Base-Catalyzed Reactions of α,β-Unsaturated Esters and Nitriles. I. Potassium-Catalyzed Dimerization of Ethyl Crotonate[1a]

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Received May 28, 1965

Ethyl crotonate undergoes fast and selective dimerization at 110° in the presence of a potassium–benzylpotassium catalyst to form the diethyl ester of 2-ethylidene-3-methylglutaric acid (III) in 90% yield. It is indicated that the vinylic hydrogen at the α-position in respect to the ester group in ethyl crotonate is more acidic than the allylic methyl hydrogens and that dimerization is initiated by metalation at the former position. Compound III is a mixture of the two possible geometric isomers; the component in which the vinylic hydrogen is *cis* to the carboethoxy group represents 81% of the dimer.

It has been reported[2] recently that α- and β-methylstyrene react readily with alkylbenzenes in the presence of promoted alkali metal catalysts to form 1,3-diphenylalkanes. On the other hand, in nonexchanging solvents, *e.g.*, alkylcyclohexanes, β-methylstyrene undergoes dimerization in the presence of a sodium catalyst or hydrodimerization in the presence of dispersed potassium.[3]

It was expected that, by substituting the phenyl function in a styrene with other electron-withdrawing groups, similar aralkylation and dimerization reactions could be applied to other types of compounds, *e.g.*, α,β-unsaturated nitriles and esters. Low molecular weight polymeric products resulting from reactions catalyzed by alkali metals, alcoholates, or phenolates, have been described in the patent literature.[4] These data, however, include only limited information on the structure of the dimeric and trimeric products obtained or on the mechanism of their formation. von Pechmann,[5] who studied the dimerization of methyl and ethyl crotonate in ether solution and in the presence of an equimolar amount of sodium methoxide as a condensation agent, assigned to the main product the structure of diester of 2-ethylidene-3-methylglutaric acid.

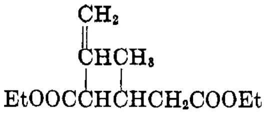
The present study deals with the reaction of ethyl crotonate in the presence of potassium–benzylpotassium as a catalyst. Preliminary experiments with Ia in excess toluene showed that, unlike β-methylstyrene,[2b] the ester does not react with the alkylbenzene to any appreciable extent and therefore the dimerization reaction can be conveniently carried out in this exchanging solvent.

The experiments were performed at the reflux temperature of toluene (110°) and the ethyl crotonate–toluene molar ratio was 1:10; 0.25 g.-atom of potassium and 0.1 mole of *o*-chlorotoluene per mole of monomer were employed in the preparation of the catalyst. Under these conditions (see Experimental Section) Ia undergoes faster dimerization compared with β-methylstyrene with almost complete exclusion of higher polymer formation. At a point of nearly quantitative conversion of the monomer, the dimer comprises about 90% of the product. The compound was purified by distillation [b.p. 84° (0.55 mm.), 243°; $n^{20}D$ 1.4512; mol. wt., 225 (calcd. for a dimer, $C_{12}H_{20}O_4$: mol. wt., 228)] and examined by a combination of infrared and n.m.r. spectroscopy, gas chromatography, and ozonation.

Three possible dimeric structures were considered.

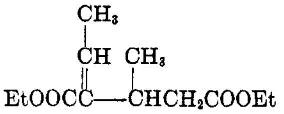
$$\mathrm{EtOOCCH{=}CHCH_2\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2COOEt}$$

I



$$\mathrm{EtOOC\overset{\overset{\overset{\displaystyle CH_2}{\|}}{\displaystyle CH}}{\overset{|}{C}}H\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2COOEt}$$

II



$$\mathrm{EtOOC\overset{\overset{\overset{\displaystyle CH_3}{|}}{\displaystyle CH}}{\overset{\|}{C}}{-\!\!-}\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2COOEt}$$

III

By analogy with β-methylstyrene[3] structures I and II could be formed if the dimerization is initiated by metalation of Ia at the allylic position. A third possibility (von Pechmann's structure III) could arise by metalation of the monomer at the α-vinylic position.[6]

Structure II is eliminated by examination of the infrared spectrum of the dimer (see Experimental Section), which shows the absence of a vinyl group in the molecule (absence of the specific absorption maxima near 910 and 990 cm.$^{-1}$, due to the $=CH_2$ and $=CH$ out-of-plane deformation, respectively). The presence of both saturated and an α,β-unsaturated ester groups is shown by the appearance of two absorption bands due to the C=O stretching vibration, *i.e.*, at 1742 and 1720 cm.$^{-1}$, respectively.[7] The presence of an α,β-unsaturated ester group is further evidenced by the two strong absorption bands at 1263 and 1183 cm.$^{-1}$ due to the C–O– stretching vibration,[8] as well as by the position of the C=C absorption band (1643 cm.$^{-1}$), which falls in the specific range for a carbonyl conjugated double bond (1647–1621 cm.$^{-1}$). Indication that the double bond is trisubstituted (struc-

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[1] (a) Paper XXXI of the series, "Base-Catalyzed Reactions." Paper XXX: N. C. Sih and H. Pines, *J. Org. Chem.*, **30**, 1462 (1965). (b) Weizmann Institute.

[2] (a) J. Shabtai and H. Pines, *J. Org. Chem.*, **26**, 4225 (1961); (b) J. Shabtai, E. M. Lewicki, and H. Pines, *ibid.*, **27**, 2618 (1962).

[3] J. Shabtai and H. Pines, *ibid.*, **29**, 2408 (1964).

[4] (a) Swiss Patent 240,616 (1946), *Chem. Abstr.*, **43**, 5792 (1949); (b) U. S. Patent 2,508,910 (1950), *Chem. Abstr.*, **44**, 7868 (1950); (c) German Patent 927,384 (1955), *Chem. Abstr.*, **50**, 8711 (1956).

[5] H. von Pechmann, *Ber.*, **33**, 3323 (1900).

[6] C. D. Broaddus, T. J. Logan, and T. J. Flautt, *J. Org. Chem.*, **28**, 1174 (1963); C. D. Broaddus, *ibid.*, **29**, 2689 (1964).

[7] *Cf.* L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1962, p. 179.

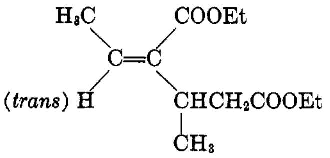
[8] Reference 7, p. 191.

ture III) is found in the presence of a medium-intensity band at 1378 cm.$^{-1}$ which is probably due to the inplane deformation of the single vinylic hydrogen.[9]

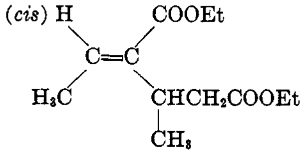
Full support for structure III is provided by the n.m.r. spectrum of the dimer. The total amount of vinylic protons (range, 5.7–7.1 p.p.m.) relative to the total amount of all protons in the molecule is in the ratio 1:21 (calcd. for III, 1:20). Also, the ratio of the total methyl *vs.* methylene protons is exactly 2:1 and that of allylic methyl protons *vs.* vinylic protons is 3:1, as expected for III. The protons of the allylic methyl group give rise to a doublet (centered at 1.82 p.p.m.) with a splitting equal to that of a pure quartet (centered at 6.8 p.p.m.) due to the vinylic proton (J = 7.2 c.p.s.). These data eliminate the possibility of structure I, which does not contain an allylic methyl group and which would require a 1:10 ratio for the vinylic *vs.* all remaining protons, as well as a 1.13:1 ratio for the methyl *vs.* methylene protons.

Hydrolysis of the dimer gives a diacid which, after recrystallization from carbon tetrachloride, has m.p. 126–127° (lit.,[5] for 2-ethylidene-3-methylglutaric acid, m.p. 127–128°). The structure of the acid was confirmed by ozonation which yielded an equimolar mixture of acetic acid and methylsuccinic acid, the latter being most likely derived by oxidation of the expected 2-oxo-3-methylglutaric acid under the conditions of oxidative decomposition of the ozonide (see Experimental Section). Final proof of structure III was provided by the n.m.r. spectrum of the free diacid which showed (1) a doublet at 1.23 p.p.m. (J = 6.5 c.p.s.) due to the secondary methyl group; (2) a doublet at 1.86 p.p.m. (J = 7.2 c.p.s.) due to the allylic methyl protons; (3) a closely spaced group of lines between 2.5 and 2.85 p.p.m. arising from the methylene protons; (4) a group of lines between 3.0 and 3.5 p.p.m. due to the methine proton; and (5) a pure quartet centered at 6.96 p.p.m. (J = 7.2 c.p.s.) due to the vinylic proton. The relative areas of the five groups of lines, in the order given, were 3:3:2:1:1 as expected for 2-ethylidene-3-methylglutaric acid (IV).

Closer examination of the n.m.r. spectrum of the diester III reveals that, in addition to the main quartet centered at 6.8 p.p.m., the vinylic proton gives rise to an additional quartet of lower intensity, centered at 5.97 p.p.m. This indicates that the dimer is a mixture of the two stereoisomers IIIa and IIIb.



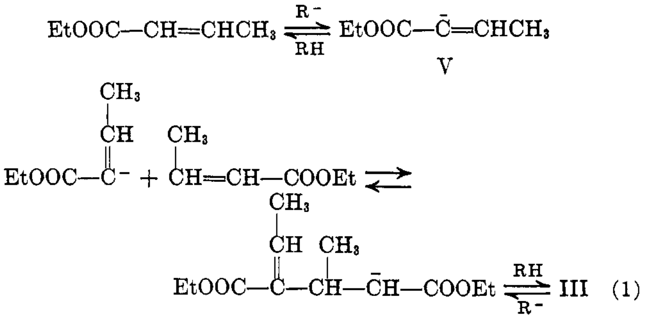
IIIa



IIIb

It is observed in the case of α,β-unsaturated esters and acids[10] that the β-carboalkoxy or carboxylic group, respectively, has a deshielding effect on the *cis*-vinylic proton. The differential shielding of the *cis*- and *trans*-vinylic protons is 0.58 p.p.m. for methacrylic acid[11] and 0.63 p.p.m. for methyl *cis*- and *trans*-crotonate.[12] The separation of the two quartets in the present case is 0.83 p.p.m. A separation effect is observed also for the doublet, due to the allylic methyl protons. The differential shielding in this case is only 0.06 p.p.m., with the methyl protons in IIIa which are *cis* to the β-carboethoxy group being more strongly deshielded (the minor doublet due to the allylic protons in the latter is centered at 1.88 p.p.m.). From the relative areas of the two quartets, due to the vinylic proton, it was calculated that isomer IIIb, in which the vinylic hydrogen is *cis* to the β-carbethoxy group, represents about 81% of the mixture obtained in the reaction. To confirm this conclusion the dimer was examined by gas chromatography. No separation was achieved on columns containing silicone gum rubber or polyester (diethylene glycol adipate or diethylene glycol succinate) as the stationary phase. The dimer was finally resolved into the two stereoisomers on a 300-ft. Golay capillary column coated with trifluoropropylmethylpolysiloxane. The isomers were in the ratio 81:19, in complete agreement with the n.m.r. determination. On the other hand, the n.m.r. spectrum of the free diacid shows that the minor component, corresponding to IIIa, is eliminated from the mixture during hydrolysis or subsequent recrystallization of the acidic product.

The exclusive formation of structure III indicates that the α-vinylic hydrogen in ethyl crotonate is considerably more acidic than the allylic methyl hydrogens and that the dimerization is most likely initiated by preferential metalation at this position.



$$\mathrm{EtOOC{-}CH{=}CHCH_3} \underset{\mathrm{RH}}{\overset{\mathrm{R^-}}{\rightleftharpoons}} \underset{\mathrm{V}}{\mathrm{EtOOC{-}\bar{C}{=}CHCH_3}}$$

$$\mathrm{EtOOC{-}\overset{\overset{\displaystyle CH_3}{|}}{\overset{CH}{\|}}{\!\!C^-}} + \mathrm{\overset{\overset{\displaystyle CH_3}{|}}{C}H{=}CH{-}COOEt} \rightleftharpoons \mathrm{EtOOC{-}\overset{\overset{\displaystyle CH_3}{|}}{\overset{CH}{\|}}{C}{-}\overset{\overset{\displaystyle CH_3}{|}}{C}H{-}\bar{C}H{-}COOEt} \underset{\mathrm{R^-}}{\overset{\mathrm{RH}}{\rightleftharpoons}} \mathrm{III} \qquad (1)$$

Rearrangement of carbanion V to a resonance-stabilized allylic carbanion would require an intramolecular proton transfer. It has been indicated[6b] that isomerization of this type occurs in the metalation of α-olefins with n-butylpotassium; however, the reaction is slower compared with the initial metalation step. In the present case no rearrangement of V is indicated, as such step is evidently much slower compared with the addition of the carbanion to a second monomer molecule.

A second but more remote possibility is that ethyl crotonate is metalated at the allylic position and the resulting carbanion ($\mathrm{EtOOC{-}CH{\overset{...}{=}}\bar{C}H{\overset{...}{=}}CH_2}$) reacts exclusively as the carbonyl-stabilized carbanion IIa

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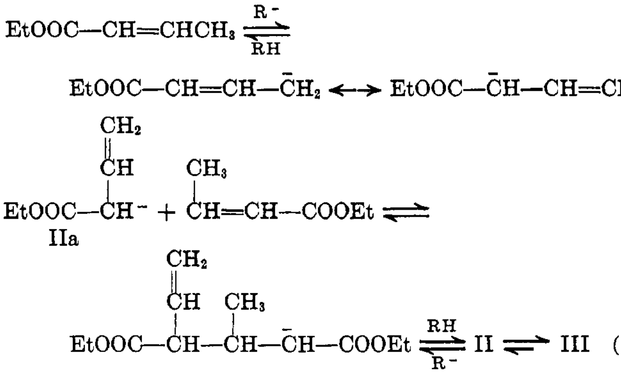
(9) Reference 7, p. 53.

(10) *Cf.* L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., Oxford, 1962, pp. 119–120.

(11) *Cf.* N. S. Bhacca, L. F. Johnson, and J. N. Schoolery, "N.M.R. Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, Spectrum No. 62.

(12) Reference 10, p. 122.



$$\mathrm{EtOOC{-}CH{=}CHCH_3} \underset{\mathrm{RH}}{\overset{\mathrm{R^-}}{\rightleftharpoons}} \mathrm{EtOOC{-}CH{=}CH{-}\bar{C}H_2} \longleftrightarrow \mathrm{EtOOC{-}\bar{C}H{-}CH{=}CH_2}$$

$$\underset{\mathrm{IIa}}{\mathrm{EtOOC{-}\overset{\overset{CH_2}{\|}}{\overset{CH}{|}}{C}H^-}} + \mathrm{\overset{CH_3}{\overset{|}{C}}H{=}CH{-}COOEt} \rightleftharpoons \mathrm{EtOOC{-}\overset{\overset{CH_2}{\|}}{\overset{CH}{|}}{C}H{-}\overset{CH_3}{\overset{|}{C}}H{-}\bar{C}H{-}COOEt} \underset{\mathrm{R^-}}{\overset{\mathrm{RH}}{\rightleftharpoons}} \mathrm{II} \rightleftharpoons \mathrm{III} \quad (2)$$

to give dimer II, which finally undergoes quantitative isomerization to the conjugated dimer III.

The intermediate II required by this mechanism could not be detected in the reaction product even at a point of only 10% conversion of the monomer.

It should be noted that, whereas β-methylstyrene is metalated preferentially at the allylic position,[3] it seems more plausible that in the present case metalation takes place at the α-vinylic position. The difference could be explained by the stronger electron-withdrawing effect of an ester as compared with a phenyl group.

Experimental Section

Materials.—The ethyl crotonate employed (Fluka A.G.) was 99.5% pure, as determined by gas chromatography. It was dried and redistilled before use: b.p. 137–139°, $n^{20}\mathrm{D}$ 1.4258. The other materials included: analytical grade toluene dried for several days over sodium, redistilled *o*-chlorotoluene, and regular grade potassium.

Dimerization Procedure. Diethyl 2-Ethylidene-3-methylglutarate (III).—The preparation of the potassium–benzylpotassium catalyst and a typical dimerization experiment were carried out as follows.

Toluene (30 g.) was introduced into a 250-ml. three-neck flask equipped with a constant-rate dropping funnel, a reflux condenser, and a high-speed (10,000 r.p.m.) dispersing stirrer. The air in the apparatus was displaced with a stream of helium, freshly cut potassium (2 g.) was added to the flask, and the mixture was brought to boiling and kept under reflux for 20 min. without mixing. The molten metal was then stirred for 1 hr. and *o*-chlorotoluene (1.2 g.) dissolved in toluene (10 g.) was added dropwise to the dispersion. The catalyst acquired at this stage a black color. Another portion of toluene (70 g.) was added (45 min.) and the mixing was extended for 30–40 min.

Ethyl crotonate (22.8 g., 0.2 mole) dissolved in toluene (74 g.) was added dropwise to the catalyst with constant stirring (45 min.). The temperature was kept at 110° throughout. After completing the addition of the ester, the reaction was continued for another 25–30 min. The mixture was quickly cooled to 0–2° with an ice–water bath and the catalyst was decomposed by slowly adding 10–15 ml. of absolute ethanol (decomposition with ethanol at room or higher temperature causes side reactions). The product was washed with 10% hydrochloric acid, 10% aqueous sodium bicarbonate, and water and then dried over anhydrous magnesium sulfate. The solvent and unreacted monomer were removed at 100 mm. and the remaining product (21.0 g., 92% conversion) was distilled through a small Vigreux column. The dimer, b.p. 80–82° (0.2 mm.), was 90 wt. % of the total. A small second fraction (6%), b.p. 138–142° (0.2 mm.), was also collected, leaving a residue and holdup of only 4%.

The dimeric product from several experiments was combined and redistilled through a 12 × 1 cm. column filled with stainless steel wire gauze packing. The diethyl 2-ethylidene-3-methylglutarate (III) obtained was more than 99.5% pure and free of any monomer or trimer: b.p. 84° (0.55 mm.), 243°; $n^{20}\mathrm{D}$ 1.4512; mol. wt. (Beckman's method), 225 (calcd. for $C_{12}H_{20}O_4$: mol. wt., 228).

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.33; H, 8.68.

Compound III shows the following infrared absorption maxima (intensity: s, strong; m, medium; w, weak): 612 (m), 764 (m), 870 (w), 950 (w), 987 (w), 1040 (s), 1080 (w), 1124 (w), 1183 (s), 1263 (s), 1293 (w), 1378 (m), 1390 (w), 1456 (m), 1469 (m), 1643 (m), 1720 (s), 1742 (s), 2990 (s) cm.$^{-1}$.

2-Ethylidene-3-methylglutaric Acid (IV).—III (4.0 g.) was hydrolyzed by refluxing with 10% aqueous sodium hydroxide (100 ml.). The hydrolysate was acidified with hydrochloric acid and continuously extracted with ether. The crystalline acid obtained after removing the solvent weighed 2.8 g. (yield 93%). It was recrystallized from carbon tetrachloride containing some ethyl acetate: m.p. 126–127° (lit.,[5] for 2-ethylidene-3-methylglutaric acid, m.p. 127–128°).

The presence of two carboxylic groups in IV was confirmed by titration in alcoholic solution: 66 mg. of IV required 7.60 ml. of a 0.09935 *N* sodium hydroxide solution (98.8% of theoretical).

Ozonation of 2-Ethylidene-3-methylglutaric Acid (IV).—A pure sample of IV (2.2 g.) was dissolved in carbon tetrachloride (70 ml.) and ozonized at −20°. After removing the solvent under vacuum, the ozonide was decomposed by stirring for 2 hr. with water (20 ml.), 30% hydrogen peroxide (20 ml.), and 10% aqueous sodium carbonate (30 ml.) and then boiling the mixture for 3 hr. Another 5 ml. of the hydrogen peroxide solution was added and the refluxing was continued for 2 hr. The solution was acidified, saturated with sodium chloride, and continuously extracted with ether. The solvent was removed, leaving 2.4 g. of a product which partially crystallized. The liquid part of the product was distilled at 25 mm. into a small liquid air trap and identified as acetic acid (0.72 g.) by its infrared spectrum. The remaining crystalline compound (1.63 g.) had m.p. 108–109°. It was purified by sublimation at 0.1 mm. to give m.p. 109–109.5° [lit.,[13] for (±)-methylsuccinic acid purified by sublimation, m.p. 108–110°]. The product did not depress the melting point of a reference sample of the acid purified by the same procedure.

The two acids (200-mg. portions) were esterified in dry ether solution with diazomethane and the methyl esters obtained were examined by gas chromatography on a polyester column (see Analytical). The retention volumes of the two compounds were identical with those of methyl acetate and the dimethyl ester of a pure sample of methylsuccinic acid, respectively. The product of a second ozonation experiment was esterified without separating the two acids and it was confirmed by gas chromatographic analysis that the two components were in equimolar amounts.

2-Ethyl-3-methylglutaric Acid (VI).—Compound III (2.076 g.) was hydrogenated in alcoholic solution in the presence of Adams catalyst (300 mg.). The volume of hydrogen absorbed was 206.0 cc. (STP) corresponding to 1.01 mole of hydrogen absorbed/mole of III. Hydrolysis of the product gave acid VI, which after recrystallization from carbon tetrachloride had m.p. 83–85° [lit.,[14] for a low-melting form of VI (apparently the pure *threo* isomer), m.p. 88°].

Analytical.—The infrared spectrum of III was measured with a Model IR7 Beckman spectrophotometer, using a microcell with capillary thickness. A Varian A-60 spectrometer was employed for the measurement of the n.m.r. spectra, using carbon tetrachloride or deuterated chloroform as a solvent and tetramethylsilane as reference compound. All n.m.r. line positions are reported in parts per million (δ).

Gas chromatographic analysis was carried out with a Model 300 F & M gas chromatograph using the following columns: (a) a 9-ft. column filled with10% silicone gum rubber on Chromosorb P; (b) two 8-ft. columns packed with 15% diethylene glycol adipate polyester and 15% diethylene glycol succinate polyester, respectively, on the same support. Separation of the two stereoisomers of III was achieved on a Perkin-Elmer 300 ft. × 0.01 in. Golay column, coated with Dow-Corning FS-1265 fluorosilicone fluid (trifluoropropylmethylpolysiloxane), using a Perkin-Elmer Fractometer with flame-ionization detector. Best resolution was obtained at 140° and a nitrogen pressure of 20 p.s.i.

Acknowledgment.—Thanks are due to Dr. B. Altman for valuable laboratory assistance and to Mr. C. Klopfenstein for helpful discussion of the n.m.r. spectral data.

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(13) G. D. Buckley, *J. Chem. Soc.*, 1325 (1953).

(14) A. Michael and J. Ross, *J. Am. Chem. Soc.*, **53**, 1156 (1931).