On heating the crystals above the melting point, acetic acid was evolved. The ultraviolet absorption spectrum corresponded exactly with that of methyl 9-oxodehydroabietate.

1,4a-Dimethyl-1-carbomethoxy-7-isopropenyl-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (VII).—A sample of the non-crystalline keto alcohol described above (2.3 g.) was heated under reflux for 6 hours with 50 ml. of acetyl chloride. The acetyl chloride was removed under reduced pressure and the residue treated at reflux temperature with 50 ml. of collidine for 17 hours. The dark, tarry product (2.2 g.) was dissolved in 25 ml. of benzene and adsorbed on an alumina column 2.2 cm. in diameter and 60 cm. high. The column was eluted with five one-liter portions of benzene to obtain five fractions of product. Fractions 4 and 5 (0.82 g.) were crystallized to constant melting point (83–84°), $[\alpha]^{22}D$ +25.0° (2% solution in $CHCl_3$) from methanol.

Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.56; H, 8.07.

The ultraviolet absorption spectrum of the compound is characterized by maxima at 240 mμ (α, 93), and 316 mμ (α, 4.7) and an inflection point at 258 mμ (α, 50). A sample of the compound (0.50 g.) was saponified by boiling in 15 ml. of diethylene glycol containing 0.30 g. of potassium hydroxide for 1.5 hours. The free acid (0.45 g.) was recovered and crystallized from benzene–petroleum ether to a constant melting point of 214–216°.

Anal. Calcd. for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74; neut. equiv., 312. Found: C, 76.67; H, 7.80; neut. equiv., 314.

A sample (1.0 g.) of the compound described above was dissolved in 50 ml. of ethyl chloride and a 4% stream of ozone (22 liters/hour) passed through the solution at −60 to −79°. The ozonization was continued for 30 min. before purging the blue solution with oxygen for a similar period of time. The solution was transferred to a flask connected with a series of traps containing an aqueous solution of 2,4-dinitrophenylhydrazine hydrochloride. A slow stream of nitrogen was passed through the solution until the ethyl chloride had been removed. After removing the ethyl chloride, 100 ml. of 25% acetic acid and 0.3 g. of zinc dust were added. The mixture was heated under gentle reflux as nitrogen was passed through the system. After 2 hours the yellow precipitate was recovered from the traps, dried and found to weigh 0.08 g. (m.p. 155°). Recrystallization from ethanol raised the melting point to 163°. The melting point was not depressed by admixture with an authentic sample of the 2,4-dinitrophenylhydrazone of formaldehyde. The non-volatile material from the ozonolysis (0.70 g.) was recovered and crystallized to constant melting point (142–143°) from methanol. The melting point was not depressed by admixture with a sample of the previously prepared 1,4a-dimethyl-1-carbomethoxy-7-acetyl-9-oxo-1,2,3,-4,4a,9,10,10a-octahydrophenanthrene.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

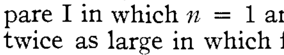
Macro Rings. III. Synthesis and Properties of *p,p'*-Tetramethylene-1,4-diphenylbutane[1]

BY DONALD J. CRAM AND NORMAN L. ALLINGER

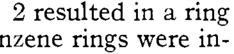
RECEIVED AUGUST 20, 1953

The compound in which two benzene rings are joined in the para positions by two four-carbon methylene bridges has been prepared. The method employed is believed to be of general application to the preparation of paracyclophanes, and involves hydrogenation of the benzene rings prior to an acyloin ring closure followed by dehydrogenation at a later stage. The stereochemical structure of the fully hydrogenated paracyclophane is established.

The previous papers of this series[2] reported the preparation of the paracyclophanes (I) in which $n = m = 2$, $n = 2$ and $m = 3$, $n = 2$ and $m = 4$, $n = 3$ and $m = 6$, and $n = 5$ and $m = 6$. Attempts to prepare I in which $n = 1$ and $m = 2$ resulted in a ring twice as large in which four benzene rings were incorporated.[2b] The spectral properties of the paracyclophanes show a gradual progression from normal (compared to open chain models, II) for I in which n and m are large (*e.g.*, $n = 5$, $m = 6$) to abnormal in which n and m are small (*e.g.*, $n = m = 2$). These abnormalities have been attributed to two effects, the distortion of the benzene rings from planarity,[3] and to a trans-annular electronic effect of one benzene on another.[4] The ultraviolet absorption spectrum of I ($n = 3$ and $m = 6$) is slightly abnormal while that of I ($n = 5$ and $m = 6$) is completely normal. Molecular models indicate that I with $n = m = 4$ possesses a geometry which allows the two phenyl groups to be completely planar, but which restricts their rotation with respect to one another. The synthesis of this compound was undertaken for two reasons: to determine the smallest ring size for the paracyclophanes compatible with a normal spectrum; and to develop a synthetic route for those substances (I, $n = m = 3$, $n = m = 4$, $n = m = 5$) whose ring size and symmetry properties were the most amenable to aromatic substitution and restricted rotation studies.



I



II

The paracyclophanes previously prepared were obtained by either of two procedures.[5] Dibro-

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[1] Research supported in part by the Office of Naval Research.

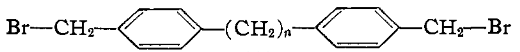
[2] (a) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951); (b) H. Steinberg and D. J. Cram, *ibid.*, **74**, 5388 (1952).

[3] C. J. Brown and A. C. Farthing [*Nature*, **164**, 915 (1949)] have demonstrated by X-ray diffraction analysis of the crystal structure of I with $n = m = 2$ that the 1,4-carbons of each benzene ring are distorted about 11° out of the plane of the other four carbons.

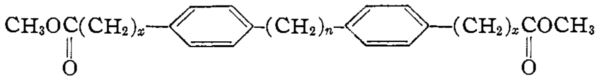
[4] Elsewhere we have used the term interstitial electronic effects (ref. 2a). The general term "trans-annular" has been used to describe the general phenomena of cross-ring reactions. [For rearrangements, see A. C. Cope, S. W. Fenton and C. F. Spencer, THIS JOURNAL, **74**, 5884 (1952); A. C. Cope, A. C. Haven, F. L. Ramp and E. R. Trumbull, *ibid.*, 4867 (1952); V. Prelog and K. Schenker, *Helv. Chim. Acta*, **35**, 2044 (1952); V. Prelog, K. Schenker and W. Kung, **36**, 471 (1953); G. Fodor and K. Nador, *J. Chem. Soc.*, 721 (1953). For elimination reactions see A. C. Cope and G. Holyman, THIS JOURNAL, **72**, 3062 (1950); K. Schenker and V. Prelog, *Helv. Chim. Acta*, **36**, 896 (1953)]. The term might be equally well applied to cross-ring electronic modifications of physical properties such as spectra. Examples of trans-annular electronic interactions are as follows: ref. 2; E. A. Braude, E. R. H. Jones, F. Sondheimer and J. B. Toogood, *J. Chem. Soc.*, 607 (1949); J. C. Lunt and F. Sondheimer, *ibid.*, 3361 (1950); P. D. Bartlett and E. S. Lewis, THIS JOURNAL, **72**, 1005 (1950).

[5] Compound I ($n = m = 2$) has also been obtained in trace amount by pyrolysis of *p*-xylene (ref. 3).

mides of type III ($n \geqq 2$) have been cyclized by a Wurtz reaction,[2] and esters of type IV ($x \geqq 2$) by an acyloin reaction.[2,6] The acyloin reaction with IV ($n = 2$ or 3, $x = 1$) failed to yield the desired compound, probably due to the activated α-hydrogen's encouragement of side reactions.[2] However, the higher yields of the acyloin ring closures compared to the Wurtz reaction made the former reaction more attractive.

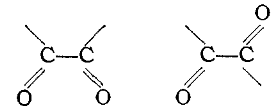


III

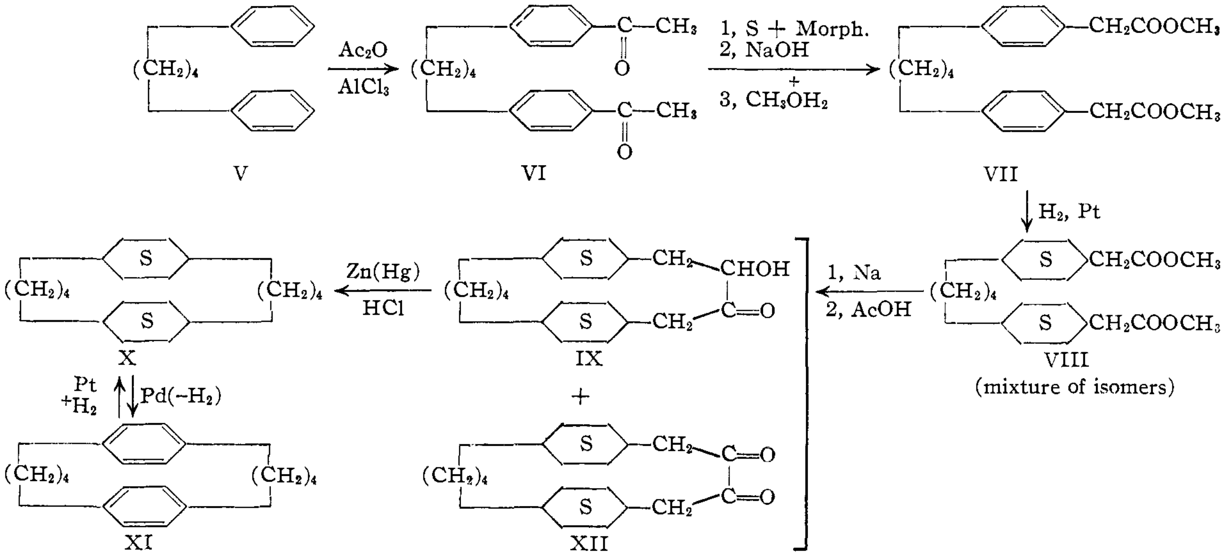


IV

The formulations summarize the synthetic sequence developed in the current investigation. Hydrocarbon V was acylated in the two *p*-positions to give diketone VI. This substance was submitted to the Schwenk–Willgerodt reaction[7] to give a thiomorpholide which upon hydrolysis and esterification gave the diester, VII. Hydrogenation of VII with platinum in acetic acid at 25° led to a mixture of the *cis–cis*, *cis–trans* and *trans–trans* isomers of VIII, from which one isomer (VIIIa) was crystallized in low yield. Attempts to isolate the other isomers from the filtrates failed, and therefore the ester in these filtrates was submitted directly to acyloin ring closure. A single acyloin was isolated in 25% yield by careful treatment of the reaction mixture, 63% of the starting material being accounted for as polymer. The yield was not changed when the dilution in the ring closure was increased by a factor of four, which fact suggests that essentially only one of the isomeric esters is giving cycle. A small amount of diketone was also isolated, and the position of the maximum in the visible spectrum at 456 mμ suggests that the carbonyl groups are in the same plane.[8] Although a selection of conformation cannot be made conclusively, molecular models suggest that the *cis* arrangement is the more comfortable. The ester obtained in a pure state (VIIIa) was also cyclized to give a poor yield of impure acyloin, identifiable only by the acyloin test with bismuth trioxide.[9]



cis *trans*



The acyloin (IX) was reduced with zinc and hydrochloric acid in acetic acid[10] to the hydrocarbon X, which could be purified only by laborious fractional crystallization. If the impure product was used directly in the next step, the final product was equally difficult to purify. Since the crude hydrocarbon (X) possessed an absorption band in the infrared at 10.21 μ (indicative of a *trans*-olefin[11]) which was absent in the pure cycle (X), the mixture was submitted to a hydrogenation, 0.2 mole of hydrogen being absorbed. With this procedure, the pure saturated hydrocarbon (X) was obtained in 87% yield from IX.[12] When the acyloin obtained by ring closure of VIIIa (crystalline ester) was submitted to the above reduction procedure, only polymeric products were obtained.

The saturated hydrocarbon X was dehydrogenated almost quantitatively with palladium-on-charcoal to give the paracyclophane XI, a small sample of which was reduced with platinum in acetic acid to give back pure X. It is therefore probable that X possesses a *cis–cis* configuration and that the two sets of six hydrogens that are *cis* to one another on each six-membered ring probably are on the outside of each ring as in Xa. This conclusion is provided by a number of considerations. (1)

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[6] R. C. Fuson and G. P. Speranza, THIS JOURNAL, **74**, 1621 (1952).

[7] E. Schwenk and E. Block, *ibid.*, **64**, 3051 (1942).

[8] N. J. Leonard and P. M. Mader, *ibid.*, **72**, 5388 (1950).

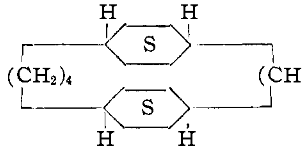
[9] W. Rigby, *J. Chem. Soc.*, 793 (1951).

[10] K. Wiesner, D. M. MacDonald, R. B. Ingram and R. B. Kelley, *Can. J. Research*, **B28**, 561 (1950).

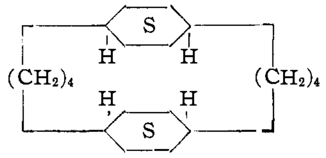
[11] N. S. Sheppard and F. B. M. Sutherland, *Proc. Roy. Soc.* (*London*), **A196**, 195 (1949).

[12] Olefins have long been recognized as side products in Clemmensen reductions [*e.g.*, see E. Muller, *Z. Elektrochem. angew. physik. Chem.*, **33**, 253 (1927)].

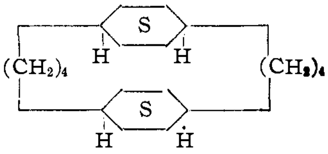
Molecular models of the three *cis–cis* isomers (Xa, Xb and Xc) suggest that the steric barrier to interconversion would be large enough under ordinary conditions to allow isolation of each isomer. (2) The space in between the two rings is too small to admit catalyst with its adsorbed hydrogen. (3) Trans-annular hydrogen migrations are improbable.



Xa



Xb



Xc

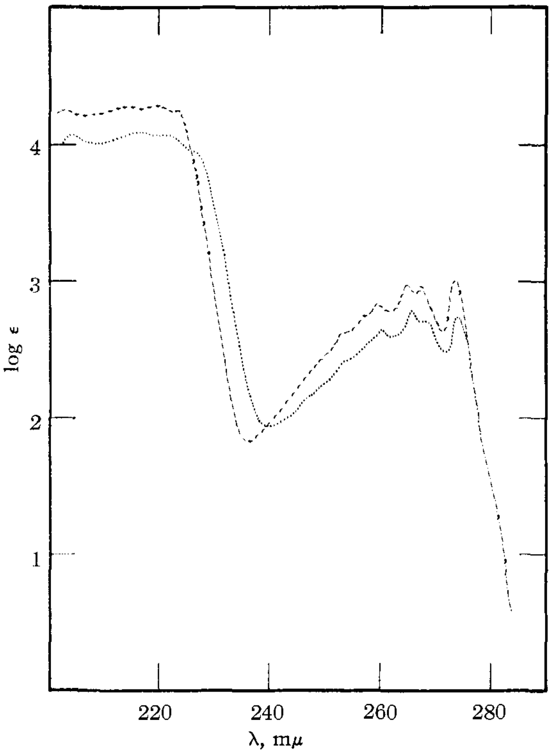
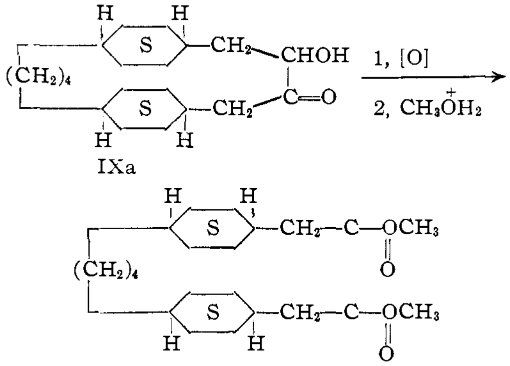


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol (Cary spectrophotometer, model 11PMS): ...., *p,p'*-tetramethylene-1,4-diphenylbutane (XI); ----, 1,4-bis-(4-ethylphenyl)-butane (XIII).

If the above conclusions are correct, then acyloin IX and diketone XII possess a configuration similar to Xa, and the starting ester that provided most of IX must have possessed the *cis–cis* configuration, VIIIb. Oxidation of IXa and esterification of the diacid produced gave an authentic crystalline sample of the *cis–cis* diester (VIIIb), which turned out to be different from the crystalline ester isolated directly from the reduction mixture (VIIIa). The latter ester is tentatively assigned the *trans–trans* structure on the following bases. The melting point of this isomer is higher than that of the *cis–cis* isomer, whereas the lack of symmetry of the alternative *cis–trans* configuration would probably result in a lower melting point.



IXa

VIIIb

Although the rule of von Auwers[13] predicts the lowest index of refraction for the *trans-trans* ester, the fact that the refractive index of the mixture rises 0.0005 unit on removal of the crystalline isomer is not proof that the crystalline isomer has the lowest index of refraction. However, the yield (7%) of isolated solid isomer (VIIIa) is consistent with the distribution of isomers calculated from the data of Miller[14] on the reduction of *p*-xylene under the conditions used in the current study. Thus, if the same relative amounts of *cis* and *trans* hydrogenation occur with ester VII (the two rings being reduced separately) as with *p*-xylene, the distribution of isomers would be 49% *cis–cis*, 42% *cis–trans* and 9% *trans–trans*. The 25% of crystalline acyloin (IXa) and 63% yield of polymer suggests that for the most part the *cis–cis* ester underwent ring closure whereas the *cis–trans* ester underwent polymerization. Attempts to oxidize the polymer back to acid with periodic acid failed, which fact suggests that the polymer does not possess 1,2-ketol linkages.

The diketone VI was converted to 1,4-bis-(4-ethylphenyl)-butane (XIII), and the spectrum of the latter is taken as "normal" for comparison with that of the paracyclophane XI. The ultraviolet absorption spectra of XI and XIII are recorded in Fig. 1, and the small differences between these spectra point to the conclusion that small trans-annular electronic effects are operative in XI, comparable in magnitude to those found in I ($n = 3$, $m = 6$). The character of these effects will be discussed in a later paper.

The infrared spectrum of XI was taken and compared to that of XIII. The band at 10.88 μ (see Experimental) that is characteristic of the smaller paracyclophanes is very weak in the spectrum of XIII.

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(13) K. von Auwers, *Ann.*, **420**, 84 (1920).

(14) O. Miller, *Bull. soc. chim. Belg.*, **44**, 513 (1935).

Experimental

Melting points are corrected, boiling points are uncorrected. **1,4-Bis-(4-acetylphenyl)-butane** (V).—The reaction of the Grignard reagent prepared from γ-phenylpropyl bromide with benzonitrile furnished γ-phenylbutyrophenone, m.p. 52–54° (hexane,), yield 78%.[15] A modified[16] Wolff–Kishner reduction of this ketone gave 1,4-diphenylbutane in 91% yield after one crystallization from methanol, m.p. 46–48°, reported[17] m.p. 52°.

A mixture of 291 g. (2.20 moles) of aluminum chloride and 300 ml. of carbon disulfide was stirred at room temperature. Acetic anhydride, 107 g. (1.05 mole), was introduced during 15 minutes, and to the resulting mixture was added over a similar period 105 g. (0.500 mole) of 1,4-diphenylbutane in 300 ml. of carbon disulfide. The solvent was then immediately distilled by heating the mixture on a steam-bath, and the warm residue was decomposed by pouring it slowly with stirring onto a mixture of 150 ml. of concd. HCl and 1 kg. of ice. The flocculent solid was collected, dried, and the crude material was dissolved in 300 ml. of hot benzene, and the solution was filtered. Hexane, 100 ml., was added to the filtrate, and after cooling to 5° the product was collected (white needles), wt. 108.7 g. (74%), m.p. 109.5–110.2°. The melting point of this material was unchanged upon recrystallization.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.49; H, 7.79.

1,4-Bis-(4-thioacetomorpholidophenyl)-butane.—The diketone V was treated with sulfur and morpholine according to the modified Willgerodt procedure[7] to give virtually a quantitative conversion to the crude thiomorpholide (yellow solid), m.p. 163.5–164.5°. For analysis, the material was recrystallized seven times from acetone (white needles), m.p. 167.4–168.0°.

Anal. Calcd. for $C_{28}H_{36}O_2N_2S_2$: C, 67.70; H, 7.31. Found: C, 67.57; H, 7.59.

1,4-Bis-(4-carboxymethylphenyl)-butane.—Hydrolysis of the above thiomorpholide with ethanolic sodium hydroxide[7] gave the crude acid as a cream-colored powder, m.p. 212–215°. A small sample was crystallized from methanol three times to give a white microcrystalline powder, m.p. 213–215°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.80. Found: C, 73.60; H, 7.00.

1,4-Bis-(4-carbomethoxymethylphenyl)-butane (VII).—Esterification of the above acid with methanol and concentrated sulfuric acid gave the ester which was distilled to give a yellow solid, b.p. 239–242° (3 mm.). The crude material (41.4 g.) was heated under reflux in 150 ml. of methanol with 1 g. of Raney nickel for two hours, the nickel was removed by filtering the hot solution, and when cooled the solution deposited white plates, wt. 33.5 g. (56% over-all from V), m.p. 70.5–72°. For analysis, a small sample was recrystallized from methanol, m.p. 71.9–72.9°.

Anal. Calcd. for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.37; H, 7.37.

1,4-Bis-(4-carbomethoxymethylcyclohexyl)-butane (VIII).—The aromatic ester (VII), 32.7 g., was hydrogenated with 3 g. of PtO_2 in 250 ml. of (fractionally distilled) acetic acid at 25° and 1 atmosphere. The reaction stopped after 4.5 hours (100% of the theoretical amount of hydrogen had been absorbed). The catalyst was removed by filtration, the solvent was evaporated under vacuum, and the product was distilled to yield a colorless liquid, b.p. 232–234° (3.5 mm.), $n^{25}D$ 1.4781, wt. 32.8 g. The ultraviolet spectrum showed no absorption above 230 mμ.

Anal. Calcd. for $C_{22}H_{38}O_4$: C, 72.09; H, 10.45. Found: C, 72.35; H, 10.65.

1,4-Bis-(4-carboxymethylcyclohexyl)-butane.—Saponification of 0.50 g. of ester VIII with ethanolic potassium hydroxide gave 0.46 g. of the acid as a white powder, m.p. 146–154°. One crystallization of this material from 80% acetic acid gave irregular needles, m.p. 150–155°. Two further crystallizations did not change the melting point.

Anal. Calcd. for $C_{20}H_{34}O_4$: C, 70.97; H, 10.12. Found: C, 71.00; H, 9.92.

1,4-Bis-(4-*trans*-carbomethoxymethylcyclohexyl)-butane (VIIIa).—The mixture of isomeric esters VIII, 31.5 g., was diluted with 70 cc. of pure pentane and kept at −10° for four hours. The solution was filtered to give 3.61 g. of white crystals, m.p. 68–76°. This material was recrystallized to give 2.09 g. (6.6% based on VIII) of white plates, m.p. 80–81°. For analysis, a sample was recrystallized from pentane–acetone, m.p. 81.1–81.8°.

Anal. Calcd. for $C_{22}H_{38}O_4$: C, 72.09; H, 10.45. Found: C, 72.13; H, 10.62.

Distillation of the ester in the filtrate gave a mixture of *cis–cis* and *cis–trans* esters, $n^{25}D$ 1.4786. Attempts were made to separate these two esters by crystallization from various solvents at temperatures ranging from −10° to −50°, but neither isomer could be isolated in a pure state. Separation by chromatography on alumina also was unsuccessful.

1,4-Bis-(4-*trans*-carboxymethylcyclohexyl)-butane.—Saponification of a 0.67-g. sample of the crystalline ester with alcoholic potassium hydroxide gave 0.57 g. of the acid. One crystallization from acetic acid gave white plates, m.p, 216–218°.

Anal. Calcd. for $C_{20}H_{34}O_4$: C, 70.97; H, 10.12. Found: C, 70.83; H, 10.19.

2-Hydroxy-3-keto-*p,p'-cis–cis*-tetramethylene-1,4-dicyclohexylbutane (IX).—The acyloin reaction was carried out under high-dilution conditions using the apparatus previously described.[2a] The ester VIII, a mixture of *cis–cis* and *cis–trans* isomers, 105.5 g. (0.288 mole), in 900 ml. of xylene was added to a suspension of 29.2 g. (1.27 moles) of sodium in 1500 ml. of xylene during 74 hours. After an additional hour of heating and stirring the mixture was cooled to 0°, and excess acetic acid was added (dropwise) to decompose the sodium and salts. Sufficient water was added to dissolve the sodium acetate. The gelatinous polymer was filtered from the solution, and, after drying, it was obtained as a gray amorphous solid, 28.8 g. (32.7%), m.p. > 250°.

The xylene filtrate was separated from the aqueous phase, washed with water, with dilute sodium bicarbonate, and dried. Acidification of the bicarbonate extracts yielded 0.76 g. (0.9%) of a white solid, presumably the acid corresponding to the starting ester. The xylene solution was concentrated to a volume of 250 ml., and, after standing at 0° for 36 hours, the solution was filtered. There was thus obtained a portion of the crude acyloin as a colorless crystalline powder, m.p. 146.5–149°. The xylene was removed from the filtrate and the residue was distilled to yield an additional 22.2 g. of crude acyloin as a yellow solid, b.p. 200–210° (1 mm.). The polymeric still residue weighed 15 g.

The two portions of crude acyloin were systematically fractionally recrystallized (10 crystallizations) from benzene–hexane to give fairly pure acyloin, 16.63 g., m.p. 152.5–153.5°. The filtrates from the above crystallizations were combined and the solvent was removed. The remaining yellow solid (27 g.) was dissolved in 150 ml. of benzene–hexane, 1:3, and absorbed on a column of 250 g. of neutral alumina of activity II.[18] The column was developed with hexane, benzene, ether and methanol, in turn. A total of thirty-eight 250-ml. fractions were taken. Fractions 1 and 2 yielded 1.83 g. of an oil which was discarded, and fractions 3–28 gave a total of 16.11 g. of crude acyloin as yellow solids with similar melting points in the range of 130–140°. The remaining fractions yielded 0.32 g. of oil and 1.99 g. of polymer in that order.

The crude acyloin obtained by chromatography was crystallized four times from benzene–hexane to give 3.20 g. of acyloin, m.p. 152–153.5°. The filtrates were combined, the solvent was removed, and the residue was fractionally distilled through a two-foot column of the Podbielniak type at 3.0 mm. After an 0.08-g. forerun, b.p. 100–193°, there was obtained the crude diketone (XII), wt. 1.74 g., b.p. 193–195°, an intermediate fraction, 1.02 g., b.p. 195–208°, and crude acyloin, 3.08 g., b.p. 208–211°. The still residue, a colorless glass, weighed 3.3 g. The crude acyloin was twice recrystallized to give 1.81 g., m.p. 152.5–154°. The total yield of acyloin was 21.64 g. (24.6%). For analysis,

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(15) A. Orekhov and M. Tiffeneau [*Bull. soc. chim.*, **41**, 1174 (1927)] reported m.p. 57–58°.

(16) Huang-Minlon, This Journal, **68**, 2487 (1946).

(17) R. Kuhn and A. Wintersteiner, *Helv. Chim. Acta*, **11**, 123 (1928).

(18) H. Brockmann and H. Schodder, *Ber.*, **74B**, 73 (1941).

a sample of the acyloin was twice recrystallized, m.p. 154–155°.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.32; H, 10.91.

The infrared spectrum in nujol showed strong bands at 3.12 and 5.75 μ, which are characteristic of O—H and C=O stretching, respectively.[19]

The crude diketone was recrystallized five times from aqueous ethanol to yield 0.52 g. (0.61%) of brilliant yellow plates, m.p. 118.7–119.8°. The compound gave no color with ferric chloride. The ultraviolet spectrum in 95% ethanol showed the following maxima: λ_{max} 272.8 mμ, ε 43; λ_{max} 283.2 mμ, ε 44; λ_{max} 294.3 mμ, ε 36; λ_{max} 307 mμ, ε 23; λ shoulder 320 mμ, ε 10; λ_{max} 456 mμ, ε 34; λ shoulder 475 mμ, ε 29. After standing for two days, an originally intensely yellow ethanol solution of the compound became colorless. The colorless solution gave no ferric chloride test and showed no maximum above 210 mμ in the ultraviolet.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.60. Found: C, 79.03; H, 10.86.

The quinoxaline derivative was prepared by the method of Leonard and Mader.[8] Two crystallizations from aqueous ethanol gave fine white needles, m.p. 100.0–101.5°.

Anal. Calcd. for $C_{26}H_{36}N_2$: C, 82.92; H, 9.64. Found: C, 83.21; H, 9.42.

A similar acyloin reaction was run using 24.2 g. of mixed *cis–cis* and *cis–trans* esters VIII. The amount of xylene and the addition time were the same as in the previous case. The relative amounts of cyclic material and polymer formed were the same as previously.

***p,p'-cis–cis*-Tetramethylene-1,4-dicyclohexylbutane (X).**—This procedure was adapted from that already recorded for a similar case.[10] Activated zinc was prepared by swirling 98.6 g. (1.51 moles) of mossy zinc with 3 g. of $HgCl_2$ and 2 ml. of concd. HCl in 300 ml. of water for 5 minutes. The liquid was then decanted and the zinc was washed twice with water. To the zinc was then added 300 ml. of glacial acetic acid, 300 ml. of concd. HCl and 10.00 g. (0.0326 mole) of the *cis–cis* acyloin (IX). The mixture was heated under reflux for 42 hours, 40-ml. portions of concd. HCl being added at 12-hour intervals. The mixture was then cooled and poured into one liter of water. The hydrocarbon was extracted with pure pentane, and the extracts were washed and dried over magnesium sulfate. Evaporation of the pentane in vacuum left a white crystalline solid, m.p. 90.5–95°, 8.98 g. (100%). The infrared spectrum of this material in carbon tetrachloride showed a band of medium intensity at 10.21 μ. This material showed no reaction with bromine in CCl_4 nor with dilute potassium permanganate in acetone.

The crude hydrocarbon was dissolved in a mixture of 120 ml. of C.P. ethyl acetate and 20 ml. of pure acetic acid. Platinum oxide (300 mg.) was added to the solution, and hydrogenation was carried out at 25° and one atmosphere. Hydrogenation was complete in four hours; 0.20 equivalent of hydrogen was absorbed.

The catalyst was collected, and the filtrates were concentrated to a volume of 60 ml. The hot solution was then diluted with 75 ml. of ethanol, cooled to −10°, and the product was collected (white needles), wt. 7.16 g., m.p. 100.4–101.1°. An additional 0.65 g. of material having the same melting point was obtained from the filtrates. The total yield was 7.81 g. (87%).

Anal. Calcd. for $C_{20}H_{36}$: C, 86.87; H, 13.13. Found: C, 86.80; H, 13.27.

The infrared spectrum was taken in CCl_4 and showed no band at 10.21 μ.

***p,p'*-Tetramethylene-1,4-diphenylbutane (XI).**—The saturated hydrocarbon X, 1.90 g. (0.00688 mole), was heated in a small flask with 190 mg. of 10% palladium-on-charcoal. The evolution of hydrogen began at 230° and ceased at 315° after 2.5 hours. The hydrogen evolved amounted to 970 ml. (25°) or 96% of the theoretical amount. The crude product was dissolved in pure pentane, the solution was filtered free of catalyst, and the solvent was removed in vacuum. The remaining white crystalline solid weighed 1.71 g. (94%), m.p. 145.5–146.5°. For analysis, the material was recrystallized from ethanol, plates, m.p. 146.2–147.3°.

The infrared spectrum from 2 to 12 μ in carbon tetrachloride showed maxima at the following wave lengths: 3.31 μ (W), 3.40 μ (S), 5.28 μ (M), 5.59 μ (W), 6.16 μ (W), 6.59 μ (S), 6.90 μ (S), 7.04 μ (W), 7.34 μ (M), 7.78 μ (W), 8.28 μ (M), 8.60 μ (W), 9.05 μ (S), 9.73 μ (M), 10.56 μ (W), 10.90 μ (W). These data were obtained with a Beckman IR2T spectrophotometer, NaCl prism.

Anal. Calcd. for $C_{20}H_{24}$: mol. wt., 264.4; C, 90.85; H, 9.15. Found: mol. wt. (Rast), 241; C, 90.87; H, 9.20.

***p,p'*-Tetramethylene-*cis–cis*-1,4-dicyclohexylbutane (X).**—The paracyclophane XI, 260 mg. (0.00098 mole) (slightly impure, m.p. 144.8–145.9°), was quantitatively hydrogenated at 25° with platinum in acetic acid, 95% of the theoretical amount of hydrogen being taken up. The solution was filtered free of catalyst. Water was added to the warm solution, and the product that crystallized upon cooling amounted to 230 mg. (91%), m.p. 98.5–99.2°. Recrystallization of this material from ethanol gave needles, m.p. 100.2–101.4°. A sample of the hydrocarbon X obtained from the Clemmensen reduction had m.p. 100.0–101.0°, and gave with the above material a mixed melting point of 100.0–101.5°.

1,4-Bis-(4-*cis*-carboxymethylcyclohexyl)-butane.—The acyloin IX, 380 mg. (0.00124 mole), was dissolved in 35 ml. of absolute dioxane. To this solution was then added 425 mg. (0.00186 mole) of paraperiodic acid in 5 ml. of water.[20] The solution was allowed to stand under nitrogen for 42 hours, and was poured into water. The product was extracted with ether, and the extracts were washed free of dioxane and dried. The ether was evaporated, and the residual oil was suspended in 50 ml. of water. Potassium hydroxide, 86 mg. (0.0015 mole), and potassium permanganate, 119 mg. (0.00075 mole), were added, and the mixture was shaken for 10 minutes. The mixture was then acidified, and sodium bisulfite was added to destroy the manganese dioxide. The product was collected and crystallized from 50% acetic acid to yield white plates, 302 mg. (72%), m.p. 168.5–171.5°. For analysis, a sample was recrystallized three times, m.p. 170–172°.

Anal. Calcd. for $C_{20}H_{34}O_4$: C, 70.97; H, 10.12. Found: C, 70.93; H, 10.15.

The dimethyl ester, prepared in 80% yield by Fisher esterification and crystallized from pentane at −80°, had m.p. 32–33°.

Anal. Calcd. for $C_{22}H_{38}O_4$: C, 72.09; H, 10.45. Found: C, 71.82; H, 10.24.

A similar oxidation experiment when carried out on a solution of polymer in ethanol or acetic acid gave back polymer unchanged.

***p,p'-trans–trans*-Tetramethylene-1,4-dicyclohexylbutane (Attempted Synthesis).**—The acyloin reaction was carried out in a manner similar to that described for the other isomers using 6.42 g. of the *trans–trans* ester VIIIA. After decomposition of the reaction mixture with acetic acid and water, the mixture was filtered to yield 2.48 g. of a white solid, m.p. 195–230° dec. This material was largely soluble in dilute alkali and appeared to consist principally of the acid corresponding to the starting ester.

The xylene layer after washing and drying was concentrated to a volume of 40 ml. and allowed to stand at −10° for 12 hours. The solid was collected to give 1.17 g. of a white powder, m.p. 140–160°. This material gave a positive acyloin test.[9] Recrystallization of this material from ethanol gave a sticky yellow solid, 0.30 g., m.p. 130–150°, positive acyloin test. This material was used in the next step without further purification. From the filtrate was obtained by dilution with water 0.80 g. of a white powder, m.p. 163–183°, negative acyloin test. Removal of the solvent from the original xylene filtrate and distillation of the residue gave 0.34 g. with a bath temperature of 135–215° (3 mm.) and 0.61 g. with a bath temperature of 245–300° (1 mm.). These fractions gave negative acyloin tests.

The fraction which gave the positive acyloin test, 0.30 g., m.p. 130–150°, was subjected to a Clemmensen reduction as described for the other isomer. The product of the reaction, obtained in virtually quantitative yield, was an amorphous brown solid, insoluble in organic solvents. It did not melt below 250°.

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(19) A. T. Blomquist and L. H. Liu, THIS JOURNAL, **75**, 2153 (1953).

(20) J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **23**, 1114 (1940).

1,4-Bis-(4-ethylphenyl)-butane (XIII).—The diketone (VI), 3.7 g., was converted to the hydrocarbon by a modified Wolff–Kishner reduction.[16] The reaction mixture was diluted with water and the product was extracted with ether. Filtration of the ether phase gave 0.65 g. of a yellow solid which was not investigated. The filtrates were washed and dried, and the ether was evaporated in vacuum. The residual oil was taken up in pentane and chromatographed on 100 g. of neutral alumina of activity II.[18] The white solid obtained from the first 100 ml. of eluate was crystallized from acetone–methanol at −80° to yield white plates, 1.45 g. (43%), m.p. 26.2–26.8°.

Anal. Calcd. for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 89.92; H, 9.55.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

The Configurations of 2,6-Bis-(iodomethyl)-*p*-dioxanes and 2,6-*p*-Dioxanedicarboxylic Acids. The Structure of Diepiiodohydrin

BY R. K. SUMMERBELL AND JAMES R. STEPHENS

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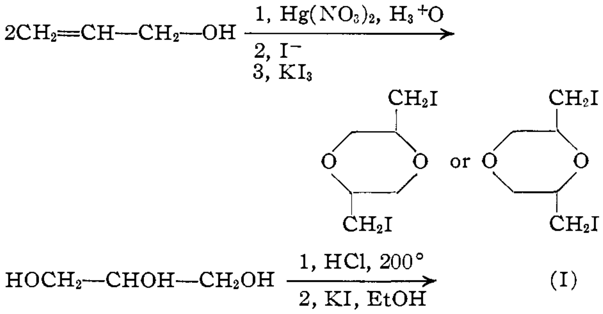
The known and a new form of 2,6-bis-(iodomethyl)-*p*-dioxane have been prepared. Their structure has been shown by oxidizing them to the corresponding 2,6-*p*-dioxanedicarboxylic acids, and the interconversion of these acids. The configurations of the compounds are indicated by the conversion of only one of the iodides to morpholine derivatives, and the hydrolysis of a monomeric acid anhydride to form one of these acids. This work constitutes the first proof of the configuration of a polysubstituted dioxane. Diepiiodohydrin has long been assigned the ambiguous structure of 2,5- or 2,6-bis-(iodomethyl)-*p*-dioxane, but since only *cis*- and *trans*-2,6-bis-(iodomethyl)-*p*-dioxanes can exist, the isomeric diepiiodohydrin must be 2,5-bis-(iodomethyl)-*p*-dioxane. The polar-equatorial substitution concept which has previously been used to explain physical properties of the *cis* and *trans* forms of disubstituted cyclohexanes seems to be applicable to the 2,6-disubstituted-*p*-dioxanes.

Previous investigators[1] who have prepared diepiiodohydrin (I) have postulated its structure as a bis-(iodomethyl)-*p*-dioxane. This has been shown to be correct by Burlingame[2] who obtained the same di-*n*-butyl-*p*-dioxane from the appropriate alkylation of either diepiiodohydrin or a dichloro-*p*-dioxane. The methods employed for the production of diepiiodohydrin (see below)

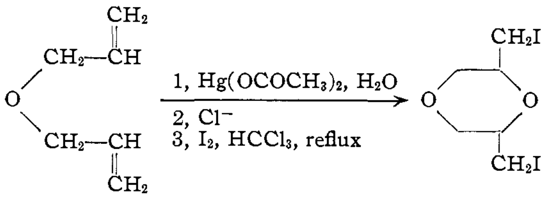


(I)

eliminate the 2,3-bis-(iodomethyl)-*p*-dioxane structure from consideration but do not permit a choice between the 2,5- or the 2,6-bis-(iodomethyl)-*p*-dioxane structure for I.

Additional but inconclusive evidence concerning diepiiodohydrin's structure was provided in 1943 by Nesmeyanov and Lutsenko[3] who cyclized allyl ether by the action of aqueous mercuric acetate to produce a dimercury derivative which could be precipitated as the chloride and then iodinated to a cyclic ether II, an isomer of I, to which they assigned the structure of 2,6-bis-(iodomethyl)-*p*-dioxane. II was not shown to be a *p*-dioxane derivative but postulated to have this structure from the method of synthesis. Even if II is proved to be 2,6-bis-(iodomethyl)-*p*-dioxane, diepiiodohydrin may have the same structure since the 2,6-derivative can exist as either the *cis* or the *trans* isomer.

We have repeated the work of Nesmeyanov and Lutsenko, and in addition to obtaining their product we have succeeded in isolating a new isomer III. If II and III are *p*-dioxanes the iodomethyl groups must be substituted in the 2,6-positions since the starting material of the synthesis was allyl ether.



II and III

Diepiiodohydrin would then be assigned the 2,5-bis-(iodomethyl)-*p*-dioxane structure.

Infrared absorption curves of II and III in chloroform solution indicated them to be different chemical entities rather than dimorphic forms of the same compound.

The *p*-dioxane structures of II and III were shown by converting them to the acids IV and V, respectively, by the action of hot concentrated nitric acid. In addition IV and V were converted to the dimethyl esters VI and VII, respectively, by reaction with diazomethane. Formation of the diesters, neutral equivalents, analysis and molecular weights indicated dicarboxylic acid structures for IV and V. The formation of these dicarboxylic acids was significant as it eliminated the possibility that either II or III could be the seven-membered ring compound 2-iodomethyl-6-iodo-1,4-dioxocycloheptane, since such a compound would be expected to lose a carbon atom on oxidation to a dicarboxylic acid. Stability of IV and

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[1] (a) C. Stoehr, *J. prakt. Chem.*, [2] **55**, 78 (1897), see also M. Fauconnier and J. Sanson, *Bull. soc. chim.*, [2] **48**, 237 (1887); (b) E. Biilman, *Ber.*, **33**, 1644 (1900), and J. Sand, *ibid.*, **34**, 1394 (1901).

[2] A. L. Burlingame, Ph.D. Dissertation, Northwestern University, 1950.

[3] A. N. Nesmeyanov and I. F. Lutsenko, *Bull. acad. sci. U.R.S.S., Classe sci. chim.*, 296–304 (1943).