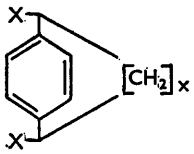
422. *The Preparation of Some* para-*Bridged Benzene Derivatives.*

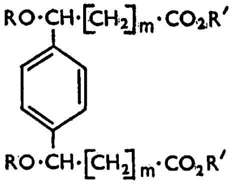
By K. Jasper Clark.

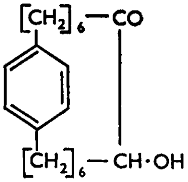
p-Tetradecamethylenebenzene has been prepared by the intramolecular condensation of *p*-di-(6-methoxycarbonylhexyl)benzene, and reduction of the resultant acyloin. Dibromination of the hydrocarbon, on the $\alpha\alpha'$-carbon atoms, was effected with *N*-bromosuccinimide, and the product converted into the $\alpha\alpha'$-diethoxy-derivative. An oxindolyl derivative of *p*-tridecamethylenebenzene is probably produced on interaction of *p*-(7-hydroxy-8-oxotetradecamethylene)benzene with phenylhydrazine. Attempts to cyclise *p*-di-(3-oxo-6-methoxycarbonylhexyl)benzene, and to prepare the *p*-nonamethylenebenzene system, failed.

It was desired to prepare compounds of type (I) with the immediate object of replacing the groups X by a second, linking alkylene chain and the ultimate object of preparing "interlocking" molecules.[1] From Catalan models it appeared that the encircling *cyclo*-alkane ring must contain at least 18 methylene groups.

Attempts to prepare dihydroxy-acids (II; $R = H$), where $m > 2$, or their diketo-analogues, for acyloin condensation and reduction, failed. The products from terephthaloyl dichloride and substituted malonic acids [2] gave poor results on hydrolysis; and the products from diethyl disodioterephthaloyldiacetate and aliphatic ω-halogeno-esters gave mainly terephthalic acid on hydrolysis.


(I)


(II)


(III)

Acyloin condensations of *p*-di-(ω-alkoxycarbonylalkyl)benzenes and subsequent reduction have recently given good yields of *p*-decamethylene-[3] and *p*-dodecamethylenebenzene,[4] and such compounds might be reactive at the α-positions. Three parallel cases have now been investigated.

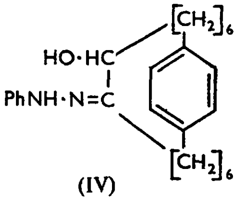
Condensation of *p*-xylylene dibromide and dihydroresorcinol, and hydrolysis of the product, gave *p*-di-(6-carboxy-3-oxohexyl)benzene, but the derived dimethyl ester gave polymers on attempted acyloin condensation, probably because of reaction of the $CO{\cdot}CH_2$ groups with the sodium used as condensing agent. However, Wolff–Kishner reduction of the diketo-acid gave *p*-di-(6-carboxyhexyl)benzene, and the derived ester was cyclised in good yield to the acyloin (III). This had the expected infrared absorption bands at 5·86 (CO) and 2·84 μ (OH) in Nujol mull, although it did not react with acetic anhydride, benzoyl chloride, aniline, or *o*-phenylenediamine, and with hydrazine gave a red oil. Clemmensen reduction then gave *p*-tetradecamethylenebenzene (I; $x = 12$, $X = H$), which with molecular bromine gave a gum but with *N*-bromosuccinimide gave a crystalline dibromo-derivative. The bromine atoms are labile towards sodium ethoxide, alcoholic potassium hydroxide, and pyridine, indicating their attachment to the aliphatic chain; and since *N*-bromosuccinimide normally attacks the α-position of aralkyl compounds, the

---

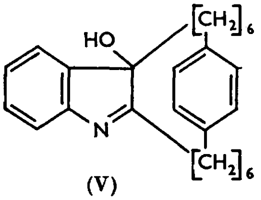
[1] Cf. Clark, *J.*, 1956 1511; 1957, 463.
[2] Parkes and Clark, *J.*, 1955, 3294.
[3] Wiesner, MacDonald, Ingraham, and Kelly, *Canad. J. Res.*, 1950, **28**, *B*, 561.
[4] Cram, Allinger, and Steinberg, *J. Amer. Chem. Soc.*, 1954, **76**, 6132.

dibromo-derivative probably has structure (I; x = 12, X = Br). However, the dibromo-compound failed to react with sodiomalonic ester or potassium cyanide, and with potassium acetate in acetic acid gave only an impure acetoxy-derivative.

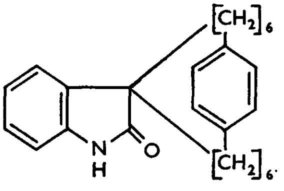
The acyloin (III) with phenylhydrazine in boiling aqueous acetic acid gave a chemically nert compound, $C_{26}H_{33}ON$, formally derived from 1 mol. of each reactant by loss of NH_4OH. This product has infrared absorption bands at 6·1 (CO·NH) and 3·01 μ (NH), and ultraviolet absorption maxima at 3150 (ε 10,400) and 2350 Å (ε 7000). It is suggested that this compound is the spiran (VI), that the phenylhydrazone (IV) first formed undergoes a Fischer reaction, giving the indole (V), which suffers Wagner–Meerwein rearrangement.



(IV)



(V)



(VI)

In a third reaction series, Friedel–Crafts reaction of δ-ethoxycarbonylvaleroyl chloride and ethyl β-phenylpropionate and Wolff–Kishner reduction of the product gave 6-(*p*-2′-carboxyethylphenyl)hexanoic acid: the orientation of this was proved by oxidation of its methyl ester to terephthalic acid, but this ester was recovered unchanged after attempted acyloin condensation.

EXPERIMENTAL

p-*Di*-(2 : 6-*dioxo*cyclo*hexylmethyl*)*benzene*.—Stetter and Dierich's method [5] was modified as follows. Dihydroresorcinol (153 g.) and *p*-xylylene dibromide (90 g.) were stirred with a solution of potassium hydroxide (38 g.) in water (153 ml.) and ethanol (30 ml.) for 6 hr. on a boiling-water bath, then ethanol (1 l.) was added, and the mixture filtered hot at the pump. Washing with boiling ethanol gave a solid (70 g., 63%), insoluble in almost all organic solvents tried, but crystallising from dimethylformamide (Found: C, 73·3; H, 6·6. Calc. for $C_{20}H_{22}O_4$: C, 73·6; H, 6·7%); the crude solid charred at 150° and was pure enough for further reaction.

p-*Di*-(6-*carboxy*-3-*oxohexyl*)*benzene*.—*p*-Di-(2 : 6-dioxo*cyclo*hexylmethyl)benzene (43·75 g.) was refluxed with 10% sodium hydroxide solution (450 ml.) for 30 hr., then diluted with water (450 ml.) and acidified to Congo-red with concentrated hydrochloric acid. The precipitated acid, crystallised from a large volume of water, had m. p. 157° (38·85 g., 80%). The *diethyl*, m. p. 49·5—50·5° (from light petroleum, b. p. 60—80°) (Found: C, 68·7; H, 8·4. $C_{24}H_{34}O_6$ requires C, 68·9; H, 8·1%), and *dimethyl ester*, m. p. 72·5° (from methanol) (Found: C, 67·0; H, 8·0. $C_{22}H_{30}O_6$ requires C, 66·7; H, 7·9%), were prepared by use of sulphuric acid as catalyst.

Adding the dimethyl ester (10 g.) in xylene (300 ml.) during 30 hr. to sodium dust (11 g.) in xylene (1·5 l.), at 115° in nitrogen, gave unchanged ester (1·1 g.) and insoluble polymer (8·4 g.).

p-*Di*-(6-*carboxyhexyl*)*benzene*.—It was not possible to prepare this acid by combined hydrolysis and reduction of *p*-di-(2 : 6-dioxo*cyclo*hexylmethyl)benzene.[5] *p*-Di-(6-carboxy-3-oxohexyl)benzene (111 g.), 100% hydrazine hydrate (90 ml.), and potassium hydroxide (120 g.) were heated in ethylene glycol (1 l.) on the water-bath for 2 hr., then slowly to the b. p. while water and excess of hydrazine distilled off. After 14 hours' refluxing, cooling, and dilution with water (2 l.), acidification with concentrated hydrochloric acid to Congo-red gave crystals, m. p. 155—156° (from ethanol) (75 g., 73%). The *diethyl*, m. p. 24°, b. p. 230—240°/0·1 mm. (Found: C, 73·7; H, 9·7. $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·7%), and *dimethyl ester*, m. p. 36·5°, b. p. 220°/0·14 mm. (Found: C, 72·9; H, 9·3. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·4%), were obtained as above.

p-(7-*Hydroxy*-8-*oxotetradecamethylene*)*benzene*.—The apparatus was essentially that described

---

[5] Stetter and Dierichs, *Chem. Ber.*, 1953, **86**, 693.

by Prelog *et al.*[6] I am indebted to Dr. R. B. Kelly[3] for further working details. The apparatus was dried for 24 hr. before use. From a mixture of sodium (11 g.) and sulphur-free xylene (1·5 l.; distilled from sodium), approx. 100 ml. of xylene were distilled; very fast stirring created a fine dust or emulsion of sodium in the boiling xylene. At 115—120°, with rapid stirring and under nitrogen, *p*-di-(6-methoxycarbonylhexyl)benzene (43·7 g.) was injected during 15—24 hr. The mixture was finally stirred for 2 hr. in nitrogen at 115°, then cooled to 0°. The temperature was kept below 30° while methanol (200 ml.) and then 20% sulphuric acid (300 ml.) were added. The xylene layer was washed with water (2 × 100 ml.), 10% sodium carbonate solution (2 × 200 ml.), and water (200 ml.), and dried (Na_2SO_4). On distillation in nitrogen yellow crystals of p-(7-*hydroxy*-8-*oxotetradecamethylene*)*benzene* (28·2 g., 79%) remained, smelling of musk. Distillation at 165—168°/0·1 mm. gave 25·55 g. (70%) of a light yellow solid which on further distillation had m. p. 67·8° (Found: C, 79·5; H, 10·1. $C_{20}H_{30}O_2$ requires C, 79·5; H, 9·9%).

p-*Tridecamethylenebenzene*-7′-spiro-3-*oxindole* (VI).—*p*-(7-Hydroxy-8-oxotetradecamethylene)benzene (1 g.) was refluxed with water (8 ml.), phenylhydrazine (5 ml.), and acetic acid (25 ml.) for 24 hr. The organic layer solidified. Pouring the whole into water gave the *spiran* (0·45 g.), m. p. 198° (from acetic acid) (Found: C, 83·3; H, 8·7; N, 3·6. $C_{26}H_{33}ON$ requires C, 83·2; H, 8·8; N, 3·7%). This product was inactive towards alcoholic potassium hydroxide, acetic anhydride, bromine in acetic acid, concentrated hydrochloric acid, and lithium aluminium hydride in ether. In concentrated sulphuric acid it gave a red solution.

p-*Tetradecamethylenebenzene*.—Amalgamated zinc wool (32 g.) and *p*-(7-hydroxy-8-oxotetradecamethylene)benzene (18 g.) in acetic acid (32 ml.) were refluxed for 24 hr., concentrated hydrochloric acid (5 × 32 ml.) being added at intervals during the first 12 hr. Dilution with water, extraction with ether, and washing with 10% sodium carbonate solution and water, drying (Na_2SO_4), evaporation, and distillation gave p-*tetradecamethylenebenzene*, (14·6 g., 90%), b. p. 120—125°/0·035—0·07 mm. (Found: C, 88·3; H, 11·8. $C_{20}H_{32}$ requires C, 88·2; H, 11·8%).

p-(1 : 14-*Dibromotetradecamethylene*)*benzene*.—*p*-Tetradecamethylenebenzene (8·4 g.) and *N*-bromosuccinimide (11 g.) with benzoyl peroxide (0·05 g.) in carbon tetrachloride (200 ml.) reacted vigorously at 100°. After refluxing for 1 hr. the mixture was filtered hot, then evaporated *in vacuo*, and the residual solid crystallised from acetone to yield p-(1 : 14-*dibromotetradecamethylene*)*benzene*, m. p. 163° (8 g.). More material (1·7 g.) was isolated by concentration of the mother-liquor. The dibromo-compound crystallised from acetone (Found: C, 56·0; H, 7·0; Br, 37·1. $C_{20}H_{30}Br_2$ requires C, 55·8; H, 7·0; Br, 37·2%). Crystallisation from alcohol lowered the yield because of formation of the ethoxy-compound.

Potassium acetate in glacial acetic acid gave an oil which could be distilled but did not give a good analysis for diacetoxy-compound despite indication of the presence of acetoxy-groups in the infrared spectrum.

p-(1 : 14-*Diethoxytetradecamethylene*)*benzene*.—To sodium (0·63 g.) in absolute alcohol (35 ml.) was added the preceding dibromo-compound (5·9 g.) in one portion. The solution was refluxed for 2 hr., cooled, and poured into dilute hydrochloric acid. The product was extracted with ether, washed with sodium carbonate solution, dried, and recovered. The *diethoxy-compound* distilled at 170°/0·03 mm. (Found: C, 80·3; H, 10·9. $C_{24}H_{40}O_2$ requires C, 80·0; H, 11·1%).

6-(p-2′-*Carboxyethylphenyl*)-2-*oxohexanoic Acid*.—Ethyl β-phenylpropionate (101 g.) was stirred with δ-ethoxycarbonylvaleryl chloride (135·5 g.) in carbon disulphide (1·2 l.). The solution was cooled to −10°, and anhydrous aluminium chloride (280 g.) added during 1 hr. After 5 hours' stirring at 0° and 18 hours' refluxing, ice and dilute hydrochloric acid were added and the organic layer separated and, with ethereal extracts of the aqueous layer, washed with water and dried (Na_2SO_4). The oil remaining on removal of the solvent was refluxed with 10% alcoholic potassium hydroxide (1·4 l.) for 3 hr. The alcohol was removed, water (1 l.) added, and the solution acidified to Congo-red with concentrated hydrochloric acid at <10°. After 1 hr. at <10° the precipitated *acid* was filtered off, washed with a little water, and crystallised from hot water (yield, 105 g., 65%). Recrystallised several times from water it had m. p. 168·5° (Found: C, 64·3; H, 6·7. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%). The *methyl*, m. p. 37°, b. p. 180—190°/0·05 mm. (Found: C, 66·9; H, 7·1. $C_{17}H_{22}O_5$ requires C,

---

[6] Prelog, Frenkiel, Kobelt, and Barman, *Helv. Chim. Acta*, 1947, **30**, 1741.

66·7; H, 7·2%), and *ethyl ester*, m. p. 43°, b. p. 190—200°/0·05 mm. (Found: C, 68·7; H, 7·9. $C_{19}H_{28}O_5$ requires C, 68·3; H, 7·8%), were prepared as above.

6-(p-2′-*Carboxyethylphenyl*)*hexanoic Acid*.—The preceding acid (100 g.) was heated in ethylene glycol (350 ml.) with 100% hydrazine hydrate (45 g.) and potassium hydroxide (90 g.) on a water-bath for 4 hr., the temperature raised slowly to the b. p., and refluxing continued for 12 hr. The mixture was cooled, diluted with water (250 ml.), and acidified to Congo-red as usual. The precipitated *acid* was kept at 10° for 1 hr., filtered off, and crystallised from a large volume of water (yield, 71·6 g., 75%). After repeated recrystallisation from water it had m. p. 126·5° (Found: C, 67·9; H, 7·8. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%). The *methyl*, m. p. 27°, b. p. 150—160°/0·06—0·09 mm. (Found: C, 69·5; H, 8·0. $C_{17}H_{24}O_4$ requires C, 69·8; H, 8·3%), and *ethyl ester*, b. p. 165—170°/0·03 mm. (Found: C, 71·4; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·7%), were prepared as above. The former with potassium permanganate gave terephthalic acid (dimethyl ester, m. p. 142°).

The author is indebted to Mr. F. Hall for some analyses and to Sir Robert Robinson, O.M., and Dr. G. D. Parkes for their interest and advice.

Dyson Perrins Laboratory, Oxford. [*Received, November* 1*st*, 1956.]