solutions resulting from titration of aliquots of each, were combined, treated with an excess of concentrated hydrochloric acid, and evaporated to dryness under reduced pressure. After 1.5 cc. of 50% potassium hydroxide solution had been added, the contents of the flask were distilled at atmospheric pressure. Addition of 1 g. of potassium hydroxide pellets to the distillate caused it to separate into two layers. The mixture was extracted with four portions of commercial *n*-hexane, the combined hexane extracts were dried over potassium hydroxide, and they were then diluted with *n*-hexane to 10 cc. in a volumetric flask. The resulting solution contained 0.432 g. of α-pipecoline, and showed, in a 1-dm. tube, a rotation of $+0.02 \pm 0.02°$. Leithe[21] reported for (+)-α-pipecoline, $[\alpha]^{15}\text{D}$ $+35.7°$; accordingly, if there had been 100% resolution, this solution would have displayed a rotation of 1.54°.

Attempts to Resolve Amines by Means of the Polymer from II.—A solution of 17.1 g. of α-methylbenzylamine in 300 cc. of 20% ethanol was allowed to pass slowly through the column. Portions constituting the first 338 cc. of effluent tested acid to litmus. The next three portions, 82 cc. in all, tested basic and were separately treated with sodium hydroxide and benzoyl chloride under Schotten–Baumann conditions, but oils were produced which solidified only on long standing. However, the following 28-cc. portion, treated the same way, gave an immediate nearly white precipitate which, when air-dried, weighed 0.246 g.; m.p. 112.5–118°. A solution of this amide in benzene to a total volume of 10 cc. showed, in a 1-dm. tube, a rotation of $-0.05 \pm 0.02°$; however, after this solution had been washed with sodium hydroxide solution, and again (because of evaporation losses) made up to 10 cc. with benzene, its rotation was $0.00 \pm 0.02°$. Although a slight loss of N-(α-methylbenzyl)-benzamide occurred during sodium hydroxide washing, the loss of optical activity is believed to be due to removal by washing of a trace of soluble polymer which had contaminated the crude amide. From the data of Pope and Read,[20] by interpolation, the benzene solution before washing would have shown a rotation of 1.06° had the solid been an optically pure antipode of the amide; after sodium hydroxide washing its rotation would have been somewhat less.

In a similar experiment, the benzoyl derivative of the first α-methylbenzylamine to break through was recrystallized prior to polarimetric examination, a procedure which admittedly might have eliminated a small excess of one optical antipode. The resulting amide, in benzene solution of concentration such that the rotation would have been 0.48° had there been complete resolution, displayed a rotation of $0.00 \pm 0.00°$.

A solution of 14 g. of α-pipecoline in 290 cc. of water was allowed to pass slowly through the column of resin from II. After 345 cc. of effluent had been collected, a 15-cc. portion containing 0.35 g. of amine was treated much as in the above experiment concerning the resin from I, in order to prepare a solution in hexane. Ten cubic centimeters of the hexane solution contained 0.269 g. of amine, and in a 1-dm. tube showed a rotation of $0.00 \pm 0.01°$; according to the data of Leithe,[21] the solution would have shown a rotation of 0.96° if there had been complete resolution.

A solution of 39.3 g. of 4-dimethylamino-2,2-diphenylvaleronitrile in 600 cc. of 95% ethanol was allowed to pass through the column which had been thoroughly washed with ethanol. The amino nitrile did not appear to be retained on the resin, for after only 107 cc. of effluent had been collected, a 25-cc. portion containing 0.50 g. of nitrile was obtained. In a 1-dm. tube, this solution showed a rotation of $+0.03 \pm 0.03°$, whereas had the nitrile been completely resolved, the rotation would have been, from data of Pohland, Marshall and Carney,[22] 1.00°; further, the nitrile recovered from this solution and recrystallized from dilute alcohol, showed (*c* 2.92, ethanol), in a 1-dm. tube, a rotation of $-0.01 \pm 0.02°$, whereas the rotation would have been 1.46° had there been complete resolution.

Acknowledgments.—The authors are deeply grateful to the Office of Naval Research and to Research Corporation, who provided financial support of this research. To Carbide and Carbon Chemicals Corporation we extend our thanks for a gift of α-methylbenzylamine, and to Eli Lilly and Co. for a gift of 4-dimethylamino-2,2-diphenylvaleronitrile.

---

[21] W. Leithe, *Monatsh.*, **50**, 40 (1928).

[22] A. Pohland, F. J. Marshall and T. P. Carney, THIS JOURNAL, **71**, 460 (1949).

PORTLAND 2, OREGON

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Mechanism of the Decarboxylation of α,β- and β,γ-Unsaturated Malonic Acid Derivatives and the Course of Decarboxylative Condensation Reactions in Pyridine[1]

BY ELIAS J. COREY

RECEIVED MARCH 20, 1952

The decarboxylation of several half-esters of α,β-unsaturated malonic acids in pyridine has been investigated for the purpose of determining the influence of the α,β-ethylenic linkage on such systems. The decarboxylation of ethyl hydrogen isopropylidenemalonate (II) proceeds rapidly in pyridine (111°) and affords a mixture of ethyl β-methyl-β-butenoate (IV) and ethyl β,β-dimethylacrylate (III) (ratio, 3:1). The reaction has been studied kinetically and has been found to take place by way of the β,γ-unsaturated acid, which decarboxylates as the conjugate base. The mesomeric anion produced by decarboxylation accepts a proton *irreversibly* at C_α or C_γ to give IV or III. Ethyl hydrogen isopropenylmethylmalonate (VIII) upon decarboxylation also yields a mixture of the isomeric β,γ- and α,β-unsaturated esters (ratio, 1:1). The rates of decarboxylation of II, ethyl hydrogen isopropylmalonate and VIII have been found to differ by factors of ten and to increase in the order: ethyl hydrogen isopropylmalonate, II, VIII. The decarboxylations of ethyl hydrogen mesitylidenemalonate (VI) and ethyl hydrogen 2,6-dichlorobenzylidenemalonate (VII) which can lose carbon dioxide only by a direct mechanism are extremely slow in pyridine near the boiling point. The significance of the results of the present study on the mechanism of decarboxylative condensation reactions is pointed out. Two new routes to α,β-unsaturated malonic acid derivatives have been devised and are illustrated herein.

The mechanism and ease of decarboxylation of α,β-unsaturated malonic acid derivatives are of special concern from both a preparative and theoretical viewpoint. The presence of an α,β-ethylenic linkage in the malonic acid system introduces interesting structural variations on the relatively well studied case of the saturated malonic acids[2] which are almost certain to manifest themselves in a divergence of mechanism. Furthermore, knowledge of the course of decarboxylative condensation reactions, such as that due to Doebner, Knoevenagel and Verley,[3] which are of fundamental significance in synthetic work, would be advanced considerably by an understanding of the behavior of α,β-unsaturated malonic acid derivatives in various

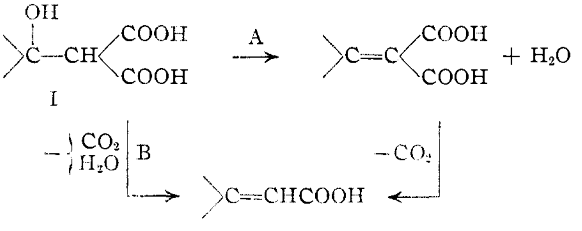
---

[1] Presented in part before the Division of Organic Chemistry at the 121st Meeting of the American Chemical Society in Buffalo, N. Y., March, 1952.

[2] B. R. Brown, *Quart. Rev.*, **5**, 131 (1951).

[3] Reviewed by J. R. Johnson in R. Adams, *et al.*, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, pp. 226–228.

media. The formation of substituted acrylic acids from carbonyl compounds and malonic acid, for example, might take place through the same intermediate β-hydroxy acid (I) by two basically different routes, represented by A and B. It has not been possible in the past to evaluate the relative importance of paths A and B or even to explain the effect of changing the reaction conditions on the amounts of acrylic acid, α,β-unsaturated malonic acid or other products produced.[4]

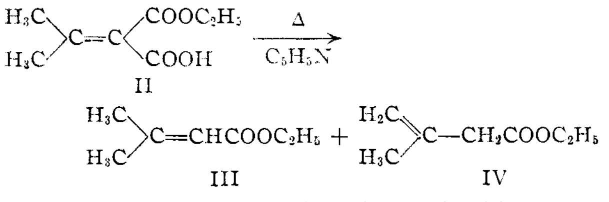


Despite the frequent use and importance of pyridine as a medium for decarboxylations little is known about its function in the reaction or the entity undergoing decarboxylation, *i.e.*, free acid or conjugate base.

In the present work the decarboxylation of the half-esters of several unsaturated malonic acids in pyridine near the boiling point has been studied and detailed information concerning the behavior of such acids in this important system has been obtained.

Results and Discussion

Decarboxylations.—The decarboxylation of ethyl hydrogen isopropylidenemalonate (II) in pyridine at 111.0° was found to proceed rapidly, the rate being approximately ten times as fast as that of the corresponding saturated compound, ethyl hydrogen isopropylmalonate. Two products are formed in the decarboxylation—the expected ethyl β,β-dimethylacrylate (III) and even larger amounts of the thermodynamically less stable β,γ-unsaturated isomer IV. The mixture or either pure isomer can be equilibrated by means of sodium ethoxide to essentially pure α,β-unsaturated ester (III). Under the conditions of the reaction, however, *i.e.*, in pyridine near the boiling point, neither the α,β-unsaturated isomer (III) nor the β,γ-unsaturated isomer (IV) is affected in the slightest, and it is therefore necessary to consider both III and IV as primary products of the reaction. The exact ratio of III to IV produced in the reaction is quite close to 1:3. The isomers can be separated by careful fractional distillation or by selective bromination of the β,γ-isomer in the mixture at −30°, separation of the resulting dibromide and debromination with zinc.

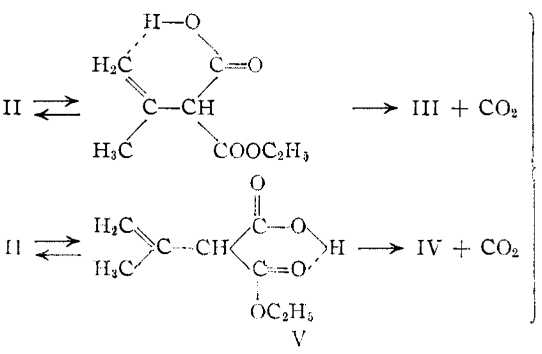


The formation of β,γ-unsaturated acids directly from α,β-unsaturated malonic acids has been observed unequivocally in only one instance previously. Rüber[5] found that γ-phenylpropylidenemalonic acid on heating yielded δ-phenyl-β-pentenoic acid. It is noteworthy that Boxer and Linstead[4] and Zaar[6] have reported the formation of mixtures of β,γ- and α,β-unsaturated acids in the condensation of *n*-butyraldehyde with malonic acid. The ratio of α,β- to β,γ-product was found to vary markedly with the amine used in the condensation and in a way which indicated that the isomers are formed by different mechanisms. γ-Phenyl-β-butenoic acid has been obtained by the condensation of phenylacetaldehyde with malonic acid in pyridine,[7] but in this instance the reaction product represents the more stable isomer and might have been formed from the less stable α,β-unsaturated isomer.

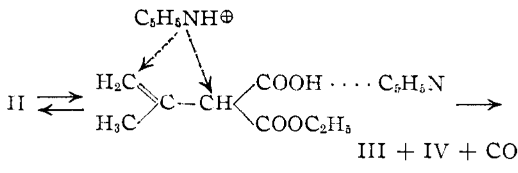
The formation of the α,β-isomer III and the β,γ-isomer IV from ethyl hydrogen isopropylidenemalonate (II) might proceed by any of a large number of paths which may involve the production of III and IV from the same intermediate, from different intermediates or a combination of both. Since the ratio of III to IV produced in the decarboxylation reaction is exactly constant under a variety of conditions which strongly affect the over-all rate, *e.g.*, with added sodium iodide, picric acid, N-ethylpiperidine and *p*-toluenesulfonic acid, it is probable that III and IV are formed predominantly from the same reactive intermediate by the same kind of reaction.[8] Only mechanisms which are consistent with this condition will be considered. These are represented by equations (1)–(5). The evidence which has been gathered from kinetic studies and use of model compounds strongly indicates that equation (5) represents the only important course of the reaction.

$$\text{II (Acid)} \longrightarrow \text{III} + \text{IV} + CO_2 \qquad (1)$$

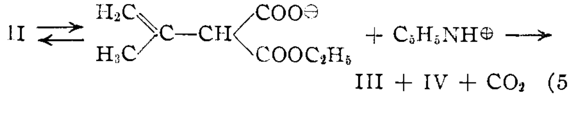
$$\text{II (Anion)} \longrightarrow \text{III} + \text{IV} + CO_2 \qquad (2)$$



(3)



(4)



(5)

---

[4] S. E. Boxer and R. P. Linstead, *J. Chem. Soc.*, 740 (1931).

(5) C. N. Rüber, *Ber.*, **38**, 2742 (1905).

(6) B. Zaar, *Ber.*, Schimmel and Co. Akt.-Ges., 299 (1929).

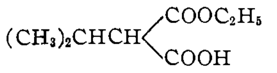
(7) D. Vorländer, *Ann.*, **345**, 244 (1906).

(8) This conclusion is supported by evidence along other lines which is discussed later.

The decarboxylation of ethyl hydrogen isopropylidenemalonate (II) (Fig. 1) follows first-order kinetics from 20% reaction to beyond 90% reaction, the plot of ln $(V_\infty^{CO_2}/V_\infty^{CO_2} - V_t^{CO_2})$, which will be designated henceforth as α_t *vs.* time, affording a reasonably good straight line. Initially, however, the reaction is quite slow and the apparent "instantaneous first-order rate constant," α_t/t, increases markedly with time. A noticeable, but much smaller, drift of α_t/t to higher values continues to occur even after 20% reaction.

The rate of decarboxylation is increased by a factor of approximately three when 0.5 *M* sodium iodide in pyridine is used as the reaction medium (Fig. 1) and by a factor of about 1.2 with 0.5 *M* pyridinium picrate in pyridine (Fig. 1). Under both conditions the reaction proceeds slowly for the first several minutes (as in the case of pure pyridine as solvent), an indication of the gradual formation of some reactive intermediate. Addition of a small amount of N-ethylpiperidine also increases the rate considerably. By increasing the amount of N-ethylpiperidine the rate of reaction can be increased some 20-fold (Table I), the plot of α_t *vs.* time giving an upward bending curve, the slope of which increases by a factor of almost three from 15% reaction to 99% reaction.

TABLE I

Reactants	*t*, min.	α_t/t $\times (10)^2$	Reacted, %
II (C_0 = 0.198 *M*) in 2.33 *M*	1	16.1	14.9
N-ethylpiperidine–pyridine	4	34.8	75.0
at 111.0°	10	44.7	99.0
 $(CH_3)_2CHCH\langle^{COOC_2H_5}_{COOH}$	14	0.20	2.5
	86	.22	17.5
(C_0 = 0.174 *M*) in pyridine			
at 111.0°	203	.24	36.7
VIII (C_0 = 0.171 *M*) in pyridine at 111.0°	2	11.7	21.3
	5	12.6	46.7
	16	15.0	91.0
VIII (C_0 = 0.170 *M*) in 0.5 *M*	1	15	14.0
sodium iodide-pyridine at	10	17	83.0
95.0°	15	17	92.0
VIII (C_0 = 0.143 *M*) in 1.4 *M*	0.5	60	23.0
N-ethylpiperidine-pyridine	1.5	63	79.0
at 95.0°	5	64	96.0

These results clearly show that mechanism (1) cannot be important since the rate of decarboxylation is increased and not decreased by the addition of sodium iodide or N-ethylpiperidine, both of which should decrease the concentration of an acid such as II in pyridine (*vide infra*). Furthermore, this mechanism requires that a plot of α_t *vs.* time should yield a curve which is *concave downward* (which is not observed) as can be shown by the following argument.

Consider an acid, HA, in equilibrium with its conjugate base, A^-, and $C_5H_5NH^+$ in pyridine solution and let $[A_t]$ represent the sum of the con-

$$K = [C_5H_5NH^+][A^-]/[HA] \qquad [A_T] = [HA] + [A^-]$$

centrations of A^- and HA. One may express the ratio of $[A^-]$ to [HA] as

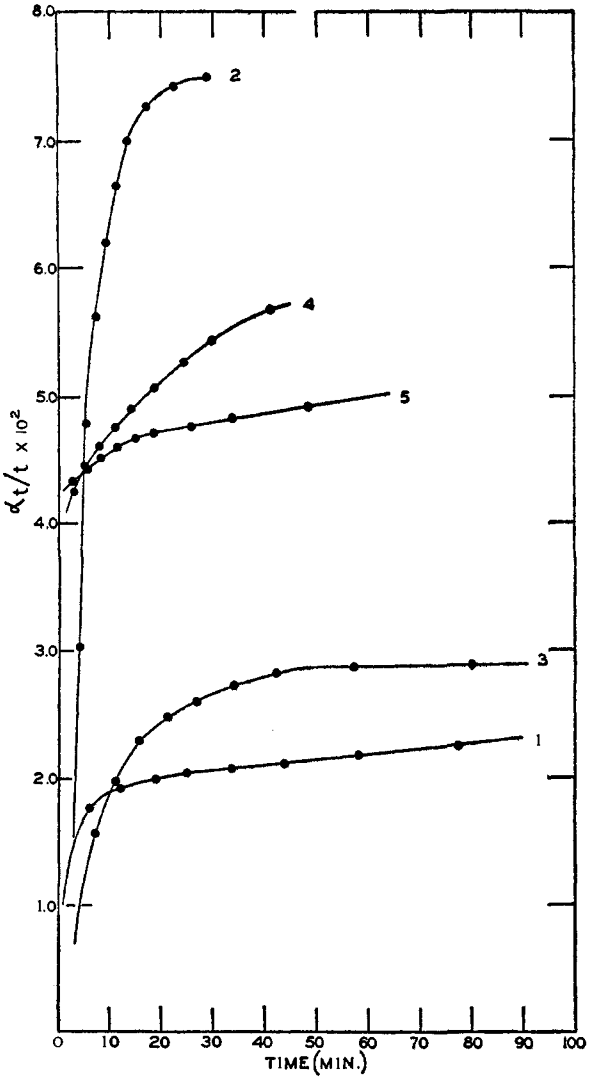


Fig. 1.—Plots of α_t/t as a function of time. The quantity α_t equals $V^{CO_2}/(V^{CO_2}_\infty - V_t^{CO_2})$ where $V_\infty^{CO_2}$ is the total volume of carbon dioxide evolved in a reaction and $V_t^{CO_2}$ is the amount of carbon dioxide evolved at time, *t*. The distances between circles on the curves represent intervals of 10% reaction, the first mark being at 10% reaction: curve (1), II (C_0 = 0.209 *M*) in pyridine at 111.0°; curve (2), II (C_0 = 0.193 *M*) in 0.5 *M* sodium iodide–pyridine at 111.0°; curve (3), II (C_0 = 0.193 *M*) in 0.5 *M* pyridinium picrate–pyridine at 111.0°; curve (4); VIII (C_0 = 0.181 *M*) in pyridine at 95.0°; curve (5), VIII (C_0 = 0.176 *M*) in 0.5 *M* pyridinium picrate–pyridine at 95.0°.

$$\frac{[A^-]}{[HA]} = {}^1/_2 \left[\frac{K}{[A_T]} + \left(\frac{K^2}{[A_T]^2} + \frac{4K}{[A_T]}\right)^{1/2}\right]$$

As $[A_t]$ decreases, the ratio $[A^-]/[HA]$ increases. Since the quantity $(V_\infty^{CO_2} - V_t^{CO_2})$ is a measure of $[A_t]$ and not $[A^-]$ or [HA], in the event that *K* is small (as appears to be the case for most carboxylic acids in pyridine),[9] the plot of α_t *vs.* time for decarboxylations proceeding through A^- should show

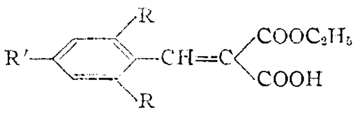
---

[9] It has been found [E. J. Corey, THIS JOURNAL, in press] that at 25° in pyridine the dissociation constant of II is about $2(10)^{-6}$. From this value using the data of Burgess and Kraus [ref. 16] a constant ($\sim 2 \times 10^{-4}$) for the ionization of II into ion pairs was obtained.

marked upward curvature.[10] The same plot for decarboxylations proceeding through HA should show slight downward curvature.

The occurrence of reaction by mechanism (2) to any appreciable extent is rendered unlikely by a number of facts. First, as is discussed in the following section, the decarboxylation of several α,β-unsaturated malonic acid derivatives which must decarboxylate by a direct mechanism is exceedingly slow. Secondly, the sodium salt of II does not undergo decarboxylation in boiling water. Such behavior would be expected, since other acids which undergo direct anionic decarboxylation in pyridine are also decarboxylated readily as their salts in aqueous solution. It seems unlikely on this basis that the conjugate base of II is capable of facile decarboxylation. Finally, the rate of decarboxylation of II during the first few minutes of contact with hot pyridine is abnormally slow. The initial rate of gas evolution, although reproducible with a given sample of II varies somewhat when different samples are used and is approximately zero in some cases. These results cannot be explained on the basis of a direct decarboxylation of II, but are consistent with mechanisms in which the β,γ-isomer of II is the species undergoing decarboxylation.

It is appropriate here to discuss a study of the ease of decarboxylation of ethyl hydrogen mesitylidenemalonate (VI) and ethyl hydrogen 2,6-dichlorobenzylidenemalonate (VII). Both compounds were found to be resistant to decarboxylation in pyridine at 111° and could be recovered essentially unchanged after exposure for several hours.[11] Since the electrical effects of the methyl and chlorine substituents are opposite in nature, the large stability of VI and VII is probably not due to the electronic influence of these groups. In fact, it might be anticipated that steric interference between the carboxyl group and the ortho substituents would favor decarboxylation. The conclusion may be drawn that the direct decarboxylation of α,β-unsaturated malonic acid derivatives in hot pyridine is in general quite slow.



VI, $R = R' = CH_3$
VII, $R = Cl, R' = H$

Mechanisms (3),[12] (4) and (5) which involve a β,γ-unsaturated intermediate are compatible with all of the data discussed thus far. Catalysis of the decarboxylation by sodium iodide, pyridinium picrate and N-ethylpiperidine could be explained on the basis that these substances increase the rate of production of β,γ-unsaturated acid or the concentration of the β,γ-unsaturated carboxylate ion.

At this point it is worthwhile to evaluate in a qualitative way the effect of adding inert electrolyte on (a) the rate of conversion of the α,β-isomer into the β,γ-isomer and (b) the ionization of the α,β- and β,γ-unsaturated acids to give the corresponding carboxylate ions. In the case of solvents of low dielectric constant such as pyridine (D = 9.4 (115.5°)[13] 12.0 (25°)[18]) it is fairly certain that addition of soluble electrolytes increases the dielectric constant of the medium[14,15] and, hence, the tendency of neutral substance to ionize.[16] The presence of ion pairs, triple ions and more complex ion aggregates[17] might also be expected to increase the degree of ionization of a neutral solute, since such species provide ion atmospheres for the charged fragments formed by the ionization. The latter effect might be especially important in pyridine, since, as has been determined from studies of ion conductances,[18] negative ions are solvated less strongly by this solvent than are positive ions. Salts such as sodium iodide, pyridinium nitrate and tetramethylammonium picrate, which have been found[18] to be strong salts (in the Walden sense[14]), are dissociated only partly ($K \cong 10^{-4}$) in dilute solutions (10^{-3}–10^{-5} M) in pyridine. In more concentrated solutions the dissociation of ion pairs and more complex ion aggregates into triple-ions greatly increases the relative concentration of charged species,[17] and, hence, increases the importance of the ion-atmosphere effect. A third and unquestionably important effect caused by the presence of moderate concentrations of salt is increased dissociation of a non-ionic substance because of the possibility of forming triple-ions with the ionic solute. This phenomenon may be illustrated for a weak acid (HA) and a salt such as sodium iodide by the equation $H{-}A + 2[Na^+I^-]^0 \rightarrow [H^+I^-Na^+]^+ + [A^-Na^+I^-]^-$. Thus, there are three factors, all operative in the same direction, which determine the consequence of added electrolyte on dissociation in pyridine solution. The first factor is dependent upon the dielectric constant and the remaining two upon the ionic strength of the medium.

A study of the decarboxylation of the β,γ-unsaturated malonic acid derivative, ethyl hydrogen

---

[10] It is recognized that both dissociated carboxylate ions and carboxylate–pyridinium ion pairs may be capable of anionic decarboxylation. However, if decarboxylation of carboxylate ions and of carboxylate ion pairs proceeds through the same transition state, then half of the carbon dioxide produced will come from each species, regardless of the relative concentrations present. Such a conclusion follows immediately from the transition state theory.

[11] Ethyl hydrogen benzylidenemalonate decarboxylates readily in hot pyridine, but the reaction is second order and the mechanism will be discussed in a separate communication.

[12] For the proposal of a cyclic intermediate in the decarboxylation of β,γ-unsaturated acids see R. T. Arnold, O. C. Elmer and R. M. Dodson, THIS JOURNAL, **72**, 4359 (1950).

[13] J. D. Cauwood and W. E. S. Turner, *J. Chem. Soc.*, **107**, 276 (1915).

[14] P. Walden, THIS JOURNAL, **35**, 1649 (1913). A. H. Scharbaugh, Jr., H. C. Eckstrom and C. A. Kraus, *J. Chem. Phys.*, **15**, 54 (1947); H. A. Strobel and H. C. Eckstrom, *ibid.*, **16**, 817 (1948).

[15] It is well known that with polar liquids such as water (D = 80) the dielectric constant is decreased by the addition of electrolytes, the decrease presumably being due to saturation of the dielectric (solvent) in the neighborhood of an ion, *i.e.*, ion–solvent dipole interaction. H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 2nd. Ed., Reinhold Publishing Corp., New York, N. Y., 1950, pp. 379–383, 604–605. This effect, which was also found by P. Walden and O. Werner, *Z. physik. Chem.*, **A124**, 405 (1926), to occur in solvents such as benzonitrile (D = 26.5) and acetone (D = 21.4), apparently diminishes in importance in liquids of low dielectric constant.

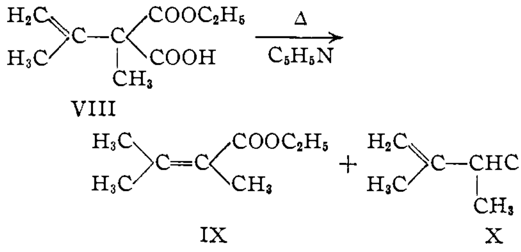
[16] See, *e. g.*, M. Kilpatrick, *Chem. Revs.*, **30**, 159 (1942).

[17] R. M. Fuoss and C. A. Kraus, THIS JOURNAL, **55**, 21, 476, 1019, 2387, 3614 (1933).

[18] W. F. Luder and C. A. Kraus, *ibid.*, **69**, 2481 (1947); D. S. Burgess and C. A. Kraus, *ibid.*, **70**, 706 (1948). *Cf.* J. N. Pearce, *J. Phys. Chem.*, **19**, 14 (1915).

isopropenylmethylmalonate (VIII), permits the elimination of (3) and (4) as possible reaction paths. The rate of decarboxylation of VIII is faster than that of II by a factor of about ten. No conclusions may be drawn from the relative rates of decarboxylation of II and VIII concerning the amount of β,γ-isomer in equilibrium with II during the decarboxylation, since the rates of decarboxylation of VIII and the β,γ-isomer of II should not be the same. It is well known that the substitution of alkyl groups on the α-carbon atom of saturated malonic acids strongly decreases the rate of decarboxylation.[19,20] In the anionic decarboxylation of VIII it is clear that the stability of the mesomeric anion formed by loss of carbon dioxide would be decreased by the presence of the methyl group on the α-carbon atom.

The product of the decarboxylation of VIII in pyridine is, as in the case of the α,β-unsaturated acid II, a mixture of α,β- and β,γ-unsaturated esters, IX and X, the ratio in this case being 1:1.


VIII

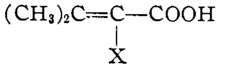
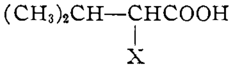
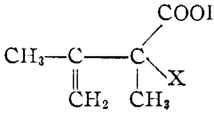
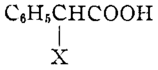
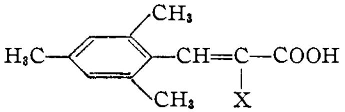
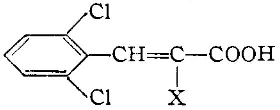
IX X

This finding strongly supports the correctness of the β,γ-unsaturated acid V as an intermediate in the formation of both isomeric esters (III and IV) by the decarboxylation of ethyl hydrogen isopropylidenemalonate (II).

The quantity α_t/t for the decarboxylation of VIII markedly increases with time, which indicates that the rate constant for anionic decarboxylation is much greater than that for the decarboxylation of the free acid. This conclusion is also reached from the fact that the rate of decarboxylation of VIII is strongly increased by the addition of sodium iodide or N-ethylpiperidine (Table II). In addition it is noteworthy that VIII may be distilled without appreciable decomposition at temperatures up to 135°.

TABLE II

RELATIVE RATES OF DECARBOXYLATION IN PYRIDINE AT 111.0° (APPROXIMATE)

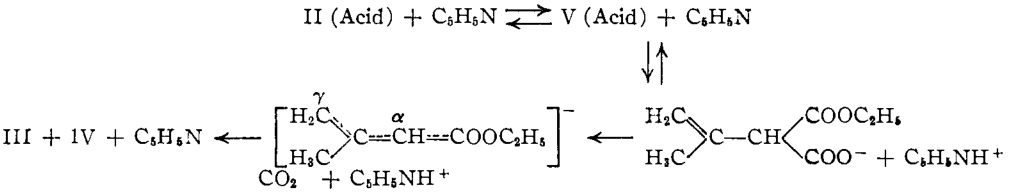
 $(CH_3)_2C{=}C(X){-}COOH$	1
 $(CH_3)_2CH{-}CH(X)COOH$	0.1
	10
 $C_6H_5CH(X)COOH$	Too fast to measure
	Too slow to measure
	Too slow to measure

$X = COOC_2H_5$

The decarboxylation of ethyl hydrogen phenylmalonate which possesses β,γ-unsaturation was studied and as expected proved to be extremely fast. Decarboxylation of the potassium salt of this acid occurred merely upon heating in aqueous or alcoholic solution. The substance undergoes decarboxylation almost immediately upon mixing with benzylamine and at a rate which is too fast to measure in pyridine at 111°. The rapid decarboxylation of such compounds containing β,γ-unsaturation is only to be expected in view of the stability of the mesomeric anion produced by anionic decarboxylation.

Returning to the decarboxylation of II, one may deduce that the β,γ-isomer V decarboxylates primarily as the anion since the rate constant for anionic decarboxylation is undoubtedly very much greater than that *via* the free acid. The fact that the relative amounts of α,β- and β,γ-unsaturated decarboxylation products are the same with added N-ethylpiperidine or sodium iodide as without provides strong evidence that essentially all of the decarboxylation of V is anionic.

In this event the rate-determining step in the conversion of II to the β,γ-isomer V must be the abstraction of a proton from the un-ionized acid II and not the conjugate base. If the rate-determining step in the isomerization were the abstraction of a proton from the conjugate base of II, the plot of α_t *vs.* time would give a line of *marked* upward curvature instead of only *slight* upward curvature as is observed. The most important mechanism for the decarboxylation of the α,β-unsaturated acid II is, therefore, established as



The addition of a proton to the mesomeric anion formed after loss of carbon dioxide is irreversible and takes place three times as fast at C_α than at C_γ. These results parallel strikingly those reported in several other cases involving the protonation or alkylation of mesomeric anions, as is evident from the ensuing discussion.

The rate of the base-catalyzed introduction of

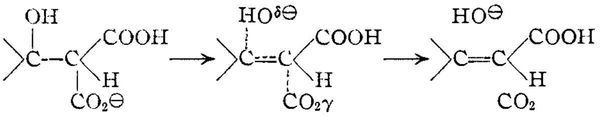
---

(19) A. L. Bernoulli and W. Wege, *Helv. Chim. Acta*, **2**, 511 (1919).

(20) A. L. Bernoulli and H. Jakubowicz, *ibid.*, **4**, 1018 (1921).

deuterium into β,γ-unsaturated nitriles, has been found to be much greater than the rate of isomerization to the α,β-unsaturated form.[21] The correspondence of this finding to the results of the present work is obvious. Kon[22] and Cope[23] have shown that the sodium salts derived from α,β-unsaturated malonic esters upon acidification or alkylation yield compounds which are β,γ-unsaturated. Other examples of the conversion of mesomeric anions into the thermodynamically less stable products are to be found in the alkylation of sodium allylbenzene,[24] the O-protonation,[25] O-alkylation[26] and O-acylation[27] of ethyl sodioacetoacetate, the Birch reduction of benzenoid systems,[28] the conversion of 3-acetoxy-$\Delta^{3,5}$-cholestadiene into Δ^5-cholesten-3-one by means of potassium amide[29] and the reduction of thebaine to phenolic dihydrothebaine.[30] The generality of these phenomena has been recognized by Birch[28] and an explanation in terms of the collision theory has been offered.[31]

The Course of Decarboxylative Condensation Reactions.—The resistance of ethyl hydrogen mesitylidenemalonate (VI) and ethyl hydrogen 2,6-dichlorobenzylidenemalonate (VII) to decarboxylation in hot pyridine indicates that the direct decarboxylation of α,β-unsaturated malonic acids and acid derivatives does not occur readily under these conditions. It seems likely that, in general, α,β-unsaturated malonic acids decarboxylate readily in hot pyridine only when a pathway is available involving an intermediate in which the α-carbon atom is not linked by a double bond. With this information we may now proceed to a consideration of the mechanism of formation of essentially pure acrylic acids from carbonyl compounds and malonic acid in pyridine. Mechanism A (see introduction) in which the intermediate β-hydroxymalonic acid (I) undergoes dehydration followed by decarboxylation cannot be correct, since the α,β-unsaturated acid should be stable or should yield a mixture of α,β- and β,γ-unsaturated products by decarboxylation *via* a β,γ-unsaturated malonic acid.[32] The reaction is better represented as proceeding by a process of decarboxylation elimination.



It is apparent that decarboxylative elimination should not be favored by solvents of high dielectric constant, since there is dispersal of charge in the transition state. Dehydration of β-hydroxymalonic acids to α,β-unsaturated malonic acids, on the other hand, should be favored by solvents of high dielectric constant, since separation of unlike charges is involved in the transition state leading to elimination of water. Furthermore, there should be an optimum basicity of the medium for each of these reactions. In summary, these factors—base strength and dielectric constant of the medium—together with the reversibility of dehydration of the β-hydroxymalonic acid should influence, in a predictable way, the amount of α,β-unsaturated malonic acid, acrylic acid and β,γ-unsaturated acid produced in the over-all reaction. It is worthy of note that triethanolamine, which has a high dielectric constant (D = about 32), has been recommended as the solvent of choice for the preparation of β,γ-unsaturated acids from carbonyl compounds and malonic acid.[4]

Synthesis.—The need of α,β-unsaturated malonic acids containing one free carboxyl group for the decarboxylation studies just described has necessitated the investigation of synthetic routes to the half-esters. Only one half ester of an α,β-unsaturated malonic acid appears to have been reported previously. Reinicke[33] prepared ethyl hydrogen benzylidenemalonate in low yield by the condensation of the potassium salt of ethyl hydrogen malonate with benzaldehyde in glacial acetic acid. This synthesis is operative only in special cases such as that studied by Reinicke.

The successful synthesis of half-esters of α,β-unsaturated malonic acids by partial hydrolysis of the corresponding diesters has not been accomplished previous to this work. It is well known that the hydrolysis of α,β-unsaturated malonic esters by aqueous bases is very slow and is accompanied to a considerable extent by cleavage to a carbonyl compound and malonic acid.[34-36] Ethyl benzylidenemalonate upon basic hydrolysis yields a mixture of malonic acid, benzylidenemalonic acid and benzaldehyde.[36]

The conversion of diethyl isopropylidenemalonate (XI) to the corresponding half-ester which is not possible by ordinary acid- or base-catalyzed hydrolysis has been accomplished using the procedure employed previously for the hydrolysis of esters of hindered aromatic acids.[37] The use of the Newman procedure was prompted by the structural similarity of diethyl isopropylidenemalonate (XI) to compounds such as XII which are hydrolyzed successfully by this method. The ester XI which dissolves in cold 96-99% sulfuric acid with the evolution of heat is converted slowly into the corresponding acid (probably *via* a short lived intermediate of the type postulated for the hindered aromatic esters, *i.e.*, XIII). This method, in all probability, provides a good route to half-esters of alkylidenemalonic acids having two alkyl groups on the β-carbon atom.

---

(21) C. K. Ingold, E. de Salas and C. L. Wilson, *J. Chem. Soc.*, 1328 (1936).

(22) G. A. R. Kon and co-workers, *ibid.*, 2727 (1926); 775 (1930); 560 (1931); 1027 (1932); 596 (1934).

(23) A. C. Cope and co-workers, THIS JOURNAL, **60**, 2644, 2901, 2903 (1938); **62**, 314, 3319 (1940).

(24) H. Levy and A. C. Cope, *ibid.*, **66**, 1684 (1944); W. G. Young, M. Kosmin, R. Y. Mixer and T. W. Campbell, *ibid.*, **74**, 608 (1952).

(25) L. Knorr, O. Rothe and H. Averbeck, *Ber.*, **44**, 1138 (1911).

(26) J. L. Simonsen and R. S. Story, *J. Chem. Soc.*, **95**, 2106 (1909).

(27) L. Claisen and E. Haase, *Ber.*, **33**, 1242 (1900).

(28) A. J. Birch, *Quart. Rev.*, **4**, 69 (1950); *J. Chem. Soc.*, 1551 (1950).

(29) A. J. Birch, *ibid.*, 2325 (1950).

(30) G. Stork, THIS JOURNAL, **74**, 768 (1952).

(31) M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, p. 103.

(32) The decarboxylation of α,β-unsaturated malonic acids appears to lead to even higher proportions of β,γ-unsaturated products than are obtained from the corresponding half esters or cyanoacetic acids. E. J. Corey, THIS JOURNAL, in press.

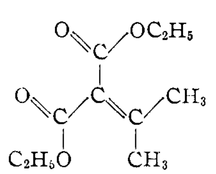
(33) G. Reinicke, *Ann.*, **341**, 80 (1905).

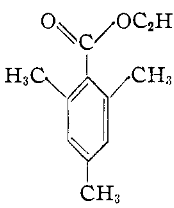
(34) A. Meyerberg, *Ber.*, **28**, 786 (1895).

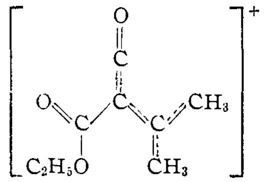
(35) J. Scheiber and F. Meisel, *ibid.*, **48**, 238 (1915).

(36) L. Claisen and L. Crismer, *Ann.*, **218**, 131 (1883).

(37) M. S. Newman, THIS JOURNAL, **63**, 2432 (1941).

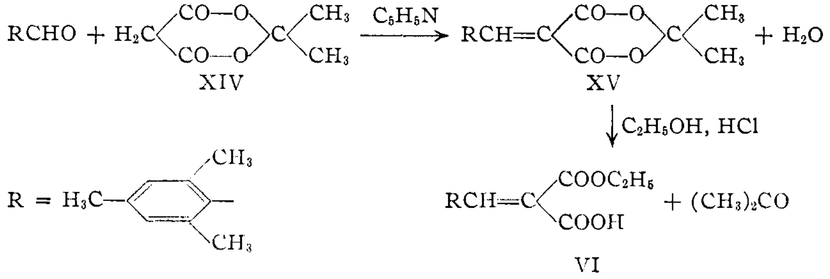

XI


XII


XIII

As might be expected the sulfuric acid procedure gives unsatisfactory results when applied to saturated malonic esters. The reaction proceeds very slowly at room temperature and, in general, is best conducted at 50–70°. The use of selective alkaline hydrolysis with one equivalent of potassium hydroxide is still to be considered the method of choice for the preparation of the half-esters of saturated malonic acids.

A second synthesis of half esters of α,β-unsaturated malonic acids has been devised which makes use of the readily available isopropylidene malonate (XIV).[38,39] Condensation of XIV with a suitable carbonyl compound leads to the isopropylidene ester of an α,β-unsaturated malonic acid which can be converted easily into the desired half-ester. The sequence may be illustrated by the preparation of ethyl hydrogen mesitylidenemalonate (VI) *via* isopropylidene mesitylidenemalonate (XV). It is interesting to note that neither ethyl hydrogen malonate nor the potassium salt will condense with mesitaldehyde. The use of isopropylidene malonate seems especially advantageous, therefore, in the preparation of α,β-unsaturated malonic acid derivatives from hindered aldehydes. The synthesis of α,β-unsaturated malonic acids free of acrylic acids obviously is also possible through the use of isopropylidene malonate.



It should be pointed out that the decarboxylation of α,β-unsaturated malonic acid derivatives provides a good route for the synthesis of β,γ-unsaturated acid derivatives. The β,γ-unsaturated compounds may be separated easily from the α,β-unsaturated isomers by recrystallization or distillation and by selective bromination of the β,γ-isomers followed by debromination.

Experimental[40]

Ethyl Hydrogen Isopropylidenemalonate (II).—Diethyl isopropylidenemalonate (XI)[23] (200 g., 1.0 mole) was added dropwise with stirring over a period of 30 minutes to 700 g. of 99% sulfuric acid (prepared from 300 g. of 30% oleum and 400 g. of 95% sulfuric acid) at 0–10°. After storage at room temperature (27°) for 16.5 hours the clear, red solution was poured with stirring into 1 l. of ice. The colorless, oily mixture was extracted with four 300-ml. portions of ether and the combined ether extracts were shaken with 440 ml. of 10% sodium hydroxide. The basic, aqueous layer was extracted with two 50-ml. portions of ether and acidified with 70 ml. of 18 *N* sulfuric acid. The ether extracts upon evaporation furnished 34.0 g. of pure XI. Extraction of the aqueous solution with five 150-ml. portions of carbon tetrachloride followed by evaporation under reduced pressure (after drying) yielded 93.0 g. (65%) of II as a clear, colorless liquid, $n^{20}\mathrm{D}$ 1.4700. Evaporative distillation of this product at 100–110° (0.05 mm.) gave pure II (recovery, 95%), $n^{20}\mathrm{D}$ 1.4693, neut. equiv., 171 (calcd. 172). A sample prepared for analysis by redistillation had $n^{20}\mathrm{D}$ 1.4692. On storage at room temperature the product solidified, m.p. 37–42°.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 56.08; H, 7.29.

Increasing the time of reaction in sulfuric acid to 26 hours decreases the yield of II to 52%. A reaction time of 5.5 hours affords a 72% yield of product, but almost 25% of the starting material is recovered. A reaction time of 5 minutes leads to almost complete recovery of the starting material.

The half-ester II is also obtained, in undiminished yield, by pouring the sulfuric acid solution (after 16 hours standing) into absolute ethanol, adding water and isolating the product in the usual way. From this result it is obvious that the intermediate XIII cannot be present in appreciable concentration.

Ethyl Hydrogen Isopropylmalonate. (A) **Potassium Hydroxide Procedure.**—Ethyl isopropylmalonate (20.2 g., 0.10 mole) was treated with a solution of 6.0 g. of potassium hydroxide in 60 ml. of absolute ethanol and the reaction mixture was allowed to stand at room temperature until neutral (20 hours). The yield of pure half-ester, $n^{20}\mathrm{D}$ 1.4315, isolated by evaporative distillation, was 13.1 g. (74.6%).

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.32; H, 8.08.

(B) **Sulfuric Acid Procedure.**—The diester (25.0 g., 0.124 mole) and 70 ml. of 95% sulfuric acid were heated at 70° for 45 minutes after which time the acid was poured into water and the product isolated in the usual way. The neutral fraction consisted of 7.2 g. of the starting material. From the acidic fraction there was obtained by evaporative distillation 9.0 g. (57%) of ethyl hydrogen isopropylmalonate as a colorless liquid, $n^{20}\mathrm{D}$ 1.4322.

Ethyl Hydrogen Phenylmalonate.—A mixture of 12.2 g. (0.0516 mole) of ethyl phenylmalonate and 2.9 g. of potassium hydroxide in 80 ml. of 50% ethanol was allowed to stand at room temperature until neutral (one-half hour). The crude half-ester was isolated in the usual way and was obtained as an oil which solidified upon storage at 4°. The crude product, m.p. 74–76.8°, amounted to 10.6 g. (98.5%). Recrystallization of the half-ester from methylene chloride-ligroin yielded pure material, m.p. 76–77°.

Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.35; H, 5.96.

Decarboxylation of II.—A mixture of 25.9 g. (0.149 mole) of II and 100 ml. of pure pyridine was heated to gentle reflux for 2 hours after which the solution was allowed to cool and poured into 160 ml. of concentrated hydrochloric acid containing 300 g. of ice. The aqueous solution was extracted with three 125-ml. portions of ether and the ether

---

[38] D. Davidson and S. A. Bernhard, THIS JOURNAL, **70**, 3426 (1948).

[39] A. N. Meldrum, *J. Chem. Soc.*, **93**, 598 (1908).

[40] All melting points and boiling points are uncorrected. We are indebted to Miss Emily Davis, Mrs. Katherine D. Pih and Mrs. Jean Fortney for the microanalyses and to Mrs. Elizabeth Leighly for the infrared determinations.

extracts were separated and washed consecutively with 25 ml. of 5% potassium bicarbonate solution. The ethereal solutions were combined, dried over calcium chloride and the ether was removed by distillation through a 30-cm. Vigreux column. The residue on distillation gave 13.5 g. (70%) of a mixture of III and IV, b.p. 64–80° (65 mm.), $n^{20}\text{D}$ 1.4231. Distillation of this mixture (13.5 g.) through a Podbielniak miniature "Hyper-Cal" column at a reflux ratio of 40:1 afforded 6.8 g. of pure β,γ-isomer (IV), b.p. 67.5–68.5° (57.8 mm.), $n^{20}\text{D}$ 1.4185. The infrared spectrum of IV manifested bands at 5.76 μ (unconjugated ester carbonyl), 6.05 μ (unconjugated C=C) and 11.1 μ (terminal methylene).

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.61; H, 9.67.

A sample of IV dissolved in carbon tetrachloride decolorized bromine instantly at 0°. No isomerization whatever occurred upon heating a solution of pure IV in pyridine to reflux for 90 minutes. The higher boiling material from the decarboxylation was collected at 76.0–76.5° (57.8 mm.), $n^{20}\text{D}$ 1.4360, and proved to be identical with a sample of ethyl β,β-dimethylacrylate (III) prepared by catalytic esterification of β,β-dimethylacrylic acid,[41] or by equilibration of the mixture obtained in the decarboxylation of II with sodium ethoxide in ethanol.

A sample of III reacted only slowly with bromine at 0°.

The pure β, γ-isomer could be obtained by treatment of the mixture of III and IV (which contained in all runs 75% of the β,γ-isomer and 25% of the α,β-isomer as found from refractive index) with 65% of the theoretical amount of bromine in carbon tetrachloride at −30°, b.p. 77–80° (1.4 mm.), $n^{20}\text{D}$ 1.5000, and debromination of the dibromide so obtained with excess zinc dust in ether–methanol (15:1) at gentle reflux. The yield of pure IV, $n^{20}\text{D}$ 1.4187–1.4190, was 83–85% based on the amount of bromine used.

Decarboxylation of II in 0.5 *M* solutions of *p*-toluenesulfonic acid, pyridinium picrate, N-ethylpiperidine, or sodium iodide in pyridine yielded exactly the same mixture of III and IV, $n^{20}\text{D}$ 1.4229–1.4232 (75% IV, 25% III) as was obtained in pure pyridine. Furthermore, the ratio of III to IV is independent of the time of reaction.

Diethyl Isopropenylmethylmalonate.—The following procedure is a modification of the method of Cope and Hancock[23] who used sodamide in toluene–ether. A mixture of 50.0 g. (0.25 mole) of diethyl isopropylidenemalonate, 200 ml. of purified, dry dioxane and 6.0 g. (0.25 mole) of finely powdered sodium hydride in a 1-l. three-necked flask equipped with stirrer, reflux condenser, dropping funnel and nitrogen inlet tube was heated to reflux for 1 hour (nitrogen atmosphere) at the end of which time all of the sodium hydride had reacted. The clear, dark gray solution was allowed to cool to room temperature and 35 g. (0.277 mole) of pure dimethyl sulfate was added dropwise. The reaction mixture was heated slowly to reflux and the heating was continued until a drop of the mixture gave no color with aqueous phenolphthalein (3 hours). The dioxane was removed by distillation under reduced pressure and the product was isolated from the residue and purified by the method of Cope and Hancock. The yield of pure diethyl isopropenylmethylmalonate, b.p. 78.5–79° (2.3 mm.), $n^{20}\text{D}$ 1.4388 (lit.[23] b.p. 110–111° (12 mm.), $n^{25}\text{D}$ 1.4370) was 38.4 g. (71%).

Ethyl Hydrogen Isopropenylmethylmalonate (VIII).—A mixture of 21.4 g. (0.1 mole) of the diester and 5.6 g. (0.1 mole) of potassium hydroxide in 110 ml. of 70% ethanol was allowed to stand at room temperature for 6 days. The solution was concentrated under reduced pressure to a volume of 20 ml., diluted to 50 ml. with water and extracted with four 50-ml. portions of ether. The combined ethereal solutions yielded 3.5 g. of the starting diester. From the aqueous layer there was obtained by acidification, extraction and distillation of the residue (100–110° at 0.05 mm.) 14.8 g. (95.5%) of pure VIII, $n^{20}\text{D}$ 1.4531, neut. equiv., 185 (calcd. 186.2). Redistillation did not change the physical properties of the product.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.85; H, 7.75.

Decarboxylation of VIII.—A mixture of 7.3 g. (0.0393 mole) of the acid VIII and 25 ml. of pure pyridine was heated at reflux temperature for 40 minutes. The resulting mixture of esters was isolated by the procedure described for III and IV. Slow distillation of the mixture through a modified semi-micro column (Holzman) yielded 0.30 g. of almost pure ethyl α,β-dimethyl-β-butenoate (X), b.p. 75–76° (48 mm.), $n^{20}\text{D}$ 1.4244 (lit.[42] b.p. 151° (735 mm.), $n^{20}\text{D}$ 1.4210), 3.27 g. of a mixture of ethyl trimethylacrylate (IX) and X, b.p. 77–87° (48 mm.), $n^{20}\text{D}$ 1.4311 and 0.66 g. of pure IX, b.p. 87–88° (48 mm.), $n^{20}\text{D}$ 1.4428 (lit.[42] b.p. 169° (733 mm.), $n^{20}\text{D}$ 1.4430). The total yield of IX and X was 4.23 g. (76%) which on the basis of refractive index consisted of exactly equal parts of IX and X.

Isopropylidene Mesitylidenemalonate (XV).—A mixture of 25.0 g. (0.169 mole) of mesitaldehyde,[43] 25.0 g. of isopropylidenemalonate (XIV)[38] and 70 ml. of pyridine was heated to 65–75° for 8 hours. The clear, red solution was cast into water and the solid which precipitated was collected by filtration and washed with water. Recrystallization of the crude product from acetone solution by adding water gave 32.5 g. (70%) of XV as fine, colorless needles, m.p. 148–149°. One recrystallization from ethanol gave analytically pure material, 30.2 g., m.p. 149–150°.

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.07; H, 6.70.

Ethyl Hydrogen Mesitylidenemalonate (VI).—A mixture of 6.0 g. (0.0219 mole) of the isopropylidene ester (XV) and 50 ml. of absolute ethanol containing a trace of dry hydrogen chloride was heated to reflux for 1.5 hours. The ethanol was removed by distillation under reduced pressure, the residue was triturated with 20 ml. of 2 *N* potassium bicarbonate solution and the mixture was filtered. The crude solid after recrystallization from ethanol afforded 2.1 g. of starting material. The bicarbonate solution was acidified with hydrochloric acid and extracted with three 25-ml. portions of ether. The ethereal solution was dried over calcium chloride, filtered and evaporated to a colorless oil which was dissolved in 15 ml. of ligroin. The product, 2.6 g. (67%), crystallized as short colorless needles, m.p. 91–95° with a small amount remaining unmelted until 105°, and is probably a mixture of *cis*- and *trans*-isomers. Recrystallization from methylene chloride–ligroin did not affect the melting point.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.58; H, 7.14.

Ethyl Hydrogen 2,6-Dichlorobenzylidenemalonate (VII).—Isopropylidene 2,6-dichlorobenzylidenemalonate was prepared from isopropylidenemalonate and 2,6-dichlorobenzaldehyde, m.p. 71–72°, using the procedure described for XV and a heating period of 16 hours. The yield of pure product, obtained as colorless plates, m.p. 150–155° after recrystallization from ethanol, was 69%.

Anal. Calcd. for $C_{13}H_{10}O_4Cl_2$: C, 51.85; H, 3.35; Cl, 23.55. Found: C, 51.94; H, 3.15; Cl, 23.45.

Treatment of isopropylidene 2,6-dichlorobenzylidenemalonate with ethanol as described for VI afforded VII as colorless prisms (from methylene chloride–ligroin), m.p. 86–100°, probably a mixture of *cis*- and *trans*-isomers.

Anal. Calcd. for $C_{12}H_{10}O_4Cl_2$: C, 49.85; H, 3.49; Cl, 24.53. Found: C, 49.76; H, 3.53; Cl, 24.62.

Decarboxylation Studies. (A) Materials.—The pyridine used for the present studies was prepared in the following way. Reagent grade pyridine (Mallinckrodt) was distilled from β-naphthyl isocyanate, dried over barium oxide and redistilled through a 30-cm. column packed with stainless steel helices. The pure pyridine so obtained (b.p. 115.3–115.6°) was saturated with carbon dioxide and stored in a tightly capped bottle.

The 0.5 *M* sodium iodide solution in pyridine was prepared from reagent grade sodium iodide, which had been dried overnight *in vacuo*, and the requisite quantity of the pure pyridine described above.

Pyridinium picrate (m.p. 164°) was prepared from pure pyridine and picric acid in hot 95% ethanol and recrystallized from ethanol to constant melting point.

N-Ethylpiperidine was prepared from ethyl sulfate and piperidine and purified by fractional distillation, b.p. 61° (70 mm.).

(B) **Apparatus and Procedure.**—The apparatus used consisted of a 50-ml. Pyrex reaction flask fitted with a mov-

---

(41) *Org. Syntheses*, **23**, 29 (1943).

(42) R. C. Huston and G. L. Goerner, THIS JOURNAL, **68**, 2504 (1946).

(43) Reference 41, p. 57.

able glass rod (held in the neck of the flask by a neoprene stopper) which protruded into the flask and a 35-cm. length of glass tubing (6 mm.) which was connected to a 100-ml. gas buret (readable to 0.05 ml. and containing mercury) through a three-way stopcock. The tube connecting the reaction flask and three-way stopcock was equipped with a 20-cm. water jacket through which cool water could be circulated. During runs the bulb of the reaction flask was immersed completely in a rapidly stirred, insulated, mineral oil-bath the temperature of which could be maintained within 0.05° in the range of 90–120°. The reaction flask was attached by a 30-cm. length of light metal rod to a separate ringstand which was caused to vibrate by the movements of a small electric motor having a 30-g. metal weight attached to one side of the rotating shaft. The flask could be shaken by this arrangement through an arc of about 0.7 cm. at a constant rate (approximately 300 times per minute).

An accurately weighed sample of the acid to be decarboxylated (0.0029–0.0038 mole) sealed in a small, thin-walled glass bulb and a measured portion of pyridine (or pyridine solution) (15–20 ml.) saturated with carbon dioxide were placed in the flask described above and the flask was immersed in the constant temperature bath, connected to the gas buret and shaken electrically. The system was allowed to attain equilibrium (about 20 minutes were usually necessary), the level of the mercury in the buret was set and the apparatus was closed to the atmosphere by manipulation of the three-way stopcock. If the buret reading remained constant for a period of 5 minutes, the reaction was started by breaking the sample bulb using the movable glass rod. Readings of the gas volume were taken every half-minute for the first 5–30 minutes of the reaction and subsequently at minute intervals. In every case studied, 95–98% yields of carbon dioxide were obtained. All runs were repeated at least once and values of α_t/t were always reproducible to within 3% for runs of the same initial acid concentration.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Stereospecificity in Rearrangements. IV. *erythro-* and *threo*-1-*p*-Chlorophenyl-1,2-diphenyl-2-bromoethanol[1]

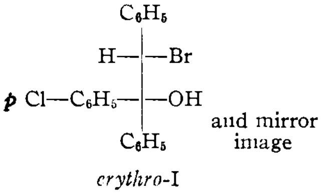
BY DAVID Y. CURTIN[2] AND ESTELLE K. MEISLICH

RECEIVED JUNE 27, 1952

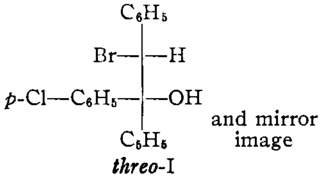
dl-erythro- and *dl-threo*-1-*p*-chlorophenyl-1,2-diphenyl-2-bromoethanol have been prepared by the bromination of 1-*p*-chlorophenyl-1,2-diphenylethanol with N-bromosuccinimide. The *erythro*-racemate rearranges with ethanolic silver nitrate to benzhydryl *p*-chlorophenyl ketone, while with ethylmagnesium bromide in boiling benzene it gives *p*-chlorobenzhydryl phenyl ketone. Conversely, the *threo*-racemate with ethanolic silver nitrate gives *p*-chlorobenzhydryl phenyl ketone and with ethylmagnesium bromide gives benzhydryl *p*-chlorophenyl ketone. The corresponding epoxides are shown not to be intermediates in the Grignard rearrangements.

In the previous papers of this series[3] it was shown that the course of the rearrangements of certain diastereoisomeric amino alcohols with nitrous acid was determined by the configuration of the reacting molecule. This paper reports a set of stereospecific rearrangements in a different system.

The two racemates of 1-*p*-chlorophenyl-1,2-diphenyl-2-bromoethanol (I) appeared to be ideally suited to the present purpose since a careful study had been made by Lane and Walters[4] of the rearrangement and related reactions under a variety of conditions of the unsubstituted analog, 1,1,2-triphenyl-2-bromoethanol.



erythro-I



threo-I

It was found that a mixture of *erythro-* and *threo*-I was readily obtained by bromination of 1-*p*-chlorophenyl-1,2-diphenylethanol with N-bromosuccinimide. (This method of synthesis was first used by Lane and Walters for the preparation of 1,1,2-triphenyl-2-bromoethanol.)

dl-erythro-I, m.p. 130°, and *dl-threo*-I, m.p. 109°, were separated from the crude bromination mixture by fractional crystallization.[5] Their configurations were established by conversion to the corresponding epoxides (II) of known configuration.[3c] Since this internal displacement reaction has been shown in other cases to occur with inversion of configuration,[6] the isomer which was converted to *trans*-II was assigned the *erythro*-configuration while that which gave *cis*-II was concluded to be *threo*.

The two racemates of I were rearranged with silver nitrate in ethanol. *dl-erythro*-I gave a 78% yield of benzhydryl *p*-chlorophenyl ketone, III, identified by ultraviolet absorption spectrum and mixed m.p., while *dl-threo*-I gave a 65% yield of *p*-chlorobenzhydryl phenyl ketone, IV. Although the IV obtained melted over a 5° range the ultraviolet absorption spectrum indicated that it was contaminated by less than 10% and probably no appreciable amount of the isomeric ketone, III. These reactions are shown for one enantiomorph of the *erythro*-series.

The results are consistent with the expectation[3] that each isomer should rearrange in such a way

---

[1] Part of the Ph.D. Thesis submitted by Estelle K. Meislich to Columbia University.

[2] Department of Chemistry, University of Illinois, Urbana, Illinois.

[3] (a) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950); (b) D. Y. Curtin and P. I. Pollak, *ibid.*, **73**, 992 (1951); (c) D. Y. Curtin, E. E. Harris and P. I. Pollak, *ibid.*, **73**, 3453 (1951).

[4] J. F. Lane and D. R. Walters, *ibid.*, **73**, 4234 (1951).

[5] The terms "*erythro*" and "*threo*" will be used here as shown below.

[6] See S. Winstein and R. B. Henderson, "Heterocyclic Compounds," Vol. I, R. C. Elderfield, Editor, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 13.