694. *The Catalytic Deuteration of Organic Compounds. Part III.* Exchange Reactions of Saturated Aliphatic Carboxylic Acids.*

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The replacement of the carbon-bound hydrogen in a number of carboxylic acids during homogeneous reaction in solution in deuterium oxide and during reaction in presence of a platinum catalyst has been re-examined, and a more detailed study made of the distribution of deuterium in propionic acid deuterated by each method. Chemical degradation of the deuterated propionic acids has shown that in the homogeneous reaction deuterium replaced only those hydrogen atoms attached to the α-carbon atom, whereas, in the reaction in presence of the catalyst, simultaneous replacement of all carbon-bound hydrogen appeared to occur. This is supported by preliminary information from a study of the cracking patterns in the mass spectrometer of specimens of methyl propionate derived from the deuterated propionic acids.

Early investigations of the homogeneous reaction involving the exchange of the carbon-bound hydrogen atoms of acetic acid dissolved in deuterium oxide led to conflicting results (Lewis and Schutz, *J. Amer. Chem. Soc.*, 1934, **56**, 493; Hall, Bowden, and Jones, *ibid.*, p. 750; Munzberg, *Z. physikal. Chem.*, 1935, **13**, *B*, 21; Lazareff, *Compt. rend.*, 1935, **200**, 1671; Erlenmeyer, Schoenauer, and Schwarzenbach, *Helv. Chim. Acta*, 1937, **20**, 726; Liotta and La Mer, *J. Amer. Chem. Soc.*, 1937, **59**, 946), but the nature of this reaction has been clarified to some extent by Bok and Gieb (*Z. physikal. Chem.*, 1939, **183**, *A*, 353) who showed that exchange with deuterium takes place readily with the hydrogen atoms of the methyl group, the reaction being promoted by acid–base catalysis. The suggested mechanism, involving enolisation, was analogous to that proposed for the deuteration of acetone, although the experimental results are not inconsistent with alternative mechanisms.

In an examination of the exchange reactions of a series of monocarboxylic acids in dilute deuterium oxide, Ives (*J.*, 1938, 81) reported that, among the saturated aliphatic acids, no detectable exchange occurred at 100° in the cases of propionic, *n*-butyric, and *iso*butyric acids, but subsequently Schanzer and Clusius (*Z. physikal. Chem.*, 1942, **190**, *A*, 241) found an exchange for the first two of these acids in presence of added alkali, the exchange being restricted to the hydrogen atoms attached to the α-carbon atom. Exclusive α-deuteration has been claimed (Schoenheimer, Rittenberg, and Keston, *J. Amer. Chem. Soc.*, 1937, **59**, 1765) on treatment of palmitic acid with concentrated deuteriosulphuric acid at 100°. On the other hand, Van Heyningen, Rittenberg, and Schoenheimer (*J. Biol. Chem.*, 1938, **125**, 495) found that higher fatty acids (C_6—C_{18}) exchange hydrogen for deuterium readily when heated to 130° in deuterium oxide in presence of alkali and a platinum catalyst. On the basis of the amount of deuterium introduced into the molecule these authors claimed that, under these conditions, many, and possibly all, of the hydrogen atoms were exchanged although equilibrium was not reached after twelve days. It is clear that the enolisation mechanism suggested for the acid–base-catalysed exchange reaction can result in exchange of the hydrogen atoms attached to the α-carbon atom only; such a mechanism cannot lead to exchange of hydrogen atoms attached to other carbon atoms.

Preliminary comparative experiments in the present study have shown that the presence of a platinum catalyst enhances the deuteration of those acids which undergo exchange in the homogeneous reaction and promotes the deuteration of other acids with which the homogeneous reaction does not take place or is too slow for detection. In these experiments, summarized in Table 1, concentrated solutions of the acids in deuterium oxide were shaken at 125—130°, in presence or absence of a platinum catalyst, for 2—10 days. The molar concentration of the acid was, in most cases, about 7—12, while that of the

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* Part II, *J.*, 1952, 576.

deuterium oxide varied between 15 and 25, but experiments have also been carried out at concentrations outside the limits of the ranges. For comparison, all the results in Table 1 have been calculated on a common concentration basis of 10M-acid and 10M-deuterium oxide, and for a period of one day, since it was found that, under the conditions employed, equilibrium was not approached in these reactions.

TABLE 1. *Overall deuterium (atom %) introduced per day.*

Concn. of acid = 10M. Concn. of D_2O = 10M.

	$CH_3{\cdot}CO_2H$	$C_2H_5{\cdot}CO_2H$	$(CH_3)_3C{\cdot}CO_2H$	$HO{\cdot}CH(CH_3){\cdot}CO_2H$	$CH_3O{\cdot}CH(CH_3){\cdot}CO_2H$
Homogeneous exchange ...	2·9	0·5	← No exchange →		
Pt-catalysed exchange ...	5·4	1·1	0·18	0·58	0·04

As shown for lactic acid in Table 2, the extent of the exchange reaction at the concentrations used was directly proportional to the weight of the platinum catalyst present; from this it may be concluded that the catalyst surface was saturated and that adsorption on the catalyst was a preliminary step in the exchange reaction.

TABLE 2.

Lactic acid (g.)	1·139	1·235	1·239	1·199
D_2O (g.)	1·109	1·109	1·112	1·109
Catalyst (g.)	—	0·025	0·050	0·100
Time (days)	2	2	2	2
Deuterium in lactate (atom %)	0·00	0·85	1·86	4·16

The deuteration of trimethylacetic acid (see Table 1) has demonstrated that hydrogen attached to a carbon atom other than the α-carbon atom can be involved in the exchange reaction catalyzed by platinum, but it is of interest, in the case where both α- and β-hydrogen atoms are available, to attempt to differentiate between the homogeneous and the heterogeneous reaction, and to determine the distribution of deuterium in the deuterated acids from both reactions. Propionic acid, deuterated with and without a catalyst, was degraded by the reactions, $CH_3{\cdot}CH_2{\cdot}CO_2H \longrightarrow CH_3{\cdot}CHBr{\cdot}CO_2H \longrightarrow CH_3{\cdot}CH(OH){\cdot}CO_2H \longrightarrow CH_3{\cdot}CO_2H$, and from determinations of the deuterium content of the propionate and the lactate or the acetate, the distribution of the deuterium between α- and β-positions was readily calculated. Table 3 shows clearly that in presence of the platinum catalyst (Expts. 1 and 3) extensive exchange had occurred involving hydrogen atoms attached to both α- and β-carbon atoms, whereas in the absence of platinum (Expts. 2 and 4) the exchange was almost wholly confined to the hydrogen atoms in the α-position. The possibility exists that a loss of deuterium may occur during the oxidative degradation of the acids but support for these results has been provided by mass-spectrometric examination of specimens of methyl propionate prepared from the deuterated propionic acids. For this purpose, consideration of a small region of the cracking patterns of the ester samples is adequate; a fuller account of these and of the cracking patterns of the parent deuterated propionic acids will be reported in due course. As the basis of comparison of the deuterated methyl propionates the large peak at mass 29, corresponding to $C_2H_5^+$ particles, was used as a standard; summarized results of the examination of the relevant portion of the cracking patterns are shown in Table 4.

TABLE 3. *Deuteration of propionic acid.*

		Deuterium content (atom %)				
		Overall			Propionate	
Expt.	Catalyst	Propionate	Lactate	Acetate	α-Position	β-Position
1	Present	10·41	7·75	—	13·30	8·47
2	Absent	5·93	3·15	—	13·92	0·60
3	Present	20·90	13·66	9·03	38·70	9·03
4	Absent	16·32	9·5	0·48	40·20	0·48

Comparison of the heights of the peaks for masses 30 and 31, corresponding to $C_2H_4D^+$ and $C_2H_3D_2^+$ respectively, in the case of experiments 1 and 2 shows that only where the deuteration of the acid had taken place in presence of the platinum catalyst is there evidence of the introduction of two deuterium atoms into the molecule. No definite conclusion regarding α- and β-substitution can be legitimately drawn from this result since the possibility exists that the two deuterium atoms may both be attached to the same carbon atom and the absence of any dideuterated radical in experiment 2 may be due simply to the relatively small amount (*ca.* 6%) of deuterium in the acid. The esters used in experiments 3 and 4 were prepared from the specimens of the deuterated acids bearing the same numbers in Table 3; and here mass spectrometry showed that, even in the absence of the platinum catalyst, more than one hydrogen atom had been exchanged. The large peak at mass 31 reported for experiment 4 could arise as the result of dideuteration in which both deuterium atoms were attached to the α-carbon atom, since the ester, in this case, was prepared from a specimen of propionic acid containing 16% of deuterium. The greater ease of introduction of further deuterium atoms, which must be attached to the β-carbon atom, when the catalyst is present can be illustrated by expressing the peak heights at the different mass numbers as percentages of the total of all the $C_2H_nD_{5-n}$ species present :

TABLE 4. *Mass-spectrometric examination of methyl propionate.*

		Peak heights				
	Mass no.	29	30	31	32	33
Expt.	Source of acid					
1	Pt-catalysed exchange	100	59·98	64·73	—	—
2	Homogeneous ,,	100	46·5	0	—	—
3	Pt-catalysed ,,	100	56·4	76·5	47·9	6·8
4	Homogeneous ,,	100	123·2	72·9	17·7	4·4

	Abundance (%)				
Mass no.	29	30	31	32	33
Expt. 3 Pt-catalysed exchange	36·3	19·2	24·9	17·2	2·4
Expt. 4 Homogeneous ,,	32·8	39·2	21·3	5·6	1·0

A rigid quantitative significance cannot yet be attached to these results owing to the possible existence of an isotope effect, but from these figures approximate values of 20·4 and 15·3 for the overall deuterium contents of the two specimens of propionic acid have been calculated. These values are subject to refinement on more detailed analysis of the mass-spectrometric data, but they are already in agreement with the direct determinations reported in Table 3.

Sufficient evidence to justify consideration of the detailed mechanism of these exchange reactions is not yet available but it is apparent that the platinum-catalysed reaction results in substitution at all carbon atoms.

EXPERIMENTAL

The methods used for the deuteration reactions, preparation of the catalyst, and determination of the deuterium content of the combustion water from the deuterated products have been described in Part I (*J.*, 1952, 572). All combustions were carried out on the silver salts prepared from the acids, after deuteration, by treatment with excess of silver carbonate or silver oxide, so that correction for the deuterium in the carboxyl group was unnecessary. In the case of lactic acid, all samples were treated with a large excess of ordinary water in order to " normalize " the hydroxyl-hydrogen.

Bromination of Propionic Acid.—α-Bromopropionic acid was prepared from the deuterated specimens of propionic acid by the method described by Marvel (*Org. Synth.*, **20**, 106). Final purification was by distillation, the fraction distilling at 100—102°/20 mm. being collected. Yields were 75—86%.

Preparation of Silver Lactate from α-Bromopropionic Acid.—Silver oxide (5·7 g.) was added during 3 hr. to a solution of α-bromopropionic acid (3·4 g.) in water (300 c.c.), the temperature being kept at 80°. The solution was filtered after being kept overnight, and the filtrate heated to 70—80° for 4 hr. with silver carbonate (2 g.). After removal of the excess of silver carbonate by filtration, the solution was evaporated to dryness and the resulting silver lactate dried *in vacuo* over concentrated sulphuric acid (yields, 78—83%).

Oxidation of Silver Lactate.—Silver lactate (2 g.), potassium permanganate (1 g.), and dilute sulphuric acid (5N; 60 c.c.) were steam-distilled until a distillate of 450—500 c.c. had been collected. The distillate was then heated for 1 hr. with silver oxide (1·4 g.) and silver carbonate (0·5 g.), filtered, and concentrated by evaporation, frequent filtration from deposited silver oxide being necessary during the concentration. Evaporation to dryness gave silver acetate in 30—36% yields.

Preparation of Methyl Propionate.—Methyl esters of the deuterated propionic acids for examination in the mass spectrometer were prepared by treatment of the silver salts with methyl iodide, and, for comparison, by the use of diazomethane.

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