

# $^{13}\text{C}$ Nuclear Magnetic Resonance Spectra of Saturated Heterocycles. 3.<sup>1a,b</sup> 1,3-Dithianes

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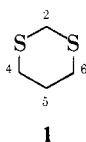
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**Abstract:**  $^{13}\text{C}$  NMR spectral data of 56 1,3-dithianes are reported. Substituent parameters for alkyl groups at C-2, C-4, C-5, and C-6 acting at C-2, C-4, C-5, and C-6 are evaluated by multiple linear regression analysis. The dithiane parameters are qualitatively similar to those in 1,3-dioxane and cyclohexane except for the  $\alpha$ -axial effect of a methyl group at C-5 which is upfield rather than downfield shifting. Also, the relative shifts of methyl substituents at C-2 are the reverse of what is found in cyclohexane and at C-2 in 1,3-dioxane, with the axial methyl group resonating downfield of the equatorial one.

Grant and co-workers, in a series of investigations,<sup>2</sup> have studied the  $^{13}\text{C}$  chemical shifts of axial and equatorial methyl groups in methylcyclohexanes and the effect such groups have on the chemical shifts of the ring carbons in the  $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$  positions. Because of the rigidity of the chair form of cyclohexane,<sup>3</sup> the spatial relationships of the substituents and ring carbons are well defined and the effect of the substituents on the chemical shifts (shift parameters) can thus be evaluated without complications due to conformation heterogeneity.

It is obviously of interest to extend such observations to ring systems containing heteroatoms, such as O, S, and N. The introduction of such heteroatoms in a conformationally well-defined framework<sup>4</sup> not only changes the basic chemical shifts of the framework carbons but also alters the effect of methyl (and other) substituents on these shifts. Hopefully such changes will eventually be interpretable in terms of a theory of the chemical shift and may serve to contribute to the development of such a theory.

In previous papers<sup>1a,5</sup> we have discussed chemical shifts in the 1,3-dioxane system. The present account deals with 1,3-dithiane (**1**), a molecule which has been extensively studied by



one of us<sup>6</sup> as well as elsewhere.<sup>7</sup> Chemical shift data for 1,3-dithiane and a number of methyl and *tert*-butyl homologues (56 compounds in all) are given in Table I. Most of the compounds listed were either available from previous work<sup>6</sup> or were obtained by standard syntheses described there;<sup>6</sup> a few special cases are discussed at the end of the Discussion section. Assignment of configuration, where diastereoisomers exist, is usually straightforward on the basis of  $^1\text{H}$  NMR spectra (see Experimental Section). Assignment of  $^{13}\text{C}$  NMR signals can be made by analogy with the  $^{13}\text{C}$  NMR spectrum of thiane:<sup>1b</sup>  $C_\alpha$ , 29.1;  $C_\beta$ , 27.8;  $C_\gamma$ , 26.5 ppm (compare cyclohexane 27.7 ppm<sup>8</sup>). Thus the most downfield signal in 1,3-dithiane (Table I, **1**), 31.95 ppm, was assigned to C-2, the next one downfield, 29.86 ppm, to C-4,6 (corroborated by double signal intensity), and the most upfield one, 26.59 ppm, to C-5. The spectra of the substituted 1,3-dithianes were in accord with these assignments and, in turn, permitted assignments of their own if one takes the Dalling-Grant parameters<sup>2c,8</sup> for methyl substituents in cyclohexanes to be qualitatively applicable to dithiane. The assignments given in Table I were made in this fashion.

It is customary,<sup>2,5</sup> in the absence of contrary indications, to assume that shift parameters are additive. For example, in *trans*-2,5-dimethyl-1,3-dithiane one assumes that the chemical

shifts at C-4,6 can be computed by adding, to the corresponding shift in 1,3-dithiane, an invariant parameter corresponding to the equatorial methyl group at C-2 ( $\gamma_e$  shift from C-2) plus a parameter corresponding to the equatorial methyl group at C-5 ( $\beta_e$  shift from C-5). Thus, in principle at least, every one of the nearly 200 chemical shifts listed in Table I can be computed by an addition of appropriate parameters to the three (2, 4-6, 5) shifts in 1,3-dithiane (entry 1) itself, i.e.,

$$\delta_x = \delta_p + \sum n_x^y \quad (1)$$

where  $\delta_x$  is the chemical shift of a given carbon atom in a substituted 1,3-dithiane,  $\delta_p$  is the shift of the same atom in the parent 1,3-dithiane, and  $n_x^y$  are parameters representing the effect of substituents  $y$  (classified as to their nature, site, and configuration or conformation) acting at position  $x$ . Equation 1 represents an overdetermined set of linear equations (since there are many more shifts than parameters) and thus optimized parameters can be determined by multiple linear regression analysis. We have done this for C-2, C-4,6, and C-5 with the results indicated in the following tables which will be discussed in the sequel.

In Table II, column 2, are listed the parameters needed to compute the shifts at C-2. In addition to parameters for equatorial and axial methyl groups at C-2, C-5, and C-4, and for several larger alkyl groups, it includes four geminal parameters required to fit compounds which have two substituents on the same carbon. With these 15 parameters it proved possible to fit 46 compounds with a mean square residual of 0.29<sub>5</sub> ppm. For 21 compounds the calculated shift agreed with the experimental to within 0.25 ppm. An error exceeding 0.5 ppm was encountered for only 13 compounds, the maximum discrepancy being 1.00 ppm (compounds **20**, **22**, and **39** were omitted in the correlation here and in later tables for lack of overlapping parameters; compounds **37**, **48**, **49**, **52**, **54**, and **56** because they exist largely in nonchair forms<sup>9</sup>). The calculated and observed parameters and residuals for these compounds are shown in Table IX in the Appendix.<sup>10</sup>

Comparison of the agreement of calculated and observed shifts in 1,3-dithianes with 1,3-dioxanes<sup>5</sup> shows that the fit is generally less good for the sulfur analogues. Very likely this is due to the energetically low-lying twist-boat form in 1,3-dithiane which causes boat or twist conformations to make appreciable contributions in even moderately congested 1,3-dithianes.<sup>6,7</sup> We therefore attempted to take twist conformations into account, calculating the approximate percentage of twist by using the energy parameters reported by Pihlaja.<sup>7</sup>

The equation corresponding to (1) for compounds partially in the twist form is

$$\delta_x = n_{\text{chair}}(\delta_p + \sum n_x^y) + n_{\text{twist}}(\delta_{p'} + \sum n_x^{y'}) \quad (2)$$

Table I. <sup>13</sup>C Chemical Shifts of 1,3-Dithianes

Dithiane	C-2	C-4	C-5	C-6	Other
1 Parent	31.95	29.86	26.59	29.86	
2 2-Methyl	42.15	30.92	25.51	30.92	2-CH <sub>3</sub> 21.12
3 2-Isopropyl	56.20	30.74	26.32	30.74	2-CH(CH <sub>3</sub> ) <sub>2</sub> 33.53 2-CH(CH <sub>3</sub> ) <sub>2</sub> 19.95
4 2- <i>tert</i> -Butyl	61.78	31.18	25.97	31.18	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.67 2-C(CH <sub>3</sub> ) <sub>3</sub> 27.85
5 2-Phenyl	51.30	31.90	25.00	31.90	
6 2,2-Dimethyl	45.05	26.97	25.18	26.97	2-(CH <sub>3</sub> ) <sub>2</sub> 30.75
7 2-Methyl-2- <i>tert</i> -butyl	59.42	26.47	25.44	26.47	2-CH <sub>3</sub> 23.51 2-C(CH <sub>3</sub> ) <sub>3</sub> 39.44 2-C(CH <sub>3</sub> ) <sub>3</sub> 25.74
8 <i>cis</i> -2,5-Dimethyl	41.56	36.26	25.20	36.26	2-CH <sub>3</sub> 21.55 5-CH <sub>3</sub> 17.44
9 <i>trans</i> -2,5-Dimethyl	41.75	38.06	30.83	38.06	2-CH <sub>3</sub> 20.20 5-CH <sub>3</sub> 22.30
10 <i>cis</i> -2- <i>tert</i> -Butyl-5-methyl	61.79	37.23	24.29	37.23	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.99 2-C(CH <sub>3</sub> ) <sub>3</sub> 27.86 5-CH <sub>3</sub> 16.37
11 <i>trans</i> -2- <i>tert</i> -Butyl-5-methyl	61.32	38.12	31.70	38.12	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.36 2-C(CH <sub>3</sub> ) <sub>3</sub> 28.05 5-CH <sub>3</sub> 22.20
12 5- <i>tert</i> -Butyl	31.25	31.02	47.25	31.02	5-C(CH <sub>3</sub> ) <sub>3</sub> 33.97 5-C(CH <sub>3</sub> ) <sub>3</sub> 27.01
13 <i>trans</i> -2-Methyl-5- <i>tert</i> -butyl	41.72	32.22	46.38	32.22	5-C(CH <sub>3</sub> ) <sub>3</sub> 33.67 5-C(CH <sub>3</sub> ) <sub>3</sub> 27.28 2-CH <sub>3</sub> 20.22
14 <i>cis</i> -2-Methyl-5- <i>tert</i> -butyl	35.86	25.30	46.87	25.30	5-C(CH <sub>3</sub> ) <sub>3</sub> 34.03 5-C(CH <sub>3</sub> ) <sub>3</sub> 27.11 2-CH <sub>3</sub> 23.61
15 <i>trans</i> -2,5-Di- <i>tert</i> -butyl	61.31	32.37	46.98	32.37	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.37 2-C(CH <sub>3</sub> ) <sub>3</sub> 28.00 5-C(CH <sub>3</sub> ) <sub>3</sub> 33.71 5-C(CH <sub>3</sub> ) <sub>3</sub> 27.24
16 <i>trans</i> -2-Phenyl-5- <i>tert</i> -butyl	51.24	33.55	46.26	33.55	5-C(CH <sub>3</sub> ) <sub>3</sub> 33.83
17 4-Methyl	32.36	38.12	35.29	30.19	4-CH <sub>3</sub> 21.98
18 <i>cis</i> -2,4-Dimethyl	43.13	39.49	34.20	31.48	4-CH <sub>3</sub> 21.70 2-CH <sub>3</sub> 20.66
19 <i>cis</i> -2-Ethyl-4-methyl	50.57	39.39	35.00	31.28	2-CH <sub>2</sub> CH <sub>3</sub> 28.45 2-CH <sub>2</sub> CH <sub>3</sub> 11.43 4-CH <sub>3</sub> 21.83
20 <i>trans</i> -2-Ethyl-4-methyl	44.27	33.06	33.78	24.73	2-CH <sub>2</sub> CH <sub>3</sub> 29.27 2-CH <sub>2</sub> CH <sub>3</sub> 12.60 4-CH <sub>3</sub> 21.09
21 <i>cis</i> -2-Isopropyl-4-methyl	57.20	39.54	35.20	31.25	2-CH(CH <sub>3</sub> ) <sub>2</sub> 33.34 2-CH(CH <sub>3</sub> ) <sub>2</sub> 19.97 4-CH <sub>3</sub> 21.93
22 <i>trans</i> -2-Isopropyl-4-methyl	49.88	33.70	33.09	25.00	2-CH(CH <sub>3</sub> ) <sub>2</sub> 32.79 2-CH(CH <sub>3</sub> ) <sub>2</sub> 20.80 4-CH <sub>3</sub> 20.86
23 <i>cis</i> -2- <i>tert</i> -Butyl-4-methyl	62.72	39.93	34.95	31.55	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.59 2-C(CH <sub>3</sub> ) <sub>3</sub> 28.09 4-CH <sub>3</sub> 22.09
24 <i>trans</i> -2- <i>tert</i> -Butyl-4-methyl	53.95	34.82	31.85	25.47	2-C(CH <sub>3</sub> ) <sub>3</sub> 36.11 2-C(CH <sub>3</sub> ) <sub>3</sub> 27.88 4-CH <sub>3</sub> 20.17
25 2,2,4-Trimethyl	47.20	35.12	34.35	27.83	2-CH <sub>3</sub> 31.50 (a or e) 2-CH <sub>3</sub> (e or a) 30.71 4-CH <sub>3</sub> 21.38
26 <i>r</i> -2- <i>tert</i> -Butyl-2, <i>cis</i> -4-dimethyl	61.39	34.65	34.85	27.38	2-C(CH <sub>3</sub> ) <sub>3</sub> 39.16 2-C(CH <sub>3</sub> ) <sub>3</sub> 25.92 2-CH <sub>3</sub> 24.18 4-CH <sub>3</sub> 21.70
27 5,5-Dimethyl	31.55	41.99	26.99	41.99	5-CH <sub>3</sub> 27.56
28 2,5,5-Trimethyl	41.88	42.78	25.64	42.78	2-CH <sub>3</sub> 20.42 5-CH <sub>3</sub> (e) 30.62 5-CH <sub>3</sub> (a) 23.53
29 2- <i>tert</i> -Butyl-5,5-dimethyl	61.74	43.21	26.51	43.21	2-C(CH <sub>3</sub> ) <sub>3</sub> 35.47 2-C(CH <sub>3</sub> ) <sub>3</sub> 27.98 5-CH <sub>3</sub> (e) 30.58 5-CH <sub>3</sub> (a) 23.39

Table I(Continued)

	Dithiane	C-2	C-4	C-5	C-6	Other	
30	2-Phenyl-5,5-dimethyl	51.46	44.25	25.75	44.25	5-CH <sub>3</sub> (e)	31.00
						5-CH <sub>3</sub> (a)	23.42
31	2,2,5,5-Tetramethyl	44.79	39.48	25.77	39.48	2-CH <sub>3</sub>	30.18
						5-CH <sub>3</sub>	26.98
32	2- <i>tert</i> -Butyl-2,5,5-trimethyl	60.84	39.68	28.15	39.68	2-C(CH <sub>3</sub> ) <sub>3</sub>	40.03
						2-C(CH <sub>3</sub> ) <sub>3</sub>	25.92
						2 or 5 (a)-CH <sub>3</sub>	24.01
						5 (a) or 2-CH <sub>3</sub>	24.78
						5-CH <sub>3</sub> (e)	29.02
33	<i>cis</i> -4,6-Dimethyl	33.34	39.21	44.57	39.21	4,6-CH <sub>3</sub>	21.90
34	<i>r</i> -2, <i>cis</i> -4, <i>cis</i> -6-Trimethyl	43.48	39.86	43.25	39.86	2-CH <sub>3</sub>	20.22
						4,6-CH <sub>3</sub>	21.43
35	<i>r</i> -2, <i>trans</i> -4, <i>trans</i> -6-Trimethyl	40.04	33.10	44.47	33.10	2-CH <sub>3</sub>	25.40
						4,6-CH <sub>3</sub>	21.66
36	<i>r</i> -2- <i>tert</i> -Butyl- <i>cis</i> -4, <i>cis</i> -6-dimethyl	62.95	40.13	43.99	40.13	2-C(CH <sub>3</sub> ) <sub>3</sub>	35.47
						2-C(CH <sub>3</sub> ) <sub>3</sub>	28.23
						4,6-CH <sub>3</sub>	21.75
37	<i>r</i> -2- <i>tert</i> -Butyl- <i>trans</i> -4, <i>trans</i> -6-dimethyl	54.46	35.85	42.33	35.85	2-C(CH <sub>3</sub> ) <sub>3</sub>	39.04
						2-C(CH <sub>3</sub> ) <sub>3</sub>	28.57
						4,6-CH <sub>3</sub>	22.34
38	<i>r</i> -2-Phenyl- <i>cis</i> -4, <i>cis</i> -6-dimethyl	52.93	40.98	43.16	40.98	4,6-CH <sub>3</sub>	21.37
						<i>ipso</i> -C	138.63
						<i>o</i> -CH	128.78
						<i>m</i> -CH	127.83
						<i>p</i> -CH	128.37
39	<i>r</i> -2-Phenyl- <i>trans</i> -4, <i>trans</i> -6-dimethyl	47.62	34.68	43.70	34.68	4,6-CH <sub>3</sub>	21.78
						<i>ipso</i> -C	140.71
						<i>o</i> -CH	128.62
						<i>m</i> -CH	128.31
						<i>p</i> -CH	126.94
40	2,2, <i>cis</i> -4,6-Tetramethyl	48.86	35.94	43.65	35.94	2-CH <sub>3</sub> (e)	30.36
						2-CH <sub>3</sub> (a)	32.39
						4,6-CH <sub>3</sub>	21.15
41	<i>r</i> -2- <i>tert</i> -Butyl-2, <i>cis</i> -4, <i>cis</i> -6-trimethyl	63.10	35.42	44.12	35.42	2-C(CH <sub>3</sub> ) <sub>3</sub>	38.97
						2-C(CH <sub>3</sub> ) <sub>3</sub>	26.04
						2-CH <sub>3</sub>	25.00
						4,6-CH <sub>3</sub>	21.50
42	<i>trans</i> -4,6-Dimethyl	26.29	32.54	41.12	32.54	4,6-CH <sub>3</sub>	20.83
43	<i>r</i> -2, <i>cis</i> -4, <i>trans</i> -6-Trimethyl	35.98	32.22	39.92	35.98	4-CH <sub>3</sub> (e)	21.75
						2- or 6-CH <sub>3</sub>	20.42
						6- or 2-CH <sub>3</sub>	20.29
44	<i>r</i> -2-Ethyl- <i>cis</i> -4, <i>trans</i> -6-dimethyl	43.45	32.35	40.84	35.74	2-CH <sub>2</sub> CH <sub>3</sub>	28.35
						2-CH <sub>2</sub> CH <sub>3</sub>	11.41
						4-CH <sub>3</sub> (e)	21.93
						6-CH <sub>3</sub> (a)	20.34
45	<i>r</i> -2-Isopropyl- <i>cis</i> -4, <i>trans</i> -6-dimethyl	49.67	32.59 or 33.09	41.04	35.57	2-CH(CH <sub>3</sub> ) <sub>2</sub> or ring C-4	33.09
						2-CH(CH <sub>3</sub> ) <sub>2</sub> or ring C-4	32.59
						2-CH(CH <sub>3</sub> ) <sub>3</sub> or 4,6-CH <sub>3</sub>	22.03
							20.29
							20.04
							19.86
46	<i>r</i> -2- <i>tert</i> -Butyl- <i>cis</i> -4, <i>trans</i> -6-dimethyl	54.96	33.11	40.77	35.66	2-C(CH <sub>3</sub> ) <sub>3</sub>	35.26
						2-C(CH <sub>3</sub> ) <sub>3</sub>	27.93
						4-CH <sub>3</sub> (e)	22.00
47	<i>r</i> -2-Phenyl- <i>cis</i> -4, <i>trans</i> -6-dimethyl	45.44	33.49	39.69	37.15	6-CH <sub>3</sub> (a)	20.17
						4-CH <sub>3</sub> (e)	21.67
						6-CH <sub>3</sub> (a)	20.11
48	2,2, <i>trans</i> -4,6-Tetramethyl	48.61	34.43	40.80	34.43	2-CH <sub>3</sub>	34.12
						4,6-CH <sub>3</sub>	21.60
49	<i>r</i> -2- <i>tert</i> -Butyl-2, <i>cis</i> -4- <i>trans</i> -6-trimethyl	64.77	35.31	42.93	38.96	2-C(CH <sub>3</sub> ) <sub>3</sub>	41.27
						2-C(CH <sub>3</sub> ) <sub>3</sub>	25.89
						2-CH <sub>3</sub>	27.30
						4- or 6-CH <sub>3</sub>	20.53
							19.63
50	4,4,6-Trimethyl	29.21	40.92	49.34	33.66	6-CH <sub>3</sub>	22.03
						4-CH <sub>3</sub> (e)	32.07
						4-CH <sub>3</sub> (a)	26.19
51	<i>cis</i> -2,4,4,6-Tetramethyl	39.14	42.76	48.29	35.07	2-CH <sub>3</sub>	20.04
						6-CH <sub>3</sub>	21.60
						4-CH <sub>3</sub> (e)	31.75
						4-CH <sub>3</sub> (a)	27.04

Table I (Continued)

Dithiane		C-2	C-4	C-5	C-6	Other	
52	<i>trans</i> -2,4,4,6-Tetramethyl	37.82	42.54	47.64	32.34	2-CH <sub>3</sub>	23.96
						6-CH <sub>3</sub>	22.20
						4-CH <sub>3</sub> (e)	32.76
						4-CH <sub>3</sub> (a)	31.00
53	2- <i>tert</i> -Butyl-4,4, <i>cis</i> -6-trimethyl	57.92	42.29	48.79	35.25	2-C(CH <sub>3</sub> ) <sub>3</sub>	35.18
						2-C(CH <sub>3</sub> ) <sub>3</sub>	28.25
						6-CH <sub>3</sub>	21.90
						4-CH <sub>3</sub> (e)	32.14
						4-CH <sub>3</sub> (a)	26.97
54	2- <i>tert</i> -Butyl-4,4, <i>trans</i> -6-trimethyl	55.93	42.76	47.92	34.65	2-C(CH <sub>3</sub> ) <sub>3</sub>	35.18
						2-C(CH <sub>3</sub> ) <sub>3</sub>	27.83
						6-CH <sub>3</sub>	21.46
						4-CH <sub>3</sub> (e)	32.14
						4-CH <sub>3</sub> (a)	30.39
55	2-Phenyl-4,4, <i>cis</i> -6-trimethyl	48.51	43.67	47.92	35.93	6-CH <sub>3</sub>	21.48
						4-CH <sub>3</sub> (e)	31.60
						4-CH <sub>3</sub> (a)	26.83
						<i>ipso</i> -C	138.01
56	<i>r</i> -2- <i>tert</i> -Butyl-2,4,4, <i>cis</i> -6-tetramethyl	62.95	39.94 or 43.63	49.04	31.84	2-C(CH <sub>3</sub> ) <sub>3</sub> or ring C-4	43.63
						2-C(CH <sub>3</sub> ) <sub>3</sub>	39.94
						2-CH <sub>3</sub>	26.19
						6-CH <sub>3</sub>	28.59
						4-CH <sub>3</sub> (e)	26.69
						4-CH <sub>3</sub> (a)	34.04
							30.98

Table II. Parameters for Shifts of C-2

Substituent	Chair only		Chair plus twist	
	Value of parameter	No. of occurrences	Value of parameter	No. of occurrences
Me-2(e)	10.09 ± 0.24	13	10.31 ± 0.11	13
Me-2(a)	5.24 ± 0.44	12	8.30 ± 1.12	10
Et-2(e)	17.61 ± 0.42	2		
<i>i</i> -Pr-2(e)	24.11 ± 0.33	3	24.39 ± 0.16	4
<i>i</i> -Pr-2(a)			25.28 ± 1.48	2
<i>t</i> -Bu-2(e)	29.43 ± 0.22	14	29.75 ± 0.10	11
Ph-2(e)	19.48 ± 0.26	6	19.65 ± 0.13	5
<i>gem</i> -Me <sub>2</sub> -2	-1.56 ± 0.56	4	-2.73 ± 1.10	4
<i>gem</i> -Me, <i>t</i> -Bu-2	-6.19 ± 0.56	4	-8.25 ± 1.11	4
Me-4(e)	1.05 ± 0.12	24	0.70 ± 0.06	21
Me-4(a)	-7.20 ± 0.24	11	-9.35 ± 0.30	13
<i>gem</i> -Me <sub>2</sub> -4	2.09 ± 0.38	4	4.61 ± 0.33	3
Me-5(e)	-0.16 ± 0.43	9	-0.45 ± 0.18	9
Me-5(a)	0.55 ± 0.47	8	0.09 ± 0.24	8
<i>t</i> -Bu-5(e)	-0.53 ± 0.29	5	-0.50 ± 0.13	4
<i>gem</i> -Me <sub>2</sub> -5	-0.51 ± 0.66	6	0.01 ± 0.30	6
2,5-Twist			29.39 ± 2.63	21
<i>sc</i> -Me-2			4.94 ± 1.24	11
<i>sc</i> - <i>i</i> -Pr-2			18.78 ± 1.96	2
<i>sc</i> - <i>t</i> -Bu-2			26.76 ± 1.29	8
<i>sc</i> -Ph-2			17.09 ± 1.89	2
<i>sc</i> -Me-5			3.69 ± 0.67	8
pseudo-(e) Me-4			6.03 ± 0.75	11

where  $n_{\text{chair}}$  and  $n_{\text{twist}}$  are the mole fractions of chair and twist form, respectively, the first set of parentheses has the same meaning as in eq 1, and in the second set of parentheses  $\delta_p$  is the (disposable) basic shift parameter for the 2,5-twist<sup>9</sup> and  $\Sigma' n_x^y$  are the substituent parameters in the twist. The new parameters are shown in the fourth column of Table II. It now takes 22 parameters to fit 42 data (shown in Table X in the Appendix<sup>10</sup>) and perhaps not unexpectedly (in view of the increased number of parameters), the fit is much improved,

the mean square residual being only 0.048 ppm. Deviations of more than 0.25 ppm between calculated and experimental shifts occur in only four cases, with a maximum of 0.45 ppm. However, the standard error of the parameters themselves is quite large and this is particularly true for all the twist parameters (last seven entries) and for axial methyl and isopropyl parameters at C-2.

In the chair-twist parameters, those for geminal substitution in chair and twist conformations are combined. An attempt

Table III. Parameters for Shifts of C-5

Parameter	Chair only		Chair plus twist	
	Value of parameter	No. of occurrences	Value of parameter	No. of occurrences
Me-2(e)	-1.33 ± 0.14	13	-1.21 ± 0.09	13
Me-2(a)	-0.38 ± 0.26	12	-1.10 ± 0.94	10
Et-2(e)	-0.52 ± 0.25	2		
<i>i</i> -Pr-2(e)	-0.31 ± 0.20	3	-0.34 ± 0.14	4
<i>i</i> -Pr-2(a)			2.78 ± 1.24	2
<i>t</i> -Bu-2(e)	-0.58 ± 0.14	14	-0.55 ± 0.09	14
Ph-2(e)	-1.49 ± 0.16	6	-1.38 ± 0.11	6
<i>gem</i> -Me <sub>2</sub> -2	0.43 ± 0.34	4	2.44 ± 0.92	4
<i>gem</i> -Me, <i>t</i> -Bu-2	0.58 ± 0.34	4	1.89 ± 0.93	4
Me-4(e)	9.00 ± 0.07	24	8.94 ± 0.05	21
Me-4(a)	5.70 ± 0.15	11	5.61 ± 0.25	13
<i>gem</i> -Me <sub>2</sub> -4	-0.85 ± 0.23	4	-0.72 ± 0.28	3
Me-5(e)	5.61 ± 0.26	9	5.55 ± 0.15	9
Me-5(a)	-1.81 ± 0.27	8	-1.85 ± 0.20	8
<i>t</i> -Bu-5(e)	20.91 ± 0.18	5	20.91 ± 0.11	4
<i>gem</i> -Me <sub>2</sub> -5	-3.11 ± 0.40	6	-3.32 ± 0.25	6
2,5-Twist			20.03 ± 2.20	20
<i>sc</i> -Me-2			-1.37 ± 1.04	11
<i>sc</i> - <i>i</i> -Pr-2			1.35 ± 1.65	2
<i>sc</i> - <i>t</i> -Bu-2			1.65 ± 1.08	8
<i>sc</i> -Ph-2			-1.13 ± 1.59	2
<i>sc</i> -Me-5			4.63 ± 0.57	7
pseudo-(e) Me-4			10.45 ± 0.63	11

to separate these entities increased the number of parameters by two and brought about no improvement in fit. Only the 2,5-twist (**57**) is considered in the treatment; insufficient data



were available to consider the 1,4-twist<sup>9</sup> (**58**). As a result, certain compounds probably existing largely in 1,4-twist conformations had to be omitted from the twist treatment (compounds **35**, **37**, **39**, **40**, **41**, **50**, **52**, **54**, and **56**; compounds **14**, **19**, **20**, and **44** were omitted for lack of overlapping parameters; corresponding omissions occur in the Tables relating to C-5 and C-4,6). To achieve the agreement found (Table X), it was necessary to adjust a few of the twist percentages from those calculated on the basis of Pihlaja's parameters; the values used are shown in Table XI (Appendix<sup>10</sup>). The only adjustments exceeding ±4% are in compounds **29**, **31**, **48**, and **49** for which amounts of twist contribution were increased from 4 to 15.8%, from 64 to 72.1%, from 80 to 99.2%, and from 80 to 99.4%, respectively.

Because of the large number of parameters in Table II, column 4, the approach including twist forms does not, perhaps, particularly recommend itself, especially since the corresponding parameters are quite imprecise. It is of interest, however, that C-2 in the (hypothetical) pure twist-1,3-dithiane resonates at substantially higher field than C-2 in the chair (29.39 vs. 31.95 ppm). It is also satisfying that most of the chair parameters shown in Table II, column 2 are not greatly altered by introduction of twist forms (compare column 4), which in fact increases confidence in the significance of the parameters. Exceptions in this regard are the parameters for axial 2-methyl, axial 4-methyl, and, to a lesser extent, axial 5-methyl. It is, of course, in the compounds with axial alkyl substituents that the twist form makes palpable contributions, so the diminished stability of the axial parameters to introduction of twist parameters is as expected.

In Table III, column 2 are given the parameters for C-5. The fit of 46 data (Table XII, Appendix<sup>10</sup>) by the 15 parameters

with a mean square residual of 0.109 is remarkably good. The parameters themselves have low standard errors and the fit of the shifts is good with only eight calculated shifts differing from the experimental by more than 0.25 ppm, and only two (the pinacolone derivatives **7** and **32**) differing by more than 0.4 ppm. When twist forms are considered, the agreement (for 42 pieces of data) improves at the expense of increasing the number of parameters to 22 (Table III, column 4). The mean square deviation of the shift data is now 0.034 ppm; all calculated data are within 0.4 ppm of the experimental and all but one (no. 32) within 0.3 ppm (Table XIII, Appendix<sup>10</sup>). The chair parameters in columns 2 and 4 of Table III are in excellent agreement with each other save for the axial 2-methyl, the 2,2-*gem*-dimethyl, and the *gem*-2-methyl-2-*tert*-butyl parameters.

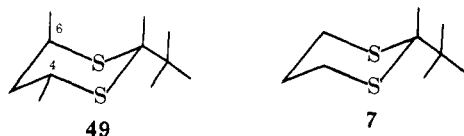
The number of shifts available for comparison with calculated values at C-4,6 is larger than at C-2 or C-5 since, for those compounds not possessing a symmetry plane bisecting the dithiane chair (passing through C-2 and C-5), the shifts at C-4 and C-6 (differently substituted in such compounds) are distinct. As a result, the 20 parameters for C-4,6 listed in Table IV, column 2 refer to 48 compounds, but 67 separate pieces of data. (Distinct 4- and 6-parameters occur for compounds **17**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **43**, **44**, **45**, **46**, **47**, **50**, **51**, **53**, and **55**.) The standard error of the parameters in Table IV is quite satisfactory save for the axial 2-isopropyl group, and the mean square residual for the experimental minus calculated values (Table XIV in the Appendix<sup>10</sup>) is 0.212. Thirty-six residuals are within 0.25 ppm and only eight are greater than 0.5 ppm (six of the latter are between 0.51 and 0.56 ppm). Two shifts (**32** and one parameter for **24**) are off by 0.72–0.73 ppm.

The twist treatment for C-4,6-substituted compounds is somewhat more complicated because the substituents at C-2 and C-5, which have hitherto been simply called "syn-clinal" in the 2,5-twist (**57**), may be either *cis* or *trans* to the substituent at C-4 or C-6. This clearly makes a difference, for example, in compound **49** where there is a difference of 3.65 ppm between C-4 (methyl *cis* to 2-*tert*-butyl group, C-4 shift 35.31 ppm) and C-6 (methyl substituent *cis* to 2-methyl group, C-6

Table IV. Parameters for Shifts at C-4,6

Parameter <sup>a</sup>	Chair only		Chair plus twist	
	Value of parameter	No. of occurrences	Value of parameter	No. of occurrences
Me-2(e)	1.21 ± 0.13	17	1.21 ± 0.14	17
Me-2(a)	-5.65 ± 0.27	14	-5.23 ± 0.35	13
Et-2(e)	1.05 ± 0.20	6		
Et-2(a)	-6.10 ± 0.52	2		
<i>i</i> -Pr-2(e)	1.05 ± 0.17	7	1.00 ± 0.20	7
<i>i</i> -Pr-2(a)	-5.90 ± 1.28	2	-7.31 ± 1.83	3
<i>t</i> -Bu-2(e)	1.36 ± 0.12	19	1.20 ± 0.14	20
Ph-2(e)	2.28 ± 0.15	8	2.17 ± 0.18	8
<i>gem</i> -Me <sub>2</sub> -2	1.67 ± 0.34	5	2.25 ± 0.56	5
<i>gem</i> -Me, <i>t</i> -Bu-2	1.17 ± 0.34	5	1.20 ± 0.61	6
Me-4(e)	8.18 ± 0.11	30	8.58 ± 0.24	24
Me-4(a)	3.89 ± 0.16	13	3.19 ± 0.46	13
<i>gem</i> -Me <sub>2</sub> -4	-1.40 ± 0.25	4	-0.78 ± 0.49	3
Me-5(e)	6.98 ± 0.27	9	7.08 ± 0.25	9
Me-5(a)	6.25 ± 0.29	8	6.52 ± 0.30	8
<i>t</i> -Bu-5(e)	1.20 ± 0.18	5	1.29 ± 0.18	4
<i>gem</i> -Me <sub>2</sub> -5	-1.01 ± 0.41	6	-1.44 ± 0.40	6
Me-6(e)	0.67 ± 0.11	30	0.53 ± 0.14	24
Me-6(a)	-6.47 ± 0.16	13	-6.93 ± 0.42	13
<i>gem</i> -Me <sub>2</sub> -6	1.52 ± 0.25	4	1.84 ± 0.46	3
2,5-Twist			25.08 ± 3.58	29
<i>sc</i> -Me-2 ( <i>cis</i> )			-4.72 ± 2.14	11
<i>sc</i> -Me-2 ( <i>trans</i> )			1.79 ± 1.90	13
<i>sc</i> - <i>i</i> -Pr-2 ( <i>cis</i> )			-2.49 ± 2.98	1
<i>sc</i> - <i>i</i> -Pr-2 ( <i>trans</i> )			5.27 ± 2.95	3
<i>sc</i> - <i>t</i> -Bu-2 ( <i>cis</i> )			-3.09 ± 2.25	8
<i>sc</i> - <i>t</i> -Bu-2 ( <i>trans</i> )			6.80 ± 1.87	8
<i>sc</i> -Ph-2 ( <i>cis</i> )			-2.78 ± 2.91	2
<i>sc</i> -Ph-2 ( <i>trans</i> )			9.23 ± 2.92	2
<i>sc</i> -Me-5 ( <i>cis</i> )			15.94 ± 1.83	7
pseudo-(e) Me-4			7.61 ± 1.23	16
pseudo-(e) Me-6			2.78 ± 1.17	16

<sup>a</sup> Note: *sc*-Me-5 (*trans*) is not included in the list; its F level or tolerance is insufficient for further computation.



shift 38.96 ppm). In such cases we have assigned *two* different parameters to the substituents at C-2 and C-5; “*cis*” for substituents which are *cis* to the substituent at C-4 or C-6, and “*trans*” for those which are *trans* (cf. Table IV, column 4). Thus C-4 in **49** has a *cis*-2-*tert*-Bu and *trans*-2-Me syn-clinal (*sc*) parameter, whereas C-6 has a *trans*-2-*tert*-Bu and *cis*-2-Me parameter. For a compound such as **7**, which has two equivalent 2,5-twist-chair forms, we have assigned half the parameter for one 2-substituent and half for the other (thus C-4,6 in **7** both have one-half a *cis*- and one-half a *trans*-2-*tert*-butyl as well as 2-methyl parameter). Finally, when there is no substituent at C-6, as in the twist form of **24**, we found, empirically, that a fit was obtained only by using the *trans* parameter. With these provisos, the data were fitted (Table XV in the Appendix<sup>10</sup>) with a mean square residual of 0.104 using 31 parameters (Table IV, column 4) for 59 data. The improvement upon introduction of twist parameters is not impressive, considering that 10 additional parameters are needed and that fewer data are fitted, but, once again, the corresponding parameters in columns 2 and 4 of Table IV are in generally good agreement.

## Discussion

In Table V are summarized the parameters for axial and

equatorial methyl substituents at C-2, C-4, C-5, and C-6 affecting the chemical shifts at these four positions. For comparison, the corresponding data for 1,3-dioxane<sup>5</sup> and cyclohexane<sup>2</sup> are included; there is, of course, a redundancy in the cyclohexane entries in Table V since the 2, 4, 5, and 6 positions in the cyclohexane are indistinguishable in the absence of the methyl substituent. The notation “ $\alpha_e$ -2” in Table V refers to an equatorial  $\alpha$ -methyl group acting at C-2. The ring carbon at C-4 has two types of  $\gamma$  substituents: “ $\gamma_e$ -2,4” refers to the equatorial  $\gamma$ -methyl group located at C-2, whereas “ $\gamma_e$ -6,4” refers to the equatorial methyl group at C-6 affecting the shift of C-4. In most cases, as indicated earlier, the chair-only and chair-twist treatments yield similar parameters and where these differ by less than 0.4 ppm, they have been statistically averaged in Table V. (When the discrepancy is more than 0.4 ppm, both chair and chair-twist values are given in that order.)

Comparison of the 1,3-dithiane parameters with those of 1,3-dioxane or cyclohexane analogues (Table V) shows that the parameters are qualitatively similar except for  $\alpha_a$ -5, which is small and *negative* in the dithiane. The cause of this reversal from the normally small but positive  $\alpha_a$  effect is not known.

Quantitatively, it is observed that the dithiane parameters are often larger than the corresponding parameters in cyclohexane and 1,3-dioxane. This is true of the  $\alpha$  parameters, both equatorial and axial, at C-2 and C-4 and also for the  $\gamma_e$  and  $\delta_e$  parameters which tend to be negligible in cyclohexane but, except for  $\delta_e$ -2, are palpable in 1,3-dithiane. An equatorial group at C-2, in particular, has quite appreciable effects at C-4 (1.2 ppm shift) and C-5 (-1.25 ppm shift).

**Table V.** Substituent Parameters for Methyl Groups<sup>a</sup> in Chair Conformations

Parameters <sup>b</sup>	Cyclohexane <sup>2b,c</sup>	1,3-Dioxane <sup>5</sup>	1,3-Dithiane
$\alpha_e-2$	5.6	5.3	10.27 ± 0.10
$\alpha_e-4$	5.6	5.7	8.33 ± 0.09
$\alpha_e-5$	5.6	3.1	5.56 ± 0.13
$\alpha_a-2$	1.1	0.3 <sup>e</sup>	5.2; <sup>c</sup> 8.3 <sup>d</sup>
$\alpha_a-4$	1.1	0.6	3.9; <sup>c</sup> 3.2 <sup>d</sup>
$\alpha_a-5$	1.1	3.1	-1.84 ± 0.16
$\beta_e-4$	8.9	5.8	7.03 ± 0.18
$\beta_e-5$	8.9	7.3	8.96 ± 0.04
$\beta_a-4$	5.2	4.5	6.37 ± 0.21
$\beta_a-5$	5.2	3.7	5.68 ± 0.13
$\gamma_e-2$	0.0	0.8	0.77 ± 0.05
$\gamma_e^{2-4}$	0.0	0.1	1.21 ± 0.10
$\gamma_e^{6-4}$	0.0	-0.1	0.62 ± 0.09
$\gamma_a-2$	-5.4	-9.0	-7.2; <sup>c</sup> -9.4 <sup>d</sup>
$\gamma_a^{2-4}$	-5.4	-7.3	-5.49 ± 0.21
$\gamma_a^{6-4}$	-5.4	-5.3	-6.53 ± 0.15
$\delta_e-2$	0.3	-0.2	-0.41 ± 0.17
$\delta_e-5$	0.3	-0.8	-1.25 ± 0.08
$\delta_a-2$	0.1	0.4	0.19 ± 0.21
$\delta_a-5$	0.1	0.1	-0.4; <sup>c</sup> -1.1 <sup>d</sup>

<sup>a</sup> These parameters are to be added to the shifts of the corresponding carbon atoms (C-2, C-4,6, C-5) in the parent cyclohexane, 1,3-dioxane, or 1,3-dithiane. For 1,3-dithiane, these shifts are: C-2, 31.95; C-4,6, 29.86; C-5, 26.59 ppm. Positive numbers indicate downfield shifts, negative numbers upfield shifts. <sup>b</sup> For notation, see text. <sup>c</sup> From chair parameters only. <sup>d</sup> Treatment includes twist form, see text. <sup>e</sup> From values for C-2 in *cis*-4,6-dimethyl-1,3-dioxane, 93.365 ppm and *r*-2,*trans*-4,*trans*-6-trimethyl-1,3-dioxane, 93.66 ppm (20% in CDCl<sub>3</sub>): G. Furst, unpublished observations.

A number of shifts of the alkyl substituents themselves are included in the last column in Table I. In Table VI, averaged shifts for equatorial and axial methyl substituents at C-2, C-4, and C-5 (selecting for the averaging only conformationally homogeneous compounds without large twist contributions) are compared with corresponding shifts in cyclohexane and 1,3-dioxane. It is clear that whereas the Me-5 shifts are "normal" in dithiane, the Me-2 shifts are "reversed". This is the opposite from what is observed in 1,3-dioxanes.<sup>1a,b,7</sup> The reason for this reversal is not clear, but it is of interest that a similar reversal is found, at least at C-2 and C-5, in the corresponding proton shifts (Table VII). Thus the axial proton at C-2 in both 1,3-dioxane and 1,3-dithiane occupies the opposite position relative to the equatorial one (upfield in dioxane, downfield in dithiane) than the axial proton at C-5 relative to its partner in the same ring system. This finding cannot be explained in terms of traditional anisotropy effects<sup>16</sup> of the S-C(4) or O-C(4) bond.<sup>17</sup>

Geminal methyl groups also deserve brief mention. At C-2, the chemical shifts of such groups are similar, differing by only 0.8–2 ppm (**25**, **40**). Larger differences (4.7–5.9 ppm) are seen at C-4 in the chair compounds **50**, **51**, **53**, and **55** (the twist-boats **52**, **54**, and **56** have lesser shift differences). The largest differences are seen at C-5: 5–7.6 ppm (**28**, **29**, **30**, and **32**). These differences may have their origin in the same factors as the differing upfield–downfield order of single methyl groups at these same positions.

In Table VIII are summarized available substituent parameters for groups other than methyl. As in cyclohexane, the  $\alpha$  parameters increase with the size of the substituent, presumably because substituents larger than methyl actually introduce both  $\alpha$  and  $\beta$  parameters. In contrast, the  $\beta_e$  parameter of the *tert*-butyl group is very small because the normally downfield shifting effect of the substituent carbon is offset by

**Table VI.** Average Value of Methyl Shifts (in ppm) in Methyl-Substituted 1,3-Dithianes, 1,3-Dioxanes, and Cyclohexane

	1,3-Dithiane	1,3-Dioxane <sup>1a</sup>	Cyclohexane <sup>2b,c</sup>
Me-2(e)	20.3	21.2	23.4; 22.7 <sup>11</sup>
Me-2(a)	23.6; <sup>a</sup> 25.4 <sup>b</sup>	17.0	19.5; 17.5 <sup>11</sup>
Me-4(e)	21.75	24.95	23.4; 22.7 <sup>11</sup>
Me-4(a)	20.25		19.5; 17.5 <sup>11</sup>
Me-5(e)	22.25	12.4	23.4; 22.7 <sup>11</sup>
Me-5(a)	16.4 <sup>c</sup>	15.9	19.5; 17.5 <sup>11</sup>

<sup>a</sup> In compd **14**. <sup>b</sup> In compd **35**. <sup>c</sup> In compd **10**.

**Table VII.** Proton Shifts (in ppm) in 1,3-Dithianes, 1,3-Dioxanes, and Cyclohexane

	1,3-Dithiane	1,3-Dioxane	Cyclohexane <sup>15</sup>
H-2(e)	3.48	4.87 <sup>13</sup>	1.65
H-2(a)	4.00	4.53 <sup>13</sup>	1.1
H-5(e)	2.09 <sup>12</sup>	1.24 <sup>14</sup>	1.65
H-5(a)	1.81 <sup>12</sup>	1.96 <sup>14</sup>	1.1

**Table VIII.** Shift Parameters for Groups Other than Methyl in Substituted 1,3-Dithianes<sup>a</sup>

	Ethyl	Isopropyl	<i>t</i> -Butyl	Phenyl
$\alpha_e-2$	17.6	24.2	29.6	19.6
$\alpha_e-5$			20.9	
$\alpha_a-2$		25.3		
$\beta_e-4$			1.2 <sub>5</sub>	
$\gamma_e-4$	1.0 <sub>5</sub>	1.02	1.3	2.25
$\gamma_a^{2-4}$	-6.1	-5.9; <sup>b</sup> -7.3 <sup>c</sup>		
$\delta_e-2$			-0.5	
$\delta_a-5$	-0.5	-0.3	-0.6	-1.4
$\delta_a-5$		2.8		

<sup>a</sup> Additive parameters; see footnote a, Table V. <sup>b</sup> From chair treatment. <sup>c</sup> From twist treatment, see text.

the  $\gamma$  or gauche effect of the methyls of the *tert*-butyl group.

**Synthesis and Assignment of Configuration.** The 1,3-dithianes were generally synthesized from the parent 1,3-dithiols<sup>18</sup> and aldehydes or ketones following precedent.<sup>6</sup> This method gives the more stable stereoisomers because of equilibration occurring during the preparation.<sup>6</sup> The less stable isomers were prepared by converting the 2-alkyl-1,3-dithianes (equatorial group at C-2, holding groups at C-5 or C-4,6; e.g., **13**, **34**) into the corresponding 2-lithio derivatives by means of butyllithium, and then quenching in acid.<sup>19</sup> Since the lithium prefers the equatorial position, the alkyl substituent at C-2 is forced into the axial conformation and remains there after the quenching with acid, presumed to proceed with retention of configuration.<sup>19</sup> The new compounds prepared by these procedures are listed in the Experimental Section.

Several of the new compounds display *cis*–*trans* isomerism. In several cases, the preparation, yielding either the stable<sup>6</sup> or the unstable<sup>19</sup> diastereomers, gives a clue to the nature of the product, e.g., for **8/9** and **13/14**. In the case of **26**, **41**, **55**, and **56** it was assumed that the more stable diastereomer was obtained. The <sup>1</sup>H and <sup>13</sup>C NMR spectra served to support the configuration assigned.

## Experimental Section

<sup>13</sup>C NMR spectra were recorded on a Varian XL-100 pulsed Fourier transform nuclear magnetic resonance spectrometer. Samples were in 10-mm diameter tubes; an internal deuterium lock was used, the solvent, CDCl<sub>3</sub>, providing the lock signal. Tetramethylsilane (2%) was the internal reference. <sup>1</sup>H NMR spectra were recorded on Jeolco

C60HL spectrometer with an external H<sub>2</sub>O lock. Samples were dissolved in CDCl<sub>3</sub> with Me<sub>4</sub>Si as an internal reference. Melting points were determined on an Electrothermal melting point apparatus. Multiple linear regression analysis was effected using the program "BMD02R-Stepwise Regression," available in the package of Bio-medical Computer Programs, University of California Press, Berkeley, Calif., 1973 (p 305). In the present treatment, the regression equation without the intercept was chosen. This is equivalent to assuming that the shift values for the parent compound (1,3-dithiane) are as found.

In the case of compounds **2**, **8**, **17**, **20**, **22**, and **42** conformational heterogeneity of the chair form was taken into account by entering two sets of independent parameters (for the two chair forms), each weighted by the appropriate mole fraction. The mole fractions used of the major conformations are as follows: **2**, 96% Me-2(e); **8**, 78% Me-2(e) (chair-only treatment), 72.5% (chair-twist treatment); **17**, 93% Me-4(e); **20**, 50% Et-2(e) (chair-only), 56% (chair-twist); **22**, 78% iPr-2(e) (chair-only), 70% (chair-twist); **42**, 50% Me-4(e).

**Starting Materials.** 1,3-Propanedithiol was obtained from Aldrich Chemical Co.

**2-Methyl-1,3-propanedithiol.**<sup>6</sup> 2-Methyl-1,3-propanediol ditosylate<sup>6</sup> was converted into the dithiol [bp 77 °C (20 Torr); lit.<sup>6</sup> 37–39 °C (2.5 Torr)] by using sodium sulfide nonahydrate and sulfur in DMF to give the intermediate di- and/or polysulfide, which was subsequently reduced to the dithiol with LiAlH<sub>4</sub>. The general procedure for this conversion has been described elsewhere.<sup>18</sup>

**2-tert-Butyl-1,3-propanedithiol.**<sup>6</sup> 2-tert-Butyl-1,3-propanediol ditosylate was converted into the dithiol [bp 81 °C (0.9–1.0 Torr); lit.<sup>6</sup> bp 40 °C (0.04 Torr)] employing the above procedure.<sup>18</sup>

**1,3-Butanedithiol** was obtained from 1,3-dibromobutane and thiourea using the procedure of Eliel and Hutchins:<sup>6</sup> bp 60 °C (9 Torr), lit.<sup>6</sup> bp 64–67 °C (10 Torr).

**2,2-Dimethyl-1,3-propanedithiol.**<sup>18</sup> Commercial 2,2-dimethyl-1,3-propanediol was converted into the ditosylate, mp 124 °C. Following the general procedure,<sup>18</sup> the dithiol was obtained from the ditosylate using sodium sulfide and sulfur in DMF followed by LiAlH<sub>4</sub> reduction in about 60% yield: bp 88–90 °C (25 Torr); lit.<sup>20</sup> bp 72 °C (12 Torr).

**meso- and dl-2,4-Pentanedithiol.** meso- and dl-2,4-pentanediol ditosylates<sup>6</sup> were separately converted into the corresponding dithiols using the polysulfide/LiAlH<sub>4</sub> method:<sup>18</sup> meso-dithiol, bp 85 °C (18 Torr), lit.<sup>21</sup> bp 74.5 °C (12 Torr); dl-dithiol, bp 60 °C (8.5 Torr), lit.<sup>21</sup> bp 65 °C (11 Torr).

**2-Methyl-2,4-pentanedithiol.** 2-Methyl-2,4-dibromopentane was obtained from 2-methyl-2,4-pentanediol and phosphorus tribromide using the procedure of Bartleson et al.<sup>22</sup> bp 60 °C (3.8 Torr), lit.<sup>22</sup> bp 61–62 °C (4 Torr). The dibromide was converted into the dithiol<sup>18</sup> in 42% yield: bp 78–80 °C (20 Torr), lit.<sup>19</sup> bp 40 °C (1.0 Torr).

**General Procedure for the Condensation of 1,3-Dithiols with Aldehydes or Ketones.** Dithiol (1 mol) was dispersed in three to four times its volume of formic acid (97%) by stirring the mixture vigorously. The aldehyde or ketone (1 mol)<sup>23</sup> was slowly added to the dithiol suspension and the mixture was stirred for 30–90 min at room temperature. The solution was transferred to a separatory funnel containing 300 ml of water, twice extracted with chloroform, washed with 100-ml portions of 5% sodium bicarbonate, then with water (twice or more), dried over anhydrous magnesium sulfate, and filtered; the solvent was evaporated. The remaining liquid or solid was either distilled or recrystallized.

**General Procedure for the Condensation of 1,3-Dithiols with Acetals.** Dithiol (0.1 mol) and 0.1 mol of the acetal,<sup>23</sup> dissolved in 20 ml of chloroform, were added dropwise to a refluxing solution of 0.2 mol of boron trifluoride etherate in 60 ml of chloroform over a period of 15 min. After the addition was completed, the solution was refluxed for 30–90 min, cooled to room temperature, transferred to a separatory funnel, and washed successively with water, 20% potassium carbonate solution, and two to three times with water. The solution was dried over anhydrous magnesium sulfate, filtered, and concentrated at reduced pressure. The resulting crude product was either recrystallized and then sublimed at reduced pressure in the case of solids, or distilled if it was a liquid.

Compounds **1**, **2**, **3**, **4**, and **5** are known.<sup>24</sup> Compounds **10**, **11**, **15**, **16**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **34**, **35**, **36**, **37**, **43**, **44**, and **45** have been previously reported,<sup>6</sup> and compounds **17**, **33**, **38**, **39**, **50**, **51**, **52**, **53**, and **54** had been prepared and described by Abatjoglou.<sup>25</sup> The new compounds listed in Table XVII (Appendix<sup>10</sup>) were prepared by one of the two general methods described above. <sup>1</sup>H NMR spectral data for new compounds are reported in Table XVI (Appendix<sup>10</sup>).

**Unstable Diastereomers.** Compounds **8**, **10**, **14**, **22**, **24**, **35**, and **37**, as well as<sup>25</sup> **39**, **52**, and **54** were prepared<sup>19</sup> from their epimers **9**, **11**, **13**, **21**, **23**, **34**, **36**, **38**, **51**, and **53** by treatment with butyllithium followed by quenching with water.

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**Supplementary Material Available.** Appendix, Tables IX–XVII, containing values of calculated and experimental NMR shift data (21 pages). Ordering information is given on any current masthead.

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