[CONTRIBUTION FROM THE HALL LABORATORY OF CHEMISTRY, WESLEYAN UNIVERSITY]

β-Pivalylpropionic Acid and Some of its Derivatives

BY G. ALBERT HILL, VICTOR SALVIN AND W. T. M. O'BRIEN, JR.

In the course of a study of certain condensation reactions in this Laboratory the need for esters of β-pivalylpropionic acid became evident. This acid had already been prepared by Wahlberg[1] by heating *t*-valeryltartaric acid. We, however, undertook another synthesis. ω-Bromopinacolone, produced by Hill and Kropa's[2] method, was treated with sodium malonic ester, yielding diethyl β-pivalylmethylmalonate. It was unusually difficult to convert this ester into the dibasic acid in good yields by the conventional method, hence the calcium salt was prepared as an intermediate. The silver salt was also isolated.

When the substituted malonic acid was heated somewhat above its melting point it decomposed and β-pivalylpropionic acid was formed. Such a compound may tautomerize, giving a γ-hydroxy-γ-lactone.[3] However, the formation of an oxime indicated the presence of a carbonyl compound. The methyl and the ethyl esters, each a liquid with licorice-like odor, were prepared in the usual way, and each in turn yielded the same amide when subjected to the action of concentrated ammonium hydroxide.

When β-pivalylpropionic acid was decomposed slowly by heat the chief product was a yellow lactone. The readiness with which it decolorized a bromine solution proved it to be unsaturated. The expected product of such a thermal decomposition would be γ-*t*-butyl-$\Delta^{\beta,\gamma}$-crotolactone. As such it should not yield a stable dihydroxylactone with potassium permanganate[4] and should be reduced to a desoxy acid.[5] Since it did give a stable dihydroxylactone with potassium permanganate, and since upon reduction it yielded the neutral saturated cyclic compound γ-*t*-butylbutyrolactone, the unsaturation must be alpha, beta and the unsaturated lactone is γ-*t*-butyl-$\Delta^{\alpha,\beta}$-crotolactone. An intramolecular rearrangement must have taken place in the process of preparation employed. Such a phenomenon is by no means unknown.[4]

Like the esters of β-pivalylpropionic acid, the unsaturated lactone reacted with ammonium hydroxide yielding the amide of the monobasic γ-ketonic acid.

A series of reduction experiments performed with the saturated lactone gave results entirely negative. A somewhat similar group carried out with β-pivalylpropionic acid led to recovery of the acid, save when sodium amalgam, in an alkaline medium, was employed: in this case the saturated lactone was obtained.

The authors wish to express their appreciation of financial assistance from the Atwater Fund.

Experimental

Diethyl β-Pivalylmethylmalonate.—Ethyl malonate (117 g.) was added slowly at 50° to a solution of 16.8 g. of sodium in 600 cc. of absolute alcohol. Subsequently, 130 g. of monobromopinacolone was introduced very slowly, with shaking. The system was refluxed for four hours. After removal of the alcohol the residue was treated with 250 cc. of water and extracted with ether. The ethereal solution was washed with saturated sodium carbonate, with 10% hydrochloric acid, and with water. It was dried with anhydrous sodium sulfate. After removal of the solvent the residue was fractionally distilled under reduced pressure. Finally 105 g. of a somewhat yellow liquid, boiling, in the main, at 151–152° at 10 mm., was obtained, a yield of 56%. *Anal.* Calcd. for $C_{13}H_{22}O_5$: C, 60.46; H, 8.52. Found: C, 60.37, 60.48; H, 8.71, 8.71.

β-Pivalylmethylmalonic Acid.—Fifty grams of the ethyl ester was mixed intimately with 50 g. of finely powdered potassium hydroxide, and the resultant solid mass was broken up during cooling. Hydrochloric acid (1:1) was added to neutrality and an excess of a saturated solution of calcium chloride was added, yielding a precipitate which was filtered with suction. *Anal.* Calcd. for $C_9H_{12}O_5Ca$: Ca, 16.69. Found: Ca, 16.57, 16.80.

The acid was liberated by the use of just sufficient concentrated hydrochloric acid, and a thick cream resulted. The whole was extracted with five 125-cc. portions of ether. The ether was removed, in a vacuum, after the solution had been dried with anhydrous sodium sulfate. Stirring caused the oily residue to crystallize. After pressing between filter papers, the solid was recrystallized from benzene. The resulting white product melted at 136°. About 2 g. of monobasic acid was recovered from the mother liquor. *Anal.* Calcd. for $C_9H_{14}O_5$: C, 53.47; H, 6.95. Found: C, 53.48, 53.60; H, 7.22, 7.24.

The silver salt, a white solid, was prepared in the usual way. *Anal.* Calcd. for $C_9H_{12}O_5Ag_2$: Ag, 51.89. Found: Ag, 51.87, 51.85.

β-Pivalylpropionic Acid.—Some of the dibasic acid heated to, and maintained at, 140°, melted and lost carbon dioxide. The solidified melt, freed from some oily

---

(1) Wahlberg, *Ber.*, **65**, 1860 (1932).

(2) Hill and Kropa, THIS JOURNAL, **55**, 2509 (1933).

(3) Bredt, *Ann.*, **236**, 225 (1886).

(4) Thiele, *ibid.*, **319**, 144 (1901).

(5) Jacobs and Scott, *J. Biol. Chem.*, **93**, 139 (1931).

product by pressing between papers, was recrystallized from a mixture of water and alcohol. It formed colorless crystals melting at 69°. It is soluble in alcohol, ether, and benzene, but only slightly soluble in water. The yield was 80%. *Anal.* Calcd. for $C_8H_{14}O_3$: C, 60.75; H, 8.86; mol. wt., 158. Found: C, 60.81, 60.77; H, 9.24, 9.12; mol. wt. (Rast method), 149, 154, 154.

Oxime of β-Pivalylpropionic Acid.—One gram of the acid and 0.5 g. of hydroxylamine hydrochloride were mixed in 30 cc. of water and treated with 0.32 g. of powdered sodium carbonate. After twenty-four hours at room temperature, white crystals had collected. They melted at 141°; the yield was 41%. *Anal.* Calcd. for $C_8H_{15}O_3N$: N, 8.09. Found: (Kjeldahl) N, 8.08, 8.05.

Methyl β-Pivalylpropionate.—Three grams of the acid was dissolved in 1 cc. of absolute methyl alcohol and two drops of concentrated sulfuric acid was added. The solution was refluxed for four hours, poured into water, treated with 10% sodium carbonate solution, and extracted with ether. This solution was dried with anhydrous sodium sulfate and distilled. The product, in 74% yield, boiled at 180° at 9 mm. It was colorless, and had a marked licorice-like odor. *Anal.* Calcd. for $C_9H_{16}O_3$: C, 62.79; H, 9.30. Found: C, 63.03, 62.92; H, 9.27, 9.33.

Ethyl β-Pivalylpropionate.—This was prepared as was its methyl analog. The colorless ester, with licorice-like odor, boiled at 118° at 9 mm. The yield was 80%. *Anal.* Calcd. for $C_{10}H_{18}O_3$: C, 64.51; H, 9.67. Found: C, 64.40, 64.70; H, 9.38, 9.87.

β-Pivalylpropionamide.—Two grams of the methyl ester and 2 cc. of concentrated ammonium hydroxide (sp. gr. 0.9) were left in a closed vessel for eighteen hours. The resulting white crystals were washed with a small quantity of cold water and, when dry, melted with decomposition at 129°. The yield was 50%. In a like manner the ethyl ester and the unsaturated lactone gave the same product, although in poorer yields. *Anal.* Calcd. for $C_8H_{15}O_2N$: N, 8.92. Found: (Kjeldahl) N, 8.76.

γ-*t*-Butyl-$\Delta^{\alpha,\beta}$-crotolactone.—Four grams of the monobasic acid was distilled slowly at 250° at atmospheric pressure. The distillate consisted of an aqueous and an oily layer. It was treated with sodium carbonate solution and extracted with ether. The ethereal solution was dried with anhydrous sodium sulfate. Subsequent distillation yielded the lactone as a yellow oil boiling at 220°. The yield was 70%. The lactone rapidly decolorized a bromine solution. *Anal.* Calcd. for $C_8H_{12}O_2$: C, 68.57; H, 8.57; mol. wt., 140. Found: C, 68.40, 68.44; H, 8.73, 8.84; mol. wt. (Rast method), 135, 138, 138.

α,β-Dihydroxy-γ-*t*-butylbutyrolactone.—Two grams of the unsaturated lactone was dissolved in 25 cc. of acetone containing 1 g. of finely powdered anhydrous magnesium sulfate. To the system a solution of 2 g. of potassium permanganate in 10 cc. of acetone was added slowly, with stirring. The temperature was kept below −4°. After half an hour the excess of permanganate was eliminated by sodium acid sulfite. The solution was filtered from the oxide mass, which was washed with acetone. All of the acetone solution was concentrated to 25 cc. in a vacuum. The residue was treated with ether, the ethereal solution being dried with anhydrous sodium sulfate and distilled. The residue, white prisms, melted at 132°. The yield was 0.5 g., 20%. *Anal.* Calcd. for $C_8H_{14}O_4$: C, 55.17; H, 8.05. Found: C, 55.28, 55.03; H, 8.21, 8.12.

γ-*t*-Butylbutyrolactone.—One gram of the unsaturated lactone was dissolved in 30 cc. of 95% alcohol. To the solution 0.25 g. of Adams platinum black catalyst was added, and reduction was carried out by shaking the system with hydrogen at two atmospheres pressure. Quantitative reduction to the saturated lactone took place in an hour. The product was recovered by filtration and distillation. It was colorless and boiled at 112° at 12 mm. *Anal.* Calcd. for $C_8H_{14}O_2$: C, 67.60; H, 9.85. Found: C, 67.45, 67.43; H, 9.94, 9.80.

Reduction of the Saturated Lactone.—Attempts were made to reduce the saturated lactone (a) by an intensification of the use of Adams catalyst, (b) by refluxing it with a glacial acetic acid solution of hydriodic acid, (c) by refluxing it with the solution used in (b) plus red phosphorus, (d) by treatment with red phosphorus and 47% hydriodic acid in a sealed tube at 200° for three hours, (e) by adding phosphorus pentachloride and subsequently carrying out the sealed tube procedure. In every case the saturated lactone was recovered or untractable oily or resinous substances resulted.

Reduction of β-Pivalylpropionic Acid.—Experiments with this ketonic acid and (a) acetic acid and zinc, (b) Adams catalyst in alcohol, (c) the Clemmensen method, (d) aluminum amalgam and acid–ether, (e) palladium on charcoal, (f) sodium amalgam and acid, (g) sodium and amyl alcohol were fruitless. In each case the original acid was recovered.

When 6 g. of the acid was refluxed for ten hours with 300 cc. of 2% sodium hydroxide containing 600 g. of 4% sodium amalgam, reduction took place. After removal of the mercury and acidification with dilute sulfuric acid, the organic product was extracted with ether. The ethereal solution was dried with anhydrous sodium sulfate. Subsequent distillation gave the saturated lactone in 50% yield. Some of the monobasic acid was recovered at 150° at the same pressure, 12 mm.

Summary

1. Diethyl β-pivalylmethylmalonate was prepared by a conventional malonic ester synthesis, and was converted into the free dibasic acid which readily gave a calcium and a silver salt.

2. Cautious heating of the dibasic acid yielded β-pivalylpropionic acid. The oxime, the methyl ester, and the ethyl ester of this compound were prepared.

3. Careful heating of the monobasic gamma ketonic acid led to the formation of an alpha-beta unsaturated gamma lactone.

4. β-Pivalylpropionic acid was reduced to the saturated lactone by the use of sodium amalgam in an alkaline medium.

MIDDLETOWN, CONN. RECEIVED SEPTEMBER 13, 1937