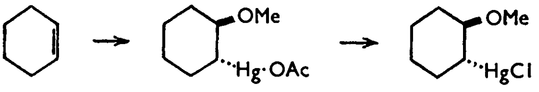
41. *Aspects of Stereochemistry. Part XII.* A Specific Directing Effect in the Mercuration of Some 4-Substituted* cyclo*Hexenes and* cis-*Hex-3-enol.*

By H. B. Henbest and B. Nicholls.

Functional groups can exert a directing effect on the stereochemistry of addition of HgX and OR at a double bond, in at least two ways. In the first, the reactions are completed by a suitably placed acid or alcohol group acting as an intramolecular nucleophile, and lactones or ethers are formed: some new examples are given in the *bicyclo*heptene series and with *trans*-hex-3-enol. A second, new directing effect [1] has been encountered with certain 4-substituted *cyclo*hexenes and *cis*-hex-3-enol: here hydroxyl or other Lewis base groups (OMe, OAc, CO_2Me, CH_2·OH, CN) promote stereospecific addition of acetoxymercuri-groups and of anions (from solvent) to the double bond. A possible mechanism for these additions is discussed. As the mercuri-groups in these adducts can be removed by reduction, a two-step method for the specific addition of water or methanol to certain double bonds becomes available.

In continuation of our studies of the stereochemistry of addition of electrophilic reagents to olefinic bonds unsymmetrically located with respect to a substituent in the remainder of the molecule,[2,3] we have examined the reactions of some unsaturated compounds with mercuric acetate in methanol and, sometimes, water. Addition of mercuri-groups [4] was chosen in the hope that crystalline products would be obtained. Thus the symmetrical *cyclo*hexene gives a high yield of the crystalline adduct (I) on treatment with mercuric acetate in methanol. Anion-exchange takes place readily with compounds RHg·OAc, and aqueous sodium chloride converts the adduct (I) into the less soluble, more stable chloromercurial (II). Most of the adducts obtained in the present work were conveniently isolated as the chloromercuri-compounds by treatment of the final reaction solutions with sodium chloride. The *trans*-configuration of the *cyclo*hexene adduct (I) has been established by *X*-ray methods,[5] and the reaction may be envisaged as proceeding through some form of mercury cation [4,6] (further discussion below).



(I) (II)

The present study began with some readily available 4-substituted *cyclo*hexenes and related *bicyclo*[2 : 2 : 1]heptenes. By the diene synthesis and other methods, a variety of compounds is available in each of which the substituent lies close enough to the double bond for electronic and/or steric effects to be expected.

Reactions with Substituted bicyclo[2 : 2 : 1]*Heptenes*.—A bromo-lactone is obtained from reaction of the unsaturated acid (III) with bromine,[7,8] and it was therefore not surprising to find that the chloromercuri-lactone (IV) was formed in high yield on treatment with mercuric acetate in methanol followed by anion-exchange with sodium chloride. Apart from the usual evidence, the structure (IV) was established by reduction of the

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* Part XI, preceding paper.

[1] Cf. Henbest and Nicholls, *Proc. Chem. Soc.*, 1957, 61.

[2] Henbest and Wilson, *J.*, 1957, 1958.

[3] Henbest and Nicholls, *J.*, 1957, 4608.

[4] Cf. Review by Chatt, *Chem. Rev.*, 1951, **48**, 7.

[5] Brook and Wright, *Acta Cryst.*, 1951, **4**, 50.

[6] Lucas, Hepner, and Winstein, *J. Amer. Chem. Soc.*, 1939, **61**, 3102.

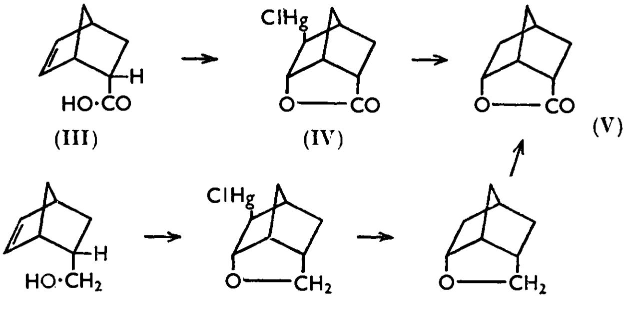
[7] Roberts, Trumbull, Bennett, and Armstrong, *ibid.*, 1950, **72**, 3116.

[8] ver Nooy and Rondestvedt, jun., *ibid.*, 1955, **77**, 3583.

compound to the known[7,9] lactone (V) by sodium borohydride in ether–methanol, use of this reagent ensuring preservation of the lactone ring.

The related unsaturated alcohol (VIII) reacts analogously, the cyclic ether (VII) being formed. This product was reduced by hydrazine[10] to the cyclic ether[11] (VI), which was oxidised by chromic acid[12] to the lactone (V) obtained previously. [Most of the mercurials obtained in this work were reduced by the hydrazine procedure.[10] This method is convenient but with methoxy-mercurials obtained from substituted hexenes and *cyclo*hexenes reduction is accompanied by extensive regeneration of the double bond (see below).]

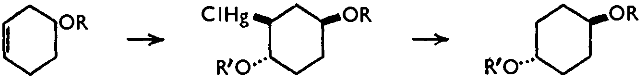
In the formation of the mercurials (IV and VII) the reactions are obviously completed by the neighbouring acid and alcohol groups which act as anion sources. Participation of these groups in the additions evidently precludes skeletal rearrangements such as are often encountered with other compounds of this series. A crystalline adduct has been obtained[13] from the reaction of the parent hydrocarbon, *bicyclo*[2 : 2 : 1]heptene, with mercuric acetate in methanol, but the published evidence does not distinguish between a rearranged or a non-rearranged structure for this product.



(III) (IV) (V)

(VIII) (VII) (VI)

Reactions with 4-Substituted cyclo*Hexenes.*—In theory, four geometrical isomers can be obtained from a 4-substituted *cyclo*hexene by *trans*-addition of HgX and MeO groups, and at least three of them are formed when the 4-substituent is a methyl group.[14] However, it has now been found that with a 4-hydroxy-substituent (IX; R = OH) a single crystalline chloromercurial is obtained in 95% yield. Reductive removal of the chloromercuri-group gave the *trans*-1 : 4-diol methyl ether (XI; R = H, R′ = Me) (independent synthesis by partial methylation of the 1 : 4-diol), and the chloromercurial is therefore formulated as (X; R = H, R′ = Me).



(IX) (X) (XI)

The methoxymercuri-derivatives from the acetate (IX; R = Ac) and the methyl and benzyl ethers (IX; R = Me and CH_2Ph) were formed by addition in the same direction as the parent alcohol. From the acetate, both the acetoxymercuri- and the chloromercuri-compound (X; R = OAc, R′ = Me) were obtained crystalline, the structures being established by alkaline hydrolysis to the mercurial (X; R = H, R′ = Me). The adducts from the two ethers were liquid but were both reduced to *trans*-1 : 4-disubstituted compounds. Thus the adduct from the methyl ether gave *trans*-1 : 4-dimethoxy*cyclo*-

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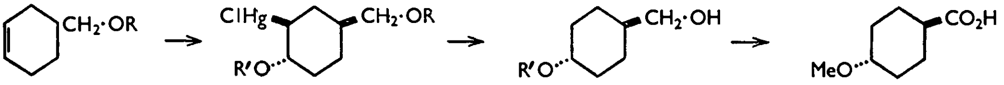
[9] Alder, Stein, Liebmann, and Rolland, *Annalen*, 1934, **514**, 197.
[10] Wright, *Canad. J. Chem.*, 1950, **30**, 268.
[11] Bruson and Riener, *Chem. Abs.*, 1948, **42**, 5471; U.S.P., 2,440,220.
[12] Cf. preceding paper.
[13] Rowland, *J. Amer. Chem. Soc.*, 1951, **73**, 2381.
[14] Park and Wright, *Canad. J. Chem.*, 1957, **35**, 1088.

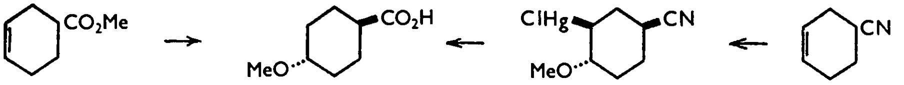
hexane (XI; R = R′ = Me) (independent synthesis), and that from the benzyl ether was reduced with hydrazine and then with lithium–ethylamine (removing the benzyl group) to give the *trans*-1 : 4-methoxy-alcohol (XI; R = H, R′ = Me).

Similar reactions in water gave the corresponding hydroxymercurials. The alcohol (IX; R = H) gave the crystalline mercurial (X; R = R′ = H) in high yield and this gave *trans*-quinitol (XI; R = R′ = H) on reduction with hydrazine. Similarly the liquid adduct from the methyl ether (IX; R = Me) was reduced to the *trans*-1 : 4-methoxy-alcohol (IX; R = Me, R′ = H), identical with that obtained by the alternative route described above.

Additions to the homologous unsaturated alcohol (XII; R = H) and its derivatives occur in the same stereochemical directions, adducts (XIII) being obtained. Thus the hydroxymercuri-product from the alcohol (XII; R = H) was reduced by hydrazine to the known *trans*-1 : 4-compound (XIV; R′ = H). The alcohol (XII; R = H), the acetate (XII; R = Ac), and the benzyl ether (XII; R = CH_2Ph) yielded similar crystalline methoxy-mercuri-adducts which were reduced to a single methoxy-alcohol. The 1 : 4-disubstituted structure (XIV; R′ = Me) for this methoxy-alcohol was confirmed by the fact that the α-naphthylurethane was identical with the lower-melting of the pair of isomers described earlier;[15] its *trans*-configuration is assigned by analogy with the reaction just described and by conversion of the adduct into the known methoxy-acid (XV) by chromic acid. This acid was also obtained from the unsaturated ester (XVI) by conversion into the methoxy-mercuri-adduct, reduction with hydrazine, and hydrolysis. Perhaps the most interesting finding in this series was that addition to the unsaturated nitrile (XVII) was also stereospecific, the crystalline adduct, formulated as (XVIII), being converted by hydrazine and hydrolysis into the same methoxy-acid (XV).



(XII) (XIII) (XIV) (XV)



(XVI) (XV) (XVIII) (XVII)

The specificity of addition of HgX and the availability of many *cyclo*hexenes with a Lewis base substituent (see below) at the 4-position means that a variety of *trans*-1 : 4-substituted *cyclo*hexanes may now be synthesized by routes not always dependent on benzenoid starting materials. From the present work where hydrazine has been generally used for removal of the mercuri-group it appears that the overall introduction of a hydroxyl group by way of a hydroxy-mercuri-derivative gives a better yield than introduction of a methoxyl group by way of the methoxy-mercuri-derivative, the drawback in the latter series being that the methyl ethers from the reduction are accompanied by about equal amounts of unsaturated compounds formed by elimination of vicinal HgX and MeO groups.

Reactions with Hexenols.—We next examined the acylic analogue, *cis*-hex-3-enol (XIX). A liquid adduct was obtained whose infrared spectrum was similar to that of the previous cyclic product (X; R = H, R′ = Me) in that bands from hydroxyl and methoxyl groups were present. Reduction with hydrazine gave a methoxy-alcohol (together with *cis*-hex-3-enol), which appeared to be largely or wholly one compound, as judged by distillation and formation of a crystalline 4-diphenylylurethane in good yield. The methoxy-alcohol must be formulated as (XXI) or (XXII), the former being the product expected by analogy

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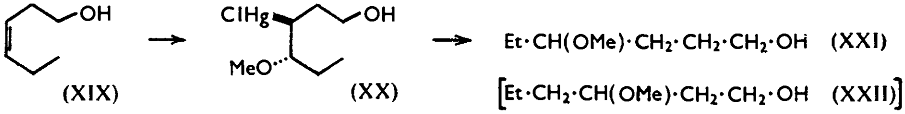
[15] Owen and Robins, *J.*, 1949, 326.

with the cyclic series. This was confirmed by exclusion, the isomeric methoxy-alcohol (XXII) being easier to synthesize by an unambiguous route. The hydroxy-ester obtained from a Reformatsky reaction between butyraldehyde and ethyl bromoacetate was methylated, and the methoxy-ester was then reduced with lithium aluminium hydride to the methoxy-alcohol (XXII), which gave a 4-diphenylylurethane different from that from the product from the mercuration sequence.

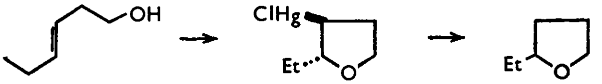


(XIX) (XX)

$\longrightarrow$ Et·CH(OMe)·CH$_2$·CH$_2$·CH$_2$·OH (XXI)

[Et·CH$_2$·CH(OMe)·CH$_2$·CH$_2$·OH (XXII)]

In contrast, the reaction of *trans*-hex-3-enol (XXIII) with mercuric acetate in methanol gave a liquid which did not show hydroxyl and methoxyl absorption in the infrared spectrum. Reduction of the product with hydrazine gave 2-ethyltetrahydrofuran (XXV), and the adduct may therefore be formulated as (XXIV; further comment on stereochemistry below), the hydroxyl group of the starting alcohol being involved as a nucleophilic component in the reaction as in the formation of the cyclic ether (VII) from the unsaturated alcohol (VIII).



(XXIII) (XXIV) (XXV)

Discussion.—These results indicate that there are at least two mechanisms by which a substituent not directly linked to the unsaturated bond can cause unidirectional addition of HgX and OR. In the first, a functional group such as hydroxyl participates in the reaction as an internal nucleophile, and cyclic ethers or lactones are obtained. The formation of the ethers (VII) and (XXV) and the lactone (IV) provide examples, but many other instances, particularly formation of cyclic ethers, have been recorded before.[16] Participation of a hydroxyl group as a nucleophilic component is, of course, also well known in the addition of halogen to many unsaturated alcohols and acids, halogeno-ethers and -lactones being obtained.

In contrast, in the specific additions of HgX and OR to the various 4-substituted *cyclo*hexenes and to *cis*-hex-3-enol, the functional groups, although obviously exerting a directing effect, were unchanged at the end of the reaction. The choice between this second mechanism and the first mechanism depends on the structure of the unsaturated component. Thus the bicyclic olefinic alcohol (VIII) reacts by the first mechanism, the hydroxymethyl group being held relatively close to the α-side[12] of the double bond and the electrophilic mercuric salt approaching from the much less hindered β-side, circumstances favouring *trans*-addition. In its monocyclic analogue (XII; R = H) the chair-like ring system is flatter and less rigid; the first mechanism is less favoured and addition occurs by the second mechanism. [Reactions of these two unsaturated alcohols with perbenzoic acid also proceeded differently.[12]]

Formation of the tetrahydrofuran (XXIV) from *trans*-hex-3-enol by the first mechanism is not surprising. The flexible hydroxyethyl group can evidently move into the requisite position to complete the reaction as an anion source. The relative configurations of the ethyl and the chloromercuri-substituents in the product will be *trans* as shown (XXIV), if normal *trans*-addition to the olefinic bond takes place. This leads to an explanation for

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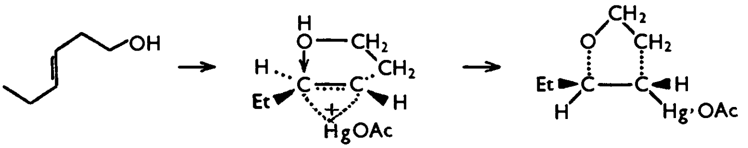
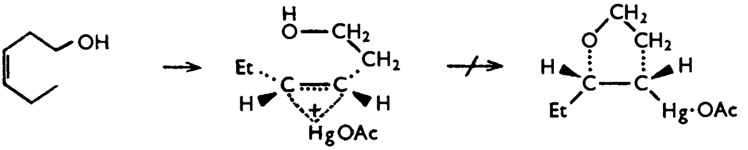
[16] Brook, Rodgman, and Wright, *J. Org. Chem.*, 1952, **17**, 988; Brook and Wright, *ibid.*, 1957, **22**, 1314; Nesmeyanov and Lutsenko, *Bull. acad. sci. U.R.S.S.*, *Cl. sci. chim.*, 1943, 296, *Chem. Abs.*, 1944, **38**, 5498; Rosen, Ziegler, and Shabica, *J. Amer. Chem. Soc.*, 1955, **77**, 762; Summerbell and Lestina, *ibid.*, 1957, **79**, 3878.

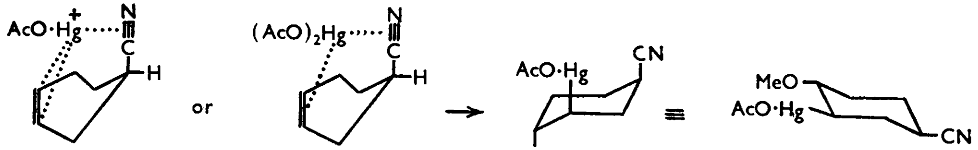
the fact that *cis*-hex-3-enol did not give a substituted tetrahydrofuran by the first mechanism, for such a reaction would have given the isomer with the bulky ethyl and acetoxymercuri-groups in a very unfavourable eclipsed *cis*-arrangement (XXVI).


(cf. XXIV)


(XXVI)

A more detailed picture of the second mechanism may be derived from the fact that in the *cyclo*hexene series compounds containing a Lewis base group (one or more unbonded electron pairs) at the 4-position undergo specific addition with final anion attack at the 1-position, to give products of the type (X, XIII, and XVIII), whereas 4-methyl*cyclo*hexene gives a mixture in which the predominant point of final anion attack has been the 2-position.[14] A partial explanation of the latter result may lie in inductive factors, and conversely it is possible that the electron-attracting properties of the Lewis base group could be responsible for final anion attack at the 1-position. However, the specificity of the formation of *trans*-1 : 4-substituted products seems to suggest that some extra factor is involved.

As the intermediate and reversible production of an organomercury salt complex (" mercurinium ion ") has been established [6] for the reaction between *cyclo*hexene and mercuric salts, it is now suggested that the presence of a Lewis base group at the 4-position may assist the formation of the complex in which the mercuric salt is held on the same side as the Lewis base group. For instance, in the reaction of 4-cyano*cyclo*hexene with mercuric acetate in methanol, the formation of a *cis*-complex (*e.g.*, XXVIIA or B) may be assisted by π-electron donation from the nitrile group. [It may be noted that acetonitrile retards the rate of mercuration [17] and that a recent study [18] of the crystal structure of the complex $(NH_3)_4Pt(MeCN)_2$ has shown the nitrile groups to be bonded to platinum in a direction perpendicular to each C≡N bond.] Ultimate reaction of this *cis*-complex with methanol (axial attack) will give a triaxial structure which may be expected to revert to the tri-equatorial form of the observed product. The specific mercuration of *cis*-hex-3-enol may be explained similarly, a quasi-ring structure being built up in the intermediate complex.


(XXVIIA) (XXVIIB) (cf. XVIII)

One possible objection to the suggestion that a *cis*-intermediate (XXVII) may be involved in the present reactions is that the Lewis base group is required to be in a quasi-axial position. However the energy differences between the quasi-equatorial and the

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[17] Birks and Wright, *J. Amer. Chem. Soc.*, 1940, **62**, 2412.

[18] Harris and Stephenson, *Chem. and Ind.*, 1957, 426.

quasi-axial 4-substituted conformations of *cyclo*hexene are probably in general much less than for the corresponding substituents in different *cyclo*hexane conformations. (Even in the latter series, reactions can take place sometimes from less favourable conformations.[3,19]) In a substituted *cyclo*hexane an axial substituent interacts sterically with two other axial groups. In a 4-substituted *cyclo*hexene, a quasi-axial group has only one other quasi-axial group with which to interact; the situation has been discussed before in greater detail.[20]

On the basis of previous evidence and on our interpretation of the *cis*- and *trans*-hex-3-enol results, we see no reason to doubt that addition of HgX and MeO or HO to unsaturated compounds is a typical electrophilic reaction in that *trans*-addition normally occurs.[4] Nevertheless doubts have been expressed [21] about the prevalence of *trans*-addition despite the apparent conclusiveness of the *X*-ray study of the *cyclo*hexene adduct.[5] These doubts apparently arise largely from an interpretation of the geometrical requirements of the general reaction of methoxy-mercurials in which the original double bond is regenerated on treatment of the adducts with mineral acid. For no very clear reasons a mechanism involving *cis*-removal of methoxy- and mercuri-groups has been favoured [21] for this type of elimination, with the consequence that, in a discussion of the addition of mercury derivatives to cinnamic acids and elimination from the adducts, the conclusion was drawn that *cis*-addition occurs. However it seems to us more likely that *trans*-addition generally takes place, and that the adducts are reconverted into the unsaturated compounds under acid conditions by an E_2 mechanism with the usual preference for a staggered *trans*-arrangement of groups to be eliminated. This general conclusion is supported by comparative kinetic studies [22] of the rates of formation of *cyclo*hexene from the *trans*-adduct (II) and from its *cis*-isomer.[23]

[*Added, October 23rd*, 1958.—Now that the stereochemical structure of *trans*-terpin has been settled (Barnes, *Austral. J. Chem.*, 1858, **11**, 134), the reactions of α-terpineol with mercuric salts can be seen to conform with the two mechanisms discussed above. According to the experimental conditions, either a mercurated cineole is formed by the first mechanism ($Me_2C{\cdot}OH$ being the internal nucleophile), or a mercurated *trans*-terpin is formed by the second mechanism. We consider therefore that this mercurated *trans*-terpin contains a *cis*-arrangement of HgX and $Me_2C(OH)$ groups, and that its isomer, formed by epimerization of the HgX group, must therefore have the mercuri-group *trans* to the $Me_2C{\cdot}OH$ group. This is a reversal of the previous suggestions by Brook and Wright (*J. Org. Chem.*, 1957, **22**, 1314).]

EXPERIMENTAL

Nomenclature and general directions are as given in the preceding paper. For many of the small-scale distillations, the bath-temperature only is given, as b. p. (b. t.).

General Procedure for the Addition of Mercury Compounds.—A solution of mercuric acetate (1 mol.) in methanol or water was added to the unsaturated compound, the mixture being shaken if necessary until it was homogeneous. It was then kept at approx. 20° until a test portion failed to give a precipitate of mercuric oxide on treatment with dilute aqueous sodium hydroxide (2—7 days). The solution, filtered if necessary from traces of mercurous salts, was usually treated with aqueous sodium chloride to give the chloromercuri-compound. With the reactions in methanol about two-thirds of the solvent was removed under reduced pressure before the addition of sodium chloride. For reduction of the mercurials, 90% hydrazine hydrate and a 3·2% w/v solution of sodium hydroxide in water were used.

[19] Turner, Mattox, Engel, McKenzie, McGuckin, and Kendall, *J. Biol. Chem.*, 1946, **162**, 565, 569, 571; Eliel, *Experientia*, 1953, **9**, 91; Noyce and Thomas, *J. Amer. Chem. Soc.*, 1957, **79**, 755.

[20] Corey and Sneen, *ibid.*, 1955, **77**, 2505.

[21] Wright, *Ann. New York Acad. Sci.*, 1957, **65**, 436.

[22] Professor S. Winstein, personal communication; T. G. Traylor, Thesis, University of California, Los Angeles, 1952.

[23] Romeyn and Wright, *J. Amer. Chem. Soc.*, 1947, **69**, 697.

Addition to bicyclo[2 : 2 : 1]*Hept-5-ene-2α-carboxylic Acid* (III).—The reaction solution from the acid (7·02 g.) and mercuric acetate (14·6 g.) in methanol (150 c.c.) was concentrated to 50 c.c. and treated with sodium chloride (3 g.) in water (20 c.c.). After being kept at 0° overnight, the product (17·1 g.) was collected. Crystallization from ethanol–ethyl acetate gave 5β-*chloromercuri*-6α-*hydroxy*bicyclo[2 : 2 : 1]*heptane-2α-carboxylic lactone* (IV), m. p. 222·5—224° (Found: C, 25·7; H, 2·3; MeO, 0. $C_8H_9O_2HgCl$ requires C, 25·75; H, 2·4; MeO, 0%). A similar experiment starting with the methyl ester (0·76 g.) of the unsaturated acid gave the same chloromercuri-lactone (1·51 g.), m. p. 222—224°.

For reduction, the organomercurial (17 g.) in ether–methanol (1 : 3; 50 c.c.) and sodium borohydride (3·8 g.) were heated under reflux for 3 hr. with stirring, and the organic product was then isolated with ether after the addition of hydrochloric acid. Crystallization from light petroleum gave the lactone (V) (5·8 g., 80%), m. p. 154—155° (lit., m. p. 155—156°). This lactone (identical m. p. and infrared spectrum) was also prepared by isomerization of the unsaturated acid with 50% sulphuric acid.[7,9]

Addition to bicyclo[2 : 2 : 1]*Hept-5-en-2α-ylmethanol* (VIII).—The reaction solution from the unsaturated alcohol (6·2 g.), mercuric acetate (16 g.), and methanol (150 c.c.) was concentrated to one-third bulk and treated with sodium chloride (3 g.) in water (20 c.c.). The precipitated 4β-*chloromercuri*-6-*oxa*tricyclo[3 : 2 : 1 : $1^{3:8}$]*nonane* (VII) (19 g.) had m. p. 227—229°. A sample recrystallized from benzene–light petroleum had m. p. 228—229° (Found: C, 26·6; H, 2·7; MeO, 0. $C_8H_{11}OHgCl$ requires C, 26·7; H, 3·1; MeO, 0%). Hydrazine hydrate (5 c.c.) was added to the organomercurial (10 g.) in sodium hydroxide solution (100 c.c.), and the mixture heated under reflux for 24 hr. Isolation with ether, sublimation under reduced pressure, and crystallization from ether–pentane gave 6-oxo*tricyclo*[3 : 2 : 1 : $1^{3:8}$]nonane (VI) (3·03 g.), m. p. 102—106° (lit.,[11] m. p. 100—105°). Reduction of the organomercurial (7·2 g.) with lithium borohydride (1 g.) in boiling ether (200 c.c.) also gave this cyclic ether (1·54 g.), m. p. 100—106°. An authentic sample was prepared [11] by heating a mixture of the unsaturated alcohol (VIII) (4·27 g.) and dilute sulphuric acid (12·5 c.c. of concentrated acid in 75 c.c. of water) under reflux for 1 hr. Part of the product sublimed into the condenser but it was all collected into ether and crystallized as before, to give the product (3·67 g.), m. p. and mixed m. p. 102—106°.

For oxidation, the ether (VI) (1·3 g.) in acetone (5 c.c.) at 0° was treated with an 8N-solution (10 c.c.) of chromic acid in sulphuric acid at $<15°$. The mixture was kept overnight at 20°, the excess of reagent reduced with sulphur dioxide, and after the addition of water the product was isolated with ether. Sublimation under reduced pressure and crystallization from light petroleum afforded the lactone (V) (1·26 g.), m. p. and mixed m. p. 154—155·5°.

Methoxy-mercurial from cyclo*Hex-3-enol* (IX; R = H).—The reaction solution from the alcohol (7·4 g.) and mercuric acetate (23 g.) in methanol (300 c.c.) was concentrated to 70 c.c. and treated with sodium chloride (6 g.) in water (40 c.c.). After the mixture had been kept overnight at 0° the chloromercurial (26·5 g.), m. p. 159—161°, was collected. Crystallization from methanol gave 3β-*chloromercuri*-4α-*methoxy*cyclo*hexan*-1β-*ol* (X; R = H, R′ = Me), m. p. 161—162° (Found: C, 23·3; H, 3·6; OMe, 8·5. $C_7H_{13}O_2ClHg$ requires C, 23·0; H, 3·6; OMe, 8·5%).

The organomercurial (7·3 g.) in boiling sodium hydroxide solution (50 c.c.) was heated with hydrazine hydrate (2·5 c.c.) under reflux for 16 hr. Mercury (3·8 g., 95%) was formed and the product was isolated with ether. Distillation gave *cyclo*hex-3-enol (1·05 g., 52%), b. p. (b. t.) 93—103°/15 mm., n_D^{19} 1·4880, and 4α-*methoxy*cyclo*hexan*-1β-*ol* (XI; R = H, R′ = Me) (1·14 g., 40%), b. p. (b. t.) 115—122°/15 mm., n_D^{21} 1·4671 (Found: C, 64·5; H, 10·65. $C_7H_{14}O_2$ requires C, 64·6; H, 10·85%). The 3 : 5-dinitrobenzoate (90% yield) of the methoxy-alcohol had m. p. 130—134° (Noyce *et al.*[19] give m. p. 125·5—126·5°) (Found: C, 51·9; H, 4·75. Calc. for $C_{14}H_{16}O_7N_2$: C, 51·85; H, 4·95%). Oxidation of the methoxy-alcohol (0·5 g.) with 8N-chromic acid (0·98 c.c.) gave 4-methoxy*cyclo*hexanone (0·316 g., 63%), b. p. (b. t.) 100—110°/15 mm., n_D^{18} 1·4572 [2 : 4-dinitrophenylhydrazone, m. p. 144—144·5° (from benzene–light petroleum) (lit.,[24] m. p. 142·5—143·5°) (Found: C, 50·5; H, 5·2. Calc. for $C_{13}H_{16}O_5N_4$: C, 50·65; H, 5·25%)].

Hydroxy-mercurial from cyclo*Hex-3-enol* (IX; R = H).—The alcohol (5 g.) and mercuric acetate (15 g.) in water (150 c.c.) were shaken at room temperature for 10 days. Sodium chloride (3 g.) was added and the solution was evaporated to dryness under reduced pressure.

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[24] Adkins and Rossow, *ibid.*, 1949, **71**, 3836.

The organomercurial (16·5 g., 94%) was extracted from the residue with ethanol. Crystallisation from benzene gave 3β-*chloromercuri*cyclo*hexane*-1β : 4α-*diol* (X; R = R′ = H), decomp. >150° (Found: C, 20·5; H, 2·9; Hg, 56·8. $C_6H_{11}O_2ClHg$ requires C, 20·5; H, 3·2; Hg, 57·1%).

Hydrazine hydrate (5 c.c.) was added to a boiling solution of the organomercurial (10·7 g.) in sodium hydroxide solution (85 c.c.), and the mixture was heated under reflux for 16 hr. The product was extracted with ethyl acetate and crystallised from acetone, to give *cyclo*hexane-1β : 4α-diol (2·95 g., 90%), m. p. 138·5—140° (dibenzoate, m. p. and mixed m. p. 150—151°) [lit.,[25] 140—141° and 149—150° respectively].

Methoxy-mercurial from cyclo*Hex-3-enyl Acetate* (IX; R = Ac).—The reaction solution from the acetate (5·6 g.), mercuric acetate (12·5 g.), and methanol (150 c.c.) was evaporated to dryness under reduced pressure. The residue was dissolved in the minimum quantity of ether and kept at 0° until the product (15·5 g., 90%) crystallized. Recrystallization from *iso*propyl ether gave 4β-*acetoxy*-2β-*acetoxymercuri*-1α-*methoxy*cyclo*hexane*, m. p. 96—98° (Found: C, 30·8; H, 4·1; OMe, 7·45. $C_{11}H_{18}O_5Hg$ requires C, 31·4; H, 4·2; OMe, 7·2%). Treatment of this compound (5 g.) in methanol (10 c.c.) with sodium chloride (1 g.) in water (10 c.c.) gave 4β-*acetoxy*-2β-*chloromercuri*-1α-*methoxy*cyclo*hexane* (X; R = Ac, R′ = Me) (4·7 g.), m. p. 111—113° (from benzene–light petroleum) (Found: C, 26·7; H, 3·7; OMe, 7·8. $C_9H_{15}O_3ClHg$ requires C, 26·55; H, 3·7; OMe, 7·6%).

A solution of the former mercurial (10·7 g.) in 5% aqueous sodium hydroxide (55 c.c.) was kept at 20° for 24 hr. Sodium chloride (2 g.) was added and carbon dioxide was passed in until the solution was neutral. The solid (8·95 g.) was crystallised from benzene, to give 3β-chloromercuri-4α-methoxy*cyclo*hexan-1β-ol, m. p. 161—162°, identical with the compound obtained from *cyclo*hex-3-enol.

4β-Acetoxy-2β-acetoxymercuri-1α-methoxy*cyclo*hexane (16·7 g.) with hydrazine hydrate (8 c.c.) in sodium hydroxide solution (150 c.c.) gave, after isolation with ether and distillation, *cyclo*hex-3-enol (1·76 g., 45%), b. p. 58—62°/15 mm., n_D^{21} 1·4861, and 4α-methoxy*cyclo*hexan-1β-ol (2·47 g., 50%), b. p. 100°/15 mm., n_D^{18} 1·4686 [3 : 5-dinitrobenzoate (90% yield), m. p. and mixed m. p. 130—134°].

Methoxy-mercurial from cyclo*Hex-3-enyl Methyl Ether* (IX; R = Me).—The reaction solution from the ether (5 g.) and methanolic 10% mercuric acetate (145 c.c.) was concentrated to one-third of its volume, and added to sodium chloride (3 g.) dissolved in water (20 c.c.); 2β-chloromercuri-1α : 4β-dimethoxy*cyclo*hexane (X; R = R′ = Me) (15·6 g.) separated as an oil. This mercurial (15 g.) with hydrazine hydrate (10 c.c.) in boiling sodium hydroxide solution (100 c.c.) gave *cyclo*hex-3-enyl methyl ether (1·55 g., 35%) and 1β : 4α-dimethoxy-*cyclo*hexane (XI; R = R′ = Me) (2·17 g., 38%), b. p. 88°/42 mm., n_D^{21} 1·4429 (lit.,[26] n_D^{18} 1·4430), whose infrared spectrum [27] was identical with that of an authentic sample prepared by methylation of the *trans*-diol.

Hydroxy-mercurial from cyclo*Hex-3-enyl Methyl Ether* (IX; R = Me).—Addition of sodium chloride (2·5 g.) in water (20 c.c.) to the reaction solution from the ether (4 g.) and mercuric acetate (11·5 g.) in water (100 c.c.) gave 2α-chloromercuri-4α-methoxy*cyclo*hexan-1β-ol (12·6 g.) as an oil. Reduction of the mercurial (10 g.) with hydrazine hydrate (10 c.c.) in aqueous sodium hydroxide solution (100 c.c.) yielded *cyclo*hex-3-enyl methyl ether (0·3 g., 10%), b. p. 30—34°/15 mm., n_D^{23} 1·4520, and 4α-methoxy*cyclo*hexan-1β-ol (2·81 g., 72%), b. p. 99—100°/15 mm., n_D^{23} 1·4655 [3 : 5-dinitrobenzoate (92% yield), m. p. and mixed m. p. 129—133°].

Methoxymercurial from Benzyl cyclo*Hex-3-enyl Ether* (IX; R = CH_2Ph).—The reaction solution from the benzyl ether (3·76 g.) and mercuric acetate (6·4 g.) in methanol (100 c.c.) was treated with sodium chloride (1·2 g.) in water (10 c.c.) to give 4β-benzyloxy-2β-chloromercuri-1α-methoxy*cyclo*hexane (8·52 g.) as a viscous oil. The mercurial (8 g.) was reduced with hydrazine hydrate (5 c.c.) and sodium hydroxide (1·9 g.) in water (60 c.c.). The product (isolated with ether) was dissolved in ethylamine (50 c.c.), cooled to 0°, and treated with finely chopped lithium (3 g.) during 30 min. The mixture was then shaken vigorously for 1 hr., and the product isolated with ether. Distillation gave *cyclo*hexanol (1·03 g., 58%), b. p. (b. t.) 100—105°/21 mm., n_D^{21} 1·4671, and 4α-methoxy*cyclo*hexan-1β-ol (0·94 g., 32%) b. p. (b. t.) 110—115°/16 mm., n_D^{21} 1·4670 (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 130—134°).

Methoxy- and Hydroxy-mercurial from cyclo*Hex-3-enylmethanol* (XII; R = H).—The

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[25] Owen and Robins, *J.*, 1949, 320.

[26] Palfray and Sabetay, *Bull. soc. chim.*, 1928, **43**, 895.

[27] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462.

reaction solution from the alcohol (11·24 g.) and mercuric acetate (32 g.) in methanol (250 c.c.) was evaporated to 100 c.c. and treated with sodium chloride (6 g.) in water (50 c.c.). The precipitated gum slowly crystallized (36 g.; m. p. 130—135°). The pure 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethanol* (XIII; R = H, R′ = Me) had m. p. 135—140° (from methanol) (Found: C, 25·45; H, 3·75. $C_8H_{15}O_2ClHg$ requires C, 25·35; H, 4·0%). The mercurial (30 g.) was reduced by hydrazine to *cyclo*hex-3-enylmethanol (5·29 g., 59%), b. p. 84—86°/14 mm., n_D^{22} 1·4807, and 4α-*methoxy*-1β-cyclo*hexylmethanol* (XIV; R′ = Me) (4·0 g., 32%), b. p. 110—111°/14 mm., n_D^{23} 1·4684 (Found: C, 66·4; H, 11·0. $C_8H_{16}O_2$ requires C, 66·65; H, 11·2%). The α-naphthylurethane separated from ligroin as needles, m. p. and mixed m. p. with an authentic sample,[28] 94—96° (Found: C, 73·3; H, 7·3. Calc. for $C_{19}H_{23}O_3N$: C, 72·8; H, 7·4%). Oxidation of the methoxy-alcohol with chromic acid in acetone gave a good yield of the *trans*-methoxy-acid, m. p. 55·5—58·5° (anilide, m. p. 180—183°) (see below).

The reaction solution from the unsaturated alcohol (5·61 g.) and mercuric acetate (16·1 g.) in water (200 c.c.) was treated with sodium chloride (3·5 g.) in water (20 c.c.), 2α-*chloromercuri*-4α-*hydroxymethyl*cyclo*hexan*-1β-*ol* (XIII; R = R′ = H) (17·2 g.), m. p. 170—172°, being precipitated. The pure compound had m. p. 179—181° (from methanol–*iso*propyl ether) (Found: C, 22·95; H, 3·7. $C_7H_{13}O_2ClHg$ requires C, 23·0; H, 3·6%). Reduction of the mercurial (15·1 g.) with hydrazine gave 4α-hydroxymethyl*cyclo*hexan-1β-ol (XIV; R′ = H) (3·47 g., 65%), m. p. 95—97·5°. The pure diol had m. p. and mixed m. p. with an authentic sample,[28] 100—102° (lit.,[25] m. p. 103°).

Methoxy-mercurial from cyclo*Hex-3-enylmethyl Acetate* (XII; R = Ac).—Addition of sodium chloride (3·5 g.) in water (20 c.c.) to the reaction solution from the unsaturated acetate (7·69 g.) and mercuric acetate (16 g.) in methanol (150 c.c.) gave 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethyl acetate* (XIII; R = Ac, R′ = Me) (19·5 g.). The pure compound had m. p. 94—96° (from methanol) (Found: C, 28·2; H, 3·9. $C_{10}H_{17}O_3ClHg$ requires C, 28·5; H, 4·05%). Reduction o the mercurial (15 g.) by the hydrazine method yielded *cyclo*hex-3-enylmethanol (2·13 g.; 53%), b. p. (b. t.) 100—105°/14 mm., n_D^{19} 1·4820 and 4α-methoxy*cyclo*hexyl-1β-carbinol (1·89 g.; 37%), b. p. (b. t.) 126—130°/14 mm., n_D^{20} 1·4707 (α-naphthylurethane, m. p. and mixed m. p. 94·5—96°).

Methoxy-mercurial from Benzyl cyclo*Hex-3-enylmethyl Ether* (XII; R = CH_2Ph).—The reaction solution from the benzyl ether (9·99 g.) and mercuric acetate (16 g.) in methanol (300 c.c.) was treated with an excess of aqueous sodium chloride to give *benzyl* 3β-*chloromercuri*-4α-*methoxy*-1β-cyclo*hexylmethyl ether* (XIII; R = CH_2Ph, R′ = Me) (23·4 g.), m. p. 75—79°. The pure mercurial had m. p. 77—81° (Found: C, 37·9; H, 4·1. $C_{15}H_{21}O_2ClHg$ requires C. 38·4; H, 4·5%). The mercurial (17 g.) was reduced with hydrazine in the usual way. The product was isolated with ether and dissolved in ethylamine (75 g.), and finely chopped lithium (5 g.) was added in portions with external cooling to moderate the reaction. Isolation in the usual way gave *cyclo*hexylmethanol (2·5 g., 60%), b. p. (b. t.) 100—102°/13 mm., n_D^{19} 1·4827, and 4α-methoxy-1β-*cyclo*hexylmethanol (0·78 g., 14%), b. p. (b. t.) 135—140°/13 mm., n_D^{21} 1·4711 (α-naphthylurethane, m. p. and mixed m. p. 94—96°).

Methoxy-mercurial from Methyl cyclo*Hex-3-enecarboxylate* (XVI).—The reaction solution from the unsaturated ester (13·9 g.) and mercuric acetate (30 g.) in methanol (300 c.c.) was concentrated to one-third of its bulk and treated with sodium chloride (6 g.) in water (30 c.c.), to give the mercurial (37·5 g.) as a gum. Reduction of the mercurial (30 g.) by the hydrazine method gave *cyclo*hex-3-enecarboxylic acid (5·84 g., 58%), b. p. 59—60°/0·1 mm., n_D^{21} 1·4789, and crude methoxy-acid (3·63 g., 30%) which partially crystallized. Further crystallization from light petroleum gave pure 4α-methoxy*cyclo*hexane-1β-carboxylic acid (XV), m. p. and mixed m. p. (see below) 55·5—58·5°. More methoxy-acid was recovered as its anilide, m. p. 181—182·5° (see below), from the mother-liquors.

*Methoxy-mercurial from 4-Cyano*cyclo*hexene* (XVII).—The reaction solution from the nitrile (11·2 g.) and mercuric acetate (32 g.) in methanol (300 c.c.) was concentrated to 100 c.c. and treated with sodium chloride (6 g.) in water (60 c.c.) to precipitate the mercurial (35·5 g.), m. p. 107—113°. Crystallization from benzene–*iso*propyl ether gave 2β-*chloromercuri*-4β-*cyano*-1α-*methoxy*cyclo*hexane* (XVIII), m. p. 125—129° (Found: C, 25·5; H, 3·4. $C_8H_{12}ONClHg$ requires C, 25·65; H, 3·2%).

The mercurial (30 g.) was reduced with hydrazine hydrate (10 c.c.) in boiling sodium

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[28] Kindly provided by Dr. L. N. Owen (Imperial College).

hydroxide solution (200 c.c.) during 16 hr. Sodium hydroxide (18 g.) was added and the solution heated under reflux for a further 24 hr. to ensure hydrolysis of the nitrile. Isolation with ether and distillation gave *cyclo*hex-3-enecarboxylic acid (4·8 g., 48%), b. p. 83—84°/0·6 mm., n_D^{22} 1·4774, and 4α-methoxy*cyclo*hexane-1β-carboxylic acid (XV) (5·72 g., 45%), b. p. 100°/0·1 mm., m. p. 56—59° (from light petroleum) (lit.,[29] 59—60°) (Found: C, 61·1; H, 8·9. Calc. for $C_8H_{14}O_3$: C, 60·75; H, 8·9%). The anilide of this acid separated from benzene–light petroleum as needles, m. p. 181—183° (lit.,[29] 186—186·5°) (Found: C, 72·1; H, 8·2. Calc. for $C_{14}H_{19}O_2N$: C, 72·05; H, 8·2%).

Methoxy-mercurial from cis-*Hex-3-enol* (XIX).—The reaction mixture from the alcohol (7·2 g.), mercuric acetate (23 g.), and methanol (150 c.c.) was concentrated to 50 c.c. and treated with sodium chloride (4·5 g.) in water (20 c.c.), the mercurial (XX) (22·5 g.) separating as an oil. Reduction of the mercurial (11·9 g.) with hydrazine hydrate (5 c.c.) in sodium hydroxide solution (100 c.c.) gave *cis*-hex-3-enol (1·32 g., 40%), b. p. 69—74°/24 mm., n_D^{19} 1·4418, and 4-*methoxyhexan*-1-*ol* (XXI) (2·07 g., 48%), b. p. 100—101°/24 mm., n_D^{19} 1·4345 (Found: C, 63·4; H, 11·9. $C_7H_{16}O_2$ requires C, 63·6; H, 12·2%). Its 4-*diphenylylurethane* had m. p. 65—67° (from ligroin) (Found: C, 73·4; H, 7·6. $C_{20}H_{25}O_3N$ requires C, 73·35; H, 7·7%): this m. p. was depressed to 52—54° on admixture with the derivative from 3-methoxyhexan-1-ol (see below).

Mercurial from trans-*Hex-3-enol* (XXIII).—The reaction solution from the alcohol (5 g.) and mercuric acetate (16 g.) in methanol (300 c.c.) was concentrated to 70 c.c. and treated with sodium chloride (3 g.) in water (20 c.c.), to give 3β-chloromercuri-2α-ethyltetrahydrofuran (XXIV) (13·8 g.). For reduction, the chloromercurial (10·5 g.) in boiling sodium hydroxide solution (150 c.c.) was treated with hydrazine hydrate (10 c.c.), the mixture then being heated under reflux for 16 hr. Distillation yielded 2-ethyltetrahydrofuran (XXV) (1·27 g., 42%), b. p. 107—108°/755 mm., n_D^{18} 1·4175 (lit., b. p. 108·5°/759 mm., n_D^{20} 1·4170), and *trans*-hex-3-enol (1·56 g., 42%), b. p. 150—152°/755 mm., n_D^{17} 1·4393. For comparison of the infrared spectrum, an authentic sample of 2-ethyltetrahydrofuran (1·46 g., 73%) was prepared by slowly heating *trans*-hex-3-enol (1·98 g.) and concentrated sulphuric acid (0·2 g.) to 150°.

Preparation of 3-*Methoxyhexan*-1-*ol* (XXII).—A mixture of *n*-butyraldehyde (70 g.) and ethyl bromoacetate (160 g.) was added to activated zinc dust (60 g.) in benzene (1 l.), with cooling. Isolation in the usual way gave the hydroxy-ester (92·7 g., 58%), b. p. 90—92°/14 mm., n_D^{22} 1·4278 (lit., b. p. 83—85°/10 mm.). A mixture of the hydroxy-ester (20·1 g.), methyl iodide (70 g.), and ether (50 c.c.) was stirred and heated under reflux while silver oxide (36 g.) was added in 1 g. portions during several hours. Heating and stirring were continued for 12 hr. and the product was isolated as usual, to yield *ethyl* 3-*methoxyhexanoate* (16·3 g., 75%), b. p. 80—82°/14 mm., n_D^{21} 1·4201 (Found: C, 61·8; H, 10·55. $C_9H_{18}O_3$ requires C, 62·05; H, 10·4%), and unchanged hydroxy-ester (3·3 g.), b. p. 88—92°/15 mm., n_D^{21} 1·4270.

A solution of the methoxy-ester (11·1 g.) in dry ether (50 c.c.) was added dropwise to a stirred suspension of lithium aluminium hydride (5 g.) in ether (100 c.c.), the mixture then being heated under reflux for 2 hr. Isolation as usual gave 3-*methoxyhexan*-1-*ol* (7·46 g., 90%), b. p. 84°/15 mm., n_D^{21} 1·4279 (Found: C, 63·85; H, 12·05. $C_7H_{16}O_2$ requires C, 63·6; H, 12·2%). Its 4-*diphenylylurethane* had m. p. 47—52° (from light petroleum) (Found: C, 73·25; H, 7·5. $C_{20}H_{25}O_3N$ requires C, 73·35; H, 7·7%).

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[29] Noyce and Weingarten, *J. Amer. Chem. Soc.*, 1957, **79**, 3093.