond between O(2) and O(4′) (80%, $x^{-1}/2$, $1^1/2 - y$, $1 - z$), 2.889(8) Å.

EXPERIMENTAL SECTION

General data. Melting points were determined with a Thomas–Hoover capillary apparatus and were uncorrected. The ^1H, ^{13}C, and ^{31}P NMR data were obtained on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 PFT accessory operating at 100.1 MHz with tetramethylsilane (TMS) as internal standard for ^1H NMR, at 25.2 MHz (with TMS) for ^{13}C and at 40.5 MHz (with 85% H_3PO_4) for ^{31}P. The ^{13}C and ^{31}P NMR spectra were obtained operating in the FT mode utilizing broad-band proton decoupling and off-resonance decoupling. Infrared spectral data were obtained on a Perkin Elmer 681 Infrared Spectrometer. Mass spectral data were collected on a high resolution CEC Model 21-110B HR mass spectrometer. Microanalyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

Starting materials. Reagents (commercially available) were purified before use when necessary. THF and ether were distilled from lithium aluminum hydride. Diisopropylamine was distilled from CaH_2. Absolute ethanol was distilled from sodium metal. The preparation of the oxiranes **1a–f** will be reported elsewhere.[8]

cis-8-Benzyl-1-oxa-8-azaspiro[4.5]decan-2-one (**2a**). To a freshly prepared solution of sodium ethoxide from sodium (0.35 g, 15.22 mg at) in absolute ethanol (35 mL) was added diethyl malonate (2.4 g, 15.0 mmol) with stirring under reflux for 30 min (N_2). A solution of *cis*-6-benzyl-1-oxa-6-azaspiro[2.5]octane[8,37] (**1a**) (2.2 g, 10.84 mmol) in ethanol (10 mL) was added dropwise, and the solution was boiled for 3 h. After cooling it to room temperature, a solution of KOH (4 g, 0.07 mol) in water (2 mL) was added, and the new solution was gently boiled for 30 min. The reaction mixture was cooled in an ice bath for 1 h, and the precipitated solid was filtered and washed (absolute alcohol; 10 mL). The solid material dissolved in minimum amount of water (ca. 10 mL) and was carefully neutralized with 5% HCl to pH ≈ 7. This aqueous solution was evaporated to give a crystalline solid (presumably crude **4a**) which was heated to 150–160°C (oil bath) for 25 min under N_2. This new mixture was cooled to room temperature and was then leached with 10% $NaHCO_3$ (3 × 10 mL); the residue was dissolved in ether (30 mL) and dried (Na_2SO_4). Evaporation of the ether gave 1.6 g (60.4%) of **2a** as an oil which solidified upon standing: mp 63–64°C (hexane). Anal. Calcd. for $C_{15}H_{19}NO_2$: 245.1416; Found: 245.1409

1-Oxa-8-thiaspiro[4.5]decan-2-one (**2b**). This lactone was prepared in a manner similar to the preparation of the lactone **2a** and in a yield of 54%: mp 52°C (hexane). Anal. Calcd. for $C_8H_{12}O_2S$: 172.0558; Found: 172.0557.

cis-8-tert-Butyl-1-oxaspiro[4.5]decan-2-one (**2c**). This lactone **2c** was also prepared in a manner similar to the preparation of the lactone **2a** and in a yield of 65%; mp 69–70°C (petroleum ether; 40–60°C). It was also possible to obtain **2c** via use of a Meyer's reagent. The procedure followed for this lactone was a modification of the method developed by Meyers and co-workers.[38] A solution of 2,4,4-trimethyl-2-oxazoline (0.68 g, 6.00 mmol) in anhydrous THF (4 mL) was cooled to −78°C, and *n*-butyllithium (4.3 mL, 1.6 M in hexane) was added dropwise under N_2. The solution was stirred for 30 min and *cis*-8-*tert*-butyl-1-oxaspiro[2.5]octane[9] (**1c**) (1.0 g, 5.95 mmol) in THF (3 mL) was added dropwise, and the solution was stirred for 4 h at −78°C. The new solution was gradually warmed to room temperature over a period of 6 h, diluted with ice cold water (75 mL), acidified to pH ≈ 2 with 1 : 1 HCl : H_2O and extracted with ether (30 mL). The ether layer was rejected, and the aqueous phase was neutralized with 10% NaOH. This basic solution was extracted with ether (2 × 20 mL). The ether extracts were combined, dried (Na_2SO_4) and evaporated to give an oily product which was stirred with 3 *N* HCl (50 mL) at 70–80°C for 30 min. After cooling, the solution was extracted with ether (2 × 25 mL). The combined ether extracts were washed with water (3 × 10 mL) and dried ($MgSO_4$). Removal of ether gave an oil which solidified upon standing. Recrystallization (petroleum ether; 40–60°C) gave 0.48 g (38.4%) of **2c**: mp 69–70°C (lit.[39] mp 69°C).

3-Methylene-cis-8-benzyl-1-oxa-8-azaspiro[4.5]decan-2-one (**5a**)

Method A. To a boiling solution of sodio malonic ester, prepared from sodium (0.7 g, 0.03 g at) and freshly distilled diethyl malonate (4.80 g, 0.03 mol) in absolute ethanol (60 mL), was added a solution of *cis*-8-benzyl-1-oxa-azaspiro[2.5]octane[8,37] (**1a**) (4.40 g, 0.022 mol) in absolute ethanol (15 mL) under N_2. The solution was stirred under gentle reflux for 3 h and cooled to room temperature. A solution of potassium hydroxide (5.0 g, 0.089 mol) in water (3 mL) was then added, and the solution was boiled for 30 min. The reaction flask was cooled in an ice-water bath, and the solid that precipitated was filtered and washed with absolute ethanol (20 mL). This remaining solid was dissolved in a minimum volume of water (ca. 20 mL), and the pH of the solution was adjusted to 4–5 by dropwise addition of 1 : 1 HCl. A mixture of diethylamine (7.3 g, 0.1 mol) and formaldehyde (37%, 20 mL) was added, and the solution was stirred at 70–75°C (water bath) for 30 min. Sodium acetate (1.50 g, 0.011 mol) and glacial acetic acid (15.0 g, 0.25 mol) were then added, and the solution was stirred at 100°C for 1 h. The reaction mixture was cooled, basified with 5% sodium hydroxide and extracted with ether (3 × 75 mL). The ether extracts were combined and washed with a saturated solution of ammonium chloride (5 × 30 mL) and water, and then the solution was dried (Na_2SO_4). Evaporation of the ether gave a yellow viscous oil. Trituration with hexane (5 mL) gave crystalline solid **5a**, 4.0 g (71.81%), which displayed a single tlc spot on silica gel. Recrystallization (hexane) gave a sample of **5a** for analysis: mp 89–90°C. Anal. Calcd. for $C_{16}H_{19}NO_2$: 257.1416; Found: 257.1413.

Method B. In a 50 mL, three-necked, round-bottom flask fitted with a condenser, addition funnel and N_2 inlet was placed activated zinc[23] (0.72 g, 0.011 g at), anhydrous ether (10 mL) and two small crystals of iodine. The system was flushed with a steady stream of N_2. In the addition funnel was placed a solution of ethyl α-bromomethylacrylate[40] (1.93 g, 0.01 mol) in ether (5 mL). A few drops of the ester solution was added until the reaction was initiated (indicated by the clouding of the reaction mixture). Upon initiation (*and not before*), stirring was begun, and the rest of the ester was admitted into the flask while the materials in the flask were kept at 40–42°C (water bath). Every 10 min, 5–7 drops of the ester solution was added dropwise over a period of 2 h. After 1 h from initiation, another 0.72 g (0.011 g at) of zinc was added. The mixture was stirred for a further period of 2 h at 40–42°C. A solution of 1-benzyl-4-piperidone (1.89 g, 0.01 mol) in THF (5 mL) was then added dropwise, and the mixture was stirred for 3 h at the same temperature and was then allowed to cool to room temperature. It was poured into 5% ice cold sulfuric acid (100 mL) and kept at 0°C for 3 h. The acidic solution was basified with 10% NaOH solution and extracted with ether (2 × 25 mL). The combined ether extracts were washed with water and dried (Na_2SO_4). Removal of ether gave a viscous yellow oil which was chromatographed over silica gel. Elutions were performed with petroleum ether (40–60°C) (200 mL) followed by $HCCl_3$. The $HCCl_3$ eluant was evaporated to give a pale yellow oil which, upon repeated chromatography, gave lactone **5a** (10%). This compound was identical with the material obtained by the Method A.

Method C. To a freshly prepared solution of sodium ethoxide from sodium (0.47 g, 20.45 mg at) and ethanol (50 mL) was added diethyl malonate (3.0 g, 18.75 mmol), and the solution was boiled for 1 h under N_2. A solution of the oxirane **1a**[8,37] (3.9 g, 19.21 mmol) in ethanol (10 mL) was added and the solution was stirred under reflux for 3 h. The reaction mixture was cooled in an ice-water bath, and a solution of potassium hydroxide (4.0 g, 0.07 mol) in water (3 mL) was added. After boiling gently for 45 min, the reaction mixture was cooled to room temperature, filtered and washed with ethanol (10 mL). The solid material was dissolved in water (15 mL) and the pH of the solution was adjusted to ≈ 7.5 (pH paper) by the careful addition of 1 : 1 HCl. A mixture of diethylamine (5.0 g, 0.068 mol) and formaldehyde (37%, 15 mL) was added, and the solution was stirred at room temperature for 1 h and then at 60°C for 15 min. The resulting solution was cooled to room temperature and 5% NaOH (10 mL) was added. The basic solution was extracted with ether (3 × 25 mL). The ether extracts were combined, washed with a saturated solution of ammonium chloride (4 × 25 mL) and dried ($MgSO_4$). Evaporation of the ether gave an oil which solidified upon standing. The solid was recrystallized (hexane) to give 2.3 g (36.3%) of **6a**: mp 124–125°C; IR (KBr) 1770 cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.0 (t, 6 H, 2 $CH_2C\underline{H}_3$, $J = 6.0$ Hz), 1.52–3.00 [m, 17 H, H(3), H(4), H(6), H(7), H(9), H(10), H(11), H(13), H(13′)], 3.52 (s, 2 H, $C\underline{H}_2C_6H_5$), 7.22 × 7.40 [m, 5 H, Ar$\underline{H}$]. Anal. Calcd. for $C_{20}H_{30}N_2O_2$: 330.2305; Found: 330.2314.

The aminolactone **6a** [1.0 g, 3.0 mmol] was dissolved in 5 mL of absolute methanol and cooled to 0°C. Methyl iodide (0.9 g, 6.34 mmol) was added and the solution was stirred at 0°C for 5 min. and at room temperature for 10 min. A 10% $NaHCO_3$ solution (15 mL) was added, and the mixture was stirred for an additional 20 min and was then extracted with ether (2 × 20 mL). The ether extracts were combined, washed with water (10 mL) and dried (Na_2SO_4). Removal of ether gave a pasty solid which was purified by chromatography over silica gel using $HCCl_3$ as the eluant to give the α-methylenelactone **5a**, [0.6 g (77.02%); 26.13% overall yield based on the oxirane **1a**]. This product was identical to the lactone obtained by the methods A and B.

3-Methylene-1-oxa-8-thiaspiro[4.5]decan-2-one (**5b**). To a freshly prepared solution of sodium ethoxide [from sodium (0.92 g, 0.04 mol) in absolute ethanol (60 mL)] was added a solution of diethyl malonate (5.92 g, 0.037 mol) in ethanol (10 mL) under N_2. This solution was stirred under reflux for 30 min, and a solution of 1-oxa-6-thiaspiro[2.5]octane[8] (**1b**) (4.2 g, 0.032 mol) in ethanol (20 mL) was added dropwise over a period of 45 min. The solution was boiled for 3 h and cooled to room temperature. To this was added a solution of KOH (6.0 g, 0.107 mol) in water (4 mL), and the mixture was gently boiled for 20 min and cooled. The precipitate that formed was filtered and washed (absolute ethanol; 20 mL). The solid material dissolved in water (ca. 15 mL) and the solution was acidified (pH ≈ 6–5). A mixture of formaldehyde (37%, 25 mL) and diethylamine (7.0 g, 0.096 mol) was added and stirred at 70–75°C for 1 h. Sodium acetate (1.0 g, 7.35 mmol) and glacial acetic acid (10.0 g, 0.17 mol) were then added and, the solution was stirred for another 1 h at 90–95°C. After cooling to room temperature, the solution was neutralized (5% NaOH solution) and extracted (ether; 3 × 40 mL). The combined ether extracts were washed with 1 : 1 HCl (10 mL), a saturated $NaHCO_3$ and brine and then were dried ($MgSO_4$). Evaporation of the ether gave 3.8 g (64.4%) of **5b**: mp 94–95°C (diethyl ether) (lit.[24] mp 94–95°C). Anal. Calcd. for $C_9H_{12}O_2S$: 184.0558; Found: 184.0564.

*Cis-***8***-tert-Butyl-3-methylene-1-oxaspiro[4.5]decan-2-one* (**5c**). *cis*-6-*tert*-Butyl-1-oxaspiro[2.5]octane[9] (**1c**) (2.52 g, 15.0 mmol) was added dropwise to a boiling solution of sodio diethyl malonate prepared from sodium (0.35 g, 15.0 mg at) and diethyl malonate (2.39 g, 15.0 mmol) in absolute ethanol (75 mL). The remaining procedure was as described previously for **5a** and gave 2.5 g (75%) of **5c**: mp 83–84°C (methanol) (lit.[25] mp 83–84°C).

3-Methylene-cis-8-phenyl-1-oxa-8-phosphaspiro[4.5]decan-2-one 8-sulfide (**5d**)

Method A. This lactone was prepared by the method described for **5a** and started from *cis*-6-phenyl-1-oxa-6-phosphaspiro[2.5]octane 6-sulfide[8] (**1d**) (2.38 g, 0.01 mol), sodium (0.46 g, 0.02 g at) and diethyl malonate (3.2 g, 0.02 mol) in absolute ethanol (40 mL). Chloroform (2 × 30 mL) was used to extract the lactone instead of ether to give **5d** (1.6 g; 54.8%): mp 185–186°C (ethanol). Anal. Calcd. for $C_{15}H_{17}O_2PS$: 292.0687; Found: 292.0695.

Method B. The Reformatsky reagent was formed as described for **5a** and started with ethyl α-bromomethylacrylate[40] (0.43 g, 2.23 mmol) and activated zinc[23] (0.30 g, 4.62 mg at). A solution of 1-phenyl-4-phosphorinanone 1-sulfide[41] (**18b**) (0.5 g, 2.23 mmol) in anhydrous THF (7 mL) was added dropwise. This product was worked up as given above. ^{31}P NMR analysis of the crude product showed the presence of the starting ketone and the α-methylenelactone in the ratio 3 : 1. This crude product was chromatographed over neutral alumina using $HCCl_3$ as the eluant. The initial fractions gave the unreacted ketone (0.28 g). Later fractions were collected and rechromatographed. The pure lactone **5d** was eluted with $HCCl_3$; yield, 0.08 g (29.6% based on the amount of unreacted ketone recovered). This compound was identical with the lactone obtained by the Method A.

3-Methylene-1,8-dioxaspiro[4.5]decan-2-one (**5e**). A solution of 1,6-dioxaspiro[2.5]octane[8] (**1e**) (1.0 g, 8.77 mmol) in absolute ethanol (5 mL) was added dropwise to a boiling solution of sodio diethyl malonate prepared from sodium (0.25 g, 10.87 mg at) and freshly distilled diethyl malonate (1.6 g, 10.00 mmol) in absolute ethanol (20 mL) under N_2. The solution was boiled for 3 h and cooled to 40°C. A solution of KOH (3.5 g, 0.063 mol) in water (3 mL) was added, and the mixture was gently boiled for 15 min. Removal of the alcohol via evaporation gave a solid mass which was dissolved in water (5 mL). The solution was acidified with 1 : 1 HCl : H_2O to pH ≃ 6.5 (pH paper) and was then heated to 65–70°C (water bath). A mixture of formaldehyde (37%, 10 mL) and diethylamine (3.5 g, 0.048 mol) was added; the resulting mixture was stirred at 70°C for 45 min. Sodium acetate (0.5 g, 3.68 mmol) and glacial acetic acid (5.0 g, 0.083 mol) were added, and this solution was stirred at 100°C for 30 min. Concentration of the solution gave a slurry mass which was leached with boiling ether (7 × 10 mL). The combined ether extracts were washed with saturated NH_4Cl solution (4 × 15 mL) and dried (Na_2SO_4). Evaporation of the ether gave a pale yellow oil which was distilled twice to give pure lactone **5e**, 0.64 g (43.5%): bp 76–77°C (1.5 mm) Anal. Calcd. for $C_9H_{12}O_3$: 168.0786; Found: 168.0781.

3-Methylene-cis-8-trans-8-dibenzyl-1-oxa-8-azaspiro[4.5]decan-2-one (**9**). To a solution of 3-methylene-*cis*-8-benzyl-1-oxa-8-azaspiro[4.5]decan-2-one (**5a**) (0.5 g, 1.95 mmol) in absolute methanol (4 mL) was added benzyl bromide (0.43 g, 2.50 mmol), and the solution was stirred at room temperature for 7 h. The new solution was diluted with anhydrous ether (25 mL) and left overnight. Shining crystals of the bromide were filtered and washed with ether (10 mL). Recrystallization (methanol/ether) gave 0.49 g (59%) of **9**: mp 181–182°C. Anal. Calcd. for $C_{23}H_{26}BrNO_2$. $1/2H_2O$: C, 63.16; H, 6.22; N, 3.20. Found: C, 63.10; H, 6.30; N, 3.20.

trans-7,9-Diphenyl-1-oxa-8-thiaspiro[4.5]decan-2-one (**12**). This method is a modified version of that of Creger.[26] To an ice-cold solution of diisopropylamine (10.1 g, 0.10 mol) in anhydrous THF (150 mL) was added *n*-butyllithium (1.6 M, 63 mL, 0.10 mol) dropwise under N_2 over a period of 15 min. The solution was stirred at 0°C for 20 min. and glacial acetic acid (3.0 g, 0.05 mol) in THF (10 mL) was added. This mixture was gradually warmed to 35–40°C and stirred at that temperature for another hour. A solution of *trans*-5,7-diphenyl-1-oxa-6-thiaspiro[2.5]octane (**1f**)[8] (2.82 g, 0.01 mol) in THF (25 mL) was added to the above mixture, and the new solution was stirred under gentle reflux (24 h). The reaction mixture was cooled to room temperature and water (100 mL) was added; the mixture was stirred at 50°C for 30 min. After cooling to room temperature, the aqueous layer was separated from the organic layer. The organic phase was washed with water (2 × 20 mL), and the washings were added to the aqueous phase. The combined aqueous layer was washed with ether (30 mL), and the ether layer was mixed with the organic phase. Removal of the organic solvents gave unreacted oxirane **1f** (0.8 g). The aqueous phase was cooled to 0°C, acidified with 5% sulfuric acid and stirred for 2 h. The solid that separated was filtered, washed with water and dried to yield 1.20 g (52.17%; based on the unreacted oxirane recovered) of **12**: mp 211–212°C (ethanol/water). Anal. Calcd. for $C_{20}H_{20}O_2S$: 324.1184; Found: 324.1190.

Addition of metalated acetic acid to cis-6-benzyl-1-oxa-6-azaspiro[2.5]-octane (**1a**). *Synthesis of* **13a**. A solution of lithium diisopropylamide (LDA) was prepared from diisopropylamine (10.1 g, 0.01 mol) and *n*-butyllithium (1.6 M, 63 mL, 0.10 mol) in THF (175 mL) at 0°C as described above. A solution of glacial acetic acid (3.0 g, 0.05 mol) in THF (7 mL) was added dropwise to the LDA solution under N_2. The mixture was stirred at 0°C for 20 min and then at 35–40°C for 45 min. A solution of *cis*-6-benzyl-1-oxa-6-azaspiro[2.5]octane[8,37] (**1a**) (2.50 g, 12.32 mmol) in anhydrous THF (10 mL) was added to the metalated acetic acid solution, and the new solution was stirred at 45–50°C for 20 h. After the reaction mixture was cooled to room temperature, water (200 mL) was added and two layers separated. The organic layer was dried (Na_2SO_4) and evaporated to give the unreacted oxirane **1a** (0.7 g). The aqueous phase was cooled to 0°C and acidified with 1 : 10 sulfuric acid : H_2O and kept at 0°C for 2 h. The acidic solution was carefully neutralized with 5% sodium hydroxide solution and extracted with ether (2 × 50 mL). The combined ether layer was washed with water and dried (Na_2SO_4). Removal of the solvent gave a white crystalline product which was recrystallized (benzene/hexane) to give 0.5 g (25.3%; based on the unreacted oxirane **1a** recovered) of **13a**: mp 124–125°C. Anal. Calcd. for $C_{28}H_{36}N_2O_3$: 448.2726; Found: 448.2731.

Addition of metalated acetic acid to 1-oxa-6-thiaspiro[2.5]octane (**1b**). *Synthesis of* **13b**. Metalated acetic acid was prepared from glacial acetic acid (3.0 g, 0.05 mol) and a solution of LDA in THF (150 mL) as described above. The oxirane **1b**[9] (1.5 g, 11.5 mmol) in THF (15 mL) was added to the metalated carboxylic acid, and the solution was gently boiled for 15 h. The reaction mixture was cooled to room temperature; water (150 mL) was added and the mixture was stirred at 50°C for 30 min. After cooling again to room temperature, ether (50 mL) was added and the aqueous layer was separated. Evaporation of ether gave the unreacted oxirane (0.35 g). The aqueous layer was cooled to 0°C and dilute sulfuric acid (1 : 10, 30 mL) was added. The solution was stirred at 0°C for 4 h and extracted with chloroform (2 × 30 mL). The combined chloroform extracts were washed with saturated $NaHCO_3$ solution and water and then were dried ($MgSO_4$). Evaporation of the chloroform layer gave a viscous oil which was leached with boiling hexane (6 × 10 mL). The hexane solution was concentrated to about 15 mL and the residual liquid was refrigerated for 24 h to give a colorless crystalline **13b** (0.3 g; 22.5%; based on the unreacted oxirane recovered). Recrystallization (benzene/hexane) produced a sample of **13b** for analysis: mp 116–117°C. Anal. Calcd. for $C_{14}H_{22}O_3S_2$: 302.1010; Found: 302.1009.

TABLE VI

Experimental X-ray data for **13b**

(a) Physical and crystallographic data

Formula	$C_{14}H_{22}O_3S_2$	
Formula wt.	302.46 g/mole	
Space group	$P2_12_12_1$ ($Z = 4$)	
Lattice constants	room temp	138(2)K
Radiation	CuKα_1	MoKα_1
a (Å)	6.0131(10)	5.916(2)
b (Å)	11.631(2)	11.585(3)
c (Å)	22.094(5)	21.986(5)
Vol (Å^3)	1545.22	1506.85
ρ^c	1.300 g/cm^3	
ρ^o	1.287 g/cm^3	
Crystal size	0.19 × 0.15 × 0.28 mm	
μ	3.04 cm^{-1}	

(b) Data collection and refinement

Radiation	MoKα
Maximum 2θ	50°
Scan mode and range	$\omega - 2\theta$, (0.70 + 0.20 tan)°
Horizontal aperture	(3.50 + 0.86 tan θ)mm
Vertical aperture	4 mm
Unique reflections	1556
Observed data	1319 ($F > 4\sigma(F)$)
R (obsd)	0.045
R_w (obsd)	0.048
R (total)	0.056

Reaction of cis-6-tert-butyl-1-oxaspiro[2.5]octane (**1c**) *with metalated acetic acid. Synthesis of* **13c**. To a solution of LDA prepared from diisopropylamine (10.1 g, 0.10 mol) and *n*-butyllithium (1.6 M, 63 mL, 0.10 mol) in THF (150 mL), a solution of glacial acetic acid (3.0 g, 0.05 mol) in THF (10 mL) was added at 0°C under N_2. After stirring the mixture at 30–35°C for 30 min., a solution of *cis*-6-*tert*-butyl-1-oxaspiro[2.5]octane (**1c**)[9] (1.68 g, 0.01 mol) in anhydrous THF (10 mL) was added, and the mixture was stirred under gentle reflux for 15 h. The reaction mixture was cooled to room temperature and diluted with water (100 mL). Ether (50 mL) was added and two layers separated. The organic layer was dried ($MgSO_4$) and evaporated to give the unreacted oxirane **1c** (0.3 g). The aqueous layer on workup as described previously gave crude **13c** as a pale brown solid, 0.5 g (32.3%; based on the unreacted oxirane **1c** recovered). An analytical sample was prepared by recrystallization (methanol/water): mp 128–130°C. Anal. Calcd. for $C_{24}H_{42}O_3$: 378.3133; Found: 378.3111.

Crystal data. A summary of the experimental data for **13b** is presented in Table VI. Colorless, rectangular prisms were grown by evaporation from a benzene/hexane solution. Lattice constants were determined by a least-squares fit of the $\pm 2\theta$ values of selected intensity maxima from all regions of reciprocal space. Both lattice constants measurements and intensity data were collected on an Enraf-Nonius CAD-4 instrument. Intensity data were measured at low temperature [138(2) K] using graphite-monochromated MoKα radiation. Three monitor reflections, remeasured after every 2 hours of X-ray exposure, showed no appreciable decomposition of the crystal during data collection. From a total of 1556 unique reflections with $2\theta < 50°$, 1319 reflections were considered observed ($F > 4\sigma(F)$) and were used in subsequent calculations. Intensity data were corrected for Lorentz and polarization effects; no absorption correction was applied ($\mu = 3.04$ cm^{-1}). The systematic absences $h00$ $h = 2n + 1$, $0k0$ $k = 2n + 1$, and $00l$ $l = 2n + 1$ uniquely determined the space group to be $P2_12_12_1$.

The positions of the sulfur atoms were determined from a Patterson map. The positions of the remaining nonhydrogen atoms were revealed in subsequent structure factor and electron density calcula-

TABLE VII

Positional ($\times 10^4$ for O(1)—S(1′A) and $\times 10^3$ for others) parameters and isotropic or isotropic equivalent ($\times 10^3$) temperature factors for nonhydrogen atoms in **13b**

	x	y	z	$U(f^2)$
O(1)	5825(6)	5538(2)	4686(1)	23(2)
C(2)	6949(7)	6539(4)	4687(2)	18(2)
O(2)	7819(6)	6900(2)	5142(1)	24(2)
C(3)	7025(9)	7040(4)	4054(2)	25(2)
C(4)	5076(10)	6455(4)	3737(2)	27(3)
C(5)	4649(8)	5340(4)	4097(2)	21(2)
C(6)	5721(10)	4293(4)	3795(2)	27(3)
C(7)	5478(11)	3172(4)	4145(2)	33(3)
S(8)	2545(3)	2788(1)	4267(1)	39(1)
C(9)	1704(10)	4106(5)	4642(2)	33(3)
C(1)	2175(10)	5163(4)	4260(2)	29(3)
C(7′)	7218(11)	8360(4)	4044(2)	27(2)
S(1′)[a]	9569(4)	10463(2)	2372(1)	33(2)
C(2′)	9577(19)	8902(8)	2411(4)	30(6)
C(3′)	8110(15)	8460(5)	2918(3)	29(4)
C(4′)	8776(12)	8871(5)	3552(3)	28(3)
O(4′)	11061(8)	8445(4)	3645(2)	34(3)
C(5′)	8787(16)	10195(6)	3596(3)	28(4)
C(6′)	10388(16)	10757(6)	3143(3)	38(5)
S(1′A)[a]	10705(21)	10431(10)	2551(5)	65(3)
C(2′A)	767(6)	1080(2)	290(1)	40(6)
C(3′A)	746(9)	1018(3)	347(2)	28(7)
C(4′A)	742(5)	885(2)	349(1)	17(5)
O(4′A)	551(3)	858(1)	301(1)	22(4)
C(5′A)	953(5)	839(2)	311(1)	25(6)
C(6′A)	1022(5)	880(3)	251(1)	5(7)

[a] Atoms S(1′) through C(6′) at 80% occupancy and atoms S(1′A) through C(6′A) at 20% occupancy.

tions. The high temperature factors in the methylene bridged sulfur ring as well as the presence of additional peaks around this ring in an electron density difference map suggested that this ring was disordered. A model which placed this sulfur ring in two orientations with an occupancy ratio of 4 : 1 gave the best agreement with the observed data. Hydrogen atoms bonded to the lactone ring, the spiro-fused sulfur ring, and the 80% sulfur ring were located on an electron-density difference map and included in subsequent refinement cycles. The function minimized was $\Sigma\omega(|F_0| - |F_c|)^2$ with weights of $w = 1/\sigma^2(F)$. The positional parameters of all atom sites were refined. The ordered, nonhydrogen atoms and the 80% sulfur ring atoms were refined anisotropically; the remaining nonhydrogen atoms were refined isotropically; and the hydrogen atoms were refined with fixed temperature factors of $U^2 = 0.04$ Å^2. The full-matrix least squares refinement converged to a final conventional R value 0.045 and weighted R_w value 0.048 for 1319 data. The final difference electron density map contained no peaks larger than 0.36 $e^-/$Å^3. An analysis of $w\Delta^2$ as a function of $\sin(\theta)$ and F revealed no significant deviations in the variance. Computer programs used for structure factor, least-squares refinement, and Fourier calculations were from the SHELX 76 package.[42] Positional and isotropic or isotropic equivalent thermal parameters for the nonhydrogen atoms are given in Table VII.[43]

ACKNOWLEDGMENTS

This work was supported in part by grants from the U.S.P.H.S. through the National Institutes of Health, National Cancer Institute, grants CA 22770 (to KDB) and CA 17562 (To DvdH). We gratefully acknowledge the help of Dr. K. Leoning, Director of Nomenclature of Chemical Abstracts, in naming some of the compounds cited herein.

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