694. *Stereochemistry of the Diels–Alder Reaction with Ethylenic Sulphoxides. Part V.*[1] *Configuration at the Sulphur Atom in the Adducts from Cyclopentadiene and 2-Phenylsulphinylacrylic Acids.*

By S. Ghersetti, H. Hogeveen, G. Maccagnani, F. Montanari, and F. Taddei.

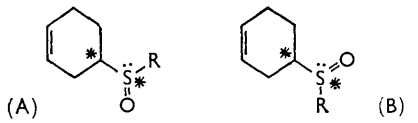
α-Ethylenic sulphoxides react with dienes to form isomeric adducts (*syn* and *anti*) which differ from each other only in the configuration at the sulphur atom. The total number of possible adducts is therefore twice that with other dienophiles. The means of identification of the *syn*- and *anti*-isomers in the adducts from cyclopentadiene and *cis*- and *trans*-2-phenylsulphinylacrylic acids are discussed: so also are the anomalous formation of iodohydrin in the *endo*-carboxy-derivatives, the stereochemistry of the reductions $>SO \rightarrow >S$ by boranes, the stereochemistry and kinetics of the oxidations $>S \rightarrow >SO \rightarrow >SO_2$, and the infrared and proton magnetic resonance spectra.

In the cases examined the *endo-syn*- are largely favoured (75—80%) over the *endo-anti*-forms. This indicates the high probability of electronic interaction between the sulphinyl group and the diene. In general it appears that the factors which influence the *syn* : *anti* ratio here are the same that determine the *endo* : *exo* ratio in the usual diene reactions.

The selective reduction of only the double bond in bicycloheptenyl sulphoxides by di-imide is also discussed.

The pyramidal structure of sulphoxides is well known, as is the possibility of optical isomerism in compounds R·SO·R′.[2] The Diels–Alder reaction with α-ethylenic sulphoxides therefore leads to isomeric adducts differing only in the configuration at the sulphur atom. The number of isomers, then, is twice that obtained from normal dienophiles. The simplest example, at least theoretically, is the reaction between butadiene and vinyl sulphoxides, $R{\cdot}SO{\cdot}CH{:}CH_2$, from which two isomers, DL-*erythro* and DL-*threo*, may be predicted (cf. A, B).

[1] Part IV, Bonincontro, Maccagnani, and Montanari, *Gazzetta*, 1962, **92**, 1182.
[2] Harrison, Kenyon, and Phillips, *J.*, 1926, 2079.



(A) (B)

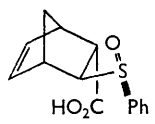
While this synthesis was not examined,* the reactions between cyclopentadiene and the sulphoxides (I)—(VI) were realised under very mild conditions.[1,3-5]

$Ph{\cdot}SO_2{\cdot}CH{:}CH{\cdot}SO{\cdot}Ph$	$Ar{\cdot}SO{\cdot}CH{:}CH{\cdot}SO{\cdot}Ar$	$Ph{\cdot}SO{\cdot}CH{:}CH{\cdot}CO_2H$
(I) *cis*	(II) *trans*-racemic	(V) *cis*
	(III) *trans*-meso	(VI) *trans*
	(IV) *cis*-racemic	

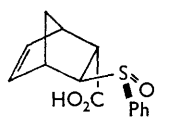
A more thorough study [1,4,5] was undertaken with the sulphoxides (V) and (VI), because of the easy separation of the *endo*- and *exo*-isomers by iodolactonisation. The predicted four *trans*-isomers (VII)—(X), and two *cis-endo*-isomers (XI) and (XII) were characterised [the two *cis-exo*-isomers, present to the extent of about 5% in the products from the sulphoxide (VI),[4] were not isolated].

To distinguish between the two isomers caused by the asymmetry at the sulphur atom, it has been assumed, somewhat arbitrarily, that the S–phenyl bond is (i) directed outwards from the bicyclic system and (ii) roughly parallel to the C:C bond. Such a conformation would be the most probable, as it allows maximum rotational freedom of the phenyl around the S–phenyl axis. Thus, the sulphoxide-oxygen atom may lie either towards or away from the C:C bond: the former we have called *syn* (as in VII, IX, XI), and the latter *anti* (as in VIII, X, XII).

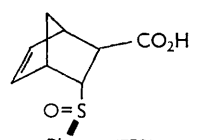
In none of the cases studied were the *syn*- and the *anti*-isomer formed in equal quantities, but their ratio varied with the nature of the substituent attached to the



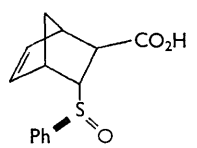
(VII) *syn*



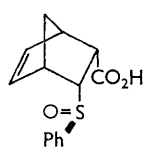
(VIII) *anti*



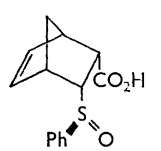
(IX) *syn*



(X) *anti*



(XI) *syn*



(XII) *anti*

SO group and with the *endo*- or *exo*-position assumed by the sulphinyl group (unpublished results from this laboratory). It is believed that electronic and/or steric factors, and the polarity of the medium, may influence the complex stereochemistry of these reactions. In any case, from these results it appears highly probable that the factors that influence the ratio of *syn*- and *anti*-isomers are the same as those [6-8] that determine the ratio of *endo*- and *exo*-isomers in normal diene syntheses.

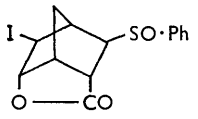
In the present report a discussion of the preliminary problem is presented: that of identification of the *syn*- and *anti*-forms, (IX), (X), and (XI), (XII). For this purpose the following were examined: the formation of iodohydrins, the stereochemistry of the

* One may predict that rather vigorous conditions would be needed for the reaction.

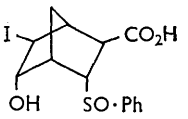
[3] Bertotti, Luciani, and Montanari, *Gazzetta*, 1959, **89**, 1564.
[4] Albera, Bonincontro, and Montanari, *Gazzetta*, 1960, **90**, 709.
[5] Ghersetti, Maccagnani, and Montanari, *Gazzetta*, 1962, **92**, 1168.
[6] Martin and Hill, *Chem. Rev.*, 1961, **50**, 537.
[7] Woodward and Katz, *Tetrahedron*, 1959, **5**, 70.
[8] Berson, Hamlet, and Mueller, *J. Amer. Chem. Soc.*, 1962, **84**, 297.

reductions $>SO \rightarrow >S$, the stereochemistry and the kinetics of the oxidation $>S \rightarrow >SO \rightarrow >SO_2$, and infrared and proton magnetic resonance spectra.

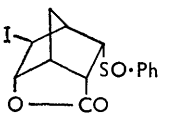
Iodohydrins.—Iodolactonisation (by iodine and sodium hydrogen carbonate in chloroform–water) of the mixture of *trans*-adducts, (VII)—(X), resulted in the formation of the iodo-lactones (XIII) and (XIV) from the *endo*-carboxy-isomers (VII) and (VIII); the reaction gave iodohydrins (XV) and (XVI) from the *exo*-carboxy-isomers (IX) and (X).



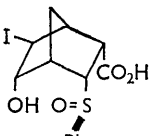
(XIII) *syn*
(XIV) *anti*



(XV) *syn*
(XVI) *anti*



(XVII) *syn*
(XVIII) *anti*



(XIX) *syn*

The reactions were quantitative, and the *syn*- and *anti*-isomers were separated by crystallisation or chromatography.[4,5] In the *cis*-series the iodo-lactones (XVII) and (XVIII) were formed from the *endo*-adducts (XI) and (XII), but for only one adduct, m. p. 194°, was the reaction quantitative; the other, m. p. 185°, which was the principal product (80%) of the diene reaction, afforded 65% of iodo-lactone and 35% of the iodohydrin (XIX).[4,5] It has been shown [5] that in neither series did a Wagner–Meerwein type of rearrangement accompany formation of the iodohydrin, and that the spatial arrangement of iodo- and hydroxy-substituents is that indicated.

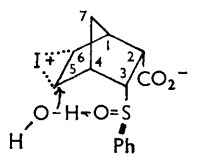
The methyl esters of the *endo-cis*-adducts behave in an even more selective manner, when subjected to iodolactonisation under the above conditions. The ester from the adduct of m. p. 185° afforded quantitatively the ester of iodohydrin (XIX), while the other remained largely unchanged, only a small amount of iodo-lactone being isolated.

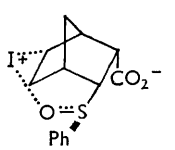
The formation of the *cis*-iodohydrin (XIX) constitutes a unique case in *endo*-carboxy-bicycloheptene systems, and depends only on the presence and particular spatial arrangement of the sulphinyl oxygen atom. The formation of the *trans*-iodohydrins (XV), (XVI) is also unexpected, as the *exo*-carboxy-isomers usually react with difficulty under the conditions of iodolactonisation.[6] In fact the *cis-endo*-sulphone and sulphide, corresponding to (XI) and (XII), gave the iodo-lactones quantitatively, while the *trans-exo*-sulphone and sulphide, corresponding to (IX) and (X), were recovered unchanged.[4,9]

The behaviour of the acids (XI), (XII) and of their esters supports the assignment of the *syn*-structure (XI) to the isomer of m. p. 185°, and the *anti*-structure (XII) to the isomer of m. p. 194°. Such assignments logically must be extended to the corresponding lactones and iodohydrins. This is concluded from the following arguments.

In both isomers (XI) and (XII) the first step in the reactions must be the electrophilic attack, from the *exo*-direction, by I^+ on the double bond of the bicyclic system,[10] followed, for the *anti*-isomer (XII), by nucleophilic attack by CO_2^-, from the favoured *endo*-direction,

(XXa)





(XXb)

on the positive position 6 of the intermediate. It is most reasonable to suppose that, with the *syn*-isomer (XI), the second step is competitive with a nucleophilic attack, from the *endo*-position, of a molecule of water hydrogen-bonded to the sulphinyl-oxygen, with simultaneous liberation of the proton (XXa). In fact it does not seem justified to postulate the competitive attack by OH^-, whose low concentration cannot compensate for the weaker nucleophilic character of water towards the carbonium ion; the nucleophilicity

[9] Albera, Luciani, and Montanari, *Boll. sci. Fac. Chim. ind. Bologna*, 1960, **18**, 52.
[10] Kaplan, Kwart, and von Schleyer, *J. Amer. Chem. Soc.*, 1960, **82**, 2341.

ratio[11] $OH^-:H_2O$ is *ca.* 10^4. Furthermore, the electrostatic repulsion by the *syn*-sulphinyl-oxygen atom must be effective on a hydroxyl ion that enters position 5 in intermediate (XXa) from the *endo*-direction. A second possibility, namely, neighbouring-group participation of the *syn*-sulphinyl-oxygen atom as in (XXb), cannot be correct, because this would exclude the structure (XIX), previously[5] demonstrated for the iodohydrin.

Moreover, lactonisation of the ester of (XI) is even less likely, as it would require hydrolysis of the methoxycarbonyl group; * therefore the ester of the iodohydrin (XIX) is the only ultimate product.

In the *trans*-series the easy formation of the two iodohydrins (XV) and (XVI) does not in itself indicate the *syn*- or *anti*-structure of (VIII) and (IX). On the other hand, molecular models demonstrate that the *exo*-arrangement of the carboxyl group allows complete rotational freedom of the phenylsulphinyl group around the *S*–bicycle bond. Thus, in both isomers, conformations are possible that are not greatly hindered sterically. In these conformations the sulphinyl-oxygen atom may favour the introduction of the hydroxyl at the 5-position, in a manner similar to that suggested for (XX).

Reductions of the SO *Group.*—It was noted earlier[4] that delactonisation with zinc and acetic acid of *trans*-iodo-lactones (XIII) and (XIV) and the *cis*-iodo-lactones (XVII) and (XVIII) to the corresponding acids (VII), (VIII), (XI), and (XII) was accompanied by partial reduction of the sulphinyl group to the sulphide. In each pair one of the isomers was more resistant to reduction, this being more evident for the *cis*-pair. As steric effects evidently play an important role in this reduction, it was reasoned that this knowledge might be useful in the identification of *syn*- and *anti*-isomers. However, a serious drawback was the lack of knowledge of the mechanism of these reductions, even though many reducing agents for sulphoxides have been known for a long time.[12]

It is known that the oxygen of sulphoxides is more nucleophilic and basic than the sulphur,[13] and in certain reactions (with hydrogen iodide, lithium aluminium hydride, etc.) an intermediate of the type $B^- \cdots \gtrless S^+-O^- \cdots A^+$ might be postulated, but one cannot separate the steric from electronic effects at the two centres of interaction or identify which attack (nucleophilic or electrophilic or both) determines the overall rate.

The problem was resolved by using diborane as the reducing agent.† Diborane is a strong Lewis acid, and must preferably attack the centre of highest electron density,[14] namely, the oxygen in sulphoxides. It is reasonable that the *anti*-isomers, in which the oxygen is less hindered, are more easily reduced than the *syn*-isomers.

The present study was limited to the *cis*-series. The acids (XI) and (XII) were first reduced with di-imide ($HN{:}NH$)[15],‡ to the corresponding norbornane derivatives (XXI)

* It should be noted that the ester of sulphide (XXXVII) was completely iodolactonised (24 hours, under the conditions stated), while that of the corresponding sulphone (XXXVI) was recovered unchanged. Under these same conditions, but in the absence of iodine, the ester of the sulphide was saponified to the extent of 18%.

† The use of diborane as a reducing agent for sulphoxides was cited for the first time by Brown and Subba Rao, *J. Amer. Chem. Soc.*, 1960, **82**, 681.

‡ In this reduction di-imide is unique. Catalytic hydrogenation over palladium or platinum was inhibited by catalyst-poisoning due to the sulphoxide, and heterolytic reagents (lithium aluminium hydride, sodium in liquid ammonia, etc.) would also reduce other groups present.

[11] Swain, Scott, and Lohmann, *J. Amer. Chem. Soc.*, 1953, **75**, 136; Swain and Scott, *ibid.*, p. 141.

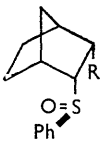
[12] Schöberl and Wagner, in Houben-Weil's "Methoden der Organischen Chemie," Vol. IX, Georg Thieme Verlag, Stuttgard, 1955, p. 218; Szmant, in Kharasch's "Organic Sulfur Compounds," Vol. I, Pergamon Press, Oxford, 1961, p. 159; Price and Oae, "Sulfur Bonding," Ronald Press Co., New York, 1962, p. 132.

[13] Smith and Winstein, *Tetrahedron*, 1958, **3**, 317; Kuhn and Trischmann, *Annalen*, 1958, **611**, 117; Laughlin, *J. Org. Chem.*, 1960, **25**, 864; Cotton, Francis, and Horrocks, *J. Phys. Chem.*, 1960, **64**, 1534.

[14] Brown, *Tetrahedron*, 1961, **12**, 117; *J. Chem. Educ.*, 1961, **38**, 173.

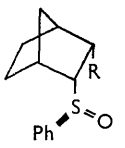
[15] Corey, Mock, and Pasto, *Tetrahedron Letters*, 1961, **11**, 347; *J. Amer. Chem. Soc.*, 1961, **83**, 2957; Hünig, Müller, and Thier, *Tetrahedron Letters*, 1961, **11**, 353; van Tamelen, Dewey, and Timmons, *J. Amer. Chem. Soc.*, 1961, **83**, 3725; Dewey and van Tamelen, *ibid.*, p. 3729; van Tamelen, Dewey, Lease, and Pirkle, *ibid.*, p. 4302.

and (XXII), to avoid eventual addition of borane to the double bond, and these were treated with an excess of diborane in diethylene glycol dimethyl ether. From each there was obtained a mixture of the sulphide alcohol (XXVI) and the sulphoxide alcohol [(XXVII) or (XXVIII)]. [The sulphoxide alcohol (XXVIII) was obtained in much higher yield from the acid (XXII) by reduction with sodium borohydride–aluminium chloride.] The sulphide alcohol, which was the principal product of the reduction of the acid (XXII), was isolated in only small quantities by reduction of the acid (XXI). Analogous results were obtained when diborane was allowed to react directly with the alcohols (XXVII) and (XXVIII). A more selective reduction of the esters (XXIV) and (XXV) was possible with bis-(1,2-dimethylpropyl)borane: the former was unaltered, while the latter was quantitatively reduced to the sulphide (XXIII). It should be mentioned that, as indicated by Brown,[14] the methoxycarbonyl group is not reduced by this dialkylborane.



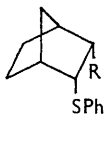
syn

(XXI) R = CO_2H
(XXIV) R = CO_2Me
(XXVII) R = $CH_2 \cdot OH$

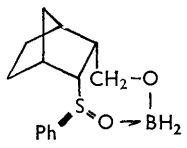


anti

(XXII) R = CO_2H
(XXV) R = CO_2Me
(XXVIII) R = $CH_2 \cdot OH$



(XXIII) R = CO_2Me
(XXVI) R = $CH_2 \cdot OH$



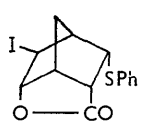
(XXIX)

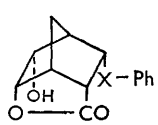
From these observations it is reasonable to assign *syn*-configurations to (XXI), (XXIV), and (XXVII), these being more resistant to reduction by boranes than are the isomers (XXII), (XXV), and (XXVIII), to which, therefore, the *anti*-configurations are assigned.* Further, reduction of the sulphoxide (XXVIII) to the sulphide (XXVI) should be favoured by the formation of a cyclic complex (XXIX) with borane. Molecular models show that formation of an analogous complex from the sulphoxide (XXVII) is less favoured sterically.

These assignments are justified by the fact that the three *syn*-compounds were derived chemically from the acid (XI), which was assigned the *syn*-form independently. Similarly, the latter three *anti*-compounds were derived from the acid (XII), to which the *anti*-configuration had been assigned.

Stereochemistry and Kinetics of Oxidations $\gtrless S \rightarrow \gtrless SO \rightarrow \gtrless SO_2$.—The sulphides (XXIII), (XXX), and (XXXI) were oxidised to sulphoxides, and the latter, in their respective *syn*- and *anti*-forms, to the sulphones.

(XXX)





(XXXI) X = S
(XXXII) X = SO *syn*
(XXXIII) X = SO *anti*
(XXXIV) X = SO_2

Mono-oxidation of the ester (XXIII) lead to about 60% of *anti*- (XXV) and 40% of *syn*-sulphoxide (XXIV). However, the ratio was reversed with (XXX), which gave 35% of *anti*- (XVIII) and 65% of *syn*-sulphoxide (XVII).[5] The kinetics of oxidation of the sulphoxides (XXIV) and (XXV) gave identical values, respectively $k_2 = 1{\cdot}15 \times 10^{-2}$ and

* It should be noted that the isomer (XII) is much more resistant than is the isomer (XI) to reduction with zinc and acetic acid or with hydrogen iodide. Earlier,[4] on this basis, the opposite configurations were provisionally assigned to the acids (XI) and (XII).

$1{\cdot}18 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ at 25° in 1 : 1 dioxan–water [for the sulphide (XXIII), $k_2 =$ 23 l. mole^{-1} sec.$^{-1}$ at 0°].

It is not possible to draw conclusions from these results, even though molecular models offer some indication that, on the basis of simple steric factors, the *anti*-isomer should be slightly favoured from the oxidation of (XXIII), and the *syn*-isomer from the oxidation of (XXX). On the other hand, it has been pointed out that, in the oxidation of sulphoxides to sulphones, steric effects are of minor importance,[16] which might explain the virtually identical rates of oxidation of esters (XXIV) and (XXV) to the sulphone.

However, more definite structural indications were obtained on oxidation of the hydroxy-lactone (XXXI) to the sulphoxides (XXXII) and (XXXIII), and the oxidation of these to the sulphone (XXXIV). The sulphoxide (XXXII) is formed by alkaline lactonisation of the iodohydrin (XIX),[1,4] and, therefore, has the same configuration at the sulphur as the lactone and the *endo-cis*-adduct (XI), which should be *syn*, as described above.

The sulphoxide (XXXIII) is formed almost exclusively on mono-oxidation of the sulphide (XXXI). The rates of oxidation, k_2, of the sulphoxides (XXXII) and (XXXIII) are, respectively, $2{\cdot}9 \times 10^{-3}$ and $4{\cdot}6 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$, at 25° in 1 : 1 dioxan–water. These results are best interpreted by assigning the *syn*-configuration to the sulphoxide (XXXII) and *anti*-configuration to (XXXIII). In fact, the hydroxyl in the *endo*-position should sterically favour oxidation of the sulphide (XXXI) to the *anti*-sulphoxide. Furthermore, the rate of oxidation of the *syn*-sulphoxide should be diminished in view of the possibility of intramolecular H-bonding (OH · · · O:S), tending to diminish the electron density at the sulphur atom.

Infrared Spectra.—Interaction between the hydroxyl and the sulphinyl group in the *trans*-iodohydrins (XV), (XVI), the *cis*-iodohydrin (XIX), and their corresponding esters, was noted in earlier infrared studies.[17] It was necessary to record the spectra of the acids in the solid state because of their very low solubility, but the iodohydrin hydroxyl frequency was very similar for the acids and the esters, those for the latter being very similar for solutions (10^{-3}M in carbon tetrachloride) and for the solid state. This confirms the earlier indication that the interaction is essentially intramolecular. The definite demonstration [5] of the position of the hydroxyl group in iodohydrins (XV), (XVI), and (XIX), now permits the following assignments: in the *trans*-series, the lower frequency (3180 cm.$^{-1}$ for the acid in Nujol mull, and 3220 cm.$^{-1}$ for the ester in carbon tetrachloride) corresponds to the *syn*-iodohydrin (XV), m. p. 213°; the higher frequency (3430 cm.$^{-1}$ for the acid in Nujol mull, and 3330 cm.$^{-1}$ for the ester in carbon tetrachloride) corresponds to the *anti*-isomer (XVI), m. p. 176°. Molecular models show that both isomers afford conformations in which intramolecular interaction OH · · · O:S is possible, but in such conformations only the *syn*-isomer allows complete rotational freedom of the phenyl around the S–phenyl bond. In the *cis*-series only one iodohydrin acid (XIX) was formed. Accordingly, no conclusion regarding its structure was possible, even though the low frequency of the iodohydrin hydroxyl (acid, 3460 cm.$^{-1}$ in Nujol mull; ester, 3465 cm.$^{-1}$ in carbon tetrachloride) indicates intramolecular interaction.

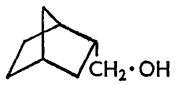
The low solubility of the hydroxy-lactones (XXXII) and (XXXIII) in non-polar solvents did not permit infrared studies of this type.

A comparison was possible for the two alcohols (XXVII) and (XXVIII). The former, m. p. 128·5°, in concentrated solution (carbon tetrachloride) exhibited two distinct hydroxyl bands, one narrow, at 3638 cm.$^{-1}$, the other wide, at 3410 cm.$^{-1}$, the latter disappearing when the solution was diluted. The isomer (XXVIII), m. p. 113°, exhibited a wide band at 3417 cm.$^{-1}$, not altered on dilution even to 3×10^{-4}M. These results are

[16] Cerniani, Modena, and Todesco, *Gazzetta*, 1960, **90**, 3; Gasperini, Modena, and Todesco, *ibid.*, p. 12.

[17] Foffani, Ghersetti, and Montanari, *Ricerca sci.*, 1960, **30**, 1010.

clearly in accord with the previous assignments, *i.e.*, *syn*-configuration to the isomer (XXVII) and *anti*- to the isomer (XXVIII). In fact, at the lowest concentrations, when all intermolecular interaction disappears, the only hydroxyl band exhibited by the isomer (XXVII) is almost identical with that exhibited by 2-*endo*-hydroxymethylbicyclo[2,2,1]heptane (XXXV) (3638 cm.$^{-1}$, 10^{-3}M in carbon tetrachloride). This indicates the absence of intramolecular interaction in the isomer (XXVII); however, such interaction is evident in the isomer (XXVIII). Molecular models indeed indicate that intramolecular interaction is much more favoured in the *anti*-isomer.



(XXXV)

The sulphide (XXVI), corresponding to the sulphoxides (XXVII) and (XXVIII), exhibits the free-hydroxyl band at 3640 cm.$^{-1}$ in carbon tetrachloride, and at higher concentrations the intermolecularly associated hydroxyl band at 3528 cm.$^{-1}$. The absence of intramolecular interaction between the sulphur and the hydroxyl group in the sulphide (XXVI) confirms, then, the indication that in the sulphoxides the inter- and intramolecular interactions between hydroxyl and sulphoxide groups involve the electrons of the sulphoxide-oxygen and not those of the sulphur. The sulphone corresponding to the sulphoxides (XXVII) and (XXVIII) exhibits a simple wide hydroxyl band at 3536 cm.$^{-1}$; this is unchanged even at concentrations of about 3×10^{-3}M (carbon tetrachloride) and probably results from intramolecular reaction between the alcoholic hydroxyl group and a sulphone-oxygen atom. The smaller frequency shift of the bonded hydroxyl here than for the sulphoxides is to be noted and is in agreement with the lower basicity of the oxygen in sulphones than in sulphoxides.[18]

Proton Magnetic Resonance Spectra.—The spectra were recorded only for the sulphoxide acids, these being studied in 0·5N-sodium deuteroxide in D_2O. In this way it was possible to overcome the obstacle of low solubility in the common spectral solvents. At the same time the alkaline solutions afforded conditions approaching those of the formation of iodo-lactones and iodohydrins. The spectra of the corresponding sulphides and sulphones of both the *cis*- and the *trans*-series were studied concurrently and will be discussed elsewhere.

The *endo-cis*-adduct (XI), to which the *syn*-configuration was assigned, showed at −360·0 c./sec. a group of lines originating from the five phenyl hydrogens (see Figure). This group, with slight variations in position and fine structure, appeared in the same region in the spectra of all the compounds of these series. The ethylenic hydrogen resonances were observed at −280 c./sec. in an AB group,[19] with additional fine structure attributed to the respective adjacent hydrogen atoms at positions 1 and 4. A narrow, intense peak at −195 c./sec. was caused by H_2O as an impurity in the D_2O, and was found unaltered in all the spectra. The multiplets at −154·3 and −108·7 c./sec. have been assigned respectively to hydrogen at positions 3 and 2. Their structure is that of an AB group, with additional fine structure caused by their respective adjacent hydrogen atoms at positions 4 and 1. The latter appeared as a multiplet at −112·3 c./sec., with wide, ill-defined structure. This confirms the interaction of hydrogen in the 1- and the 4-position with many other hydrogen atoms, the four cited above in the 2-, 3-, 5-, and 6-positions, and the two at the methylene bridge (position 7). The latter were observed as an AB quartet at −19·2 c./sec.[20]

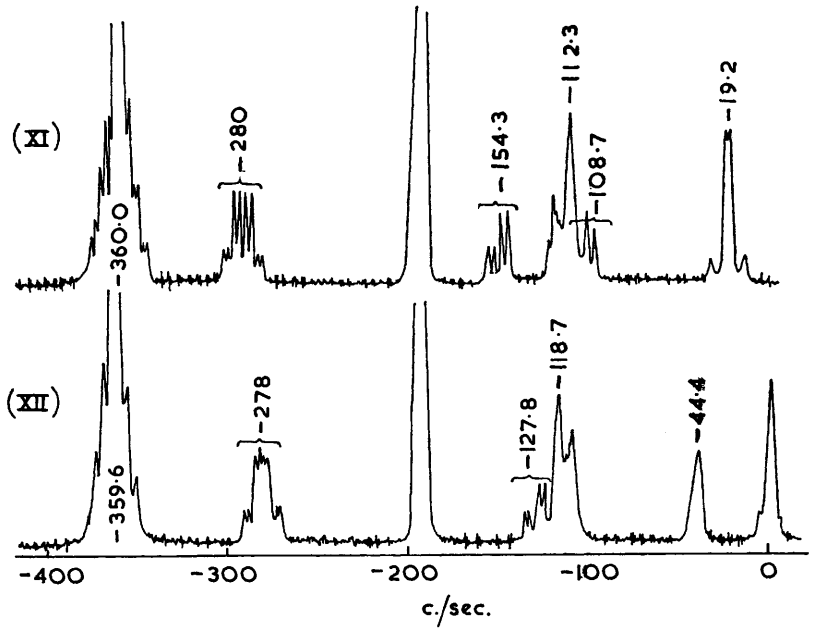
The hydrogen resonances of the phenyl group, the double bond, and the methylene bridge of the *anti*-isomer (XII), were found to differ little from those of isomer (XI); however, substantial differences were noted for the other hydrogen resonances (see Figure). The hydrogen at position 1 was shifted slightly and fell under the multiplet at −127·8 c./sec.; but that at position 4 was shifted to −44·4 c./sec.,

[18] Barnard, Fabian, and Koch, *J.*, 1949, 2442; Amstutz, Hunsberger, and Chessick, *J. Amer. Chem. Soc.*, 1951, **73**, 1220.

[19] Pople, Schneider, and Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, pp. 119 *et seq.*

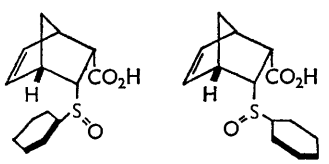
[20] Hogeveen, Maccagnani, Montanari, and Taddei, unpublished work.

which is a displacement of 67·9 c./sec. from that of isomer (XI) towards higher magnetic field. These differences between isomers (XI) and (XII) are directly associated with configuration at the sulphur atom. The *anti*-isomer (XII) easily attains a



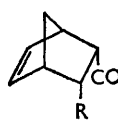
Proton magnetic resonance spectrum of acids (XI) and (XII).

conformation in which the plane of the phenyl group is adjacent to the 4-hydrogen atom. This is much less probable for the *syn*-isomer (XI), in which a conformation is easily attained having the sulphoxide-oxygen adjacent to the 4-hydrogen atom. On the other hand, it was noted [21] that the applied magnetic field H_0 induces within the aromatic

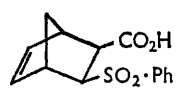


anti

syn



(XXXVI) R = SO_2·Ph
(XXXVII) R = SPh



(XXXVIII)

nucleus a secondary magnetic field in the opposite direction. The protons lying above the aromatic plane are affected in such a way by the induced diamagnetism that they resonate in a higher magnetic field, which is exactly what happens to the 4-hydrogen atom of isomer (XII).

The spectra are in accord, therefore, with the configurational assignments of isomers (XI) and (XII), as noted above.

In the sulphone (XXXVI) the presence of the two oxygen atoms symmetrically bonded to sulphur probably favours a conformation in which the phenyl is in a position intermediate between that of the extremes possible for the corresponding sulphoxides. In the sulphide (XXXVII) an even greater rotational freedom is possible, the phenyl group

[21] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Oxford, 1959; Pople, *J. Chem. Phys.*, 1956, **24**, 1111; Waugh and Fessenden, *J. Amer. Chem. Soc.*, 1957, **79**, 846.

moving either near to, or far from, the 4-hydrogen atom, so that its average position is similar to that in the sulphone. The spectra of isomers (XXXVI) and (XXXVII) reflect this situation, and the 4-hydrogen resonance was found at intermediate positions, −80·0 and −84·0 c./sec., respectively. For the *cis-exo*-sulphone (XXXVIII) the undisturbed 4-hydrogen was observed at −96·7 c./sec.

The study of the bicyclo[2,2,1]heptane analogues was complicated by the saturation of the double bond: there was disappearance of absorption between −290 and −270 c./sec., but increase in that between −20 and 0 c./sec. because of the four new methylenic hydrogens. Apart from this, the spectra are similar to those of the unsaturated series. With the *anti*-sulphoxide (XXII) the 4-hydrogen resonance was observed at −22·7 c./sec.; for the *syn*-isomer (XXI) at −84·7 c./sec.; and for the corresponding sulphone at −51·5 c./sec.

For the *trans*-iodohydrins, the 4-hydrogen resonance of the *syn*-isomer (XV) was observed at −184·5 c./sec., and that of the *anti*-isomer (XVI) at −61·0 c./sec. The relative shifts of the magnetic fields are of the same order of magnitude as those noted above. Moreover, a diminution of the screening by the hydroxyl group was observed with both isomers (XV) and (XVI); in the former the deshielding effect was furthered by that derived from the sulphoxide group. These results confirm the independent conclusions of the infrared studies.

Acidities.—It can be further noted that the acidities of the *anti*-isomers were consistently lower than those of the *syn*-isomers; in 48% v/v aqueous ethanol at 25°, the difference in pK_a in the *cis*-series was 0·27 unit, in the *trans*-series 0·15—0·17 unit. This might logically arise from the influence of the negative charge at the sulphinyl-oxygen atom, which in the *anti*-isomer, but not in the *syn*-isomer, is sufficiently close to the carboxyl group to reduce its acidity. These assignments are in accord with those discussed above. The influence of the field effect of the sulphinyl group on acidity has been recently discussed.[22] A complete discussion of our acidity studies (sulphides, sulphoxides, and sulphones) will be published shortly.

Conclusions.—Each of the methods discussed above allows an independent, even if not rigorous, identification of the *syn*- and *anti*-isomers from the Diels–Alder reaction of α-ethylenic sulphoxides with cyclopentadiene. In all cases the assignments were consistent. In both pairs of adducts examined [*cis*-(XI) and -(XII), and *trans*-(IX) and -(X)] the phenylsulphinyl group was in the *endo*-position. In both cases the *syn*-isomer was favoured, 80% in the *cis*- and 75% in the *trans*-series.[4,5] It appears very likely that electronic interactions involving the sulphinyl group play the principal role in determining the ratio of *syn*- and *anti*-isomers. Further study is in progress to clarify this point.

Experimental

Spectra.—Infrared spectra were recorded with a Beckman I.R. 4 spectrometer equipped with sodium chloride and lithium fluoride prisms, for Nujol or hexachlorobutadiene mulls or carbon tetrachloride solutions. The hydroxyl bands were analysed with cell paths up to 5 cm.

Proton magnetic resonance spectra were recorded with a Varian D.P. 60 spectrometer operating at 56·4 Mc./sec. The multiplet areas were checked by using a Varian 3521 integrator. Calibration of the peaks was done by the " side band " technique,[23] with t-butyl alcohol as an internal standard.

Iodolactonisation.—The following general procedure was used. A solution of ester (0·01 mole) in chloroform (70 ml) was shaken for 24 hr. with a solution of iodine (0·015 mole.), potassium iodide (0·045 mole), and sodium hydrogen carbonate (0·02 mole) in water (90 ml.).

[22] Meyers, *Tetrahedron Letters*, 1962, **24**, 1125; Meyers, Lombardini, and Bonoli, *J. Amer. Chem. Soc.*, 1962, **84**, 4603.
[23] Arnold and Packard, *J. Chem. Phys.*, 1951, **19**, 1608.

The excess of iodine was reduced with sodium thiosulphate, and the chloroform layer was separated, washed with water, dried, and evaporated, to give the product.

In these conditions, methyl 3-*endo*-*syn*-phenylsulphinylbicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylate [4] (cf. XI) gave 98% of methyl 5-*endo*-hydroxy-6-*exo*-iodo-3-*endo*-*syn*-phenylsulphinylbicyclo[2,2,1]heptane-2-*endo*-carboxylate [4] (cf. XIX), m. p. 162—163°.

Treatment of 3-*endo*-*anti*-phenylsulphinylbicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid [4] (XII) in tetrahydrofuran with ethereal diazomethane gave the *methyl ester*, m. p. 133—135°. Crystallisation from light petroleum (b. p. 75—120°) raised the m. p. to 136—137° (Found: C, 65·4; H, 5·9. $C_{15}H_{16}O_3S$ requires C, 65·2; H, 5·8%). Iodolactonisation of this ester (0·25 g.) afforded a mixture (0·26 g.), m. p. 120—162°, of the initial ester and of 6-*endo*-hydroxy-5-*exo*-iodo-3-*endo*-*anti*-phenylsulphinylbicyclo[2,2,1]heptane-2-*endo*-carboxylic acid lactone [4] (XVIII). The infrared spectra (in Nujol) showed carbonyl bands at 1784 [lactone (XVIII)], and 1737 cm.$^{-1}$ [ester of the acid (XII)]. Quantitative infrared analysis in chloroform indicated a mixture of lactone (XVIII), 38%, and ester of acid (XII), 59%.

3-*endo*-Phenylthiobicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid [4] (XXXVII) was esterified with diazomethane in ether. The oily ester was not characterised, but was lactonised directly, yielding 98% of 6-*endo*-hydroxy-5-*exo*-iodo-3-*endo*-phenylthiobicyclo[2,2,1]heptane-2-*endo*-carboxylic acid lactone [4] (XXX), m. p. 143—145°. After crystallisation from ethanol this had m. p. 150—151°.

3-*endo*-Phenylsulphonylbicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid (XXXVI) in tetrahydrofuran was esterified with ethereal diazomethane. The *ester*, after crystallisation from benzene, had m. p. 150—151° (Found: C, 61·6; H, 5·4. $C_{15}H_{16}O_4S$ requires C, 61·6; H, 5·5%). All the ester was recovered in attempted iodolactonisations.

Reaction of the Ester of Sulphide (XXXVII) *with Sodium Hydrogen Carbonate*.—The ester of the sulphide acid (XXXVII) (0·56 g.) in chloroform (12 ml.) was shaken for 24 hr. with sodium hydrogen carbonate (0·37 g.) in water (6 ml.). From the chloroform layer the unaltered ester (0·45 g., 80%) was recovered, and from the acidified water layer the acid (XXXVII) (0·10 g., 18%).

3-endo-*Phenylsulphinylbicyclo*[2,2,1]*heptane*-2-endo-*carboxylic Acids*, syn (XXI), anti (XXII).—The *syn*-acid (XI) (6·0 g.) in methanol (200 ml.) was neutralised with methanolic potassium hydroxide. To this, under nitrogen and with agitation, was added potassium azodicarboxylate (11·7 g.), and, during 3 hr., a solution of acetic acid (13·8 g.) in methanol (75 ml.). Stirring was prolonged for another hour, and the methanol was evaporated in a vacuum. The residue was dissolved in chloroform, the solution washed with dilute sulphuric acid and water, and the solvent evaporated to give a quantitative yield (6·0 g.) of the syn-*acid* (XXI), m. p. 183—184°. Crystallised from ethyl acetate this had m. p. 184—185°, ν 1713 (CO), ~980 (SO) cm.$^{-1}$ (Found: C, 63·5; H, 6·2. $C_{14}H_{16}O_3S$ requires C, 63·6; H, 6·1%). Oxidation of the acid (XXI) with peracetic acid gave a sulphone, m. p. 202—204°, identical with that [24] obtained previously.

Similarly, the saturated anti-*acid* (XXII) was obtained from the *anti*-acid (XII); crystallised from ethanol–ethyl acetate, it had m. p. 194° (Found: C, 63·6; H, 6·1%).

Proton magnetic resonance spectra indicated the absence of a double bond in the compounds (XXI) and (XXII) (no bands observed in the region between −290 and −270 c./sec.).

Reduction of the syn-*Acid* (XXI) *with Diborane*.—To a stirred solution of acid (XXI) (0·50 g.) and sodium borohydride (0·28 g.) in diethylene glycol dimethyl ether (10 ml.) a solution of boron trifluoride–ether complex (1·38 g.) in the same solvent (3 ml.) was added under nitrogen during 3 hr. Stirring was prolonged for 1 hr., and after 20 hr. at room temperature the excess of hydride was decomposed. The product was diluted with chloroform and washed with aqueous sodium carbonate. The chloroform was evaporated, and the residue was chromatographed on acidified alumina. Benzene eluted 2-endo-*hydroxymethyl*-3-endo-*phenylthiobicyclo*[2,2,1]-*heptane* (XXVI) (50 mg., 11%), and subsequently chloroform eluted 2-endo-*hydroxymethyl*-3-endo-syn-*phenylsulphinylbicyclo*[2,2,1]*heptane* (XXVII) (0·28 g., 58%). The sulphide (XXVI), after crystallisation from light petroleum (b. p. 40—60°), had m. p. 54—55° (Found: C, 71·1; H, 7·8. $C_{14}H_{18}OS$ requires C, 71·7; H, 7·7%). The sulphoxide (XXVII), after crystallisation from light petroleum (b. p. 75—120°), had m. p. 129—130°, ν 3638 (free OH), 3410 (associated OH) (in CCl_4), and ~995 (SO) cm.$^{-1}$ (in Nujol) (Found: C, 66·7; H, 7·3. $C_{14}H_{18}O_2S$ requires C, 67·1; H, 7·25%).

[24] Luciani, Montanari, and Tramontini, *Gazzetta*, 1960, **90**, 731.

Reduction of the anti-*Acid* (XXII) *with Diborane.*—The *anti*-acid (XXII), reduced under the above conditions, gave the sulphide alcohol (XXVI) (79%) and 2-endo-*hydroxymethyl*-3-endo-anti-*phenylsulphinylbicyclo*[2,2,1]*heptane* (XXVIII) (11%), m. p. 115—116° (from light petroleum; b. p. 75—120°) [the m. p. of the mixture with the isomer (XXVII) was depressed], ν ~3417 (associated OH) (in CCl_4), ~1015 (SO) cm.$^{-1}$ (in Nujol) (Found: C, 66·6; H, 7·25. $C_{14}H_{18}O_2S$ requires C, 67·1; H, 7·25%).

Reduction of sulphoxides (XXI) and (XXII) with twice the proportion of sodium borohydride and half the proportion of boron trifluoride–ether (to keep the diborane in solution) yielded almost quantitatively the sulphide alcohol (XXVI) from isomer (XXII), and the *syn*-sulphoxide alcohol (XXVII) from isomer (XXI). The sulphoxide (XXVII) was not reduced under these conditions (95% recovered); the *anti*-sulphoxide (XXVIII) was reduced to the sulphide (XXVI) (75%).

Reduction of the anti-*Acid* (XXII) *with Sodium Borohydride–Aluminium Trichloride.*—The *anti*-acid (XXII) (0·5 g.) and aluminium trichloride (0·5 g.) were dissolved in diethylene glycol dimethyl ether (20 ml.) and stirred under nitrogen for 15 min. Sodium borohydride (0·42 g.) in diethylene glycol dimethyl ether (20 ml.) was added during 20 min. After a few hours at room temperature, the mixture was stirred at 70° for 2 hr., then the excess of hydride was decomposed with ethanol. The solvent was evaporated in a vacuum, and the residue dissolved in chloroform and washed with dilute sulphuric acid and aqueous sodium carbonate. From the chloroform layer the *anti*-sulphoxide alcohol (XXVIII), m. p. 113—114°, was isolated, and from the alkaline solution some acid (XXII) (30 mg.).

Reduction of Methyl 3-endo-*Phenylsulphinylbicyclo*[2,2,1]*heptane*-2-endo-*carboxylates* (XXIV) *and* (XXV) *with bis*-(1,2-*dimethylpropyl*)*borane.*—The *anti*-acid (XXII) in tetrahydrofuran with ethereal diazomethane gave the *ester* (XXV) (100%), m. p. 100—102° (from light petroleum; b. p. 75—120°) (Found: C, 64·3; H, 6·8. $C_{15}H_{18}O_3S$ requires C, 64·7; H, 6·5%). A stirred solution of 2-methylbut-2-ene (1·45 g.) and sodium borohydride (0·30 g.) in diethylene glycol dimethyl ether (7 ml.) was cooled at 0° under nitrogen. Boron trifluoride–ether (1·47 g.) in diethylene glycol dimethyl ether (2 ml.) was added during 30 min. The solution was left at 0° for 1 hr., after which the ester (XXV) (0·28 g.) in diethylene glycol dimethyl ether (2 ml.) was added in one portion. The mixture was left at room temperature for 17 days. After this the excess of hydride was eliminated, the solvent evaporated, and the residue chromatographed on acidified alumina. Benzene eluted the sulphide ester (XXIII) (0·1 g., 38%) as an oil (its proton magnetic resonance spectrum was identical with that of the product obtained as described below).

The *syn*-acid (XXI) gave the *syn*-ester (XXIV), m. p. 119—120° (from light petroleum; b. p. 75—120°) (Found: C, 64·7; H, 6·6. $C_{15}H_{18}O_3S$ requires C, 64·7; H, 6·5%). This ester, treated as above, was recovered to an extent of 68%.

Methyl 3-endo-*Phenylthiobicyclo*[2,2,1]*heptane*-2-endo-*carboxylate* (XXIII).—The *sulphide ester* (XXIII) was obtained as an oil, n_D^{25} 1·5720, by treatment of the sulphide-acid (XXXVII) with diazomethane, followed by reduction with di-imide and chromatography in benzene on acidified alumina (Found: C, 68·7; H, 7·0. $C_{15}H_{18}O_2S$ requires C, 68·7; H, 6·9%).

2-endo-*Hydroxymethylbicyclo*[2,2,1]*heptane* (XXXV).—Bicyclo[2,2,1]heptane-2-*endo*-carboxylic acid (5·0 g.) was esterified with ethereal diazomethane and then reduced in 5 hr. with an excess (2·8 g.) of lithium aluminium hydride in boiling ether, to give the alcohol (XXXV) (2·7 g., 60%), b. p. 98—100°/17 mm. (lit.,[25] b. p. 93—95°/14 mm.).

Mono-oxidation of the Iodo-lactone Sulphide (XXX).—The iodo-lactone sulphide [4] (XXX) (1·0 g.) was oxidised at 0° with perbenzoic acid (2 equiv.) in chloroform. The solution was washed with aqueous sodium hydrogen carbonate and evaporated, and a mixture (1·03 g.; m. p. 152—155°) of the sulphoxides (XVII) and (XVIII) was isolated. Infrared analysis in acetone of the 730 cm.$^{-1}$ band, observed in the spectrum of the *syn*-isomer (XVII) [4] [absent in that of the *anti*-isomer (XVIII)] indicated 60—70% of sulphoxide (XVII) in the mixture.

Mono-oxidation of 5-endo,6-endo-*Dihydroxy*-3-endo-*phenylthiobicyclo*[2,2,1]*heptane*-2-endo-*carboxylic Acid* 6-*Lactone* (XXXI).—The hydroxy-lactone sulphide (XXXI) [1] (1·03 g.) was oxidised at 0° with perbenzoic acid (2 equiv.) in chloroform. The solution was left for 12 hr. at room temperature, and the *anti*-sulphoxide (XXXIII), m. p. 248—252° (0·84 g.), was then isolated by filtration. The chloroform solution was washed with aqueous sodium hydrogen carbonate and evaporated, and a further amount (0·23 g.; m. p. 235—240°) of sulphoxide (XXXIII) was isolated. The total yield was 98%. Crystallisation from acetic acid raised the

[25] Alder and Stein, *Annalen*, 1936, **525**, 247.

m. p. to 258° [a mixture of this compound with the isomer (XXXII) [4] depressed the m. p.], ν 3290 (OH), 1770 (CO), and 1019—1026 (SO) cm.$^{-1}$ (in Nujol) (Found: C, 60·4; H, 5·2. $C_{14}H_{14}O_4S$ requires C, 60·4; H, 5·1%). The infrared spectra of the two fractions were identical with that of the pure product.

Mono-oxidation of Methyl 3-endo-*Phenylthiobicyclo*[2,2,1]*heptane*-2-endo-*carboxylate* (XXIII).—Under the conditions used with the sulphides (XXX) and (XXXI), the sulphide ester (XXIII) was oxidised to a mixture of the sulphoxides (XXIV) and (XXV). Quantitative proton magnetic resonance spectroscopy was based on the peak of the methyl group, which for the *syn*-isomer (XXIV) was at −116·8 and for the *anti*-isomer at −124·4 c./sec. from the reference (cyclohexane) in carbon disulphide solution. It indicated 60% of the *anti*-isomer (XXV) and 40% of the *syn*-isomer (XXIV) in the mixture.

Kinetics.—The rates of oxidation of sulphides and sulphoxides with perbenzoic acid were measured in dioxan–water (1 : 1 v/v) at 0·0° or 25·0°, by titration of the excess of peracid with potassium iodide and thiosulphate.[26] The second-order rate constants k_2 were determined graphically by plotting log $[(a - x)/(b - x)]$ against time. Straight lines were obtained up to at least 75% conversion.

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[26] Maioli and Modena, *Gazzetta*, 1957, **87**, 1306; Cerniani and Modena, *ibid.*, 1959, **89**, 843.