Stereochemistry of Sulphur Organic Compounds. Part 24.[1] Synthesis and Conformational Analysis of *cis*- and *trans*-2-Methoxy-5-methylthio Derivatives of Oxane

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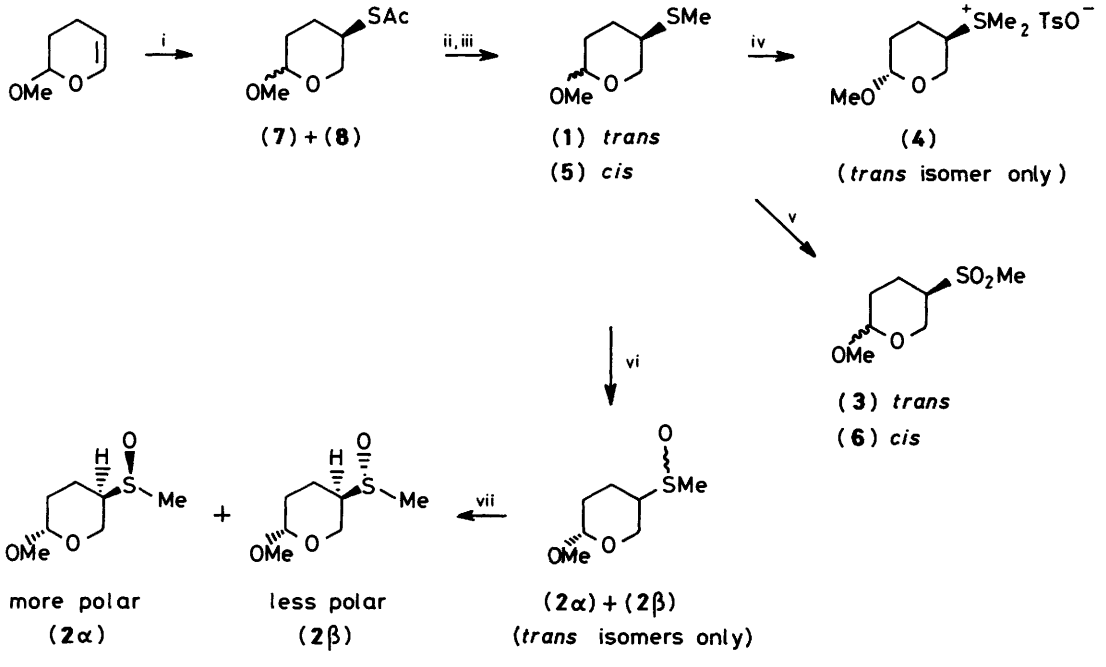
The synthesis and conformational analysis of *cis*- and *trans*-2-methoxy-5-X-oxane, by ^{13}C n.m.r. at low temperature in several solvents, are reported. $\Delta G°$ Values in CD_2Cl_2 of *trans*-isomers are −0.61 (X, SMe), +1.65 (X, SOMe more polar isomer), +0.57 (X, SOMe less polar isomer), −0.50 (X, SO_2Me), and ⩾ +1.4 (X, $^+SMe_2$) kcal mol^{-1}, negative values indicating a preference for the diequatorial conformer. In all *cis*-compounds only one conformation is present. By comparison of these values with those calculated from 2-methoxyoxane and 3-methylthio derivatives of oxane the role played by the anomeric effect on the (oxygen–sulphur)$_{1,2\text{-}g}$ interaction can be inferred.

Recently, we studied the conformational equilibria of oxanes substituted at C(3) with sulphide, sulphoxide, sulphone, and sulphonium functions.[1] The conformational behaviour of these compounds was notably influenced by both steric factors and the interaction between the non-bonding electrons of the heterocyclic oxygen and the sulphur function. On the other hand, the anomeric effect in the oxane ring is nowadays explained in terms of the stereoelectronic interaction of non-bonding electrons on the heterocyclic oxygen with the σ^*_{C-O} orbital of the exocyclic C–O bond (endo-anomeric effect).[2] This effect modifies the electronic density on the heterocyclic oxygen atom and will obviously affect both the polar and stereoelectronic interactions of this atom with other groups on the ring.

The conformational equilibria of *cis*- and *trans*-2-methoxy-5-methylthio derivatives of oxane (**1**)—(**6**) is reported here (see Scheme). These compounds show the same relative arrangement between the oxygen and the sulphur atom as do 3-thio derivatives of oxane, the only difference being the presence of the methoxy group at C(2) which presents the anomeric effect mentioned above (Figure 1).

Results and Discussion

(a) *Synthesis.*—Compounds (**1**)—(**6**) were synthesized as shown in the Scheme. Free-radical-catalysed addition of thiolacetic acid to 2-methoxy-3,4-dihydro-2*H*-pyran gave the 2-methoxy-5-*S*-thioacetyltetrahydropyrans (**7**) and (**8**) as a



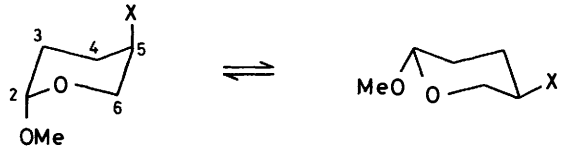
Scheme. *Reagents and procedure:* i, AcSH–$(PhCO_2)_2$; ii, KOH–H_2O; iii, MeI; iv, TsOMe; v, excess of $NaIO_4$; vi, 1 equiv. $NaIO_4$; vii, chromatographic separation

Table 1. Room-temperature ^{13}C n.m.r. chemical shifts of *cis*- and *trans*-2-methoxy-5-methylthio derivatives of oxane[a]

Substituent (Compound)	Solvent	C(2)	C(3)	C(4)	C(5)	C(6)	OMe	SMe
SMe (1)	CD_2Cl_2	101.8	30.1	27.4	42.4	67.7	55.7	14.1
SOMe (2α)	CD_2Cl_2	99.5	27.7	19.7	58.0[b]	59.9[b]	55.4	37.6
SOMe (2β)	CD_2Cl_2	100.1	27.6	17.7	58.8	60.5	55.6	37.1
SO_2Me (3)	CD_2Cl_2	101.2	28.3	20.5	58.9	60.8	56.0	40.0
$^+SMe_2$ (4)	CD_2Cl_2:CD_3OD[c,d]	98.7	26.2	20.4	55.2	57.9	55.5	*e*
SMe (5)	$CDCl_3$	97.2 (97.3)[f]	30.3 (27.9)	24.7 (24.3)	41.6 (41.1)	63.2 (63.1)	54.4	13.1
SO_2Me (6)	$CDCl_3$	96.6 (97.3)	28.5 (27.5)	17.9 (16.8)	58.9 (58.2)	56.8 (56.6)	54.8	38.4

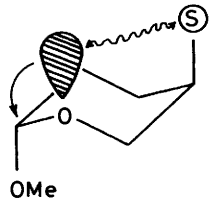
[a] In p.p.m. from Me_4Si. [b] The assignment may be reversed. [c] 1:1 v/v. [d] Signals for *p*-$MeC_6H_4SO_3^-$ ion at 21.4 (Me), 141.3 (*ipso* and *p*), 129.6 and 126.5 (*o* and *m*). [e] Signals at δ 23.9 and 23.5 belong to the $^+SMe_2$ group. [f] Calculated values in parentheses.

Table 2. Low-temperature ^{13}C n.m.r. chemical shifts of compounds (1)—(4)[a]



X	Solvent	*T*/K	Conformations	C(2)	C(3)	C(4)	C(5)	C(6)	OMe	SMe
SMe (1)	CD_2Cl_2	173	A[b]	97.7 (97.6)[c]	24.9 (24.7)	20.8 (21.7)	42.5 (42.5)	60.9 (60.0)	54.6[d]	14.7
			E[b]	102.8 (102.6)	31.6 (31.4)	28.6 (28.9)	40.9 (41.1)	69.7 (70.1)	56.7	14.4
SOMe (2α)	CD_2Cl_2	163	A	97.2 (98.0)	25.8 (25.3)	18.1 (17.4)	59.7 (59.4)	55.0 (55.3)	55.0	37.2
			E	102.5 (102.3)	30.0 (30.0)	22.9 (22.4)	*e* (55.9)	64.8 (64.3)	57.0	35.1[d]
SOMe (2β)	CD_2Cl_2	163	A	97.6 (98.2)	25.4 (24.7)	16.5 (15.9)	59.7 (59.6)	57.4 (57.2)	54.9[d]	37.3
			E	102.7 (102.4)	29.7 (29.9)	18.0 (17.9)	53.8[d] (54.2)	65.1 (65.0)	*e*	35.9
SO_2Me (3)	CD_2Cl_2	153	A	97.7 (97.5)	24.7 (24.3)	16.9 (15.9)	*e* (57.8)	*e* (55.7)	*e*	40.3
			E	102.6 (102.6)	29.5 (29.2)	21.7 (21.4)	57.4[f] (58.2)	63.5 (63.6)	57.2[f]	39.4
$^+SMe_2$ (4)	CD_2Cl_2–CD_3OD[g]	173[h]	A	97.8 (98.4)	25.4 (24.1)	19.5 (18.5)	53.7 (52.9)	56.8 (57.0)	55.2	*i*
			E[j]							

[a] In p.p.m. from Me_4Si. [b] A, diaxial conformer; E, diequatorial conformer. [c] Calculated values in parentheses. [d] Signal corresponding to $CFCl_3$–$CDCl_3$ (17:3 v/v) spectrum in CD_2Cl_2 signal not seen. [e] Signal not seen. [f] The assignment may be reversed. [g] 1:1 v/v. [h] Signals for the *p*-$C_6H_4SO_3^-$ ion at δ 21.6 (Me), 142.1 and 141.8 (*ipso* and *p*), 129.4 and 126.3 (*o* and *m*). [i] Signals at δ 23.2 and 22.9 for the $^+SMe_2$ group. [j] Conformer not seen.



S : SMe ; SOMe ; SO_2Me ; $^+SMe_2$

Figure 1. Decrease of $(S–O)_{1.2-g}$ interaction brought about by the anomeric effect

2:3 *cis–trans* mixture (g.c. and ^1H n.m.r.). Saponification to mercaptide followed by methylation yielded the sulphides (**1**) and (**5**) as a 3:2 mixture (g.c. and ^1H n.m.r.).

The sulphides were separated by column chromatography and the isomer configurations assigned by ^1H and ^{13}C n.m.r. Both diastereoisomers showed the lowest-field signal for H(2). In the *cis* isomer (**5**), the conformation with the methoxy group axial has less energy (indeed this compound is conformationally homogeneous) and, therefore, the chemical shift for δ H(2) and its coupling constants must be typical for the equatorial position. On the other hand, in the *trans* isomer (**1**), both conformers are likely to be populated.* The ^{13}C n.m.r. values

* Experimental values: *cis*-isomer H(2), δ 4.58 (m, $^3J_{2,3eq} + {}^3J_{2,3ax} + {}^4J_{2,6eq}$ 4.1 Hz); *trans*-isomer H(2), δ 4.11 (dd, *J* 6.8 and 2.7 Hz).

are in agreement with this assignment [see for instance the chemical shift for C(2) in Table 1].

The *trans*-sulphide (**1**) was oxidized with one equivalent of sodium periodate to a diastereoisomeric mixture of sulphoxides (**2α**) and (**2β**), separated by chromatography (the α denomination corresponds to the more polar isomer). Oxidation of both sulphides (**1**) and (**5**) with excess of periodate gave the sulphones (**3**) and (**6**); the sulphonium salt (**4**) was prepared from methyl toluene-*p*-sulphonate and sulphide (**1**) (Scheme). All the configurations were in concert with previous assignments for sulphides (**1**) and (**5**).

(b) *Conformational Analysis.*—The room-temperature ^{13}C n.m.r. spectra for compounds (**1**)—(**6**) are shown in Table 1. All the assignments were confirmed by DEPT and supported by the effects of the functions attached to the ring. Compounds (**5**) and (**6**) exist very largely with an axial OMe and an equatorial sulphur function. The calculated chemical shifts (in parentheses) for these compounds are in agreement with the assignment made (Table 1).

Table 2 shows low-temperature ^{13}C spectra for *trans*-isomers (**1**)—(**4**). ^{13}C Signals in these compounds were assigned by taking into account the ^{13}C chemical shift for 2-methoxyoxane[3] and the effects of sulphur functions in both axial and equatorial 3-position in oxanes on ^{13}C shifts.[1] The calculated values (in parentheses) are also in agreement with the assignments for these compounds, especially considering that the calculated values refer to room temperature and that the basic values are for $CDCl_3$ solutions.

The spectroscopic behaviour of the diastereoisomeric sulphoxides (**2α**) and (**2β**) permits the assignment of the relative configuration at both chiral centres C(5) and sulphur. Table 3 shows the chemical-shift differences, for the most meaningful carbons, between axial sulphoxides (**2α**) and (**2β**) and are compared with the corresponding ones for analogous sulphoxides[1] (5-methylsulphinyloxanes,* 5-benzylsulphinyloxanes,* and *cis*-2-methyl-5-methylsulphinyloxanes*). The spectroscopic differences between diastereoisomeric sulphoxides can be correlated with the relative configurations at both chiral centres C(5) and sulphur. Taking into account the *X*-ray diffraction data of the less polar (β) benzyl sulphoxide which showed[1] that this compound is racemic with a $C^RS^R + C^SS^S$ configuration, spectroscopic analogies among α-sulphoxides, on the one hand, and β-isomers, on the other, in all compounds mentioned, are straightforward to assign. Thus, the configuration of the more polar isomer (**2α**) will be the same as that of the other more polar isomers (α) (*i.e. RS/SR*) and that of the less polar isomer (**2β**) agrees with that of the other less polar isomers (β) (*RR/SS*). The lower chemical shifts for C(4) in β-isomers and C(2) in α-sulphoxides are due to the greater effect of the sulphinyl oxygen (see drawing in Table 3).

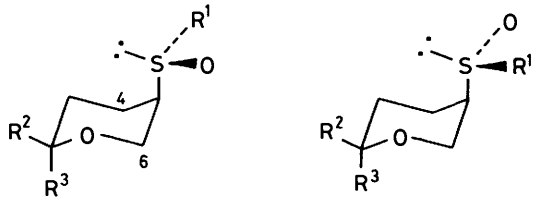
Table 4 lists the free-energy differences calculated from the intensity of the ^{13}C signals in the low-temperature spectra of the *trans*-isomers. These values refer to the equilibrium from the diaxial towards the diequatorial conformer, *i.e.* negative numbers imply that the diequatorial conformer is the more stable.

The factors that affect the conformational equilibrium of the *trans*-2-methoxy-5-methylthio derivatives of oxane can be divided into two types. On the one hand, the interactions of the sulphur function with both the heterocyclic oxygen (dipolar, electronic, and electrostatic) and the methylene C(3) (steric) and, on the other, the dipolar, steric, and stereoelectronic interactions that make up the anomeric effect of the methoxy group at C(2). As a first approximation, one might expect that if all the above interactions were brought together as an energy term, the result would be similar to the experimental $\Delta G°$ value. If that was not true, there would be some peculiarites in these compounds, as a result of both the sulphur function and the anomeric methoxy being present. Therefore, the conjunction between the experimental $\Delta G°$ values for the 5-methylthio derivatives of oxane[1] and the corresponding magnitude for 2-methoxyoxane, will give, by comparison with those experimental $\Delta G°$ values indicated in Table 4, the modifications that bring about the anomeric effect in the conformational behaviour of the sulphur function at C(5) in oxane.

Table 5 records the experimental $\Delta G°$ values (in CD_2Cl_2) of the *trans*-2-methoxy-5-methylthio derivatives of oxane and compares them with those calculated from 5-methylthio derivatives of oxane[1] (in CD_2Cl_2) and 2-methoxytetrahydropyran (CD_2Cl_2). The $\Delta\Delta G°$ values, corresponding to $\Delta G°$(exp.) − $\Delta G°$(theor.), denote a higher stability of the diaxial conformation in these compounds than one might expect by considering the present groups and these values rise with the electronegativity of sulphur.

The results make it clear that the anomeric methoxy group conditions all the interactions that arise from the axial disposition of the sulphur function. Table 5 shows that the OMe group tends to adopt the axial disposition more than the sulphur function (this is true except for the sulphonium salt, nevertheless this compound is conformationally homogeneous).

Table 3. Differences of ^{13}C chemical shifts between C(6) and C(4) of diastereoisomer sulphoxides of oxane



α β

			$\delta_\alpha - \delta_\beta$	
R^1	R^2	R^3	C(6)	C(4)
CH_2Ph	H	H	−1.8	+1.9
Me	H	H	−2.0	+1.5
Me	Me	H	−2.1	+1.4
Me	H	OMe	−2.4	+1.6

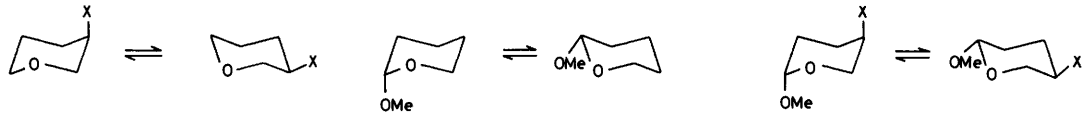
Table 4. $\Delta G°$ Values of *trans*-2-methoxy-5-methylthio derivatives of oxane obtained from ^{13}C signal intensity[a]

Substituent (Compound)	Solvent	*T*/K	$\Delta G°$/kcal mol^{-1}
SMe	$CFCl_3$–$CDCl_3$[b]	163	−0.32 ± 0.06
(**1**)	CD_2Cl_2	173	−0.61 ± 0.05
SOMe	$CFCl_3$–$CDCl_3$[b]	153	+0.60 ± 0.01
(**2α**)	CD_2Cl_2	163	+0.65 ± 0.03
SOMe	$CFCl_3$–$CDCl_3$[b]	148	+0.47 ± 0.02
(**2β**)	CD_2Cl_2	163	+0.57 ± 0.03
SO_2Me	CD_2Cl_2	153	−0.50 ± 0.02
(**3**)			
$^+SMe_2$	CD_2Cl_2–CD_3OD[c]	173	⩾ + 1.4[d]
(**4**)			

[a] See section on conformational analysis. [b] 85:15 v/v. [c] 1:1 v/v. [d] Sole conformer seen.

* The correct position numbering for these compounds is 3-X-sulphinyloxanes. The alternative numbering system was chosen to preserve analogy of positions with those in (**2α**) and (**2β**).

Table 5. Comparison between experimental $\Delta G°$ for *trans*-2-methoxy-5-methylthio derivatives of oxane and calculated $\Delta G°$ from 3-methylthio derivatives of oxane and 5-methoxyoxane



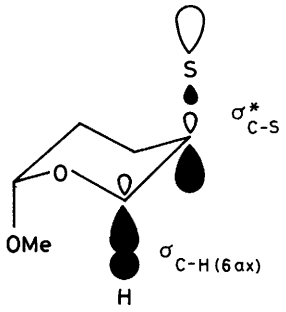
X	$\Delta G°_{Experimental}$	$\Delta G°_{Experimental}$	$\Delta G°_{Theoretical}$	$\Delta G°_{Experimental}$	$\Delta\Delta G°$
SMe	−1.18		−0.86	−0.61	0.25
SOMe α	−0.10		+0.22	+0.65	0.43
SOMe β	−0.43	+0.32	−0.11	+0.57	0.68
SO_2Me	≃ −1.45		≃ −1.13	−0.50	≃ 0.63
$^+SMe_2$	+0.55		+0.87	⩾ +1.40	⩾ 0.53

Therefore, one may think that the anomeric effect controls the conformational equilibrium for these compounds. So, if we analyse the modifications that the anomeric effect brings about in the molecule, the conformational behaviour of compounds (**1**)—(**4**) can be explained. From the methoxy group at C(2) in oxane, it could be inferred that: (a) the *endo*-anomeric effect[2] decreases the electronic density at the heterocyclic oxygen, lowering both attractive and repulsive $(O–S)_{1,2\text{-}g}$ interactions, (b) protons at C(6) increase their acidity as a result of the higher electronegativity of the oxygen function and, in addition, the above mentioned *endo*-anomeric effect increases the H(6ax) acidity,[4] (c) geometrical modifications mainly affect C(2)[2b] and, therefore, do not have an appreciable influence on the sulphur function.

The $\Delta\Delta G°$ values (Table 5) do not provide support for the *endo*-anomeric effect [point (a)] being the main factor in the high stability of diaxial conformations. So, in the sulphide (**1**) the (S–O) interaction is destabilizing but in sulphonium salt (**4**) there is a stabilizing electrostatic interaction between these groups.[1] A reasonable explanation for the conformational behaviour of (**1**)—(**4**) is based on the acidity of H(6) [point (b)]. If we take the 5-methylthio derivatives of oxane as a model, the factors included in this point will increase the energy of the $\sigma_{C–H(6ax)}$ orbital in compounds (**1**)—(**4**). In this way, taking into account the structural and energy demands of the generalized *gauche* effect[2b,5] it would imply a greater facility of interaction between this $\sigma_{C–H(6ax)}$ orbital and the antibonding $\sigma^*_{C–S}$ bond (Figure 2). This stereoelectronic stabilizing factor justifies the direction of $\Delta\Delta G°$ variation. Thus, the more electronegative the sulphur function, the less energy the $\sigma^*_{C–S}$ orbital has and, therefore, the more stabilizing the interaction.

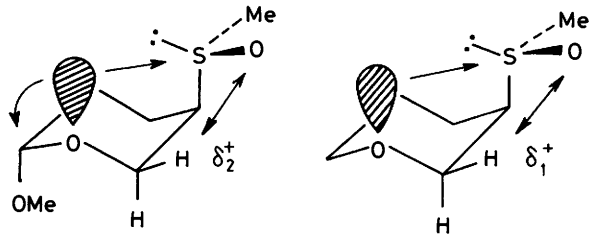
Diastereoisomeric sulphoxides (**2α**) and (**2β**) need special attention. In a previous paper[1] it was found that in the conformational equilibrium of the more polar isomer of 5-methylsulphinyloxane (α-isomer), the axial conformation was more populated ($-\Delta G°$ smaller, Table 5) than that in the corresponding less polar isomer (β-sulphoxide). Two possible explanations were then given. In axial conformers of α-sulphoxides there is possibility of overlap of an unoccupied sulphur *d*-orbital with an occupied sp^3-orbital of the ring oxygen (for details on $n \longrightarrow d$ effect see Figure 3 in ref. 6). The second explanation is based on the fact that the equatorial H(6) is more electropositive (due to its proximity to ring oxygen) than the equatorial H(4) and thereby the axial sulphoxide conformation in which the sulphoxide oxygen is close to H(6), *i.e.* α-isomers, may be preferred by electrostatic factors (Figure 3).

In sulphoxides (**2α**) and (**2β**), experimental $\Delta G°$ values (Table 4) point in the same direction; the more polar isomer has a higher conformational preference for the diaxial conformer. However, as shown by the $\Delta\Delta G°$ values, its 'stabilization factor' $\Delta\Delta G°$ is smaller. This implies that the $n \longrightarrow d$ effect could be meaningful for this kind of compound. The reasons for this arise from Figure 3 which shows a comparison of the stabilizing factors in α-sulphoxides between our compound and 5-methylsulphinyltetrahydropyran[1] (see above). If we take the later sulphoxide as a model, the higher acidity of H(6eq) in (**2α**) does not give rise to a greater conformational differentiation between sulphoxides (**2α**) and (**2β**), while the lower availability of the lone pair at oxygen for the $n \longrightarrow d$ interaction, as a result of the anomeric effect, points in the right direction.



$$SMe < SOMe < SO_2Me < {}^+SMe_2$$

Figure 2. Stereoelectronic *gauche* interaction between $\sigma_{C–H(6ax)}$ and $\sigma^*_{C–S}$ orbitals



$$(n \rightarrow d)_{(2\alpha)} < (n \rightarrow d)_{model}$$

$$\delta_1^+ < \delta_2^+ \Longrightarrow (O/H)_{(2\alpha)} > (O/H)_{model}$$

Figure 3. Comparison of $n \longrightarrow d$ effect and $(O–H)_{1,3\text{-}p}$ interaction between α sulphoxides

Conclusions.—The presence of a 2-methoxy group in 5-methylthio derivatives of oxane modifies the conformational behaviour of these compounds and the experimental $\Delta G°$ values do not match with the conformational effects of the groups present. The differences between experimental and theoretical $\Delta G°$ values are mainly explained by taking into account the $\sigma_{C-H(6ax)} \longrightarrow \sigma^*_{C-S}$ (*gauche* effect) interaction which is significant in diaxial conformers of these compounds. On the other hand, the drop in electronic density at the ring oxygen, as a result of the anomeric effect, justifies the importance of the $n \longrightarrow d$ interaction on the conformational analysis of diastereoisomeric sulphoxides.

Experimental

M.p.s were determined on an Electrothermal apparatus in open capillary tubes and are uncorrected. Elemental analyses were performed by the 'Instituto de Química Orgánica (CSIC)' in Madrid with a Perkin-Elmer analyser. I.r. spectra were obtained using a Perkin-Elmer model 1310 spectrometer. Mass spectra were recorded on an AEI model MS-30 spectrometer at 70 eV. ^1H and ^{13}C n.m.r. spectra were recorded on Bruker WM-200-SY or WP-80-SY instruments. Shifts are reported in p.p.m. downfield from internal tetramethylsilane. Silica gel used in chromatography was Merck F-254 (t.l.c.) or 60 (70—230 mesh) (column).

cis- *and* trans-2-*Methoxy*-5-S-*thioacetyltetrahydropyran* (**7**) *and* (**8**).—To a mixture of thiolacetic acid (7.1 ml, 7.612 g, 0.1 mol) and benzoyl peroxide (0.5 g), cooled to 0 °C, was added 2-methoxy-3,4-dihydro-2*H*-pyran (11.4 ml, 11.415 g, 0.1 mol). The solution was allowed to stand overnight and then was treated with aqueous 10% sodium hydrogen carbonate (100 ml) and extracted with ether (4 × 75 ml). The organic layer was washed with water (50 ml), dried (Na_2SO_4), and evaporated to give thioacetates (17.12 g, 90%) as a *cis–trans* mixture (2:3) which was used in the following reaction without prior purification; $\nu_{max.}$(film) 1 690 cm^{-1} ($SCOCH_3$); δ_H ($CDCl_3$) 4.75 [0.4 H, m, 2-H(eq) *cis*], 4.55 (0.6 H, m, 2-H *trans*), 3.40 (1.8 H, s, OMe *trans*), 3.37 (1.2 H, s, OMe *cis*), 2.32 (1.8 H, s, $SCOCH_3$ *trans*), and 2.30 (1.2 H, s, $SCOCH_3$ *cis*).

trans- *and* cis-2-*Methoxy*-5-*methylsulphenyltetrahydropyran* (**1**) *and* (**5**).—The above *cis–trans* mixture of thioacetates (12.98 g, 0.068 mol), aqueous 20% potassium hydroxide (100 ml), and methanol (50 ml) were refluxed for 1 h. Then methyl iodide (8.5 ml, 19.366 g, 0.1364 mol) was added and refluxing continued for 30 min. The mixture was cooled and extracted with ether (3 × 100 ml). The organic layer was washed with water (2 × 50 ml), dried (K_2CO_3), and concentrated to yield *cis–trans* sulphides (7.69 g, 70%) in a 2:3 ratio (g.c. and ^1H n.m.r.). The isomers were separated by column chromatography (ether–hexane, 1:19).

cis-*Isomer* (**5**). This had R_F (ether–hexane, 1:9) 0.25; $\nu_{max.}$(film) 2 930, 2 825, 1 440, 1 365, 1 200, 1 125, 1 110, 1 050, 1 025, 1 000, 900, and 840 cm^{-1}; δ_H($CDCl_3$) 4.57 [1 H, m, 2-H(eq)], 3.68—3.48 [2 H, part AB of an ABX system, 6-H(ax)], 3.29 (3 H, s, OMe), 2.65 (1 H, m, 5-H), 2.04 (3 H, s, SMe), and 1.84—1.62 [4 H, m, 3-H(eq), 3-H(ax), 4-H(eq), 4-H(ax)]; *m/z* 164 (M^+ + 2, 1.1%), 162 (M^+, 20.5), 131 (15.9), 130 (6.7), 115 (0.7), 102 (13.7), 87 (13.7), 74 (100), 61 (29.5), 58 (7.8), 55 (22.7), 54 (11.8), and 41 (18.2).

trans-*Isomer* (**1**). This had R_F (ether–hexane, 1:9) 0.19; $\nu_{max.}$(film) 2 940, 2 920, 2 830, 1 440, 1 385, 1 215, 1 175, 1 130, 1 060, 1 040, and 1 020 cm^{-1}; δ_H($CDCl_3$) 4.41 (1 H, dd, *J* 6.8 and 2.7 Hz, 2-H), 4.11 [1 H, ddd, *J* −11.7, 3.9, and 1.8 Hz, 6-H(eq)], 3.45 (3 H, s, OMe), 3.42 [1 H, dd, *J* −11.7 and 8.2 Hz, 6-H(ax)], 2.73 (1 H, m, 5-H), 2.30—1.86 [2 H, m, 4-H(eq), 3-H(eq)], 2.12 (3 H, s, SMe), and 1.79—1.41 [2 H, m, 4-H(ax), 3-H(ax)]; *m/z* 164 (M^+ + 2, 0.2%), 162 (M^+, 5.1), 131 (7.8), 130 (25.0), 115 (3.8), 102 (16.4), 88 (22.4), 87 (12.5), 74 (100), 61 (33.4), 58 (25.0), 55 (27.1), 54 (13.8), and 41 (22.9).

trans-2-*Methoxy*-5-*methylsulphinyltetrahydropyran* (**2α**) *and* (**2β**).—To an ice-cooled solution of sodium metaperiodate (1.283 g, 6 mmol) in water (10 ml) was added (**1**) (0.973 g, 6 mmol) dissolved in ethanol (3 ml). The mixture was stirred at 0 °C for 4 h and was then allowed to stand overnight at room temperature. The mixture was concentrated to dryness and the resulting material was extracted several times with methylene dichloride. The extracts were dried (Na_2SO_4) and concentrated (rotary evaporator) to afford the two diastereoisomeric sulphoxides as an oil (quantitative yield). Separation of the isomers (**2α**) and (**2β**) was carried out by column chromatography (CCl_4–Pr^iOH, 9:1).

More polar diastereoisomer (**2α**). This had R_F (CCl_4–Pr^iOH, 4:1) 0.23; m.p. 76—77 °C (CCl_4) (Found: C, 47.0; H, 8.1; S, 17.7. $C_7H_{14}SO_3$ requires C, 47.2; H, 7.9; S, 18.0%); $\nu_{max.}$(KBr) 2 980, 2 950, 2 930, 2 900, 1 445, 1 370, 1 355, 1 300, 1 290, 1 200, 1 125, 1 080, 1 035, and 1 015 cm^{-1}; δ_H($CDCl_3$) 4.62 (1 H, t, *J* 3.7 Hz, 2-H), 4.22—4.02 [2 H, part AB of an ABX system, *J* −12.4, 4.3, and 3.4 Hz, 6-H(eq), 6-H(ax)], 3.45 [1 H, m, 4-H(eq)], 2.63 (3 H, s, SOMe), and 2.34—1.53 [3 H, m, 4-H(ax), 3-H(ax), 3-H(eq)].

Less polar diastereoisomer (**2β**). This had R_F (CCl_4–Pr^iOH, 4:1) 0.24; m.p. 80—81 °C (CCl_4) (Found: C, 47.4; H, 8.1; S, 18.2. $C_7H_{14}SO_3$ requires C, 47.2; H, 7.9; S, 18.0%); $\nu_{max.}$(KBr) 2 995, 2 980, 2 950, 2 850, 1 460, 1 390, 1 220, 1 175, 1 130, 1 065, 1 050, and 1 030 cm^{-1}; δ_H(CD_2Cl_2) 4.54 (1 H, dd, *J* 4.7 and 2.8 Hz. 2-H), 4.15 (1 H, dd, *J* −12.6 and 3.6 Hz, 6-H), 3.58 (1 H, ddd, *J* −12.6, 5.2, and 0.9 Hz, 6-H), 3.38 (3 H, s, OMe), 2.63 (1 H, m, 5-H), 2.57 (3 H, s, SOMe), 2.28—1.92 [3 H, m, 4-H(eq), 4-H(ax), 3-H(eq)] and 1.66—1.51 [1 H, m, 3-H(ax)].

trans-2-*Methoxy*-5-*methylsulphonyltetrahydropyran* (**3**).—To a solution of sodium metaperiodate (1.45 g, 6.78 mmol) in water (20 ml) was added sulphide (**1**) (0.4868 g, 3 mmol). The solution was warmed at 50 °C for 1 h. The mixture was then evaporated to dryness and the residue was extracted several times with methylene dichloride. The extracts were dried (Na_2SO_4) and concentrated to give an oil, which was purified on column chromatography ($CHCl_3$); yield 88%; m.p. 104—105 °C (EtOH) (Found: C, 43.0; H, 7.3; S, 16.25. $C_7H_{14}SO_4$ requires C, 43.3; H, 7.3; S, 16.5%); $\nu_{max.}$(KBr) 3 010, 3 000, 2 960, 2 940, 2 920, 2 880, 1 475, 1 450, 1 400, 1 310, 1 300, 1 275, 1 140, 1 055, 950 and 750 cm^{-1}; δ_H($CDCl_3$) 4.50 (1 H, dd, *J* 6.9 and 3.8 Hz, 2-H), 4.28 [1 H, part A of and AMX system, ddd, *J* −12.3, 4.4, and 1.5 Hz, 6-H(eq)], 3.92 [1 H, part M of an AMX system, dd, *J* −12.3 and 7.0 Hz, 6-H(ax)], 3.45 (3 H, s, OMe), 3.14—3.00 (1 H, m, 5-H), 2.92 (3 H, s, SO_2Me), 2.41—2.22 [1 H, m, 4-H(eq)], 2.15—1.95 [2 H, m, 4-H(ax), 3-H(eq)], and 1.68—1.46 [1 H, m, 3-H(ax)].

cis-2-*Methoxy*-5-*methylsulphonyltetrahydropyran* (**6**).—Sulphide (**5**) was oxidized with sodium metaperiodate as indicated above for (**3**). It was purified on column chromatography ($CHCl_3$), yield 92%; m.p. 60—61 °C (EtOH) (Found: C, 43.1; H, 7.5; S, 16.1. $C_7H_{14}SO_4$ requires C, 43.3; H, 7.3; S, 16.5%); $\nu_{max.}$(KBr) 3 010, 3 000, 2 970, 2 940, 2 920, 1 450, 1 365, 1 300, 1 280, 1 210, 1 140, 1 030, 950, 900, 830, and 760 cm^{-1}; δ_H($CDCl_3$) 4.66 (1 H, dd, *J* 2.9 and 1.8 Hz, 2-H), 4.00—3.90 [2 H, part AB of a degenerated ABX system, 6-H(eq), 6(H(ax)], 3.37 (3 H, s, OMe), 3.15 (1 H, m, 5-H), 2.84 (3 H, s, SO_2Me), and 2.50—1.60 [4 H, m, 4-H(eq), 4-H(ax), 3-H(eq), 3-H(ax)].

Dimethyl-(5-trans-2-*methoxytetrahydropyranyl*)*sulphonium Toluene*-p-*sulphonate* (**4**).—A mixture of (**1**) (0.486 g, 3 mmol)

and methyl toluene-*p*-sulphonate (1.32 g, 7.08 mmol) was stirred at 30 °C for 8 h. The mixture was washed with anhydrous ether and filtered to afford (**4**) (0.784 g, 75%), m.p. 149—150 °C (ethanol–hexane, 1:2) (Found: C, 51.45; H, 7.0; S, 18.2. $C_{15}H_{24}S_2O_5$ requires C, 51.7; H, 6.9; S, 18.4%); $\nu_{max.}$(KBr) 3 020, 3 000, 2 990, 2 920, 2 830, 1 595, 1 495, 1 460, 1 390, 1 205, 1 190, 1 125, 1 070, 820, and 680 cm^{-1}; $\delta_H(CDCl_3)$ 7.80—7.05 (4 H, AA′BB′ system, C_6H_4), 4.65 (1 H, t, *J* 2.6 Hz, 2-H), 4.22 (1 H, m, 5-H), 4.12 [1 H, dd, *J* −13.9 and 2.1 Hz, 6-H(ax)], 3.76 [1 H, dt, *J* −13.9 and 3.2 Hz, 6-H(eq)], 3.33 (3 H, s, OMe), 3.22 (6 H, s, $^+SMe_2$), 2.35 (3 H, s, $ArCH_3$), 2.35 [1 H, m, 4-H(eq)], 2.35 [1 H, m, 4-H(eq)], and 2.60—2.10 [3 H, m, 4-H(ax), 3-H(eq), 3-H(ax)].

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