# 946. *Cyclisations and Rearrangements in the Isodrin–Aldrin Series.*

By C. W. Bird, R. C. Cookson, and E. Crundwell.

Treatment of the stereoisomeric insecticides, isodrin and aldrin, with acid induces a series of cyclisation, rearrangement, and hydride transfer to form a mixture of saturated and unsaturated products, the most stable of which is the saturated isomer with a cyclobutane ring in place of the two double bonds of isodrin. On reaction with acid and on acetolysis of the methanesulphonates of related alcohols five different ring systems are produced.

The results, *inter alia*, prove the configurations previously assumed for isodrin and aldrin, whose ring systems have now been interconverted.

The isomeric chlorohydrocarbon insecticides, aldrin and isodrin, offer attractive frameworks for the study of transannular interactions, both chemical and spectroscopic: but first their configurations must be considered.

Aldrin is made [1] by the addition of bicycloheptadiene to hexachlorocyclopentadiene: knowing the tendency for *exo*-addition of dienes to bicycloheptadiene [2] and allowing for the large size of the *gem*-dichloro-group, one might expect aldrin to have the configuration (I) rather than any of the other three possibilities. Isodrin is made [3] by addition of hexachlorobicycloheptadiene (II) to cyclopentadiene: here the large *gem*-dichloro-group in the dienophile (II) is likely to force addition of cyclopentadiene from the *endo*-side. Of the two structures resulting from *endo*-addition, (III) avoids the repulsion between the methylene and dichloroethylene groups present in the other.

The double bonds in a diene of structure (III) are very close to one another and on irradiation would be expected to join up forming a cyclobutane ring.[4] We therefore applied the test of irradiating a solution of isodrin in a silica vessel with a mercury arc. That the product was saturated was shown by the usual chemical tests, and the disappearance of the dichloroethylene chromophore was confirmed by the absence of its characteristic, strong band at about 1600 cm.$^{-1}$. The low end-absorption of the product at 200 mμ, where the dichloroethylene compounds have ε about 9000, definitely established that the product was saturated. Since systematic names in this series are so cumbersome * we shall refer to this isomer as the cage-compound (IV). Its formation by treatment that left aldrin unchanged proves the configuration of isodrin (III). The isodrin and aldrin series are interconvertible by rearrangements that affect only the unchlorinated part of the molecule (see below): aldrin must, therefore, have the configuration (I).

Attention was next turned to the action of electrophilic reagents on isodrin (III), as its stereochemistry clearly favours transannular reactions. Indeed the products obtained on treatment of isodrin with sulphuric acid in wet dioxan were entirely saturated. The two main components were the cage-compound (IV) and an alcohol, m. p. 204°. We learnt later that Lidov and Bluestone had described in a patent [5] the conversion of isodrin

* In a preliminary note (Cookson and Crundwell, *Chem. and Ind.*, 1958, 1004) we wrote that we were tempted to call this isomer " photodrin: " the Editors have since persuaded us to resist the temptation. The following descriptive names are used in this paper: isodrin (III), cage-compound (IV), *endo-endo*-alcohol (V; R = H), aldrin (I), *endo-exo*-alcohol (IX; R = H), half-cage *exo*-alcohol (VI; H = R), half-cage *endo*-alcohol (XII; R = H). Systematic names are given in the Experimental section. We are most grateful to the Editors for their assistance in naming these molecules on the " polycyclo " convention, to which α- and β-prefixes have been added to distinguish stereoisomers (see footnote, p. 4814.)

[1] Lidov, U.S.P. 2,635.977; Lidov and Soloway, B.P. 692,547.

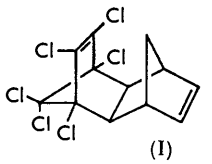
[2] Alder, Mönch, and Wirtz, *Annalen*, 1959, **627**, 47; Stille and Frey, *J. Amer. Chem. Soc.*, 1959, **81**, 4273.

[3] Bluestone, U.S.P. 2,676,132; Lidov, U.S.P. 2,717,851; Arvey Corp., B.P. 714,688.

[4] Cookson, Crundwell, and Hudec, *Chem. and Ind.*, 1958, 1003; Schönberg, " Präparative Organische Photochemie," Springer-Verlag, Berlin, 1958, p. 22.

[5] Lidov and Bluestone, U.S.P. 2,714,617.

into a substance clearly the same as (IV) by hydrogen bromide in ether or acetic acid. Lidov [3] had added acetic acid to isodrin (III) in the presence of sulphuric acid to form an acetate, which he assumed had the unrearranged structure (V). Hydrolysis of the acetate yielded the alcohol, m. p. 204°, which could be re-acetylated to Lidov's acetate. The absence of the dichloroethylene chromophore and their complete saturation rule out structures (V) for the alcohol and its acetate. The ketone got by oxidation of the alcohol had $\nu_{max.}$ 1755 cm.$^{-1}$ and no band at 1420 cm.$^{-1}$, so that the carbonyl group must be in a five-membered ring with no α-methylene group. These features are accommodated by structure (VI; R = H) for the alcohol, m. p. 204°, and (VII) for the ketone. Boron trifluoride in benzene rearranged isodrin epoxide (VIII) quantitatively to the ketone (VII).†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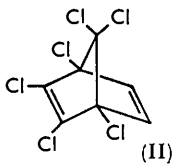
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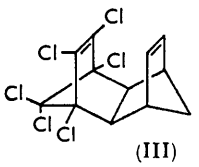
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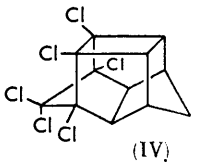
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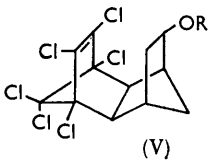
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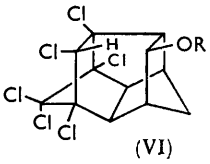
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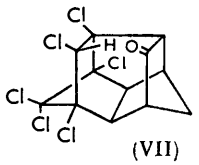
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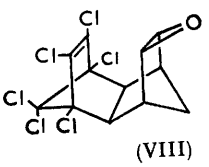
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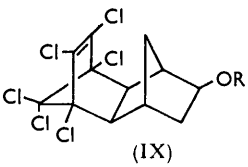
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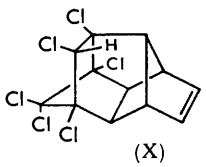
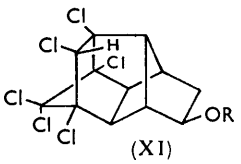
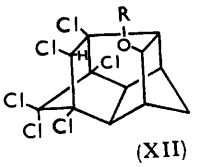

(X)


(XI)


(XII)

The genuine, unrearranged hydroxydihydro-derivative (V; R = H), still showing the dichloroethylene chromophore, was made from isodrin by Brown and Zweifel's reaction.[6]

Acetic acid containing sulphuric acid turned aldrin (I) almost entirely into the *endo-exo*-acetate (IX; R = Ac), accompanied by traces of half-cage acetate (VI; R = Ac) and cage-compound (IV). From its mechanism of formation the acetate (IX) was expected to be the *exo*-epimer, and this configuration was confirmed by the compound's being different from the known [7] *endo*-epimer, made by addition of *endo*-acetoxybicycloheptene to hexachlorocyclopentadiene.

To examine the kinetically controlled, consecutive rearrangements of the intermediate carbonium ions, the methanesulphonates of the *endo-endo*-alcohol (V), half-cage alcohol (VI), and *endo-exo*-alcohol (IX) were heated in acetic acid containing sodium acetate. The last (IX) gave mostly aldrin (I) with some *endo-exo*-acetate (IX; R = Ac) and *endo-endo*-acetate (V; R = Ac), but major products from the other two methanesulphonates, which were acetolysed far more rapidly, were a new acetate and a chlorohydrocarbon. The dichloroethylene chromophore was absent from the spectra of both, so that we assumed at first that they were the acetate (XI; R = Ac) and the olefin (X) formed by further rearrangement of a carbonium ion related to the half-cage structure (VI). On

† In the ultraviolet region the three isomeric ketones, *endo-endo*-ketone (as V), half-cage ketone (VII; X = O), and *endo-exo*-ketone (as IX) all had very similar long-wavelength absorption, with $\lambda_{max.}$ between 295 and 300 mμ and $\varepsilon_{max.}$ 30—60, so that the dichloroethylene group has little effect on the $n \longrightarrow \pi^*$ transition of the first ketone (as V).

[6] Brown and Zweifel, *J. Amer. Chem. Soc.*, 1959, **81**, 247.

[7] Lidov, U.S.P. 2,635,979; Lidov and Soloway, B.P. 692,545; Vol'fson, Mel'nikov, Plate, Sapozhkov, and Taits, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 1252.

TABLE 1. *Solvolysis products of methanesulphonates in acetic acid–sodium acetate.*

| Methanesulphonate | Isodrin (III) | *endo-endo*-Acetate (V) | *exo*-Half-cage acetate (VI) | Cage compound (IV) | Chlorohydrocarbon (XIII) | Half-cage *endo*-acetate (XII) | Aldrin (I) | *endo-exo*-Acetate (IX) |
|---|---|---|---|---|---|---|---|---|
| *endo-endo*- (V) ..... | 38 | 7·4 | 8 | — | 21 | 25 | — | — |
| *exo*-Half-cage (VI) ..... | — | — | 14 | — | 34 | 52 | — | — |
| *endo*-Half-cage (XII) ..... | — | — | 16 | — | 40 | 44 | — | — |
| *endo-exo*- (IX) ..... | — | 10 | — | — | — | — | 75 | 15 |

that assumption we supplied samples and experimental details to Professor S. Winstein and Dr. P. Carter, who were also interested in relating the supposed structures to their unchlorinated analogues.[8,9] Surprisingly, on reduction with lithium and t-butyl alcohol in tetrahydrofuran the alcohol derived from the new acetate gave the cyclic ether with the half-cage skeleton, presumably derived from the *endo*-half-cage alcohol (XII; R = H). In agreement with the revised structure (XII; R = Ac), the infrared spectrum of the acetate shows a sharp band at 3140 cm.$^{-1}$ and that of the alcohol one at 3100 cm.$^{-1}$. These exceptionally high frequencies can be attributed only to the C–H stretching mode of a severely congested hydrogen atom:[10] in fact, the methanesulphonate (XII; R = Me·$SO_2$) has the highest frequency recorded for a hydrogen atom linked to saturated carbon (3145 cm.$^{-1}$). The structure of the alcohol (XII; R = H) was made secure by its oxidation to the same half-cage ketone (VII) as was obtained from its epimer (VI; R = H).

The new chlorohydrocarbon, isomeric with isodrin and aldrin, was found to be saturated, and its precise structure is not yet known. Acid converts it into the cage-compound (IV), so that it may have a structure such as (XIII) (in Scheme 1).

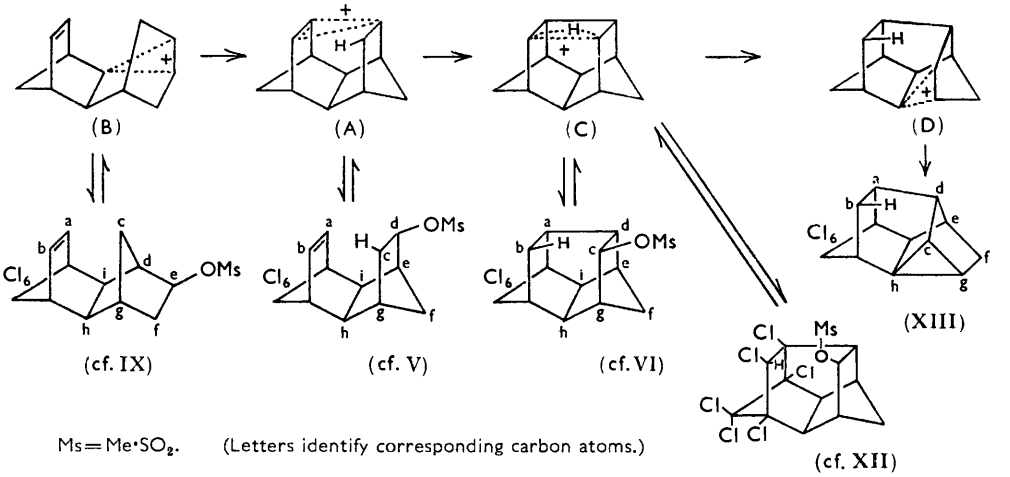
The methanesulphonates were then all solvolysed under identical conditions (18 hr. in boiling acetic acid containing 5% of sodium acetate), and the products were analysed by careful chromatography on silica gel. Separation of the eight possible components was usually good: occasional small intermediate fractions were analysed by infrared spectroscopy. [Rather surprisingly the cage-compound (IV) travelled more slowly down the column than isodrin.] Table 1 records the molar percentage yields of the products from these solvolyses: the figures for the *endo-exo*-methanesulphonate (IX: R = Me·$SO_2$) refer to 190°, since it was quite stable under the standard conditions.

The ionisation of the other three sulphonates must be accelerated very substantially, either through relief of strain or delocalisation of charge in the transition state. The obvious factor in the *endo-endo*-ester (V; R = Me·$SO_2$) is the ability of the electrons of the double bond to participate,[8] so that the first carbonium ion it forms is (A), in Scheme 1. In any case, the quite different distribution of products (unlikely to be entirely due to the difference in temperature) shows that it does not give the same ion (B) as the *endo-exo*-methanesulphonate (IX; R = Me·$SO_2$). Release of pressure between the hydrogen atoms attached to $C_{(b)}$ and $C_{(c)}$ must contribute to the accelerated solvolysis of the half-cage *exo*-sulphonate (VI; R = Me·$SO_2$). Further help may come from involvement of electrons from the $C_{(b)}$–H bond [to give the ion (C)], from the $C_{(a)}$–$C_{(d)}$ bond, or from the $C_{(g)}$–$C_{(h)}$ bond [to give ion (D)]. For the sake of illustration, the first alternative is implied in the diagram. Ionisation of the half-cage *endo*-sulphonate (XII; R = Me·$SO_2$), which must receive even more steric acceleration, may proceed initially to an ion-pair such as (H; R = Me·$SO_2$). The chlorohydrocarbon (XIII) is supposed to be formed by loss of a proton from the bornyl type of bridged ion (D). In the presence of acid the rearrangements become reversible: a proton adds to the $C_{(h)}$–$C_{(g)}$ bond of the cyclopropane (XIII) to regenerate the ion (D), which eventually loses a proton, perhaps *via* (C), to give the

[8] Winstein, *Experientia*, Suppl. II, 1955, 137.
[9] Bruck, Winstein, and Thompson, *Chem. and Ind.*, 1960, 590.
[10] de Vriess and Ryason, *J. Org. Chem.*, 1961, **26**, 62; Kivelson, Winstein, Bruck, and Hansen, *J. Amer. Chem. Soc.*, in the press.

cage-compound (IV). [If an ion like (C) exists it must be unsymmetrical in this system, the proton being nearer $C_{(b)}$ than to $C_{(c)}$. We hope to find which proton is actually lost in the cyclisation of (V), (VI), and (XII) to the cage-compound (IV) by using deuterated compounds.]

*Scheme* I.




The most extraordinary feature of these rearrangements, however, is that the very strained half-cage *endo*-acetate (XII; R = Ac) is formed from the sulphonates (V), (VI), and (XII) (R = Me·$SO_2$) about three times as fast as is the *exo*-acetate (VI; R = Ac). All the obvious ways of delocalising the positive charge in the half-cage carbonium ion operate from the inside (*endo*), and even apart from steric hindrance would lead to the confident expectation of *exo*-attack by acetate ion. Perhaps the relatively acidic hydrogen atom attached to $C_{(b)}$ can help to pull the acetate into the inside of the molecule by hydrogen-bonding in a transition state resembling (H; R = Ac).

Although the differences in ratios of half-cage *exo*-acetate (VI; R = Ac) to *endo*-acetate (XII; R = Ac) to the chlorohydrocarbon (XIII?) seem outside the experimental error, the ratios are nevertheless rather close in all three acetolyses, so that these three products may all arise from a common ion (D). In acetolysis the hydride migration is irreversible, and no trace of product with the isodrin or aldrin skeleton could be found from the half-cage methanesulphonates. Although the cage-compound (IV) was never detected from acetolysis of the methanesulphonates, preliminary experiments show that it is formed on treatment of the half-cage amine with nitrous acid. The *endo-exo*-sulphonate (IX; R = Me·$SO_2$) gave some *endo-endo*-acetate (V; R = Ac), presumably through the ion (A). It is remarkable, then, that no isodrin or rearranged products could be isolated, which seem to be derived from the ion (A) in acetolysis of the *endo-endo*-methanesulphonate (V; R = Me·$SO_2$). Although the difference in temperature may be partly responsible, this may mean that different ions are involved.

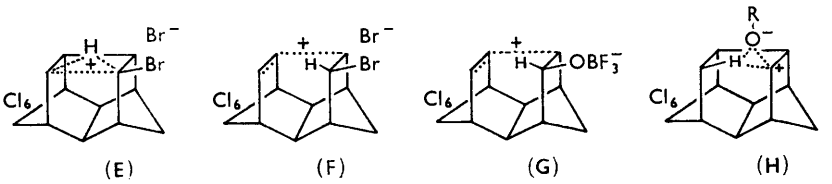
Table 2 shows the result of heating compounds of the four ring systems with 5% sulphuric acid in acetic acid for $\frac{1}{2}$ hr. Under these conditions of equilibration the isodrin skeleton (III and V; R = Ac) soon disappears; the aldrin skeleton (IX; R = Ac) is relatively stable, but gradually goes over to the half-cage *exo*-acetate (VI; R = Ac) and the cage-compound (IV); the *endo*-acetate (XII; R = Ac) and chlorohydrocarbon (XIII?) soon rearrange to the same two systems; and the half-cage *exo*-acetate (VI: R = Ac) itself slowly cyclises to the cage-compound, the most stable system, which eventually constitutes almost the sole product.

From the addition of acetic acid to isodrin (III) the half-cage acetate (VI; = Ac) R

TABLE 2. *Products of heating with* $H_2SO_4$–AcOH.

| | Half-cage *exo*-acetate (VI) | Cage compound (IV) | Half-cage *endo*-acetate (XII) | *endo-exo*-Acetate (IX) |
|---|---|---|---|---|
| Isodrin (III) | 57 | 37 | 4·5 | 2 |
| Half-cage *exo*-acetate (VI) | 73 | 27 | — | — |
| Product of acetolysis of half-cage mesylate | 53 | 45 | 1·8 | — |
| Aldrin (I) | 1·8 | 1·5 | — | 97 |

should contain both the added hydrogen and the acetate on the same carbon atom. Addition of deutero-acid gave a sample of acetate (VI; R = Ac) containing deuterium, which was lost on oxidation to the ketone (VII).




(E) (F) (G) (H)

Bromine in carbon tetrachloride transformed isodrin (III) mainly into the cage-compound (IV). Hydrogen bromide was also produced, which might have catalysed the cyclisation, but that the cage-compound was still formed in the presence of a suspension of finely divided calcium carbonate, when no free hydrogen bromide could be detected, shows that bromine does catalyse the cyclisation. Presumably the cage-compound comes from some such ion-pair as (E) or (F) by removal of $Br^+$ in preference to $H^+$ by $Br^-$. It amounts to an electrophilic displacement *with inversion* on $C_{(c)}$.

In contrast, the corresponding dipolar ions (*e.g.*, G) from isodrin oxide (VIII) and boron trifluoride, being unable to lose oxygen by reduction, preferentially undergo hydride migration to give the stable carbonyl group, rather than to lose the inside proton to give the cage-alcohol.

There are several differences in the behaviour of the compounds in the isodrin–aldrin series and of their unchlorinated analogues, on which Winstein and his colleagues [8,9] have published some preliminary results: the most obvious are (1) the much reduced reactivity of the chlorinated double bond (a,b), and (2) the necessity for hydride transfer to $C_{(b)}$ to accompany bridging to $C_{(a)}$ in the chlorinated compounds.

(1) The relative reluctance of the chlorinated double bond to participate in carbonium ion reactions is shown, for example, by the far slower solvolysis of the chlorinated sulphonate (V; R = Me·$SO_2$) than of the unchlorinated analogue, which cannot even be isolated.[9] Although the cage-compound (IV) is not formed in our acetolyses, the cage-hydrocarbon is an important product in the chlorine-free series.[8,9]

(2) The reluctance of the carbon atoms carrying chlorine to accept a positive charge or a nucleophile means that the half-cage and the skew skeleton can be formed only after hydride migration. In the unchlorinated series the occurrence of hydride migration cannot be detected, because of the symmetry of the system: the use of optically active or isotopically labelled esters would be needed.

[Added 13th March, 1961.] Since this paper was submitted, one has appeared by Soloway, Damiana, Sims, Bluestone and Lidov (*J. Amer. Chem. Soc.*, 1960, 82, 5377), in which they accept structures (VI) and (VII).

## EXPERIMENTAL

Infrared spectra were recorded for Nujol or Fluorlube mulls, unless otherwise stated, on a Unicam S.P. 100 spectrophotometer. Ultraviolet spectra were measured for ethanol solutions on a Unicam S.P. 500 or S.P. 700 instrument. Solutions for chromatography were prepared in light petroleum (b. p. 60—80°) and chromatographed on silica gel (activity about 1 on Brockmann's scale) with light petroleum containing increasing proportions of benzene. Compounds were eluted in the following order: (III), (XIII ?), (V; R = Ac), (XII; R = Ac), (VI;

R = Ac), and (IV), (I), (V; R = Ac), (IX; R = Ac), (XII; R = Ac), (VI; R = Ac). Where compounds were obtained by alternative routes their identity was established by mixed m. p. and infrared spectra.

*Photoisomerisation of Isodrin.*—1α,2β,3α-1,8,9,10,11,11-Hexachlorotetracyclo[6,2,1,$1^{3,6}$,$0^{2,7}$]dodeca-4,9-diene * (isodrin) (III) (1 g.) dissolved in ethyl acetate (50 ml.) was irradiated for 7 days in a quartz tube, in an atmosphere of carbon dioxide. The solvent was evaporated, and the residue dissolved in acetone (20 ml.) and treated with potassium permanganate (1·6 g.) in acetone (20 ml.) under reflux for 30 min. Water and sodium metabisulphite were added and the product was isolated by chloroform extraction. The 1,2,3,3,4,11-*hexachlorohexacyclo*-[5,4,1,0,$^{2,6}$,$0^{4,11}$,$0^{5,9}$,$0^{10,12}$]*dodecane* (cage compound; IV) thus obtained crystallised from ethanol in needles, m. p. 298° (decomp.) (Found: C, 39·6; H, 2·3; Cl, 57·8. $C_{12}H_8Cl_6$ requires C, 39·5; H, 2·2; Cl, 58·3%); ε at 200 mμ was 630; no maximum around 1600 cm.$^{-1}$.

*Acid Treatment of Isodrin.*—Sulphuric acid (5 ml.) was added to isodrin (2 g.) dissolved in dioxan (20 ml.) containing water (0·2 ml.). The solution was kept on a steam-bath for 14 hr., then cooled, and water was added. The ether extract was washed with sodium hydrogen carbonate solution, dried ($Na_2SO_4$) and evaporated. The residue was chromatographed to give the cage-compound (IV) (0·28 g.) and 1,9,10,10,11,exo-12-*hexachloropentacyclo*[7,2,1,$0^{2,6}$,$0^{4,8}$,$0^{7,11}$]-*dodecan*-3α-*ol* (half-cage alcohol; VI; R = H) (0·62 g.) which crystallised from aqueous ethanol in needles, m. p. 204° (Found: C, 38·1; H, 2·5; Cl, 55·5. $C_{12}H_{10}Cl_6O$ requires C, 37·6; H, 2·6; Cl, 55·5%), no maximum around 1600 cm.$^{-1}$. The half-cage alcohol was acetylated with acetic anhydride in pyridine to give the *acetate* (VI; R = Ac), needles (from ethanol), m. p. 218° (Found: C, 39·9; H, 2·1; Cl, 49·5; Ac, 11·1. $C_{14}H_{12}Cl_6O_2$ requires C, 39·5; H, 2·8; Cl, 50·2; Ac, 10·1%), $\nu_{max.}$ 1740 cm.$^{-1}$; no band around 1600 cm.$^{-1}$. The acetate was reconverted into the alcohol by basic hydrolysis.

*Oxidation of the Half-cage Alcohol* (VI).—The alcohol (1·25 g.), dissolved in acetic acid (40 ml.), was treated at 70° dropwise, during 40 min., with aqueous potassium permanganate (0·82 g. in 40 ml.). The temperature was raised to 110° and then kept at 90° for 3 hr. The mixture was cooled and filtered. The organic material, separated from the precipitate by extraction with acetone, was chromatographed to give 1α,9,10,10,11,exo-12-*hexachloropentacyclo*-[7,2,1,$0^{2,6}$,$0^{4,8}$,$0^{7,11}$]*dodecan*-3-*one* (VII) (0·82 g.) that, crystallised from benzene–light petroleum, had m. p. 285° (decomp.) (Found: C, 38·1; H, 2·3; Cl, 55·8. $C_{12}H_8Cl_6O$ requires C, 37·8; H, 2·1; Cl, 55·8%), $\lambda_{max.}$ 300 mμ (ε 35); ε at 205 mμ = 480; $\nu_{max.}$ 1755 cm.$^{-1}$; no band around 1600 or 1400 cm.$^{-1}$.

*Rearrangement of Isodrin Epoxide.*—The epoxide (VIII) (1·26 g.) was dissolved in dry benzene (20 ml.) and saturated with boron trifluoride. The solution was refluxed on the steam-bath for 30 min. and then evaporated to dryness. The residue was chromatographed to give the half-cage ketone (VII) as the sole product.

*The* endo-endo-*Alcohol* (V; R = H).—Diborane, prepared from sodium borohydride (1·2 g). and boron trifluoride–ether complex (6·4 g.),[11] was passed into an ice-cooled solution of isodrin (11 g.) in dry ether (50 ml.) during 70 min. and the mixture was left at room temperature for 70 min. Ice was then added, followed by sodium hydroxide (0·5 g.) in water (4 ml.). Subsequently a 30% solution (3·75 ml.) of hydrogen peroxide was added during an hour with stirring, which was continued for a further 40 min. The resultant emulsion was washed with ether and the extract washed with 4N-sulphuric acid and water. Evaporation of the ether gave a white, frothy solid (11 g.) which did not crystallise. The product was characterised by acetylation with acetic anhydride in pyridine to 1α,2β,3α,1,8,9,10,11,11-*hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]-*dodec*-9-*en*-4β-*yl acetate* (V; R = Ac); crystallised from ethanol, this had 194—195° (Found: Cl, 49·9; Ac, 9·3. $C_{14}H_{12}Cl_6O_2$ requires Cl, 50·2; Ac, 10·1%), $\nu_{max.}$ 1725, 1600 cm.$^{-1}$.

* The symbols α and β in this and similar names are used to distinguish stereoisomers that would otherwise have identical polycyclo-names. They denote the relative stereochemistry of hydrogen or a substituent at the positions enumerated; the largest ring (*i.e.*, that stated first in the square brackets) is considered to be flat; hydrogen or the substituent at position 1 (which must necessarily be a bridge-head) is arbitrarily assigned an α-prefix; hydrogen and the substituents at other positions are then given α- or β-prefixes according to whether they are on the same or different sides of the " plane " of the large ring. Cage and half-cage structures, at least in this series, can exist in only one configuration and no such stereochemical designation is necessary for these parent structures. It is not necessary to consider here the extension of this system needed for asymmetry on a bridge (here a methylene group of the five-membered rings).

[11] Brown and Rao, *J. Org. Chem.*, 1957, **22**, 1135.

1α,2β,3α,1,8,9,10,11,11-*Hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]*dodec*-9-*en*-4-*one* was prepared by oxidation of the *endo-endo*-alcohol (V; R = H) with chromium trioxide in pyridine [12] and, crystallised from ethanol, had m. p. 220° (Found: C, 38·1; H, 2·4; Cl, 56·0. $C_{12}H_8Cl_6O$ requires C, 37·8; H, 2·1; Cl, 55·8%), $\lambda_{max.}$ 298 mμ (ε 30), $\nu_{max.}$ 1750, 1600, 1425 cm.$^{-1}$.

*Preparation of Methanesulphonates.*—The appropriate alcohol was dissolved in pyridine, treated with a slight excess of methanesulphonyl chloride, and set aside overnight. Water was cautiously added and the crystals that separated were filtered off and recrystallised. In this way were prepared:

*The half-cage* exo-*methanesulphonate* (VI; R = $SO_2Me$), rods (from chloroform), m. p. 201° (decomp.) (Found: C, 33·9; H, 2·9; S, 6·8. $C_{13}H_{12}Cl_6O_3S$ requires C, 33·8; H, 2·6; S, 6·9%).

*The* endo-endo-*methanesulphonate* (V; R = $SO_2Me$), flakes (from ethanol), m. p. 135—137° (Found: C, 34·3; H, 2·6%).

*The* endo-exo-*methanesulphonate* (IX; R = $SO_2Me$) (from chloroform–light petroleum), m. p. 177—179° (decomp.) (Found: C, 34·4; H, 2·8; S, 6·9%).

*The half-cage* endo-*methanesulphonate* (XII; R = $SO_2Me$), needles (from chloroform–light petroleum), changing gradually to rhombs, m. p. 150—152° (decomp.) (Found: C, 33·9; H, 2·6; S, 6·4%).

*Solvolysis of the Sulphonates.*—The appropriate methanesulphonate (*ca.* 1·3 g.) was refluxed for 18 hr. in acetic acid (20 ml.) containing sodium acetate (5 g. in 100 ml.). The solution was then poured into water and extracted with chloroform. The extract was successively washed with water, aqueous sodium hydrogen carbonate, and water and dried ($Na_2SO_4$). The residue after evaporation was chromatographed and the molar percentage yields based on material recovered (*ca.* 90%) are recorded in Table 1. The *endo-exo*-methanesulphonate (IX; R = $SO_2Me$) was recovered unchanged from the above treatment, which was repeated at 190° in a sealed tube. The half-cage acetate (VI; R = Ac) was stable under the standard conditions. Two new compounds were isolated:

The chlorohydrocarbon (XIII ?) had m. p. 262°, after sublimation in a high vacuum (Found: C, 39·9; H, 2·45; Cl, 57·9. $C_{12}H_8Cl_6$ requires C, 39·5; H, 2·2; Cl, 58·3%); it gave no band around 1600 cm.$^{-1}$.

The endo-*acetate* (XII; R = Ac) was sublimed in a high vacuum for analysis and had m. p. 153—154° (Found: C, 39·8; H, 2·8; Cl, 50·0%), $\nu_{max.}$ 3140 and 1750 cm.$^{-1}$, no band around 1600 cm.$^{-1}$. Basic hydrolysis gave the half-cage *endo*-alcohol (XII; R = H), m. p. 260° (decomp.) after sublimation in a high vacuum (Found: C, 37·7; H, 3·0; Cl, 55·0%).

*Oxidation of the* endo-*Alcohol* (XII; R = H).—The alcohol (201 mg.) was dissolved in acetic acid (2 ml.), and chromium trioxide (48 mg.) in a few drops of water was added. After 24 hr. water was added and the mixture was extracted with chloroform. The chloroform was washed with water, sodium hydrogen carbonate solution, and water and dried ($Na_2SO_4$). The product was chromatographed and crystallised from chloroform–light petroleum; it had m. p. 296—298° (Found: C, 38·0; H, 2·35; Cl, 55·7%), $\lambda_{max.}$ 294 mμ (ε 40). The infrared spectrum was identical with that of compound (VII) above.

*Analysis of Products from Treatment with Acid.*—The compound (1—2 g.) was refluxed for 30 min. in acetic acid (20 ml.) with sulphuric acid (4 ml.) and then worked up as for the solvolyses. The results are recorded in Table 2. Thus was obtained the endo-exo-*acetate* (IX; R = Ac) (from ethanol), m. p. 144—145° (Found: C, 39·9; H, 3·5; Cl, 50·7; Ac, 10·1. $C_{14}H_{12}Cl_6O_2$ requires C, 39·5; H, 3·5; Cl, 50·7; Ac, 10·1%), $\nu_{max.}$ 1730, 1600 cm.$^{-1}$. Basic hydrolysis gave 1α,2β,3β,1,8,9,10,11,11-*hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]*dodeca*-9-*en*-4α-*ol* (*endo-exo*-alcohol; IX; R = H); crystallised from ether–light petroleum, this had m. p. 124—125° (Found: C, 37·5; H, 2·7; Cl, 54·5%). Oxidation with chromium trioxide gave the endo-exo-*ketone* (from ether–light petroleum), m. p. 124—125° (Found: C, 37·5; H, 2·4; Cl, 55·6%), $\lambda_{max.}$ 294 mμ (ε 64), $\nu_{max.}$ 1760, 1600, 1415 cm.$^{-1}$.

*Deuterium Experiments.*—Sulphur trioxide (6·4 g.) was added slowly to deuterium oxide (4 g.) with cooling and stirring, followed by acetic anhydride (13 ml.). Isodrin (7·3 g.) was added and the mixture was stirred and heated to 120°. After 30 min. it was kept at 90° for a further 90 min. The product was worked up in the usual way. Basic hydrolysis and chromatography gave the cage-compound (IV) (2·64 g.) and half-cage alcohol (VI; R = H) (2·55 g.), m. p. 203° after crystallisation from chloroform (Found: C, 37·6; H and D, 2·6; Cl, 55·6.

[12] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

$C_{12}H_9Cl_6DO$ requires C, 37·5; H and D, 2·6; Cl, 55·5%), $\nu_{max.}$ 2241, 2255sh cm.$^{-1}$ (C–D). Oxidation of this alcohol as before gave a sample of half-cage ketone (VII) in which no band characteristic of C–D could be detected.

*Treatment of Isodrin with Bromine.*—Bromine (0·4 ml.) in carbon tetrachloride was added dropwise with stirring to a solution of isodrin (5 g.) in carbon tetrachloride (25 ml.). The solution was left overnight and then washed with a solution of potassium iodide and sodium thiosulphate. After removal of solvent the total product was dissolved in acetone (150 ml.) and refluxed for 1 hr. with an excess of potassium permanganate. Most of the acetone was then evaporated and water and sodium metabisulphate were added. The cage-compound (IV) (2·69 g.) was obtained by chloroform extraction.

The cage-compound (IV) was also obtained when the reaction was repeated in the presence of finely divided calcium carbonate (5 g.).

One of us (E. C.) acknowledges a grant from Shell Research Ltd. We are grateful also to the Royal Society and Imperial Chemical Industries Limited for financial support, to Dr. J. Hudec for much helpful advice, and to Professor S. Winstein and Dr. P. Carter for informing us of the nature of the solvolysis product of the ester (VI; R = Me·$SO_2$).

THE UNIVERSITY, SOUTHAMPTON. [*Received, September 22nd,* 1960.]