Thermal Racemisation of 1,4-Thiazine Oxides: Evidence for a Sigmatropic Pathway

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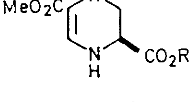
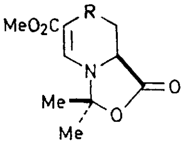
Summary The thermally induced racemisation of methyl (4*R*,6*R*)-9,9-dimethyl-7-oxo-8-oxa-4-thia-1-azabicyclo-[4,3,0]non-2-ene-3-carboxylate 4-oxide (**5**) probably involves the intermediacy of the sulphenic acid (**9**), which is formed by a sigmatropic hydrogen shift.

The sulphoxide (**1**),† m.p. 158—160° (decomp.), $[\alpha]_D + 222°$ (H_2O), was prepared (70%) by oxidation of the acid (**2**)[1] with *m*-chloroperbenzoic acid (in dioxan at 12°). Compound (**5**),† m.p. 180—185° (decomp.), $[\alpha]_D$ 0° ($CHCl_3$), was obtained (51%) from the corresponding oxidation (in dichloromethane at −78°) of the lactone (**6**).[1] O.r.d. spectroscopy indicated that (**5**) was a racemate; moreover, when treated with 1 mol equiv. of sodium hydroxide it was converted into the racemate of (**1**).

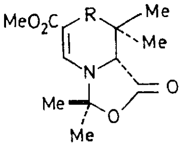
The lactone sulphoxide (**5**) was obtained in optically active form $\{[\alpha]_D + 105°$ ($CHCl_3$)$\}$ when isolated and recrystallised (chloroform–ether) at or below 10°; but when recrystallised from hot chloroform–ether, it was obtained as a racemate. The racemisation is therefore thermally induced. Furthermore, when optically active (**5**) was left for 24 h at room temperature in dichloromethane containing 10% MeOD, the racemic product was 75% monodeuteriated and 24% undeuteriated on the basis of mass spectroscopy; the isotope was located (76%) at position 6 by n.m.r. spectroscopy.



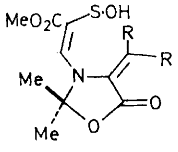
(1) R^1 = SO, R^2 = H
(2) R^1 = S, R^2 = H
(3) R^1 = SO, R^2 = Me
(4) R^1 = S, R^2 = Me



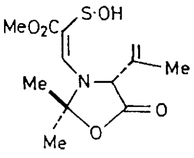
(5) R = SO
(6) R = S



(7) R = SO
(8) R = S



(9) R = H
(10) R = Me



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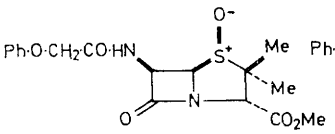

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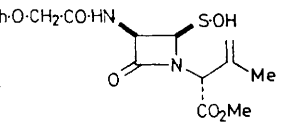

(13)

Compound (**3**),† m.p. 144—145° (decomp.), $[\alpha]_D + 235°$ (H_2O), was prepared (30%) by *m*-chloroperbenzoic acid oxidation (in dichloromethane at −78°) of the ester (**4**).[1] It also underwent racemisation in chloroform although the reaction was 1·7 times slower than in the case of (**5**). The rate of racemisation of (**3**) was markedly solvent dependent; the reaction occurred 82 times faster in chloroform than in water.

Compound (**7**),† m.p. 187—188°, $[\alpha]_D - 126°$ ($CHCl_3$), was obtained (48%) by *m*-chloroperbenzoic acid oxidation of (**8**).[2] It rapidly racemised in chloroform [*ca.* 6·7 times faster than (**5**)] and in dichloromethane containing 10% MeOD. In the latter instance the racemic product (isolated after 24 h) was 24% monodeuteriated and 72% undeuteriated on the basis of mass spectroscopy; the isotope was located (25%) at position 6 by n.m.r. spectroscopy.

An interesting feature of the foregoing reactions is that the sulphoxides interconvert with their enantiomers but not with their diastereoisomers, suggesting that the achiral intermediates "memorise" the stereochemistry of their precursors. We suggest that the sulphenic acids *e.g.*, (**9**) are the intermediates and that their formation involves a concerted hydrogen shift. This sigmatropic process can only occur when the sulphoxides possess a *syn*-axial arrangement of the sulphinyl group and the tertiary hydrogen atom. Consequently, (**3**) and (**5**) are the (*R*)-oxides and (**7**) is the (*S*)-oxide.

Sigmatropic reactions of the above type[3] have recently been observed in the penicillin field;[4] for example, (**12**) underwent deuterium exchange specifically at the 2*β*-methyl group when heated for several hours in benzene containing deuterium oxide. A similar pathway is probably responsible[5] for the ring-opening of *trans*-2,3-dimethylthiiran 1-oxide, which occurs at 35°.

The present results indicate that sigmatropic hydrogen shifts can be markedly accelerated when the migrating hydrogen is adjacent to a carbonyl group and that such reactions occur much more readily in chloroform than in water. On the basis of the deuterium incorporation result, it is clear that (**10**) is formed more readily than (**11**) from (**7**). This result contrasts with that observed for (**12**), which equilibrates only with (**13**).

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† The composition of all new compounds was confirmed by elemental analysis and by mass spectroscopy. Structural assignments are based on i.r., u.v., and n.m.r. spectroscopic evidence.

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

[3] The pyrolytic conversion of sulphoxides, containing a hydrogen atom at the *β*-carbon atom, into olefins has been studied on numerous occasions; cyclic transition states have been postulated for these eliminations (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).

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