Anal. Calcd. for $C_{25}H_{22}O$: C, 88.72; H, 6.55. Found: C, 88.67; H, 6.58.

The infrared spectrum (chloroform) of this substance shows absorption at 1677 cm.$^{-1}$ assignable to the conjugated carbonyl group.

The ultraviolet spectrum (ethanol) shows a single absorption maximum at 268 mμ with a molar extinction coefficient of 7810.

URBANA, ILL.

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

Some Condensation Reactions of Isopropylidene Malonate[1]

JOHN A. HEDGE,[2] CARL W. KRUSE,[3] AND H. R. SNYDER

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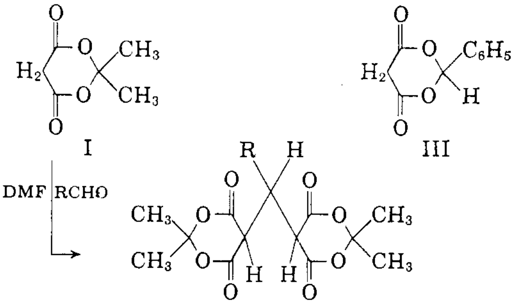
Isopropylidene malonate undergoes condensation with formaldehyde, acetaldehyde and benzaldehyde in dimethylformamide at room temperature with no added catalyst to give the corresponding aldol-Michael products in excellent yields. The condensation of isopropylidene malonate with other carbonyl compounds is also discussed.

Isopropylidene malonate (I) contains a methylene group of unusually great acidity and an ester group that undergoes hydrolysis under extremely mild conditions. These features make it appear an attractive alternative to malonic ester as a reagent for the synthesis of compounds containing very sensitive functions that might be altered under the conditions of the ordinary malonic ester syntheses. Some reactions of the reagent I with carbonyl compounds and alkyl halides have been reported[4-7]; in this paper several new aldol and Michael condensation products of isopropylidene malonate and of the similar ester, benzylidene malonate[8] (III) are described.

Although the structure of isopropylidene malonate (I) has been proved conclusively,[4] benzylidene malonate has been regarded[8,9] as a carboxy-β-lactone as recently as 1954, this formulation being patterned after the "Meldrum's Acid" structure originally suggested[10] for I. To make certain that III is the analog of I, its infrared spectrum was examined; the absence of carboxyl bands confirmed the structure III.

Condensations of I with aqueous formaldehyde, with acetaldehyde, and with benzaldehyde, all in dimethylformamide (DMF) at room temperature and with no added catalyst, gave nearly quantitative yields of the aldol-Michael products II. The product IIb from acetaldehyde was also obtained in moderate yield from crotonaldehyde, obviously as the result of the occurrence of a reverse aldol reaction. Benzylidene malonate and formaldehyde also reacted readily to form the product similar to IIa.



I

III

IIa. R = H
b. R = CH_3
c. R = C_6H_5

When the reaction of benzaldehyde and isopropylidene malonate was carried out in dimethyl sulfoxide (DMSO) or glacial acetic acid, a mixture of the aldol-Michael product (IIc) and the unsaturated (aldol) product, isopropylidene benzalmalonate, was formed. These solvents evidently are less favorable to the Michael reaction than is dimethylformamide. The same solvent effect also was noted in the reaction of isopropylidene malonate with the less reactive aldehyde, *p*-nitrobenzaldehyde. With this combination in dimethyl sulfoxide only the unsaturated product, isopropylidene *p*-nitrobenzalmalonate, was obtained (74%), but in dimethylformamide a mixture of this substance and the Michael product formed. In dimethylformamide cinnamaldehyde reacted to form only the aldol product, isopropylidene cinnamalmalonate (82%). It is interesting that in this experiment, unlike that with crotonaldehyde, there was no indication of the formation of products resulting from a reverse aldol reaction. The reaction

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[2] Sun Oil Co. Fellow, 1959–60.

[3] Phillips Petroleum Co. Fellow, 1956–57.

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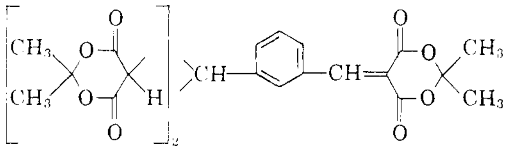
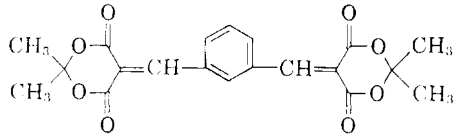
of benzaldehyde and benzylidene malonate (III) in dimethyl sulfoxide afforded the unsaturated product, benzylidene benzalmalonate. Benzylidene benzalmalonate was also obtained as a by-product in the reaction used to prepare benzylidene malonate.

Reactions of isophthalaldehyde and terephthalaldehyde were of interest because of the several possible reaction courses with such bifunctional aldehydes. In dimethylformamide, isophthalaldehyde yielded only one product, triisopropylidene *m*-(β,β,β′,β′-isopropyl)-β,β-styrenehexacarboxylate (IV), resulting from aldol reaction at one aldehyde function and both aldol and Michael reactions at the other. In each of several experiments in which the molar ratio of isopropylidene malonate to isophthalaldehyde was varied from 4:1 to 2:1, only IV was isolated; however, the crude products from runs with molar ratios of 3:1 and 2:1 were apparently less pure and may have contained some of the other possible products, including V. With dimethyl sulfoxide as the solvent and a 2:1 molar ratio a product that was insoluble in aqueous potassium carbonate (in which IV is soluble) was obtained in poor yield. The infrared spectrum indicated this material to be principally diisopropylidene isophthalaldimalonate (V), but a pure sample was not obtained.



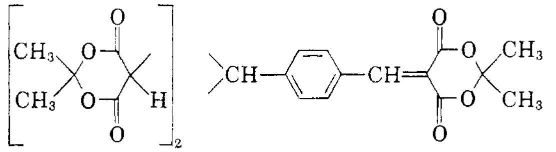
IV



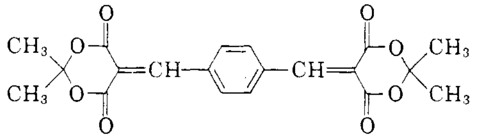
V

Terephthalaldehyde in dimethylformamide also reacted to form the product (VI) resulting from a double aldol reaction and a single Michael addition. It was obtained in excellent yields with molar ratios of 3.5:1 to 6:1 of isopropylidene malonate to the aldehyde, and no evidence of the formation of the double Michael addition product was observed. The substance VI proved quite unstable with respect to the reverse Michael reaction leading to VII. Attempted recrystallization of VI in warm aqueous acetone or in cold aqueous acetonitrile gave bright yellow crystals of VII, identical with samples prepared in poor yield from isopropylidene malonate and terephthalaldehyde (2:1) in dimethyl sulfoxide.

The failure to obtain the double Michael product from isophthalaldehyde might be attributed to steric interference of the two bulky substituents, even in the *meta* position to each other. Models indicate that the interference would be substantial. However, the same explanation is not applicable to the *para* isomer. The apparently greater tendency of VI to undergo the reverse Michael reaction, as compared to IV, probably results from the formation of the more highly conjugated system in VII, as compared to V.



VI



VII

Since acetone was used in working up some of the crude products it was desirable to learn whether it reacts with isopropylidene malonate under mild conditions. No reaction was observed in dimethylformamide, but with acetone itself as the solvent and in the presence of piperidine and glacial acetic acid, condensation occurred to give isopropylidene isopropylidenemalonate in 58% yield. This product, like the cyclohexanone condensation product,[6] readily underwent a reverse aldol reaction.

EXPERIMENTAL[11–13]

Isopropylidene malonate was prepared according to the procedure described by Davidson and Bernhard[4] and benzylidene malonate by that of Michael and Weiner.[8]

Diisopropylidene methylenedimalonate (IIa). A solution of 14.4 g. (0.1 mole) of isopropylidene malonate and 4.05 g. (0.05 mole) of 37% aqueous formaldehyde in 40 ml. of dimethylformamide was allowed to stand at room temperature. Crystals began to deposit at the end of 1 hr. After 2 hr., 25 ml. of water was added. The mixture was cooled, filtered and washed well with cold water to give 14.2 g. of diisopropylidene methylenedimalonate, m.p. 143–146° dec. A second crop (0.4 g.) formed in the filtrate. The total yield was 14.6 g. (97%). The product was dissolved in acetone and reprecipitated by adding twice the volume of cold water. A second such purification gave the analytical sample, m.p. 144.5–146° dec.

Anal. Calcd. for $C_{13}H_{16}O_8$: C, 52.00; H, 5.37. Found: C, 52.00; H, 5.44.

When equimolar amounts of isopropylidene malonate and formaldehyde were used, only a clear gum was obtained.

Diisopropylidene ethylidenedimalonate (IIb). A. *Acetaldehyde condensation.* A solution of 0.25 g. (5.7 mmoles) of acetaldehyde and 0.8 g. (5.6 mmoles) of isopropylidene malonate in 4 ml. of dimethylformamide was allowed to

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(11) All melting points were taken on a Kofler micro hot stage unless otherwise specified.

(12) The infrared spectra were determined by P. McMahon and his associates with a Perkin-Elmer model 21 double beam recording spectrophotometer equipped with sodium chloride optics.

(13) The microanalyses were performed by J. Nemeth, Mrs. Ruby Ju, Miss Claire Higham, Mrs. A. S. Bay, and Miss Jane Liu.

stand at room temperature for 3.5 hr. The reaction mixture was poured into cold 5% sodium bicarbonate solution, filtered to remove a small amount of undissolved material and acidified to cause precipitation of a white solid. Filtration and drying yielded 0.86 g. (98%) of crude IIb, m.p. 115–120° dec. Purification accomplished by pouring an acetone solution of the crude product into cold water afforded nearly pure IIb which began to decompose at 150°. The infrared spectrum of the purified product was identical to that of the analytical sample prepared from crotonaldehyde (see part B).

B. *Crotonaldehyde condensation.* A solution of 7.2 g. (0.05 mole) of isopropylidene malonate and 0.88 g. (0.0125 mole) of crotonaldehyde in 1.5 ml. of water and 20 ml. of dimethylformamide was left at room temperature for 6 hr. Addition of cold water to the reaction mixture caused the formation of a precipitate. The precipitate was collected and dried to yield 5.35 g. (67%) of crude IIb, m.p. 147–150° dec. Recrystallization from acetone-water afforded the analytical sample which melted with decomposition starting at 155°.

Anal. Calcd. for $C_{14}H_{18}O_8$: C, 53.50: H, 5.77. Found: C, 53.75; H, 5.85.

Diisopropylidene benzylidenedimalonate (IIc). A solution of 1.44 g. (10 mmoles) of isopropylidene malonate and 1.06 g. (10 mmoles) of benzaldehyde in 5 ml. of dimethylformamide deposited a few crystals within 5 hr. at room temperature. The entire reaction mixture was poured into 10 ml. of cold water. The resulting precipitate was filtered, washed with water, and dried to yield 1.75 g. (93%) of crude IIc. Recrystallization from dimethylformamide-water, followed by trituration in refluxing acetone, gave the analytical sample, m.p. 180–182° dec.

Anal. Calcd. for $C_{26}H_{24}O_8$: C, 60.63, H, 5.36. Found: C, 60.45; H, 5.45.

Dibenzylidene methylenedimalonate. A solution of 0.96 g. (5 mmoles) of benzylidene malonate (III) and 0.21 g. (2.6 mmoles) of 37% aqueous formaldehyde in 10 ml. of dimethylformamide was left at room temperature for 5.25 hr. Cold water was added and a gummy white precipitate formed. The precipitate was collected and purified by dissolving in acetone and adding water to give 0.57 g. (58%) of dibenzylidene methylenedimalonate, m.p. 203–207° dec. The product was soluble in 5% sodium bicarbonate solution.

Isopropylidene benzalmalonate. A. *With dimethyl sulfoxide as solvent.* A solution of 1.06 g. (10 mmole) of benzaldehyde and 1.44 g. (10 mmoles) of isopropylidene malonate in 5 ml. of dimethyl sulfoxide was allowed to stand at room temperature for 18 hr. Filtration of the reaction mixture yielded 0.75 g. (41%) of IIc, m.p. 155° dec. Water was added to the filtrate and the resulting precipitate was collected and triturated in 5% sodium carbonate to give 0.7 g. (30%) of crude isopropylidene benzalmalonate, m.p. 80 84°. The analytically pure material was obtained by recrystallization from cyclohexane. This material melts near 75°, resolidifies, and melts again at 85–86°.

Anal. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 66.84; H, 5.14.

B. *With glacial acetic acid as solvent.* A solution of 1.06 g. (10 mmoles) of benzaldehyde and 1.44 g. (10 mmoles) of isopropylidene malonate in 5 ml. of glacial acetic acid was left at room temperature for 35 hr. The crystals which had formed were removed by filtration and washed with a small amount of glacial acetic acid to yield 0.9 g. (49%) of IIc, m.p. 175–177° dec. The addition of water to the filtrate caused the precipitation of 1.0 g. (43%) of isopropylidene benzalmalonate, m.p. 83–85°.

The infrared spectrum of compound IIc has carbonyl bands at 1777 and 1740 cm.$^{-1}$ in Nujol, while that of isopropylidene benzalmalonate has bands at 1760 and 1728 cm.$^{-1}$ in chloroform.

Isopropylidene p-nitrobenzalmalonate. A. *With dimethyl sulfoxide as solvent.* A solution of 1.0 g. (6.6 mmole) of *p*-nitrobenzaldehyde and 1.1 g. (7.6 mmole) of isopropylidene malonate in 4 ml. of dimethyl sulfoxide was allowed to stand at room temperature for 10 hr. Filtration afforded 1.35 g. (74%) of isopropylidene *p*-nitrobenzalmalonate, m.p 210–215°. Recrystallization of the crude product from benzene gave the analytically pure material, m.p. 216–217°.

Anal. Calcd. for $C_{13}H_{11}NO_6$: C, 56 32; H, 4.00; N, 5.05. Found: C, 56.62; H, 3.88; N, 4.94.

B. *With dimethylformamide as solvent.* A solution of 1.0 g. (6.6 mmoles) of *p*-nitrobenzaldehyde and 1.9 g. (13.2 mmoles) of isopropylidene malonate was left at room temperature for 22 hr. By filtration, 1.5 g. of a mixture of isopropylidene *p*-nitrobenzalmalonate and another compound, believed to be diisopropylidene *p*-nitrobenzylidenedimalonate, was obtained. Trituration of the mixture in hot chloroform dissolved the benzal derivative and left 0.75 g. (27%) of undissolved material, m.p. 166–170° dec. The infrared spectrum of this undissolved material showed that it was almost certainly diisopropylidene *p*-nitrobenzylidenedimalonate, but an analytically pure sample was not obtained. An additional 0.4 g. of isopropylidene *p*-nitrobenzalmalonate was obtained by the addition of water to the dimethylformamide filtrate. The total yield of crude isopropylidene *p*-nitrobenzalmalonate was 1.15 g. (63%).

Isopropylidene cinnamalmalonate. A solution of 3.6 g. (25 mmoles) of isopropylidene malonate and 1.65 g. (12.5 mmoles) of cinnamaldehyde in 20 ml. of dimethylformamide was left at room temperature for 10 hr. At the end of this period, cold water was added and a cloudy yellow mixture resulted. Acetone was added until the mixture became clear. After standing overnight in the refrigerator, the mixture was filtered with difficulty to yield 2.65 g. (82%) of yellow, crude isopropylidene cinnamalmalonate, m.p. 92–105°. The crude product was dissolved in acetone and reprecipitated by adding water to give 2.6 g. of purer product, m.p. 103–106°. Two recrystallizations from ethanol-water gave product which melted at 109.5–110.5°. The product was insoluble in 5% sodium bicarbonate solution and had a bright yellow color, indicating that a conjugated double bond system was present. An analytical sample, m.p. 106.5–108° in a capillary tube, was obtained by dissolving the product in hot benzene, adding petroleum ether (b.p. 30–60°), and cooling slowly.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46. Found: C, 69.81; H, 5.60.

In another experiment, with equimolar amounts of cinnamaldehyde and isopropylidene malonate, isopropylidene cinnamalmalonate, m.p. 109.5–110.5°, was obtained in 75% yield.

Benzylidene benzalmalonate. A. *With dimethyl sulfoxide as solvent.* A mixture of 0.9 g. (4.7 mmoles) of benzylidene malonate (III) and 0.5 g. (4.7 mmoles) of benzaldehyde in 5 ml. of dimethyl sulfoxide was left at room temperature for 48 hr. Water was added and the mixture was left at room temperature for 48 hr. The solid which had formed during this period was collected and recrystallized from acetone to yield 0.45 g. (35%) of benzylidene benzalmalonate. A mixed melting point of the product and the pure analytical sample (see part B) of benzylidene benzalmalonate showed no depression (m.p. 147.5–148.5° with no evident decomposition).

B. *As a by-product in the benzylidene malonate preparation.* A mixture of 20.0 g. (0.192 mole) of malonic acid and 5 drops of concd. sulfuric acid in 80 ml. of acetic anhydride was left at room temperature for 36 hr. A slight amount of undissolved malonic acid was removed by filtration, and the filtrate was concentrated under reduced pressure (2 mm.) in a 40° bath. To the residue from the concentration was added 20.0 g. (0.189 mole) of freshly distilled benzaldehyde. Heat was evolved and the mixture, upon being cooled under the water tap, began to thicken and solidify. After storage overnight in the refrigerator, a thick red oil resulted. Ether (200 ml.) was added to the red oil and a powdery precipitate formed. The precipitate was filtered and washed with ether to give 4.35 g. (12%) of crude III, m.p. 116–118° dec. The mother liquors were concentrated *in vacuo*, dissolved in 300 ml. of acetone, and poured into 300 ml. of water. Filtration afforded 5.7 g. (22%) of benzylidene benzalmalonate, m.p. 144–146°. The product was recrystallized twice from acetone to give the analytical sample, m.p. 148–149°.

Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.81; H, 4.60.

The infrared spectrum of benzylidene malonate in methylene chloride shows a split carbonyl band at 1800 and 1780 cm.$^{-1}$ while the conjugated carbonyls of benzylidene benzalmalonate show a split band at 1770 and 1750 cm.$^{-1}$ in Nujol.

Triisopropylidene m-(β,β,β′,β′-isopropyl)-β,β-styrenehexacarboxylate (IV). A solution of 5.76 g. (40 mmoles) of isopropylidene malonate and 1.34 g. (10 mmoles) of isophthalaldehyde in 15 ml. of dimethylformamide was left at room temperature for 6.75 hr. The addition of cold water caused a gummy precipitate to form. Acetone was added until the solution became clear. The solution was allowed to evaporate slowly overnight to form a white precipitate. Upon filtration, 3.15 g. of white powder (IV), m.p. 159–169° dec., was obtained. By further evaporation a second crop (0.14 g.) was obtained. The total yield was 3.29 g. (62%). By dissolving the product in acetone-benzene and adding petroleum ether, the analytically pure material, m.p. 148–152° dec., was obtained.

Anal. Calcd. for $C_{26}H_{26}O_{12}$: C, 58.86; H, 4.94. Found: C, 59.06; H, 5.23.

A mixture of 2 moles of isopropylidene malonate to 1 mole of isophthalaldehyde left at room temperature for 10 hr. formed a less pure product, m.p. 131–137° dec., in 94% yield (based on isopropylidene malonate). The product was slowly soluble in 5% sodium bicarbonate solution. This indicated that IV was the principal product. With a 3:1 ratio of isopropylidene malonate to isophthalaldehyde left at room temperature for 10.5 hr. an even less pure product, m.p. 110–122° dec., was obtained in 86% yield. Since no acetone was used in the work-up of these latter two reactions and since the reaction times of the latter two reactions were slightly longer, no really valid comparisons of the various ratios can be made.

The infrared spectrum of IV in Nujol shows a broad carbonyl band with four peaks at 1790, 1770, 1745, and 1720 cm.$^{-1}$ Bands at 1610 and 1587 cm.$^{-1}$ show that a double bond conjugated with an aromatic ring is present.

Diisopropylidene isophthalaldimalonate (V). A solution of 2.88 g. (20 mmoles) of isopropylidene malonate and 1.34 g. (10 mmoles) of isophthalaldehyde in 15 ml. of dimethyl sulfoxide was left at room temperature for 15 hr. The addition of water caused a white gummy precipitate to form. Acetone was added until the solution was clear. The solution was allowed to evaporate slowly to give a filterable precipitate. Filtration gave 0.65 g. of a white mixture, m.p. 150–152° dec. The mixture was triturated in 5% potassium carbonate solution, filtered, and washed with water to give 0.45 g. (12%) of crude V, m.p. 147–149° dec. An infrared spectrum of this compound was definitely not the same as the spectrum of IV. Acidification of the basic filtrate gave 0.2 g. of crude IV, m.p. 140–143° dec.

An attempt to purify the crude diisopropylidene isophthalaldimalonate V by stirring in 5% potassium carbonate solution resulted in the decomposition of most of the product. Further work-up gave only isophthalaldehyde.

The infrared spectrum of V in Nujol shows split carbonyl absorption at 1760 and 1735 cm.$^{-1}$ and double bond absorption at 1620 cm.$^{-1}$

Triisopropylidene p-(β,β,β′,β′-isopropyl)-β,β-styrenehexacarboxylate (VI). A. *With a four to one ratio of the reactants.* A solution of 5.76 g. (40 mmoles) of isopropylidene malonate and 1.34 g. (10 mmoles) of terephthalaldehyde in 15 ml. of dimethylformamide was left at room temperature. After 3 hr., crystals had begun to deposit from the yellow solution. After 10 hr., acetone and cold water were added, and the mixture was cooled for 45 min., filtered, and washed with cold water to yield 5.05 g. of crude product (VI), m.p. 154.5–156° dec. A second crop (0.17 g.) was obtained from the filtrate to give a total yield of 5.22 g. (98%) of crude material. The product (VI) was slowly soluble in 5% potassium bicarbonate solution.

Triturating the product in hot acetonitrile, filtering the undissolved portion (m.p. 157–158.5° dec.), cooling the filtrate, and adding water gave a light yellow mixture, m.p. 152.5–154° dec. The mixture was stirred in acetone and filtered to give white product (VI), m.p. 155.5–156° dec. Addition of water to the acetone filtrate gave yellow needles of diisopropylidene terephthalaldimalonate (VII), m.p. 207.5–209° dec. Stirring the product (VI) in acetonitrile at room temperature, filtering, and adding water to the filtrate caused decomposition of the product to a small amount of VII. No VI was recovered.

B. *With a six to one ratio of the reactants.* A solution of 8.65 g. (60 mmoles) of isopropylidene malonate and 1.34 g. (10 mmoles) of terephthalaldehyde in 30 ml. of dimethylformamide deposited crystals after standing for 5 hr. at room temperature. After 10 hr., cold water was added, and the mixture was cooled for 20 min., filtered, and washed well with cold water. After drying overnight, the white solid weighed 4.4 g., m.p. 125–130° dec. A second crop (0.35 g.) was obtained from the filtrate. The total yield of crude product (VI) was 4.75 g. (90%).

The product was triturated in a warm acetone-water solution, and the undissolved portion (VI), m.p. 158–159.5° dec., was collected. Addition of water to the filtrate gave a mixture of products apparently resulting from partial decomposition. The mixture was stirred in acetone to dissolve the diisopropylidene terephthalaldimalonate (VII), and the undissolved portion (VI), m.p. 150.5–153° dec., was collected. Addition of water to the filtrate gave analytically pure diisopropylidene terephthalaldimalonate (VII), m.p. 182.5–184.5° dec.

Anal. Calcd. for $C_{20}H_{18}O_8$: C, 62.17; H, 4.70. Found: C, 62.30; H, 4.66.

A second recrystallization of VII from acetone-water gave a higher melting material, m.p. 202–205° dec. The twice recrystallized material was recrystallized twice more from acetone to give a sample of VII, m.p. 194–196.5° dec., which was also analytically pure.

C. *With a three and one-half to one ratio of the reactants.* A solution of 5.04 g. (35 mmoles) of isopropylidene malonate and 1.34 g. (10 mmoles) of terephthalaldehyde in 25 ml. of dimethylformamide was stirred magnetically at room temperature. The color of the solution changed from colorless to yellow within 1 hr. and solid formed within 3 to 6 hr. After 10 hr., 50 ml. of reagent grade benzene was added and stirring was continued for 15 min. The mixture was filtered, washed thoroughly three times with reagent grade benzene, and dried to give 2.95 g. of fine white powder (VI), m.p. 161.5–163.5° dec. Analysis showed this fraction to be analytically pure.

Anal. Calcd. for $C_{26}H_{26}O_{12}$: C, 58.86; H, 4.94. Found: C, 59.05; H, 5.01.

The benzene was evaporated from the dimethylformamide solution and water was added to the dimethylformamide residue. Collection of three additional crops gave 0.95 g. of product. The total yield was 3.90 g. (74%).

Diisopropylidene terephthalaldimalonate (VII). A solution of 1.44 g. (10 mmoles) of isopropylidene malonate and 0.67 g. (5 mmoles) of terephthalaldehyde in 10 ml. of dimethyl sulfoxide was left at room temperature. The color of the solution changed from light yellow to orange to red. After 10 hr., the red solution was poured into cold water. A gummy yellow precipitate formed. Acetone was added until the solution was clear. Slow addition of water to this clear solution gave a filterable precipitate. Filtration and drying gave 0.21 g. of crude diisopropylidene terephthalaldimalonate (VII). The crude product melted partially at 174–180° dec. Part of the melt resolidified as long needles which melted at 193–198.5° dec. Two additional crops gave 0.13 g.

of crude product. The total yield of crude VII was 0.34 g. (18%). Recrystallization from acetone gave long yellow needles, m.p. 191.5–194.5° dec. See the preceding section, part B, for analysis of compound VII.

Isopropylidene isopropylidenemalonate. To a solution of 3.6 g. (0.025 mole) of isopropylidene malonate in 11.6g. (0.2 mole) of reagent grade acetone were added 5 drops of piperidine and 1 drop of glacial acetic acid. After 12.5 hr. at room temperature, cold water was added to the yellow solution. An oil formed, which upon cooling and scratching, crystallized. Filtration gave 2.65 g. (58%) of crude isopropylidene isopropylidenemalonate, m.p. 70–78°. The crude product was triturated in 5% potassium carbonate solution, filtered, and washed with water to give 0.6 g. (13%) of pure product, m.p. 73–78.5°. Over 2 g. had been lost by this mild treatment. Two recrystallizations accomplished by dissolving the product in methanol and adding water gave the analytical sample, m.p. 75–78.5°.

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.78; H, 6.60.

URBANA, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY]

Small-Ring Heterocyclic Compounds. I. Aldehydes in the Darzens Synthesis of Glycidic Esters[1a]

LAMAR FIELD AND CLAYTON G. CARLILE[1b]

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The base-catalyzed condensation of ethyl chloroacetate with benzaldehyde gives ethyl *trans*-2,3-epoxy-3-phenylpropanoate (I) contaminated by varying amounts of ethyl *trans*-α-chlorocinnamate. The proportion of the glycidate I is greatest when the cation associated with the base is large, when the solvent is polar, and when the temperature of reaction is about 0–5°. Use of diethylene glycol dimethyl ether, or a combination of higher temperature and polar solvent, results in I which contains a considerable amount of an isomer, possibly the hitherto unreported *cis*-glycidate I. A typical aliphatic aldehyde gave poor results in the Darzens synthesis because of aldol condensation; although formaldehyde also gave poor results, pivalaldehyde, lacking α-hydrogen atoms, gave a glycidic ester in 67% yield. An effort to improve the Darzens condensation by use of a chlorothiol ester was unpromising.

The reaction of benzaldehyde and ethyl chloroacetate in the Darzens condensation produces ethyl 2,3-epoxy-3-phenylpropanoate (I) as the main product. Under the usual conditions employed,[2,3] *trans*-I results,[4] a plausible consequence of "overlap control."[5]

With potassium *t*-butoxide as the base, glycidate I results in good yield and purity.[6] Sodamide, however, results in glycidate I containing about 25% of ethyl α-chlorocinnamate (II).[7] In our hands, incidental use of sodium ethoxide also resulted in a mixture of I and II. These differences in results pointed to the desirability of studying the controlling factors in this typical Darzens condensation.

Table I shows that yields and relative amounts of I and II vary significantly with the base used and with certain of the conditions. As the chlorocinnamate II is not easily separated from the glycidate I by distillation, yields of I and II were calculated

TABLE I

VARIATIONS IN YIELD OF GLYCIDATE I AND CHLOROCINNAMATE II

Expt. No.	Base	Glycidate Yield, %	Ratio of Yields, $\frac{\text{Glycidate I}}{\text{Cinnamate II}}$	Solvent[a]
1	Lithium hydride[b,c]	49	3	E
2	Sodium hydride	61	7	E
3	Lithium ethoxide	85, 65	26, 13	EA
4	Sodium ethoxide[b]	45	6	E and B
5	Sodium ethoxide	49	11	EA
6	Potassium ethoxide	63	13	EA
7	Tetramethylammonium ethoxide	60	100	EA
8	Lithium *t*-butoxide[d]	52	10	TB
9	Potassium *t*-butoxide	71	12	E and TB
10	Potassium *t*-butoxide	61	130	TB
11	Potassium *t*-butoxide[d]	77	45	TB
12	Lithium *t*-pentoxide	38	7	TP

[a] E, ether; EA, ethyl alcohol; B, benzene; TB, *t*-butyl alcohol; TP, *t*-pentyl alcohol. [b] Introduced as the solid. [c] Temperature 53–58°. [d] Reaction effected at room temperature.

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