

and anhydrous ammonia was introduced until about 4 ml. had condensed. Clean sodium (43 mg.) was added in small pieces with shaking, while the solution was maintained just below the boiling point. After completion of the reduction, ethanol (ca. 1 ml.) was added, and the ammonia was boiled off. The mixture was taken up in chloroform and water, washed with sodium bicarbonate, sodium hydroxide, and water, and evaporated to dryness *in vacuo*. The 154 mg. of bright yellow crystals were chromatographed in benzene over alumina to give 76 mg. of white crystals. Sublimation at 100° at 14 mm. gave 73 mg. (47.7% yield) of biphenyl, m.p. 68–70° (corr.).

Reduction of 9-phenanthrol. A 100-mg. sample of 9-phenanthrol was dissolved in 1.0 ml. of a solution of diethyl phosphite¹⁴ in carbon tetrachloride (75 mg./ml.). To this solution was added 0.09 ml. of triethylamine, and after standing overnight, the solution was worked up as above to give 165 mg. of crude ester. This material was dissolved in 2 ml. of ether. Sufficient ammonia was introduced into the solution, cooled as above, to raise the total volume to 7 ml. A 23-mg. sample of sodium cut in small pieces was slowly added to the reaction mixture. At the end of the addition a deep black color persisted. The reaction mixture was then worked up as described to give, after chromatography and sublimation at 150° and 14 mm., 23.1 mg. (25% yield) of phenanthrene, m.p. 96–98° (corr.).

Reduction of 2,7-naphthalenediol. To a solution of 161 mg. of 2,7-naphthalenediol in 0.3 ml. of tetrahydrofuran was added 4.05 ml. of a solution of diethyl phosphite¹⁴ in carbon tetrachloride (75 mg./ml.) and 0.35 ml. of triethylamine. After standing over the week end, the reaction was worked up as above to give 460 mg. of crude ester. The ester was dissolved in 3 ml. of tetrahydrofuran, and 8 ml. of liquid ammonia was added. Clean sodium (85 mg.) was then added. The yellow-brown solution was worked up in the usual fashion to give 22.5 mg. (17.5%) of naphthalene.

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1-Keto-3-methyl-2-tetralylacetic Acid from Cyclization of β -Carboxy- γ -methyl- δ -phenylvaleric Acid

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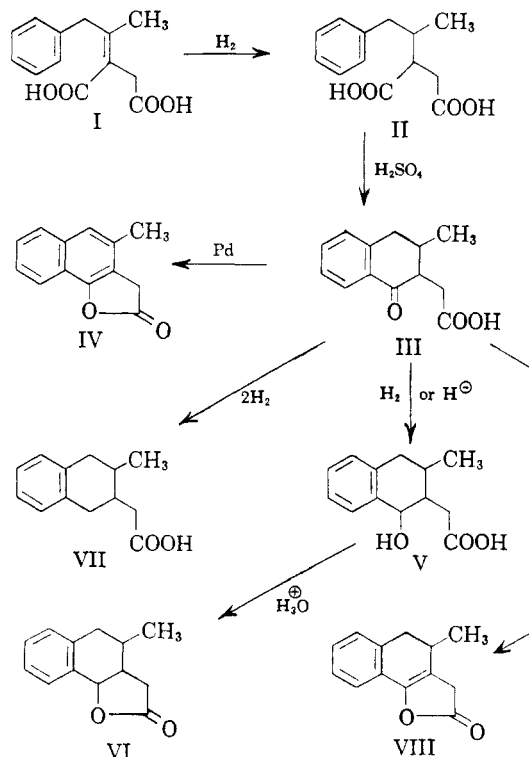
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It has been reported¹ that acid-esters derived by Stobbe condensation of succinates with phenylacetone are cyclized to benzosuberones. Different

results have now been observed with corresponding saturated di-acids obtained from the same reaction.

The di-acid I described earlier¹ was prepared in 40% yield by Stobbe condensation of phenylacetone and ethyl succinate in the presence of sodium methoxide, and subsequent alkaline hydrolysis. The location of the double bond as shown in I was established previously¹ through ozonolysis, and further evidence for this assignment is now found in the fact that the infrared spectrum of I clearly shows the presence of both unconjugated (5.84 μ) and conjugated (5.93 μ) carboxyl groups. Hydrogenation of I in the presence of palladium-charcoal gave a mixture of two stereoisomers of II, an outcome which might be anticipated in analogy with Newman's finding,² that two isomers of β -carboxy- γ,δ -diphenylvaleric acid are formed in hydrogenation of a phenyl-(in place of methyl) substituted di-acid similar to I. Likewise in a sense similar to that of cyclizations reported by Newman,² it was found that cyclization of the mixture of acids II with sulfuric acid at room temperature gave the tetralone derivative III in 56% yield.

Structure III was established by the following facts, which exclude the alternative cyclization product, 3-carboxy-4-methylbenzosuberene-1-one. Keto acid III was esterified very readily. In fact it was not possible to prepare a 2,4-dinitrophenylhydrazone of III itself, for in the presence of alcohol and dilute sulfuric acid at room temperature, esterification took place during the preparation of the derivative, giving the 2,4-dinitrophenylhydrazone



(1) J. R. Dice and G. R. Allen, *J. Am. Chem. Soc.*, **74**, 1231 (1952).

(2) M. S. Newman and R. T. Hart, *J. Am. Chem. Soc.*, **69**, 298 (1947).

of the corresponding ester. This behavior indicates interaction of the ketone and carboxyl groups. Aromatization of III in the presence of palladium at 180° was accompanied by lactone formation, giving naphthalenelactone IV, the structure of which follows from the infrared spectrum (five-membered enol-lactone band at 5.55 μ) and the characteristic naphthalenoid ultraviolet spectrum (see Experimental part). Hydrogenation of III under neutral conditions (in ethyl acetate) in the presence of palladium-charcoal at room temperature, or reduction of III with sodium borohydride followed by acidification at ice temperature, gave hydroxy-acid V (same stereoisomer obtained in both experiments), which lactonized readily to VI. When the same hydrogenation of III was done at 80° in ethyl acetate, hydrogenolysis of the ketone took place and compound VII was formed in quantitative yield. Again, this result may be due to interaction of the ketone and carboxyl groups.

Attempts were made to prepare enol-lactone VIII, and a small amount of material, m.p. ca. 80° (infrared absorption at 5.56 and 5.70 μ), believed to be this compound, was eventually obtained when III was distilled, or refluxed in xylene in the presence of a trace of benzenesulfonic acid. It was evident, however, that enol-lactones of this type are less stable and less readily formed than corresponding compounds derived from benzosuberenes.³ It was interesting to observe that a small amount of naphthalene lactone IV was formed upon treating II, or the crude acid-ester obtained by reduction of the acid-ester precursor of I, with polyphosphoric acid at 100°. Evidently dehydrogenation or disproportionation of III or VIII takes place readily at elevated temperatures.

EXPERIMENTAL⁴

β -Carboxy- γ -methyl- δ -phenylvaleric acid (I). A solution of 36 g. (0.268 mole) of phenylacetone and 54 g. (0.310 mole) of ethyl succinate was added to a solution of 14.5 g. (0.631 atom) of sodium in 500 ml. of absolute methanol. The mixture was refluxed and stirred for 3 hr., and was distilled with stirring for another hour to remove excess methanol (350 ml.). Water (200 ml.) was added to the cooled residue. The mixture was refluxed for 1.5 hr. and was allowed to stand overnight. The alkaline solution was decanted from gummy material, washed with ether and ethyl acetate, and acidified with hydrochloric acid at ice temperature. The product was collected, washed with 3 portions of water, air dried, and triturated with 2 portions of ether. The yield of acid, m.p. 173–177°, was 25.5 g. (40.5%). Recrystallization from ethyl acetate raised the m.p. to 180–181° (reported¹ m.p. 178–180°). The infrared spectrum (Nujol) had an intense doublet 5.84 and 5.93 μ . A neutral equivalent of 116 (calcd. 117) was found.

When the hydrolysis step was omitted in this experiment, acidification afforded a mixture of crystals and oil. The organic material was isolated by extraction with ethyl

acetate and evaporation of the solvent from the water washed and dried solution. Trituration with ether afforded 16.5 g. of di-acid, m.p. 173–177°, and 24 g. of crude acid-ester, a viscous, orange oil which was sufficiently pure for further work.

β -Carboxy- γ -methyl- δ -phenylvaleric acid (II). Hydrogenation of 22.5 g. of di-acid I in the presence of 6 g. of 10% palladium-charcoal in 400 ml. of ethyl acetate at 75° and 40 lb. resulted in absorption of one mole of hydrogen. Filtration of the catalyst and evaporation of the solvent gave 23 g. of colorless crystals, m.p. 113–140°. The higher-melting isomer was obtained in pure condition by recrystallization from ethyl acetate; colorless crystals, m.p. 169–170°, showing intense infrared absorption (chf.) at 5.87–5.89 μ .

Anal. Calcd. for C₁₃H₁₆O₄: C, 66.08; H, 6.83. Found: C, 66.12; H, 6.73.

The low-melting isomer remaining in the filtrates could not be purified completely by recrystallization.

The acid-ester obtained in the preceding experiment was hydrogenated in the same way. One mole of hydrogen was absorbed, and the product, isolated as usual, was viscous oil.

1-Keto-3-methyl-2-tetralylacetic acid (III). The crude acid (mixture of isomers) obtained in the preceding experiment (22 g.) was treated with 120 ml. of concd. sulfuric acid at room temperature, and the mixture was stirred for 2 hr. During this time the solid material dissolved slowly, and the temperature of the solution rose for a time to 45°. The red solution was poured over ice. When hydrolysis was complete, the solid product was collected, washed with water, and air dried. Recrystallization from ethyl acetate (2 crops) afforded 11.4 g. (56%) of colorless crystals, m.p. 141–145°; further recrystallization raised the m.p. to 148–150°. The infrared spectrum (chf.) had peaks at 2.84, 5.85, and 5.97 μ . The compound was soluble in sodium bicarbonate solution.

Anal. Calcd. for C₁₃H₁₄O₃: C, 71.54; H, 6.46. Found: C, 71.57; H, 6.74.

The 2,4-dinitrophenylhydrazone of the corresponding methyl ester was prepared from III in methanol in the usual way. Recrystallization from methanol-ethyl acetate gave red-orange crystals, m.p. 167–169°. The infrared spectrum of the derivative had an intense peak at 5.79 μ , in addition to the usual features.

Anal. Calcd. for C₂₀H₂₀O₆N₄: C, 58.24; H, 4.89. Found: C, 58.03; H, 4.96.

1-Hydroxy-3-methyl-2-naphthylacetic acid lactone (IV). A solution of 0.5 g. of III in 60 ml. of redistilled *p*-cymene containing 1.0 g. of 10% palladium-charcoal was refluxed vigorously for 2 hr. Filtration of the hot suspension gave a solution which was colorless at first, but which soon developed a greenish color upon exposure to air. The solvent was evaporated as rapidly as possible. The residue, a mixture of crystals and green oil, was triturated with methanol, which gave 0.24 g. of yellow crystals, m.p. 163–165°. Recrystallization from methanol afforded colorless or very pale yellow needles, m.p. 165–166°. The infrared spectrum (chf.) had an intense peak at 5.54–5.56 μ and a small peak at 6.05 μ . The ultraviolet spectrum (ethanol) had λ_{\max} 227, 288, 310, and 325 m μ (log ϵ 4.83, 3.78, and 3.14, respectively).

Anal. Calcd. for C₁₃H₁₆O₂: C, 78.77; H, 5.09. Found: C, 78.82; H, 5.38.

Cyclization of 2.8 g. of acid II with 30 g. of polyphosphoric acid at 95° for 15 min., and hydrolysis of the cooled mixture with ice and water, gave mainly an alkali-soluble dark gum and 0.5 g. of yellow, neutral material. Trituration of the neutral fraction with ether gave 0.2 g. of yellow crystals, recrystallization of which (methanol or ethyl acetate) gave crystals, m.p. 164–166°. The mixed melting point with IV as obtained above was undepressed, and the infrared spectra of the two samples were identical.

Cyclization of 7.8 g. of hydrogenated acid-ester corresponding to II with 35 g. of polyphosphoric acid afforded

(3) P. D. Gardner and W. J. Horton, *J. Am. Chem. Soc.*, **75**, 4976 (1953).

(4) Melting points are corrected (capillary).

3.6 g. of partly-crystalline, neutral material, trituration of which with methanol afforded 0.4 g. of compound IV, identical with the compound obtained as described above by the same criteria.

1-Hydroxy-3-methyl-2-tetralylacetic acid (V). (A) Hydrogenation (40 lb.) of 1.0 g. of III in the presence of 1.2 g. of 10% palladium-charcoal in 200 ml. of ethyl acetate at 25° for 1.5 hr. gave 1.0 g. of colorless crystals, m.p. 135–138°. The infrared spectrum of this crude product was virtually identical with that of purified material (*vide infra*) and showed no lactone band. Recrystallization from cyclohexane-ethyl acetate raised the m.p. to 147–148°; the infrared spectrum (chf.) had broad, moderately intense absorption at 3.1–3.25 μ and an intense peak at 5.87 μ . The compound was soluble in sodium bicarbonate solution.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 70.89; H, 7.32. Found: C, 70.75; H, 7.48.

(B) A suspension of III (1.0 g.) in 30 ml. of water was treated with excess sodium borohydride (*ca.* 4 g.) in portions, which resulted in solution of the compound. The solution was warmed on a steam cone for 1.5 hr., was chilled in ice, and was acidified slowly with cold hydrochloric acid. The product, after washing with cold water and drying in the air, was recrystallized from ethyl acetate; colorless crystals, m.p. 147–148°. The mixed melting point with V obtained as described above was not depressed, and the infrared spectra of the samples were identical.

1-Hydroxy-3-methyl-2-tetralylacetic acid lactone (VI). A pure sample of acid V was treated with 10% hydrochloric acid at 45° and the suspension was allowed to stand overnight at room temperature. The crystals were collected, washed with water, and air dried. The melting point of the crude lactone was 124–130°; the infrared spectrum showed a new, intense peak at 5.66 μ and no longer had bands at 3.1–3.25 or 5.87 μ . The compound was insoluble in sodium bicarbonate solution. Recrystallization from cyclohexane gave pure material, m.p. 135–136°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.18; H, 6.68.

3-Methyl-2-tetralylacetic acid (VII). Hydrogenation of 0.65 g. of III in the presence of 1.2 g. of 10% palladium-charcoal and 170 ml. of ethyl acetate at 80° and 40 lb. for 2 hours gave a quantitative yield of colorless crystals, m.p. 98–103°. Recrystallization from cyclohexane raised the m.p. to 107–109°. The infrared spectrum (chf.) had an intense peak at 5.87 μ .

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.65; H, 7.81.

1-Hydroxy-3-methyl-3,4-dihydro-2-naphthylacetic acid lac-

The cooled solution was diluted with ether, was washed with 2 portions of sodium bicarbonate solution and 2 portions of water, and was dried over magnesium sulfate. Evaporation of the solvents gave 2.0 g. of bright yellow crystals. Trituration with ether afforded pale yellow crystals, m.p. 72–77°. Recrystallization from ether gave nearly pure material, m.p. 74–80°. The compound was somewhat contaminated with a persistent yellow impurity which could not be removed entirely. The infrared spectrum (chf.) showed a doublet, 5.57 μ (intense) and 5.70 μ (moderately-intense).

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.97; H, 6.04. Found: C, 77.26; H, 6.32.

A sample (2.2 g.) of III was melted *in vacuo* (1.0 mm.). The melt was refluxed at this pressure for 10 minutes, and was distilled. A few drops of orange distillate, b.p. 166–168° (0.8 mm.) were obtained before the remaining material decomposed, and this product crystallized rapidly. Recrystallization from ether gave pale yellow crystals, m.p. 79–83°. The infrared spectrum (chf.) of this material also had peaks at 5.56 and 5.70 μ and was virtually the same as the spectrum of material obtained as described above.

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Esters of *p*-Methyl- and *p*-Isopropylmandelic Acids as Mosquito Repellents

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In a previous paper¹ the preparation and mosquito repellent action of esters of mandelic acids were reported. Although substitution in the aromatic nucleus seemed to decrease the repellent effect of the esters against mosquitoes, further confirmation of this finding was sought.

TABLE I
ESTERS OF *p*-SUBSTITUTED MANDELIC ACIDS, $R-C_6H_4-CHOHCOOR'$

| R' | n_D^{25} | B.P., °C./Mm. | Yield, % | Analyses, % | | | |
|--|---------------|---------------|----------|-------------|-------|----------|-------|
| | | | | Carbon | | Hydrogen | |
| | | | | Calcd. | Found | Calcd. | Found |
| R = Methyl (yield based on <i>p</i> -tolualdehyde method E, ref. 1) | | | | | | | |
| Propyl | 1.5055 | 157/12 | 30 | 69.21 | 69.19 | 7.75 | 7.51 |
| Butyl | 1.4999 | 162–6/13 | 48 | 70.05 | 70.18 | 8.10 | 8.11 |
| Pentyl | 1.4995 | 174/12 | 43 | 70.52 | 70.95 | 8.45 | 8.45 |
| R = Isopropyl (yield based on <i>p</i> -isopropylmandelic acid method D, ref. 1) | | | | | | | |
| Methyl | M.p. 81–82°C. | 160–1/10 | 45 | 69.21 | 68.93 | 7.75 | 7.20 |
| Ethyl | M.p. 39–41°C. | 166/10 | 60 | 70.24 | 69.91 | 8.16 | 7.92 |
| Propyl | 1.4938 | 174/10 | 62 | 71.16 | 71.23 | 8.53 | 8.35 |
| Allyl | 1.5118 | 177/10 | 53 | 71.77 | 71.58 | 7.74 | 7.58 |
| Butyl | 1.4955 | 182–3/10 | 61 | 71.97 | 71.96 | 8.96 | 8.54 |
| Pentyl | 1.4926 | 189–90/10 | 59 | 72.69 | 72.34 | 9.15 | 8.88 |
| Hexyl | 1.4918 | 201–2/10 | 66 | 73.34 | 73.37 | 9.41 | 8.73 |

tone (VIII). A solution of 2.3 g. of III in 50 ml. of dry xylene was treated with 4 drops of benzenesulfonic acid, and the solution was refluxed under a water separator for an hour.

(1) W. F. Barthel, J. Leon, and S. A. Hall, *J. Org. Chem.*, 19, 485 (1954).