Steroidal Sulphur Compounds. Part I. Pyrolysis and Absolute Configuration of Steroidal Phenyl Sulphoxides

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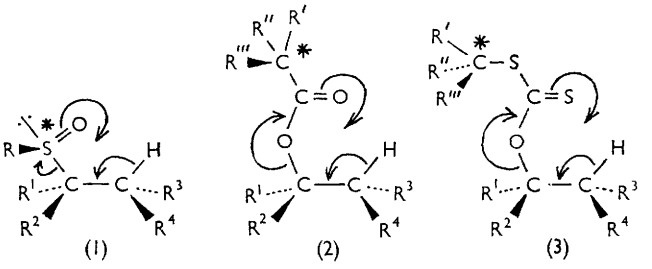
The chirality of the sulphur atom in eight steroidal sulphoxides has been shown to influence the direction of pyrolytic elimination to give olefins. Consideration of the product ratios and relative stabilities of the transition states lead to the assignment of absolute configuration to the sulphoxides, and provided evidence that the incipient double bonds are well developed in the transition states. Axial sulphoxides eliminate faster than equatorial sulphoxides. The ultraviolet and optical rotatory dispersion characteristics of the sulphoxides were recorded; the *R*- and *S*-sulphoxides displayed positive and negative Cotton effects, respectively, which were independent of the configuration of the steroidal residue.

THE formation of olefins by pyrolysis of esters,[1] xanthates,[2] amine oxides,[3] and sulphoxides [4] proceeds predominantly by a cyclic intramolecular mechanism which results in *cis* elimination. Steric influences upon the direction of elimination,[3a,5] and the ratio of *cis*- to *trans*-olefin obtained [3b] were explained in terms of non-bonded interactions in the cyclic transition state between substituents on the α- and β-carbon atoms,[3,5] until it was shown that in some cases steric effects due to the

[1] D. H. R. Barton, *J. Chem. Soc.*, 1949, 2174.
[2] W. Huckel, W. Tappe, and G. Legutke, *Annalen*, 1940, **543**, 191.
[3] (*a*) A. C. Cope, N. A. LeBel, H. H. Lee, and W. R. Moore, *J. Amer. Chem. Soc.*, 1957, **79**, 4720; (*b*) M. R. V. Sahyan and D. J. Cram, *J. Amer. Chem. Soc.*, 1963, **85**, 1263.
[4] C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, 1960, **82**, 1810.
[5] A. C. Cope and E. M. Acton, *J. Amer. Chem. Soc.*, 1958, **80**, 355; A. C. Cope, E. Ciganek, and J. Lazar, *ibid.*, 1962, **84**, 2591.

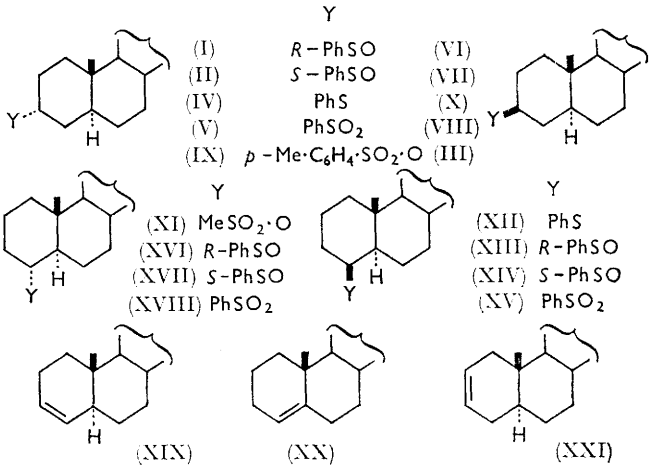
leaving group are also important.[6] The chirality of the sulphur atom was shown to influence the direction of elimination in a pair of steroidal methyl sulphoxides [6a] and in 4-methylcyclohexyl *p*-tolyl sulphoxide,[6b] and a similar but less pronounced effect occurred with asymmetric esters.[6c]

In a systematic examination of the scope and application of steric effects of the leaving group upon olefin composition in pyrolytic elimination, we have examined the pyrolysis of eight steroidal sulphoxides. Sulphoxides were chosen because the steric effect should be larger for these compounds than for esters or xanthates, because in sulphoxides (1) the asymmetric centre is adjacent to the developing double bond, whereas it is further removed in esters (2) and xanthates (3). Asymmetric amine oxides should also produce a significant steric effect, but are less easily prepared stereochemically pure than sulphoxides. Phenylsulphinyl steroids were especially convenient because they were easily prepared, and the presence of the bulky phenyl group would promote a high degree of asymmetric selection; the ultraviolet maxima [7] and associated o.r.d. curves [8] of alkyl aryl sulphoxides also occur in more accessible spectral regions than those of dialkyl sulphoxides, and the relationship between chirality and optical rotatory dispersion of sulphoxides is currently of interest.[8,9]



(1) (2) (3)

Preparation of Starting Materials.—In order to simplify presentation, the absolute configurations of the phenylsulphinyl compounds are given in this section, and the evidence for these configurations is given later in the text. *R*-3α-Phenylsulphinyl-5α-cholestane (I) and *S*-3α-phenylsulphinyl-5α-cholestane (II) were prepared from 3β-toluene-*p*-sulphonyloxy-5α-cholestane (III) by treatment with benzenethiolate ion in ethanol, and oxidation of the resulting 3α-phenylthio-5α-cholestane (IV). The diastereoisomeric sulphoxides were readily separated by preparative thin-layer chromatography.* In initial experiments the sulphide was oxidised by hydrogen peroxide in acetic acid,[11] but later peroxylauric acid [12] in light petroleum was used, since peroxyacid oxidation of sulphides is known to proceed faster in aprotic than in protic solvents.[13] The reaction time was consequently reduced from 24 hr. to 15 mins., and the work-up procedure simplified. We consider this the most convenient method for the oxidation of sulphides to sulphoxides.[14] As with other methods of oxidising sulphides in media of relatively low acidity,[7c] there was some overoxidation to sulphone even when only 1 mol. of peroxylauric acid was used, but this was avoided by using a deficiency of peroxylauric acid, and repeating the oxidation on the easily recovered starting material. Oxidation of the sulphoxides (I) and (II) with peroxylauric acid gave the same sulphone (V), illustrating that the sulphoxides differed only in the configuration about sulphur.



R-3α-Phenylsulphinyl-5α-cholestane (I) with potassium t-butoxide in dimethyl sulphoxide gave *R*-3β-phenylsulphinyl-5α-cholestane (VI), a transformation which is consonant with the conversion of a bulky phenylsulphinyl group from an axial to the more stable equatorial orientation. This was expected, since the phenylsulphinyl group has a strong preference for the equatorial orientation, having a conformational free-energy difference of 1·9 kcal./mole.[15] Similar treatment of *S*-3α-phenylsulphinyl-5α-cholestane (II) afforded *S*-3β-phenylsulphinyl-5α-cholestane (VII). The 3β-sulphoxides (VI) and (VII) differed only in the chirality of

* The sequence used in assigning the configuration of the steroidal phenyl sulphoxides is O, phenyl, steroid residue, pair of electrons.[10]

[6] (*a*) D. N. Jones and M. A. Saeed, *Proc. Chem. Soc.*, 1964, 81; (*b*) S. I. Goldberg and M. S. Sahli, *Tetrahedron Letters*, 1965, 4441; (*c*) S. I. Goldberg and F.-L. Lam, *Tetrahedron Letters*, 1964, 1893.

[7] (*a*) H. P. Koch, *J. Chem. Soc.*, 1950, 2892; (*b*) H. Bredereck, G. Brod, and G. Hoschele, *Chem. Ber.*, 1955, **88**, 438; (*c*) F. G. Bordwell and P. J. Boutan, *J. Amer. Chem. Soc.*, 1957, **79**, 717.

[8] (*a*) K. K. Anderson, W. Gaffield, N. E. Papanikolaou, J. W. Foley, and R. I. Perkins, *J. Amer. Chem. Soc.*, 1964, **86**, 5637; (*b*) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, *J. Amer. Chem. Soc.*, 1965, **87**, 1958.

[9] K. Mislow, A. L. Ternay, and J. T. Melillo, *J. Amer. Chem. Soc.*, 1963, **85**, 2329; K. Mislow, M. M. Green, P. Laur, and D. R. Chisholm, *ibid.*, 1965, **87**, 665; W. Gaffield, F. F. Wong, and J. F. Carson, *J. Org. Chem.*, 1965, **30**, 951.

[10] See R. S. Cahn, *J. Chem. Educ.*, 1964, **41**, 116.

[11] D. N. Kirk and V. Petrow, *J. Chem. Soc.*, 1962, 1091; R. E. Schaub and M. J. Weiss, *J. Org. Chem.*, 1962, **27**, 2221.

[12] W. E. Parker, C. Ricciuti, C. L. Ogg, and D. Swern, *J. Amer. Chem. Soc.*, 1955, **77**, 4037.

[13] C. G. Overberger and R. W. Cummins, *J. Amer. Chem. Soc.*, 1953, **75**, 4250.

[14] C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 1109, give a comprehensive list of methods for oxidising sulphides to sulphoxides.

[15] E. L. Eliel, E. W. Della, and M. Rogic, *J. Org. Chem.*, 1965, **30**, 855.

the sulphur atom, since oxidation of both compounds with peroxylauric acid gave the same sulphone (VIII). Each 3α-sulphoxide gave only one 3β-sulphoxide on treatment with base, and since these product sulphoxides were different and were not interconvertible under the reaction conditions it appears that equilibration at carbon was not accompanied by equilibration at sulphur, in accord with previous observations.[16] There is no precedent for the alternative conclusion that inversion at carbon is attended by concomitant and stereospecific inversion at sulphur, and we consider it very unlikely.

The n.m.r. spectra of the sulphides, sulphoxides, and sulphones substantiated the assignments of configuration at C-3 (Table 1). The equatorial 3β-hydrogens in the

TABLE 1

N.m.r. data (τ) of 5α-steroidal phenyl sulphides, phenyl sulphoxides, and phenyl sulphones

		Geminal H *		$W_{\frac{1}{2}}$ †	C-19 Me	C-18 Me
(IV)	3α-PhS	3β(e)	6·43	7	9·20	9·34
(X)	3β-PhS	3α(a)	7·08	25	9·22	9·36
(I)	*R*-3α-PhSO	3β(e)	7·17	10	9·16	9·32
(VI)	*R*-3β-PhSO	3α(a)	7·53	26	9·18	9·37
(II)	*S*-3α-PhSO	3β(e)	7·18	11	9·16	9·33
(VII)	*S*-3β-PhSO	3α(a)	7·47	23	9·18	9·36
(V)	3α-$PhSO_2$	3β(e)	7·01	9	9·17	9·35
(VIII)	3β-$PhSO_2$	3α(a)	7·12	28	9·18	9·35
(XII)	4β-PhS	4α(e)	6·74	8	9·00	9·35
(XIII)	*R*-4β-PhSO	4α(e)	7·55	13	8·82	9·32
(XVI)	*R*-4α-PhSO	4β(a)	7·04	20	9·08	9·33
(XIV)	*S*-4β-PhSO	4α(e)	7·36	9	8·70	9·33
(XVII)	*S*-4α-PhSO	4β(a)	7·21	24	9·17	9·33
(XV)	4β-$PhSO_2$	4α(e)	6·78	11	8·76	9·32
(XVIII)	4α-$PhSO_2$	4β(a)	7·04	26	8·73	9·35

* e = Equatorial, a = axial. † Width of band at half height (c./sec.).

3α-phenyl sulphide (IV), the 3α-sulphoxides (I) and (II), and the 3α-sulphone (V) gave rise to signals at lower fields than the axial 3α-hydrogen in the respective epimeric compounds (X), (VI), (VII), and (VIII), the signals being sharper in the first group than in the second; this behaviour is characteristic of equatorial and axial protons in a six-membered ring.[17] 3β-Phenylthio-5α-cholestane (X) was prepared from 3α-toluene-*p*-sulphonyloxy-5α-cholestane (IX) by treatment with benzenethiolate ion in ethanol. Oxidation of the sulphide (X) with peroxylauric acid gave a mixture of the *R*-3β-sulphoxide (VI) and the *S*-3β-sulphoxide (VII) which could not be separated chromatographically, but which gave the *R*-3β-sulphoxide (VI) on fractional crystallisation.

4α-Methanesulphonyloxy-5α-cholestane (XI) with sodium benzenethiolate in refluxing ethanol gave 4β-phenylthio-5α-cholestane (XII), which was oxidised by peroxylauric acid in light petroleum to give a mixture of *R*-4β-phenylsulphinyl-5α-cholestane (XIII) and *S*-4β phenylsulphinyl-5α-cholestane (XIV). These were cleanly separated by preparative thin-layer chromatography. Further oxidation of the 4β-sulphoxides (XIII) and (XIV) by peroxylauric acid gave the same sulphone (XV), confirming that the sulphoxides differed only in the configuration about sulphur. Treatment of the *R*-4β-sulphoxide (XIII) with potassium t-butoxide in dimethyl sulphoxide gave only the *R*-4α-sulphoxide (XVI), and the *S*-4β-sulphoxide (XIV) likewise gave only the *S*-4α-sulphoxide (XVII). In view of the pronounced preference of the phenylsulphinyl group to be equatorially orientated, these transformations under equilibrating conditions are rational only in terms of the conversion of the phenylsulphinyl groups from an axial to an equatorial orientation, and therefore establish the configuration of the sulphoxides. Oxidation of the *R*-4α-sulphoxide (XVI) and the *S*-4α-sulphoxide (XVII) with peroxylauric acid gave the same 4α-sulphone (XVIII). The n.m.r. spectra (Table 1) of the 4α- and 4β-sulphones were consistent with their allocated configurations, showing signals due to the C-4 hydrogens in the expected positions (equatorial at lower field than axial) and of the expected relative band width (axial broader than equatorial). The C-19 methyl group resonates at lower field in the 4β-sulphoxides than in the 4α-sulphoxides, which is consistent with the close proximity of the phenylsulphinyl group and the C-19 methyl group in the former,[18] substantiating the assignment of configuration at C-4. However the positions of the C-4 hydrogen signals in the sulphoxides were the reverse of those expected, being at lower fields in the 4α-sulphoxides than in the 4β-sulphoxides. This may be due to a deformation of ring A in the 4β-sulphoxides from a chair into either a half-chair or flexible conformation in order to relieve the considerable repulsive steric interaction between the phenylsulphinyl group and the C-19 methyl group;[18] the 4α-hydrogen, instead of being equatorially orientated, adopts either a quasi-equatorial or boat-axial position, with a consequent alteration in its n.m.r. characteristics. This explanation is not entirely satisfactory, because the n.m.r. spectra of the 4β- and 4α-sulphones are not inconsistent with the chair conformation for ring A in both compounds, which leads to the doubtful conclusion that the repulsion between the phenylsulphonyl group and the C-19 methyl group is appreciably less than the phenylsulphinyl–C-19 methyl group repulsion.

Pyrolysis of the Sulphoxides.—*R*-4β-Phenylsulphinyl-5α-cholestane (XIII) decomposed after 12 hr. in boiling benzene (80°), to give only 5α-cholest-3-ene (XIX) in 85% yield, whilst under the same conditions *S*-4β-phenylsulphinyl-5α-cholestane (XIV) was inert. Since the 4β orientation of the phenylsulphinyl group in the *R*-4β-sulphoxide (XIII) has been established, the production of only 5α-cholest-3-ene on pyrolysis provides further proof of the *cis* stereochemical course of the pyrolytic elimination of sulphoxides.[4] The remarkable difference in reactivity between the *R*- and *S*-4β-sulphoxides is best rationalised in terms of the non-bonded

[16] D. J. Cram and S. H. Pine, *J. Amer. Chem. Soc.*, 1963, **85**, 1096.

[17] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, New York, 1959, p. 115.

[18] K. Tori and T. Komeno, *Tetrahedron*, 1965, **21**, 309.

interactions of the phenylsulphinyl group in the transition state. In both sulphoxides *cis* elimination by the Hurd [19] cyclic intramolecular mechanism (*Ei*) can occur only in one direction to give 5α-cholest-3-ene (XIX), and it is likely that the most favoured conformation of the transition state for this concerted elimination is that with a *syn*-periplanar arrangement of leaving groups, where the dihedral angle between the 3β C–H bond and the 4β C–S bond is either small or zero.[20] This may readily be achieved by distortion of ring A into the half-chair conformation. Examination of Dreiding models shows that a transition state of this type is very unfavourable for conversion of the *S*-4β-sulphoxide into 5α-cholest-3-ene because of severe steric interactions between the phenyl group and the 10-methyl group and 6α-hydrogen atom (4), whereas in the transition state from the *R*-4β-sulphoxide (XIII) these interactions are absent (5). Hence, the pyrolytic decomposition of the *R*-4β-sulphoxide should proceed more readily than that of the *S*-4β-sulphoxide. The relative configuration of the two 4β-sulphoxides were assigned on this basis. Since the absolute configuration of the steroid skeleton is known,[21] the absolute configurations of *R*-4β-phenylsulphinyl-5α-cholestane (XIII) and *S*-4β-phenylsulphinyl-5α-cholestane (XIV) were therefore established

The *S*-4β-sulphoxide (XIV) decomposed slowly at 100° in toluene to give a 1 : 1 mixture of 5α-cholest-3-ene (XIX) and cholest-4-ene (XX). Whereas 5α-cholest-3-ene (XIX) could have been produced by the *cis* intramolecular mechanism, through the high-energy transition state depicted in (4), cholest-4-ene (XX), the product of *trans* elimination, must have been produced by a different mechanism. Control experiments showed that epimerisation at neither carbon nor sulphur occurred under the reaction conditions, so 4α-sulphoxides are not intermediates in the decomposition of the 4β-sulphoxides, and similarly 5α-cholest-3-ene (XIX) is not formed from the *S*-4β-sulphoxide through the *R*-4β-sulphoxide (XIII). Henbest and Khan [22] had shown that epimerisation at sulphur occurs when sulphoxides are heated to 180°, a temperature far higher than that used in this work. Kingsbury and Cram [4] had shown that in the pyrolysis of sulphoxides the cyclic intramolecular mechanism leading to stereospecific *cis* elimination was accompanied to a limited extent by a less stereoselective radical pair mechanism which becomes more important as the temperature is increased. It seems likely that the cholest-4-ene (XX) and possibly some of the 5α-cholest-3-ene (XIX) was produced by this mechanism.

Since the absolute configuration of the two 4β-sulphoxides had been determined, the absolute configurations of the two 4α-sulphoxides (XVI) and (XVII) obtained from them by isomerisation at C-4 were also known. In both the *R*-4α-sulphoxide (XVI) and the *S*-4α-sulphoxide (XVII) *cis* elimination of benzenesulphenic acid can occur in two directions, to give 5α-cholest-3-ene (XIX) and cholest-4-ene (XX). If the cyclic intramolecular mechanism applies, and steric effects due to the phenyl group are important in the transition state, then the *R*-4α-sulphoxide (XVI) would give predominantly cholest-4-ene (XX), and the *S*-4α-sulphoxide would give mostly 5α-cholest-3-ene (XIX). These predictions were arrived at in the following way. In the transition state (6) from the *R*-4α-sulphoxide (XVI) to cholest-4-ene (XX) the phenyl group is not sterically compressed, whilst the transition state (7) leading to 5α-cholest-3-ene (XIX) is destabilised by strong steric interactions between the phenyl group and the 5α-, 6α-, and 7α-hydrogen atoms. Similarly, the transition state (8) from the *S*-4α-sulphoxide (XVII) to 5α-cholest-3-ene is not destabilised by steric interactions of the phenyl group, whereas the transition state (9) leading to cholest-4-ene (XX) is rendered unfavourable by steric interactions between the phenyl group and the 1α- and 2α-hydrogen atoms.

Pyrolysis of the *R*-4α-sulphoxide (XVI) at 100° in toluene gave 5α-cholest-3-ene (XIX) and cholest-4-ene (XX) in the ratio 46 : 54. Under the same conditions the olefins were obtained from the *S*-4α-sulphoxide (XVII) in the ratio 7 : 3. In each case the ratio of products is in the direction predicted, substantiating our assumptions about the nature of the transition state. However, the preponderance of cholest-4-ene (XX) from the *R*-4α-sulphoxide was not as large as expected from a consideration only of steric interactions in the transition state. This may be due to the rigidity at C-5, because of the ring fusion, which means that the conformational distortion of ring A required to bring the 4α–S and 5α–H bonds into the required *syn*-periplanar arrangement is greater than that required to bring the 4α–S and 3α–H bonds into coplanarity; in the latter case coplanarity may be achieved by torsional adjustment at both C-4 and C-3, but only C-4 can be torsionally adjusted to make the 4α–S and 5α–H bonds coplanar. A similar explanation has been provided to account for the production of only 5α-cholest-6-ene by pyrolysis of 6α-dimethylamino-5α-cholestane *N*-oxide.[23]

Pyrolysis of the *R*-3α-sulphoxide (I) at 100° in toluene gave 5α-cholest-3-ene (XIX) and 5α-cholest-2-ene (XXI) in the ratio 3 : 2, whilst under the same conditions the *S*-3α-sulphoxide (II) gave a 4 : 1 mixture of the olefins; these results revealed the configurations about sulphur in these compounds. Examination of models shows that steric interaction between the phenyl group and the 4α-hydrogen in the transition state (10) leading from the *R*-3α-sulphoxide to 5α-cholest-2-ene (XXI)

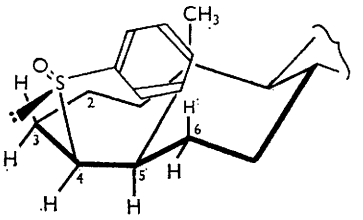
[19] C. D. Hurd and F. H. Blunck, *J. Amer. Chem. Soc.*, 1938, **60**, 2419.

[20] D. J. Cram, "Steric Effects in Organic Chemistry," ed. M. S. Newman, Wiley, New York, 1956, p. 310; E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, p. 232.

[21] J. A. Mills, *J. Chem. Soc.*, 1952, 4976; V. Prelog and H. L. Meier, *Helv. Chim. Acta*, 1953, **36**, 320; B. Riniker, D. Arigoni, and O. Jeger, *ibid.*, 1954, **37**, 546; J. W. Cornforth, I. Youhotsky, and G. Popjak, *Nature*, 1954, **173**, 536.

[22] H. B. Henbest and S. A. Khan, *Proc. Chem. Soc.*, 1964, 56.

[23] R. Ledger, A. J. Smith, and J. McKenna, *Tetrahedron*, 1964, **20**, 2413.



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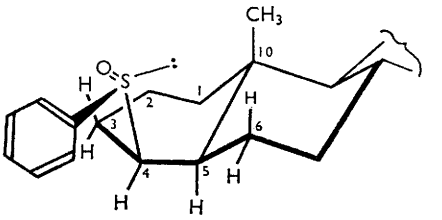

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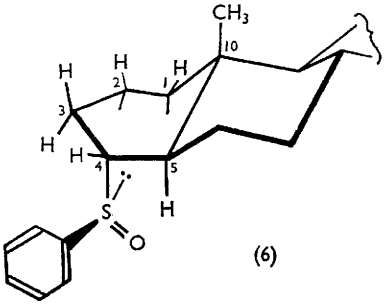

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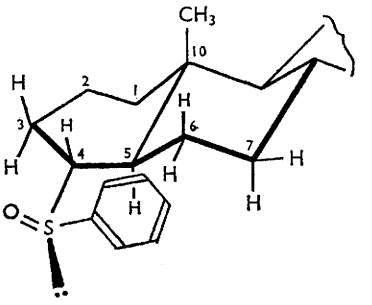

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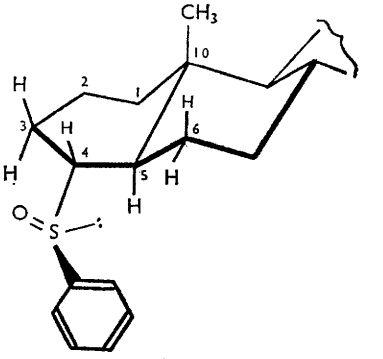

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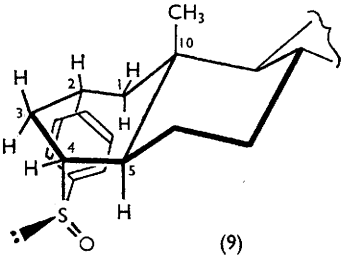

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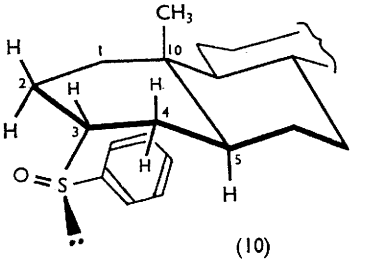

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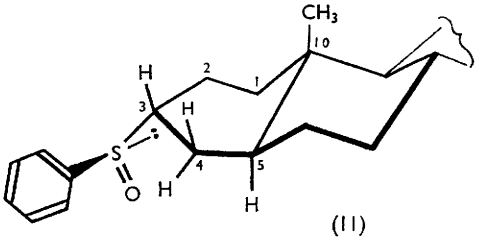

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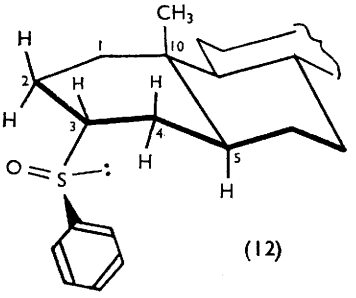

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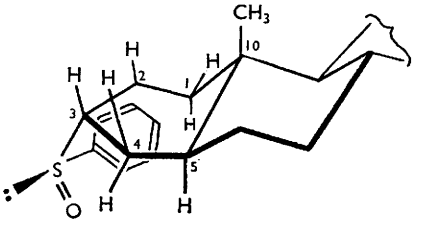

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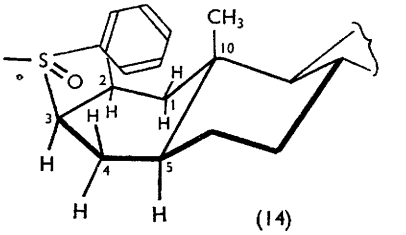

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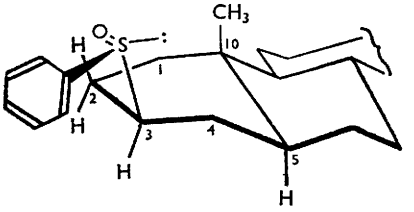

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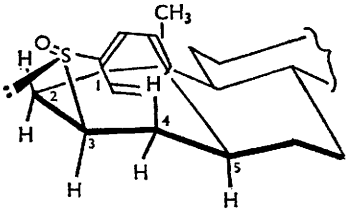
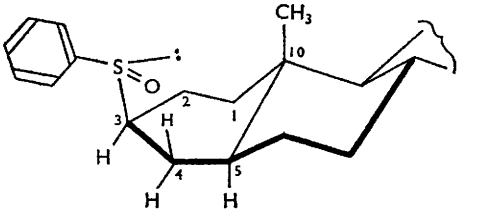


(16)



(17)

render it less favourable (on steric grounds alone) than the transition state (11) leading to 5α-cholest-3-ene (XIX), where the phenyl group is not sterically compressed. Similarly, the transition state (12) from the *S*-3α-sulphoxide (II) to 5α-cholest-2-ene (XXI) is not sterically compressed by the phenyl group, but the transition state (13) leading to 5α-cholest-3-ene (XIX) is destabilised by steric interactions between the phenyl group and the 1α- and 2α-hydrogens.

The allocation of absolute configuration to the *R*-3α-sulphoxide (I) and *S*-3α-sulphoxide (II) also leads to the assignment of absolute configuration to the *R*-3β-sulphoxide (VI) and the *S*-3β-sulphoxide (VII), since these were obtained from (I) and (II), respectively, by epimerisation at C-3. Application of the previous arguments leads to the prediction that pyrolysis of *R*-3β-phenylsulphinyl-5α-cholestane (VI) should give mainly 5α-cholest-2-ene (XXI), because the transition state (14) leading to 5α-cholest-3-ene (XIX) is destabilised by steric interaction between the phenyl group and 10β-methyl group and 2β-hydrogen, whereas the transition state (15) leading to 5α-cholest-2-ene (XXI) is free from steric compressions involving the phenyl group. *S*-3β-Phenylsulphinyl-5α-cholestane (VII) should give predominantly 5α-cholest-3-ene (XIX), since the transition state leading to 5α-cholest-2-ene (XXI) is less favourable on steric grounds than that leading to 5α-cholest-3-ene (XIX), the former (16) involving repulsion between the phenyl group and 10β-methyl and 4β-hydrogen, whereas in the latter (17) the phenyl group is unhindered. These predictions were realised in practice, the *R*-3β-sulphoxide (VI) giving 5α-cholest-2-ene (XXI) and 5α-cholest-3-ene (XIX) in the ratio 82 : 18 on heating at 100° in toluene, whilst the *S*-3β-sulphoxide (VII) gave the same two olefins in the ratio 47 : 53 at the same temperature. The assumptions that steric interactions of the phenyl group are important in the transition state were therefore justified.

It appears that the transition states leading to 5α-cholest-2-ene and to 5α-cholest-3-ene (XIX) from all four C-3 sulphoxides have an appreciable amount of double bond character. This may be deduced from the fact that there was not a marked preponderance of 5α-cholest-3-ene in any of the olefin mixtures, even when steric factors favoured its formation. 5α-Cholest-2-ene is thermodynamically more stable than 5α-cholest-3-ene,[24] and the greater tendency to form 5α-cholest-2-ene may be understood if the transition states contained partially developed double bonds, so that the relative thermodynamic stability of the products was reflected in that of the transition states. In the pyrolytic elimination of amine oxides the double bond has also been shown to be well developed in the transition state.[25]

TABLE 2

Olefin yield in the pyrolysis of steroidal sulphoxides

	Configuration of sulphoxide group *	Temp.	Time (hr.)	% Yield starting material recovered	% Yield olefins †	% Composition of olefins 2	3	4
(VI)	*R*-3β(e)	110°	24	85	80	82	18	0
(I)	*R*-3α(a)	100	20	50	78	62	38	0
(VII)	*S*-3β(e)	110	160	67	76	48	52	0
(II)	*S*-3α(a)	100	20	50	95	83	17	0
(XVI)	*R*-4α(e)	100	70	40	85	0	46	54
(XIII)	*R*-4β(a)	80	12	0	85	0	100	0
(XVII)	*S*-4α(e)	100	70	40	80	0	71	29
(XIV)	*S*-4β(a)	100	72	26	70	0	50	50

* e = Equatorial, a = axial. † Based on starting material consumed.

The rate of elimination of axial sulphoxides was greater than that of the equatorial sulphoxides (Table 2), although accurate rate studies were not carried out. A similar relationship between orientation and reactivity exists for nucleophilic substitutions[26] and base-catalysed eliminations of alicyclic halides[27] and sulphonate esters.[28] In *E*2 eliminations the difference in reactivity is attributed largely to stereoelectronic factors, the presence of the preferred *anti*-periplanar relationship of leaving groups in axial compounds and its absence in equatorial compounds rendering the former more reactive.[29] However, in the *E*i elimination of cyclohexyl phenyl sulphoxides the same degree of conformational distortion is required to bring both an axial sulphoxide and an equatorial sulphoxide into the preferred *syn*-periplanar relationship of leaving groups, because of the axial–equatorial relationship between leaving groups (hydrogen and phenylsulphinyl) in each case; therefore the difference in reactivity is not stereoelectronic in origin and must be attributed to steric factors. The epimerisation experiments described earlier show that the axial sulphoxides are less stable than their equatorial epimers. This difference in

[24] (*a*) P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch, and G. W. Wood, *J. Chem. Soc.*, 1951, 2402; (*b*) R. B. Turner, W. R. Meador, and R. W. Winkler, *J. Amer. Chem. Soc.*, 1957, **79**, 4116, 4122.

[25] A. C. Cope, R. A. Pike, and C. F. Spencer, *J. Amer. Chem. Soc.*, 1953, **75**, 3212.

[26] E. L. Eliel and R. G. Haber, *J. Amer. Chem. Soc.*, 1959, **81**, 1249; E. L. Eliel and R. S. Ro, *ibid.*, 1957, **79**, 5995.

[27] D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1951, 1048; E. D. Hughes, C. K. Ingold, and J. B. Rose, *ibid.*, 1953, 3839; G. H. Alt and D. H. R. Barton, *ibid.*, 1954, 4284.

[28] (*a*) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 1127; (*b*) W. Stoll, *Z. physiol. Chem.*, 1937, **246**, 1; (*c*) H. R. Nace, *J. Amer. Chem. Soc.*, 1952, **74**, 5937.

[29] D. H. R. Barton, *J. Chem. Soc.*, 1953, 1027.

ground state energy may be attributed largely to the difference in steric compression of the phenylsulphinyl group. In the transition states this difference is reduced, because the orientation of the phenylsulphinyl groups becomes more similar, being intermediate between axial and equatorial in each case. Hence the activation energy for elimination of the axial sulphoxide is less than that for the equatorial sulphoxide. This is apparently a case of " steric acceleration," and the explanation is similar to that used to interpret the difference in the rates of solvolysis of *cis*- and *trans*-4-t-butylcyclohexyl tosylates.[30] However, the assumption inherent in this argument, that steric and hence enthalpy factors predominate in the free energy differences, may not be valid in view of the conformational mobility of the phenylsulphinyl group, and we are investigating the role of entropy factors in the relative stability and reactivity of these sulphoxides.

The pyrolytic decomposition of *R*-4β-phenylsulphinyl-5α-cholestane (XIII) to give only 5α-cholest-3-ene (XIX) indicates that when steric effects are unimportant *cis* elimination proceeds exclusively even when statistical factors favour *trans* elimination; in this case there are two *trans* β-hydrogens and one *cis* β-hydrogen. However, when steric considerations inhibit *cis* elimination, *trans* elimination can occur, as in the formation of cholest-4-ene (XX) from *S*-4β-phenylsulphinyl-5α-cholestane (XIV). In the other steroidal sulphoxides there are two *cis* β-hydrogens available for abstraction, so, whilst steric considerations inhibit *cis* elimination in one direction, *cis* elimination in the alternative direction can readily occur, and we have assumed that it competes successfully with *trans* elimination. The assumption was verified by the pattern of results, which is rational only on the basis of a *cis* elimination mechanism. However, these results do not distinguish between a concerted cyclic elimination mechanism and a radical pair mechanism, which was suggested as an alternative by Kingsbury and Cram.[4] The radical pair mechanism involves initial homolysis of the C–S bond followed by abstraction of the β-hydrogen by the phenylsulphinyl radical. If this mechanism is important in the present cases, it would be necessary to postulate that hydrogen abstraction by the phenylsulphinyl radical occurred much faster than racemisation at both carbon and sulphur, in order to rationalise the olefin compositions obtained. We consider this to be unlikely, but if configurational stability did apply then the steric factors controlling the direction of elimination are the same as in the cyclic concerted mechanism, so the configurational assignments would still be valid.

The composition of the olefin mixtures was determined by optical rotatory dispersion techniques, which proved to be far more accurate and convenient than methods based on infrared [24a] and ultraviolet spectroscopy.[31] Whereas the olefins themselves showed plain o.r.d. curves, the pyridine adducts of the osmate esters derived from the olefins showed Cotton effects of large amplitude.[32] The adduct from 5α-cholest-2-ene showed a positive Cotton effect, whilst those from 5α-cholest-3-ene and cholest-4-ene displayed negative Cotton effects of different amplitude. In the case of the Δ^2- and Δ^3-olefins, the composition of the mixtures was determined by measuring the molecular rotations at 446 mμ, and for the Δ^3- and Δ^4-olefin mixtures the amplitude was measured. The percentage compositions could be determined to ±2% by this technique. Although osmium tetroxide attacks 5α-cholest-2-ene exclusively from the α side of the molecule,[33] in Δ^4-steroids attack can occur from both the α and the β side.[34] The products of reaction between 5α-cholest-3-ene and osmium tetroxide have not been reported to our knowledge, but it is possible that both the α- and β-ester–pyridine complexes are formed, with that of α configuration predominating. However, the ratio of α to β attack was constant with both 5α-cholest-3-ene and 5α-cholest-4-ene, since identical o.r.d. curves were obtained from a series of preparations. Furthermore, a precise linear relationship existed between measured amplitude (for the osmate ester–pyridine complexes) and olefin composition in a large number of synthetic olefin mixtures.

Ultraviolet spectra of the sulphoxides in cyclohexane solution are recorded in Table 3. The position of the band at *ca.* 260 mμ due to the benzenesulphinyl chromophore [7a,35] occurred at higher wavelengths (264 mμ) in the axial 3α-sulphoxides than in the equatorial 3β-sulphoxides (257 mμ); the band was also less intense in the 3α-sulphoxides. It appears that, as with acyclic alkyl aryl sulphoxides, increase in steric compression is accompanied by a red shift in the position of this band.[8b,36] Whereas the spectra of these sulphoxides depended upon the configuration at C-3, they were not influenced by the chirality of the sulphur atom, the *R*- and *S*-3β-sulphoxides displaying almost identical spectra, as did also the *R*- and *S*-3α-sulphoxides. In contrast, there was a marked difference in the spectra of the *R*-4β-sulphoxide and the *S*-4β-sulphoxide, the former absorbing at 260 and the latter less strongly at 270 mμ. If these spectral differences are associated with differences in steric compression of the phenylsulphinyl chromophore, as it seems in the C-3 sulphoxides and in other examples, then the *S*-4β-sulphoxide is appreciably more hindered than the *R*-4β-sulphoxide. There was also a smaller

[30] E. L. Eliel, " Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, p. 223.
[31] P. Bladon, H. B. Henbest, and G. W. Wood, *J. Chem. Soc.*, 1952, 2737.
[32] E. Bunnenberg and C. Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5953.
[33] H. B. Henbest and M. Smith, *J. Chem. Soc.*, 1957, 926; C. W. Shoppee, D. N. Jones, and G. H. R. Summers, *ibid.*, 1957, 3100.
[34] A. R. Davies and G. H. R. Summers, *J. Chem. Soc.* (*C*), 1966, 1012.
[35] P. Karrer, N. J. Antia, and R. Schwyzer, *Helv. Chim. Acta*, 1951, **34**, 1392.
[36] A. Cerniani, G. Modena, and P. E. Todesco, *Gazzetta*, 1960, **90**, 3; G. M. Gasperini, G. Modena, and P. E. Todesco, *ibid.*, p. 12; I. V. Baliah and R. Varadachari, *J. Indian Chem. Soc.*, 1960, **37**, 321.

TABLE 3

Ultraviolet spectral data and optical rotatory dispersion characteristics of steroidal sulphoxides

	Configuration of sulphoxide group *	Ultraviolet		Optical rotatory dispersion †		
				Zero rotation		
		λ (mμ); ε	λ (mμ); ε	Peak	point	Trough
(I)	*R*-3α(a)	210; 8100	264; 3150	285 (+29,800)	270	238 (−147,000)
(II)	*S*-3α(a)	209; 7850	264; 3150	233 (+172,000)	274	283 (−26,800)
(VI)	*R*-3β(e)	210; 8200	257; 4700	278 (+29,100)	261	237 (−101,000)
(VII)	*S*-3β(e)	208; 8600	257; 4500	233 (+123,000)	268	280 (−25,300)
(XIII)	*R*-4β(a)	210; 8000	260; 4500	281 (+23,600)	267	243 (−102,000)
(XIV)	*S*-4β(a)	210; 9600	270; 2900	234 (+122,000)	275	293 (−30,300)
(XVI)	*R*-4α(e)	211; 7500	265; 4100	285 (+16,500)	280	238 (−134,000)
(XVII)	*S*-4α(e)	209; 6350	260; 4200	239 (+109,000)	264	281 (−30,600)

* e = Equatorial, a = axial. † Figures in mμ, with molecular rotations in parenthesis.

but significant difference in the ultraviolet spectra of the diastereomeric 4α-sulphoxides; in this case the *R*-4α-sulphoxide absorbed at higher wavelength and was

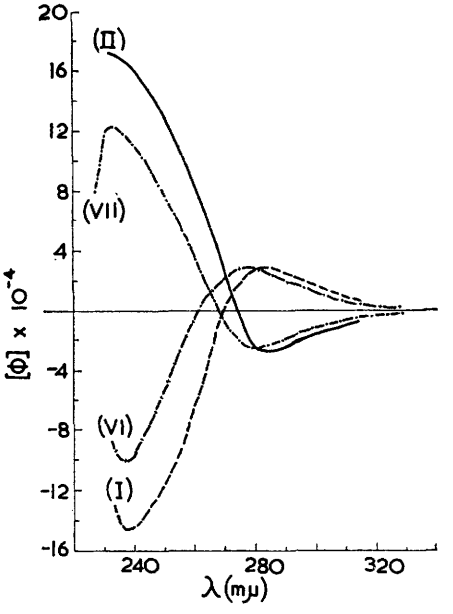


FIGURE 1

apparently the more hindered. In both the 4β- and 4α-sulphoxides, the reasons for the differences in steric hindrance between the compounds epimeric at sulphur was not obvious from an examination of Dreiding models.

The benzenesulphinyl chromophore is inherently dissymmetric, and it has been shown that a relationship exists between the chirality of alkyl aryl sulphoxides and the sign of the relevant Cotton effect.[8] The absolute configurations of the sulphoxides were assigned by stereospecific synthesis from (−)-menthyl (−)-*p*-iodobenzenesulphinate,[8b] in which the configuration about sulphur had been established by *X*-ray analysis.[37] Seven alkyl *p*-tolyl sulphoxides with the *R* configuration at sulphur prepared in this manner gave rise to positive Cotton effect curves, but unfortunately the enantiomeric sulphoxides with the *S* configuration were not available.

The o.r.d. curves of the eight steroidal phenyl sulphoxides prepared in this investigation are shown in Figures 1 and 2, and the relevant data are given in Table 3. The four sulphoxides with *R* configuration at sulphur gave positive Cotton effect curves, whilst the four enantiomers with *S* configuration at sulphur gave negative Cotton effect curves of similar shape but opposite sign. The results with the *R*-sulphoxides are in accord with those previously recorded, and a direct illustration is now provided of the reversal in sign of the Cotton effect associated with inversion of chirality about sulphur in diastereoisomeric alkyl phenyl sulphoxides. The o.r.d. behaviour of this series of sulphoxides is consistent with their allocated absolute configurations, verifying the validity of the methods used to determine them. The agreement between these results and those hitherto recorded also serves to substantiate the assumption that sulphinate esters react

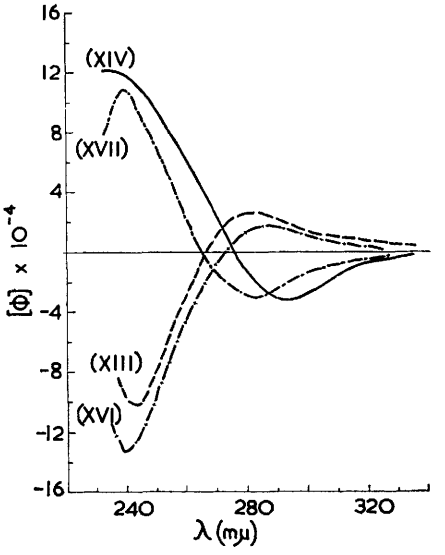


FIGURE 2

with Grignard reagents with inversion of configuration at sulphur,[8] upon which the validity of previous allocations of absolute configurations of sulphoxides depended.

[37] E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, 1964, **86**, 3395.

The close similarity of the o.r.d. curves of the four *R*-sulphoxides on the one hand, and of the four *S*-sulphoxides on the other demonstrates clearly that the configuration of the alkyl group in alkyl phenyl sulphoxides does not influence the sign of the Cotton effect, and has very little influence upon its amplitude. This provides convincing evidence, additional to that previously presented,[8] that the phenylsulphinyl chromophore is inherently dissymmetric.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. Preparative thin-layer chromatography was performed on glass plates 25 cm. square, with a layer of Silica Gel G (Merck) 1 mm. thick. The silica gel was mixed with 6% aqueous silver nitrate solution to make silver nitrate impregnated plates for separation of olefins.[38] Infrared spectra were measured on a Unicam SP 100 spectrophotometer, and ultraviolet spectra were determined in cyclohexane on a Perkin-Elmer Ultracord spectrophotometer. Rotations cited are for chloroform solutions. Optical rotatory dispersions were measured in cyclohexane on a Bendix Polaromatic 62 automatic recording instrument. N.m.r. spectra were determined on a Varian A 60 spectrometer for carbon tetrachloride and deuteriochloroform solutions, and are recorded on the τ scale. Light petroleum refers to the fraction of b. p. 40—60°.

3α-*Phenylthio*-5α-*cholestane* (IV).—3β-Toluene-*p*-sulphonyloxy-5α-cholestane (IX) [28c] (8 g.) was added to a solution of sodium (3·5 g.) in a mixture of ethanol (300 ml.) and thiophenol (14 ml.). After 18 hr. under reflux, the mixture was poured into ice-cold aqueous potassium hydroxide (2N), extracted with ether, and the ethereal extract washed with water and dried (Na_2SO_4). Evaporation gave a yellow gum (8 g.) which was chromatographed on alumina (240 g.). Elution with light petroleum (900 ml.) gave 5α-cholest-2-ene, m. p. 72—74° (1·8 g., 24%) (from ether–methanol), and further elution (2600 ml.) gave the *product* (IV) (4·85 g., 68%), needles, m. p. 106—108° (from ether–methanol), $[\alpha]_D$ +20° (*c* 1·45) (Found: C, 82·1; H, 11·1; S, 6·5. $C_{33}H_{52}S$ requires C, 82·45; H, 10·9; S, 6·7%).

R-3α- *and* S-3α-*Phenylsulphinyl*-5α-*cholestane* (I) *and* (II).—Peroxylauric acid [12] (96% pure; 0·459 g., 2·04 mmoles) in light petroleum (50 ml.) was added to 3α-phenylthio-5α-cholestane (IV) (3·91 g., 8·1 mmoles) at 20°, and after 15 min. the solution was passed on to alumina (120 g.). Elution with light petroleum (1 l.) gave (IV) (3·056 g., 78%), m. p. 106—108°, and elution with ether (1 l.) gave a mixture of the sulphoxides (0·784 g., 21%). This procedure was repeated twice with the recovered sulphide, to give finally (IV) (1·562 g., 40%), m. p. 106—108°, and a mixture of the sulphoxides (I) and (II) (2·35 g., 58%) which was chromatographed on 40 silica plates developed in chloroform–benzene (1 : 1). The two layers were severally extracted with ether, to give the *sulphoxide* (I) (0·94 g., 40%), needles, m. p. 145—147° (from methanol), $[\alpha]_D$ +43° (*c* 1·4), $\nu_{max.}$ (KBr) 1035, (CCl_4) 1049 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 264, 210 mμ (ε 3150, 8100), o.r.d. $[\phi]_{285}$ +29,800, $[\phi]_{270}$ 0, $[\phi]_{238}$ −147,000° (Found: C, 80·1; H, 10·3; S, 6·6. $C_{33}H_{52}OS$ requires C, 79·8; H, 10·6; S, 6·45%), and the *sulphoxide* (II) (0·83 g., 35%), needles, m. p. 148—149° (from methanol) $[\alpha]_D$ +12° (*c* 1·5), $\nu_{max.}$ (KBr) 1034, 1040, (CCl_4) 1042 1053 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 264, 209 mμ (ε 3150, 7850), o.r.d. $[\phi]_{283}$ −26,800, $[\phi]_{274}$ 0, $[\phi]_{233}$ +172,000° (Found: C, 79·9; H, 10·8; S, 6·7%).

3α-*Phenylsulphonyl*-5α-*cholestane* (V).—Peroxylauric acid (96% pure; 200 mg., 0·89 mmole) was added to *R*-3α-phenylsulphinyl-5α-cholestane (I) (110 mg., 0·22 mmole) in light petroleum (25 ml.) at 20°. After 15 min. the solution was diluted with ether (100 ml.) and filtered through alumina (3 g.). Evaporation of the filtrate and crystallisation from methanol gave the *product* (V) (108 mg., 95%), plates, m. p. 158—160°, $[\alpha]_D$ +18° (*c* 1·5) (Found: C, 77·4; H, 10·1; S, 6·1. $C_{33}H_{52}O_2S$ requires C, 77·3; H, 10·2; S, 6·25%). Oxidation of *S*-3α-phenylsulphinyl-5α-cholestane in the above manner gave the same sulphone, m. p. and mixed m. p. 157—160°. The infrared spectra and t.l.c. behaviour of the two samples were identical.

3β-*Phenylthio*-5α-*cholestane* (X).—3α-Toluene-*p*-sulphonyloxy-5α-cholestane [28c] (9·3 g.) was added to a solution of sodium (3·75 g.) in a mixture of ethanol (300 ml.) and thiophenol (14 ml.). After boiling for 2 days, the solution was worked up in the usual manner, to give a yellow gum which was chromatographed on alumina (300 g.). Elution with light petroleum (750 ml.) gave 5α-cholest-2-ene (XXI) (2·36 g.), m. p. 72—74°; further elution (500 ml.) gave a mixture (3·13 g.), and final elution (2 l.) gave the *product* (X) (3·16 g.), m. p. 76—78° (from ether–methanol), $[\alpha]_D$ +28° (*c* 1·5) (Found: C, 82·5; H, 11·2; S, 6·9%). Re-chromatography of the mixture gave a further 994 mg. of the sulphide (total yield, 4·16 g., 51%).

R-3β-*Phenylsulphinyl*-5α-*cholestane* (VI).—(*a*) Peroxylauric acid (96% pure; 0·5 g., 2·2 mmoles) in light petroleum (150 ml.) was added to 3β-phenylthio-5α-cholestane (4·1 g., 8·5 mmoles). After 15 min. at 20° the mixture was passed on to alumina (120 g.). Elution with light petroleum (2 l.) gave 3β-phenylthio-5α-cholestane (X) (3·00 g., 73%), m. p. 76—78°, and elution with ether (2 l.) gave a mixture (1·2 g., 27%) of the 3β-sulphoxides which could not be separated by chromatography. Crystallisation from ether–methanol gave the *product* (VI), needles, m. p. 177—179°, $[\alpha]_D$ +72° (*c* 1·5), $\nu_{max.}$ (KBr) 1046, (CCl_4) 1052 cm.$^{-1}$, $\lambda_{max.}$ 257, 210 mμ (ε 4700, 8200), o.r.d. $[\phi]_{278}$ +29,100, $[\phi]_{261}$ 0, $[\phi]_{237}$ −101,000° (Found: C, 80·1; H, 10·5; S, 6·5%).

(*b*) *R*-3α-Phenylsulphinyl-5α-cholestane (I) (1·2 g.) and potassium t-butoxide (1 g.) in dimethyl sulphoxide (35 ml.) was kept at 65° for 2·5 hr., and poured into water. Isolation by ether extraction and crystallisation from methanol gave (VI) (1·14 g., 95%), m. p. and mixed m. p. 177—179°.

S-3β-*Phenylsulphinyl*-5α-*cholestane* (VII).—*S*-3α-Phenylsulphinyl-5α-cholestane (II) (151 mg.) was equilibrated in the above manner, to give the *product* (VII) (121 mg., 80%), m. p. 165—167° (from ether–methanol), $[\alpha]_D$ −74° (*c* 0·6), $\nu_{max.}$ (KBr) 1045, (CCl_4) 1050, 1048 cm.$^{-1}$, $\lambda_{max.}$ 257, 208 mμ (ε 4500, 8600), o.r.d. $[\phi]_{280}$ −25,300, $[\phi]_{268}$ 0, $[\phi]_{233}$ +123,000° (Found: C, 79·7; H, 10·4; S, 6·7%).

3β-*Phenylsulphonyl*-5α-*cholestane* (VIII).—(*a*) Peroxylauric acid (96% pure; 50 mg., 0·21 mmole) in light petroleum (10 ml.) was added to *R*-3β-phenylsulphinyl-5α-cholestane (60 mg., 0·12 mmole) at 20°. After 15 min. the solution was diluted with ether (10 ml.) and filtered through alumina (3 g.). Evaporation and crystallisation from methanol gave the *product* (VIII) (55 mg., 89%), m. p. 180—183°, $[\alpha]_D$ +21° (*c* 1·2) (Found: C, 77·1; H, 10·3; S, 6·4%).

(*b*) Oxidation of *S*-3β-phenylsulphinyl-5α-cholestane (VII)

[38] L. J. Morris, *Chem. and Ind.*, 1962, 1238.

(40 mg.) in the above manner gave the same sulphone, m. p. and mixed m. p. 183—186°. The two samples displayed identical infrared spectra and t.l.c. behaviour.

4α-*Methanesulphonyloxy-5α-cholestane* (XI).—Methanesulphonyl chloride (5 ml.) was added to 5α-cholestan-4α-ol [39] (3 g.) in pyridine (100 ml.). After 3 hr. the usual work-up gave the *product* (XI) (3·1 g., 89%), fine needles, m. p. 146—149° (from ether–methanol), $[\alpha]_D$ +18° (*c* 1·75) (Found: C, 72·2; H, 10·75; S, 6·95. $C_{28}H_{50}O_3S$ requires C, 72·0; H, 10·8; S, 6·9%).

4β-*Phenylthio-5α-cholestane* (XII).—4α-Methanesulphonyloxy-5α-cholestane (1·7 g.) was added to a solution of sodium (1·5 g.) in a mixture of ethanol (100 ml.) and thiophenol (5 ml.). After boiling for 18 hr. the product was extracted with ether and worked up in the usual way, to give a yellow gum (1·86 g.) which was chromatographed on alumina (60 g.). Elution with light petroleum (200 ml.) gave a mixture (0·96 g.) of 5α-cholest-3-ene and -4-ene, and further elution (1 l.) gave the *product* (XII) (0·768 g., 45%), needles, double m. p. 109—112/127—129°, $[\alpha]_D$ +47° (*c* 1·3) (Found: C, 82·7; H, 10·9; S, 6·5%).

R-4β- *and* S-4β-*Phenylsulphinyl-5α-cholestane* (XIII) and (XIV).—Peroxylauric acid (96% pure; 360 mg., 1·6 mmoles) in light petroleum (10 ml.) was added to 4β-phenylthio-5α-cholestane (XII) (768 mg., 1·6 mmoles). After 30 min. the solution was diluted with ether (30 ml.) and filtered through alumina (30 g.). Evaporation gave a solid (788 mg.) which was chromatographed on 10 silica plates developed in ether–benzene (1 : 9). Two bands were severally extracted with ether, to give the *sulphoxide* (XIII) (274 mg., 35%), needles, m. p. 143—145° (from ether–methanol), $[\alpha]_D$ +91° (*c* 1·2), $\nu_{max.}$ (KBr) 1048, (CCl_4) 1058 cm.$^{-1}$, $\lambda_{max.}$ 260, 210 mμ (ε 4500, 8000), o.r.d. $[\phi]_{281}$ +23,600, $[\phi]_{267}$ 0, $[\phi]_{243}$ −102,000° (Found: C, 79·5; H, 10·4; S, 6·5%), $C_{33}H_{52}OS$ requires C, 79·8; H, 10·6; S, 6·45%), and the *sulphoxide* (XIV) (370 mg., 48%), needles, m. p. 172—173° (from ether–methanol), $[\alpha]_D$ −44° (*c* 1·4), $\nu_{max.}$ (KBr) 1046, (CCl_4) 1052 cm.$^{-1}$, $\lambda_{max.}$ 270, 210 mμ (ε 2900, 9600), o.r.d. $[\phi]_{293}$ −30,300, $[\phi]_{275}$ 0, $[\phi]_{234}$ +122,000° (Found: C, 79·9; H, 10·7; S, 6·5%).

4β-*Phenylsulphonyl-5α-cholestane* (XV).—(*a*) *S*-4β-Phenylsulphinyl-5α-cholestane (XIV) (52 mg., 0·11 mmole) was treated with peroxylauric acid (96% pure; 110 mg., 0·49 mmole) in light petroleum (20 ml.) for 30 min. at room temperature, then diluted with ether (20 ml.) and filtered through alumina (4 g.). Evaporation gave the *product* (XV) (48 mg., 90%), needles, m. p. 217—220° (from methanol), $[\alpha]_D$ +20° (*c* 0·7) (Found: C, 77·3; H, 10·3; S, 6·5%).

(*b*) *R*-4β-Phenylsulphinyl-5α-cholestane (XIII) (28 mg.) was treated with peroxylauric acid in the above manner, to give the sulphone (XV), m. p. and mixed m. p. 220—223°, which displayed identical infrared spectra and t.l.c. behaviour with the sample prepared previously.

R-4α-*Phenylsulphinyl-5α-cholestane* (XVI).—A solution of *R*-4β-phenylsulphinyl-5α-cholestane (XIII) (40 mg.) and potassium t-butoxide (100 mg.) in dimethyl sulphoxide (5 ml.) was kept at 65° for 3 hr. The usual work up gave the *sulphoxide* (XVI) (32 mg., 80%), needles, m. p. 125—126° (from ether–methanol), $[\alpha]_D$ −53° (*c* 1·2), $\nu_{max.}$ (KBr) 1045, (CCl_4) 1045 cm.$^{-1}$, $\lambda_{max.}$ 265, 211 mμ (ε 4100, 7500), o.r.d. $[\phi]_{285}$ +16,500, $[\phi]_{280}$ 0, $[\phi]_{238}$ −134,000° (Found: C, 79·85; H, 10·6; S, 6·6%).

S-4α-*Phenylsulphinyl-5α-cholestane* (XVII).— *S*-4β-Phenylsulphinyl-5α-cholestane (XIV) (68 mg.) was treated with potassium t-butoxide in dimethyl sulphoxide in the above manner, to give the *product* (XVII) (54 mg., 80%), needles, double m. p. 154—157/175—178° (from ether–methanol), $[\alpha]_D$ −57° (*c* 1·2), $\nu_{max.}$ (KBr) 1039, (CCl_4) 1050 cm.$^{-1}$, $\lambda_{max.}$ 260, 209 mμ (ε 4200, 6350), o.r.d. $[\phi]_{281}$ −30,600, $[\phi]_{264}$ 0, $[\phi]_{239}$ +109,000° (Found: C, 79·6; H, 10·3; S, 6·4%).

4α-*Phenylsulphonyl-5α-cholestane* (XVIII).— (*a*) *S*-4α-Phenylsulphinyl-5α-cholestane (XVII) (110 mg., 0·23 mmole) was treated with peroxylauric acid (96% pure; 120 mg., 0·53 mmole) in light petroleum (30 ml.) for 30 min. at room temperature. The solution was diluted with ether (30 ml.) and filtered through alumina (3 g.). Evaporation and crystallisation from ether–methanol gave the *product* (XVIII) (90 mg., 82%), m. p. 209—211°, $[\alpha]_D$ −20° (*c* 1·4) (Found: C, 77·2; H, 10·5; S, 6·45%).

(*b*) Oxidation of *R*-4α-phenylsulphinyl-5α-cholestane (XVI) (30 mg.) with peroxylauric acid in the above manner gave the sulphone (XVIII) (27 mg.), m. p. and mixed m. p. 209—212°, having infrared and t.l.c. behaviour identical with that of the previous sample.

Pyrolysis of the Sulphoxides.—Pyrolyses at 80° were performed in boiling benzene, at 110° in boiling toluene, and at 100° in toluene heated in a steam-jacket. Each pyrolysis was performed at least twice, and reproducible results were obtained in every case. The procedures described below are typical.

(*a*) *R*-4β-Phenylsulphinyl-5α-cholestane (76 mg.) was dissolved in boiling benzene (25 ml.), and after 12 hr. poured into water, extracted with ether, and the ethereal extract washed with water, dried, and evaporated, to give 5α-cholest-3-ene (48 mg., 85%), m. p. and mixed m. p. 73—74° (from ether–methanol). Thin-layer chromatography of the crude product on silver nitrate impregnated plates confirmed the absence of cholest-4-ene.

(*b*) *S*-3β-Phenylsulphinyl-5α-cholestane (VII) (270 mg.) was dissolved in boiling toluene (15 ml.). After 160 hr. the mixture was worked up as above, to give an oily solid (231 mg.) which was chromatographed on silica (thin-layer technique). Development with light petroleum gave a band at the solvent front and another at the origin, which were severally extracted with ether. The band at the origin gave *S*-3β-phenylsulphinyl-5α-cholestane (VII) (180 mg., 67%), m. p. and mixed m. p. 165—167° (from methanol), whilst the band at the solvent front gave a mixture of olefins (51 mg.) which was re-chromatographed on silver nitrate impregnated silica plates. Development with light petroleum gave one band of R_F 0·1, which was extracted with ether. Evaporation afforded a solid mixture of 5α-cholest-2-ene (XXI) and 5α-cholest-3-ene (XIX) in the ratio 48 : 52, analysed by the method described below.

Analysis of Olefin Mixtures.—5α-Cholest-2-ene (XXI) was prepared from 5α-cholestan-3-one by the published method.[24b] 5α-Cholest-3-ene (XIX) and cholest-4-ene (XX) were conveniently obtained from the reaction of 4α-methanesulphonyloxy-5α-cholestane (XI) with benzenethiolate ion (see above). The Δ^3- and Δ^4-olefins were readily separated by thin-layer chromatography on silver nitrate impregnated silica plates. The Δ^2- and Δ^3-olefins could not be separated by this chromatographic procedure.

The osmate ester–pyridine complexes of the olefins were

[39] S. Wolfe, M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, 1959, **24**, 1034.

prepared as follows. 5α-Cholest-2-ene (XXI) (4·72 mg., 0·013 mmole) was dissolved in carbon tetrachloride (2 ml.) and osmium tetroxide (5 mg., 0·02 mmole), and pyridine (2 drops) added. The solution was made up to 20 ml. with carbon tetrachloride and left at 20° for 24 hr. The o.r.d. spectrum, determined directly on this solution displayed $[\phi]_{526}$ −8800, $[\phi]_{483}$ 0, $[\phi]_{391}$ +24,000°. The solution obtained in the same way from 5α-cholest-3-ene (XIX) (7·68 mg., 0·021 mmole) and osmium tetroxide (8 mg., 0·032 mmole) gave $[\phi]_{552}$ +16,600, $[\phi]_{500}$ 0, $[\phi]_{400}$ −33,800°. The same procedure was used to prepare the osmate ester–pyridine complex from cholest-4-ene (16·246 mg., 0·044 mmole) and osmium tetroxide (17 mg., 0·066 mmole), except that the solution was allowed to stand for 48 hr. before the o.r.d. spectrum was determined; the spectrum then showed $[\phi]_{535}$ +4200, $[\phi]_{462}$ 0, $[\phi]_{400}$ −6150°. For a typical mixture of 5α-cholest-2-ene (XXI) and 5α-cholest-3-ene (XIX), 9·88 mg. (0·027 mmole) was allowed to react with osmium tetroxide (10 mg., 0·04 mmole) in the above manner, and the o.r.d. spectrum determined after 24 hr. Similarly, in a typical case, 7·78 mg. (0·021 mmole) of a mixture of 5α-cholest-3-ene (XIX) and cholest-4-ene (XX) was allowed to react with osmium tetroxide (8·1 mg., 0·032 mmole), and the o.r.d. spectrum of the solution determined after 48 hr.

The following method is typical of that used to determine the percentage composition of the mixtures of 5α-cholest-2-ene (XXI) and 5α-cholest-3-ene (XIX). The o.r.d. curves of standard solutions of the osmate ester–pyridine complexes of 5α-cholest-2-ene, 5α-cholest-3-ene, and of a mixture of the two olefins were recorded, and the deflection at 446 mμ was measured in each case. For a series of known mixtures the percentage composition determined by this method was accurate to ±3%; by using a linear correction factor derived from these data the method was refined to determine the percentage composition of other mixtures to within ±2%. The data for the determination of the ratio of olefins obtained by pyrolysis of *R*-3α-phenylsulphinyl-5α-cholestane (I) are detailed below, where c = concentration of olefin in mg. per ml., and d = deflection in mm.

		Ratio (XXI) : (XIX)		
Known value		1 : 0·20	1 : 0·53	1 : 0·86
Determined by o.r.d.		1 : 0·23	1 : 0·61	1 : 1·10

	Run	1	2	3	4	
(XXI)	*c*	0·236	0·212	0·289	0·240	
	d	+62	+54	+74	+60	
	d/*c*	+260	+255	+256	+250	Mean +254
	Run	1	2	3		
(XIX)	*c*	0·384	0·395	0·333		
	d	−109	−115	− 96		
	d/*c*	−284	−291	−295	Mean −290	
	Run	1	2	3		
Mixture of (XXI) and (XIX)	*c*	1·53	1·39	1·11		
	d	+54	+50	+40		
	d/*c*	+39	+36	+36	Mean +37	

Hence ratio (XXI) : (XIX) is 1 : 0·66; correction is 0·065.
Therefore true ratio is 1 : 0·6, *i.e.*, contains 62% (XXI).

The percentage composition of mixtures of 5α-cholest-3-ene (XIX) and -4-ene (XX) was determined in the same way, except that the amplitudes of the o.r.d. curves were taken as a measure of the concentration of each constituent. This method was more accurate than that using deflections at 446 mμ. The results, which are typical, for the olefin mixture obtained by pyrolysis of *R*-4α-phenylsulphinyl-5α-cholestane (XVI) are detailed below, where a = amplitude in mm., and c = concentration in mg. per ml.

	Run	1	2	3	4	5
(XIX) (*c* 0·2668)	*a*	17·0	16·9	16·7	16·8	16·9
	a/*c*	63·7	63·4	62·6	63·0	63·4
					Mean *a*/*c* 63·2	
(XX) (*c* 0·8123)	*a*	12·9	13·0	13·1	12·9	12·9
	a/*c*	15·9	16·0	16·1	15·9	15·9
					Mean *a*/*c* 15·9	
Mixture of (XIX) and (XX) (*c* 0·3890)	*a*	14·3	14·4	14·3	14·5	14·3
	a/*c*	36·7	37·0	36·7	37·1	36·7
					Mean *a*/*c* 36·9	

Therefore mixture contained 54% (XX).

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