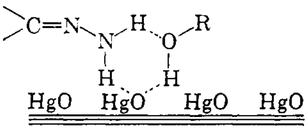
time an active site is destroyed by reacting a new one is produced, the reaction system would be expected to exhibit zero order kinetic behavior.[15] A transition state (II) for reaction at an active site can be written so that the water (or alcohol)



II

molecule involved in the six membered cyclic complex is well situated to activate an adjacent mercuric oxide site, after reacting.

EXPERIMENTAL

Analytical grade mercuric oxide (yellow), freshly prepared camphor hydrazone,[16] and carefully purified solvents were used throughout the investigation. Unless otherwise stated, the oxidations were carried out in refluxing solvents with rapid agitation by a Hershberg type stirrer. An electrically heated oil bath controlled to ±2° was used as a source of heat. The volatile products were analyzed by the infrared method of Swann and Cripwell[17] and by vapor phase chromatography using a standard 2-meter column having butyl phthalate on firebrick as the fixed phase.

d-Camphor hydrazone. The hydrazone was prepared by refluxing *d*-camphor with 4 moles of 95% hydrazine and 1 mole of acetic acid in three times its weight of absolute ethanol for 4 hr. After removing the ethanol at aspirator pressure, the reaction mixture was brought to its original volume with ether, the lower hydrazine layer was removed and the reaction mixture was washed with 10% sodium hydroxide saturated with sodium chloride followed by saturated sodium chloride alone. Removal of the solvents under aspirator pressure followed by distillation at reduced pressure gave camphor hydrazone, m.p. 55°, b.p. 68° (5 mm.), in about 75% yield.

Kinetic procedure. A solution of 3 g. of camphor hydrazone in 25 ml. of the solvent being investigated was placed in a three necked flask equipped with a Hershberg stirrer, a condenser, and a solid addition tube. The solution was then heated to the desired temperature, the stirring was begun and the mercuric oxide (8 g.) was quickly added in one portion. The nitrogen evolved was measured by a gas burette attached to the condenser. Under these conditions the apparent zero order rate constant for the reaction in refluxing ethanol was 7×10^{-4} moles/min.

Oxidation in ethanol-d_1. Ten grams of camphor hydrazone was dissolved in 20 ml. of ethanol-d_1 at room temperature. After a few minutes 20 g. of mercuric oxide was added, and the mixture was refluxed with stirring for 2 hr. Ethanol (10 ml.) was added to the cooled reaction mixture, the slurry was filtered and the clear filtrate was quickly distilled over a short path leaving the higher boiling, nonvolatile products behind. The addition of an equal volume of cold water to the distillate gave a cloudy solution which was extracted four times with pentane. Careful removal of the solvent from the dried pentane extracts left a thick oil consisting largely of tricyclene. The tricyclene was freed from traces of camphene by treatment with alkaline permanganate. Two distillations at atmospheric pressure gave 2.8 g. of tricyclene (35%), m.p. 64.5°.

DEUTERIUM ANALYSIS

Reaction Solvent	% Tricyclene-d_1
Ethanol	0.05
Ethanol-d_1	0.41[18]

Acknowledgment. We are grateful to Mr. Seymour Meyerson, Whiting Research Laboratories, Standard Oil Company (Indiana), for the mass spectral analysis. We also thank Dr. G. J. Karabatsos for many helpful discussions.

EAST LANSING, MICH.

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[15] K. J. Laidler, *Chemical Kinetics,* McGraw-Hill, New York, 1950, 154.

[16] Camphor hydrazone is quite hygroscopic and the hydrate decomposes to camphor azine at room temperature. We have also detected the presence of camphor in older samples.

[17] G. Swann and F. J. Cripwell, *Ind. Chem.,* **24** 573 (1948).

[18] The small but real deuterium content observed is probably due to enolization of the hydrazone prior to being oxidized.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, CASE INSTITUTE OF TECHNOLOGY]

Cation-Exchange Resin Catalyzed Hydrolysis and Decarboxylation of Esters of Acetoacetic and Malonic Acids

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The simultaneous hydrolysis and decarboxylation of negatively substituted esters as catalyzed by cation-exchange resins was compared to similar reactions catalyzed by equivalent amounts of sulfuric acid. In the acetoacetic ester system the resin was found to be more efficient than an equivalent amount of sulfuric acid. With diethyl malonate and ethyl hydrogen malonate the resin system specifically favored the formation of ethyl acetate, seemingly a product of decarboxylation of the half-ester. Essentially no difference was obtained, however, in the relative efficiencies of the two catalysts for the overall reaction. The resin again was found to be the more effective catalyst for the hydrolysis and decarboxylation of α-ethylmalonic ester.

Esters of acetoacetic and malonic acids are usually hydrolyzed in mild alkaline solution to give the alkali metal salts of the acids. Heating the acidified solutions resulting from these hydrolyses results in decarboxylation and the formation of a methyl ketone or an acid. Acid catalyzed hydrolysis of these esters would be expected to be

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[1] Taken from the Ph.D. thesis of John A. Oscar.

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accompanied by decarboxylation, but these reactions appear not to have been investigated very extensively. Ion exchange resins have proved to be interesting catalysts and have been used by Hammett and co-workers[3–7] in the hydrolysis of esters.

Haskell and Hammett[6] conclude that the major factor determining the difference in rates between the heterogeneous and the homogeneous catalysts appear to be the loss in internal entropy of the ester molecule which accompanies its fixation on the skeleton of the resin particle in the formation of the transition state.

Riesz and Hammett[7] report that the activity of the resin can be modified by changing the resin surface by formation of amine salts. The effect of surface modification on the effectiveness of the resin as a catalyst was also indicated by the work of Astle and Gergel,[8] using anion exchange resins in the Knoevenagel reaction.

It was the purpose of this investigation to study the simultaneous hydrolysis and decarboxylation of acetoacetic and malonic esters in the presence of cation exchange resins of the polystyrenesulfonic acid type and to compare their effectiveness with equivalent amounts of a conventional acid such as sulfuric acid.

EXPERIMENTAL

Cation exchange resin catalyzed hydrolysis and decarboxylation of acetoacetic esters. Dry Dowex 50W × 2 resin (6.0 g., 30 meq.), ethyl acetoacetate (65.0 g., 0.5 mole) and 35.6 g. of water were added to a 300-ml. round bottom, three neck flask equipped with thermometer. An Ace "Trubore" stirrer and an efficient reflux condenser were connected to a Dry Ice–acetone trap. The reaction mixture was heated with constant stirring at 75° for 6 hr. during which time a total of 24.9 g. of volatile material was collected in the Dry Ice–acetone trap. The reaction residue was filtered, the resin washed with water, and the filtrate fractionated in a 90-cm. column, 2 mm. I. D. packed with a spiral wire helix. The distillation residue was analyzed for carbonyl according to the method of Bryant and Smith [9] to determine the amount of unchanged ethyl acetoacetate. This procedure indicated a conversion of 88.6%. The volatile material collected during reaction was combined with the distillate and analyzed for carbonyl in order to obtain the quantity of acetone formed. This indicated a conversion of 88.5% to acetone.

Sulfur acid catalyzed hydrolysis and decarboxylation of ethyl acetoacetate. The procedure was the same as above except that 30 meq. of concd. sulfuric acid was added to the 36 g. of water. At the end of 6 hr. the catalysst was just neutralized with sodium carbonate solution, the reaction residue was fractionated and the products analyzed as above.

Cation exchange resin catalyzed hydrolysis and decarboxylation of ethyl α-n-propylacetoacetate. Dowex 50W × 2 (6.0 g., 30 meq.); ethyl α-*n*-propylacetoacetate (86.4 g., 0.5 mole); and 36.0 g. (2 moles) water were added to the apparatus described above. The reaction mixture was heated with constant stirring at 75° for 40 hr. The reaction residue was filtered, and the resin washed with 125 ml. of methanol. The filtrate was analyzed without further separation as follows: The total milliequivalents of carbonyl and the total milliequivalents of ester were found. The milliequivalents of 2-hexanone was taken as the difference between these two values. The conversion to 2-hexanone was found to be 21.8%.

Cation exchange resin catalyzed hydrolysis and decarboxylation of diethyl malonate. The reaction apparatus was the same as described above except that an azeotrope trap and reflux condenser were replaced by a 200-mm. long, 12 mm. I.D. 1/8 in. glass helices packed distillation column and distillation head. Reactants were added as follows: 6.0 g. (30 meq.) of Dowex 50W × 2, 80.2 g. (0.5 mole) diethyl malonate and 36.0 g. (2.0 moles) water. The reaction mixture was heated with constant stirring for 8 hr. at a temperature of 95–111° during which time 56.6 g. of volatile material was collected at a head temperature of 70–74°. The reaction residue was filtered and the resin washed with water. The reaction distillate was titrated with standard base to obtain the milliequivalents of acid and saponified to obtain milliequivalents of ethyl acetate formed. The reaction residue was titrated to obtain the total milliequivalents of acid present and saponified to obtain the milliequivalents of unchanged diethyl malonate. From these data the yield of ethyl acetate was found to be 47%, of acetic acid 24%, and malonic acid 33%.

DISCUSSION

Acetoacetic esters: The results of the hydrolysis of acetoacetic esters are summarized in Table I. It is noted that in each case the rate of hydrolysis and decarboxylation is significantly greater in the presence of the cation exchange resin than when an equivalent amount of sulfuric acid was used as the catalyst. In no case could acetoacetic acid be detected, suggesting that the rate of decarboxylation may be faster than the rate of hydrolysis. Steric factors seem to be most important in affecting the rate of hydrolysis and decarboxylation, since introduction of one group (methyl) on the

TABLE I

ACID-CATALYZED HYDROLYSIS AND DECARBOXYLATION OF ACETOACETIC ESTERS AT 75°

Ester[a]	Catalyst[b]	Time, Hr.	Reaction,[e] %
Acetoacetic ester	Resin	6	88
	Resin	6	89
	H_2SO_4	6	58
α-Methylacetoacetic ester[c]	Resin	6	13
α-Ethylacetoacetic ester	Resin	6	17
	H_2SO_4	6	1
α-*n*-Propylacetoacetic ester	Resin	40	22
	H_2SO_4	40	2
α-*n*-Butylacetoacetic ester	Resin	40	12
	H_2SO_4	40	2
α-Isopropylacetoacetic ester	Resin	40	12
	H_2SO_4	40	1
α,α-Diethylacetoacetic ester[d]	Resin	40	1

[a] As mole ester with 2.0 mole water. [b] Resin = Dowex 50 × 2; 30 meq. acid in each case. [c] 0.27 mole ester employed. [d] 0.36 mole ester employed. [e] Only reaction product methyl ketones and carbon dioxide.

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(3) S. A. Bernhard and L. P. Hammett, *J. Am. Chem. Soc.*, **75**, 1798 (1953).

(4) S. A. Bernhard and L. P. Hammett, *J. Am. Chem. Soc.*, **75**, 5834 (1953).

(5) S. A. Bernhard, A. Garfield, and L. P. Hammett, *J. Am. Chem. Soc.*, **76**, 991 (1954).

(6) V. C. Haskell and L. P. Hammett, *J. Am. Chem. Soc.*, **71**, 1284 (1949).

(7) P. Riesz and L. P. Hammett, *J. Am. Chem. Soc.* **76**, 992 (1954).

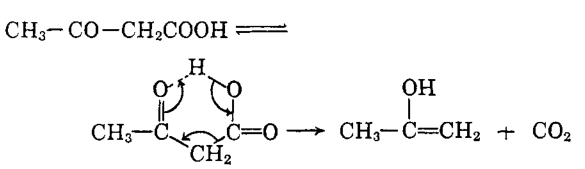
(8) M. J. Astle and W. C. Gergel, *J. Org. Chem.*, **21**, 493 (1956).

(9) W. M. D. Bryant and D. M. Smith, *J. Chem. Soc.*, **57**, 57 (1935).

methylene group causes a large reduction in the reaction rate, some 80% under the same conditions. The effect of other substituents supports the large role played by steric hindrance in the reaction rate. The diethyl derivative showed essentially no reaction after forty hours. Examination of molecular models of the Fischer-Hirschfelder type demonstrates clearly the spatial interference of alpha substituted alkyl groups toward the hydrolysis of the acetoacetic esters. The interference not only renders attack by a water molecule on the carbonyl carbon more difficult, but contributes greatly to the extreme crowding in the transition state.

The greater rate of hydrolysis in the presence of the cation exchange resin can be explained on the basis of the suggestion of Hammett. The ester becomes oriented on the resin surface forming an intermediate complex which is more readily attacked by water than is the ester in the presence of a homogeneous catalyst. Steric hindrance seems to be decreased in the formation of the intermediate complex on the resin surface.

Westheimer and Jones[10] postulate that it is the undissociated β-keto acid which is decarboxylated and that the decarboxylation occurs through a chelated cyclic intermediate.



It is quite possible that the ester is oriented on the resin surface in much the same way as is postulated for the acid and that as the alcohol is lost at the resin surface as a result of hydrolysis the free acid remains as the cyclic structure, probably activated by association with the resin so that decarboxylation is greatly facilitated and a ketone is formed. The hydrolysis and decarboxylation is then essentially a single process. The magnitude in the differences in the rates of hydrolysis in the presence of homogeneous and heterogeneous catalysts is surprising and cannot be accounted for quantitatively at the present time.

TABLE II

EFFECT OF CROSS LINKING ON THE CATALYTIC EFFICIENCY OF DOWEX 50 × n IN THE HYDROLYSIS AND DECARBOXYLATION OF ETHYL ACETOACETATE AT 75°

Resin	Meq. Cat.	Moles H_2O	Moles Ester	Time Hr.	Reaction, %
Dowex 50 × 1	30	2.0	0.5	6	87.8
Dowex 50 × 2	30	2.0	0.5	6	88.6
Dowex 50 × 8	30	2.0	0.5	6	59.2
Dowex 50 × 16	30	2.0	0.5	6	47.6

A decrease in the pore size of the resin, resulting from increased cross-linking with divinyl benzene, causes a decrease in the rate of hydrolysis as indicated in Table II. There is no appreciable difference in rate when 1 or 2% divinylbenzene is used as a cross-linking agent, but 8 and 16% divinylbenzene show a considerable decrease in the hydrolysis rate. This may result from a partial exclusion of the ester relative to water from the active sites within the resin. This is supported by the fact that whereas considerable swelling of the resin occurs in water, very little or no swelling of the resin occurs in ethyl acetoacetate. At any rate the decreased pore size interferes with the formation of the intermediate complex with the ester.

Malonic esters. Malonic esters are more difficult to hydrolyze than acetoacetic esters, requiring higher temperatures and longer reaction times. The results are summarized in Table III. In contrast with acetoacetic esters relatively large amounts of free malonic acid were obtained, and there is little difference in over-all reaction rates between homogeneous and heterogeneous catalyst systems unless one of the methylene hydrogens is replaced by an alkyl group.

It should be noted that appreciably larger quantities of ethyl acetate are obtained when cation exchange resins are used as catalysts and that this probably results from the decarboxylation of the half-ester.

The preferential hydrolysis to the half-ester could conceivably be attributed to the fact that the resin is a heterogeneous catalyst rather than to any decrease in internal entropy in the formation of the intermediate complex. It is reasonable to assume that a diethyl malonate molecule could approach a resin particle with only one ester group in position to be catalytically hydrolyzed, and decarboxylated then wander into a portion of the solution containing no catalyst where no further reaction occurs.

The greater effectiveness of the resin in the catalysis of hydrolysis of alkylmalonic esters can be explained by the assumption that the alkyl group interferes less in the formation of the intermediate complex on the resin surface than in the homogeneous solution.

Attempts to hydrolyze the negatively substituted esters, ethyl cyanoacetate and ethyl phenylacetate were not very successful. The hydrolysis rate was very slow and no decarboxylation was observed.

CLEVELAND, OHIO

TABLE III

ACID-CATALYZED HYDROLYSIS AND DECARBOXYLATION OF MALONIC ESTERS

Ester	Catalyst[a]	Mole H_2O	Temp.	Time, Hr.	Ethyl Acetate	Acetic Acid	Malonic Acid	Total, %
Monoethyl malonate	Resin	2.0	99–108	2.25	10	38	51	99
	H_2SO_4	2.0	99–108	2.25	8	42	49	99
Diethyl malonate	Resin	1.25	99–114	8	41	22	31	94
	Resin	2.0	95–111	8	42	24	33	99
	Resin	2.9	97–107	8	22	35	42	99
	H_2SO_4	2.0	96–111	8	30	25	44	99
	H_2SO_4	3.1	97–107	8	13	39	47	99
Malonic acid[b]	Resin	1.45	102–105	6	—	53	47	53
	H_2SO_4	1.40	102–105	6	—	50	50	50
α-Ethyl	Resin	2.0	100	16	11[c]	42[d]	9[e]	62
Malonic ester	H_2SO_4	2.0	101	16	2	5	5	12

[a] Resin = Dowex 50W × 2; 30 meq. in each case. [b] Decarboxylation only. [c] % Ethyl butyrate. [d] % Butyric acid. [e] % Propane-1,1-decarboxylic acid.

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[10] F. H. Westheimer and W. A. Jones, *J. Am. Chem. Soc.*, 63, 3283 (1941).