hindrance, might be expected to give not an acid but a ketone, showed no reaction with benzene and aluminum chloride.

2. When coumarine reacts with benzene and aluminum chloride the ring is not broken but an addition compound with benzene is formed. This corresponds with the results of Lorriman, who found no reaction with naphthalic anhydride, which also has a six-membered ring containing oxygen in the formula.

3. In the reaction with coumarilic acid and with pyromucic acid, addition compounds are formed but the ring is not broken.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WESLEYAN UNIVERSITY]

BROMINE DERIVATIVES OF SOME DELTA KETONIC ESTERS

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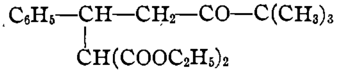
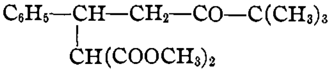
The bromination of certain δ-ketonic esters, such, for example, as dimethyl β-phenyl-γ-benzoyl-ethylmalonate, has already been investigated by Kohler.[1] The esters utilized in this study are closely related to the compound mentioned above, but have a pivalyl group in place of the benzoyl.



$$\begin{array}{l} C_6H_5\text{—}CH\text{—}CH_2\text{—}CO\text{—}C(CH_3)_3 \\ \qquad\quad | \\ \qquad\quad CH(COOC_2H_5)_2 \end{array}$$



$$\begin{array}{l} C_6H_5\text{—}CH\text{—}CH_2\text{—}CO\text{—}C(CH_3)_3 \\ \qquad\quad | \\ \qquad\quad CH(COOCH_3)_2 \end{array}$$

The bromine derivatives prepared from them will be used in this Laboratory in a continuation of work in the cyclopropane series.

With benzalpinacolone and sodium ethoxide, ethyl malonate yielded the ethyl ester of β-phenyl-γ-pivalyl-ethylmalonic acid. By brominating this in carbon tetrachloride, only one product, a monobromo compound, was isolated. This substance was quite stable at elevated temperatures, successfully withstanding heating for an hour at 200°.

Because of the generally superior crystallizing power of methyl compounds, work with ethyl esters was temporarily discontinued and methyl derivatives utilized thenceforth. When benzalpinacolone and methyl malonate were treated with sodium methoxide, the methyl ester of β-phenyl-γ-pivalyl-ethylmalonic acid was obtained, and the corresponding ester acid isolated as a by-product. When esterified, the ester acid yielded the dimethyl ester mentioned above.

When the methyl ester obtained by the Michael reaction was brominated in carbon tetrachloride, two crystalline monobromo derivatives melting, respectively, at 83.5° and 85°, were obtained. By gentler bromination of the ester in methyl alcohol, the same products resulted, but in

[1] Kohler, THIS JOURNAL, **44**, 840 (1922).

a different ratio. An attempt was made to brominate the lower-melting bromine compound, but no crystalline product could be isolated.

That neither isomer is a β-halogen derivative was proved by the formation from each of the same ring compound, the dimethyl ester of 2-phenyl-3-pivalyl-cyclopropane-1,1-dicarboxylic acid, melting at 86°. This substance showed the resistance to the action of aqueous permanganate characteristic of some similarly substituted cyclopropanes.[2] The lower-melting bromine compound yielded this cyclopropane when treated with sodium methylate, potassium acetate and magnesium methylate. The isomer more readily yielded the ring compound, producing it upon treatment with sodium methylate, *p*-toluidine and ammonia. The last two reagents, under precisely similar circumstances, did not react with the compound melting at 83.5°.

In seeking to convert one of the halogen compounds into the other or into the same iodine compound, each was treated with potassium iodide, but no change took place. Hydrobromic acid in methyl alcohol was subsequently utilized, and while the lower-melting compound was unaffected, the higher-melting substance was converted into the compound melting at 83.5°. This indicated that these substances were stereo-isomers rather than structural isomers, and therefore γ-bromine derivatives.

When the bromine compound melting at 83.5° was heated at 200° for an hour, no change took place. Repeating the experiment at 250° led to the formation, through loss of methyl bromide, of a methyl ester of α-carboxy-β-phenyl-γ-pivalyl-butyrolactone. Thus the identity of the lower-melting bromine compound as the dimethyl ester of β-phenyl-γ-bromo-γ-pivalyl-ethylmalonic acid was established.

The structure of the lactone ester was confirmed by an independent synthesis. By saponification and acidification, β-phenyl-γ-pivalyl-ethylmalonic acid was obtained from the product of the Michael reaction. The constitution of this substance was shown by its ready conversion on heating into β-phenyl-γ-pivalyl-butyric acid,[3] and by regeneration of the Michael reaction product upon esterification. The crude dibasic acid was treated with bromine, and hydrobromic acid was evolved, but no crystalline lactone acid could be obtained. By esterification of the oil, there crystallized a lactone ester, identical with that obtained by heating the 83.5° bromine compound.

When the bromine compound melting at 85° was heated, it decomposed at 150°, and yielded crystals, melting at 103.5°, of a substance isomeric with the lactone ester prepared by synthesis and melting at 128°. Attempts were made by heating to 250°, and by the use of hydrogen bromide and hydrogen chloride, in methyl alcohol, to relate this compound to the

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[2] Kohler and Conant, This Journal, **39**, 1404 (1917).

[3] Vorländer and Kalkow, *Ber.*, **30**, 2271 (1897).

lactone ester melting at 128° (only one of four possible stereo-isomers), but without success. The ester melting at 103.5° was recovered unchanged in each instance. When this ester was saponified, it yielded upon acidification an acid melting at 135°, which regenerated the original compound with methyl alcoholic hydrogen chloride solution.

Experimental Part

Ethyl β-Phenyl-γ-pivalyl-ethylmalonate.—A solution of 9.4 g. benzalpinacolone[4] and 8.5 g. of ethyl malonate in 10 cc. of dry ethyl alcohol was treated with sodium ethoxide until it was distinctly alkaline to moist litmus. Acidification, after three hours' refluxing, precipitated the organic material which was taken up in ether. After washing with sodium carbonate, the dried ether gave 16.9 g. of the ester; m. p., 44.5°; yield, 97.1%. It was recrystallized from a mixture of acetic acid, water and ether.

Anal. Subs., 0.1836, 0.1777: CO_2, 0.4609, 0.4497; H_2O, 0.1364, 0.1344. Calcd. for $C_{20}H_{28}O_5$: C, 68.90; H, 8.13. Found: C, 68.46, 69.01; H, 8.25, 8.40.

When ether was used as a solvent and sodium replaced the sodium ethoxide, the yield was 96.4%. A small amount of acidic product removed by the sodium carbonate was not investigated.

Bromination of the Ethyl Ester.—To 10 g. of the ethyl ester in 10 cc. of carbon tetrachloride, 5.1 g. of bromine in 4 cc. of carbon tetrachloride was slowly added. After standing for an hour, and subsequent removal of the solvent by an air blast, 12.1 g. of an oil, which slowly solidified, remained. About one-half of this was obtained from ethyl alcohol as white crystals; m. p., 80–81°. The residue remained oily. The crystalline, material amounted to a 47% yield.

Anal. Subs., 0.2674, 0.2439: AgBr, 0.1186, 0.1073. Calcd. for $C_{20}H_{27}O_5Br$: Br, 18.74. Found: 18.88, 18.72.

Heating the Bromine Derivative of the Ethyl Ester.—One g. of the bromine compound, m. p. 80–81°, was heated to 200° for an hour under a pressure of 35 mm. Subsequent treatment of the cold melt with ethyl alcohol yielded crystals which by a mixed-melting-point determination, were found to be unchanged brominated ethyl ester; m. p., 80–81°.

Methyl β-Phenyl-γ-pivalyl-ethylmalonate.—To a solution of 19 g. of benzalpinacolone and 15 g. of methyl malonate in 16 cc. of absolute methyl alcohol, a 10% solution of sodium methoxide in the same solvent was added until the solution was distinctly alkaline to moist litmus. Upon standing, 24.8 g. of white crystals appeared and was filtered. After removal of the alcohol, the residue was treated with ether and dil. hydrochloric acid. The ether solution was freed of acidic products by sodium carbonate. From the dried ether 1.5 g. of crystals was recovered. The methyl ester was recrystallized from methyl alcohol; m. p., 82.5°; yield, 26.3 g., or 82.2%.

Anal. Subs., 0.2273, 0.2097: CO_2, 0.5589, 0.5172; H_2O, 0.1557, 0.1431. Calcd. for $C_{18}H_{24}O_5$: C, 67.45; H, 7.55. Found: C, 67.05, 67.26; H, 7.61, 7.58.

Monomethyl Ester of β-Phenyl-γ-pivalyl-ethylmalonic Acid.—Acidification of the sodium carbonate, referred to above, yielded 0.7 g. of an oil which crystallized from hot water; m. p., 103°.

Anal. Subs., 0.2551, 0.2483: Ag, 0.0702, 0.0684. Calcd. for $C_{17}H_{21}O_5Ag$: Ag, 26.14; for $C_{16}H_{18}O_5Ag_2$: Ag, 42.69. Found: 27.52, 27.55.

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[4] Hill and Bramann, "Organic Syntheses, John Wiley and Sons, Inc., New York, **1925**, vol. 5, p. 15.

By treatment with methyl iodide the silver salt yielded the dimethyl ester; m. p., 82.5°.

Bromination of Methyl β-Phenyl-γ-pivalyl-ethylmalonate.—Fifty g. of the methyl ester in 75 cc. of dry carbon tetrachloride was slowly treated with a carbon tetrachloride solution of bromine, 27.5 g. in 20 cc. After standing 15 hours, most of the solvent and the excess of reagent were removed by a steam-bath, and a 63g. residue, solid when cool, resulted. By the use of methyl alcohol 41.45 g. of white crystals, m. p. 83.5°, was obtained.

Anal. Subs., 0.2333: AgBr, 0.1096. Calcd. for $C_{18}H_{23}O_5Br$: Br, 20.04. Found: 19.99.

The residue yielded crystals; m. p., 85°. These resembled in appearance the crystals that melted at 83.5°, but a mixture melted at 70°.

Anal. Subs., 0.2345, 0.1922: AgBr, 0.1098, 0.0905. Calcd. for $C_{18}H_{23}O_5Br$: Br, 20.04. Found: 19.93, 20.04.

The yield in this instance was practically quantitative for a monobromo derivative and the isomers were formed in a 2:1 ratio, the lower-melting predominating.

When methyl alcohol was used as a solvent, the same isomers were produced, but in a 1:1 ratio, and the total yield of monobromo compounds was 92.7%.

Bromination of the Compound Melting at 83.5°.—Seven g. of the bromine compound, m. p. 83.5°, in 10 cc. of carbon tetrachloride was treated with 3.3 g. of bromine. The solution stood at room temperature for 15 hours, and was refluxed for two and one-half days. Hydrogen bromide was evolved. Attempts to isolate a solid from this material failed consistently.

Dimethyl 2-Phenyl-3-pivalyl-cyclopropane Dicarboxylate.—Two g. of the bromine compound, m. p. 83.5°, was treated in 5 cc. of warm, dry benzene with a methyl alcoholic solution of sodium methoxide, until a permanent yellow color appeared. After acidification with dil. acetic acid, and washing with sodium carbonate, the dried benzene yielded 1.23 g. of solid. By crystallization from methyl alcohol, this halogen-free substance, which resisted the action of potassium permanganate, was obtained; m. p., 86°; yield, 77%.

Anal. Subs., 0.1940: CO_2, 0.4831; H_2O, 0.1165. Calcd. for $C_{18}H_{22}O_5$: C, 67.94; H, 6.92. Found: C, 67.90; H, 6.67.

Potassium acetate and magnesium methylate produced the same cyclopropane with this bromine compound, but *p*-toluidine and ammonia were without action. The isomer melting at 85° yielded the cyclopropane ester melting at 86° with sodium methylate with *p*-toluidine and with ammonia.

Treatment with Potassium Iodide.—One-half g. of the bromine compound, m. p. 83.5°, was refluxed for one and one-half hours with 0.5 g. of potassium iodide in 5 cc. of methyl alcohol. After evaporation of the solvent the residue, taken in ether, washed and dried, yielded 0.3 g. of the original substance.

The higher-melting bromine compound was subjected to similar treatment and was unaffected.

Treatment with Hydrogen Bromide.—A solution of 1 g. of the bromine compound melting at 85° in 10 cc. of absolute methyl alcohol was saturated cold with hydrogen bromide. After standing for several days, most of the solvent was removed by an air blast, and the residue dissolved in ether. Upon washing with dil. sodium carbonate solution, and subsequent drying, the ether yielded white crystals, which were found to melt at 83.5°, and were shown by a mixed-melting-point determination to be the lower-melting bromine ester.

The lower-melting isomer was recovered unchanged when subjected to like treatment.

Effect of Heat on the Bromine Compound Melting at 83.5°.—When a sample of the lower-melting bromine compound was heated for an hour at 200° and at 35 mm., it was recovered unaltered. However, when some of the same ester was heated to 250° at 35 mm. for an hour, by means of moist litmus and by silver nitrate the presence of an acid and a bromide was detected in the decomposition products. The cooled melt, with methyl alcohol, yielded some unchanged substance, chiefly a red oil and a small quantity of halogen-free crystals; m. p., 124–126°. This material was subsequently shown, by a mixed-melting-point determination, to be a rather crude sample of a methyl ester of α-carboxy-β-phenyl-γ-pivalyl-butyrolactone; m. p., 128°.

Synthesis of the 128° Methyl Ester of α-Carboxy-β-phenyl-γ-pivalyl-butyrolactone. Preparation of β-Phenyl-γ-Pivalyl-Ethylmalonic Acid.—Twenty-one and eight tenths g. of dimethyl β-phenyl-γ-pivalyl-ethylmalonate in 50 cc. of absolute methyl alcohol was treated hot with a solution of 21 g. of potassium hydroxide in 30 cc. of methyl alcohol diluted with 20 cc. of water. A semi-solid mass formed and after standing 15 hours was filtered, washed with dry alcohol and acetone. Twenty-five and seven-tenths g. of a salt was obtained. When gradually treated with 1:3 hydrochloric acid, the salt yielded an oil which was separated as crystals from neutral substances by solution in ether, extraction with sodium bicarbonate and acidification; m. p., 137°, with evolution of gas; yield, 16.75 g., or 82.9%. The silver salt was prepared through the ammonium salt and analyzed.

Anal. Subs., 0.2415, 0.2474: Ag, 0.0996, 0.1015. Calcd. for $C_{16}H_{18}O_5Ag_2$: Ag, 42.69. Found: 41.25, 41.03.

A sample of the acid saturated with hydrogen chloride in dry methyl alcohol yielded crystals which, by a mixed-melting-point determination, were shown to be dimethyl β-phenyl-γ-pivalyl-ethylmalonate; m. p., 82°.

Effect of Heat on the Acid Melting at 137°.—Attempts to purify this acid by recrystallization from hot water led to the formation of a known acid, β-phenyl-γ-pivalylbutyric acid, melting without decomposition at 122°.

Anal. Subs., 0.1636: Ag, 0.0501. Calcd. for $C_{15}H_{19}O_3Ag$: Ag, 30.42. Found: 30.62.

Preparation of the Lactone Ester Melting at 128°.—Five g. of the crude β-phenyl-γ-pivalyl-ethylmalonic acid in 30 cc. of dry chloroform was gradually treated cold with a chloroform solution of 3 g. of bromine. After standing for an hour, the solution was diluted to double its volume with ice and water, and extracted with considerable ether. After washing with sodium carbonate, the dried ether left 1 g. of oil, presumably a mixture of lactones.

Acidification of the sodium carbonate and extraction with ether yielded, upon evaporation of this solvent, 3.9 g. of a yellow oil. This, dissolved in a saturated absolute methyl alcohol solution of hydrogen chloride, deposited 0.7 g. of crystals of the lactone ester, m. p. 128°, and about 1.5 g. of oil was obtained by evaporation.

Anal. Subs., 0.1924, 0.1587, 0.1499: CO_2, 0.4802, 0.3881, 0.3679; H_2O, 0.1157, 0.0961, 0.0897. Calcd. for $C_{17}H_{20}O_5$: C, 67.10, H, 6.58. Found: C, 66.83, 66.67, 66.92; H, 6.68, 6.73, 6.65.

Effect of Heat on the Bromine Compound Melting at 85°.—Three g. of the higher-melting bromine compound was heated for an hour at 150°, and at 25 mm.; by means of moist litmus and silver nitrate the presence of an acid and a bromide in the decomposition products was established. The cooled melt, red in color, yielded white, halogen-free crystals from methyl alcohol; m. p., 103.5°; yield, 2.2 g., or 80%. It was only very slowly attacked by permanganate. This is apparently a methyl ester of α-carboxy-β-phenyl-γ-pivalyl-butyrolactone.

Anal. Subs., 0.1904: CO_2, 0.4674; H_2O, 0.1148. Calcd. for $C_{17}H_{20}O_6$: C, 67.10; H, 6.58. Found: C, 66.94; H, 6.70.

Heating the Lactone Ester Melting at 103.5°.—Some of the lactone ester, m. p. 103.5°, was heated for three hours under diminished pressure at 250°. Bubbling occurred and some darkening, but the cooled melt yielded with methyl alcohol nothing but the original compound; m. p., 103.5°.

Action of Halogen Acids on the Lactone Ester Melting at 103.5°.—Twenty-five hundredths g. of the lower-melting lactone ester was dissolved in 3 cc. of absolute methyl alcohol saturated with hydrogen bromide. During a period of two days' standing, crystals formed which, by a mixed-melting-point determination, were proved to be identical with the starting material.

An analogous experiment wherein hydrogen chloride was substituted for hydrogen bromide yielded a precisely similar result.

Action of Alkali on the Lower-Melting Lactone Ester.—One g. of the lactone ester, m. p. 103.5°, suspended in 20 cc. of water, was warmed with sodium methylate, gradually added until the system was homogeneous. Upon acidification and standing, 0.85 g. of solid material was obtained; yield, 90%. This was purified from ether-petroleum ether and melted at 135°, with abundant evolution of gas. It dissolved readily in sodium carbonate solution and gradually reduced potassium permanganate. It is an α-carboxy-β-phenyl-γ-pivalyl-butyrolactone.

Anal. Subs., 0.1548: CO_2, 0.3764; H_2O, 0.0891. Calcd. for $C_{16}H_{18}O_5$: C, 66.21; H, 6.21. Found: C, 66.33; H, 6.39.

Esterification of the Acid Melting at 135°.—One-tenth g. of the lactone acid was dissolved in a methyl alcoholic solution of hydrogen chloride. After 24 hours, the solution was diluted and extracted with ether. The ether, washed with sodium carbonate solution and dried, yielded crystals, m. p. 103°, which, by the mixed-melting-point method, were shown to be the methyl lactone ester; m. p., 103.5°.

The writer desires to express his appreciation of the advice given him by Professor E. P. Kohler during this investigation.

Summary

Some new bromine compounds, derivatives of esters of β-phenyl-γ-pivalyl-ethylmalonic acid, have been described.

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