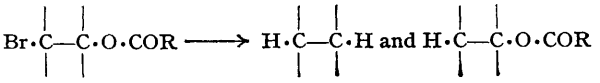
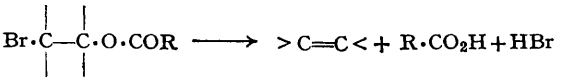
# 1062. *Mechanisms of Hydrogenation. Part IV.* Substitution and Elimination in the Hydrogenolysis of Halogen Compounds.*

By D. A. Denton, F. J. McQuillin, and P. L. Simpson.

In hydrogenolysis of certain α-bromo-lactones, elimination of the lactonic group may accompany displacement of the halogen and lead to two reaction products:



Examples are described to show that loss of the lactone occurs through an elimination step:



brought about by the catalyst.

For a series of α-halogeno-steroid ketones, hydrogenolysis is shown to be influenced principally by a mutual polarisation in a type of neighbouring-group effect and to only a lesser extent by the nature of a second substituent. The catalyst is considered to act in a nucleophilic fashion in halogen hydrogenolysis. Attention is drawn to the importance of buffering the acidity of the medium as a condition of maintaining the catalytic metal in a low oxidation state.

The close relationship of chemisorption and co-ordination-complex formation is illustrated by the behaviour of a catalyst made using a Dowex chelating resin as catalyst support.

Experimental evidence[1] indicates the similar nature of the bond formed in chemisorption of an olefin at, *e.g.*, palladium, and in an olefin–transition-metal complex. However, whilst chemisorption of π-bonding donor molecules is easily rationalised in this way, there are also many instances to be considered of absorption and reaction with scission of a σ-bond. So as to obtain information on examples of this kind, we have examined the hydrogenolysis of the carbon–halogen bond, particularly in certain α-bromo-lactones and α-halogeno-ketones.

Catalytic hydrogenolysis of halogen is a well established method.[2] Reaction is very generally impeded or inhibited by the halogen acid released,[2–5] and a base is usually added.

* Part III, *J.*, 1963, 5996.

[1] F. J. McQuillin, W. O. Ord, and P. L. Simpson, *J.*, 1963, 5996.

[2] Cf. M. Busch and H. Stove, *Ber.*, 1916, **49**, 1063; E. Ott and K. Kramer, *Ber.*, 1935, **68**, 1655; V. Prelog and E. Zalan, *Helv. Chim. Acta*, 1944, **27**, 535; R. Baltzly and A. P. Phillips, *J. Amer. Chem. Soc.*, 1946, **68**, 261; W. von E. Doering and E. F. Schoenewaldt, *ibid.*, 1951, **73**, 2333; W. R. Boehme, *ibid.*, 1958, **80**, 4740; H. Stettner, O. E. Bander, and W. Neumann, *Chem. Ber.*, 1956, **89**, 1922; H. Kamerer, L. Horner, and H. Beck, *ibid.*, 1958, **91**, 1376; T. G. Halsall, E. R. H. Jones, and G. D. Meakins, *J.*, 1952, 2862.

[3] M. Busch and W. Schmidt, *Ber.*, 1929, **62**, 2612.

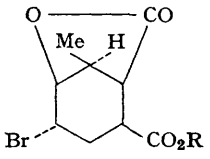
[4] W. F. Whitmore and A. J. Revukas, *J. Amer. Chem. Soc.*, 1940, **62**, 1687.

[5] J. S. Campbell and C. Kemball, *Trans. Faraday Soc.*, 1963, **59**, 2583.

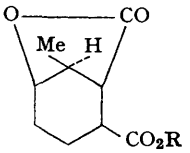
Many authors have used alkali hydroxide or alkoxide; we have made addition of potassium acetate our standard procedure.

Although formation of a dimeric product has been reported,[3] hydrogenolysis of halide more generally leads to quantitative displacement of halogen by hydrogen. In the hydrogenation of a bromo-lactone (I; R = H or Me) which we examined for another purpose, we encountered phenomena which suggested that direct replacement of halogen by hydrogen may not be an obligatory mechanism.

Hydrogenolysis of the bromo-lactone (I) was intended as a method of synthesis of the debrominated lactone (II). In absence of added base the bromo-lactone (I; R = H) and its methyl ester (I; R = Me) did not react with hydrogen at a palladised-charcoal catalyst, whilst in potassium acetate solution, however, some 1·6 mol. of hydrogen were fairly easily absorbed to give a large proportion of the cyclohexanedicarboxylic acid (III; R = H), or its ester (III; R = Me), in addition to the expected lactonic product (II; R = H or Me). The bromo-lactone (I; R = H) was hydrogenated as its monosodium salt with the same result, and the relative proportion of the two products was essentially unaltered by changing the catalyst




(I)

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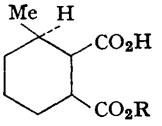


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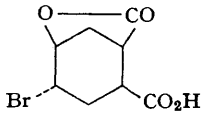


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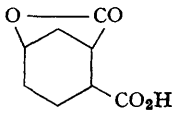


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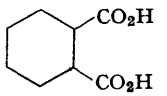


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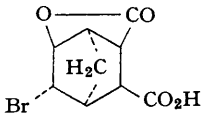


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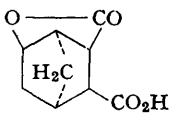


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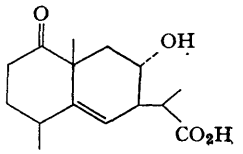


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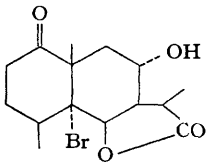


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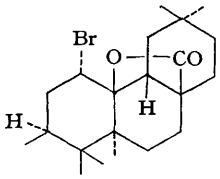


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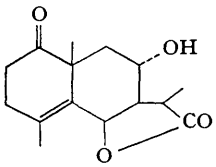


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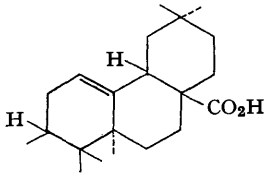
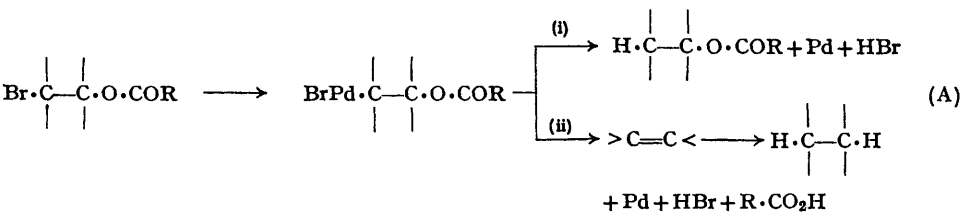



(XIII)

(palladium or nickel) or the solvent (aqueous alcohol or dioxan). The lactonic group in the debrominated product (II) was resistant to hydrogenolysis, and the dicarboxylic acid (III) must therefore arise during displacement of the halogen.

A related bromo-lactone (IV) behaved similarly, and in this case the dicarboxylic acid (VI) was formed in greater amount than the debrominated product (V). The bromo-lactone (VII) from bicycloheptenedicarboxylic acid,[6] when hydrogenated under the same conditions, was debrominated to give the lactone (VIII) unaccompanied by any product of fission of the lactone ring. Alder *et al.*[6b] reported the same result from hydrogenolysis of compound (VII) in a strongly alkaline solution.

From these examples, in which ring-opening of the lactone is evidently contingent on fission of the halogen bond, but ultimately dependent on some structural factor, we were led to infer two modes of displacement of halogen as in (A).




(A)

As a test of this hypothesis we examined the bromo-lactone[7] (X) since the derived olefinic product, dihydro-ψ-santonin (IX), is rather resistant to further reduction at the olefinic bond.[8] This bromo-lactone, when hydrogenated at palladised charcoal in alcoholic potassium acetate solution, absorbed one mol. of hydrogen to reform dihydro-ψ-santonin (IX) quantitatively. Also oleanolic acid bromo-lactone[9] (XII) was reconverted into oleanolic acid (XIII) on hydrogenolysis under the same conditions.

These various bromo-lactones were stable to alcoholic potassium acetate solution at room temperatures and the instances of elimination, (X) → (IX) and (XII) → (XIII), are therefore acceptable evidence in support of step (ii) postulated in the scheme (A). This conclusion is consistent also with the relative ease of scission of the lactone ring in the examples which we have examined. The infrared carbonyl frequencies (Table 1) indicate no correlation between

TABLE 1.

Infrared absorption of the lactonic carbonyl group.

| Bromo-lactones | $\nu_{max.}$ (cm.$^{-1}$) | Lactones | $\nu_{max.}$ (cm.$^{-1}$) |
|---|---|---|---|
| (I; R = H) | 1779 | (II; R = H) | 1751 |
| (I; R = Me) | 1779 | (II; R = Me) | 1773 |
| (IV) | 1764 | (V) | 1761 |
| (VII) | 1770 | (VIII) | 1757 |
| (X) | 1764 | (XI) | 1751 |
| (XII) | 1786 | | |

ease of hydrogenolysis and the relative degree of strain in these bromo-lactones. A parallel is apparent, however, between the ease of scission and the order of stabilities of the double bond introduced into the olefinic intermediates, *i.e.*, (IX) and (XIII) > (XIV) and (XV) > (XVI). This result led us to discount explanations based on factors such as variable availability of hydrogen at the catalyst and to consider the intervention of a "chemisorbed"

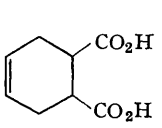
[6] (*a*) K. Alder, G. Stein, W. Eckardt, R. F. V. Buddenbrock, and S. Schneider, *Annalen*, **1933**, **504**, 216; (*b*) K. Alder, G. Stein, R. F. V. Buddenbrock, W. Eckardt, W. Frercks, and S. Schneider, *ibid.*, **1934**, **514**, 1.

[7] W. G. Dauben and P. D. Hance, *J. Amer. Chem. Soc.*, 1955, **77**, 2451; W. Cocker and S. Hornsby, *J.*, 1947, 1157.

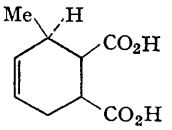
[8] G. R. Clemo and W. Cocker, *J.*, 1946, 30.

[9] A. Winterstein and G. Stein, *Z. physiol. Chem.*, 1952, **211**, 56.

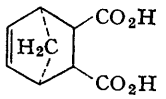
organometallic intermediate which may react by alternative paths as in (A). We were impressed also by the similarity in behaviour of the bromo-lactones on hydrogenation and of a series of methoxycyclohexylmercury halides (XVII; R = $CO_2H$, $CH_2OH$, OMe, or $OCH_2Ph$) on reductive removal of the chloromercury substituent with alkaline hydrazine.[10]



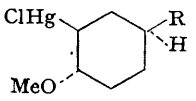

(XIV)




(XV)




(XVI)

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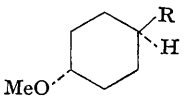
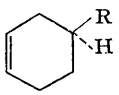
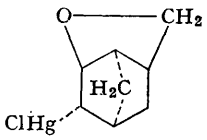



(XVIII)




(XIX)




(XX)

The product of direct reduction, *i.e.*, (XVIII; R = $CO_2H$, $CH_2OH$, OMe, $OCH_2Ph$), was accompanied in each case by a considerable proportion of the cyclohexene derivative (XIX). Significantly, the bicycloheptanemercury halide (XX) could be reduced without the formation of any accompanying bicycloheptene derivative.

Although these parallels strengthen the case for regarding the mechanism (A) as a reasonable basis for further discussion, fuller information is required concerning the mode of interaction of the bromo-lactone with the catalyst. The halogen and the lactonic group are electronically similar and either or both may take part in "absorption." We note, however, that the debromo-lactones appear to be quite stable to hydrogenolysis, and in the case of the bromo-lactone (XII) from oleanolic acid there is evident steric difficulty in both bromo- and lactonic-substituents being engaged by the catalyst at the same time. We are inclined therefore to regard chemisorption through the halogen as the operative process and, so as to obtain more insight into the nature of the interaction of the halide and the catalyst, we compared the rates of hydrogenolysis of some differently constituted halides.

The results (Table 2) illustrate (*a*) the relative order of hydrogenolysis: C–Br > C–Cl, (*b*) the assistance given by electrophilic groups: Ph, >C:O, $CO_2Et$, and (*c*) the considerable acceleration in presence of added potassium acetate.

TABLE 2.

Initial rates of hydrogenation (c.c./min./mg. catalyst × $10^3$) (i) in methanol and (ii) in methanol with potassium acetate (1 equiv.).

| Halide* | (i) | (ii) | Halide | (i) | (ii) |
|---|---|---|---|---|---|
| n-$C_7H_{15}Br$ | nil | nil | $Ph{\cdot}[CH_2]_3{\cdot}Br$ | 7·5 | 17 |
| PhCl | 10 | 75 | $Ph{\cdot}CO{\cdot}CH_2Br$ | 122 | 165 |
| PhBr | 79 | 125 | $EtO{\cdot}CO{\cdot}CH_2Br$ | 11 | 68 |
| $Ph[CH_2]_2{\cdot}Cl$ | nil | 2·5 | $EtO{\cdot}CO{\cdot}[CH_2]_2{\cdot}Br$ | 4 | 10 |
| $Ph[CH_2]_2{\cdot}Br$ | 6·5 | 25 | | | |

* Concentration $5 \times 10^{-2}$M.

The influence of added potassium acetate (see Figure) appears to be due to buffering the acidity of the solution. A quantity of slightly alkaline chromatographic alumina added

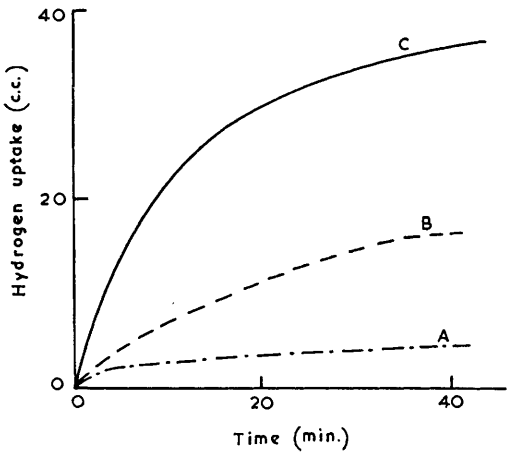
[10] H. B. Henbest and B. Nicholls, *J.*, 1959, 227.

to the reaction medium provided sufficient buffering for complete, albeit slow, hydrogenation of the bromo-lactone (I; R = Me) and we infer that the hydrogen ion rather than the halide ion is the effective inhibitor.

By absorption and reaction with hydrogen ion, a catalytic metal will be converted into a condition of higher ionisation energy, or a state of higher positive valency:

$$n\mathrm{Pd} + 2m\mathrm{H}^+ \rightleftharpoons (n\text{-}2m)\mathrm{Pd} + 2m(\mathrm{PdH})^+ \rightleftharpoons m\mathrm{Pd}^{++} + m\mathrm{H}_2$$

Hydrogen absorption may be somewhat reduced in acid solution,[11] but since hydrogenation of many substances is with advantage carried out in a strongly acid solution we do not regard hydrogen absorption as a limiting factor. There is often objective evidence of the oxidation of the metal; not infrequently in hydrogenolysis of halides the reaction solution becomes coloured by extracted $Pd^{II}$ ions and an alkaline buffer will assist re-reduction.




Hydrogenation of phenethyl bromide ($6{\cdot}5 \times 10^{-2}$M) in ethanol: (A) alone, (B) with 0·5 equiv., and (C) with 1, 2, or 3 equiv. of potassium acetate.

There appear therefore to be good general grounds for associating hydrogenolysis of halides with maintaining a low valency or nucleophilic state in the catalytic metal. The relatively inhibitory effect of weak bases such as acetate ion on the hydrogenation of olefins[1] suggests that the process designated as "chemisorption" depends on a complementary character in the electronic state of the metal and of the bond with which it interacts.

TABLE 3.

Rates of hydrogenation (c.c./min./mg. catalyst × $10^2$). Concentration $3{\cdot}5 \times 10^{-2}$M in methanol–acetone (1:1) with potassium acetate (1 equiv.).

| Derivative | $\Delta\nu$(CO) (cm.$^{-1}$) | $\Delta\lambda$(CO) (m$\mu$) | Rate | Product |
|---|---|---|---|---|
| | Cholestan-3-one derivatives | | | |
| 2,2-$Br_2$ | +17 | +12 | 4·5 | 2α-Br |
| 2α, 4α-$Br_2$ | +38 | — | 4·2 | — |
| 2α-Br, 2β-Me | 0 | +29 | 3·8 | 2β-Me |
| 2α-Br | +12 | −4 | 3·5 | — |
| 2β-Br, 2α-Cl | +26 | +4 | 3·5 | 2α-Cl |
| 2α-Br, 2β-Cl | +27 | +11 | 3·2 | ,, |
| 2,2-$Cl_2$ | +30 | +15 | 2·5 | ,, |
| 4α-Br, 2α-Cl | +39 | — | 0·9 | ,, |
| 2α-Cl | +15 | −7 | 0·7 | — |
| 2α-I | +3 | | 0·6 | — |
| | Lanost-8-en-3-one derivatives | | | |
| 2α-Br | +25 | +3 | 3·0 | |
| 2β-Br | +31 | −6 | 2·1 | |

[11] D. V. Sokolskii, *Trudy Inst. khim. Nauk, Akad. Nauk Kazakh. S.S.R.*, 1959, **5**, 146.

Whilst the relative order of ease of hydrogenolysis, C–Br > C–Cl, is reasonable in reflecting the order of bond strengths, the relative ease of hydrogenolysis of halogen attached to an aromatic ring or with a neighbouring carbonyl group requires further consideration. We therefore examined the hydrogenolysis of the series of α-halogeno-oxo-steroids shown in Table 3. In comparison with these ketones 2α-bromocholestan-3β-ol and 2β-bromocholestan-3α-ol underwent hydrogenolysis of halogen only extremely slowly.[12] The oxo-group is therefore clearly a principal factor in assisting hydrogenolysis.

The figures for rates of hydrogenation given in Table 3 are based on several concordant rate measurements in each case and, although the differences are not large, we consider that the indicated order of relative reactivity of these halogeno-ketones is reasonably correct. Iodide ion is a known[1] hydrogen inhibitor (Table 4). An iodo-group is therefore probably displaced rather more easily than is indicated by the value for 2α-iodocholestanone. From

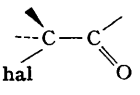
TABLE 4.

Rates of hydrogenation (c.c./min./mg. catalyst × $10^3$) for phenethyl bromide in methanol with various additives.

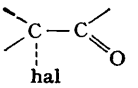
| Additive | Rate | Additive | Rate |
|---|---|---|---|
| None | 6·5 | HBr | 3·3 |
| KOAc | 26 | NaI | 0·4 |
| LiBr | 4·4 | PhEt | 8 |

the remaining examples, however, it is clear that reaction is determined primarily by the polarisation introduced by the oxo-group and the polarisability of the halogen, and is influenced to only a limited degree by the second substituent on the carbon atom carrying the halogen.

Interaction of adjacent carbonyl and halogen groups is reflected in enhanced reactivity of the halogen towards nucleophilic substitution[13] and, for example, in the steric control by the halogen of addition of nucleophiles to the carbonyl group.[14] The nature of the interaction is, however, more apparent in the displacements by α-halogen of the carbonyl absorption in the ultraviolet[15] and in the infrared,[16] which emphasise also the importance of the relative orientation of the respective bond dipoles. In an eclipsed conformation (XXI)




(XXI)

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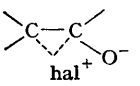
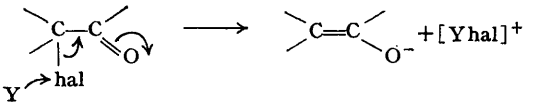



(XXIII)

dipole repulsion reduces the bond polarities and displaces the carbonyl infrared[16] band to higher frequencies (Δν). The staggered arrangement (XXII) minimises the dipole field interaction, but permits a type of "neighbouring-group polarisation" as in (XXIII), recognised in a displacement (Δλ) in the ultraviolet carbonyl absorption[15] to longer wavelengths. The polarisation (XXIII) is, in effect, a reversion towards the transition state in halogen substitution of a ketone, and it appears most reasonable to associate activation of the halogen by the carbonyl with an interaction of this kind. It may be noted that in polarographic reduction of α-halogenocyclohexanones reduction is easier for axially rather than for

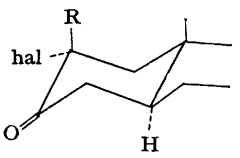
[12] Cf. L. F. Fieser and R. Ettorre, *J. Amer. Chem. Soc.*, 1953, **75**, 1700; L. F. Fieser and W. Y. Huang, *ibid.*, p. 4837.
[13] Cf. E. S. Gould, "Mechanism and Structure in Organic Chemistry," Hold, Rinehart, and Winston, New York, 1959, p. 283.
[14] J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J.*, 1959, 112.
[15] H. H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York, 1962, p. 181.
[16] Cf. L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd edn., Methuen, London, 1958, pp. 140, 401.

equatorically oriented halogen.[17] The halogen of α-bromo-ketones may also be removed by bromide ion,[18] by triphenylphosphine,[19] and, in some instances by sodium borohydride reduction[20] in processes which may be represented collectively as in (XXIV) where Y = $Br^-$, $Ph_3P$, or $BH_4^-$. Displacements of this kind are consistent with an activating process as in (XXIII).

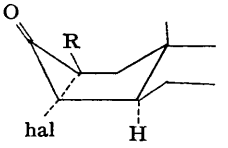



(XXIV)

In the steroid halogeno-ketones, dipole interaction may be important also in controlling the conformational equilibrium[21] (XXV) ↔ (XXVI). 2α-Bromo-2β-methylcholestanone, for example, adopts the boat (XXVI; R = Me) as the preferred conformation,[22] whilst the 2,2-dihalogeno-cholestanones are maintained in the chair form (XXV; R = hal) by the 2β-halogen dipole,[23]




(XXV)



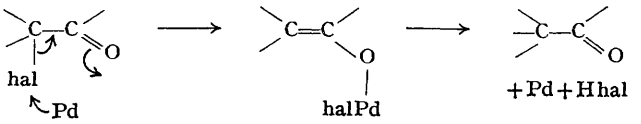

(XXVI)

This is relevant in determining the type of group interaction, *i.e.*, (XXI) and (XXIII). In the relative order of reactivity noted in Table 3, *i.e.*, 2,2-dibromo- > 2α-bromo-2β-methyl- > 2β-bromo-2α-chloro- > 2α-bromo > 2α-bromo-2β-chloro-cholestanone, it may be significant that in the first three of these substances there is axially oriented halogen, and that the 2β-chloro-substituent in the last example will introduce resistance to deformation of the molecule in the sense of (XXV) → (XXVI). A significant difference also emerges between the reactivity of the 4α-bromo-substituent in 2α-chloro-4α-bromo- and 2α,4α-dibromo-cholestanone, which in the former is displaced quite slowly, but in the latter so quickly that no monobromo-intermediate could be observed. The 4α-bromo-group is clearly not seriously hindered, nor from the other examples, does a 2α-chloro-substituent appear to be intrinsically deactivating. The result suggests that reaction of the readily removed 2α-bromo-group potentiates displacement at C-4. This could arise if the 2α-bromine is displaced not directly by hydrogen but through some adsorbed intermediate. In correspondence with the scheme (XXIV) and with the evidence for an organometallic intermediate in the hydrogenolysis of the α-bromo-lactones, it is possible to consider the sequences (XXVII). It may be noted that bromobenzene and related bromo-aromatics, under suitable conditions,[3] give biphenyls on hydrogenation, *i.e.*, that the halogen may be displaced at the catalyst other than by hydrogen. It is of interest too that organometallic intermediates are mentioned also in connection with the reduction of organic halides by chromous salts.[24]

[17] A. M. Wilson and N. L. Allinger, *J. Amer. Chem. Soc.*, 1961, **83**, 1999.
[18] I. M. Heilbron, H. Jackson, E. R. H. Jones, and F. S. Spring, *J.*, 1938, 102; R. C. Cookson and S. H. Dandegaonker, *J.*, 1955, 352.
[19] I. J. Borowitz and R. Virkhaus, *J. Amer. Chem. Soc.*, 1963, **85**, 2183; A. J. Speziale and L. R. Smith, *ibid.*, 1962, **84**, 1868; B. Miller, *J. Org. Chem.*, 1963, **28**, 345.
[20] H. B. Henbest, E. R. H. Jones, A. A. Wagland, and T. I. Wrigley, *J.*, 1955, 2477; E. R. H. Jones and D. J. Wluka, *J.*, 1959, 907.
[21] D. H. R. Barton, D. A. Lewis, and J. F. McGhie, *J.*, 1957, 2907.
[22] C. Djerassi, N. Finch, and R. Mauli, *J. Amer. Chem. Soc.*, 1959, **81**, 4997; C. Djeressi, N. Finch, R. C. Cookson, and C. W. Bird, *ibid.*, 1960, **82**, 5488; R. Villotti, H. J. Ringold, and C. Djerassi, *ibid.*, p. 5693.
[23] E. W. Warnhoff, *J. Org. Chem.*, 1963, **28**, 889.
[24] F. A. Anet and E. Leblanc, *J. Amer. Chem. Soc.*, 1957, **79**, 2649; C. E. Castro and W. C. Kray, *ibid.*, 1963, **85**, 2768.

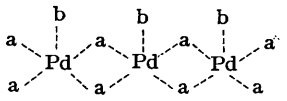
In chemisorption the detailed nature of the bonding will evidently be complex; in addition to the halogen, the carbonyl group, aromatic ring, or other π-bonding residue must certainly be engaged.

We have already noted[1] the highly inhibiting influence of chelating ligands on the hydrogenation of olefins, which we attributed to the blocking of catalyst co-ordination sites.




(XXVII)

This deduction is confirmed by the inactivity of a palladium catalyst prepared on Dowex A1 chelating resin. On this resin, which carries imido-diacetic acid residues, $Pd^{++}$ ions were readily absorbed and could be reduced *in situ* by either hydrogen or alkaline formalin[25] with characteristic colour change of the resin from brown to black. This preparation, however, failed to promote hydrogen uptake by benzoquinone or by a simple olefin. Since in previous work[1] we have employed both acidic and basic ion-exchange resins as catalyst supports, we must attribute the inactivity of the palladised Dowex A1 resin to the imido-diacetic acid chelating groups blocking chemisorption of reducible substances.




(XXVIII)

The clear implication of the presence of closely related "co-ordination sites" leads us to picture the catalyst in an idealised way as an aggregate, (XXVIII), of a series of "atomic" units which contribute co-ordination sites "a" and "b", as in simple metal complexes. This kind of model seems to be necessary if polyfunctional molecules such as halogeno-ketones, bromo-lactones, and aryl halides are to be brought together with hydrogen in an absorbed reaction complex.

## Experimental

*Bromo-lactone* (IV) *from Cyclohex-4-ene-*cis*-1,2-dicarboxylic Acid.*—The diacid (1·7 g.) in water (25 c.c.) at 35° was stirred whilst *N*-bromosuccinimide (1·8 g.) was added. The solution was stirred at approx. 35° for 2 hr. and extracted with chloroform after saturating with ammonium sulphate. The product, freed from succinimide by means of a little sulphur dioxide and washing with water, was recrystallised from ethyl acetate and light petroleum to give the *γ-lactone*, m. p. 158° (Found: C, 38·2; H, 3·7. $C_8H_9O_4Br$ requires C, 38·5; H, 3·6%).

Hydrogenolysis of this lactone (0·497 g.) in ethanol (25 c.c.) with potassium acetate (0·25 g.) and palladised charcoal (0·149 g.) required 48 hr. for complete uptake of hydrogen (66·5 c.c., 1·38 mol.). The product could be separated into two components by water, cyclohexane-1β,2β-dicarboxylic acid (0·12 g.), m. p. 190°, being the more soluble, and 4β-*hydroxycyclohexane*-1β,2β-*dicarboxylic acid* 2→4-*lactone*, m. p. 186° (from water), $\nu_{max.}$ 1760 and 1730 cm.$^{-1}$ (Found: C, 56·5; H, 6·1. $C_8H_{10}O_4$ requires C, 56·4; H, 5·9%) the less soluble.

*Hydrogenolysis of* 3α-*Bromo*-4β-*hydroxy*-5β-*methylcyclohexane*-1β,2β-*dicarboxylic Acid* 2→4-*Lactone.*—The lactone (0·5 g.) was hydrogenolysed in alcohol (25 c.c.) with palladised charcoal (0·15 g.) and potassium acetate (0·19 g.) to give 3β-methylcyclohexane-1β,2β-dicarboxylic acid (0·2 g.), m. p. 168°, and 4β-hydroxy-3β-methylcyclohexane-1β,2β-dicarboxylic acid 2→4-lactone (0·14 g.), m. p. 160°, in complete agreement with previous experiments (see preceding Paper).

*Hydrogenolysis of the Bromo-lactone* (VII).—This bromo-lactone was obtained, m. p. 160°, by the method of Alder *et al.* (cf. ref. 6*b*). The bromo-lactone (0·5 g.), in ethanol (25 c.c.)

[25] R. P. Linstead and S. L. Thomas, *J.*, 1940, 1127.

with palladised charcoal (0·15 g.) and potassium acetate (0·5 g.), absorbed 1 equivalent(47 c.c.) of hydrogen in 40 hr. to give 5-hydroxybicyclo[2,2,1]heptane-2,3-dicarboxylic acid 3 → 5-lactone,[26] m. p. 199°.

*Hydrogenolysis of the Bromo-lactone* (X) *from Dihydro-ψ-santonin.*—The bromo-lactone, m. p. 180°, was prepared by the action of bromine on a solution of dihydro-ψ-santonin in aqueous potassium carbonate. A sample (0·102 g.) in ethyl acetate (7 c.c.), with palladised charcoal (27 mg.) and potassium acetate (35 mg.), absorbed 1 mol. of hydrogen (6·9 c.c.) in 18 hr. to reform dihydro-ψ-santonin, m. p. and mixed m. p. 189°.

*Hydrogenolysis of 12-Bromo-oleanolic Acid Lactone* (XII).—The lactone (28 mg.), obtained, m. p. 235—240°, by the action of bromine–acetic acid on oleanolic acid, was hydrogenated in acetone (10 c.c.) with palladised charcoal (8 mg.) and potassium acetate (10 mg.). It absorbed 1·02 mol. hydrogen (1·3 c.c.) to reform oleanolic acid, m. p. 305° (lit.,[9] 306—308°).

*Hydrogenolysis of 2-Halogeno-3-oxo-steroids.*—The conditions were as indicated in Table 3. Products were identified as under. (*a*) 2α-Bromocholestan-3-one[27a] gave cholestan-3-one, m. p. 129°. (*b*) 2,2-Dibromocholestan-3-one gave 2α-bromocholestanone, m. p. 169° (80%), 2,2-dibromocholestanone,[27b,c,d] m. p. 145—147° (5%), and cholestanone (10%) which were separated by chromatography on silica in benzene. (*c*) From 2α,4α-dibromocholestanone[27c] the product, on chromatography on silica, gave cholestanone (45%), 2α,4α-dibromocholestanone (40%), and some 5% of unresolved material. (*d*) 2α-Bromo-2β-methylcholestanone[27d] gave a product which was separated on alumina with benzene–hexane to give 2α-methylcholestanone,[27e] m. p. 119—120° (12%), and 2β-methylcholestanone,[27d] m. p. 92° (70%), eluted by benzene–ether. (*e*) 2α-Chlorocholestanone[28a] gave cholestanone, m. p. 129—130°. (*f*) 2,2-Dichlorocholestanone[28b] gave a product which was separated by chromatography on silica to give 2α-chlorocholestanone, m. p. 173° (85%) and 2—3% of each of cholestanone and 2,2-dichlorocholestanone, m. p. 151°. (*g*) The product from 2α-bromo-2β-chlorocholestanone,[18] on silica, gave 2α-chlorocholestanone (90%), m. p. 172°, and a little low-melting material. (*h*) 2β-Bromo-2α-chlorocholestanone[18] gave a similar result. (*i*) 4α-Bromo-2α-chlorocholestanone[28b] yielded 2α-chlorocholestanone. (*j*) Both 2α- and 2β-bromolanost-8-en-3-one[16] absorbed 1 mol. of hydrogen to give lanost-8-en-3-one, m. p. 119°.

The following $R_F$ values were found for the cholestan-3-one derivatives chromatographed on silica plates in benzene: cholestan-3-one 0·132, 2α-bromo- 0·335, 2,2-dibromo- 0·625, 2α,4α-dibromo- 0·47, 2α-methyl- 0·33, 2β-methyl- 0·81, 2α-bromo-2β-methyl- 0·47, 2α-chloro- 0·32, 2,2-dichloro- 0·61, 2β-bromo-2α-chloro- 0·65, 2α-bromo-2β-chloro- 0·66, 2α-chloro, 4α-bromo- 0·40, 2α-iodo- 0·44.

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[26] D. Ver Nooy and C. S. Rondestvedt, *J. Amer. Chem. Soc.*, 1955, **77**, 3583.

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[28] (*a*) J. J. Beereboom, C. Djerassi, D. Ginsburg, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 3500; (*b*) B. Ellis and V. Petrow *J.*, 1953, 3869.