[Contribution from the Department of Chemistry of the University of California at Los Angeles]

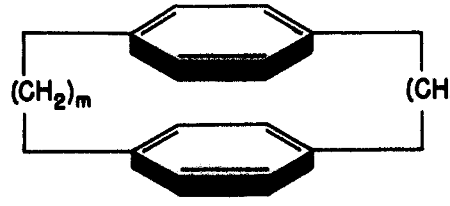
Macro Rings. II. Polynuclear Paracyclophanes[1]

By H. Steinberg[2] and Donald J. Cram[3]

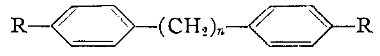
Received June 16, 1952

Two members of a new class of compound have been prepared in which four benzene rings are held together in a macro ring through methylene bridges attached to their para positions. The paracyclophane containing two benzene rings and a five- and a six-membered methylene bridge is reported. All three compounds have normal ultraviolet absorption spectra, and the infrared spectra of the two cycles whose spectra were taken were found to contain an identifying band common to all paracyclophanes prepared thus far.

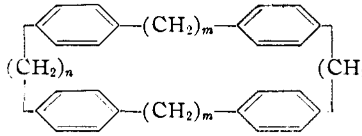
The first paper of this series[4] reported the preparation of compounds of class I in which $n = m = 2$; $n = 2, m = 3$; $n = 2, m = 4$; and $n = 3, m = 6$. The ultraviolet and infrared absorption spectra of these cycles showed a number of abnormalities as compared to the open chain model compounds of structure II. These differences were attributed to two novel structural characteristics of compounds such as I: when n and m are small, the benzene rings assume a puckered configuration; when the benzene rings are pressed together, interstitial electronic effects are possible due to the proximity of the π-orbitals of the two aromatic nuclei. Support for this interpretation was found in the gradual approach of the spectral properties of compounds I to those of II as n and m became larger and the two benzene rings were thrust further apart. However, none of the paracyclophanes previously reported became completely normal in either set of spectral properties.



I



II

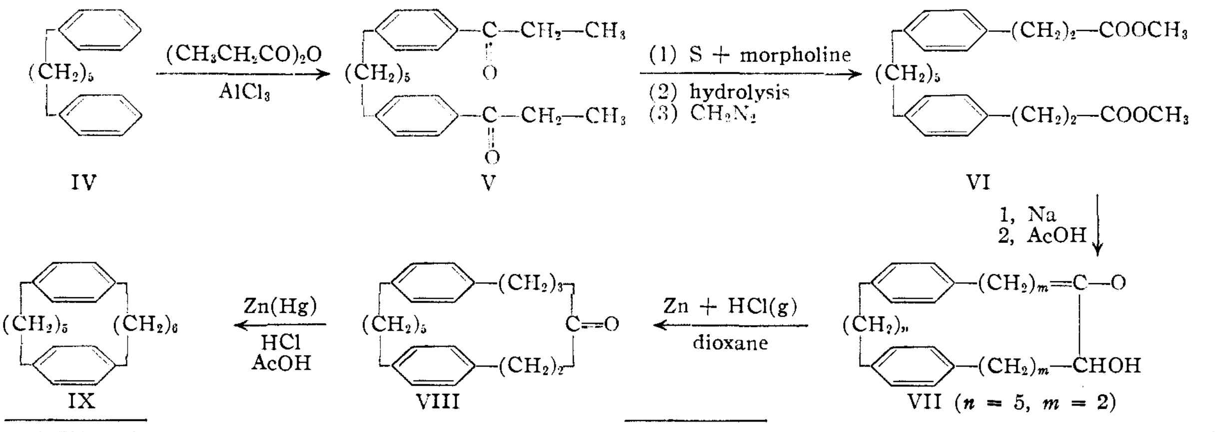


III

The present study reports the syntheses and properties of three new paracyclophanes which possess ultraviolet absorption spectra comparable to that of the open chain compounds (II). The first of these substances belongs to class I ($n = 5$, $m = 6$) whereas the other two belong to a new class of cycle in which *four* benzene rings are held together in a macro ring through methylene bridges attached to their para positions (III).

The cycle belonging to class I was prepared by the sequence shown in the diagram.[5] Hydrocarbon IV was propionylated in the two *p*-positions to give the diketone V, which was submitted to the Schwenk modification of the Willgerodt reaction[6] to give a thiomorpholide, hydrolysis and esterification of which gave the diester, VI. This material was submitted to the acyloin reaction[7] to give cycle VII which was reduced first to the ketone VIII and finally to the paracyclophane IX in a 58% over-all yield.

Cycle XIII is the smallest paracyclophane which has been prepared,[4] and to determine whether steric factors place a limit on the ring size at this point, an attempt was made to prepare XII utilizing the same general methods used to prepare XIII, XIV and XV. Only reduced material [bis-(*p*-tolyl)-methane] was isolated from the lower boiling fraction of the products of the Wurtz reaction, and the ultraviolet absorption spectrum of this fraction



---

[1] This work was supported in part by a generous grant from the Research Corporation.

[2] Atomic Energy Commission Predoctoral Fellow.

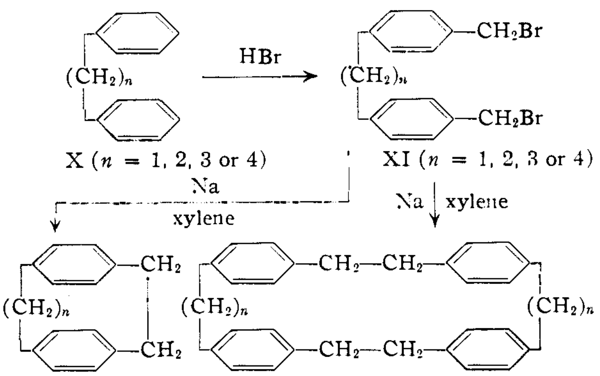
[3] Requests for reprints should be addressed to this author.

[4] D. J. Cram and H. Steinberg, This Journal, **73**, 5691 (1951).

[5] Recently R. C. Fuson and G. P. Speranza [*ibid.*, **74**, 1621 (1952)] reported the synthesis of three acyloins of the same type as VII in which $n = 2$ and $m = 3$, 5 or 9.

[6] E. Schwenk and E. Bloch, *ibid.*, **64**, 3051 (1942).

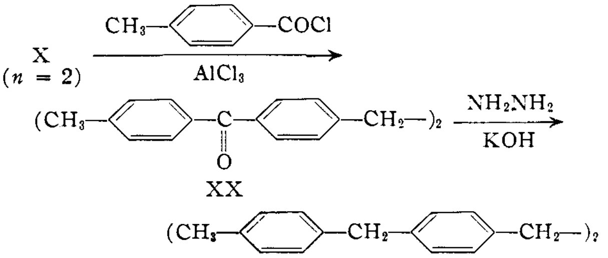
[7] See ref. 4 for a summary of recent literature references.



X (n = 1, 2, 3 or 4) XI (n = 1, 2, 3 or 4)

XII (n = 1); XIII (n = 2) XVI (n = 1); XVII (n = 2)
XIV (n = 3); XV (n = 4) XVIII (n = 3); XIX (n = 4)

was normal, which suggests that little or no XII was produced in the reaction. From the higher boiling materials, compound XVI was isolated in 0.1% yield. The cyclic structure was assigned to this substance on the basis of its analysis and molecular weight. To prove that the compound was cyclic and not the linear reduction product, XXI, the latter compound was prepared. Dibenzyl was treated with *p*-toluyl chloride to give the diketone XX, which was reduced to XXI, the



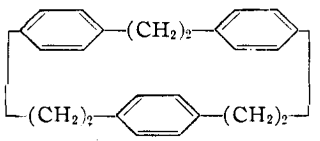
XX

XXI

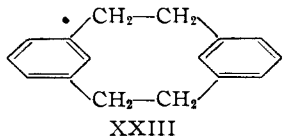
linear counterpart of XVI. The two latter compounds had quite different properties.

Since the three reactions that led to the paracyclophanes XIII, XIV and XV[4] were carried out in a fashion identical to that which gave XVI, the higher-boiling fractions obtained from the products of the three original Wurtz reactions were examined for XVII, XVIII and XIX, respectively. Only cycle XVIII was isolated, and in only trace amounts.

The two reactions leading to the paracyclophanes containing four aromatic nuclei are not unlike those of Baker, McOmie and Norman[8] who obtained cycles XXII and XXIII by the treatment of *p*- and *m*-xylylene bromide, respectively, with sodium. The former substance represents the first synthesis of a paracyclophane containing three aromatic nuclei.



XXII



XXIII

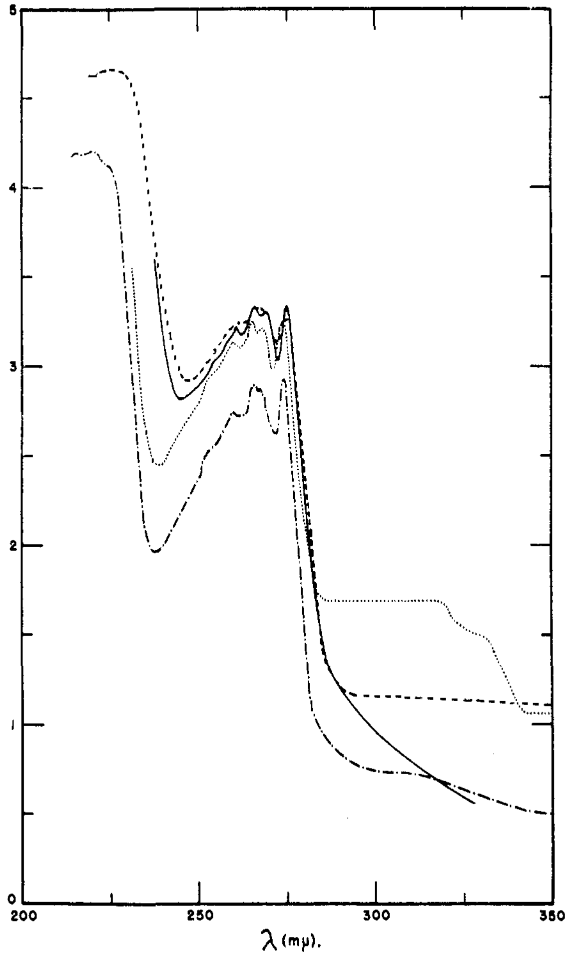
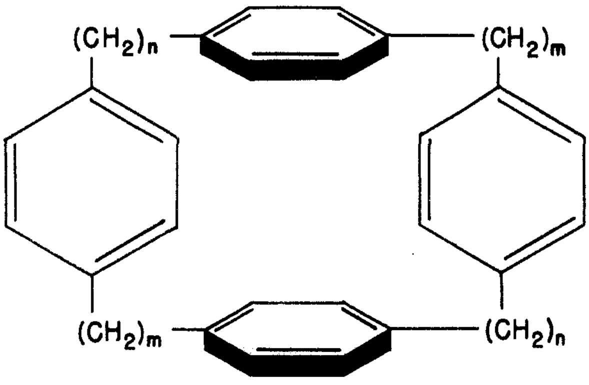


Fig. 1.—Ultraviolet absorption spectra in cyclohexane (Cary recording spectrophotometer, model 11 PMS): curve —, *p,p'*-bis-(4-methylbenzyl)-dibenzyl (XXI); curve -.-, *p,p'*-hexamethylene-1,5-diphenylpentane (IX); curve ---, cycle XVI; curve ...., cycle XVIII.

Figure 1 records the ultraviolet absorption spectra of the three new cyclic hydrocarbons as well as that of the linear model, XXI. The spectra of these cycles do not depart from that of the model compound, and therefore the aromatic nuclei would appear to be too far apart for interstitial resonance effects to operate. Since IX (I with n = 5, m = 6) has a normal and I with n = 3, m = 6 has an abnormal ultraviolet absorption spectrum, the smallest paracyclophane with a normal spectrum should contain methylene bridges of intermediate length, possibly I with n = m = 4 or 5. An examination of molecular models of the polynuclear cycles XVI and XVIII reveals the interesting possibility that these molecules can assume the geometry of a rather wide belt with a large hole in the middle. A spacially more economical and more probable geometry is shown in structure XXIV. Either type of configuration places the π-orbitals of the benzene rings well out of each others way.

---

[8] W. Baker, J. F. W. McOmie and J. M. Norman, *J. Chem. Soc.*, 1114 (1951). See also W. Baker, F. Glockling and J. F. W. McOmie, *ibid.*, 1118 (1951).



XXIV

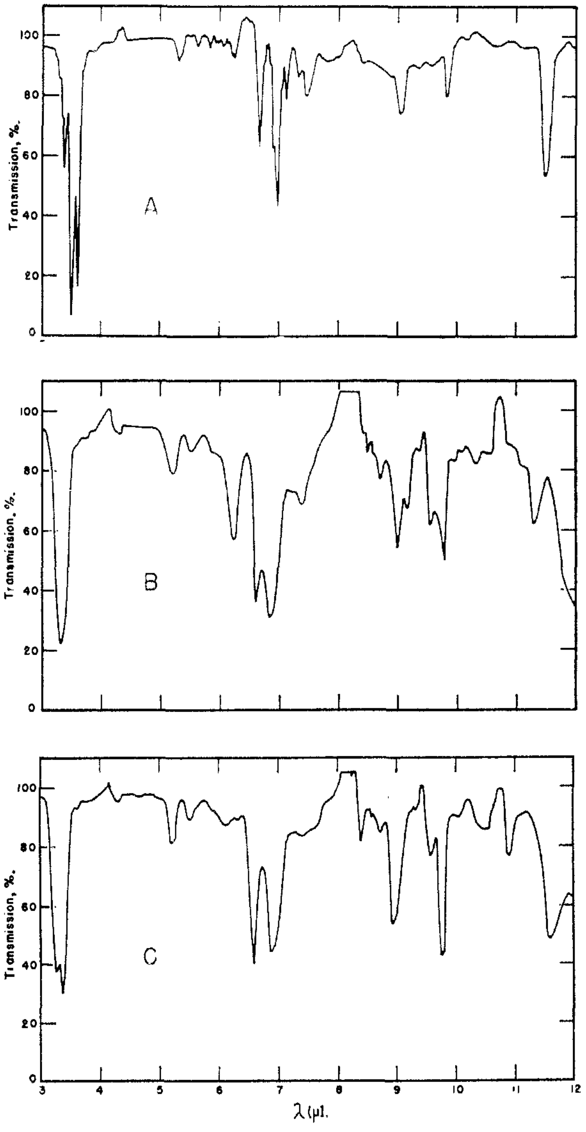


Fig. 2.—Infrared absorption spectra (Beckman spectrophotometer, model IR2T) with rock salt prisms and cells: curve A, *p,p'*-hexamethylene-1,5-diphenylpentane (IX), solution (6.3% by weight) in carbon tetrachloride; curve B, cycle XVI, solution (22% by weight) in chloroform; curve C, *p,p'*-bis-(4-methylbenzyl)-dibenzyl (XXI), solution (19% by weight) in chloroform.

The absorption bands in the infrared that seemed to be associated with non-planar benzene rings in cycles XIII, XIV and XV[4] are absent in the spectra of IX and XVI (see Fig. 2). On the other hand, strong absorption bands have appeared in the six paracyclophanes whose spectra have been taken in the region of 11.20 to 11.85 μ, and these bands have appeared in the spectra of only one (XXI) of the open chain models that have been examined.[4] These bands have already been of diagnostic use in detecting the presence of these cycles in mixtures of hydrocarbons.

Experimental Part

1,5-Bis-(4-propionylphenyl)-pentane (V).—Cinnamylideneacetophenone (m.p. 101–103°) was prepared in 70% yield by the method of Scholtz,[9] and was reduced to 1,5-diphenylpentane (IV) by an adaptation of the procedure of Strauss and Grindell[10] in a 42% yield, b.p. 138–140° (0.3 mm.). In the present work, a pressure of 100 atmospheres of hydrogen and a relatively large batch size (122 g.) were employed. This material was treated with propionic anhydride by a procedure analogous to B of paper I of this series.[4] The product instead of being crystallized was distilled (b.p. 201–203° at 0.08 mm.) to give a 44% yield of an oil which solidified to a crystalline mass melting at 47–51°. This material was used directly in the next step. A small sample was recrystallized five times from petroleum ether to give large white plates, m.p. 54–55°.

Anal. Calcd. for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39. Found: C, 81.92; H, 8.65.

1,5-Bis-[4-(β-carboxyethyl)-phenyl]-pentane.—This procedure is a modification of that reported by Schwenk and Block[6] for a similar reaction. A mixture of 64 g. of V (crude), 21 g. of sulfur and 165 ml. of morpholine was held at reflux temperature for 18 hours. The dark brown reaction mixture was poured into 1 liter of water, and the crude morpholide was extracted with chloroform. The organic extracts were concentrated, the residual oil was diluted with a solution of 1 liter of 70% ethanol and 160 ml. of a 50% sodium hydroxide solution, and the resulting mixture was held at reflux temperature for 19 hours. The ethanol was then evaporated under reduced pressure, and the residual solution was partially neutralized with 180 ml. of concentrated hydrochloric acid. The mixture was brought to a boil, treated with 8 g. of Norite, and filtered through a cake of Celite. The filtrate was acidified with concentrated hydrochloric acid, cooled in an ice-bath, and filtered. The filter cake was dried and recrystallized twice from glacial acetic acid (Norite treatment) to give 15.9 g. (23% yield) of white granules, m.p. 174–179°. A sample recrystallized four times from ethanol gave white platelets, m.p. 185–186°.

Anal. Calcd. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66; neut. equiv., 184. Found: C, 74.73; H, 7.75; neut. equiv., 184.

1,5-Bis-[4-(β-carbomethoxyethyl)-phenyl]-pentane (VI).—A solution of 15 g. of crude acid (see above) dissolved in 300 ml. of absolute dioxane was added to an ether solution (200 ml.) of diazomethane prepared from 20 g. of nitrosomethylurea.[11] The excess reagent was destroyed with glacial acetic acid, the ether and dioxane were evaporated under reduced pressure, and the yellow residue was dissolved in benzene. This solution was washed with water, with sodium hydroxide solution, and again with water. After the solution had been dried, the solvent was evaporated, and the crystalline residue was recrystallized from 1200 ml. of hot methanol (Norite treatment) to give 13.1 g. of ester (80% yield) as white plates, m.p. 108–110°. A small sample recrystallized from methanol gave m.p. 108.5–110°.

Anal. Calcd. for $C_{25}H_{32}O_4$: C, 75.72; H, 8.14. Found: C, 75.52; H, 8.02.

3-Keto-4-hydroxy-*p,p'*-hexamethylene-1,5-diphenylpentane (VII).—The general acyloin cyclization procedure de-

---

(9) M. Scholtz, *Ber.*, **28**, 1730 (1895).

(10) F. Strauss and H. Grindell, *Ann.*, **439**, 306 (1924).

(11) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 165.

scribed in paper I of this series[4] was employed. In this manner 12.2 g. of VI was added over 46 hours to 3 g. of sodium stirred at 7800 r.p.m. The color of the reaction mixture progressed from light gray at the beginning to light yellow-green at the mid-way point to olive green at the end. The usual work-up gave 0.84 g. of polymer and an orange oil which solidified to a mush when cooled. This material was triturated with cold pentane, filtered, and the solid was recrystallized from petroleum ether (Norite treatment) to give 6.06 g. of hard white rosettes, m.p. 121–124°, 0.96 g. of a second crop, m.p. 119–123°, and 0.32 g. of a third crop, m.p. 119–123° (total crude yield, 71%). A small sample recrystallized three times from petroleum ether gave white needles, m.p. 124–124.5°.

Anal. Calcd. for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39; mol. wt., 336. Found: C, 82.03; H, 8.67; mol. wt., 326 (Rast).

***p,p'*-Hexamethylene-1,5-diphenylpentane (IX).**—The acyloin, IX (2.0 g.) was reduced in a solution of hydrogen chloride in dioxane with zinc by the method of Stoll[12] to give upon distillation of the reaction product (bath temperature of 188–200° at 0.13 mm.) 1.84 g. (96% yield) of ketone VIII which crystallized in the receiver. This material was reduced directly to the hydrocarbon with amalgamated zinc, hydrochloric and acetic acid by the procedure described in paper I of this series[4] for the reduction of 3-keto-*p,p'*-hexamethylene-1,3-diphenylpropane. The product was extracted into ether, and the ether layer was washed with water, a 10% solution of sodium hydroxide, and again with water. The solution was then dried, the solvent was evaporated, and the remaining white solid was recrystallized from methanol to give 1.0 g. (57% yield) of white needles, m.p. 125–131°. Three recrystallizations of this material from methanol gave white needles, m.p. 131.5–133°.

Anal. Calcd. for $C_{23}H_{30}$: C, 90.13; H, 9.87; mol. wt., 306. Found: C, 89.87; H, 9.90; mol. wt., 310 (Rast).

Di-(*p*-bromomethylphenyl)-methane (XI, n = 1).—Procedure G was erroneously omitted from paper I of this series[4] and is recorded here as applied to XI, $n = 1$.[13] To a stirred mixture of 65 g. (0.72 mole) of paraformaldehyde, 165 ml. of 48% hydrobromic acid, 123 ml. of phosphoric acid, 204 ml. of glacial acetic acid and 84 g. (0.5 mole) of diphenylmethane held at 100° was added through a delivery tube dry hydrogen bromide gas. After five hours the flow of gas was interrupted, the mixture was allowed to stand for eight hours, and was again stirred and heated at 100° for an additional eight hours. The warm reaction mixture was then poured into 2 liters of water and cooled to 0°. The supernatant liquid was decanted from the semi-solid oil, which was triturated with cold acetone to give a gray solid. Two recrystallizations of this material from benzene gave 45 g. (25% yield) of white prisms, m.p. 152.5–154°. An analytical sample melted at 153–154.5°.

Anal. Calcd. for $C_{15}H_{14}Br_2$: C, 50.87; H, 3.99. Found: C, 50.58; H, 4.05.

Attempted Preparation of *p,p'*-Dimethylenediphenylmethane (XII).—The cyclization procedure previously described[4] was employed. In this manner 41.8 g. (0.118 mole) of di-(*p*-bromomethylphenyl)-methane was added over 48 hours to 11.4 g. (0.496 mole) of sodium stirred in boiling xylene at 7500 r.p.m. The color of the reaction mixture progressed from light gray at the beginning to slate gray at the end. The usual work-up of the reaction mixture[4] gave 10.4 g. of polymer which did not melt below 340° and which was insoluble in common organic solvents. Concentration of the xylene filtrates gave a yellow colloidal mixture which was triturated with 100 ml. of cold ether and filtered free of a sticky tan material. The filtrate was saved, and the tan material was sublimed at 0.3 mm. to give two fractions: (1) 0.38 g., bath temperature 90–150°, yellow oil; (2) 0.37 g., bath temperature 190–250°, yellow solid. Fraction (1) was dissolved in pentane and passed through a 50-g. column of alumina with pentane as an eluting agent. The column filtrates when evaporated gave 0.24 g. of a colorless oil whose ultraviolet absorption spectrum was "normal" as compared to that of di-*p*-tolylmethane. Fraction (2) was dissolved in a 50% benzene–50% pentane mixture and absorbed on a 50-g. column of alumina. The column was developed with the same solvent, and evaporation of the column filtrates gave solid residues which were combined and recrystallized three times from acetone to give 25 mg. of white platelets of compound XVI, m.p. 151–153°.

Anal. Calcd. for $C_{30}H_{28}$: C, 92.74; H, 7.26; mol. wt., 388.5. Found: C, 92.78; H, 7.26; mol. wt., 399 (Rast).

The original ether solution was evaporated, and the residual brown oil was distilled at 0.3 mm. to give two fractions: (1) 3.5 g., bath temperature 125–170°, colorless oil; (2) 1.55 g., bath temperature 180–250°, glass. The polymeric still residue amounted to 6.0 g. Fraction (1) was crystallized in methanol at −80° to give white plates of di-*p*-tolylmethane, m.p. 26–28°. The material in the filtrate had a "normal" ultraviolet absorption spectrum as compared to di-*p*-tolylmethane.

Isolation of Paracyclophane XVIII from Products of Wurtz Reaction with *1,3-Bis-(4-bromomethylphenyl)-propane*.—In paper I of this series[4] was reported the preparation of *p,p'*-trimethylene-1,2-diphenylethane from the treatment of 1,3-bis-(4-bromomethylphenyl)-propane with sodium. From the higher boiling fraction of the products of this reaction (1.07 g. of yellow oil distilling at a pot temperature of 200–250° at 0.3 mm.) was isolated compound XVIII in the following manner. The oil was dissolved in 5 ml. of pentane and decolorized with Norite, and the mixture was filtered. The filtrate was evaporated, and the residue was distilled in a short-path still. At a bath temperature of 145–150° (0.09 mm.), 0.22 g. of a colorless oil was collected, and at 185–190° (0.08 mm.), 0.43 g. of a viscous yellow oil was obtained. The latter fraction was crystallized from pentane at −80° to give material which upon recrystallization from pentane gave 90 mg. of XVIII, m.p. 58.5–61.5°. Another recrystallization gave small irregular prisms, m.p. 61–62°.

Anal. Calcd. for $C_{34}H_{36}$: C, 91.84; H, 8.16; mol. wt., 444. Found: C, 91.85; H, 8.18; mol. wt., 431 (Rast).

4,4'-Bis-(*p*-toluyl)-dibenzyl (XX).—A mixture of 25 g. of *p*-toluic acid and 100 ml. of thionyl chloride and two drops of dry pyridine was held at reflux temperature for 10 hours, and the thionyl chloride was evaporated under reduced pressure. The acid chloride was distilled to give 26 g. of material which was used directly in the next step. To a stirred mixture of the acid chloride, dibenzyl (14.6 g.) and 60 ml. of pure carbon disulfide was added in small portions over a period of 15 minutes 56 g. of dry, powdered aluminum chloride. The mixture was stirred for an additional 30 minutes and then mixed with cracked ice and concentrated hydrochloric acid. The organic layer was separated, and the carbon disulfide was evaporated to give a sludge which was dissolved in ether. The ether solution was washed with water, with sodium carbonate solution and again with water and was then dried. When evaporated to a low volume the solution deposited white needles (11.0 g.), m.p. 152–153°, second crop (3.6 g.), m.p. 151–153°. Recrystallization of this material from a chloroform–ether mixture gave 12.3 g., m.p. 153–154°. An analytical sample melted at 154.5–155°.

Anal. Calcd. for $C_{30}H_{26}O_2$: C, 86.09; H, 6.26. Found: C, 85.91; H, 6.33.

***p,p'*-Bis-(4-methylbenzyl)-dibenzyl (XXI).**—A mixture of 5.0 g. of the diketone XX, 6 g. of potassium hydroxide, 5 ml. of 85% hydrazine hydrate and 30 ml. of triethylene glycol was heated to 150°, and the water and excess hydrazine were allowed to escape. The solution was then held at 210° for 12 hours, cooled, and shaken with water. The solid that separated was collected and washed first with water and then with acetone. One recrystallization of the material from glacial acetic acid and two from chloroform and ether provided 2.4 g. of white scales, m.p. 124.5–125°. A mixed melting point of this material (XXI) and cycle XVI melted at 92–110°.

Anal. Calcd. for $C_{30}H_{30}$: C, 92.26; H, 7.74; mol. wt., 390. Found: C, 92.13; H, 7.74; mol. wt., 370.

LOS ANGELES, CALIFORNIA

---

[12] M. Stoll, *Helv. Chim. Acta*, **30**, 1837 (1947).

[13] This procedure is analogous to that developed by J. A. Goodson, *et al.*, *Brit. J. Pharmacol.*, **3**, 62 (1948).