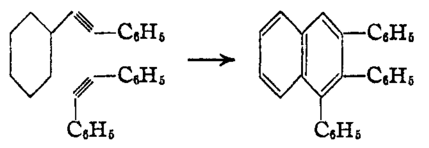
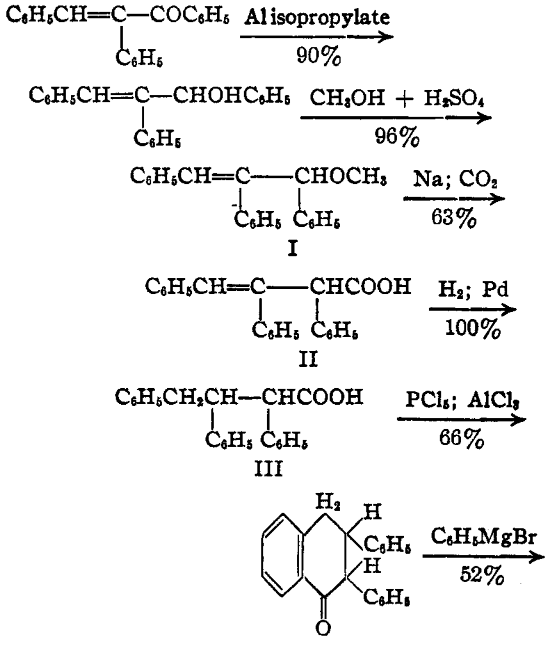
[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

Polyphenylnaphthalenes. II. 1,2,3-Triphenylnaphthalene

BY FELIX BERGMANN, DAVID SCHAPIRO AND H. EMILE ESCHINAZI

1,2,3-Triphenylnaphthalene (VI) has been prepared by Schlenk[1] by dimerization of tolane in a process analogous to the formation of 1-phenylnaphthalene-2,3-dicarboxylic acid from phenylpropiolic acid.[2] This method, however, is unsuitable for the preparation of large amounts of the above hydrocarbon. Another route to VI would be Grignardization of 2,3-diphenyl-α-tetralone (IV) which was synthesized by Crawford[3] from α,β-diphenyl-β-benzoyl-propionic acid via the α,β,γ-triphenylbutyric acid (III). The overall yield of IV in this two-step process, is, however, only about 15%. We have therefore worked out a new method for the triphenylbutyric acid, based on the fact that α,β,γ-triphenylallyl methyl ether (I) readily yields the α,β,γ-triphenylallylsodium.[4] The reaction scheme is





$$C_6H_5CH{=}\underset{C_6H_5}{C}{-}COC_6H_5 \xrightarrow[90\%]{\text{Al isopropylate}}$$

$$C_6H_5CH{=}\underset{C_6H_5}{C}{-}CHOHC_6H_5 \xrightarrow[96\%]{CH_3OH + H_2SO_4}$$

$$C_6H_5CH{=}\underset{C_6H_5}{C}{-}\underset{C_6H_5}{C}HOCH_3 \xrightarrow[63\%]{Na;\ CO_2}$$

I

$$C_6H_5CH{=}\underset{C_6H_5}{C}{-}\underset{C_6H_5}{C}HCOOH \xrightarrow[100\%]{H_2;\ Pd}$$

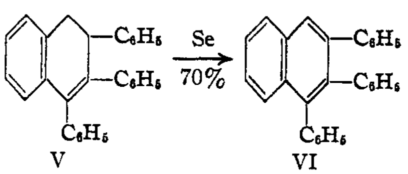
II

$$C_6H_5CH_2\underset{C_6H_5}{C}H{-}\underset{C_6H_5}{C}HCOOH \xrightarrow[66\%]{PCl_5;\ AlCl_3}$$

III

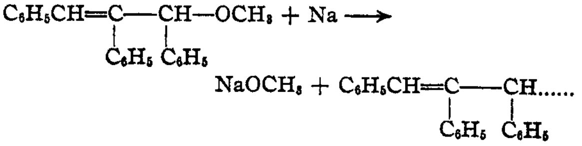
$$\xrightarrow[52\%]{C_6H_5MgBr}$$

IV



V VI

When the sodium substitution product of I was decomposed with carbon dioxide at 0°, it yielded the α,β,γ-triphenylvinylacetic acid (II) only in 63% yield, although apparently all of the methyl ether had entered the reaction with alkali metal. From the neutral part of the reaction mixture, no starting material could be isolated and no methoxyl was found in its analytical investigation. On the other hand, it was observed that an appreciable amount of sodium remained unreacted, even after shaking for seven days. This is an indication that the intermediary triphenylallyl radical, which is formed according to the scheme



$$C_6H_5CH{=}\underset{C_6H_5}{C}{-}\underset{C_6H_5}{C}H{-}OCH_3 + Na \longrightarrow NaOCH_3 + C_6H_5CH{=}\underset{C_6H_5}{C}{-}\underset{C_6H_5}{C}H\ldots\ldots$$

may undergo side reactions, and therefore partly escape the combination with a second sodium atom. The neutral by-products of II are still under investigation. One of them has been identified as 1,2,3-triphenylpropylene, by cyclization to 1,2-diphenylindene.

Cyclization of III, the hydrogenation product of II, was effected with a somewhat better yield (66%) than that recorded by Crawford (58%), when phosphorus pentachloride was used for the preparation of the acid chloride and benzene as solvent instead of carbon disulfide in the Friedel-Crafts reaction.

The tetralone IV reacted with phenylmagnesium bromide only at 100°. The crude carbinol was directly dehydrated to 1,2,3-triphenyl-3,4-dihydronaphthalene (V), which was smoothly dehydrogenated by selenium at 280-300°. After extraction with acetone, the dehydrogenation product (VI) was directly obtained in crystalline state.

α,β,γ-Triphenylbutyric acid (III) exists in two racemic stereoisomeric forms. In the procedure of Crawford, the configuration of III is determined

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[1] Schlenk and E. Bergmann, *Ann.*, **463**, 71 (1928).

[2] Lanser, *Ber.*, **32**, 2478 (1899); Michael, *ibid.*, **39**, 1908 (1906).

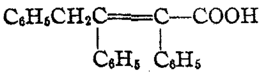
[3] Crawford, THIS JOURNAL, **61**, 608 (1939).

[4] F. Bergmann, THIS JOURNAL, **64**, 69 (1942).

by the choice of either of the two forms of α,β-diphenyl-β-benzoylpropionic acid. Apparently the configuration of the asymmetric carbon atoms of the keto acid is preserved during reduction of the carbonyl group. On the other hand, de Schüttenbach[5] obtained in the Grignard reaction of benzylmagnesium chloride with the nitrile of α-phenylcinnamic acid a mixture of the two possible racemic nitriles of III. This result is to be expected in view of the fact that the two asymmetric centers are introduced here simultaneously. During the catalytic hydrogenation of II, *one* new asymmetric center is established at the β-carbon atom; therefore a mixture of the two possible stereoisomers should be obtained. However, only the higher melting form of III was isolated in quantitative yield. In this connection it may be recalled that the benzaldesoxybenzoin used, and therefore also the triphenylvinylacetic acid, possesses the *trans* structure with regard to the double bond.

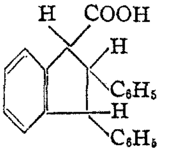
In view of this result, it would be of interest to examine the reduction of a compound of formula VII to III. VII should result from an allylic rearrangement of II. This reaction is now under investigation.

Owing to the allylbenzene structure present, II is easily cyclized by cold concentrated sulfuric acid to 2,3-diphenylhydrindene-1-carboxylic acid (VIII).



$$C_6H_5CH_2\underset{C_6H_5}{\underset{|}{C}}{=\!=}\underset{C_6H_5}{\underset{|}{C}}{-}COOH$$

VII



VIII

Experimental

Desoxybenzoin was prepared according to "Organic Syntheses," Vol. XII, p. 16, with the following modifications. The aluminum chloride was added portionwise at 40–50°. By this procedure, the amount of benzene can be reduced to 250 cc. for 0.5 mole of phenylacetic acid. The crude reaction product, after removal of the benzene, was triturated with a little methanol in a mortar. The main bulk of desoxybenzoin was obtained directly in pure, crystalline form, and only the remaining sirup (about 10%) had to be distilled *in vacuo;* yield, 80%.

Benzaldesoxybenzoin was obtained in 55% yield according to Kohler.[6]

1,2,3-Triphenylallyl alcohol[4] was obtained in 90% yield from benzaldesoxybenzoin (95 g.) and aluminum isopropylate (40 g.) in isopropanol (400 cc.). The alcohol (80 g.) was etherified with methanol (150 cc.) by addition of 1 cc. of concd. sulfuric acid and heating on a steam-bath with occasional shaking. The ether (I) crystallized immediately. Recrystallization from ligroin gave a yield of 96%.

1,2,3-Triphenylvinylacetic Acid (II).—Fifty grams of I ($^1/_6$ mole) and 8.5 g. of sodium (2.2 atoms) were shaken in ether for ninety-six hours. Reaction started immediately and the solution acquired a deep wine-red color. During reaction with carefully dried carbon dioxide gas at 0°, the color changed first to orange and then to lemon-yellow. On acidification, a white gum-like mass was precipitated. It was dissolved in sodium carbonate solution, ethanol was added until the solution became turbid, and the acidification was performed at 0°. From a mixture of benzene and ligroin white needles were obtained, m. p. 132–135°; yield, 33 g. or 63%. The acid II did not decolorize bromine.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.1; H, 5.7. Found: C, 83.8; H, 5.7.

The neutral part of the reaction product was distilled in a high vacuum. The lower-boiling fraction, b. p. 185–188° (0.03 mm.), a thick yellow oil, crystallized almost completely on standing, m. p. 62°. With bromine in carbon tetrachloride, a liquid addition product was obtained. After evaporation of the solvent, it was triturated with ligroin. A strong evolution of hydrobromic acid set in, and the mass crystallized immediately,[7] from high-boiling petroleum ether as long needles, m. p. 177–178°; mixed m. p. with 1,2-diphenylindene, 178°. The higher-boiling fraction, 225–230° (0.03 mm.) formed a brown resin, which could not be induced to crystallize.

The methyl ester of II was prepared by means of diazomethane and first obtained as a thick oil. On boiling with methanol, it was induced to crystallize; from isopropanol, short needles, m. p. 107°.

Anal. Calcd. for $C_{23}H_{20}O_2$: OCH_3, 9.5. Found: OCH_3, 9.8.

The ethyl ether was obtained in 90% yield by boiling with ethanolic hydrogen chloride for six hours, and distillation, b. p. 190–193° (0.3 mm.). Because of its low melting point, 59°, the ester could not be recrystallized satisfactorily.

Anal. Calcd. for $C_{24}H_{22}O_2$: OC_2H_5, 13.1. Found: OC_2H_5, 12.8.

2,3-Diphenylhydrindene-1-carboxylic Acid (VIII).—One gram of the acid II was thoroughly mixed with 1 cc. of concd. sulfuric acid. An exothermic reaction set in, yielding a brown sirup. After two minutes, the reaction product was precipitated by ice water as a yellow powder. VIII crystallized from dilute ethanol in white needles, m. p. 161°; yield, quantitative. The sodium salt of VIII, in contrast to the salt of the acid II, dissolved easily in dilute sodium carbonate solution.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.1; H, 5.7. Found: C, 84.3; H, 5.4.

The methyl ester was prepared with diazomethane and crystallized from methanol as clusters of needles, m. p. 116–117°.

Anal. Calcd. for $C_{23}H_{20}O_2$: OCH_3, 9.5. Found: OCH_3, 9.5.

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[5] De Schuttenbach, *Ann. chim.*, [11] **6**, 90 (1936).

[6] Kohler and Nygaard, THIS JOURNAL, **52**, 4128 (1930).

[7] Orechoff, *Ber.*, **47**, 89 (1914), obtained the cyclization product simply on boiling with glacial acetic acid.

α,β,γ-Triphenylbutyric Acid (III).—During the catalytic hydrogenation of II in dioxane, it was necessary to add fresh catalyst several times.[8] Apparently the hydrogenation product, like other known phenylbutyric acids, was intensly adsorbed at the active surface, thereby hindering the attack on new unsaturated molecules. After evaporation of the dioxane, there was left a crystalline mass. Recrystallization from benzene–ligroin yielded the acid III in beautiful needles, m. p. 158°. The methyl ester, prepared by means of diazomethane, melted at 158° (isopropanol).

Anal. Calcd. for $C_{23}H_{22}O_2$: OCH_3, 9.4. Found: OCH_3, 9.5.

III gave no reaction with concd. sulfuric acid. When III was dissolved in boiling sodium carbonate solution, its sodium salt crystallized on cooling. It is easily soluble in ethanol, and can be recrystallized from isopropanol as long, fine needles, m. p. 278–280°. Twenty-one grams of III and phosphorus pentachloride (15 g.) in benzene (175 cc.) were heated on a steam-bath for four hours. The solvent and phosphorus oxychloride were removed *in vacuo*, whereafter the acid chloride remained as a yellow solid. On trituration with concd. ammonia, the α,β,γ-triphenylbutyramide was formed; from ethanol as fine needles, m. p. 168–169°.

Anal. Calcd. for $C_{22}H_{21}ON$: N, 4.4. Found: N, 4.7.

2,3-Diphenyl-1-keto-1,2,3,4-tetrahydronaphthalene (IV).—The above acid chloride was dissolved in benzene, and after addition of aluminum chloride (11 g.) stirred for four hours at 0°, and eight hours at room temperature. The mixture was then decomposed with ice and hydrochloric acid, and the solvent removed by steam. The crude ketone was dissolved in carbon tetrachloride and washed with sodium carbonate solution. About one-half of the tetralone IV crystallized directly, the second part crystallized only after distillation, b. p. 205–207° (0.02 mm.) and trituration with ligroin; m. p. 146–147°; yield, 13.5 g.

1,2,3-Triphenyl-3,4-dihydronaphthalene (V).—To a Grignard solution, prepared from bromobenzene (4 g.) and magnesium (0.6 g.) the above tetralone (4 g.) was added in benzene solution. No reaction occurred. The solvent was then distilled off and the residue heated to 100° for twelve hours. After decomposition with ice and sulfuric acid, carbon tetrachloride was added in order to dissolve the sirupy organic material. The crude carbinol (3.5 g., 70%) could not be induced to crystallize, apparently because it presented a mixture of stereoisomers. It was therefore directly dehydrated with potassium bisulfate (6 g.) at 160° for two hours, and the reaction product again dissolved in carbon tetrachloride. The main bulk of V (2 g.) crystallized immediately after evaporation of the solvent, on trituration with acetone and methanol. An additional crop (0.5 g.) was obtained by distillation of the filtrate, b. p. 215° (0.5 mm.). Recrystallization from high-boiling petroleum ether gave plates of m. p. 176°; yield, 2.5 g., 52%.

Anal. Calcd. for $C_{28}H_{22}$: C, 93.9; H, 6.1. Found: C, 93.6; H, 6.1.

1,2,3-Triphenylnaphthalene (VI).—0.5 gram of the foregoing dihydronaphthalene derivative was heated with an equal weight of selenium to 280–300° for eighteen hours. The hard material was pulverized and extracted several times with boiling acetone. The residue of this solution crystallized directly from ligroin as yellowish needles, m. p. 153–154°; yield, 0.35 g., 70%. No picrate could be obtained in alcohol–benzene solution.

Summary

Reaction of 1,2,3-triphenylallylsodium with carbon dioxide opens a new route to α,β,γ-triphenylbutyric acid, and therefore to 2,3-diphenyl-α-tetralone and its derivatives. The synthesis of 1,2,3-triphenylnaphthalene by this method is described.

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[8] Hydrogenation of 50 g. of II required about nine hours.

[CONTRIBUTION FROM THE MEDICAL CLINIC OF THE PETER BENT BRIGHAM HOSPITAL, AND THE DEPARTMENT OF MEDICINE, HARVARD MEDICAL SCHOOL]

Preparation and Properties of Renin[1]

BY OTTO SCHALES

Tigerstedt and Bergman[2] found that the intravenous injection of saline extracts made from fresh kidneys, causes a prolonged rise in blood pressure. They named the substance responsible for this effect *Renin* and concluded that it is a protein, soluble in water and dilute salt solutions, insoluble in alcohol and inactivated by heat. Bingel and Strauss[3] confirmed these results and purified crude kidney press juice to a certain extent by isolating the fraction soluble in $^1/_3$ saturated and precipitated by $^7/_{12}$ saturated ammonium sulfate solution. Hessel[4] gave a general outline of a further purification of renin, but has not published the detailed procedure.

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[1] Presented before the Division of Biological Chemistry at the Atlantic City meeting of the American Chemical Society, September 11, 1941.

[2] R. Tigerstedt and P. G. Bergman, *Skand. Arch. Physiol.*, **8**, 223 (1898).

[3] A. Bingel and E. Strauss, *Deutsch. Arch. klin. Med.*, **96**, 476 (1909).

[4] G. Hessel, *Klin. Wchnschr.*, **17**, 843 (1938).