[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

A Study of the Esterification of Benzoic Acid with Methyl Alcohol Using Isotopic Oxygen

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There has been much discussion as to which linkages are broken in the two reactions: (a) the saponification of an ester, and (b) the esterification of a carboxylic acid. The first of these was studied by Polanyi and Szabo,[1] who demonstrated that the saponification of amyl acetate in heavy oxygen water results in amyl alcohol of ordinary isotopic composition. The solution of the second problem, for which evidence has been inconclusive up to the present, is the subject of this paper.

The formation of water by the acid-catalyzed esterification of benzoic acid with methyl alcohol may be represented by either of the equations

$$C_6H_5CO \,\vdots\, OH + H \,\vdots\, O\,CH_3 \longrightarrow C_6H_5COOCH_3 + H_2O \quad (1)$$

$$C_6H_5CO\,O \,\vdots\, H + HO \,\vdots\, CH_3 \longrightarrow C_6H_5COOCH_3 + H_2O \quad (2)$$

The purpose of this work is to distinguish between (1) and (2) by allowing ordinary benzoic acid to react with methyl alcohol containing an increased concentration of oxygen 18. If mechanism (1) is correct, such an experiment will yield water of ordinary isotopic composition (0.200% oxygen 18), whereas by mechanism (2), heavy oxygen water will be obtained.

Attempts to make the reaction go to completion in a short time resulted in esterification of the large amount of hydrochloric acid catalyst which must be used. Therefore the concentrations of catalyst and reactants were so adjusted as to give a half-time of about two weeks at 25°, and samples were withdrawn at known intervals for determination of the heavy oxygen content of the water. The reaction mixtures had the following composition: methyl alcohol, 68.6% by volume; hydrochloric acid, 0.123 *M*; benzoic acid, 2.70 *M*; water, 2.72 *M* (4.9% by volume). A large concentration of benzoic acid was necessary in order to have appreciable amounts of water formed by the esterification. The initial presence of the water, although it would dilute any heavy oxygen water formed, made it possible in the first stages of the reaction to recover enough water for analysis.

Rate of the Reaction.—In order to calculate the concentration of heavy oxygen in the water at any point, the amount of water formed by the esterification must be known. 20.4 cc. of reaction mixture of the above composition was prepared by dissolving in 14.00 cc. of a freshly prepared methanol–hydrochloric acid solution (0.1803 *M*), 1.00 cc. of water and 6.72 g. of benzoic acid. After putting the solution into the thermostat, 1.00-cc. samples were withdrawn and titrated with standard 0.1121 *N* sodium hydroxide to determine the benzoic acid remaining. The results are given in Table I. A plot of these data was made so that, in the experiments given below, one could readily determine at any time the percentage of reaction and therefore the number of moles of water formed.

TABLE I

RATE OF ESTERIFICATION AT 24.93°

Time, hours	Titer, cc.	% reaction
0.0	25.40	0.00
22.0	23.56	7.58
43.3	21.89	14.46
96.4	19.34	24.97
144.0	17.41	32.92
209.9	15.65	40.17
383.0	12.01	55.17

The amount of the reverse reaction which takes place was determined by allowing a methyl alcohol solution containing 2.50 *M* methyl benzoate, 2.50 *M* water and 0.114 *M* hydrochloric acid to stand in the thermostat. Samples withdrawn for titration of the benzoic acid formed showed that over a period of 196.5 hours, only 1.3% of the possible hydrolysis had taken place. This error is negligible, since in this work the esterification was never continued beyond 55% reaction.

Exchange Experiments.—It is obvious that exchange of oxygen between the water in the system and the methyl alcohol, methyl benzoate or benzoic acid, will give rise to errors whose magnitudes must be determined.

The fact that methyl alcohol does not exchange in the presence of hydrochloric acid already has been reported.[2]

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[1] Polanyi and Szabo, *Trans. Faraday Soc.*, **30**, 508 (1934).

[2] Roberts, *J. Chem. Phys.*, **6**, 294 (1938).

To determine whether methyl benzoate exchanges, a methyl alcohol solution containing 2.49 *M* methyl benzoate, 0.123 *M* hydrochloric acid and 2.96 *M* heavy oxygen water was allowed to stand in the thermostat. Twenty-five-cc. samples were taken and the water was recovered by fractional distillation and analyzed (see experimental part). Table II shows the results obtained. It can be seen that within experimental error no exchange of the methyl benzoate has taken place.

TABLE II

EXCHANGE EXPERIMENT WITH METHYL BENZOATE

Time, hours	H_2O recovered, cc.	% H_2O^{18}
0	....	0.462
172	0.43	.464
314	.67	.460

The amount of exchange of the benzoic acid was determined as follows: 102 cc. of a reaction mixture, having the composition originally given, was set up, using ordinary benzoic acid, ordinary methyl alcohol and water containing 0.509% oxygen 18. If no exchange of the benzoic acid were taking place, the heavy oxygen content of the water would be lowered by dilution with the ordinary water arising from the esterification. The amount of such lowering could be determined by taking the weighted mean of the composition of the water originally present and the water formed. If, on the other hand, the benzoic acid were exchanging, the heavy oxygen content of the water would be decreased even further than that calculated. Table III shows the results obtained.

TABLE III

EXCHANGE OF BENZOIC ACID UNDER CONDITIONS OF ESTERIFICATION

Initial composition: 0.2752 mole benzoic acid, 0.2775 mole of H_2O^{18}, 70 cc. of methanol, HCl 0.123 *M*.

Time, hours	% reaction	Mole H_2O formed	% H_2O^{18} calcd.	H_2O recovered, cc.	% H_2O^{18} found
0	0.0	0.0000	0.509	0.08	0.510
94.0	24.5	.0674	.449	.28	.431
206.4	39.9	.1098	.421	.29	.400
378.8	54.7	.1505	.400	.34	.371

A comparison of the fourth and sixth columns will show that some exchange of the benzoic acid is taking place. This observation is in accord with the fact that benzoic acid has been shown to exchange both its oxygens rather readily.[2] That the exchange occurring in these experiments is small can be seen from the following consideration. If immediate complete exchange of the benzoic acid had taken place, the composition of the water would drop to 0.304% oxygen 18. The differences in Table III are of much smaller magnitude than this decrease. Rough calculations of the amount of exchange were made by separating the two simultaneous processes, *i. e.*, by assuming that first the known amount of esterification takes place and then the remaining benzoic acid exchanges with the water. It must be remembered that both oxygens of the benzoic acid are available for the exchange process. The results of these calculations are given in the second column of Table IV.

Esterification with $CH_3O^{18}H$.—The final experiment, performed at the same concentrations, contained ordinary benzoic acid, ordinary water and methyl alcohol containing 0.372% oxygen 18. In calculating the results to be expected by mechanism (2), a correction must be made for the decrease in heavy oxygen content of the water due to exchange with the benzoic acid. This was done by separating the two reactions as outlined above, and using the data on the benzoic acid exchange from the above experiment. These calculations result in the values given in Table IV. It can be seen that the corrections are comparatively small, and that they have very little effect upon the difference of oxygen content to be expected by the two mechanisms.

TABLE IV

CORRECTIONS FOR EXCHANGE OF BENZOIC ACID IN DATA CALCULATED FOR MECHANISM (2)

% reaction	Equivalents of benzoic acid exchanged	% H_2O^{18} expected for mechanism (2) Original	Corr.
24.5	0.0269	0.234	0.232
39.9	.0407	.249	.244
54.7	.0726	.260	.251

The results of the heavy oxygen methyl alcohol experiment are given in Table V.

TABLE V

ESTERIFICATION USING $CH_3O^{18}H$

Time, hours	Percentage H_2O^{18} calculated Mechanism (1)	Mechanism (2)	H_2O recovered, cc.	H_2O^{18} found, %
0	0.200	0.200	....	.....
94.0	.200	.232	0.28	0.204
212.4	.200	.244	.42	.200
334.0	.200	.250	.78	.200

These experiments demonstrate that in the esterification of benzoic acid with methyl alcohol, the oxygen in the water formed originates entirely from the benzoic acid. It is notable that this is in accord with the conclusions drawn from experiments with mercaptans and thioacids.[3]

Experimental

Materials.—Methyl alcohol was purified by the method of Lund and Bjerrum.[4] Benzoic acid of the Mallinckrodt "Analytical Reagent" grade was found by titration to contain a maximum of 0.2% of impurity, and was therefore used directly. Hydrochloric acid was of the C. P. reagent quality. Hydrochloric acid solutions in methanol were prepared by passing the gas into anhydrous methanol; the solutions were used immediately after preparation. Standard 0.1 *N* sodium hydroxide, made up from a saturated carbonate-free solution, was standardized against Bureau of Standards potassium acid phthalate. Methyl benzoate was shaken three times with sodium carbonate solution, three times with water, dried over calcium chloride, and fractionated.

Heavy oxygen water, prepared by fractional distillation,[5] was refluxed with alkaline permanganate for one hour, fractionated and distilled from chromic acid. Heavy oxygen methyl alcohol, also prepared by fractional distillation,[6] was treated with magnesium and iodine in the same manner as the ordinary material[4] and fractionated. The middle fraction was further fractionated after the addition of two drops of phosphoric acid. The middle fraction, which distilled constantly at 65°, contained traces of volatile amines from which the methanol could not be freed completely. These small amounts of impurity caused the slow formation of a light yellow color in the reaction mixture when the methanol was used for the esterification.

Analyses.—The mass spectrograph was of the type described by Bleakney[7]; the procedure for analysis of the water was that of Cohn and Urey.[8] In the present work, the water recovered from the experiments was shaken with 26 cc. of ordinary carbon dioxide gas at atmospheric pressure for five hours. The precision of analyses was generally 1% or better.[9]

The heavy oxygen methyl alcohol was analyzed for its oxygen content by converting it to water and analyzing the water as above. This was done by passing a mixture of the methanol vapor and hydrogen through a quartz tube which contained a nickel spiral at about 650° and a thoriated nickel catalyst[10] at about 400°. The water was caught in a trap enclosed in solid carbon dioxide–acetone mixture; the yields were practically quantitative. Heavy oxygen water, passed through the apparatus under the same conditions, was recovered with no decrease in heavy oxygen content, demonstrating that exchange with the quartz tube or with any oxide in the catalyst had not taken place. Analysis of ordinary methyl alcohol by this method gave 0.204% oxygen 18.

Esterification Experiments.—All operations were carried out in glass apparatus fitted with interchangeable ground joints. Esterification experiments were carried out in the thermostat kept at 24.93 ± 0.02°. Twenty-five cc. samples of reaction mixture were pipetted for recovery of the water, and from these the methanol, water and a small amount of the methyl benzoate were distilled *in vacuo* at room temperature. This initial process took thirty minutes at a maximum, thus causing a negligible error in the reaction time recorded. The distillate was then fractionated at atmospheric pressure, the water and methyl benzoate remaining behind. In the final step, the water was distilled off *in vacuo* from the methyl benzoate. The water samples obtained by this method were always contaminated by small amounts of methanol and methyl benzoate; these impurities can have no effect on the results obtained by the method of analysis given above.

Summary

Ordinary benzoic acid has been esterified with heavy oxygen methyl alcohol in the presence of a small amount of hydrochloric acid catalyst. The water resulting from the reaction is of ordinary isotopic composition, demonstrating that the oxygen in the water formed originates entirely from the benzoic acid. Slow exchange of the benzoic acid proceeds simultaneously with the esterification, necessitating a small correction in the calculated results.

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[3] Reid, *Am. Chem. J.*, **43**, 489 (1910).

[4] Lund and Bjerrum, *Ber.*, **64**, 210 (1931).

[5] Huffman and Urey, *Ind. Eng. Chem.*, **29**, 531 (1937).

[6] Unpublished work of Huffman and Keston in this Laboratory.

[7] Bleakney, *Phys. Rev.*, **40**, 496 (1932).

[8] Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).

[9] Mass spectrograph analyses done by Dr. John E. Gorham.

[10] Russell and Fulton, *Ind. Eng. Chem., Anal. Ed.*, **5**, 384 (1933).