[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

A SYNTHESIS OF α-ETHOXYMETHYLENE AND α-CHLOROMETHYLENE CARBOXYLIC ESTERS[1, 2]

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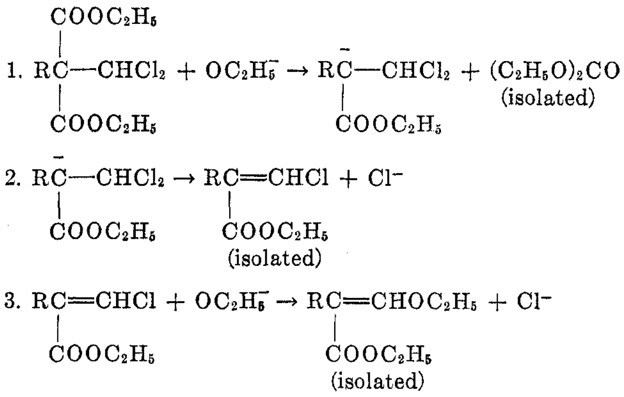
It has been found that substituted dichloromethyl malonic esters react rapidly above 65° in inert solvents with one equivalent of ethoxide ion to give α-chloromethylene carboxylic esters in yields generally over 90%. The other products are diethyl carbonate and chloride ion. If two equivalents of ethoxide ion are used the organic product is the corresponding α-ethoxymethylene carboxylic ester.

If the reaction between a substituted dichloromethyl malonic ester and two equivalents of ethoxide ion is carried out in absolute ethanol, two and possibly three kinds of fission of the molecule take place:

1. Fission of diethyl carbonate to yield α-ethoxymethylene carboxylic esters.
2. Fission of ethyl orthoformate to yield the simple substituted malonic ester.
3. Fission of diethyl carbonate and ethyl orthoformate to yield the ester of the acid which would have been obtained by hydrolysis and decarboxylation of the mono-substituted malonic ester.

The following equations represent the reactions and some proposed mechanisms for the formation of the products:

In inert solvent (eg. xylene, ether):



$$1.\ R\overset{COOC_2H_5}{\underset{COOC_2H_5}{C}}—CHCl_2 + OC_2H_5^- \rightarrow R\overset{-}{\underset{COOC_2H_5}{C}}—CHCl_2 + \underset{\text{(isolated)}}{(C_2H_5O)_2CO}$$

$$2.\ R\overset{-}{\underset{COOC_2H_5}{C}}—CHCl_2 \rightarrow \underset{\text{(isolated)}}{R\underset{COOC_2H_5}{C}{=}CHCl} + Cl^-$$

$$3.\ R\underset{COOC_2H_5}{C}{=}CHCl + OC_2H_5^- \rightarrow \underset{\text{(isolated)}}{R\underset{COOC_2H_5}{C}{=}CHOC_2H_5} + Cl^-$$

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[1] A U. S. Patent Application covering the subject matter of this paper has been filed by Research Incorporated, N. Y., N. Y., Assignee of the second author.

[2] Requests for reprints should be sent to The Librarian, Frick Chemical Laboratory, Princeton University, Princeton, N. J.

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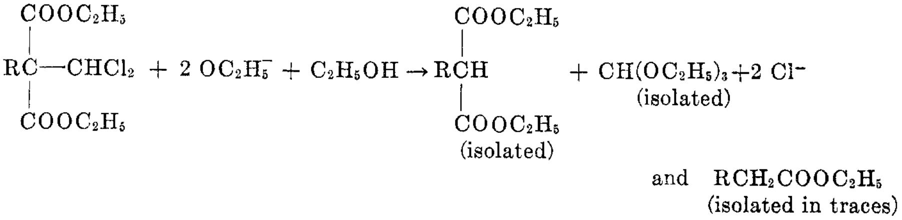
In ethanol:

Reactions 1, 2, and 3 plus the following:

4. 

$$\underset{\mathrm{COOC_2H_5}}{\overset{\mathrm{COOC_2H_5}}{\mathrm{RC}}}\!-\!\mathrm{CHCl_2} + 2\,\mathrm{OC_2H_5^-} + \mathrm{C_2H_5OH} \rightarrow \underset{\substack{\mathrm{COOC_2H_5}\\ \text{(isolated)}}}{\overset{\mathrm{COOC_2H_5}}{\mathrm{RCH}}} + \underset{\text{(isolated)}}{\mathrm{CH(OC_2H_5)_3}} + 2\,\mathrm{Cl^-}$$

$$\text{and}\quad \underset{\text{(isolated in traces)}}{\mathrm{RCH_2COOC_2H_5}}$$

The reactions appear to be general. They have been applied in ethanol to the compound where R = *n*-butyl and in xylene to compounds where R = *n*-butyl, benzyl, and carbethoxymethyl. In the series of *n*-aliphatic substituents the reaction is general at least through *n*-dodecyl since, although intermediates were not isolated, the product could be hydrolyzed and decarboxylated to yield the correct aldehyde.

Reactions 1 and 2 (and 3 if two equivalents of ethoxide ion are used) begin at a practical rate in xylene solutions (about 1 *molar*) at 65°, and, at the reflux temperature, are complete in 15 to 20 mins.

In all cases examined the double bond remains in the position required by the general equations above. That the double bond does not move into conjugation with the phenyl ring in the case where R = benzyl is shown by comparison of ultraviolet absorption spectra in cyclohexane of the benzyl derivatives (chloroethyl ester $\lambda_{\max}$ 223 mμ; ethoxyethyl ester $\lambda_{\max}$ 239 mμ) and ethyl cinnamate ($\lambda_{\max}$ 272 mμ). The ultraviolet absorption spectrum of 1-phenyl-2-carbethoxy-3-ethoxypropene-2 is essentially the sum of those of toluene (1) and ethyl β-ethoxycrotonate (2).

The dichloromethyl substituted malonic esters are conveniently prepared by reaction of the sodium derivative of the substituted malonic ester with excess chloroform in xylene solution. This is an improvement over the method of Kötz and Zörnig (3) who used the dry sodium derivative with excess chloroform in a sealed tube. The amounts of chloroform and xylene should be adjusted so that the reflux temperature of the mixture is at least 95° since below this temperature the reaction is impracticably slow. Too much chloroform, in addition to depressing the boiling point of the mixture, tends also to precipitate the sodium derivative. It was found that a mixture of 1 mole of sodium derivative to 10 moles of chloroform with sufficient xylene to bring the reflux temperature of the mixture to 95° is near optimum for ordinary equipment. The yields are generally 50 to 70%.

If the substituted malonic ester is prepared by halide alkylation of malonic ester in an inert solvent such as xylene, it is possible to proceed without isolation of intermediates from a suitable alkyl halide to the ethoxymethylene derivative. Hydrolysis and decarboxylation of the latter product provides an aldehyde containing two carbons more than the original halide.

Tschitschibabin (4) prepared a few α-alkoxymethylene carboxylic esters by reaction of α halo esters with ethyl orthoformate and zinc. As a structure proof, the method was applied to the preparation of 1-ethoxy-2-carbethoxyhexene-1 from ethyl α-bromocaproate. In our hands the yield of crude product was 30.6 % based on bromo ester. The preparation of α-chloromethylene carboxylic esters by a systematic method is not reported in the literature.

EXPERIMENTAL

1,1-Dichloro-2,2-dicarbethoxyhexane. Chloroform (47.8 g., 0.4 mole) was added to the room temperature solution of sodium (4.6 g., 0.2 g.-atom) in diethyl *n*-butylmalonate (43.29 g., 0.2 mole) and xylene (400 cc.). The solution was refluxed 15 minutes when 5 cc. of the mixture required one drop of 0.2 *N* HCl to reach the phenolphthalein end-point.

The brownish mixture was poured into H_2SO_4-acidulated ice-water. The residue from the H_2O-washed organic layer was fractionally distilled under reduced pressure through a 15-plate column.

The product in 50.2% yield boiled at 155–168° (20 mm.), n_D^{25} 1.4520–1.4533. Refractionation yielded the pure substance of b.p. 152° (20 mm.), n_D^{25} 1.4536.

Anal.[5] Calc'd for $C_{12}H_{20}Cl_2O_4$ (299.194): C, 48.17; H, 6.74; Cl, 23.70.

Found: C, 48.36; H, 6.66; Cl, 23.55.

1-Ethoxy-2-carbethoxyhexene-1, preparation in xylene. 1,1-Dichloro-2,2-dicarbethoxyhexane (11.37 g., 0.038 mole) was added to a sodium ethoxide dispersion in xylene prepared by dissolving sodium (1.75 g., 0.076 g.-atom) in a mixture of ethanol (30 cc.) and xylene (80 cc.) and subsequently removing the excess ethanol by distillation.

After 15 minutes reflux, 5 cc. of the mixture required one drop of 0.2 *N* HCl to the phenolphthalein end-point. The mixture was poured into H_2SO_4-acidulated ice-water. The residue from the H_2O-washed organic layer was fractionally distilled.

The only distillate was 1-ethoxy-2-carbethoxyhexene-1 [b.p. 130–131° (20 mm.), n_D^{25} 1.4489] identical with that obtained by similar reaction in ethanol and by the method of Tschitschibabin (4). The yield was 93.4%.

1-Ethoxy-2-carbethoxyhexene-1, preparation in ethanol. To a solution of sodium (11.5 g., 0.5 g.-atom) in ethanol (340 cc.) was added diethyl *n*-butylmalonate (108.1 g., 0.5 mole). After cooling to room temperature, chloroform (59.7 g., 0.5 mole) was added. At about 65° reaction began and cooling of the reaction flask was necessary. After the reaction had subsided the mixture was refluxed for one hour when it was neutral to wet litmus. After removal of most of the ethanol, the mixture was poured into water and extracted with ether. The residue from the ether layer was fractionally distilled through a 15-plate column. There was isolated diethyl carbonate (4.2 g., b.p. 126°, d_{23}^{23} 0.970, n_D^{20} 1.3852), ethyl orthoformate (44.8 g., b.p. 145°, n_D^{25} 1.3919), 1-ethoxy-2-carbethoxyhexene-1 (separated on redistillation from diethyl *n*-butylmalonate) (42.0 g., b.p. 136–138° (20 mm.), n_D^{25} 1.4490, $d_{25}^{31.5}$ 0.9326), diethyl *n*-butylmalonate (19.0 g., b.p. 142.5° (20 mm.) n_D^{25} 1.4267), and 9.1 g. of yellow products boiling above 210° (20 mm.) which are probably related to chloroform disubstitution products.

Diethyl *n*-butylmalonate was identified by hydrolysis to crystalline *n*-butylmalonic acid of m.p. 103°.[6] Authentic *n*-butylmalonic acid caused no m.p. depression. Other known products were identified by reference to their physical constants.

1-Ethoxy-2-carbethoxyhexene-1 was identified as follows:

Anal.[5] Calc'd for $C_{11}H_{20}O_3$ (200.270): C, 65.97; H, 10.07.

Found: C, 65.61, 65.61; H, 10.27, 10.17: *Mol. wt. detn.* (camphor), 237.

Saponification equivalent. (3 hours reflux dilute ethanol-NaOH and back titration with HCl to phenolphthalein end-point). Found: 230.

The acidic oil which separated from the acidified NaOH saponification mixture was heated until foaming ceased. The product deposited a 2,4-dinitrophenylhydrazone of

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[5] Analysis by Joseph F. Alicino, P.O. Box 267, Metuchen, N. J.

[6] All melting points are micro. corr.

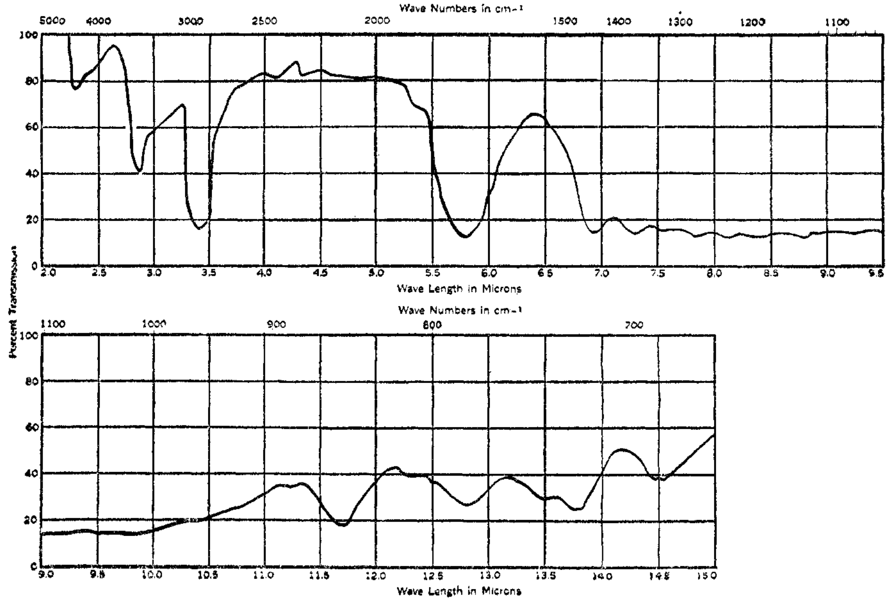

FIGURE 1. INFRARED ABSORPTION SPECTRUM OF 1-ETHOXY-2-CARBETHOXYHEXENE-1.

m.p. 102–104° which was identical with authentic caproic aldehyde 2,4-dinitrophenylhydrazone.

The index of refraction, b.p., ultraviolet absorption spectrum (λ_{max} 243.5 log ϵ 3.835) and infrared absorption spectrum which follows (Fig. 1) were identical with those of 1-ethoxy-2-carbethoxyhexene-1 prepared according to the method of Tschitschibabin (4).

Reactions of 1,1-dichloro-2,2-dicarbethoxyhexane with ethanolic sodium ethoxide. 1,1-Dichloro-2,2-dicarbethoxyhexane (5 g., 0.0167 mole) was added to the solution of sodium (0.95 g., 0.0418 g.-atom) in absolute ethanol (20 cc.) and the mixture was refluxed one hour. The reaction mixture was poured into water and extracted with ether. The brownish ether residue was fractionally distilled under reduced pressure through a 15-plate concentric tube column. Of the 5.0 g. of distillate, the first 1.5 g. (which reduced dilute $KMnO_4$-Na_2CO_3 rapidly at room temperature) consisted of impure 1-ethoxy-2-carbethoxyhexene-1 and the remainder was diethyl *n*-butylmalonate.

1-Ethoxy-2-carbethoxyhexene-1 [method of Tschitschibabin (4)]. The product was prepared according to the method of Tschitschibabin from ethyl α-bromocaproate (51.1 g., 0.23 mole), ethyl orthoformate (41.5 g., 0.28 mole), and etched zinc (19.0 g., 0.29 g.-atom). Completion of the reaction required 5 hours reflux. Fractional distillation of the washed (dil. HCl, dil. NaOH) mixture separated the crude product of b.p. 117–131.5° (20 mm.), n_D^{25} 1.4299–1.4485 in 30.6% yield. Refractionation yielded the pure product of b.p. 131.5° (20 mm.), n_D^{25} 1.4491, d_{22}^{23} 0.9326.

Anal.[5] Calc'd for $C_{11}H_{20}O_3$ (200.270): C, 65.97; H, 10.07.

Found: C, 66.08; H, 9.94.

1-Phenyl-2,2-dicarbethoxy-3,3-dichloropropane. The hot solution of sodium (4.6 g., 0.2 g.-atom) in diethyl benzylmalonate (50 g., 0.2 mole) and xylene (200 cc.) was dripped rapidly into a refluxing solution of $CHCl_3$ (364 g., 1.88 moles) in xylene (200 cc.). After 15 minutes reflux the solution was neutral to wet litmus. Fractional distillation of the H_2O-washed reaction mixture separated the dichloride in 60% yield (b.p. 205–205.5° (20 mm.) n_D^{25} 1.4970–1.5113). Refractionation yielded the pure substance of b.p. 206° (20 mm.), n_D^{25} 1.5082.

Anal.[5] Calc'd for $C_{15}H_{18}Cl_2O_4$ (333.188): C, 54.07; H, 5.45; Cl, 21.28.
Found: C, 54.24; H, 5.45; Cl, 21.10.

The use of sodium hydride raised the yield to 67%.

1-Phenyl-2-carboxy-3-chloropropene-2. Sodium (2.3 g., 0.1 g.-atom) was dissolved in a mixture of absolute ethanol (20 cc.) and xylene (90 cc.). Excess ethanol was removed by distillation through a Vigreux column. The sodium ethoxide dispersion was cooled to 50° and 1-phenyl-2,2-dicarbethoxy-3,3-dichloropropane (30 g., 0.09 mole) was added. Reaction began at once and diethyl carbonate appeared at the head of the column.

After 20 minutes reflux, the mixture was poured into H_2SO_4-acidulated ice-water. The residue from the H_2O-washed organic layer was fractionally distilled. Of the 20 g. of distillate, about half boiled at 150–160° (20 mm.) (n_D^{25} 1.5231–1.5150) and the remainder at 160–190° (20 mm.) (n_D^{25} 1.5130–1.5060). No esters were obtained in the pure state.

All fractions, after alkaline hydrolysis (10% aqueous KOH—1 hr. reflux) and acidification with conc'd HCl, deposited colorless needles which after recrystallization from dilute ethanol or benzene—petroleum ether melted at 107.4°.

The substance was unaltered by heating to 200°, reduced alkaline and neutral $KMnO_4$ rapidly at room temperature, failed to absorb bromine from CCl_4 solution, distilled unaltered at atmospheric pressure, and crystallized unchanged from hot conc'd HI; λ_{max} 223 mμ (cyclohexane) log ϵ 4.114.

Anal.[5] Calc'd for $C_{10}H_9ClO_2$ (196.629): C, 61.08; H, 4.61.
Found: C, 61.28, 61.16; H, 4.83, 4.98; *Mol. wt. detn.* (camphor), 219.

The *amide*, prepared in the usual way using thionyl chloride and conc'd NH_4OH, melted, after recrystallization from benzene-petroleum ether, at 118–118.5°.

Anal.[5] Calc'd for $C_{10}H_{10}ClNO$ (195.645): C, 61.39; H, 5.15; N, 7.16.
Found: C, 61.61; H, 5.19; N, 7.52.

The *anilide* prepared in a similar manner melted at 106°.

1-Phenyl-2-carbethoxy-3-ethoxypropene-2. 1-Phenyl-2,2-dicarbethoxy-3,3-dichloropropane (10 g., 0.03 mole) was treated with sodium ethoxide (from 2.8 g., 0.12 g.-atom) as described under *1-ethoxy-2-carbethoxyhexene-2.* The distillate contained only 1-phenyl-2-carbethoxy-3-ethoxypropene-2 of b.p. 171–172° (12 mm.) n_D^{25} 1.5135–1.5136 in 92.5% yield.

The product reduced dilute $KMnO_4$-$MgSO_4$ rapidly at room temperature and absorbed bromine from CCl_4 solution; λ_{max} 239 mμ, log ϵ 3.699 (cyclohexane). A fraction of n_D^{25} 1.5135 was analyzed.

Anal.[5] Calc'd for $C_{14}H_{18}O_3$ (234.284): C, 71.77; H, 7.74.
Found: C, 71.65, 71.55; H, 7.44, 7.48.

1-Phenyl-2-carboxy-3-ethoxypropene-2. Acidification with conc'd HCl in the cold of an alkaline hydrolysis mixture (10% aqueous KOH—overnight reflux) of 1-phenyl-2-carbethoxy-3-ethoxypropene-2 deposited on oil which on crystallization from ethanol and repeated recrystallization from benzene melted at 115–115.5°.

The product reacted in the same way with $KMnO_4$ and Br_2 as did its ethyl ester above; λ_{max} 245.5 mμ, log ϵ 3.888 (cyclohexane).

Anal.[7] Calc'd for $C_{12}H_{14}O_3$ (206.232): C, 69.88; H, 6.84; C_2H_5O, 21.82.
Found: C, 70.13, 70.32; H, 6.87, 6.98; C_2H_5O, 20.46.

1,1-Dichloro-2,2,3-tricarbethoxypropane. Chloroform (125.5 g., 1.05 moles) was added to a solution at room temperature of sodium hydride (4.0 g., 0.17 mole) and diethyl 2-carbethoxysuccinate (37.0 g., 0.15 mole) in xylene (500 cc.). The solution was refluxed for 3.5 hours when 3 drops of 0.2 *N* HCl were required to neutralize 5 cc. of the mixture to phenophthalein.

The reaction mixture was poured into H_2SO_4-acidulated ice-water. The residue from the H_2O-washed organic layer was fractionally distilled. The crude product in 40% yield boiled at 165–187° (20 mm.), n_D^{25} 1.4370–1.4560. Refractionation yielded the pure product of b.p. 183.5° (20 mm.); n_D^{25} 1.4565.

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[7] Analysis by Clark Micro Analytical Laboratory, P.O. Box 17, Urbana, Ill.

Anal.[5] Calc'd for $C_{12}H_{18}Cl_2O_6$ (329.178): C, 43.78; H, 5.51; Cl, 21.54.
Found: C, 44.01; H, 5.62; Cl, 21.50.

1-Ethoxy-2,3-dicarbethoxypropene-1. Sodium (2.5 g., 0.11 g.-atom) was added to a mixture of ethanol (25 cc.) and xylene (190 cc.) and, after reaction, the excess ethanol was removed by distillation. To the suspension 1,1-dichloro-2,2,3-tricarbethoxypropane (16.5 g., 0.05 mole) was added and the mixture was refluxed for 3.5 hours.

The reaction mixture was poured into water, and the organic layer was fractionally distilled. The crude product in 52%[8] yield boiled at 148–174° (20 mm.), n_D^{25} 1.4452–1.4500. Refractionation provided the pure product of b.p. 158° (20 mm.), n_D^{25} 1.4460.

Anal. Calc'd for $C_{11}H_{18}O_5$ (230.254): C, 57.38; H, 7.88; C_2H_5O, 58.71.
Found:[9] C, 57.00; H, 7.97; C_2H_5O, 58.53.

Acknowledgment. Mr. Kenneth R. Mitchell assisted in demonstrating that the reaction in ethanol to produce products hydrolyzable to aldehydes is general in the *n*-alkyl series of substituted malonic esters.

SUMMARY

It is shown that substituted dichloromethyl malonic esters react in inert solvent with one equivalent of ethoxide ion to yield α-chloromethylene esters and diethyl carbonate: with two equivalents of ethoxide ion to yield diethyl carbonate and the corresponding α-ethoxymethylene ester.

The reactions of substituted dichloromethyl malonic esters with two equivalents of ethoxide ion in ethanol produce diethyl carbonate, α-ethoxymethylene esters, ethyl orthoformate, and traces of the ester corresponding to the hydrolysis and decarboxylation of the original substituted malonic ester.

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(4) TSCHICHIBABIN, *J. prakt. Chem.*, [2] **73**, 326 (1906).

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[8] The low yield is probably a result of mechanical loss due to the small amount of material reacted.

[9] Analysis by Geller Laboratories, 473 Blanchard Terrace, Hackensack, N. J.