Pyrolysis of Esters. XXVI. Synthesis of Half Acids by the Pyrolysis of Diesters

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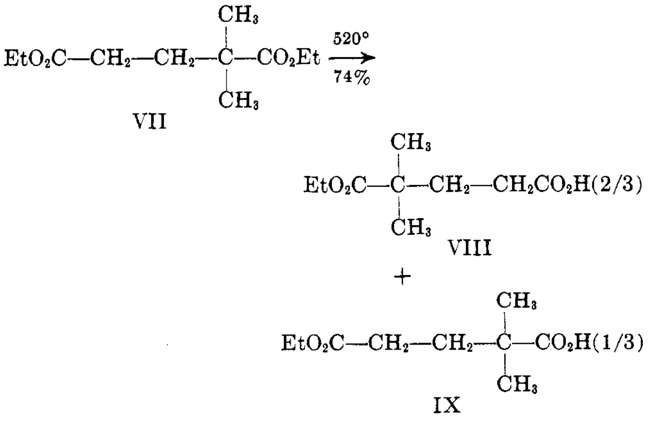
Since it was shown in these laboratories that the pyrolysis of esters was an excellent tool for the synthesis not only of olefins but also a variety of compounds derived from the acid portion, such as acids,[3,4] ketones,[5] nitriles,[6] and esters,[4] a search for other synthetic applications was undertaken. Because of the convenience of recycling unchanged starting material, it appeared that the pyrolysis of esters could be successfully applied to the preparation of half esters of dibasic acids. Three general methods for the synthesis of half esters have been used: the first involves the esterification of the dibasic acid under conditions mild enough to permit only one of the acid groups to be esterified; the second employs the partial saponification of a diester; and the third involves the disproportionation of a diester and a diacid. Applied to the preparation of ethyl hydrogen sebacate (I), the first method generally gives poor yields.[7] The second method, although very satisfactory where steric factors are important, gives low yields for the preparation from diethyl sebacate (II).[8] Fourneau and Sebetay[9] used the third method to prepare ethyl hydrogen sebacate (I) in a 54% yield by heating a mixture of diethyl sebacate (II) and sebacic acid at 280–300° for 5 hr. This procedure has the disadvantage that both the diester and diacid are required. Swan, Oehler, and Buswell[10] used a combination of the first and third methods to give, in the best available synthesis, a 60 to 65% yield of ethyl hydrogen sebacate (I). In this preparation sebacic acid (1 mole), diethyl sebacate (0.58 mole), ethanol (1.3 moles), dibutyl ether, and concentrated hydrochloric acid are heated for four hours in a complex procedure. The presence of the diethyl ester suppresses formation of additional diester and is recovered for use in a subsequent run. It seemed likely that pyrolysis of diethyl sebacate could be a simpler synthesis for the preparation of the half acid.

$$\underset{\text{II}}{\mathrm{EtO_2C{-}(CH_2)_8CO_2Et}} \xrightarrow[69\%]{440^\circ} \underset{\text{I}}{\mathrm{EtO_2C{-}(CH_2)_8{-}CO_2H}}$$

$$\underset{\text{IV}}{\mathrm{EtO_2C{-}(CH_2)_4CO_2Et}} \xrightarrow[78\%]{470^\circ} \underset{\text{III}}{\mathrm{EtO_2C{-}(CH_2)_4{-}CO_2H}}$$

$$\underset{\text{VI}}{\mathrm{EtO_2C{-}(CH_2)_3CO_2Et}} \xrightarrow[80\%]{500^\circ} \underset{\text{V}}{\mathrm{EtO_2C{-}(CH_2)_3{-}CO_2H}}$$



$$\underset{\text{VII}}{\mathrm{EtO_2C{-}CH_2{-}CH_2{-}C(CH_3)_2{-}CO_2Et}} \xrightarrow[74\%]{520^\circ} \underset{\text{VIII}}{\mathrm{EtO_2C{-}C(CH_3)_2{-}CH_2{-}CH_2CO_2H}}(2/3) + \underset{\text{IX}}{\mathrm{EtO_2C{-}CH_2{-}CH_2{-}C(CH_3)_2{-}CO_2H}}(1/3)$$

When diethyl sebacate (II) was added dropwise to a Vycor pyrolysis tube packed with Pyrex helices at 440°, a 28% conversion to ethyl hydrogen sebacate (I), a 7.7% conversion to sebacic acid, and a 59% recovery of starting material II were noted. The yield of half ester, based on unrecovered starting diester II, was, therefore, 69%. (The yield, based on both unrecovered diester and diacid, was 85%.) The temperature of pyrolysis was critical; at 430° a 21% conversion to ethyl hydrogen sebacate (I) or a 50% yield, based on unrecovered diester II, was realized, while at 450° a 34% conversion to half ester or a 50% yield, based on unrecovered diester II, was obtained. At lower temperatures less of the diester is pyrolyzed while at higher temperatures secondary pyrolysis of the ethyl hydrogen sebacate (I) to sebacic acid becomes more important.

When diethyl adipate (IV) was pyrolyzed at 470°, a 28% conversion to ethyl hydrogen adipate (III) was obtained, at the same time a 7.5% conversion to adipic acid plus a 64% recovery of starting material IV were realized. The yield of half ester III, based on unrecovered diester IV, was, therefore, 78%, while the yield, based on both unrecovered diester and diacid, was 99%. The 78% yield of ethyl hydrogen adipate (III) compares favorably with the 71 to 75% yield obtained by the method of Swan, Oehler, and Buswell.[10]

Pyrolysis of diethyl glutarate (VI) at 500° gave a 41% conversion to ethyl hydrogen glutarate (V) plus a 48.5% recovery of starting diester VI. The yield of half ester V, based on unrecovered diester VI, was 80%. Bachmann, Kushner, and Stevenson[11] reported a 90% yield of ethyl hydrogen glutarate (V) from glutaric anhydride for a small run with a short reaction time. In this laboratory, however, large runs with a necessarily longer reaction time gave only a 60% yield of half ester plus considerable quantities of diethyl glutarate and glutaric acid. Apparently ethyl hydrogen glutarate (V) is a strong enough acid to catalyze the disproportionation during the 10-hr. heating period. If the reaction mixture of glutaric anhydride and ethanol was allowed to stand several days at room temperature, a 78% yield of the half ester was obtained.

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[1] Previous paper in this series, *J. Org. Chem.*, **29**, 1249 (1964).

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[3] W. J. Bailey and W. N. Turek, *J. Am. Oil Chemists' Soc.*, **33**, 317 (1956).

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Since it appeared that the pyrolysis of diesters to half esters was a useful synthetic method, it was of interest to determine the influence of steric hindrance on the selectivity of the elimination reaction. Diethyl α,α-dimethylglutarate (VII), which has one hindered ester group and one unhindered group, was prepared in 55% yield by the oxidation of commercially available 2,2-dimethyl-4-cyanobutyraldehyde with a mixture of nitric and sulfuric acids, followed by esterification of the resulting diacid. A high selectivity was not expected, since it was shown previously[3] that ethyl 2,4,6-trimethylbenzoate pyrolyzed at 560° to give a 90% yield of the corresponding acid. Since the coordination numner of the carbonyl carbon atom apparently is not increased beyond three during cleavage, the pyrolysis does not exhibit the great sensitivity to steric hindrance that do reactions involving addition to the carbonyl group. When the diethyl α,α-dimethylglutarate (VII) was saponified with 0.7 molar equivalent of potassium hydroxide, a 65% yield of 4-methyl-4-carbethoxypentanoic acid (VIII), which gave only a single peak on vapor phase chromatography, was obtained. However, when the diester was pyrolyzed at 520°, a 51% conversion to a mixture of half esters VIII and IX was obtained. Since 32% of starting ester VII also was recovered, the yield of half esters, based on unrecovered starting materials, was 74%. Vapor phase chromatography indicated that the mixture of half esters consisted of about two-thirds 4-methyl-4-carbethoxypentanoic acid (VIII) and one-third 2,2-dimethyl-4-carbethoxybutanoic acid (IX). It can be concluded that steric hindrance plays a small but definite role in the pyrolysis of esters.

Experimental[12]

Pyrolysis of Diethyl Sebacate (II).—Preliminary pyrolyses of diethyl sebacate (II) (Eastman Kodak Co., n^{25}D 1.4333) at 475 and 450° with the apparatus described previously[13] indicated the formation of 140 and 77% of one molar equivalent of titratable hydrogen ion, respectively. These amounts were determined by solution of the pyrolysates in 250 ml. of alcohol, followed by titration of 25-ml. aliquots with standard sodium hydroxide, with phenolphthalein as the indicator.

At a nitrogen flow rate of 60 bubbles per min., 233 g. (0.903 mole) of diethyl sebacate (II) was added dropwise to the Vycor pyrolysis tube packed with 1/8-in. Pyrex helices and externally heated at 440° over a period of 11 hr. To avoid any charring, the pyrolysis tube was changed after approximately half the material had been added. The pyrolysate, 218.7 g., was fractionated under reduced pressure through a 10-in., helix-packed column to yield 59.1 g. (28%) of ethyl hydrogen sebacate (I), b.p. 152° (0.6 mm.), m.p. 35° [reported[14] b.p. 210° (18 mm.), m.p. 36°]; 137.5 g. (59% recovery) of diethyl sebacate (II); and 12.3 g. of sebacic acid, m.p. 135°. The yield of ethyl hydrogen sebacate (I), based on unrecovered diester II, was 69%.

Pyrolysis of Diethyl Adipate (IV).—Preliminary runs at 430 and 450° indicated that the extents of pyrolysis at these temperatures were 38.5 and 86.5%, respectively, of one molar equivalent of titratable hydrogen ion.

By the procedure described for diethyl sebacate (II), 96.5 g. (0.477 mole) of diethyl adipate (IV) (Eastman Kodak Co., n^{25}D 1.4240) was pyrolyzed at 470° over a period of only 1 hr. Fractionation of the 89.9 g. of pyrolysate through a 10-in. Vigreux column under reduced pressure produced 23.6 g. (28%) of ethyl hydrogen adipate (III), b.p. 98° (0.03 mm.), m.p. 29° [reported[15] b.p. 180° (19 mm.), m.p. 29°]; and 61.5 g. (64% recovery) of diethyl adipate (IV). At the end of the distillation a considerable amount of solid adipic acid was observed in the column. In order to recover this, 100 ml. of ethanol was added to the distillation flask and refluxed into the column and distillation head until all the adipic acid was washed into the flask. Evaporation of the ethanol produced 5.2 g. (7.5%) of adipic acid. The yield of ethyl hydrogen adipate (III), based on unrecovered diester IV, was 78%.

Pyrolysis of Diethyl Glutarate (VI).[16]—Over a period of 3.5 hr., 224 g. (1.19 moles) of diethyl glutarate (VI) was pyrolyzed at 500°. Fractionation of the pyrolysate through a 12-in., helix-packed column gave 77.7 g. (41%) of ethyl hydrogen glutarate (V), b.p. 126–130° (3.2 mm.), n^{26}D 1.4350 [reported[11] b.p. 159–165° (17 mm.)]; and 108.5 g. (48.5% recovery) of starting diester VI. The yield of V, based on unrecovered VI, was, therefore, 80%.

Diethyl α,α-Dimethylglutarate (VII).—By the method of Hoch and Karrer[17] 2,2-dimethyl-4-cyanobutyraldehyde[18] was oxidized with a mixture of nitric and sulfuric acids to form the dimethylglutaric acid, m.p. 82° (reported[17] m.p. 84–85°), in a 55% yield. To a 1-l. flask equipped with a 10-in. Vigreux column were added 173 g. (1.08 moles) of α,α-dimethylglutaric acid, 378 ml. (6.49 moles) of absolute alcohol, 195 ml. of toluene, and 0.94 ml. of concentrated sulfuric acid. The azeotrope was removed by distillation until the temperature of the vapors rose to 78°. The distillate then was dried over 150 g. of potassium carbonate and returned to the reaction flask. The distillation was continued until the temperature again rose to 78°. (The oil-bath temperature did not exceed 150°.) The residue was then fractionated through a 10-in., helix-packed column to give 194.9 g. (77%) of diethyl α,α-dimethylglutarate (VII), b.p. 128° (28 mm.), n^{25}D 1.4250.

Anal. Calcd. for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.12; H, 9.37.

Vapor phase chromatography of VII on a commercial Tide column at 327° with helium flow of 0.25 ml. per sec.; sensitivity: 7, and detector current of 25 ma. gave a single peak with a retention time of 1.6 min.

Pyrolysis of Diethyl α,α-Dimethylglutarate (VII).—Pyrolysis of 5- to 10-g. quantities of diethyl α,α-dimethylglutarate (VII) by the procedure described above indicated that, at 450, 500, 520, and 550°, 13, 58, 98, and 147% of one molar equivalent of titratable hydrogen ion, respectively, were liberated.

At 520°, 42.7 g. (0.198 mole) of diethyl α,α-dimethylglutarate (VII) was pyrolyzed over a period of 2.5 hr. The pyrolysate (37.5 g.) was fractionated through a 2-ft., spiral-wire column to yield 18.8 g. (51%) of material, b.p. 98° (0.05 mm.), n^{25}D 1.4406, assumed to be a mixture of 4-methyl-4-carbethoxypentanoic acid (VIII) and 2,2-dimethyl-4-carbethoxybutanoic acid (IX). In addition to the half esters, 13.5 g. (32% recovery) of starting material and 3.6 g. (11%) of α,α-dimethylglutaric acid were obtained. The yield of half esters, based on unrecovered starting material, was 74%.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.44; H, 8.57. Found: C, 57.40; H, 8.27.

Examination of crude pyrolysate before fractionation, under conditions identical with those described for 4-methyl-4-carbethoxypentanoic acid (VIII), revealed three peaks: (1) a large peak (1.6 min.) which corresponded to the diester starting material (VII); (2) a peak (2.5 min.) which was assumed to be the other possible half ester, 2,2-dimethyl-4-carbethoxybutanoic acid (IX); and (3) a peak identified by its retention time (4.6 min.) to be 4-methyl-4-carbethoxypentanoic acid (VIII). With the assumption that the total area under the second and third peaks represents only the two half esters, it can be said that, of the total amount of half esters formed by pyrolysis of diethyl α,α-dimethylglutarate, about two-thirds was 4-methyl-4-carbethoxypentanoic acid (VIII) and about one-third was 2,2-dimethyl-4-carbethoxybutanoic acid (IX).

4-Methyl-4-carbethoxypentanoic Acid (VIII).—To a 1-l., three-necked flask, equipped with a dropping funnel, a thermometer,

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(12) The authors are grateful to Mrs. Kathryn Baylouny and Mrs. Jane Ratka for the microanalyses.

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(16) The authors are grateful to Dr. John J. Daly, Jr., for this pyrolysis.

(17) D. Hoch and P. Karrer, *Helv. Chim. Acta*, **37**, 397 (1954).

(18) The authors are grateful to the Tennessee Eastman Co., Kingsport, Tenn., for a generous sample of this material.

and a stirrer, were added 24.1 g. (0.122 mole) of diethyl α,α-dimethylglutarate (VIII), 10 ml. of water, and 200 ml. of methyl alcohol. A solution of 4.5 g. (0.08 mole) of potassium hydroxide in 15 ml. of water was then added at a rate sufficient to keep the reaction mixture below 26° over a period of 6 hr. The mixture was then stirred at room temperature for an additional 10 hr. After the major portion of the methyl alcohol was removed by distillation under reduced pressure, 300 ml. of water was added and the residue was acidified to pH 4 by the dropwise addition of concentrated hydrochloric acid. The aqueous solution was then extracted with four 100-ml. portions of ether. After the ether extracts had been dried over anhydrous magnesium sulfate, the mixture was fractionated through a 2-ft. spiral-wire column to yield 13.7 g. (65%) of 4-methyl-4-carbethoxypentanoic acid (VIII), b.p. 100° (0.4 mm.), $n^{25}\mathrm{D}$ 1.4355.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.44; H, 8.57. Found: C, 57.36; H, 8.72.

Vapor phase chromatography under the exact conditions described above for diethyl α,α-dimethylglutarate (VII) gave only one peak with a retention time of 4.6 min.

Reduction of the Double Bond in Ethylidenemalonic Ester by Lithium Aluminum Hydride

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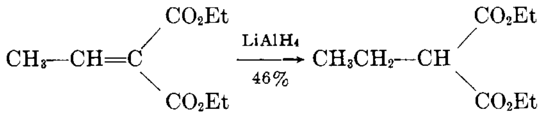
In an attempt to prepare a sample of 2-hydroxymethyl-2-buten-1-ol, ethylidenemalonic ester was treated with a large excess of lithium aluminum hydride. Surprisingly, the product was not the unsaturated diol but the saturated ester, ethyl ethylmalonate.



$$\mathrm{CH_3{-}CH{=}C(CO_2Et)_2 \xrightarrow[46\%]{LiAlH_4} CH_3CH_2{-}CH(CO_2Et)_2}$$

The reduction of the double bond in several unsaturated esters with lithium aluminum hydride has been previously reported in the literature. Ethyl *o*-hydroxycinnamate was reduced to *o*-(3-hydroxypropyl)-phenol[2] and methyl α-cyanocinnamate was reduced to 2-benzyl-3-amino-1-propanol[3] in a 30% yield. Cinnamaldehyde is also reduced to 3-phenylpropanol, but in this case it has been shown that the mechanism of the reduction involves the reduction of the carbonyl group to give a salt of cinnamyl alcohol which is subsequently reduced to the saturated alcohol.[4] In fact cinnamyl alcohols can be prepared in good yields by the reverse addition of the lithium aluminum hydride to various ethyl cinnamates.[5] A few other cases are reported in which a carbon–carbon double bond is reduced in preference to a highly reducible group in the same molecule. Gilsdorf and Nord[6] found that the reverse addition of the hydride to 1-phenyl-2-nitropropene at −40 to −50° gave a 56% yield of 1-phenyl-2-nitropropane. At higher temperature they isolated some benzylacetoxime. Since this work was completed LeMoal, Carrie, and Bargain[7] reported the reduction of α-cyano-β-phenylcinnamonitrile and the related cyanoacetic ester to the corresponding dihydro derivatives with several complex hydrides. Surprisingly they also reported that it was not possible to reduce the α-carbethoxy-β-phenylcinnamic ester to its dihydro derivatives with any of the hydrides used.

Since prolonged reflux during the reduction of unsaturated esters with lithium aluminum hydride resulted in lower yields[8] than with the saturated esters, ethylidenemalonic ester was reduced with a large excess (eight equivalents) of hydride for 1 hr. at 15° to give a 31% yield of ethyl ethylmalonate. Vapor phase chromatography showed that the material gave only one symmetrical peak and its infrared spectrum was identical with that for an authentic sample of ethyl ethylmalonate. When the reduction was carried out with a 10% excess of hydride, a 43% yield of ethylmalonic ester was obtained, together with a large amount of polymeric residue. With two equivalents of hydride a 46% yield of the ethylmalonate was obtained plus a somewhat smaller amount of polymeric residue.

Brown, Mead, and Subba Rao[9] showed that sodium borohydride plus lithium bromide in diglyme gave excellent yields of alcohols from esters. Its increased selectivity was illustrated by the reduction of ethyl cinnamate to cinnamyl alcohol in high yields. However, the reduction of ethyl ethylidenemalonate with an excess of this reagent gave a 30% yield of ethylmalonate plus a large amount of a high boiling residue. With an equivalent amount of this hydride, a 20% yield of the ethylmalonate resulted.

One can rationalize the results described by the assumption that the hydride ion preferentially adds in a 1,4 manner to the ethylidenemalonate to produce the stable enolate of ethylmalonic ester. The charge on the enolate retards further reduction to the saturated diol. With only a slight excess of hydride the low concentration of enolate favors the Michael addition to the starting unsaturated ester to produce the polymeric residue.

Experimental[10]

Reduction of Ethyl Ethylidenemalonate with Lithium Aluminum Hydride.—To a slurry of 2.36 g. (0.0625 mole) of lithium aluminum hydride in 100 ml. of dry ether was added a solution of 23.2 g. (0.125 mole) of ethyl ethylidenemalonate in 50 ml. of ether at a rate such as to keep the temperature of the reaction mixture below 15° while the flask was immersed in an ice bath. After the mixture had been stirred for an additional hour, it was poured into a mixture of ice and dilute hydrochloric acid. The aqueous layer was extracted with two 50-ml. portions of ether. After the combined ether layer and ether extracts were dried over anhydrous magnesium sulfate and the ether had been removed by distillation at atmospheric pressure, the residue was fractionated through a 10-in. Vigreux column to give 11.1 g. (46%) of ethyl ethylmalonate, b.p. 70° (4 mm.), $n^{25}\mathrm{D}$ 1.4172 [lit.[11] b.p. 94–96° (13 mm.), $n^{20}\mathrm{D}$ 1.4170].

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.81; H, 8.55.

V.p.c. of this ester at 205° on a silicone grease–Chromosorb column gave only one symmetrical peak; under the same condi-

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