Studies Related to Dihydro-1,4-thiazines. Part VI.[1] Thermal Racemisation of Sulphoxides [2]

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Oxidation of the dihydrothiazine lactone (17) and the ester (2) with *m*-chloroperbenzoic acid yields the respective (*R*)-oxides (18) and (10); the analogous (*S*)-oxides (33) and (30) are obtained from the dimethyl derivatives (31) and (28). The foregoing sulphoxides undergo thermally induced racemisation under mild conditions: deuterium-incorporation experiments implicate the sulphenic acids, *e.g.* (23), as the reaction intermediates.

The hydroxymethylthiazine ester (7), prepared from the ester (2) and formaldehyde in the presence of an acid catalyst, is converted into the ethoxymethylthiazine ester (8) by ethanolic hydrochloric acid. Oxidation of the derivative (8) with *m*-chloroperbenzoic acid gives a mixture of the (*S*)-oxide (15) and the racemate of the (*R*)-oxide (13). The former sulphoxide is stable in boiling dichloromethane, whereas the latter interconverts with the sulphenic acid (24) in dichloromethane at room temperature. This result, which emphasises that a *syn*-axial arrangement of the sulphinyl group and the tertiary hydrogen atom is a prerequisite for the racemisation, suggests that the sulphenic acid is formed by a concerted intramolecular hydrogen shift.

In the presence of 1,5-diazabicyclo[4.3.0]non-5-ene, the (*R*)- (13) and the (*S*)-oxide (15) are equilibrated (as their racemates) to give a mixture containing *ca.* 18% of the former derivative and 82% of the latter.

The ethoxysulphonium salts (20) and (34), formed from the reaction of the lactone sulphoxides (18) and (33) with triethyloxonium tetrafluoroborate, are transformed into the respective ethoxy-lactones (38) and (36) and hydroxy-lactones (39) and (37) by sodium hydroxide.

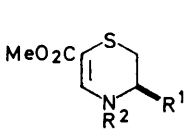
RECENTLY we have examined [3] the conformational behaviour of a series of 1,4-thiazine 1-oxides. The single sulphoxides obtained by oxidation of the acid (1) and the alcohol (3) and the major sulphoxides produced by oxidation of the acetate (4) and the mesylate (5) were inter-related by chemical means and they were considered to possess the *R*-configuration at position 1. We have discussed previously [3] the n.m.r. spectroscopic evidence on which this assignment was

[1] Part V, J. Kitchin and R. J. Stoodley, *J.C.S. Perkin I*, 1973, 2464.

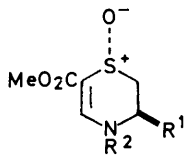
[2] Preliminary communication, A. G. W. Baxter, J. Kitchin, R. J. Stoodley, and R. B. Wilkins, *J.C.S. Chem. Comm.*, 1973, 285.

[3] J. Kitchin and R. J. Stoodley, *Tetrahedron*, 1973, **29**, 3023.

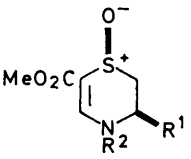
based. We now present chemical evidence which unequivocally establishes that the sulphoxide derived from the acid (1) is the (*R*)-isomer (9).



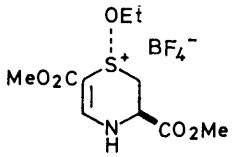
(1) R^1 = CO_2H, R^2 = H
(2) R^1 = CO_2Me, R^2 = H
(3) R^1 = CH_2·OH, R^2 = H
(4) R^1 = CH_2·OAc, R^2 = H
(5) R^1 = CH_2·OMs, R^2 = H
(6) R^1 = CH_2·OH, R^2 = Pr^i
(7) R^1 = CO_2Me, R^2 = CH_2·OH
(8) R^1 = CO_2Me, R^2 = CH_2·OEt



(9) R^1 = CO_2H, R^2 = H
(10) R^1 = CO_2Me, R^2 = H
(11) R^1 = CH_2·OH, R^2 = H
(12) R^1 = CH_2·OH, R^2 = Pr^i
(13) R^1 = CO_2Me, R^2 = CH_2·OEt



(14) R^1 = CH_2·OH, R^2 = Pr^i
(15) R^1 = CO_2Me, R^2 = CH_2·OEt



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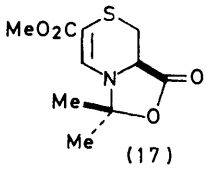

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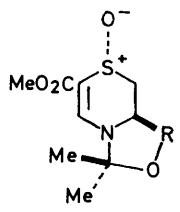


(18) R = CO
(19) R = CH_2

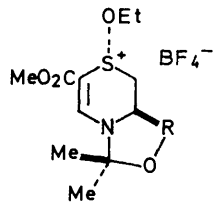
Oxidation of the lactone (17) [4] with *m*-chloroperbenzoic acid yielded a single sulphoxide which, after recrystallisation from boiling chloroform–ether, exhibited no detectable optical rotation. This observation was surprising since the sulphoxide obtained from the acid (1) showed $[\alpha]_D$ +222° (H_2O).[3] Saponification of the lactone sulphoxide gave an optically inactive material, identical (n.m.r. sprctroscopy) with the sulphoxide prepared by oxidation of the acid (1). Evidently, therefore, the lactone sulphoxide was the racemate.

The foregoing result implied either that the lactone (17) underwent racemisation prior to oxidation or that the derived sulphoxide was racemised under the reaction (or work-up) conditions. A mixture of the lactone (17) and the lactone sulphoxide, obtained from the reaction of the lactone (17) with *ca.* 0·5 mol. equiv. of *m*-chloroperbenzoic acid, was treated with sodium hydroxide and the resultant acids were esterified by diazomethane. The product was fractionated (silica gel chromatography) to give the optically pure ester (2).[4] Thus the lactone (17) was shown to be optically stable under the reaction conditions.

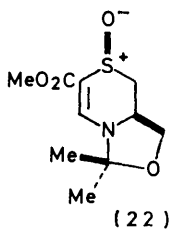
The lactone sulphoxide was obtained in optically active form {$[\alpha]_D$ +119° ($CHCl_3$)} when its isolation was effected at low temperature. It was estimated to be optically pure by converting a sample into the acid sulphoxide {$[\alpha]_D$ +224° (H_2O)}. When the optically active lactone sulphoxide was recrystallised from hot chloroform–ether, the resultant material possessed no detectable optical rotation, indicating that the racemisation was thermally induced.

The ester sulphoxide was prepared by oxidation of the ester (2) with *m*-chloroperbenzoic acid. A sample recrystallised from chloroform–ether at room temperature showed $[\alpha]_D$ +230° (H_2O); it was considered to be optically pure since it was converted into the acid sulphoxide {$[\alpha]_D$ +213° (H_2O)} by alkali. After recrystallisation from boiling chloroform–ether, the ester sulphoxide was obtained in optically inactive form, illustrating that it also underwent a thermally induced racemisation.

Oxidation of the acid (27) [5] with *m*-chloroperbenzoic acid afforded the acid sulphoxide {$[\alpha]_D$ −76° (H_2O)}, which was converted into the racemate in boiling chloroform.



(20) R = CO
(21) R = CH_2



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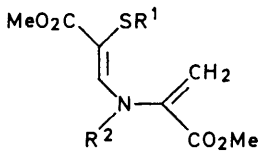
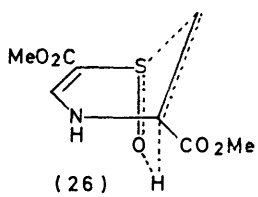


(23) R^1 = OH, R^2 = H
(24) R^1 = OH, R^2 = CH_2·OEt
(25) R^1 = O^-, R^2 = CH_2·OEt



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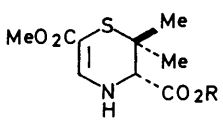
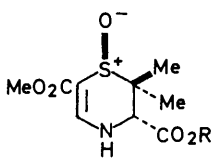


(27) R = H
(28) R = Me



(29) R = H
(30) R = Me

The lactone (31)[6] was similarly oxidised to the sulphoxide, which was isolated in optically active form {$[\alpha]_D$ −47° ($CHCl_3$)} when its isolation was conducted at low temperature. An attempt to determine the optical

[4] A. R. Dunn, I. McMillan, and R. J. Stoodley, *Tetrahedron*, 1968, **24**, 2895.

[5] I. McMillan and R. J. Stoodley, *Tetrahedron Letters*, 1966, 1205; *J. Chem. Soc.* (*C*), 1968, 2533.

[6] J. Kitchin and R. J. Stoodley, *J.C.S. Perkin I*, 1973, 22.

purity of the lactone sulphoxide, by converting it into the acid sulphoxide, was unsuccessful because the material underwent partial racemisation under the saponification conditions. However, the derivative was estimated to be optically pure by transforming a sample {[α]$_D$ −41° ($CHCl_3$)]} into the lactone sulphone (32) {[α]$_D$ −96° ($CHCl_3$)} with *m*-chloroperbenzoic acid. Low temperature oxidation of the lactone (31) with an excess of *m*-chloroperbenzoic acid gave the lactone sulphone (32) {[α]$_D$ −98° ($CHCl_3$)}. The lactone sulphoxide was transformed into the racemate by recrystallisation from boiling chloroform–ether.

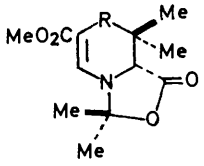
Oxidation of the ester (28) with sodium periodate afforded the ester sulphoxide {[α]$_D$ −83° ($CHCl_3$)}, which was considered to be optically pure since it was converted into the acid sulphoxide {[α]$_D$ −73° (H_2O)} by alkali. Crystallisation from boiling chloroform–light petroleum gave the ester sulphoxide in optically inactive form.

An interesting feature of the foregoing reactions is that the sulphoxides interconvert with their enantiomers but not with their diastereoisomers. There are two possible explanations for this result: either the diastereoisomeric sulphoxides are kinetically inaccessible from the achiral intermediate or they are formed but are thermodynamically unstable with respect to the starting sulphoxides. We favour the former interpretation. Thus, when left for 24 h in dichloromethane containing 10% methan[^{2}H]ol, the racemates of the sulphoxides obtained from the lactones (17) and (31) incorporated *ca.* 75 and 25% $^2H_1$, respectively, at position 6.

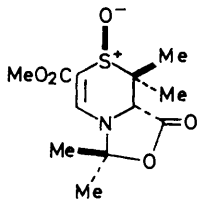
The foregoing observations indicate that the sulphenic acids, *e.g.* (23), intervene in the racemisations. We suggest that the intermediates are formed by a sigmatropic process [*e.g.* (26)], which demands that the sulphoxides possess a *syn*-axial arrangement of the sulphinyl group and the tertiary hydrogen atom. Consequently, the sulphoxides derived from the lactone (17) and the ester (2) are the (*R*)-oxides (18) and (10); those obtained from derivatives (31), (27), and (28) are the (*S*)-oxides (33), (29), and (30).

If the sulphenic acid formation requires a concerted intramolecular hydrogen shift, an inversion of the configuration of the sulphinyl group will preclude the thermal racemisation of the sulphoxides. Attempts were therefore made to convert the derivatives (33), (18), and (10) into their diastereoisomers by Johnson's method.[7]

When treated with triethyloxonium tetrafluoroborate followed by sodium hydroxide, the lactone sulphoxide (33) afforded two new neutral products which were separated (silica gel chromatography); neither component was the required sulphoxide. Analytical and spectroscopic considerations left little doubt that the less polar minor constituent was the ethoxy-lactone (36) and that the more polar component was the hydroxy-lactone (37). The latter substance was transformed into the former in the presence of ethanolic hydrogen chloride; moreover, it was also converted into the previously characterised hydroxy-ester (40)[8] by methanolic sodium methoxide.



(31) R = S
(32) R = SO_2



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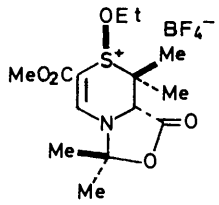

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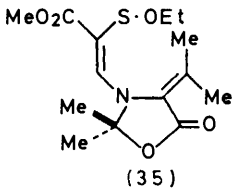

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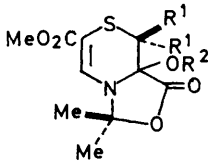
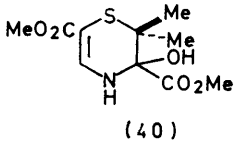


(36) R^1 = Me, R^2 = Et
(37) R^1 = Me, R^2 = H
(38) R^1 = H, R^2 = Et
(39) R^1 = R^2 = H



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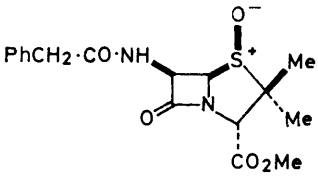

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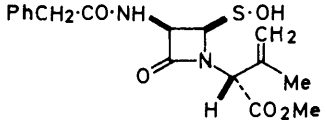

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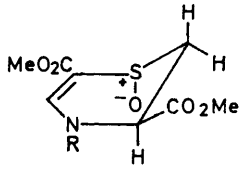
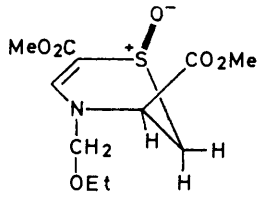


(43) R = H
(44) R = CH_2·OEt



(45)

Under corresponding conditions, the lactone sulphoxide (18) afforded a mixture of the ethoxy- (38) and the hydroxy-lactone (39).

These findings can be accounted for by invoking the intermediacy of the sulphenates, *e.g.* (35), formed by a base-induced β-elimination. The acidity of the 6-hydrogen atom is evidently responsible for such reactions since

[7] C. R. Johnson, *J. Amer. Chem. Soc.*, 1963, **85**, 1020.
[8] R. J. Stoodley, *J. Chem. Soc.* (*C*), 1968, 2891.

the ethoxysulphonium salt (21) yielded the (*S*)-oxide (22) in the presence of sodium hydroxide.[3]

An attempt to convert the ester sulphoxide (10) into its diastereoisomer by treatment with triethyloxonium tetrafluoroborate followed by sodium hydroxide was also unrewarding.

Previously we have shown [3] that the alcohol (3) was oxidised to the (*R*)-oxide (11), whereas its *N*-isopropyl derivative (6) afforded a mixture (*ca.* 7 : 3) of the (*S*)- (14) and the (*R*)-oxide (12), respectively. It was hoped therefore that oxidation of the ethoxymethylthiazine ester (8) would lead to a mixture of sulphoxides.

The hydroxymethylthiazine ester (7), formed from the reaction of the ester (2) with formaldehyde in the presence of hydrochloric acid, was converted into the ethoxymethyl analogue (8) by ethanolic hydrochloric acid. Oxidation of the derivative (8) with *m*-chloroperbenzoic acid yielded a mixture (*ca.* 1 : 1) of sulphoxides which were separated (silica gel chromatography).

The less polar major sulphoxide was devoid of optical activity, suggesting that it was the racemate of the (*R*)-oxide (13). Moreover, when left dissolved for 4 days in dichloromethane containing 10% methan-[^{2}H]ol, it incorporated *ca.* 16% $^2H_1$ at position 3. The minor (*S*)-oxide (15) was isolated in optically active form {$[\alpha]_D$ −104° ($CHCl_3$)}; it was optically stable in boiling dichloromethane or benzene.

The foregoing result provides compelling support for the view that the sulphenic acids, which participate in the thermal racemisation of sulphoxides, are produced by a concerted intramolecular hydrogen shift.

It is well known [9] that the thermolysis of sulphoxides containing a hydrogen atom at the β-carbon atom yields olefins. Since there is good evidence to indicate that these reactions involve cyclic transition states, it has been assumed that the sulphenic acids are the other products. These derivatives, which have been observed only rarely,[10] have recently been studied by several groups; they have proved to be versatile intermediates, particularly in the penicillin field.[11] It has been established that sigmatropic hydrogen shifts are involved in the formation of the sulphenic acids, *e.g.* (42), from penicillin ester *S*-oxides, *e.g.* (41), at 80°.[12] A similar pathway is probably responsible for the ring-opening of *trans*-2,3-dimethylthiiran 1-oxide; this reaction, which occurs at 35°, is evidently facilitated by the relief of ring strain in forming the sulphenic acid intermediate.[13]

The present results demonstrate that sigmatropic hydrogen shifts can be markedly influenced by the acidity of the migrating hydrogen atom. For example, whereas the lactone sulphoxide (18) was readily racemised in chloroform at room temperature, the derivative (19) [3] showed no loss of optical activity when heated in refluxing chloroform, benzene, or toluene.

An interesting difference exists between the thiazine sulphoxide (33) and the penicillin *S*-oxide (41). In the latter case only the hydrogen atoms of the 2β-methyl group undergo the sigmatropic shift, on the basis of deuteriation experiments,[12] in spite of the greater acidity of the 3-hydrogen atom.

Finally we comment on the conformational properties of the sulphoxides (10), (13), and (15). The n.m.r. spectrum ($CDCl_3$) of the derivative (10) contained a triplet at τ 7·66 ($J_{2\alpha,2\beta} = J_{2\beta,3} = 13$ Hz) for the 2β-proton and a double doublet at 6·59 ($J_{2\alpha,2\beta}$ 13, $J_{2\alpha,3}$ 2 Hz) for the 2α-proton; that of the compound (13) possessed a triplet at 7·41 ($J_{2\alpha,2\beta} = J_{2\alpha,3} = 13{\cdot}4$ Hz) for the 2β-proton and a double doublet at 6·76 ($J_{2\alpha,2\beta}$ 13·4, $J_{2\alpha,3}$ 2·8 Hz) for the 2α-proton. These values of the vicinal coupling constants established [3] that the sulphoxides adopted the conformations (43) and (44). The (*S*)-oxide (15) showed in its n.m.r. spectrum ($CDCl_3$) double doublets at τ 7·46 ($J_{2\alpha,2\beta}$ 14, $J_{2\alpha,3}$ 5·2 Hz) and 6·13 ($J_{2\alpha,2\beta}$ 14, $J_{2\beta,3}$ 2·8 Hz) for the 2α- and the 2β-proton, respectively, indicating [3] that it existed as the conformer (45). These findings are in complete accord with the previous results, which illustrated that the sulphoxides exhibited a marked preference for the conformer possessing an axial oxide function.[3]

When treated with 1,5-diazabicyclo[4.3.0]non-5-ene in dichloromethane, the racemate of the (*R*)-oxide (13) was converted mainly into the racemate of the (*S*)-oxide (15) [ratio of (15) to (13), *ca.* 4·5 : 1]. A similar mixture of isomers, which was devoid of optical activity, was produced from the (*S*)-oxide (15) under corresponding conditions, establishing that the sulphoxides were at equilibrium. This interconversion almost certainly occurs by way of the sulphenate anion (25), formed from the sulphoxides (13) and (15) by a base-induced β-elimination.

The foregoing result indicated that the (*S*)-oxide (15) was more stable than the (*R*)-isomer (13) by *ca.* 3·8 kJ mol^{-1} (at 300 K). This value, which also must reflect the free-energy difference between the conformers (44) and (45), can be approximately equated to the additional energy of the adjacent methoxycarbonyl and ethoxymethyl groups [$A^{(1,2)}$ strain [14]] compared with the *syn*-axially arranged oxide and methoxycarbonyl functions.

EXPERIMENTAL

For general experimental details see Part I.[15] 60 MHz N.m.r. spectra were recorded with a Varian EM-360

[9] C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, 1960, **82**, 1810; J. F. King and M. J. Coppen, *Canad. J. Chem.*, 1971, **49**, 3714.

[10] J. A. Shelton and K. E. Davis, *J. Amer. Chem. Soc.*, 1967, **89**, 718.

[11] 'Cephalosporins and Penicillins: Chemistry and Biology,' ed. E. H. Flynn, Academic Press, New York, 1972; R. J. Stoodley, *Progr. Org. Chem.*, 1973, **8**, 102.

[12] D. H. R. Barton, F. Comer, D. G. T. Greig, G. Lucente, P. G. Sammes, and W. E. G. Underwood, *Chem. Comm.*, 1970, 1059; D. H. R. Barton, F. Comer, D. G. T. Greig, P. G. Sammes, C. M. Cooper, G. Hewitt, and W. G. E. Underwood, *J. Chem. Soc.* (*C*), 1971, 3540; R. D. G. Cooper and F. L. José, *J. Amer. Chem. Soc.*, 1970, **92**, 2575; R. D. G. Cooper, *ibid.*, p. 5010.

[13] J. E. Baldwin, G. Höfle, and S. C. Choi, *J. Amer. Chem. Soc.*, 1971, **93**, 2810.

[14] F. Johnson, *Chem. Rev.*, 1968, **68**, 375.

[15] A. R. Dunn and R. J. Stoodley, *J.C.S. Perkin I*, 1972, 2509.

spectrometer. Methan[^{2}H]ol (99%) was purchased from Fluorochem Ltd.

Reaction of the Lactone (17) *with* m-*Chloroperbenzoic Acid.*—(*a*) A solution of *m*-chloroperbenzoic acid (2·00 g, 11·6 mmol) in dichloromethane (40 ml) was added dropwise to a stirred, cooled (acetone–solid carbon dioxide) solution of the lactone (17) [4] (2·43 g, 10 mmol) in dichloromethane (40 ml). After 2 h the mixture was allowed to warm to room temperature and washed with sodium hydrogen carbonate solution (3 times) followed by water. Evaporation of the dried ($MgSO_4$) organic layer left a residue (2·28 g, 88%), which was recrystallised from boiling chloroform–ether to give the *racemate* of *methyl* (4R,6R)-9,9-*dimethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*azabicyclo*[4.3.0]*non*-2-*ene*-3-*carboxylate* 4-*oxide* (18), m.p. 180—185° (decomp.), $[\alpha]_D$ 0° (1·5% in $CHCl_3$). Although possessing a slightly different i.r. spectrum, the sample was identical with the optically active material [3] by mass and n.m.r. spectroscopy (Found: C, 46·7; H, 5·1; N, 5·1%; M^+, 259. $C_{10}H_{13}NO_5S$ requires C, 46·3; H, 5·1; N, 5·4%; *M*, 259).

(*b*) The lactone (17) (1·215 g, 5 mmol) was treated with *m*-chloroperbenzoic acid (0·400 g, 2·3 mmol) as in method (*a*). Work-up afforded a residue (1·240 g) shown to contain a mixture (*ca.* 1·5 : 1) of the lactone (17) and the lactone sulphoxide (18) by n.m.r. spectroscopy. Since the lactone (17) was unstable on silica gel, the mixture was treated with M-sodium hydroxide (5 ml, 5 mmol) followed by Amberlite IR 120 (H^+) resin. Evaporation gave a product which, after esterification with diazomethane in ether, was fractionated by silica gel chromatography (chloroform as eluant).

The first-eluted material (0·550 g, 51%), m.p. 102—103° (from chloroform–ether), $[\alpha]_D$ +86° (0·44% in $CHCl_3$), was identical with the ester (2) [4] by i.r. and n.m.r. spectroscopy.

(*c*) In a modification of the previously described procedure,[3] the lactone (17) (0·445 g, 1·83 mmol) was treated with *m*-chloroperbenzoic acid as in method (*a*). After 0·5 h an excess of diazomethane in ether followed by ether was added to the cooled mixture; the precipitated sulphoxide (18) (0·300 g, 63%), m.p. 188—190°, $[\alpha]_D$ +119° (1·2% in $CHCl_3$), was filtered off.

Reaction of the Lactone Sulphoxide (18) *with Sodium Hydroxide.*—(*a*) The racemate of the lactone sulphoxide (18) (0·130 g, 0·5 mmol) was suspended in water (5 ml) and 0·1M-sodium hydroxide (5 ml, 0·5 mmol) was added. After 5 min the solution was deionised with Amberlite IR 120 (H^+) resin and evaporated to leave the *racemate* of (1R,3R)-3,4-*dihydro*-6-*methoxycarbonyl*-2H-1,4-*thiazine*-3-*carboxylic acid* 1-*oxide* (9) (0·104 g, 95%), m.p. 157—159° (from methanol), $[\alpha]_D$ 0° (0·5% in H_2O). The sample, although possessing a slightly different i.r. spectrum, was identical with the optically active acid sulphoxide (9) [3] by n.m.r. spectroscopy (Found: C, 38·0; H, 4·0; N, 6·2. $C_7H_9NO_5S$ requires C, 38·4; H, 4·2; N, 6·4%).

(*b*) The lactone sulphoxide (18) {$[\alpha]_D$ +119° (1·2% in CHCl)} (0·195 g, 0·15 mmol) was suspended in water (5 ml) and 0·1M-sodium hydroxide (3·75 ml, 0·375 mmol) was added. After 5 min the solution was extracted with chloroform (twice). Evaporation of the dried ($MgSO_4$) organic layer left unchanged starting material (0·091 g, 47%), m.p. 188—189° (from chloroform–ether at room temperature), $[\alpha]_D$ +107° (1·5% in $CHCl_3$). The aqueous layer was deionised with Amberlite IR 120 (H^+) resin and evaporated to give material (0·065 g, 40%), m.p. 157—159° (from methanol), $[\alpha]_D$ +224° (1·0% in H_2O), which was identical with the acid sulphoxide (9) [3] by i.r. and n.m.r. spectroscopy.

Reaction of the Ester (2) *with* m-*Chloroperbenzoic Acid.*—The ester (2) [4] (2·17 g, 10 mmol) was treated with *m*-chloroperbenzoic acid as described for the lactone (17) [method (*a*)]. After 1·5 h the mixture was extracted with water (3 times). Evaporation of the aqueous layer gave *dimethyl* (1R,3R)-3,4-*dihydro*-2H-1,4-*thiazine*-3,6-*dicarboxylate* 1-*oxide* (10) (0·06 g, 45%), m.p. 145—146° (decomp.) (from chloroform–ether at room temperature), $[\alpha]_D$ +230° (1·18% in H_2O), $\nu_{max.}$ (KBr) 3560, 3500, and 3430 (NH), 1745 (ester C=O), 1700 and 1675 (each unsat. C=O), and 1590 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 273 nm (ε 14,800), τ ($CDCl_3$) 7·66 (1H, t, $J_{2\alpha.2\beta} = J_{2\beta.3}$ = 13 Hz, 2β-H), 6·59 (1H, dd, $J_{2\alpha.2\beta}$ 13, $J_{2\alpha.3}$ 2 Hz, 2α-H), 6·22 and 6·12 (each 3H, s, MeO), 5·44 (1H, dd, $J_{2\beta.3}$ 13, $J_{2\alpha.3}$ 2 Hz, 3-H), 2·63br (1H, d, *J* 8 Hz, NH), and 2·06 (1H, d, *J* 8 Hz, 4-H) (addition of D_2O caused the signal at τ 2·63 to disappear and that at 2·06 to collapse to a singlet) (Found: C, 40·9; H, 5·0; N, 6·3%; M^+, 233. $C_8H_{11}NO_5S$ requires C, 41·2; H, 4·7; N, 6·0%; *M*, 233).

When recrystallised from boiling chloroform–ether, the ester sulphoxide (10) was converted into the *racemate*, m.p. 144—146° (decomp.), $[\alpha]_D$ 0° (1·0% in H_2O). The sample, although possessing a slightly different i.r. spectrum, was identical with the optically active material by mass and n.m.r. spectroscopy (Found: C, 40·9; H, 4·7; N, 5·8%; M^+, 233).

Reaction of the Ester Sulphoxide (10) *with Sodium Hydroxide.*—The ester sulphoxide (10) {$[\alpha]_D$ +234° (0·5% in H_2O)} (0·117 g, 0·5 mmol) was treated with sodium hydroxide as described for the lactone sulphoxide (18) [method (*a*)]. Work-up gave a material (0·092 g, 84%), m.p. 156—158° (from methanol), $[\alpha]_D$ +213° (1·3% in H_2O), which was identical with the acid sulphoxide (9) [3] by i.r. and n.m.r. spectroscopy.

Reaction of the Acid (27) *with* m-*Chloroperbenzoic Acid.*—A solution of *m*-chloroperbenzoic acid (0·380 g, 2·24 mmol) in dioxan (4 ml) was added to the acid (27) [5] (0·462 g, 2 mmol) dissolved in dioxan (4 ml). After 45 min the mixture was diluted with chloroform and extracted with water (3 times). Evaporation of the aqueous layer afforded (1*S*,3*S*)-2,3-dihydro-6-methoxycarbonyl-2,2-dimethyl-2*H*-1,4-thiazine-3-carboxylic acid 1-oxide (29) as a crisp foam, $[\alpha]_D$ −76° (1·18% in H_2O), $\nu_{max.}$ (KBr) 3400br (OH and NH), 1700br (CO_2H and unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 275 nm (ε 10,300), τ [$(CD_3)_2SO$] 9·17 and 8·62 (each 3H, s, *gem*-Me_2), 6·30 (3H, s, MeO), 6·00 (1H, s, 3-H), 4·4br (*ca.* 4H, s, $2H_2O$), 2·15 (1H, d, *J* 7 Hz, 5-H), and 1·0br (1H, d, *J* 7 Hz, NH) (addition of D_2O caused the signals at τ 4·4 and 1·0 to disappear and that at 2·15 to collapse to a singlet).

When heated in boiling chloroform, the acid sulphoxide (29) was converted into the *racemate*, m.p. 140—142° (from chloroform), $[\alpha]_D$ 0° (1·1% in H_2O). The sample, although possessing a different i.r. spectrum, was identical with the optically active material by n.m.r. spectroscopy except that the signal at τ 4·4 was absent (Found: C, 42·9; H, 5·2; N, 5·6. $C_9H_{13}NO_5S$,0·25H_2O requires C, 42·9; H, 5·4; N, 5·6%).

Reaction of the Lactone (31) *with* m-*Chloroperbenzoic Acid.*—(*a*) The lactone (31) [6] (0·271 g, 1 mmol) was treated with *m*-chloroperbenzoic acid as described for the derivative (17) [method (*a*)]. After 0·5 h an excess of diazomethane

in ether, followed by ether, was added to the cooled mixture; the precipitated *methyl* (4S,6S)-5,5,9,9-*tetramethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*azabicyclo*[4.3.0]*non*-2-*ene*-3-*carboxylate* 4-*oxide* (33) (0·33 g, 48%) was filtered off; m.p. 187—188°, $[\alpha]_D$ −47° (1·6% in $CHCl_3$), $\nu_{max.}$ (KBr) 1785 (γ-lactone C=O), 1685 (unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 284 nm (ε 12,900), τ ($CDCl_3$) 9·13, 8·34, and 8·24 (3H, 6H, and 3H, s, 2 *gem*-Me_2), 6·24 (3H, s, MeO), 5·69 (1H, s, 6-H), and 2·20 (1H, s, 2-H) (Found: C, 50·0; H, 5·6; N, 4·8%; M^+, 287. $C_{12}H_{17}NOS$ requires C, 50·2; H, 5·9; N, 4·9%; *M*, 287).

When recrystallised from boiling chloroform–ether, the lactone sulphoxide (33) was converted into the *racemate*, m.p. 186—188° (decomp.), $[\alpha]_D$ 0° (0·8% in $CHCl_3$). The sample, although possessing a slightly different i.r. spectrum, was identical with the optically active material by mass and n.m.r. spectroscopy (Found: C, 49·9; H, 6·1; N, 4·8%; M^+, 287).

(*b*) A solution of the lactone (31) (0·324 g, 1·2 mmol) in dichloromethane (8 ml) was treated at −10° with *m*-chloroperbenzoic acid (0·516 g, 3 mmol) in dichloromethane (8 ml). The mixture was left at −10° for 48 h, diluted with dichloromethane, and washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried ($MgSO_4$) organic layer gave *methyl* (6R)-9,9-*dimethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*azabicyclo*[4.3.0]*non*-2-*ene*-3-*carboxylate* 4,4-*dioxide* (32) (0·330 g, 86%), m.p. 228—230° (from chloroform–ether), $[\alpha]_D$ −98° (1·0% in $CHCl_3$), $\nu_{max.}$ (KBr) 1790 (γ-lactone C=O), 1685 (unsat. C=O), and 1590 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 276 nm (ε 13,100), τ ($CDCl_3$) 8·66, 8·33, 8·27, and 8·17 (each 3H, s, 2 *gem*-Me_2), 6·17 (3H, s, MeO), 5·27 (1H, s, 6-H), and 2·23 (1H, s, 2-H) (Found: C, 47·4; H, 5·5; N, 4·6%; M^+, 303. $C_{12}H_{17}NO_6S$ requires C, 47·5; H, 5·6; N, 4·6%; *M*, 303).

Reaction of the Lactone Sulphoxide (33) *with* m-*Chloroperbenzoic Acid*.—A solution of the lactone sulphoxide (33) {$[\alpha]_D$ −41° (2·1% in $CHCl_3$)} (0·086 g, 0·3 mmol) in dichloromethane (3 ml) was treated at −10° with *m*-chloroperbenzoic acid (0·073 g, 0·42 mmol) in dichloromethane (4 ml). The mixture was left at −10° for 24 h and worked up to give a substance (0·080 g, 89%), m.p. 228—230° (from chloroform–ether), $[\alpha]_D$ −96° (2·56% in $CHCl_3$), which was identical with the lactone sulphone (32) by i.r. and n.m.r. spectroscopy.

Reaction of the Lactone Sulphoxide (33) *with Sodium Hydroxide*.—The lactone sulphoxide (33) {$[\alpha]_D$ −38° (1·65% in $CHCl_3$)} (0·143 g, 0·5 mmol) was treated with sodium hydroxide as described for the derivative (18) [method (*b*)]. Work-up gave unchanged starting material (0·060 g, 42%), m.p. 186—188° (from chloroform–ether at room temperature), $[\alpha]_D$ −14° (1·5% in $CHCl_3$), and an amorphous solid (0·051 g, 39%), $[\alpha]_D$ −12° (0·6% in H_2O), which was identical with the acid sulphoxide (29) by n.m.r. spectroscopy.

Reaction of the Ester (28) *with Sodium Periodate*.—A solution of the ester (28)[5] (0·490 g, 2 mmol) in methanol (16 ml) was treated with sodium periodate (0·464 g, 2·2 mmol) in water (16 ml). After 35 min the mixture was diluted with water and extracted with chloroform (3 times). The organic layer was washed with water, dried ($MgSO_4$), and evaporated to leave *dimethyl* (1S,3S)-3,4-*dihydro*-2,2-*dimethyl*-2H-1,4-*thiazine*-3,6-*dicarboxylate* 1-*oxide* (30) (0·350 g, 67%) as a syrup, $[\alpha]_D$ −83° (1·4% in $CHCl_3$), $\nu_{max.}$ (film) 3400br (NH), 1740 (ester C=O), 1690 (unsat. C=O), and 1590 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 275 nm (ε 7600), τ ($CDCl_3$) 9·07 and 8·50 (each 3H, s *gem*-Me_2), 6·21 and 6·12 (each 3H, s, MeO), 5·72 (1H, s, 3-H), 2·6br (1H, d, *J* 7 Hz, NH), and 2·09 (1H, d, *J* 7 Hz, 5-H) (addition of D_2O caused the signal at τ 2·6 to disappear and that at 2·09 to collapse to a singlet) (Found: M^+, 261·0660. $C_{10}H_{15}NO_5S$ requires *M*, 261·0671).

When heated in boiling chloroform the ester sulphoxide (30) was converted into the *racemate*, m.p. 114—116° (from chloroform–light petroleum), $[\alpha]_D$ 0° (1·0% in $CHCl_3$). The sample, although possessing a slightly different i.r. spectrum, was identical with the optically active material by n.m.r. spectroscopy (Found: C, 45·8; H, 5·7; N, 5·3. $C_{10}H_{15}NO_5S$ requires C, 46·0; H, 5·7; N, 5·4%).

Reaction of the Ester Sulphoxide (30) *with Sodium Hydroxide*.—The ester sulphoxide (30) {$[\alpha]_D$ −76° (2·0% in $CHCl_3$)} (0·130 g, 0·5 mmol) was treated with sodium hydroxide as described for the lactone sulphoxide (18) [method (*b*)]. Work-up gave a syrup (0·061 g, 50%), $[\alpha]_D$ −77° (1·94% in $CHCl_3$), identical with the starting material by n.m.r. spectroscopy, and an amorphous solid (0·054 g, 43%), $[\alpha]_D$ −73° (1·5% in H_2O), which was identical with the acid sulphoxide (29) by n.m.r. spectroscopy.

Reaction of the Lactone Sulphoxide (33) *with Triethyloxonium Tetrafluoroborate–Sodium Hydroxide*.—Triethyloxonium tetrafluoroborate (0·285 g, 1·5 mmol), dissolved in dry dichloromethane (0·5 ml), was added to a solution of the lactone sulphoxide (33) (0·213 g, 0·75 mmol) in dry dichloromethane (1 ml). After 24 h the mixture was evaporated to leave the crude sulphoxonium salt (34) (0·348 g), $\nu_{max.}$ (film) 1795 (γ-lactone C=O), 1700br (unsat. C=O), and 1595 cm^{-1} (C=C); no starting material was detected (n.m.r. spectroscopy and t.l.c.).

A solution of the crude salt (34) (0·302 g) in water (12 ml) was treated with 0·1M-sodium hydroxide (7·5 ml, 0·75 mmol). After 5 min the mixture was extracted with chloroform (3 times). Evaporation of the dried ($MgSO_4$) organic layer gave a crystalline residue (0·146 g), shown to contain a mixture of derivatives (37) and (33) (*ca.* 5 : 1, respectively) by n.m.r. spectroscopy; a small amount of a third component was detected on t.l.c. The mixture was fractionated by silica gel chromatotography [benzene–ether (8 : 1) as eluant].

The first-eluted material (0·012 g, 3%) was *methyl* 6-*ethoxy*-5,5,9,9-*tetramethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*azabicyclo*-[4.3.0]*non*-2-*ene*-3-*carboxylate* (36), m.p. 148—149° (from ethanol–water), $[\alpha]_D$ 0° (0·55% in $CHCl_3$), $\nu_{max.}$ (KBr) 1785 (γ-lactone C=O), 1695 (unsat. C=O), and 1600 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 226 (ε 4400), 268sh (1900), and 312 nm (7000), τ ($CDCl_3$) 8·92, 8·33, and 8·23 (3H, 6H, and 3H, s, 2 *gem*-Me_2), 8·79 (3H, t, *J* 7 Hz, $MeCH_2$·O), 6·63 (2H, q, *J* 7 Hz, $MeCH_2$·O), 6·23 (3H, s, MeO), and 2·53 (1H, s 2-H) (Found: C, 53·3; H, 6·8; N, 4·3%; M^+, 315. $C_{14}H_{21}NO_5S$ requires C, 53·3; H, 6·7; N, 4·4%; *M*, 315).

The second-eluted substance (0·040 g, 20%) was *methyl* 6-*hydroxy*-5,5,9,9-*tetramethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*azabicyclo*[4.3.0]*non*-2-*ene*-3-*carboxylate* (37), m.p. 176—178° (from ethanol–water), $[\alpha]_D$ 0° (0·55% in $CHCl_3$), $\nu_{max.}$ (KBr) 3400 (OH), 1785 (γ-lactone C=O), 1675 (unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 221 (ε 6500) and 311 nm (12,000), τ ($CDCl_3$) 8·90, 8·36, 8·30, and 8·22 (each 3H, s, 2 *gem*-Me_2), 6·87 (1H, s, OH), 6·23 (3H, s, MeO), and 2·43 (1H, s, 2-H) (addition of D_2O caused the signal at τ 6·87 to disappear) (Found: C, 50·1; H, 6·2; N, 5·0%; M^+, 287. $C_{12}H_{17}NO_5S$ requires C, 50·2; H, 5·9; N, 4·9%; *M*, 287).

The third-eluted substance (0·032 g, 14%) was identical with the lactone sulphoxide (33) by n.m.r. spectroscopy.

Reaction of the Hydroxy-lactone (37) *with Ethanolic Hydrogen Chloride.*—The hydroxy-lactone (37) (0·057 g, 0·2 mmol) was dissolved in ethanolic hydrogen chloride [prepared by adding acetyl chloride (2 drops) to ethanol (5 ml)]. After 15 h the solution was diluted with chloroform and washed with water (twice). Evaporation of the dried ($MgSO_4$) organic layer gave a residue (0·057 g, 90%), m.p. 148—149° (from ethanol–water), which was identical with the ethoxy-lactone (36) by i.r. and n.m.r. spectroscopy.

Reaction of the Hydroxy-lactone (37) *with Sodium Methoxide.*—A solution of the hydroxy-lactone (37) (0·057 g 0·2 mmol) in methanol (5 ml) was treated with 0·1M-sodium methoxide (0·4 ml, 0·04 mmol). After 0·75 h the mixture was diluted with dichloromethane and washed with water. Evaporation of the dried ($MgSO_4$) organic layer yielded a residue, which was purified by silica gel chromatography [benzene–ether (12 : 1) as eluant]. The derived product (0·040 g, 73%), m.p. 112—114° (from ether–light petroleum), was identical with the hydroxy-ester (40) [8] by i.r. and n.m.r. spectroscopy.

Reaction of the Lactone Sulphoxide (18) *with Triethyloxonium Tetrafluoroborate–Sodium Hydroxide.*—The lactone sulphoxide (18) (0·518 g, 2 mmol) was treated with triethyloxonium tetrafluoroborate as described for the derivative (33). Evaporation of the mixture after 12 h afforded the crude sulphoxonium salt (20) (0·700 g), $\nu_{max.}$ (KBr) 1805 (γ-lactone C=O), 1730 (unsat. C=O), and 1595 cm^{-1} (C=C); no starting material was detected (t.l.c.).

A solution of the crude salt (20) (0·690 g) in water (50 ml) was treated with 0·1M-sodium hydroxide (20 ml, 2 mmol). After 5 min the mixture was extracted with chloroform (3 times). Evaporation of the dried ($MgSO_4$) organic layer gave a syrup (0·355 g), shown to contain a mixture of the derivatives (39), (18), and (38) (*ca.* 8 : 7 : 1, respectively) by n.m.r. spectroscopy. The mixture was fractionated by silica gel chromatography [benzene–ether (8 : 1) as eluant].

The first-eluted material (0·015 g, 3%) was *methyl 6-ethoxy-9,9-dimethyl-7-oxo-8-oxa-4-thia-1-azabicyclo*[4.3.0]*non-2-ene-3-carboxylate* (38), m.p. 117—119° (from carbon tetrachloride), $[\alpha]_D$ 0° (0·56% in $CHCl_3$), $\nu_{max.}$ (KBr) 1780 (γ-lactone C=O), 1700 (unsat. C=O), and 1590 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 224 (ε 4400), 261 (2400), and 310 nm (7000), τ ($CDCl_3$) 8·79 (3H, t, *J* 7 Hz, $MeCH_2$·O), 8·40 and 8·23 (each 3H, s, *gem*-Me_2), 7·76 and 6·63 (each 1H, d, *J* 13 Hz, 5-H_2), 6·41 (2H, q, *J* 7 Hz, $MeCH_2$·O), 6·23 (3H, s, MeO), and 2·50 (1H, s, 2-H) (Found: C, 50·1; H, 6·0; N, 4·7%; M^+, 287. $C_{12}H_{17}NO_5S$ requires C, 50·2; H, 5·9; N, 4·9%; *M*, 287).

The second-eluted component (0·090 g, 17%) was *methyl 6-hydroxy-9,9-dimethyl-7-oxo-8-oxa-4-thia-1-azabicyclo*[4.3.0]*non-2-ene-3-carboxylate* (39), m.p. 122—124° (from chloroform–light petroleum), $[\alpha]_D$ 0° (0·72% in $CHCl_3$), $\nu_{max.}$ (KBr) 3380 (OH), 1775 (γ-lactone C=O), 1675 (unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 220 (ε 6200), 258 (3000), and 310 nm (9800), τ ($CDCl_3$) 8·31 and 8·23 (each 3H, s, *gem*-Me_2), 7·66 and 6·86 (each 1H, d, *J* 12 Hz, 5-H_2), 6·56 (1H, s, OH) 6·23 (3H, s, MeO), and 2·40 (1H, s, 2-H) (addition of D_2O caused the signal at τ 6·56 to disappear) (Found: C, 46·6; H, 5·0; N, 5·4%; M^+, 259. $C_{10}H_{13}NO_5S$ requires C, 46·3; H, 5·0; N, 5·4%; *M*, 259).

Further elution [chloroform–ethyl acetate (9 : 1)] gave a third component (0·140 g, 27%), which was identical with the lactone sulphoxide (18) by n.m.r. spectroscopy.

Reaction of the Hydroxy-lactone (39) *with Ethanolic Hydrogen Chloride.*—The hydroxy-lactone (39) (0·052 g, 0·2 mmol) was treated with ethanolic hydrogen chloride as described for the derivative (37). Work-up after 5 h yielded a product (0·049 g, 85%), m.p. 115—118° (from carbon tetrachloride), which was identical with the ethoxy-lactone (38) by i.r. and n.m.r. spectroscopy.

Reaction of the Ester Sulphoxide (10) *with Triethyloxonium Tetrafluoroborate–Sodium Hydroxide.*—The ester sulphoxide (10) (0·233 g, 1 mmol) was treated with triethyloxonium tetrafluoroborate as described for the derivative (37). The mixture was evaporated after 2 h to give the crude sulphoxonium salt (16) (0·270 g), $\nu_{max.}$ (KBr) 1755 (ester C=O), 1700br (unsat. C=O), and 1600 cm^{-1} (C=C); no starting material was detected (t.l.c.).

A solution of the crude salt (16) (0·270 g) in water (10 ml) was treated with 0·1M-sodium hydroxide (10 ml, 1 mmol). After 5 min the mixture was extracted with chloroform (3 times). Evaporation of the dried ($MgSO_4$) organic layer yielded a syrup (0·040 g), which contained a complex mixture of products (t.l.c.). The aqueous layer was deionised with Amberlite IR 120 (H^+) resin and evaporated to give a syrup (0·110 g), shown to contain mainly the ester sulphoxide (10) by n.m.r. spectroscopy.

Reaction of the Ester (2) *with Formaldehyde.*—A solution of the ester (2) [4] (2·17 g, 10 mmol) in 50% aqueous dioxan (20 ml) was treated with M-hydrochloric acid (1 ml) followed by aqueous 40% formaldehyde (4 ml). After 24 h the mixture was diluted with water and extracted (3 times) with chloroform. Evaporation of the dried ($MgSO_4$) organic layer gave *dimethyl* (3R)-3,4-*dihydro*-4-*hydroxymethyl*-2H-1,4-*thiazine*-3,6-*dicarboxylate* (7) (2·23 g, 90%), m.p. 120—122° (from chloroform–ether), $[\alpha]_D$ +220° (0·92% in $CHCl_3$), $\nu_{max.}$ (KBr) 3460 (OH), 1755 (ester C=O), 1685 (unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 219 (ε 7400), 260 (4700), and 310 nm (10,700), τ ($CDCl_3$) 7·20 (1H, dd, $J_{2\alpha.2\beta}$ 12·8, $J_{2\beta.3}$ 3·0 Hz, 2α-H), 6·66 (1H, dd, $J_{2\alpha.2\beta}$ 12·8, $J_{2\beta.3}$ 3·0 Hz, 2β-H), 6·21 (6H, s, 2 MeO), 5·50 (1H, t, $J_{2\alpha.3} = J_{2\beta.3}$ = 3·0 Hz, 3-H), 5·34 (2H, s, N·CH_2), and 2·45 (1H, s, 4-H) (Found: C, 44·0; H, 5·3; N, 5·4%; M^+, 247. $C_9H_{13}NO_5S$ requires C, 43·7; H, 5·3; N, 5·7%; M^+, 247).

Reaction of the Hydroxymethylthiazine Ester (7) *with Ethanolic Hydrochloric Acid.*—The ester (7) (0·620 g, 2·5 mmol) was dissolved in ethanol (100 ml) containing concentrated hydrochloric acid (1 ml). After 12 h the solution was diluted with chloroform and washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried ($MgSO_4$) organic layer gave *dimethyl* (3R)-4-*ethoxymethyl*-3,4-*dihydro*-2H-1,4-*thiazine*-3,6-*dicarboxylate* (8) (0·410 g, 70%), m.p. 67—68° (from ether–light petroleum), $[\alpha]_D$ +124° (1·9% in $CHCl_3$), $\nu_{max.}$ (KBr) 1750 (ester C=O), 1685 (unsat. C=O), and 1605 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 312 nm (ε 11,800), τ ($CDCl_3$) 8·82 (3H, t, *J* 6·8 Hz, $MeCH_2$·O), 7·26 (1H, dd, $J_{2\alpha.2\beta}$ 13·6, $J_{2\alpha.3}$ 3·2 Hz, 2α-H), 6·66 (1H, dd, $J_{2\alpha.2\beta}$ 13·6, $J_{2\alpha.3}$ 3·2 Hz, 2β-H), 6·56 (2H, q, *J* 6·8 Hz, $MeCH_2$·O), 6·32 and 6·29 (each 3H, s, MeO), 5·40 (1H, t, $J_{2\alpha.3} = J_{2\beta.3}$ = 3·2 Hz, 3-H), 5·38 (2H, ABq, *J* 9 Hz, N·CH_2), and 2·36 (1H, s, 5-H) (Found: C, 48·1; H, 6·2; N, 5·2%; M^+, 275·0764. $C_{11}H_{17}NO_5S$ requires C, 48·0; H, 6·2; N, 5·1%; *M*, 275·0827).

Reaction of the Ethoxymethylthiazine Ester (8) *with* m-*Chloroperbenzoic Acid.*—The ester (8) (0·825 g, 0·3 mmol)

was treated with *m*-chloroperbenzoic acid as described for the lactone (17) [method (*a*)]. After 2·5 h the mixture was washed with sodium hydrogen carbonate solution (3 times) followed by water. Evaporation of the dried ($MgSO_4$) organic layer gave a syrup, shown to contain mainly two components (*ca.* 1 : 1) by n.m.r. spectroscopy. The mixture was fractionated by silica gel chromatography (chloroform as eluant).

The first-eluted component (0·321 g, 36% was the *racemate* of *dimethyl* (1R,3R)-4-*ethoxymethyl*-3,4-*dihydro*-2H-1,4-*thiazine*-3,6-*dicarboxylate* 1-*oxide* (13), m.p. 75—76° (from ether), $[\alpha]_D$ 0° (0·6% in $CHCl_3$), $\nu_{max.}$ (KBr) 1745 (ester C=O), 1695 (unsat. C=O), and 1600 cm^{-1} (C=C), $\lambda_{max.}$ (EtOH) 277 nm (ε 14,600), τ ($CDCl_3$) 8·83 (3H, t, *J* 7·5 Hz, $MeCH_2$·O), 7·41 (1H, t, $J_{2\alpha.2\beta} = J_{2\alpha.3} = 13·4$ Hz, 2β-H), 6·76 (1H, dd, $J_{2\alpha.2\beta}$ 13·4, $J_{2\alpha.3}$ 2·8 Hz, 2α-H), 6·60 (2H, q, *J* 7·5 Hz, $MeCH_2$·O), 6·23 and 6·19 (each 3H, s, MeO), 5·50 (1H, dd, $J_{2\beta.3}$ 13·4, $J_{2\alpha.3}$ 2·8 Hz, 3-H), 5·13 (2H, ABq, *J* 10 Hz, CH_2·N), and 2·13 (1H, s, 5-H) (Found: C, 48·1; H, 5·9; N, 4·8%; M^+, 291. $C_{11}H_{17}NO_6S$ requires C, 45·4; H, 5·8; N, 4·8%; *M*, 291).

The second-eluted component (0·279 g, 32%) was *dimethyl* (1S,3R)-4-*ethoxymethyl*-3,4-*dihydro*-2H-1,4-*thiazine*-3,6-*dicarboxylate* 1-*oxide* (15), m.p. 74—75° (from ether–light petroleum), $[\alpha]_D$ −104° (0·6% in $CHCl_3$), $\nu_{max.}$ (KBr) 1760 and 1740 (each ester C=O), 1690 (unsat. C=O), and 1595 cm^{-1} (C=C), $\lambda_{max.}$ 276 nm (ε 16,500), τ ($CDCl_3$) 8·76 (3H, t, *J* Hz, $MeCH_2$·O), 7·46 (1H, dd, $J_{2\alpha.2\beta}$ 14, $J_{2\alpha,3}$ 5·2 Hz, 2α-H), 6·48 (2H, q, *J* 7 Hz, $MeCH_2$·O), 6·27 and 6·20 (each 3H, s, MeO), 6·13 (1H, dd, $J_{2.\alpha2\beta}$ 14, $J_{2\alpha.3}$ 2·8 Hz, 2β-H), 5·40 (1H, dd, $J_{2\alpha.3}$ 5·2, $J_{2\beta.3}$ 2·8 Hz, 3-H), 5·18 (2H, ABq, *J* 10 Hz, CH_2·N), and 2·02 (1H, s, 5-H) (Found: C, 45·1; H, 5·7; N, 4·8%; M^+, 291. $C_{11}H_{17}NO_6S$ requires C, 45·4; H, 5·8; N, 4·8%; *M*, 291).

Equilibration of the (R)-*Oxide* (13) *and the* (S)-*Isomer* (15).—(*a*) A solution of the racemate of the (*R*)-sulphoxide (13) (0·200 g, 0·69 mmol) in deuteriochloroform (1·5 ml) was treated with 1,5-diazabicyclo[4.3.0]non-5-ene (1 drop) and the reaction was monitored by n.m.r. spectroscopy. After 5 min the mixture was diluted with chloroform and washed with 0·2M-hydrochloric acid followed by water. Evaporation of the dried organic layer left a syrup (0·130 g), shown to contain a mixture (*ca.* 4·5 : 1) of the sulphoxides (15) and (13) by n.m.r. spectroscopy. The mixture was separated by silica gel chromatography (chloroform as eluant).

The first-eluted material (0·017 g, 9%) was identical with the starting material (t.l.c. and n.m.r. spectroscopy).

The second-eluted substance (0·080 g, 40%) was the *racemate* of the (*S*)-oxide (15), m.p. 111—112° (from ether). The sample, although possessing a slightly different i.r. spectrum, was identical with the optically pure material by mass and n.m.r. spectroscopy (Found: C, 45·5; H, 5·8; N, 4·7%; M^+, 291. $C_{11}H_{17}NO_6S$ requires C, 45·4; H, 5·8; N, 4·8%; *M*, 291).

(*b*) The (*S*)-oxide (15) (0·050 g, 0·17 mmol) was treated with 1,5-diazabicyclo[4.3.0]non-5-ene as described in method (*a*). Work-up after 5 min yielded a syrup (0·020 g), $[\alpha]_D$ 0° (1·4% in $CHCl_3$), shown to contain a mixture (*ca* 4·6 : 1) of the sulphoxides (15) and (13) by n.m.r. spectroscopy.

Deuteriation of the Sulphoxides (18), (33), *and* (13).—(*a*) A solution of the lactone sulphoxide (18) (0·101 g, 0·39 mmol) in dichloromethane (9 ml) and methan[^{2}H]ol (1 ml) was left at room temperature for 24 h. The material obtained by evaporation of the solvent was 24% $^2H_0$, 75% $^2H_1$, and 1% $^2H_2$ (mass spectroscopy); τ ($CDCl_3$) as for the sulphoxide (18) except 7·69 (1H, d, $J_{2\alpha.2\beta}$ 13 Hz, 5β-H), 6·56 (1H, d, $J_{2\alpha,2\beta}$ 13 Hz, 5α-H), and 5·30 (0·25H, dd, $J_{2\beta,3}$ 13, $J_{2\alpha.3}$ 3 Hz, 6-H).

(*b*) The racemate of the lactone sulphoxide (33) (0·112 g, 0·39 mmol) was treated as described in method (*a*). The product was 72% $^2H_0$, 27% $^2H_1$, and 1% $^2H_2$ (mass spectroscopy); τ ($CDCl_3$) as for the sulphoxide (33) except 5·65 (0·75H, s, 6-H).

(*c*) The racemate of the ethoxymethylthiazine ester *S*-oxide (13) (0·113 g, 0·39 mmol) was treated as described in method (*a*). The product was 94% $^2H_0$, 5% $^2H_1$, and 1% $^2H_2$ (mass spectroscopy). After resubjection to the reaction conditions for 72 h, the sample was 83% $^2H_0$, 16% $^2H_1$, and 1% $^2H_2$: τ ($CDCl_3$) as for the sulphoxides (13) except 7·41 (0·89H, t, $J_{2\alpha.2\beta} = J_{2\beta.3} = 13$ Hz and 0·11H, d, $J_{2\alpha.2\beta}$ 13 Hz, 2β-H) and 5·50 (0·89H, dd, $J_{2\beta.3}$ 13, $J_{2\beta.3}$ 2·8 Hz, 3-H).

Thermal Behaviour of the Sulphoxides (15) *and* (19).—(*a*) A solution of the (*S*)-oxide (15) (0·058 g, 0·2 mmol) in dichloromethane (10 ml) was heated under reflux for 4 h. Evaporation gave the starting material, m.p. 74—75° (from ether), $[\alpha]_D$ −100° (0·7% in $CHCl_3$). A similar result was obtained when the sample was heated under reflux in benzene (2 h)

(*b*) A solution of the (*R*)-oxide (19) (0·090 g) in chloroform (10 ml) was heated under reflux for 24 h. Evaporation gave the starting material, m.p. 165—169° (from chloroform–ether), $[\alpha]_D$ +305° (0·9% in $CHCl_3$). A similar result was obtained when the sample was heated under reflux in benzene (3 h) or toluene (5 h).

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