for 2.5 hr. at 40 p.s.i. Evaporation of the filtrate gave an oil, which was dissolved in petroleum ether (b.p. 60–80°) and chloroform (1:1) and refrigerated for several weeks. A solid separated and was crystallized from ethanol to yield 0.47 g. (47%) of α-benzyl-γ-phenylbutyrolactone, m.p. 78–80°, $\nu_{\max}^{\mathrm{KBr}}$ 1775 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.07; H, 6.51.

Reaction of 2 with Benzylamine.—A solution of 5 ml. of benzylamine in 25 ml. of dry benzene was refluxed with 500 mg. of **2** for 48 hr. The contents were taken up in 50 ml. of ether and extracted several times with 18% hydrochloric acid, followed by water. Evaporation of the solution gave an oil, which was treated with a large volume of petroleum ether and heated on a steam bath until all of the oil had been converted to a white solid. Filtration of the mixture under suction gave 300 mg. of material, m.p. 125–130°. Crystallization from ethyl acetate gave several mg. of solid **9**, m.p. 135–139°, $\nu_{\max}^{\mathrm{KBr}}$ 1760 (α,β-unsaturated lactone), 1660 cm.$^{-1}$ (amide), and 3300–3400 cm.$^{-1}$ (-OH and -NH). The filtrate yielded **2**, m.p. 155–160°, upon evaporation.

When 200 mg. of **2** was heated under reflux with a solution of 2 ml. of benzylamine in 10 ml. of dry benzene for 5.5 days, and the reaction worked up as described previously, 40 mg. of a substance, m.p. 120–125°, was obtained. After crystallization from ethyl acetate–petroleum ether the melting point was 120–121°, $\nu_{\max}^{\mathrm{KBr}}$ 1660, 3490, and 3350 cm.$^{-1}$. This compound gave a positive test when treated with bromine in carbon tetrachloride.

Anal. Calcd. for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.48; mol. wt., 357. Found: C, 80.46; H, 6.31; mol. wt. (Rast), 337.

Reduction of 1 with LiAlH$_4$ at Low Temperature.—One gram (0.026 mole) of lithium aluminum hydride in 150 ml. of anhydrous ether was stirred vigorously and heated under reflux for 0.5 hr. A suspension of 3.1 g. (0.012 mole) of **1** in 125 ml. of ether was added to the slurry, which was maintained at $-25 \pm 5°$, in a carbon tetrachloride–Dry Ice bath. After 40 min., addition was complete and the mixture was stirred for 5.5 hr. The contents were hydrolyzed with 20 ml. of wet ether followed by 4 ml. of water. The filtrate was dried over anhydrous magnesium sulfate and evaporated to an oil. A solution of the oil in acetone was stored in a refrigerator for several days to yield 0.62 g. (20%) of a compound, m.p. 224–226° (red decomposition), $\lambda_{\max}^{\mathrm{EtOH}}$ end absorption, $\nu_{\max}^{\mathrm{KBr}}$ 1759 and 1550 cm.$^{-1}$. Crystallization from ethyl acetate narrowed the melting point to 225–226°.

Anal. Calcd. for $(C_{17}H_{13}O_2)_2$: C, 81.91; H, 5.25; mol. wt., 498. Found: C, 81.84; H, 5.17; mol. wt. (Signer–Barbier), 340.

The molecular weight was obtained only after many months of equilibration. We suspect that decomposition may have occurred during this time giving rise to the low value. Similar results were obtained using tetrahydrofuran in place of ether.

Reaction of Keto Acid 8 with Acetic Anhydride.—A mixture of 500 mg. (1.9 mmoles) of **8** and 5 ml. of acetic anhydride in an Erlenmeyer flask was heated on a hot plate, maintained at 70–80°, for 3 hr. After partial evaporation of the solvent by air, the heavy white precipitate was filtered by suction, washed with ethyl acetate, and dried *in vacuo*. A product, 133 mg., 28%, m.p. 226°, was obtained. Admixture of a sample with that obtained from the low temperature reduction of **1** failed to depress the melting point.

The aforementioned procedure was repeated, except that the reaction was conducted in a 50-ml. three-necked flask, equipped with a reflux condenser and gas inlet tube through which nitrogen was passed. After 3 hr., the acetic anhydride was removed under reduced pressure in a rotating evaporator. Only an oil was obtained, from which the product described previously could not be obtained. The oil was redissolved in 5 ml. of acetic anhydride and heated for 2 hr. while air was bubbled through the solution. Evaporation in air caused 40 mg. of product **12** to precipitate from solution.

Hydrogenation of 12.—The bislactone (30 mg.) was suspended in 60 ml. of methanol and hydrogenated for 3 hr. over palladium on charcoal at 2400 p.s.i. and 60°. A large volume of acetone was added to dissolve the suspended white solid. Evaporation of solvent yielded 10 mg. of a fine, white solid, m.p. 250–254°. Crystallization from benzene gave several milligrams of product, m.p. 256–257°, $\nu_{\max}^{\mathrm{KBr}}$ 1775 (saturated butyrolactone), no band at 1650 cm.$^{-1}$.

Anal. Calcd. for $(C_{17}H_{15}O_2)_2$: C, 81.25; H, 6.02. Found: C, 80.11; H, 6.23.

Attempted hydrogenation of **12** at 40 p.s.i. with palladium on charcoal or platinum oxide failed.

Reduction of 1 with Sodium Borohydride.—Sodium borohydride (0.85 g., 0.022 mole) was dissolved in 50 ml. of 95% ethanol and cooled in an ice-water bath. The solution was stirred magnetically and a suspension of 2.78 g. (0.011 mole) of **1** in 125 ml. of ethanol was added over a period of 30 min. After addition was complete, the contents were stirred for 4 hr. while the temperature was maintained at 0°. The reaction mixture was carefully poured into cold 18% HCl, and a white solid separated. Suction filtration gave 1.82 g. (66%) of product, m.p. 260–270°. This material was insoluble in all solvents tried and could only be purified in the following manner: The compound was refluxed in a large volume of chloroform for 12 hr. Undissolved solid was removed and the filtrate evaporated to an oily residue. Methanol was added to precipitate a white solid, m.p. 278–280° (red decomposition), $\nu_{\max}^{\mathrm{KBr}}$ 1760 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.21; H, 5.21.

Acknowledgment.—The authors thank Professor Scott Searles for helpful discussions.

3,3-Diphenylglutaric Acid. A Novel Carbanion Condensation Reaction

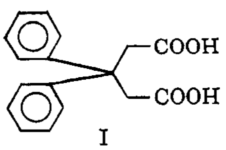
THOMAS C. BRUICE AND WILLIAM C. BRADBURY[1]

The Department of Chemistry, Cornell University, Ithaca, New York

Received July 1, 1963

A compound previously assigned the structure of 3,3-diphenylglutaric acid has been established to be β-(4-carboxymethylphenyl)hydrocinnamic acid (II). The preparation of II *via* condensation of dichlorodiphenylmethane with sodium diethyl malonate represents a novel carbanion condensation reaction on an aromatic ring. Details are provided for the synthesis of 3,3-diphenylglutaric acid (I).

In extending the studies of the Thorpe–Ingold effect[2] on the rates of anhydride formation from the monoesters of 3,3-disubstituted glutaric acids and the rates of hydrolysis of the intermediate anhydrides[3] we desired to obtain 3,3-diphenylglutaric acid (I). The present paper describes the synthesis of 3,3-diphenylglutaric acid and the correct assignment of structure to a structural isomer of I that had previously been assumed to be I. In the course of this study a novel carbanion condensation reaction was encountered.



I

---

[1] The experimental data contained herein will form a portion of the Ph.D. dissertation of W. C. B.

[2] R. M. Beesley, C. K. Ingold, and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1080 (1915).

[3] T. C. Bruice and U. K. Pandit, *J. Am. Chem. Soc.*, **82**, 5858 (1960).

The synthesis of I was reported in 1936 by Phalnikar and Nargund[4] who condensed dichlorodiphenylmethane with ethyl sodiomalonate in a sealed tube at 100° employing benzene as solvent. The condensation reaction was repeated in this laboratory[5] employing the modified procedure of heating the reactants in refluxing benzene under anhydrous conditions. The same dicarboxylic acid could be obtained in 20% yield and the analysis agreed with that of structure I. The observations of Phalnikar and Nargund that this dicarboxylic acid could not be converted into a cyclic anhydride were confirmed. Treatment of the dicarboxylic acid in the appropriate fashion with acetyl chloride, acetic anhydride, oxalyl chloride, phosphorus pentoxide in dioxane or toluene, or simple heating at 160–170° did not afford an anhydride. This observation alone is sufficient to show that the dicarboxylic acid obtained *via* condensation of diethyl sodiomalonate and dichlorodiphenylmethane is not I which, due to an anticipated large *gem* effect, should form a cyclic anhydride with great facility. The inability to form an anhydride suggested the dicarboxylic acid of Phalnikar and Nargund to be an isomer of I in which the carboxyl groups are located at some distance from each other or are sterically unable to approach each other. That this is so is confirmed by the finding of the original investigators[6] who determined the apparent distance between the carboxyl groups as being 38.8 Å. This value was calculated from the determined pK_1 and pK_2 values by the method of Bjerrum[7] and may be compared to that of 7.52 Å. as determined for 3-phenyl-3-methylglutaric acid by the same workers.

Structure of Phalnikar's and Nargund's Acid.—By titration with standard base the unknown acid was found to have an equivalent weight of 144 and an analysis corresponding to 3,3-diphenylglutaric acid (I). The molecular weight of I is 284 with a theoretical neutralization equivalent of 142. The unknown acid was, therefore, established to be a structural isomer of I. The infrared spectrum of the unknown acid exhibited doublets at 6.70, 6.78 and 9.68, 9.77; and a strong singlet at 12.4 μ. The observed pattern suggested the presence of a 1,4-disubstituted benzene ring. This would indicate that the first malonate carbanion displaced one of the two chloro groups as expected, but the second malonate anion, because of reasons which would include steric hindrance, appeared to have attacked the *para* position of one of the phenyl rings. If this were so then, after hydrolysis and decarboxylation, there should be obtained β-(4-carboxymethylphenyl)hydrocinnamic acid (II). This supposition, inferred from the infrared spectra, has been shown to be correct and II represents the structure of the acid obtained by Phalnikar and Nargund.

Oxidation of Phalnikar and Nargund's acid yielded *p*-benzoylbenzoic acid (III) and pyrolysis in lime yielded 1-*p*-tolyl-1-phenylethylene (IV) (Chart I) whose structure was established *via* alternate synthesis.[8]

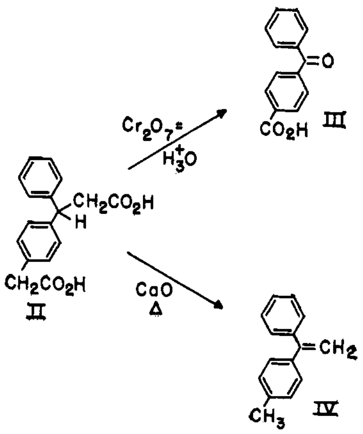


CHART I

The unequivocal synthesis of II is shown in Chart II. 4-Benzoylphenylacetic acid (V)[9] was converted by the Reformatskiĭ reaction[10] on the ethyl ester to ethyl β-(4-carbethoxymethylphenyl)-β-hydroxyhydrocinnamate (VII). Hydrolysis of VII with methanolic potassium hydroxide provided VIII which could be dehydrated to β-(4-carboxymethylphenyl)cinnamic acid (IX) with dry HCl in ether. The procedure for the hydrogenation of IX to give β-(4-carboxymethylphenyl)hydrocinnamic acid (II) was that outlined by Papa and co-workers.[11a] The infrared spectra of the compound II, prepared in this manner, was superim-

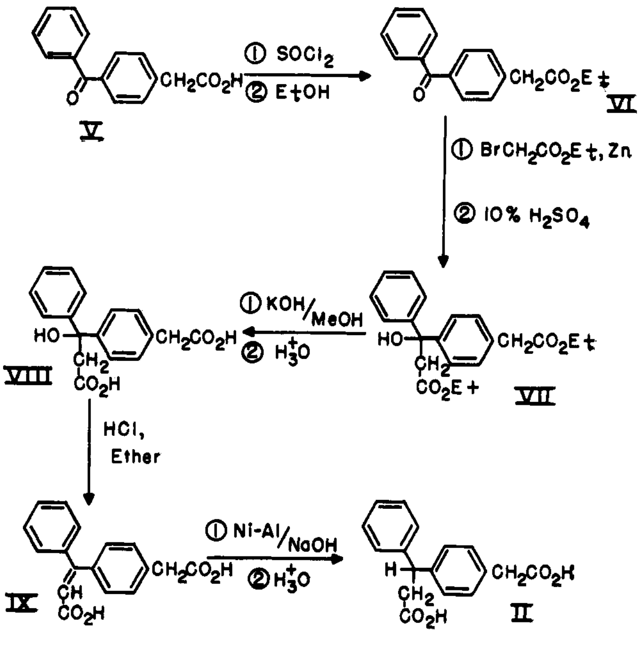


CHART II

---

[4] N. L. Phalnikar and K. S. Nargund, *J. Univ. Bombay*, **5** (Pt. 2), 105 (1936).

[5] T. C. Bruice and U. K. Pandit, unpublished initial studies leading to the present manuscript.

[6] N. L. Phalnikar and B. V. Bhide, *J. Univ. Bombay*, **10** (Pt. 5), 147 (1942).

[7] N. Bjerrum, *Z. Physik. Chem.* (Leipzig), **106**, 219 (1923).

[8] G. R. Gogte and M. S. Pavri [*J. Univ. Bombay*, **27**, (Pt. 3A), 35 (1958); *Proc. Ind. Acad. Sci.*, **5A**, 535 (1937)] using lime, pyrolyzed 3,3-bis(4-methoxyphenyl)glutaric acid and isolated, as a primary product, 1,1-bis(4-methoxyphenyl)ethylene. The other pyrolysis products were acetic acid and carbondioxide.

[9] R. P. Zelinski, B. W. Turnquest, and E. C. Martin, *J. Am. Chem. Soc.*, **73**, 5521 (1951).

[10] H. Rupe and E. Busolt, *Ber.*, **40**, 4537 (1907).

[11] (a) D. Papa, E. Schwenk, and B. Whitman, *J. Org. Chem.*, **7**, 587 (1942); (b) pertinent references cited in M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p. 229.

posable on that of the acid as prepared by the method of Phalnikar and Nargund.

The mechanism for the introduction of the malonate anion at the *para* position to provide the precursor of II has not been elucidated nor can it be certain what order is followed in the nucleophilic displacements which must occur at the *para* position and at the methylene carbon by malonate anions. It would appear most reasonable to suppose that the initial reaction involves displacement of Cl^- by attack of diethyl malonate anion at the methylene carbon. The second malonate anion not being capable, for steric reasons, of reacting at the methylene group, could then attack at the *para* position of one of the aromatic rings with displacement of the second Cl^-. Alternatively, and in view of the strongly basic conditions and the temperature involved, it is probably more reasonable to suppose that the initial reaction of malonate anion at the methylene carbon is followed by a rapid dehydrohalogenation reaction and a subsequent "extended Michael condensation" (Chart III). Though "extended Michael condensations," as depicted in Chart III, have apparently not previously been noted, it should be pointed out that the conditions employed are unusual in solvent and temperature (benzene, 80°). The mechanism of Chart III has some analogy in the abnormal addition of Grignard reagents to sterically hindered phenyl ketones.[11b]

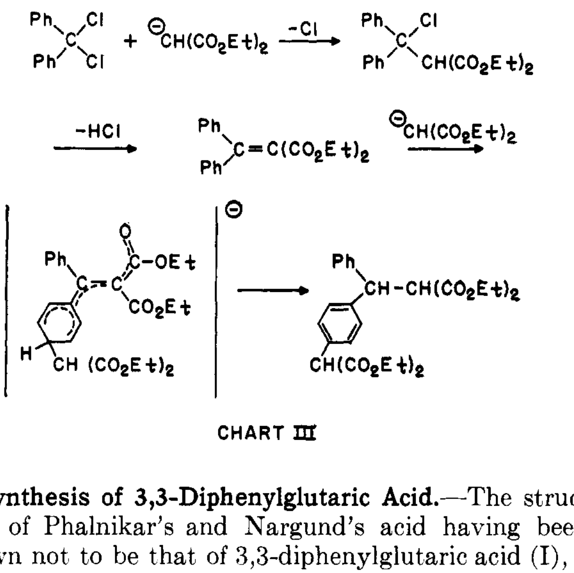


CHART III

Synthesis of 3,3-Diphenylglutaric Acid.—The structure of Phalnikar's and Nargund's acid having been shown not to be that of 3,3-diphenylglutaric acid (I), a synthesis of I was devised (Chart IV). Knoevenagel condensation of benzophenone with ethyl cyanoacetate[12] or malononitrile afforded ethyl 2-cyano-3,3-diphenylacrylate (XI) or 1,1-diphenyl-2,2-dicyanoethylene (X), respectively. The best yields were obtained when malononitrile was employed. Michael addition of malononitrile to X or XI gave XII. It was not possible to obtain reproducible analysis for XII (see Experimental) but, on hydrolysis in refluxing concentrated hydrochloric acid, XII was converted to 3,3-diphenyl-2,4-dicyanoglutarimide (XIII). 3,3-Dialkyl-2,4-dicyanoglutarimides have been hydrolyzed and decarboxylated by Thole and Thorpe[13] with 70% sulfuric acid to provide the 3,3-dialkylglutaric acids in excellent yield. When this technique was employed with XIII only tars were obtained. Base hydrolysis was found to be ineffective due to the known resistance of the glutarimide anion to attack by OH^- ions.[14] The glutarimide XIII when refluxed with a H_2O–H_2SO_4–HoAc mixture[15] was converted to the diimide of 2,2-diphenylpropane-1,1,3,3-tetracarboxylic acid (XIV) The bicyclodiimide XIV was then hydrolyzed and de-

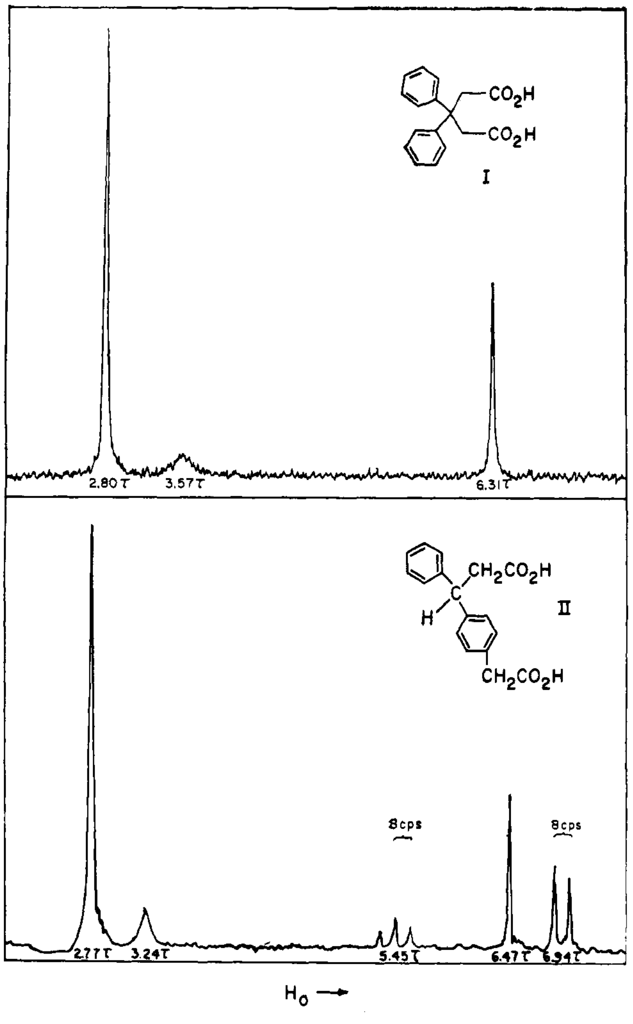


Fig. 1.—N.m.r. spectra of I and II taken in deuterated acetone with tetramethylsilane as standard.

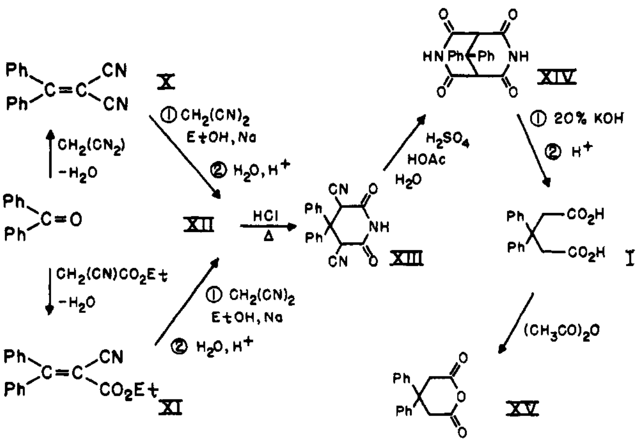


CHART IV

---

(12) A. C. Cope, *et al.*, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

(13) F. B. Thole and J. F. Thorpe, *J. Chem. Soc.*, **99**, 422 (1911).

(14) J. T. Edwards and K. A. Terry, *ibid.*, 3527 (1957).

(15) S. M. McElvain and D. H. Clemens, *J. Am. Chem. Soc.*, **80**, 3915 (1958).

carboxylated by refluxing first with alkali and then acid giving I in good yield.

Unlike II, I formed a cyclic anhydride very readily upon treatment with acetic anhydride or acetyl chloride. The features of the n.m.r. spectra taken in deuterated acetone with tetramethylsilane as standard are provided in Fig. 1. The spectrum of II showed absorption at 2.77, nine aromatic H; 3.24, two carboxyl H; 5.45, one methylene H; 6.47, two methylene H; 6.94 τ, two methylene H. The spectrum of I showed absorption at 2.80, ten aromatic H; 3.57, two carboxyl H; 6.31 τ, four methylene H. The simple and nearly perfect n.m.r. spectra of I and II offered strong supporting evidence for the structures assigned.

As further confirmation of the structures of I and II, as synthesized in this paper, their pK_a values were determined titrimetrically (see Table I). The determined values for II agree approximately with those determined by Phalnikar and Bhide[6] (pK_1 4.37, pK_2 4.98, ΔpK_a 0.61) and indicates virtual isolation of the carboxyl groups from each other. The ΔpK_a value for I, on the other hand, indicates considerable compression of the carboxyl groups as anticipated from the decrease in rotamer distribution due to the bulky *gem*-diphenyl substituents.[3]

TABLE I

Acid	pK_1	pK_2	ΔpK_a
I	3.91	6.71	2.80
II	4.14	4.91	0.77

Experimental[16]

1,1-Diphenyl-2,2-dicyanoethylene (X).—Benzophenone (100 g., 0.55 mole), malononitrile (33 g., 0.50 mole), ammonium acetate (7.7 g., 0.10 mole), and glacial acetic acid (24 g.) were added to 150 ml. of benzene in a 500-ml. flask arranged for refluxing and continuous removal of water. The reaction mixture was refluxed until 16 ml. of water had been collected (~12 hr.). Upon cooling the reaction mixture, crystallization of the product occurred. After collecting and recrystallization from aqueous ethanol there was obtained 80 g. (70%) of X as white needles, m.p. 140°, lit.[17] m.p. 136°.

3,3-Diphenyl-2,4-dicyanoglutarimide (XIII).—The procedure for the Michael addition was adapted from that employed by McElvain and Clemens.[16] A solution of sodium ethoxide was prepared from 7 g. sodium (0.3 mole) and 400 ml. of absolute ethanol. To the solution of sodium ethoxide there was then added 20 g. of malononitrile (0.3 mole) followed by 46 g. of 1,1-diphenyl-2,2-dicyanoethylene (0.20 mole). The reaction mixture was stirred under anhydrous conditions for 0.5 hr. at room temperature, allowed to stand for two additional hours and then diluted with 750 ml. of water. By filtration 9 g. (0.14 mole) of the starting diphenyldicyanoethylene was collected and the filtrate acidified by addition of 100 ml. of concentrated hydrochloric acid. From the acidified solution there precipitated a yellow oil. The heterogeneous mixture was extracted with ether. From the ether layer there precipitated a granular crystalline material which was collected and recrystallized from aqueous ethanol. In this manner there was obtained 25.4 g. of XII, m.p. 210–211°.

Anal. Found: C, 77.06; H, 5.85; N, 13.29.

XII was recrystallized from acetone–benzene–petroleum ether (b.p. 60–70°), m.p. 210–211°.

Anal. Found: C, 75.66; H, 5.65; N, 14.05.

XII was repeatedly recrystallized from the same solvent, m.p. 209–210°.

Anal. Found: C, 76.22; H, 5.78; N, 13.88.

The n.m.r. spectrum in deuteriodimethyl sulfoxide revealed that an ethyl group was most probably present in the form of an ethoxide group.

XII (0.77 g.) was boiled for 15 min. in 25 ml. of hydrochloric acid (20 ml. concentrated, plus 5 ml. of water), cooled, and the product collected. In this manner there was obtained 0.67 g. of XIII as white flakes, m.p. 234° dec.

Anal. Calcd. for $C_{19}H_{13}N_3O_2$: C, 72.37; H, 4.16; N, 13.33. Found: C, 72.03; H, 4.24; N, 13.38.

Diimide of 2,2-diphenylpropane-1,1,3,3-tetracarboxylic Acid (XIV).—3,3-Diphenyl-2,4-dicyanoglutarimide (XIII, 3.95 g., 0.125 mole) was refluxed for 10 hr. in a solution composed of 40 ml. of water, 40 ml. of acetic acid, and 28 ml. of concentrated sulfuric acid. After diluting with 200 ml. of water, cooling, and collecting there was obtained 3.51 g. (84%) of product as white flakes, m.p. 330° with sublimation. An analytical sample was prepared by recrystallization from 95% ethanol. XIV did not melt even when sealed in a capillary but sublimed as high as 360°.

Anal. Calcd. for $C_{19}H_{14}N_2O_4$: C, 68.25; H, 4.22; N, 8.38. Found: C, 68.05; H, 4.34; N, 8.45.

3,3-Diphenylglutaric Acid (I).—XIV (0.44 g., 1.32 mole) was refluxed for 24 hr. in 10% aqueous sodium hydroxide (30 ml.) and cooled. After addition of 30 ml. of 50% aqueous sulfuric acid refluxing was resumed for 3 hr. Acetic acid (10 ml.) was added and refluxing again resumed for another 3 hr. After cooling to room temperature inorganic salts were removed by filtration and the filtrate was chilled in the refrigerator until further precipitation had ceased. The product was then collected as white flakes (0.27 g., 72%, m.p. 159°). After recrystallization from water, the melting point was 161–162°.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.83; H, 5.63. Found: C, 71.77; H, 5.68.

3,3-Diphenylglutaric anhydride (XV) was prepared by refluxing the dicarboxylic acid I with acetic anhydride or acetyl chloride for 4–7 hr. After recrystallization from benzene, the anhydride melted at 147–148° with sublimation.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.64; H, 5.30. Found: C, 76.88; H, 5.32.

β-(4-Carboxymethylphenyl)hydrocinnamic Acid (II).—The following is an adaptation of the procedure of Phalnikar and Nargund.[4] To 6.9 g. (0.30 mole) of freshly cut sodium in 300 ml. of anhydrous benzene there was added 48 g. of diethyl malonate (0.30 mole) followed by 36 g. (0.152 mole) of dichlorodiphenylmethane.[18,19] The mixture was refluxed under anhydrous conditions for 23 hr. The resultant dark red solution was acidified with 6 *N* hydrochloric acid, the benzene and aqueous layers separated and the aqueous layer washed with 25 ml. of benzene. The benzene fractions were combined and washed with three 100-ml. portions of 5% aqueous sodium carbonate solution and dried overnight with anhydrous magnesium sulfate. Removal of the benzene solvent on the flash evaporator provided a brown oil which was refluxed with 300 ml. of concentrated hydrochloric acid for 27 hr. The resulting glomerate of amorphous and crystalline material was removed by filtration and dissolved in 10% aqueous sodium carbonate, the resultant solution extracted with ether, and the aqueous layer acidified. Recrystallization of the product from water yielded 8.6 g. (20%) of II, m.p. 164–165°, lit. m.p. 162–163°. Alteration in reaction times, etc., did not improve the yield.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.83; H, 5.63. Found: C, 71.73; H, 5.66. Found: C, 71.58; H, 5.84.

The diamide was prepared by the procedure of Phalnikar and Nargund,[4] m.p. 172°, lit. m.p. 172°.

Anal. Calcd. for $C_{17}H_{18}N_2O_5$: C, 72.38; H, 6.38. Found: C, 72.25; H, 6.25.

Degradation of II. A.—Oxidation with dichromate solution[20] gave a 55% yield of 4-benzoylbenzoic acid, m.p. 198–199°, lit.[21] m.p. 197–200°, mixture melting point with authentic sample of 4-benzoylbenzoic acid,[22] 199–200°. The following derivatives of the oxidation product were prepared in the normal manner.

---

[16] Analysis were performed by Scandinavian MicroAnalytical Laboratory, Box 25, Herlev, Denmark. Melting points are uncorrected and determined on a hot stage with polarizing microscope. Infrared spectra were determined in potassium bromide disks.

[17] R. Schenck and H. Finken, *Ann.*, **462**, 272 (1928).

[18] R. E. Buckles and G. Matlack, *Org. Syn.*, **31**, 104 (1951).

[19] H. Staudinger and H. Freudenberger, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1934, p. 573.

[20] A. I. Vogel, "Practical Organic Chemistry," Longmans Green and Co., New York, N. Y., 1954, p. 529.

[21] S. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1952, p. 260.

[22] 4-Benzoylbenzoic acid acquired from Aldrich Chemical Co.

2,4-Dinitrophenylhydrazone had m.p. 250–251°, and the **amide,** m.p. 161–162°.

Anal. Calcd. for $C_{21}H_{16}N_4O_6$: C, 59.11; H, 3.47; N, 13.79. Found: C, 58.82; H, 3.79; N, 13.45.

Anal. Calcd. for $C_{15}H_{13}NO_2$ (amide): C, 74.65; H, 4.92; N, 6.22. Found: C, 74.29; H, 5.00; N, 6.18.

B.—Pyrolysis of II in lime produced a red oil as distillate which on redistillation (b.p. 88–100° at 1–2 mm.) gave three fractions having the following refractive indices: $n^{27}\text{D}$ 1.5821, 1.5833, 1.5859. The pyrolysis product was identified as 1-*p*-tolyl-1-phenylethylene (IV) *via* an independent synthesis.

Acetophenone was allowed to react with *p*-tolylmagnesium bromide to give *p*-tolylphenylmethylcarbinol which was dehydrated upon distillation to give IV, b.p. 120–130° (5–10 cm.), $n^{25}\text{D}$ 1.5862 (lit.[23] $n^{20}\text{D}$ 1.5862). The infrared spectra of the third fraction of the pyrolysis product and product obtained from independent synthesis were superimposable.

Ethyl *p*-Benzoylphenylacetate (VI).—*p*-Benzoylphenylacetic acid (7.8 g., 32.5 mmoles) was refluxed in thionyl chloride (20 ml., 0.38 mole) for 3 hr. when most of the thionyl chloride was removed with the aid of chloroform using a flash evaporator. The residual acid chloride was then refluxed with excess absolute ethanol under anhydrous conditions for 3 hr., the solution cooled, and the ester collected by filtration. Recrystallization from an alcohol–water mixture yielded the product as white needles, m.p. 62°, 7.5 g., 87%, lit.[24] m.p. 61–63°.

β-(4-Carboxymethylphenyl)-3-hydroxyhydrocinnamic Acid (VIII).—Ethyl bromoacetate (2 g., 8 mmoles) dissolved in sodium-dried benzene was added dropwise to a mixture of dry benzene (30 ml.), ethyl *p*-benzoylphenyl acetate (1.0 g., 3.75 mmoles), and zinc (0.740 g., 11.3 mmoles) previously etched in HCl. The reaction mixture was refluxed on a water bath under dry nitrogen with mechanical stirring until most of the zinc had dissolved. The reaction mixture was cooled in an ice bath and added to 6 ml. of concentrated sulfuric acid on ice. The resultant mixture was then extracted with ether, the ethereal extract dried over anhydrous magnesium sulfate, and the solvent removed by aspiration leaving a yellow oil. The oil was taken up in 40 ml. of 20% methanolic potassium hydroxide solution and refluxed for 24 hr. After cooling the methanolic solution was extracted once with ether, acidified, cooled, and 630 mg. of the crude product collected by filtration. Concentration of the mother liquor yielded an additional 410 mg. of crude product (a total crude yield of 93%, m.p. 173–178°). The crude material was crystallized from an ether–acetone mixture by addition of petroleum ether (b.p. 60–70°) to the warm solution until cloudy, rewarming until clear, and allowing to cool in the refrigerator. In this manner the product was obtained as white flakes which formed over a period of 3 days, m.p. 181–182°.

Anal. Calcd. for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.86; H, 5.39.

β-(4-Carboxymethylphenyl)cinnamic Acid (IX).—VIII (0.07 g., 0.25 mmole) was dissolved in ether and hydrogen chloride gas bubbled through the ether solution at room temperature for 1–2 hr. The ether was removed, the residue dissolved in 10% sodium carbonate solution, the solution treated with charcoal, and after filtering the filtrate was acidified. The acidic mixture was extracted with ether and dried over anhydrous magnesium carbonate. After removing the solvent 67 mg. (89%) of IX was obtained, m.p. 178–181°. Recrystallized IX was obtained as needles from 10% aqueous ethanol.

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.34; H, 5.00. Found: C, 71.84; H, 5.08.

β-(4-Carboxymethylphenyl)hydrocinnamic Acid (II).—IX (75 mg., 0.25 mmole) was dissolved in 20 ml. of a 10% sodium hydroxide solution and heated on a water bath to 90–100°. The solution was mechanically stirred while Raney nickel-aluminum catalyst powder[25] (0.3 g.) was added in small portions. After addition was completed heating was continued for an additional hr. The solution was filtered and allowed to cool while 7 ml. of concentrated hydrochloric acid was added. The acidic mixture was next extracted with ether, the ethereal solution dried over magnesium sulfate, and the ether solvent removed. In this manner 52 mg. (70%) of white crystalline material was obtained which after recrystallization from water melted at 164–165°.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.83; H, 5.63. Found: C, 71.75; H, 5.76.

pK_a Determinations.—The pK_a values were determined by titration employing a Radiometer TTT1b titrator equipped with a Radiometer PHA 630Ta scale expander and a Radiometer SBR2c Titrigraph with a Radiometer SBU1a micrometer syringe drive which accommodated a 1-ml. Agla Trubore syringe which led to a three-neck ₸ Metrohm microtitration cell by way of a glass capillary. The glass capillary buret tip extended half way into the solution to be titrated passing through an air tight ₸ fitting. The other two necks of the microtitration vessel were fitted with a ₸ Metrohm type X glass electrode and a ₸ salt bridge leading to an external calomel electrode. The tip of the ₸ salt bridge was fitted with an asbestos wick to prevent large changes in μ during the course of the titration. The cell had a 2-ml. capacity and was maintained at constant temperature by circulation of water through the water jacket from a Hake water bath which permitted temperature control at 25.0 ± 0.1°. Carbonate free base, 0.100 *N* potassium hydroxide, and 1.25×10^{-3} *M* carbon dioxide-free aqueous acid solutions were used. Before titrating, the pH meter scale expander was standardized against buffer solutions at pH 4.00 and pH 7.00 and checked after titrating. Direct readings were taken from the micrometer arrangement driving the Trubore syringe and from the scale expander.

Since the ΔpK_a of II was less than I, the data were treated by Britton's modification of the method of Noyes.[26,27] The data for I (ΔpK_a >2.7) were treated by the sample expressions by Albert,[27] the determination of the ionization constant of a monobasic acid requiring correction for the concentration of hydrogen ions. Corrections for liquid potentials and salt errors were not attempted at this time. The titration technique and calculation method (Britton) were tested by titrating 1.25×10^{-3} *M* succinic acid. The result was pK_1 4.20 and pK_2 5.56 as compared with 4.20 and 5.60,[28] 4.22 and 5.67,[29] and 4.20 and 5.62,[30] respectively. As a check to the purity as well as the authenticity of the runs neutralization equivalents were calculated from the pH data and were generally within 1% of the correct value.

Acknowledgment.—This work was supported by a grant from the National Institutes of Health.

---

[23] M. S. Kharasch, *et al.*, *J. Org. Chem.*, **15**, 775–778 (1950).

[24] J. A. Zderic, *et al.*, *ibid.*, **26**, 1635 (1961).

[25] Raney nickel–aluminum catalyst powder, Gilman Paint and Varnish Co., Chattanooga, Tenn.

[26] H. Britton, "Hydrogen Ions," Chapman and Hall, London, 1955, p. 217; A. A. Noyes, *Z. Physik. Chem.* (Leipzig), 11, 495 (1893).

[27] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., London, and John Wiley and Sons, Inc., New York, N. Y., 1962, p. 52.

[28] W. L. German and A. I. Vogel, *J. Am. Chem. Soc.*, **58**, 1546 (1936).

[29] J. C. Speakman, *J. Chem. Soc.*, 855 (1940).

[30] H. S. Sims, *J. Am. Chem. Soc.*, **48**, 1251 (1926).