of this ether extract with brine was followed by drying and evaporation to give the keto acid **14b** (2.96 g, 98%): IR (KBr) 3540, 2600 (hydroxyl, carboxyl), 1730 (ketone), 1705 (carboxyl), 1040 (hydroxyl) cm^{-1}; ^1H NMR (acetone-d_6) 0.80, 0.83, (2s, 6 H, 18,19-methyls), 3.8 (br, 1 H, 3α-H) ppm. This compound (2.96 g, 8.17 mmol) was dissolved in methylene chloride (150 mL) and the solution treated with acetic anhydride (30 mL) and perchloric acid (2 drops, 70%). After stirring for 5 h at room temperature the solution was washed successively with water (100 mL), $NaHCO_3$ solution (100 mL, 5%), and brine (100 mL), followed by drying and evaporation. The gummy product was treated with methanol (50 mL) and the solution evaporated to yield a brown solid, which was chromatographed on silica gel using 8% ethyl acetate in hexane. The enol lactone **15** was eluted as the second component following an unidentified forerunner. Recrystallization of **15** from ethanol-water gave microcrystalline needles (1.33 g, 42%): mp 172-74 °C; IR (KBr) 1770 (lactone), 1732 (acetate), 1040, 1025 (lactone, acetate) cm^{-1}; ^1H NMR 0.85 (s, 3 H, 19-CH_3), 0.91 (s, 3 H, 18-CH_3), 2.00 (s, 3 H, 3-acetate), 2.32, 2.62 (br, 4 H, 3',4'-H), 4.51 (br, 1 H, 3α-H) ppm; MS, *m/e* 386 (71), 371 (100), 358 (M*), 312 (64), 269 (6), 262 (*m**), 218 (22). Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87; O, 16.65. Found: C, 74.71; H, 8.91; O, 16.50.

Formation of [16,17-*e*] Fused Lactone 2a. The unsaturated keto ester 11 (2.79 g, 7.2 mmol) was dissolved in methanol (25 mL) to which a solution of KOH (1.5 g) in water (7.5 mL) had been added. This solution was refluxed for 30 min, diluted with water, and washed with ether. The aqueous layer was acidified with dilute hydrochloric acid to give a yellow solution, which was extracted with ether (4 × 100 mL). The organic extract was washed with brine (100 mL), dried, and evaporated to form a yellow gum, which was dissolved in acetone and evaporated again to yield a yellow powder (2.52 g, 97%) of the unsaturated keto acid **16**: IR (KBr) 3420, 2500 (hydroxyl, carboxyl), 1720 (carboxyl, ketone), 1645 (double bond), 1042, 1035 (hydroxyl) cm^{-1}; ^1H NMR (acetone-d_6) 0.83 (s, 3 H, 19-CH_3), 1.03 (s, 3 H, 18-CH_3), 3.15 (d, 2 H, 16^2-H), 4.3-4.9 (br, 2 H, 3α-H, 16^1-H), 5.20 (br, 1 H, 6-H) ppm. This crude product (4.5 g, 2.5 mmol) was dissolved in acetic anhydride (125 mL) and refluxed for 4.5 h with sodium acetate (950 mg) followed by cooling, dilution with ether, and successive washing with water (3 × 100 mL), 5% aqueous Na_2HPO_4 (3 × 100 mL), and brine (3 × 100 mL). The product was treated with methanol (50 mL) and pyridine (0.5 mL) with subsequent drying overnight and solvent removal to furnish a viscous brown liquid, which was chromatographed on Florisil starting with hexane and progressing to 15% ethyl acetate in hexane. The major component was the fused pyrone **2a**, which was recrystallized from ethanol-water as needles (340 mg, 7%): mp 191-92 °C; IR (KBr), 1730 (lactone, acetate), 1620, 1535 (conjugated diene), 1235, 1030 (lactone, acetate) cm^{-1}; ^1H NMR 1.01 (s, 3 H, 19-CH_3), 1.05 (s, 3 H, 18-CH_3), 2.00 (s, 3 H, 3-acetate), 4.50 (br m, 1 H, 3-H), 5.32 (m, 1 H, 6-H), 6.00 (d, 1 H, J = 9 Hz, 3'-H), 7.20 (d, 1 H, J = 9 Hz, 4'-H) ppm; MS, *m/e* 382 (32), 323 (100), 322 (39), 307 (18), 295 (25), 281 (7). Anal. Calcd for $C_{24}H_{30}O_4$: C, 75.36; H, 7.91; O, 16.73. Found: C, 75.23; H, 7.83; O, 16.84.

A minor component (80 mg) which eluted from the column before **2a** was the unsaturated enol ester **17a**: mp 175-76 °C; IR (KBr) 1778 (enol ester), 1735 (methyl ester), 1720 (acetate), 1638 (double bonds), 1438, 1245, 1180 (esters) cm^{-1}; ^1H NMR 0.95 (s, 3 H, 19-CH_3), 1.05 (s, 3 H, 18-CH_3), 2.00 (s, 3 H, 3-acetate), 2.20 (s, 3 H, 17-acetate), 3.70 (s, 3 H, OCH_3), 4.55 (br, 1 H, 3α-H), 5.40 (m, 1 H, 6-H), 5.40 (d, 1 H, J = 16 Hz, 16^2-H), 7.27 (d, 1 H, J = 16 Hz, 16^1-H) ppm. Anal. Calcd for $C_{27}H_{36}O_6$: C, 71.02; H, 7.95. Found: C, 71.05; H, 8.09.

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Registry No. **2a**, 94459-33-3; **2b**, 94459-34-4; **2d**, 94459-35-5; **3a**, 94535-34-9; **6**, 94459-36-6; **9**, 3127-21-7; **10**, 94459-37-7; **11**, 94459-38-8; **14a**, 94459-39-9; **14b**, 94459-40-2; **15**, 94459-41-3; **16**, 94459-42-4; **17a**, 94459-43-5; cyanoacetyl chloride, 16130-58-8; titanium tetrachloride, 7550-45-0; dimethyl malonate, 108-59-8; 5α-androstan-17-one, 963-74-6; (carbethoxymethylene)triphenylphosphorane, 1099-45-2; ethyl formate, 109-94-4.

Conformational Analysis. 25.[1] ^{13}C NMR Chemical Shifts—Sensitive Detectors in Structure Determination. 3.[2] The Proposal for Non-Chair Conformations in Methyl-Substituted 2-Oxo-1,3,2-dioxathianes Challenged

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The ^{13}C chemical shifts of 2-oxo-1,3,2-dioxathiane and 39 methyl derivatives as analyzed from the derived substituent effects show that the 2-oxo-1,3,2-dioxathiane ring attains exclusively chair conformations, preferably with an axial (19 cases) but often also with an equatorial S=O group (8 cases). Of the remaining 13 derivatives 11 fit excellently into the shift increment parameterization as mixtures of two interconverting chair forms. Only two of the most heavily substituted derivatives appear in a chair-chair equilibrium which cannot be precisely defined. These results are in close agreement with conclusions based on ^1H NMR spectra, dipole moments, IR, and mass spectrometry but challenge some recent reports on the (frequent) participation of twist forms in this system.

Introduction

In 1976 we first pointed out that the ^1H NMR spectra of a number of methyl-substituted 2-oxo-1,3,2-dioxathianes[3] (**14**, **21-26**, **31**, and **33**) are, in contrast to earlier reports on the significant contribution of twist forms, indicative of a single chair form or a chair-chair equilibrium. In 1982 we briefly reviewed the publications on the structure and conformations of alkyl-substituted 2-oxo-1,3,2-dioxathianes[4,5] and carried out a thorough analysis of the ^1H NMR spectra of all methyl-substituted and several other alkyl-substituted 2-oxo-1,3,2-dioxathianes.[4]

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Table I. ^{13}C Chemical Shifts (δ) of 2-Oxo-1,3,2-dioxathiane and Its Methyl Derivatives

no.	substitution	C(4)	C(5)	C(6)	C(Me)
1	parent	57.30	25.99	57.30	
2	*r*-2-*t*-4-Me	64.24	33.38	57.54	21.3 (4e)
3	*r*-2-*c*-4-Me[a]	74.23	31.31	63.51	21.6 (4)
4	*r*-2-*c*-5-Me	62.29	30.01	62.29	13.2 (5e)
5	*r*-2-*t*-5-Me	62.86	29.68	62.86	15.0 (5a)
6	4,4-Me_2[a]	80.28	36.14	55.55	30.9 (4e), 28.9 (4a)
7	5,5-Me_2	66.44	31.67	66.44	22.6 (5av)
8	*r*-2-*t*-4-*c*-5-Me_2	70.17	36.79	61.76	18.4 (4e), 13.2 (5e)
9	*r*-2-*c*-4-*c*-5-Me_2[a]	76.91	32.77	66.64	19.6 (4), 11.1 (5)
10	*r*-2-*t*-4-*t*-5-Me_2	66.23	34.15	64.16	18.3 (4e), 9.9 (5a)
11	*r*-2-*c*-4-*t*-5-Me_2[a]	79.47	35.21	69.04	17.7 (4), 12.6 (5)
12	*r*-2-*t*-4-*t*-6-Me_2	64.73	40.73	64.73	21.2 (4/6e)
13	*r*-2-*c*-4-*c*-6-Me_2	73.83	38.70	73.83	21.3 (4/6e)
14	*r*-2-*c*-4-*t*-6-Me_2[a]	71.63	37.93	62.01	21.0 (4), 22.5 (6)
15	*r*-2,4,4,*c*-5-Me_3	85.56	39.47	58.40	29.5 (4e), 23.7 (4a), 13.0 (5e)
16	*r*-2,4,4,*t*-5-Me_3[a]	84.91	36.91	64.32	29.6 (4), 23.8 (4), 12.9 (5)
17	*r*-2-*t*-4,5,5-Me_3	71.75	34.96	67.65	14.4 (4e), 22.3 (5e), 17.2 (5a)
18	*r*-2-*c*-4,5,5-Me_3[a]	81.06	34.19	73.05	16.1 (4), 22.0 (5), 18.3 (5)
19	*r*-2,4,4,*t*-6-Me_3	80.73	43.48	60.67	32.2 (4e), 28.8 (4a), 21.2 (6e)
20	*r*-2,4,4,*c*-6-Me_3	81.99	41.91	70.45	31.5 (4e), 26.3 (4a), 21.9 (6e)
21	*r*-2-*t*-4-*c*-5-*t*-6-Me_3	69.08	43.74	69.08	18.7 (4/6e), 12.8 (5e)
22	*r*-2-*c*-4-*t*-5,*c*-6-Me_3	78.70	41.70	78.70	19.5 (4/6e), 12.3 (5e)
23	*r*-2-*t*-4-*t*-5-*t*-6-Me_3	68.59	38.78	68.59	18.3 (4/6e), 4.1 (5a)
24	*r*-2-*c*-4-*c*-5-*c*-6-Me_3	77.50	37.00	77.50	18.5 (4/6e), 14.4 (5a)
25	*r*-2-*c*-4-*c*-5-*t*-6-Me_3[a]	75.69	40.28	66.96	16.4 (4), 12.0 (5), 21.3 (6)
26	*r*-2-*c*-4-*t*-5-*t*-6-Me_3[a]	78.09	39.23	65.62	17.7 (4), 12.7 (5), 19.0 (6)
27	*r*-2,4,4,*c*-5-*t*-6-Me_3	84.83	46.13	64.89	29.8 (4e), 24.3 (4a), 12.5 (5e), 21.7 (6e)
28	*r*-2,4,4,*t*-5-*c*-6-Me_4	85.85	43.69	75.25	29.4 (4e), 21.7 (4a), 12.5 (5a), 20.3 (6e)
29	*r*-2,4,4,*t*-5-*t*-6-Me_4	84.42	41.13	63.35	30.0 (4e), 28.9 (4a), 7.3 (5a), 19.0 (6e)
30	*r*-2,4,4,*c*-5-*c*-6-Me_4	85.90	40.40	72.50	28.5 (4e), 27.0 (4a), 7.3 (5a), 18.9 (6e)
31	*r*-2-*t*-4,5,5,*t*-6-Me_4	72.48	38.70	72.48	14.4 (4/6e), 21.3 (5e), 11.6 (5a)
32	*r*-2-*c*-4,5,5,*c*-6-Me_4	81.70	37.12	81.70	15.3 (4/6e), 20.7 (5e), 12.0 (5a)
33	*r*-2-*c*-4,5,5,*t*-6-Me_4[a]	80.24	38.58	69.72	16.8 (4), 20.5 (5), 14.5 (5), 19.7 (6)
34	4,4,5,5-Me_4[a]	87.90	36.70	64.80	26.8 (4), 24.8 (4), 21.7 (5)
35	4,4,6,6-Me_4	79.23	44.79	79.23	32.9 (4/6e), 30.4 (4/6a)
36	*r*-2,4,4,5,5,*t*-6-Me_5	88.24	39.92	66.92	26.6 (4e), 25.2 (4a), 21.0 (5e), 15.3 (6e)
37	*r*-2,4,4,5,5,*c*-6-Me_5	89.46	39.23	76.46	25.2 (4e), 23.5 (4a), 20.5 (5e), 15.0 (5a), 15.3 (6e)
38	*r*-2,4,4,*c*-5,6,6-Me_5	83.69	47.96	83.69	31.7 (4/6e), 24.8 (4/6a), 12.5 (5a)
39	*r*-2,4,4,*t*-5,6,6-Me_5	83.94	45.16	83.94	31.8 (4/6e), 24.1 (4/6a), 12.4 (5e)
40	4,4,5,5,6,6-Me_6	87.71	42.52	87.71	28.7 (4/6e), 27.9 (4/6a), 22.1 (5e), 21.9 (5a)

[a] The favored orientation as shown in Table IV.

The results confirmed unambiguously the postulate that substituted 2-oxo-1,3,2-dioxathianes exist preferentially either in a chair conformation with an axial S=O group or as a mixture of S=O axial and S=O equatorial chair forms. In some cases substitution at C-4, C-5, and C-6 caused the predominance of the S=O equatorial chair form.[4] We also utilized chemical equilibration and dipole moment measurements to strengthen our conformational conclusions.[4,5]

Also in 1982 we studied the IR spectra of 2-oxo-1,3,2-dioxathiane and 49 alkylated homologues[5,6] and found that characteristic stretching vibrations are 1185–1203 cm^{-1} for axial S=O groups and 1238–1247 cm^{-1} for equatorial S=O groups. These observations were ascribed to S=O axial or S=O equatorial chair forms (or their mixtures) but not to twist forms. Nevertheless some recent reports on IR[7,9] and ^{13}C NMR[8,10] studies of methyl-substituted 2-oxo-1,3,2-dioxathianes emphasize the frequent participation of twist forms.

The above situation prompted us to reanalyze the ^{13}C NMR chemical shifts of all possible methyl-substituted 2-oxo-1,3,2-dioxathianes thereby deriving the values of the different substituent effects from the equation

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

where δ_x is the chemical shift of a given carbon atom in a substituted derivative, δ_p is that of the same carbon atom in the parent compound, and n_x^y are the parameters caused by n substituents y acting at carbon x.[2,11–16] Significant contribution of non-chair forms would require modification of eq 1 into eq 2.[17]

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

Results

The experimental combinations of substituent effects on 2-oxo-1,3,2-dioxathianes were derived from the ^{13}C NMR chemical shifts shown in Table I. The parent compound is axial 2-oxo-1,3,2-dioxathiane (1) with the axial sulfoxide oxygen since 1,3,2-dioxathiane itself does not seem to be a stable compound.[18]

The shift parameters summarized in Tables II and III were derived with the shift data for compounds **1**, **2**, **4**, **5**,

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Table II. The Shift Parameters at C(4/6) of 2-Oxo-1,3,2-dioxathianes

source of substituent effect	C(4/6)		no. of occurrences
4e	α_e	6.95 ± 0.15	44
4a	α_a	8.01 ± 0.17	24
5e	β_e	4.66 ± 0.13	35
5a	β_a	5.41 ± 0.16	33
6e	γ_e	−0.71 ± 0.24	44
6a	γ_a	−5.56 ± 0.43	24
4e5e	$\alpha_e\beta_e$	1.22 ± 0.19	23
4e5a	$\alpha_e\beta_a$	−3.09 ± 0.15	22
4a5e	$\alpha_a\beta_e$	−0.75 ± 0.18	13
5a6e	$\beta_a\gamma_e$	1.46 ± 0.16	21
4e6e	$\alpha_e\gamma_e$	0.59 ± 0.20	24
4e6a	$\alpha_e\gamma_a$	−0.94 ± 0.22	16
2e4a	$\alpha_a\gamma_a^2$	7.97 ± 0.20	16
2a6a	$\gamma_a^2\gamma_a^6$	−0.51 ± 0.21	16
2a6e	$\gamma_a^2\gamma_e^6$	0.60 ± 0.21	25
2e − 2a	$\gamma_e^2 - \gamma_a^2$	9.81 ± 0.17	33
5,5	$\beta_e\beta_a$	−1.00 ± 0.14	14
6,6	$\gamma_e^6\gamma_a^6$	2.85 ± 0.27	12
4e5e6e	$\alpha_e\beta_e\gamma_e^6$	−1.18 ± 0.18	12
4e4a5e5a	$\alpha_e\alpha_a\beta_e\beta_a$	0.85 ± 0.18	3
5a6e6a	$\beta_a\gamma_e^6\gamma_a^6$	−1.25 ± 0.18	6
	rms	0.247 ppm	
	av diff	0.17 ppm	
	range	33.91 ppm	

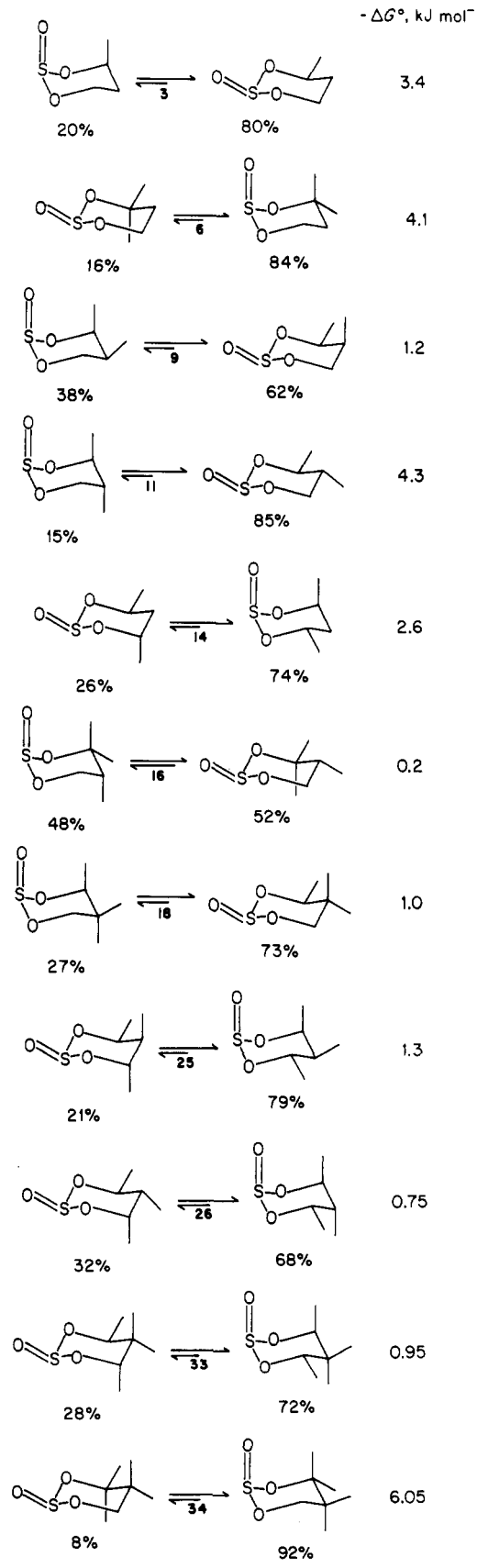
Table III. The Shift Parameters at C(5) of 2-Oxo-1,3,2-dioxathianes

source of substituent effect	C(5)		no. of occurrences
4e	β_e	7.34 ± 0.08	49
4a	β_a	5.29 ± 0.21	21
5e	α_e	4.14 ± 0.19	21
5a	α_a	4.30 ± 0.30	20
4,4	G_β	−1.91 ± 0.17	12
5,5	G_α	−2.17 ± 0.30	9
4e5e	$\alpha_e\beta_e$	−0.49 ± 0.14	25
4e5a	$\alpha_a\beta_e$	−2.86 ± 0.16	25
4a5e	$\alpha_e\beta_a$	−1.03 ± 0.18	12
2e − 2a	$\delta_e^2 - \delta_a^2$	−2.08 ± 0.15	19
2a4a	$\beta_a\delta_a^2$	−0.32 ± 0.18	16
2a5a	$\alpha_a\delta_a^2$	−0.65 ± 0.20	14
4e5e5a	$\alpha_e\alpha_a\beta_e$	−0.52 ± 0.21	12
4e4a5a	$\alpha_a\beta_e\beta_a$	−0.39 ± 0.20	6
	rms	0.240 ppm	
	av diff	±0.13 ppm	
	range	18.80 ppm	

7, **8**, **10**, **12**, **13**, **15**, **17**, **19–21**, **23**, **27–32**, and **36**, which were known to exist in the anancomeric chair conformations[3-6,10,15,19] shown in Chart I with two sets of simultaneous equations [one for C-4/6 and one for C-5]. Then the data for compounds **3**, **6**, **9**, **11**, **16**, **18**, **25**, **26**, **33**, and **34**, consisting of two unequal chair conformations,[3-5] (Scheme I) were weighted and added. The best fit, however, was obtained by slight adjustment of the mole fraction values from those reported earlier (cf. Table IV). Finally the data for compounds **22**, **24**, and **37** were added by assuming them conformationally homogeneous (cf. Chart I).

The shift parameters remained practically the same thus confirming the anancomeric nature of the latter compounds. The data for compounds **35** and **38–40** were not used for deriving the chemical shift parameters reported in Tables II and III because they are the only compounds

Scheme I



with independent 4a6a, 4a5e6a, and 4a5a6a increments and, furthermore, they may not be anancomeric but include both S=O axial and S=O equatorial chair forms.

The rms values are 0.247 ppm at C-4/6 and 0.240 ppm at C-5. The average differences between the observed and calculated ^{13}C chemical shifts are 0.17 ppm at C-4/6 and

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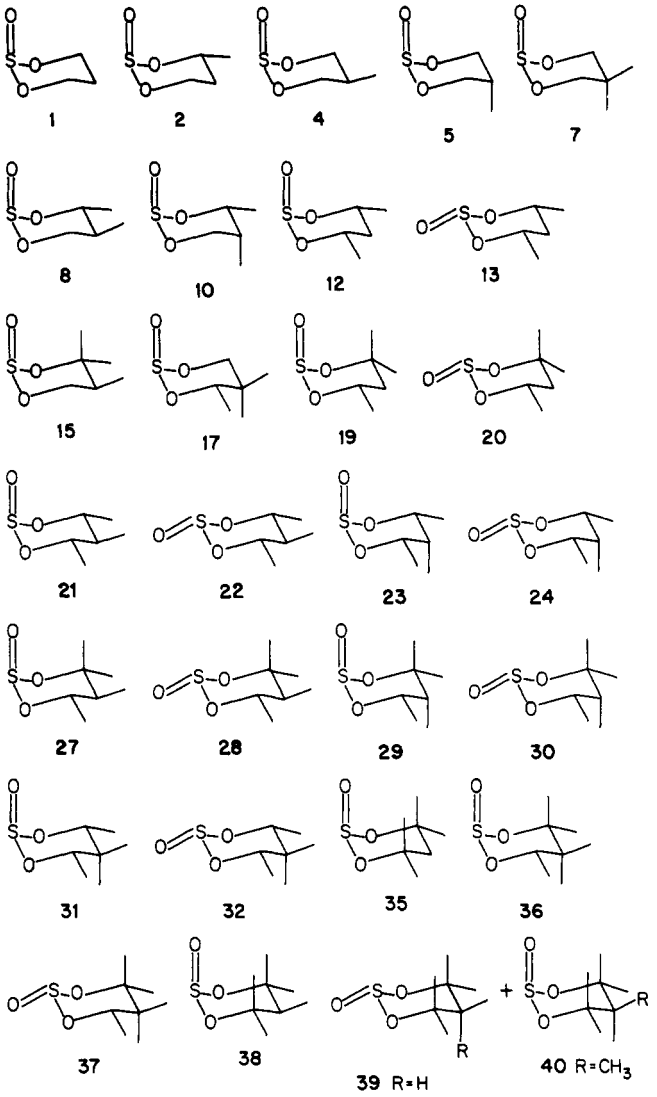
Chart I



0.13 ppm at C-5 which, however, are only 0.50% and 0.75% from the respective shift ranges (Tables II and III).

Discussion

In order to calculate methyl substituent effects on the ^{13}C NMR chemical shifts of 2-oxo-1,3,2-dioxathianes by eq 1 a basic condition is that all derivatives included in the calculations have the same ring conformation, for example the chair form. A change of ring conformation, e.g., from a chair to a twist form, obviously leads to different chemical shifts in the parent compound, δ_p. That is why chair and twist derivatives are no longer comparable, an observation that can be utilized in looking for twist-shaped derivatives. In other words, if ^{13}C chemical shifts of all methyl-substituted 2-oxo-1,3,2-dioxathianes can be correlated with anancomeric chair forms or chair–chair equilibria the argument can be made that non-chair forms have negligible contributions. A multilinear regression program[2,14] was used to solve eq 1 on a DEC-20 computer. The values of the shift parameters are considered significant if they are 0.3 ppm or larger and/or at least two times their standard deviations. With this in mind, the final mole fractions of the two chair forms of the conformationally inhomogeneous compounds were obtained iteratively to discover the best fit for the substituent effect correlations.

The equatorial α effect of a methyl group at C-4/6 is about 1 ppm more deshielding than that in 1,3-dioxanes (Table II) but about 1 ppm less deshielding than that in 2-oxo-1,3-dioxanes[15,21] (6.95, 5.76, and 7.83 ppm, respectively). The axial α effect is increasingly more deshielding than in 2-oxo-1,3-dioxanes and 1,3-dioxanes (8.01, 5.37 and 0.95 ppm, respectively). This trend can be partly ascribed to the lack of an axial hydrogen at atom 2 but perhaps even more so to the capacity of the axial methyl at C-4 to bend outward from the ring when moving from 1,3-dioxanes to 2-oxo-1,3,2-dioxathianes.[2-6,15,16]

At C-5 the equatorial and axial α effects (Table III) are very similar and close to those observed in 2-oxo-1,3-dioxanes[1] but about 1 ppm more deshielding than those in 1,3-dioxanes.[2]

The geminal α effect (G_α) at C-4 is negligible as in 2-oxo-1,3-dioxanes[1] whereas that in 1,3-dioxanes is −2.60 ppm.[2] This reflects at least the moderate or weak ionic character of the SO_3 and CO_3 moieties, the easier outward bending of the axial 4-methyl group, and weak interactions between it and position 2 in these compounds.[15,16]

Both equatorial and axial β effects of a methyl group at C-4/6 parallel α effects. In other words, the equatorial effect is again less deshielding than the axial one. At C-5 $\beta_e - \beta_a$ decreases in the order 1,3-dioxanes > 2-oxo-1,3,2-dioxathianes > 2-oxo-1,3-dioxanes (3.26, 2.05, and 1.36 ppm, respectively) which seems to correlate roughly with the flattening of the acetal or ester end of the molecules and also with the ionic character of the ester moieties.[2-6,15,16]

The geminal β effect (G_β) at C-5 becomes less shielding in the order 2-oxo-1,3,2-dioxathiane > 2-oxo-1,3-dioxane > 1,3-dioxane (−1.91, −1.21, and −0.74 ppm, respectively). The differences are small and can be understood in the light of small differences in electronic environment of this carbon affected by the group at position 2.[15]

It has been stated[20,21] that when the S=O group in 2-oxo-1,3,2-dioxathianes is axial the γ gauche effect causes a substantial upfield shift at C-4/6 relative to that in the conformer where the S(=O) group is equatorial. This difference can be expected to be −9.1 ppm between **12** in which the S=O bond is gauche and **13** where it is antiperiplanar (or γ anti) to the O–C_4 and O–C_6 bonds.[20]

This effect has been thought to be of steric origin. In the present study we have used this difference as a $\gamma_e^2 - \gamma_a^2$ parameter (Table II) which is effective at C-4/6 of compounds with the equatorial S=O group since in the parent compound 2-oxo-1,3,2-dioxathiane, the S=O group is axial. The weighted value of this effect, +9.81 ppm, at C-4/6 is not far from the difference mentioned above. The δ_e^4 effect at C-6 is shielding and very close to those of 2-oxo-1,3-dioxanes[1] and 1,3-dioxanes[2] (−0.71, −0.91, and −0.38 ppm, respectively). The γ_a^4 effect at C-6 is about 1 ppm more shielding than that in 1,3-dioxanes (−5.56 vs. −4.74 ppm, respectively). However, this minor difference can be expected, e.g., because of the different ring sizes and interatomic distances. These effects are nevertheless close enough to each other to postulate that an axial lone pair orbital at position 2 behaves similarly to the axial hydrogen at C-2 in 1,3-dioxanes.

In the parent compound (1) the axial S=O group[4,5,10] (Chart I) shields C-4/6 since it is gauche to the O–C_4 and O–C_6 bonds, whereas the equatorial S=O bond is antiperiplanar (γ anti).[16] As a matter of fact, the axial oxygen perturbs the electronic environment around C(4) and C(6) and increases their shielding in very much the same manner as an axial methyl group at C-2 in 1,3-dioxanes.[2,14]

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Since the S=O group is exclusively axial in the parent compound (1), a $\delta_e - \delta_a$ effect has been measured from the substituted homologues and probably reflects the different polarizability of the sulfoxide group in the equatorial and axial orientations.[4,5,6] By comparison, $\delta_e - \delta_a$ at C-5 of 1,3-dioxanes is practically zero.[2]

As to the vicinal and polysubstitution effects it is interesting to note that despite their general similarity for 2-oxo-1,3,2-dioxathianes (1–40), 1,3-dioxanes,[2,14] and 2-hydroxy-1,3,2-dioxaborinanes[15] they also reflect their particular conformational features and relative differences.

The buttressing $\alpha_e\gamma_e$ and $\alpha_e\gamma_a$ effects at C-4/6 are very close to those in 1,3-dioxanes,[2,16] 2-oxo-1,3-dioxanes,[1] and 2-hydroxy-1,3,2-dioxaborinanes.[15] The δ syn-axial 2a4a and 2a6a effects (Table II and III) are very similar to those in 1,3-dioxanes,[2,16] although $\alpha_a\gamma_a{}^2$ at C-4/6 is ca. 1 ppm more deshielding than that in 1,3-dioxanes (7.93 vs. 6.99 ppm, respectively) and $\gamma_a{}^2\gamma_a{}^6$ at C-4 is slightly shielding in comparison with that of 1,3-dioxanes (−0.51 vs. 0.74 ppm). At C-5 2a4a (=2a6a) effects in both compounds are slightly shielding (−0.72 vs. −0.44 ppm, respectively). The similarity of these δ syn-axial effects emphasizes the importance of the replacement of the axial group at position 2 whether a lone pair orbital or a hydrogen with an axial substituent CH_3 or S(=O) and at the same time the conformational resemblance between 1,3-dioxanes[2,16] and 2-oxo-1,3,2-dioxathianes.

Chair–Chair Equilibria and the ^{13}C Chemical Shifts. Compounds **3, 6, 9, 11, 14, 16, 18, 25, 26, 33,** and **34** exist as equilibria of two chair forms (Scheme I) the positions of which have been estimated earlier[3,5,6] by means of ^1H NMR, dipole moment data, chemical equilibration, and mass spectrometry.[6,22] In the present study the conformer populations were slightly adjusted to reach the best possible fit for the set of the substituent effect equations. The final conformer populations of the chair–chair equilibria **3, 6, 9, 11, 14, 16, 18, 25, 26, 33,** and **34** do not usually differ significantly from those reported before.[3,5,6]

Compounds **9** and **18** (Scheme I) turn out, however, to prefer the conformer with equatorial 4-methyl. Initially they were reported[5,6] as near equimolar mixtures of the two chair forms. Probably the model values of the proton–proton coupling constants used when evaluating the conformer ratio of **9**[5,6] were not accurate enough. In the cases of **18** and **34**, the original estimates[5,6] were based on the ^1H chemical shifts of the methyl groups, for which it is generally more difficult to find model values. It appears then that ^{13}C chemical shift correlations give more precise estimates of these conformational equilibria. Hellier and Phillips[10] also found that **18** favors the S=O equatorial chair form (Scheme I).

As to the other compounds in Scheme I Hellier and Phillips[10] assign **14, 16, 25, 26, 33,** and **34** as having non-chair (twist) forms simply because their treatment of the ^{13}C NMR shift data was too qualitative to allow an exact solution of the conformer equilibria. The present analysis shows, however, that the contribution of the twist forms can be precluded. Hellier and Phillips[10] state also that **6** and **18** exist preferentially in chair forms with an axial and equatorial S=O group, respectively, whereas **3** is a mixture of two chair conformations, results which are all in qualitative agreement with our conclusions (Scheme I).

Finally even **35** and **38–40**, which were not used for deriving the chemical shift parameters, favor chair conformations. We conclude that both **35** and **38** (Chart I) exist preferentially in the S=O axial chair form since in those cases with axial methyl groups at C-4/6 in both conformers in question (cf. **6, 14, 25, 26, 33,** and **34**) the S=O axial chair form is always clearly more abundant with the exception of **16** where the methyl substituent at C-5 counterbalances the equilibrium. Hence the 4a/6a substitution pattern in **35** and **38** makes the S=O axial chair form more favored and the anancomerism of **15** shows that an equatorial methyl group at C-5 of **38** does not alter its conformation in relation to that of **35**. This conclusion is in agreement with the postulate based on the ^1H NMR chemical shifts[4] and is further supported by our IR results since both **35** and **38** show strong absorption bands (1200 and 1198 cm^{-1}, respectively) corresponding to that of the axial S=O group but not to that of the equatorial S=O group.[6]

With an approach described earlier[4] the conformational equilibria for **3, 9, 11, 14, 18, 25,** and **26** (Scheme I) let us estimate the conformational energy of the axial methyl group at C-5, $\Delta G°(5a\text{-}CH_3)$ at 2.5 ± 0.3 kJ mol^{-1}, that of the 4e5e gauche interaction at 1.6 ± 0.4 kJ mol^{-1}, that of the 2e4a syn interaction at 2.1 kJ mol^{-1}, and finally the difference $\Delta G°(2a - 2a4a)$ at 0.4 kJ mol^{-1}, in other words the interaction and stabilization are fairly close to each other. These results are in good agreement with the previous estimates.[6] From the chair–chair equilibria of **6** and **16** we can then draw the conclusion that 4,4,5a-Me_3 substitution causes an extra destabilization of 3.4 kJ mol^{-1} similar to that in 1,3-dioxanes.[23] Hence **39** favors the equatorial orientation of the 5-methyl group at C-5 by about two times this amount (6.8 kJ mol^{-1}). Taking this and the equilibria for **6** and **16** into account we can estimate that **39** is about 4:1 mixture of the S=O equatorial and axial chair forms, respectively (Chart I). Finally a comparison of **16** with **34** and **39** with **40** shows that **40** is about a 4:1 mixture of the S=O axial and equatorial chair forms, respectively. The above conclusions are supported also by the IR spectra of **39** and **40** which show absorptions for both the equatorial (1243 cm^{-1}) and the axial S=O groups (1198 cm^{-1}, 1203 cm^{-1}).[5,6]

The Non-Chair Forms of 2-Oxo-1,3,2-dioxathianes Challenged. As we have already stated, our previous investigations on the ^1H NMR spectra,[3,5,6] dipole moments,[3,5,6] chemical equilibration,[3,5,6] and mass spectra[5,22] of methyl-substituted 2-oxo-1,3,2-dioxathianes do not support the existence of twist forms. This is confirmed by the present correlation of ^{13}C NMR chemical shift data. The few recent reports which, mainly due to an inadequate analysis of the available data, still emphasize the frequent participation of twist forms are worth a closer examination. First of all, Hellier and Phillips[10] analyzed the ^{13}C chemical shift data of methyl-substituted 2-oxo-1,3,2-dioxathianes in a qualitative manner and were hence unable to define the conformer populations accurately. It is, however, noteworthy that they assign twist conformations (**3, 14, 16, 25, 26, 33, 34**) or predominant chair conformations (**10, 18**) to the derivatives which according to our various experimental approaches, including the present ^{13}C NMR analysis, exist in chair–chair equilibria.

Cazaux et al.[7,9] on the basis of IR and ^1H NMR spectra of several substituted 2-oxo-1,3,2-dioxathianes favor non-chair conformations. However, the band in the region 1216–1232 cm^{-1} which they assign to ν_{SO} isoclinal in the twist conformations can be found as a sharp band or a shoulder of a band at 1200–1212 cm^{-1} for almost all the compounds[6] including **1, 12, 13,** and **19** which even ac-

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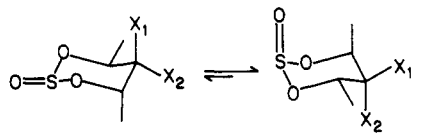
(23) Pihlaja, K.; Äyräs, P. *Suom. Kemistil. B* **1969**, *42*, 65, 74.

Scheme II



	e		a
25	21%	X_1=CH_3, X_2=H	79%
26	32%	X_1=H, X_2=CH_3	68%
41	15%	X_1=H, X_2=Cl	85%
42	40%	X_1=Cl, X_2=H	60%

cording to the above authors attain chair forms. Changing the solvent from nonpolar to polar did not change the relative intensity of the band although the twist form should be more polar than the chair conformation with an axial S=O group and the relative intensity of the band should increase.[6] Hence we believe that the 1216–1232 cm^{-1} band is due to the C–C(–H) stretching vibrations rather than to isoclinal S=O groups.[6]

Very recently Gorrichon et al.[8] reported that **41** and **42** exist appreciably in twist conformations. Their conclusions are based on a poor correlation of the ^{13}C NMR chemical shift data for these and some model compounds. Using the substituent effects given in Tables II and III, we can estimate chemical shifts for the conformations in Scheme II when $X_1 = X_2 = H$ and from the paper of Gorrichon et al.[8] we obtain the α and β effects due to an equatorial or an axial Cl-atom and a few correction terms due to the gauche interactions. Taking these into account together with our knowledge about the other possible effects we can easily estimate that **41** is about an 85:15 mixture of the S=O axial (a) and S=O equatorial (e) chair forms. In the case of **42** it is more difficult to estimate all of the necessary substituent effects (due to the lack of model compounds[8]) but roughly the proportion of the S=O axial (a) chair form is now about 60%. These estimates are supported by the conformer ratios of **25** and **26** since it can be expected that an axial chlorine atom at C-5 is favored in relation to an axial methyl group at C-5.

In the light of the above discussion we conclude that there is no reason to believe that methyl-substituted 2-oxo-1,3,2-dioxathianes attain other than chair conformations.

Experimental Section

The ^{13}C spectra were recorded at 298 K on Jeol FX-60 NMR spectrometer operating at 15.03 MHz with 8 K data points. Samples were prepared in 10-mm od tubes as 10% w/v solutions in $CDCl_3$ with 2% Me_4Si as a reference. Most shift data (Table I) were extracted from Nikander's dissertation[5] (compounds **1–8**, **10**, **12–21**, **23**, **27–29**, and **31–40**) but those of compounds **9**, **11**, **25**, and **26** were redetermined. Shift data for compounds **22**, **24**, and **30** were taken from Hellier and Phillips.[10] All methyl-substituted 2-oxo-1,3,2-dioxathianes were available from our earlier studies.[3-6] Gorrichon et al.[8] report for **41** and **42** the following ^{13}C chemical shifts. **41**: C-4 77.1, C-5 62.7, and C-6 63.25 ppm. **42**: C-4 72.9, C-5 62.3, and C-6 67.9 ppm.

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Registry No. **1**, 4176-55-0; **2**, 32644-05-6; **3**, 32644-06-7; **4**, 37989-54-1; **5**, 37989-53-0; **6**, 4493-97-4; **7**, 1003-85-6; **8**, 58240-37-2; **9**, 81800-23-9; **10**, 58210-19-8; **11**, 81800-24-0; **12**, 25845-28-7; **13**, 25845-29-8; **14**, 29882-38-0; **15**, 81756-33-4; **16**, 81756-34-5; **17**, 81756-35-6; **18**, 81756-36-7; **19**, 25545-81-7; **20**, 25545-82-8; **21**, 29265-49-4; **22**, 29288-15-1; **23**, 36044-84-5; **24**, 36044-85-6; **25**, 61665-27-8; **26**, 61665-28-9; **27**, 81756-38-9; **28**, 81800-26-2; **29**, 81800-25-1; **30**, 81800-27-3; **31**, 29288-16-2; **32**, 36297-36-6; **33**, 34513-18-3; **34**, 81756-37-8; **35**, 32475-82-4; **36**, 81756-39-0; **37**, 81756-40-3; **38**, 81756-42-5; **39**, 81756-41-4; **40**, 81756-43-6.

Rapid Scan UV Spectroscopic and Kinetic Studies of the Reaction of Methyl 4-Methoxy-3,5-dinitrobenzoate with Pyrrolidine in Dimethyl Sulfoxide

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An intermediate complex in the aromatic nucleophilic substitution reaction of methyl 4-methoxy-3,5-dinitrobenzoate with pyrrolidine in dimethyl sulfoxide has been observed by rapid scan UV spectroscopy, and kinetic and equilibrium constants have been obtained for its formation and decomposition. The observable intermediate is the conjugate base (I^-) of the zwitterionic form (IH). The formation of I^- is base catalyzed and the decomposition of I^- is first order in pyrrolidine hydrochloride. The possible mechanism is that proton transfer between IH and I^- is not more rapid than the k_{-1} step and that general acid catalyzed leaving group departure from I^- is rate limiting.

In kinetic studies of the reactions of 1-ethoxy-2,4-dinitronaphthalene with primary and cyclic secondary amines in dimethyl sulfoxide, Bunnett observed that proton transfer is rapid and that the rate-limiting decomposition of X^- is general acid catalyzed (Scheme I).[1,2]

This work provided direct evidence for the specific base–general acid (SB–GA) mechanism of the S_NAr reaction.[3,4] Recently evidence in favor of the SB–GA mechanism has been presented in the reactions of methyl 4-methoxy-3,5-dinitrobenzoate (MDNB)[5] and 2,4,6-trinitrophenetole[6] with *n*-butylamine in Me_2SO.

A series of papers have revealed that the kinetics are greatly different between pyrrolidine and piperidine as nucleophiles.[2,4,7] It has been reported that proton transfer

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