101. *The Catalytic Deuteration of Organic Compounds. Part I. Deuteration and Disproportionation.*

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Bloch and Rittenberg's method of preparing deuteriocholesterol by a platinum-catalysed exchange reaction between the sterol and deuterium oxide has been applied to a series of simpler compounds. Each contained representative features of sterol molecules, and the deuteration results have allowed these compounds to be placed in order of increasing facility of exchange. Considerable amounts of deuterium were found in the products when the original compounds underwent a disproportionation reaction in deuterium oxide.

THE preparation of deuteriocholesterol containing up to 5% of deuterium by the treatment of cholesterol with deuterium oxide and acetic acid at 120° in presence of a platinum catalyst has been described by Bloch and Rittenberg (*J. Biol. Chem.*, 1943, **149**, 505). According to these workers the deuterium was introduced into the side chain and the ring system of the sterol, while a destruction of cholesterol took place parallel with the extent of deuteration.

In the present investigation the applicability of this reaction to the deuteration of some simpler compounds has been studied, and the resulting information has been used (see following paper) in a re-examination of Bloch and Rittenberg's work on cholesterol and in a deuteration of ergosterol by similar methods.

The simpler compounds were chosen from saturated and unsaturated aliphatic and alicyclic hydrocarbons: benzene and *cyclo*hexanol were also examined for further comparisons.

Some indication of the influence of structure on the extent of the exchange reaction may be seen in Table 1 which shows the amounts of deuterium introduced under comparable reaction conditions into the reaction products, results being included for two series of experiments in which the catalyst preparations were of different activity.

It is seen that, whereas relatively little exchange of the hydrogen atoms in the saturated *n*-hexane and *cyclo*hexane molecules took place, the introduction of a double bond resulted in considerably greater exchange, a similar effect being also produced to a lesser extent by the presence of a hydroxyl group. An exchange reaction between ethylene and deuterium oxide in presence of a nickel catalyst has been discussed by Horiuti and Polanyi (*Trans. Faraday Soc.*, 1934, **30**, 1164); the mechanism suggested involved chemisorption at the double bond accompanied by bond-opening, transfer of a hydrogen atom, and either removal or addition of a further hydrogen atom. Comparison of the values obtained for the two octenes examined shows a slight but reproducible difference in deuteration depending on the position of the double bond, suggesting that its presence may not be the sole factor determining the extent of deuteration.

TABLE 1. *Comparative deuterations.*

Compound	Relative no. of D atoms introduced into product		Relative no. of D atoms introduced into methyl group of acetic acid solvent	
	Catalyst I	Catalyst II	Catalyst I	Catalyst II
*cyclo*Hexane	0·121	0·027	0·802	0·775
n-Hexane	0·187	0·133	1·02	0·836
*cyclo*Hexanol	0·534	0·209	0·224	0·203
*cyclo*Hexa-1 : 3-diene	0·635	0·473	0·346	0·618
Pent-1-ene	0·980	0·458	0·945	0·588
Oct-2-ene	1·01	0·717	0·702	0·668
Oct-1-ene	1·13	0·885	0·798	0·548
*cyclo*Hexa-1 : 4-diene	2·70	2·37	0·165	0·347
Benzene	2·74	2·73	0·132	0·224
*cyclo*Hexene	2·76	2·87	0·120	0·399

Consideration of the relatively large amounts of deuterium found in the products in the cases of *cyclo*hexene and *cyclo*hexa-1 : 4-diene suggested that here the reaction took place in two steps—a disproportionation reaction resulting in the production of *cyclo*hexane and benzene, followed by the deuteration of the latter hydrocarbon which was shown to exchange extensively under the conditions of these experiments. Comparison of boiling ranges before and after deuteration, and estimation, by titration, of the number of ethylenic bonds present (Table 2) indicated that such disproportionation had occurred. Zelinsky and Pavlow (*Ber.*, 1924, **56**, 1066; 1925, **58**, 185; cf. Corson and Ipatieff, *J. Amer. Chem. Soc.*, 1939, **61**, 1056; Taylor and Turkevitch, *Trans. Faraday Soc.*, 1939, **35**, 921) showed that *cyclo*hexene, when passed over a palladium catalyst at temperatures between 92° and 230°, isomerised according to the equation :

TABLE 2. *Boiling ranges and double-bond estimations.*

	Boiling range :		Double-bond content after deuteration
	before deuteration	after deuteration	
*cyclo*Hexene	83—84·5°	77·5—78·5°	0·01
	83—84·5	77—79	0·18
*cyclo*Hexa-1 : 4-diene	87	77—78	0·10
	87	77—78	0·04
*cyclo*Hexa-1 : 3-diene	83—86	80—84	0·56
	83—86	80—84	0·59

$$3C_6H_{10} = 2C_6H_{12} + C_6H_6$$

On the assumption that benzene and *cyclo*hexane had been formed in these proportions and by use of the values obtained separately for these hydrocarbons, calculation has shown that if the disproportionation took place independently as a first stage and was followed by deuteration of the resulting *cyclo*hexane and benzene the value for the deuterium content of the mixed products would not be more than 5%. If, however, conversion of the *cyclo*hexene into *cyclo*hexane proceeded by addition of hydrogen in equilibrium with the deuterium present in the solvent the calculated deuterium content would be raised to 7·5%, a value approximating more closely to the experimentally determined value of 8%.

Similar considerations apply to the case of *cyclo*hexa-1 : 4-diene. Here (cf. Zelinsky and Pavlow, *Ber.*, 1933, **66**, 1420) the disproportionation might be represented by the equation :

$$3C_6H_8 = C_6H_6 + 2C_6H_{12}$$

Calculation showed that random addition of deuterium and hydrogen atoms from the solvent to *cyclo*hexadiene would produce a deuterium content in the *cyclo*hexane of 13·9%. The *cyclo*hexane was separated in this case and the atom % of deuterium found to be 11·70.

The fall of the bromine absorption of *cyclo*hexa-1 : 3-diene to a value corresponding to about 0·5 double bond on treatment with palladium had been noted by Zelinsky and Pavlow (*loc. cit.*), who suggested the reactions

$$2C_6H_8 = C_6H_6 + C_6H_{10} \text{ (rapid)}$$

followed by

$$3C_6H_{10} = C_6H_6 + 2C_6H_{12} \text{ (slow)}$$

The comparatively low results obtained in the experiments with the 1 : 3-diene do not appear to be in conformity with this mechanism which would require more extensive deuteration of the products.

The small but significant changes in the boiling ranges of the samples of the octenes seem to indicate that some isomerisation may have occurred.

Of the exchange reactions reported in this paper those affording maximum deuteration of the products involved either a platinum-catalysed exchange reaction between benzene and deuterium oxide or a platinum-catalysed disproportionation occurring in deuterium oxide. To the established classes of exchange reactions involving ionisable hydrogen atoms, incipiently ionised hydrogen atoms or tautomeric changes, might therefore be added deuterations accompanying disproportionation or isomerisation in heavy water induced by heterogeneous catalysis.

EXPERIMENTAL

Deuterations.—All deuterations were carried out in presence of a platinum black catalyst in a medium of acetic acid and heavy water. The purified reactants were weighed into Pyrex tubes in quantities shown in Table 3, the weights of hydrocarbons being in approximately equimolecular proportions.

After being charged, the tubes were cooled in liquid air, evacuated, sealed, and shaken for 3 days at 123—133°.

TABLE 3. *Contents of reaction tubes : boiling ranges before and after deuteration.*

	Compound (g.)	Catalyst (g.)	D_2O (g.)	AcOH (g.)	Boiling range starting material	Boiling range product
Catalyst I						
n-Hexane	3·106	0·0805	0·427	1·635	68°	67—68°
*cyclo*Hexane	3·011	0·0810	0·427	1·636	80—80·2	80
*cyclo*Hexanol	2·934	0·0810	0·433	1·653	161	158—160
*cyclo*Hexene *	2·973	0·0810	0·435	1·645	83—84·5	77·8—78·5
Pent-1-ene	2·567	0·0810	0·429	1·641	38—39	38—39
Oct-1-ene	3·977	0·0810	0·433	1·651	119—121	120—122·5
Oct-2-ene	3·976	0·0810	0·431	1·644	122—124·5	123—124·5
*cyclo*Hexa-1 : 4-diene *	2·841	0·0810	0·434	1·640	87	77—78
*cyclo*Hexa-1 : 3-diene *	2·855	0·0810	0·437	1·651	83—86	80—84
Benzene	2·771	0·0810	0·434	1·640	80—80·5	78
Catalyst II						
n-Hexane	3·128	0·0810	0·431	1·646	68	67—68
*cyclo*Hexane	3·034	0·0810	0·432	1·648	80—80·2	80—80·5
*cyclo*Hexanol	3·017	0·0810	0·439	1·674	161	160—163
*cyclo*Hexene *	2·989	0·0810	0·434	1·653	83—84·5	77—79
Pent-1-ene	2·583	0·0810	0·433	1·654	38—39	37—39
Oct-1-ene	3·977	0·0810	0·432	1·651	120—121	120—122
Oct-2-ene	3·973	0·0810	0·431	1·648	123·5—125	122—124
*cyclo*Hexa-1 : 4-diene *	2·853	0·0810	0·431	1·643	87	77—78
*cyclo*Hexa-1 : 3-diene *	2·833	0·0810	0·432	1·646	83—86	80—84
Benzene	2·790	0·0810	0·432	1·647	80—80·5	77

* Disproportionation of the hydrocarbon took place.

Isolation of the Products.—The reaction tubes were cooled in liquid air and opened. Where possible, the two layers of liquid were separated and the hydrocarbons dried and freed from traces of acid with solid sodium hydroxide. The hydrocarbons were distilled and the ranges over which they boiled observed : in a few cases, some drops of a higher-boiling, coloured liquid remained. The residues contained considerably more deuterium than the parent hydrocarbons.

The *cyclo*hexanol samples required a different method of separation as the product in the reaction tube was homogeneous and probably contained some *cyclo*hexyl acetate. After removal of the catalyst this liquid was refluxed for 3 hours with aqueous sodium hydroxide (3 g. in 25 ml. of water), and the *cyclo*hexanol recovered by ether-extraction.

The products from the *cyclo*hexadienes were washed with water and dried ($CaCl_2$) to avoid the possibility of polymerisation. The only losses occurring were due to the slight solubility of the hydrocarbons in the acetic acid–water mixture and also to the minute quantities of polymer formed.

The acetic acid–water solvent from each reaction mixture was converted into silver acetate by the addition of aqueous acetic acid to a 30% excess of silver oxide, a quantity known to produce 99·9% conversion into silver acetate. The silver acetate was recovered by crystallisation from water after removal of the excess of silver oxide. Investigation showed that this recovery process caused negligible loss of deuterium from the methyl group of the acetic acid.

Isolation of the acetic acid from the *cyclo*hexanol deuteration involved steam-distillation of the acidified aqueous layer after ether-extraction of the *cyclo*hexanol. The acetic acid was converted into silver acetate by the method indicated above.

Preparation of Reactants.—Acetic acid. " AnalaR " acid was refluxed with chromium trioxide and purified by distillation and crystallisation.

Heavy water. " Norsk Hydro " product of 99·75% deuterium oxide by weight was used.

cyclo*Hexane,* n-*hexane,* cyclo*hexene, oct-*1*-ene, and oct-*2*-ene.* These were purified by distillation.

cyclo*Hexanol.* This was shaken with aqueous alkali, washed with water, dried (K_2CO_3), and distilled.

*Pent-*1*-ene.* *n*-Amyl alcohol was dehydrated with sulphuric acid (Adams, Kamm, and Marvel, *J. Amer. Chem. Soc.*, 1918, **40**, 1950). The product was fractionated in a Widmer column.

cyclo*Hexa-*1 : 4*-diene.* Quinol was hydrogenated under pressure with Raney nickel (Adkins and Cramer, *J. Amer. Chem. Soc.*, 1930, **52**, 4349). The diol produced was dehydrated with concentrated sulphuric acid, and the product fractionated in a Widmer column (Senderens, *Compt. rend.*, 1923, 1183).

cyclo*Hexa-*1 : 3*-diene.* 1 : 2-Dibromo*cyclo*hexane was prepared by bromination of *cyclo*hexene (*Org. Synth.*, Coll. Vol. II, Wiley, 1943, p. 171). Dehydrobromination was accomplished by boiling the dibromide in quinoline (Zelinsky and Gorsky, *Ber.*, 1908, **41**, 2479).

Benzene. " Crystallisable " benzene was shaken several times with concentrated sulphuric acid, washed with water, dried, crystallised, and distilled.

Platinum black on asbestos catalyst. Formaldehyde reduction of a platinum salt solution containing a suspension of purified asbestos produced the catalyst (Vogel, " Textbook of Practical Organic Chemistry," Longmans, 1948, p. 842, Method A).

Separation of the Saturated Disproportionation Product of cyclo*Hexa-*1 : 4*-diene.*—A portion of the product (1·11 g.) from the reaction mixture was treated with 30% oleum (an equal volume), and the mixture set aside for 15 minutes at room temperature. The unchanged hydrocarbon was separated after dilution of the mixture with water. This portion was assumed to be *cyclo*hexane and was washed with water and dried ($CaCl_2$) (yield, 0·05 g.).

Refractive Index Measurements on the Products of cyclo*Hexene Disproportionation.*—Zelinsky and Pavlow (*Ber.*, 1924, **57**, 1066; 1925, **58**, 185) observed that passage of *cyclo*hexene over palladium at 164° and 223° gave products of n_D^{20} 1·4448 and 1·4489 respectively. These values they compared with a 1 : 2 benzene–*cyclo*hexane mixture with n_D^{20} 1·4455. Measurements on the *cyclo*hexene before deuteration gave n_D^{18} 1·4484 and on the products after deuteration n_D^{18} 1·4422.

Estimation of Deuterium.—The water produced by combustion of the deuterio-compounds in air or oxygen was purified by a modification of the method used by Keston, Rittenberg, and Schoenheimer (*J. Biol. Chem.*, 1937, **122**, 227), and the deuterium content of the water measured by the " Gradient Tube " method (Linderstrøm-Lang, Jacobsen, and Johansen, *Compt. rend. Trav. Lab., Carlsberg*, 1938, **23**, 17; Linderstrøm-Lang and Lanz, *ibid.*, 1938, **21**, 315).

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