STUDIES OF CYCLIC HYDROCARBONS.

By

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ABSTRACT.

This thesis is presented in three sections.

Section I deals with the synthesis of *spiro*-hydrocarbons. The two compounds *spiro*(5:2)octane and *spiro*(4:2)heptane were prepared; the latter compound has not previously been described. It was not found possible to synthesise a series of *spiro*-compounds containing varying numbers of *cyclo*butane rings, because of the failure to isolate pure intermediate products.

Section II describes the formation of *o*-xylene through 4:5-dimethylene*cyclo*hexene. The scheme to prepare this *cyclo*hexene involved the Hofmann degradation of the quaternary ammonium hydroxide derived from *cis*-4:5-*bis*(dimethylaminomethyl)*cyclo*hexene dimethiodide. 4:5-Dimethylene*cyclo*hexene was not isolated, but a sample of *o*-xylene was obtained which was identified by the preparation of its sulphonamide.

Section III is subdivided into three parts.

Part 1 deals with the study of the anomalous reductions of 2:2'-diacetyldiphenyl under different conditions. The reductions were carried out in an attempt to devise a scheme for the preparation of 2:2'-dialkyldiphenyls. The Clemmensen reduction yielded 9:10-dimethylphenanthrene; the products isolated from the Huang Minlon reduction on the same diketone were an unsaturated hydrocarbon $C_{16}H_{14}$, and 9:10-dimethylphenanthrene. The course of this reaction is studied in detail.

No pure compounds were isolated from the product of the Meerwein-Ponndorf-Verley reaction, but the reduction with lithium aluminium hydride gave the expected carbinol.

Part 2 is devoted to the condensation reactions of 2:2'-bis(bromomethyl)diphenyl with 1:1:2:2-tetracarbethoxyethane, 1:1:3:3-tetracarbethoxypropane, and diethyl methylmalonate. The reaction with 1:1:3:3-tetracarbethoxypropane and the dibromide produced a compound which was not identified, but possible structures are proposed. The condensation reaction with diethyl methylmalonate gave the expected product, which led to the preparation of several new compounds.

Part 3 describes several methods of preparation of 2:2'-diphenyl diacetic acid, which is considered to be a suitable starting compound in the syntheses of some large-membered ring compounds of diphenyl.

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Section I

The syntheses of spiro-hydrocarbons.

Introduction.

Cyclohexane was the first member in the series of alicyclic compounds to be prepared and studied. As recently as 1880, it was generally accepted that only rings containing six carbon atoms existed (V. Meyer, Annalen., 1876, 180, 192), and all attempts to synthesise smaller rings had been fruitless. In the early 1880's, W.H. Perkin began his classical investigations which changed the ideas of many eminent contemporary chemists on ring compounds, and laid the foundations of modern alicyclic chemistry (Pedler Lecture, J., 1929, 1347). The first alicyclic compound to be prepared by Perkin was cyclobutane 1:1-dicarboxylic acid (Ber., 1883, 16, 1793), and a little later three- and five-membered systems were obtained. Cyclo-butane and cyclopropane-1:3-dicarboxylic acid had been previously prepared but not recognised (Markovnikov and Krestnovnikov, Annalen., 1881, 208, 333; Freund, Monatsh., 1882, 3, 626).

The existence of three- and four-membered rings called for a revision in ideas on the stereochemistry of the carbon atom, and an explanation was required for the variations in the stability of the different ring systems.

A. von Baeyer (Ber., 1885, 18, 2277; 1890, 23, 1275), introduced the Strain Theory (Spannungtheorie) which employed the Le Bel-van't Hoff tetrahedral model of the carbon valencies (1874), and postulated that the carbon atoms in any alicyclic ring were uniplanar. This made it necessary for the bond angles to be capable of alteration, thus setting up a condition of strain in the ring. Baeyer calculated the strain and assumed that it was a rough measure of the instability of the various rings, but had few facts with which to test this hypothesis since the hydrocarbons cyclobutane and cyclopentane had not then been synthesised.

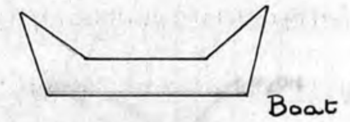
Number of carbon atoms in ring.	3	4	5	6
Calculated deflection from normal valency angle.	$+24^{\circ}44'$	$+9^{\circ}44'$	$0^{\circ}44'$	$-5^{\circ}16'$

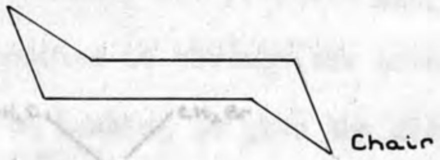
Perkin exploited the use of diethyl malonate to synthesise some four-, five-, and six-membered rings, and found that the yields corresponded approximately to predictions based on the assumption that the tendency for ring formation is governed by the degree of strain it possesses, i.e. $C_5 > C_6 > C_4 > C_3$.

The Baeyer theory proved fairly satisfactory for rings smaller than cyclohexane, but broke down completely when applied to macrocyclic systems.

In 1918, Mohr (J.pr. Chem., 1918, (ii), 98, 349; 1922, (ii), 103, 316) revived and elaborated a theory introduced by Sachse in 1890, that not all alicyclic rings are coplanar, but from cyclohexane upwards, puckered, multiplanar configurations may be formed involving little or no deflection of the tetrahedral valency angles. It has since been shown by Ruzicka, Ziegler, Huckel, and many others (Ruzicka, Chemistry and Industry, 1935, 54, 2) that there are no theoretical barriers for the existence of macrocyclic rings.

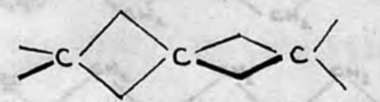
In cyclohexane, for example, two strainless configurations can be visualised,

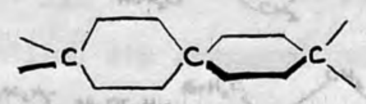




All the experimental evidence, however, actually indicates that practically all cyclohexane molecules correspond to the chair form, both in the vapour and in the liquid phase (Hassel, Quart. Reviews., 1953, VII, 221). It has been calculated that the thermal energy is sufficient to cause facile interconversion between the boat and chair forms. (Shoppee, J., 1946, 1138; Barton, ibid., 1948, 340; Hazelbrock and Oosterhoff, Discuss. Faraday Soc., 1951, 10, 87.).

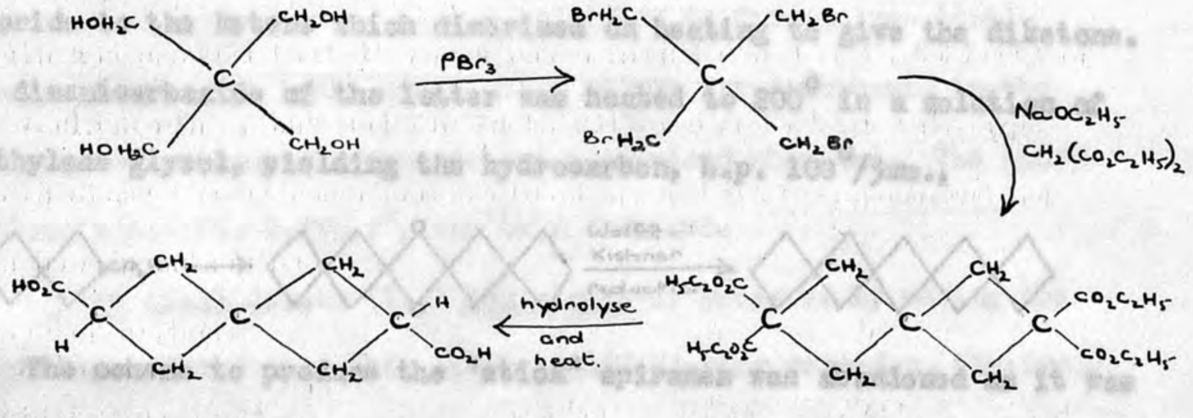
In 1875, van't Hoff pointed out that an allene of the formula ${}^{a}_{b}\!>\!C=C=C\!<\!{}^{c}_{d}$ should be capable of existing in two optically isomeric forms, assuming that the carbon atoms possess tetrahedral configurations. It was later realised that it is not necessary for four different groups to be present, but that ${}^{a}_{b}\!>\!C=C=C\!<\!{}^{a}_{b}$ should similarly exist as two isomers. Just as the hydrocarbon ethylene $H_2C=CH_2$ may be regarded as the first in the series of alicyclic compounds, so allene which contains two such simple rings, may be regarded as the first of a large number of spiro-compounds with a greater number of carbon atoms in these rings. e.g.





The models of these molecules show that the planes of the rings are perpendicular to each other.

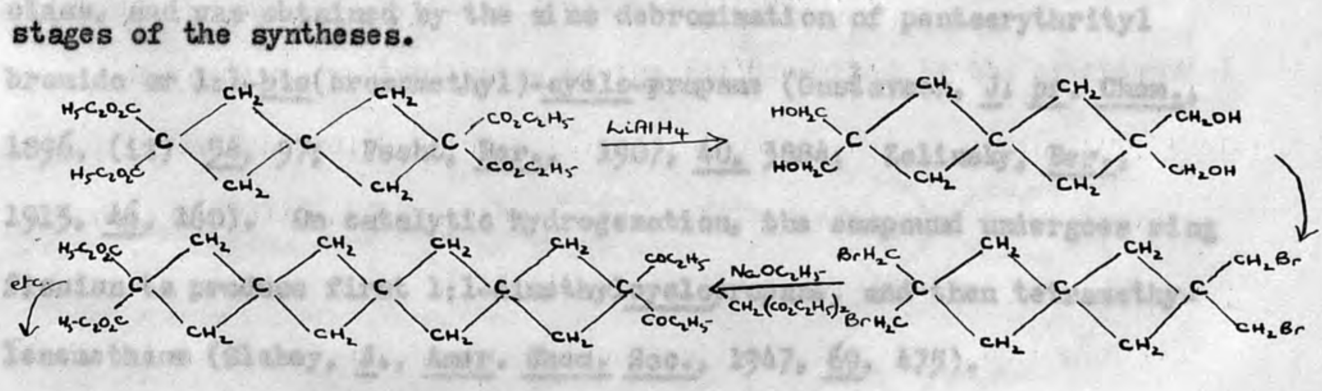
In the ring closure reactions with diethyl malonate which make use of the active methylene group, the preparation of the resolvable spiro-(3:3)-heptane dicarboxylic acid is of particular interest. This acid was first synthesised by Fecht (Ber., 1907, 40, 3883), by the following method,



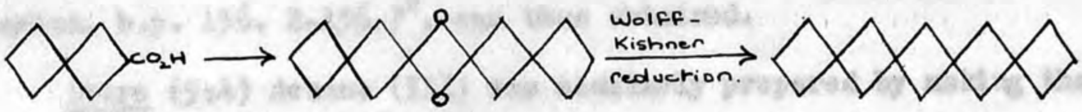
and was later resolved by Backer and Schurink (Rec. Trav. chim., 1931, 50, 921).

The object of starting the work in this section was to synthesise a series of "stick" spiranes of the type

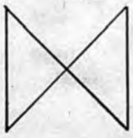
with varying numbers of four-membered rings, and to investigate the optical properties of their derivatives. The simple Perkin ring closure reaction with dihalides and diethyl malonate was to be used in several stages of the syntheses.



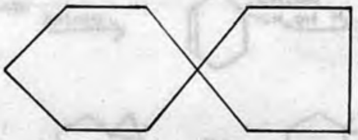
One such compound, tetraspirohexadecane, has been recorded; this was synthesised by Buchman and Madoff (California Institute of Technology, Private Communication, Institute of Petroleum), who prepared spiro (3:3) heptane-2-carboxylic acid and converted it through the acid chloride to the ketene which dimerised on heating to give the diketone. The disemicarbazide of the latter was heated to 200° in a solution of diethylene glycol, yielding the hydrocarbon, b.p. 100°/3mm.,



The scheme to produce the "stick" spiranes was abandoned as it was not possible to isolate pure products in the early stages of the syntheses (see p.11-13). Attention was then given to the synthesis of simpler spiranes, few of which have been prepared; of the simple ones based on the allene structure only the following are known.


I


II


III

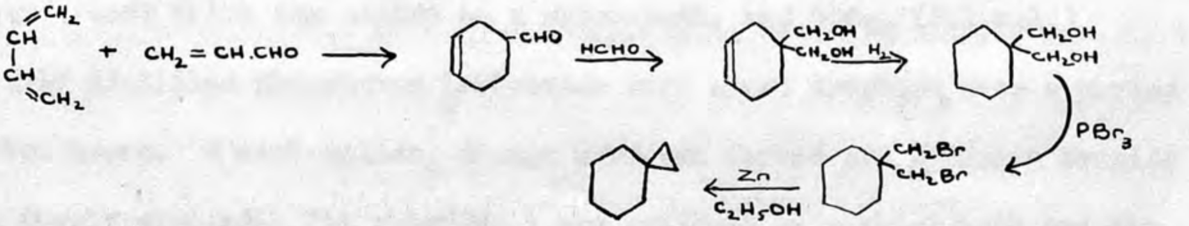

IV

Spiro (2:2) pentane (I) is the simplest representative of the spirane class, and was obtained by the zinc debromination of pentaerythrityl bromide or 1:1-bis(bromomethyl)-cyclo-propane (Gustavson, J. pr. Chem., 1896, (ii) 54, 97; Fecht, Ber., 1907, 40, 3884; Zelinsky, Ber., 1913, 46, 160). On catalytic hydrogenation, the compound undergoes ring fission to produce first 1:1-dimethylcyclopropane, and then tetramethylenemethane (Slabey, J., Amer. Chem. Soc., 1947, 69, 475).

Spiro (4:4) nonane (II) has been prepared by Zelinsky and Elagina (Compt. rend. Acad. Sci. U.R.S.S. 1945, 49,568). These workers started by reducing cyclopentanone to 1:1'-dihydroxy-1:1'-dicyclopentyl and treating this with dilute sulphuric acid to give spiro (4:5) decane-6-one. This spiro-ketone was oxidised with nitric acid, and the product was heated in the presence of barium hydroxide to form spiro- (4:4)-nonane-1-one. The hydrazone of this ketone was decomposed in the presence of potassium hydroxide and platinised charcoal. The hydrocarbon, b.p. 156. 2-156.7°, was thus obtained.

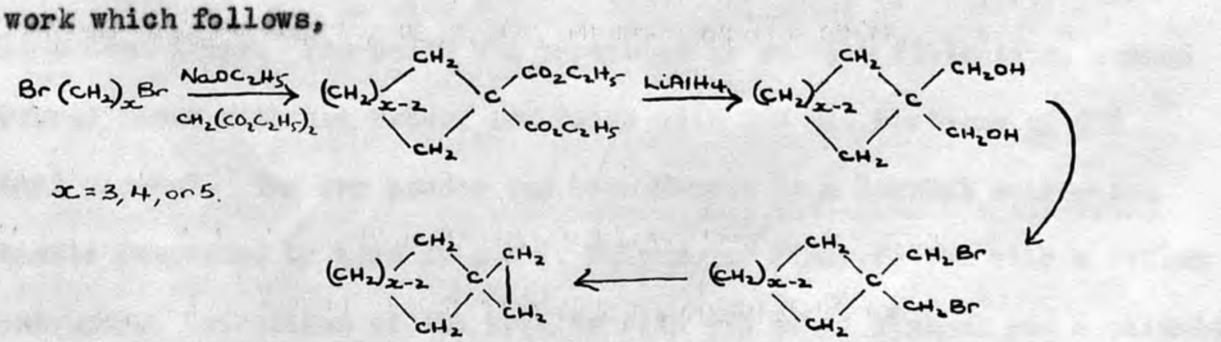
Spiro (5:4) decane (III) was similarly prepared by making the 5-ketone, and reducing this by the Wolff-Kishner reaction. (Zelinsky and Schuikin, Ber., 1929, 62, 2184)

Spiro (5:2) octane (IV) was synthesised by Shortbridge, Craig, Greenlee, Derfer, and Boord, (J. Amer. Chem. Soc., 1948, 70, 946) using the following scheme,



This compound and its derivatives are distinguished from other spiranoid compounds by their great stability.

The scheme outlined below is the one described in the experimental work which follows,



Considerable difficulty was encountered in preparing the 1:1-bis-(bromomethyl) compounds, and the yields were low. However, spiro (4:2)-

heptane and spiro (5:2) octane were obtained by this method.

Spiro (4:2) heptane has not previously been synthesised although many of its derivatives including the cis and trans acids have been prepared (Thorpe, J., 1920, **117**, 1579: 1922, **121**, 1821).

Experimental.

I. Attempted Synthesis of Trispirotridecane.

(a) Preparation of pentaerythrityl bromide.

The methods of (i) Backer and Schurink (Rec. Trav. chim., 1931, 50, 921), and (ii) Herzog (Org. Synth., 1951, 31, 82), were used for this preparation.

Purification of materials.

Phosphorus tribromide was distilled, the fraction, b.p. 173°, being used. Technical pentaerythritol, m.p. 244°, was recrystallised twice from 2.5% v/v hydrochloric acid. The melting point was raised to 260°.

(i) 125 G. (1.0 mol.) pentaerythritol were placed in a 500 ml. two-necked flask which was heated on a water-bath, and 500g. (2.1 mol.) freshly distilled phosphorus tribromide were added dropwise over a period of two hours. A semi-molten, orange mass was formed and hydrogen bromide was freely evolved. The water-bath was replaced by a metal-bath and the temperature of the reaction mixture was slowly raised to 170° and maintained at 170°±10° for twenty hours. The orange-red product was transferred to a beaker containing 1 l. water, and vigorously stirred to disperse the flocculent lumps. The solid was separated by suction filtration, washed several times with hot water, and twice with 200 ml. portions of 95% ethyl alcohol. The dry powder was transferred to a Sohxlet extraction thimble suspended by wire in a 1 l. Erlenmeyer flask fitted with a reflux condenser. Extraction of the bromide with 95% ethyl alcohol was continued for several days. Off-white crystals having a musty odour were precipitated from the alcohol when it was cooled; these were recrystallised from alcohol and heated to 120° to remove phosphorus compounds. Odourless, crystals, m.p. 161.5°, were obtained. Yield 234g. (66%)

(ii) $C(CH_2OH)_4 + 4C_6H_5SO_2Cl \xrightarrow{C_6H_5N} C(CH_2OSO_2C_6H_5)_4 + 4HCl$

$C(CH_2OSO_2C_6H_5)_4 + NaBr \longrightarrow C(CH_2Br)_4 + 4C_6H_5SO_3Na$

375G. (4.2 mol.) benzene sulphonyl chloride were added dropwise to a mixture of 65g. (1.0 mol.) pentaerythritol and 325 ml. pyridine in a 3 l. three-necked flask fitted with a dropping funnel, thermometer, and mechanical stirrer, at such a rate as to maintain the temperature of the reaction mixture between 30-35°. The temperature was then kept at 40° for one hour. The mixture was added slowly, and then more rapidly to a vigorously stirred solution of 400 ml. concentrated hydrochloric acid in 500 ml. water and 1 l. methyl alcohol in a 5 l. beaker. Crystallisation of pentaerythrityl benzene sulphonate was induced by seeding with a small portion of extracted product which had been treated separately. The suspension was cooled in ice, and the product was filtered off under suction, washed with several litres of water and finally with 500 ml. of methyl alcohol.

The crude pentaerythrityl benzene sulphonate was added to 500 ml. diethylene glycol in a 2 l. Erlenmeyer flask fitted with a Hershberg stirrer, and 300g. (5.8 mol.) sodium bromide were introduced. The mixture was heated with slow stirring on a metal-bath at 140-150° for sixteen hours. The reaction mixture was cooled to about 90°, and

1 l. of ice-water was rapidly stirred in. The mixture was finally cooled by the addition of ice until a temperature of 10° was attained. The precipitate was filtered off under suction, washed with water, and pressed dry. The brown crystalline solid was dissolved in 1 l. boiling acetone and filtered by gravity through a heated funnel. Colourless plates of pentaerythrityl bromide separated out as the solution cooled, these were filtered off and washed with 100 ml. 95% ethyl alcohol. More product was obtained by concentrating the mother liquor.
Yield 139g. (75%), m.p. 160°.

(b) Preparation of 1:1:5:5- tetracarbethoxyspiroheptane

The method of Backer and Schurink was used (*Rec. Trav. chim.*, 1931, *50*, 921).

Purification of reagents.

iso-Amyl alcohol was dried over calcium sulphate and the fraction, b.p. 129.5-131°, was distilled into a dry flask. Diethyl malonate was dried over calcium sulphate, and distilled under reduced pressure. Fraction, b.p. 87-89°/16 mm., was used in the preparation.

28.75G. (5 mol.) freshly cut sodium were added to 1.25 l. *iso*-amyl alcohol contained in a 3 l. three-necked flask, fitted with a mechanical stirrer sealed with a polythene gland, a dropping funnel, and a reflux condenser; the latter two were equipped with calcium chloride traps. 200G. (4.9 mol.) dry diethyl malonate were slowly added and the mixture was gently warmed. 100g. (1.0 mol.) pentaerythrityl bromide were then added. The condenser was replaced by a distillation head, and the mixture was distilled until the thermometer reading was 128°. The distillate, about 500 ml., contained some ethyl alcohol formed by double decomposition between diethyl malonate and <u>iso</u>-amyl alcohol in the presence of sodium. 500 ml. dry <u>iso</u>-amyl alcohol were added to the reaction mixture which was heated under reflux for fifty-six hours. A large quantity of the <u>iso</u>-amyl alcohol was then removed by distillation, water was then added to the remaining mixture and the rest of the alcohol was distilled over as an azeotropic mixture. More water was added to dissolve all the precipitated sodium bromide, and a dark brown oil separated out. The product was extracted several times with ether, and the combined extracts were dried over anhydrous potassium carbonate. The ether was removed by distillation, and attempts were made to purify the product by distillation under reduced pressure.

An 8" column packed with Fenske helices was used, but at 1 mm. pressure rapid decomposition of the ester fraction took place, and it was necessary to stop the distillation. Several variations in technique were tried, but each time the ester decomposed producing a dark yellow distillate. One third of the crude ester product was distilled at atmospheric pressure. After the lower fractions up to, b.p. 132°, had been removed, a pungent smelling, colourless liquid commenced to distil, but rapid decomposition occurred in the distillation flask and heating had to be stopped. The distillate had a refractive index of n_D^{20}1.4245, and the following analysis:

Found: C, 67.0 ; H, 11.1

Required for $C_{19}H_{28}O_8$: C, 59.4 ; H, 7.3%

An attempt was made to isolate the pure ester by the formation of its amide. 20g. crude product were shaken at regular intervals with ammonia (d. 0.880) solution. No amide was produced.

5.0G. crude product were left to stand for two days in a stoppered flask with 100 ml. alcoholic 20% potassium hydroxide solution. The bulk of the alcohol was distilled off, and the remaining potassium salt was dissolved in water. The solution was boiled with decolourising charcoal, filtered, and the filtrate was acidified with concentrated hydrochloric acid and extracted with ether. The ether was evaporated from the extract and the 2 ml. liquid which remained were heated in a test-tube on a metal-bath at 210-220° for thirty minutes; effervescence due to the liberation of carbon dioxide was observed. When the liquid was cooled, a crystalline mass was formed which was extracted with hot water and recrystallised from ethyl acetate. Well-defined crystals, m.p. 211°, were obtained; this agrees with the m.p. given by Backer and Schurink. The isolation of 1:5-spiroheptane dicarboxylic acid confirms the presence of 1:1:5:5- tetracarbethoxy-spiro-heptane in the crude product.

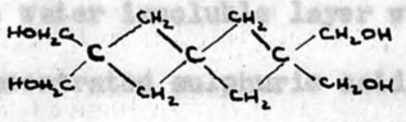
(c) Attempt to reduce the product of the reaction between diethyl malonate and pentaerythrityl bromide.

Low b.p. fractions were distilled from the crude product, and 50g. of the remaining liquid were added dropwise to a suspension of 10g. lithium aluminium hydride in 500 ml. anhydrous ether, at such a rate as to maintain steady boiling of the ether. The reaction mixture was heated under reflux for two hours on a water-bath. The excess of reducing agent was decomposed by the addition of water, and 5% v/v sulphuric acid was added until the solution was clear. The ethereal layer was isolated, and the aqueous layer was extracted several times with ether. The combined extracts were dried over anhydrous potassium carbonate, and, after the ether had been removed by distillation, the remaining liquid was distilled under reduced pressure. 5.0G. colourless, viscous, pungent-smelling liquid, b.p. 140°/5mm., n_D^{20} 1.4705, were collected. The residue was a brown waxy solid.

Analysis of liquid.

Found: C, 68.4 ; H, 11.4

$C_{11}H_{20}O_4$ requires C, 61.1 ; H, 9.3 %



$C_{11}H_{20}O_4$

II Attempted Synthesis of Spiro (3:2) hexane.

(a) Preparation of 1:3-dibromopropane.

The method of Kamm and Marvel, (*Org. Synth.*, 1921, *1*, 8) was used.

657G. (2.0 mol.) concentrated sulphuric acid were slowly added to a mixture of 250g. (1.0 mol.) trimethylene glycol, 1360g. (2.5 mol.) 48% hydrobromic acid solution and 412g.(1.3 mol.) concentrated sulphuric acid in a 3l. flask. The mixture was heated under reflux for one hour and then distilled until no water insoluble product appeared in the distillate. The water insoluble layer was isolated and washed with water, 50g. concentrated sulphuric acid, and finally 10% sodium carbonate solution. The oil was dried over calcium chloride, and then distilled. 595g. (89.5%) 1:3-dibromopropane, b.p. 162-165°, were collected.

(b) Preparation of 1:1-dicarbethoxycyclobutane.

A method was used similar to that of Cason and Allen, (*J. Org. Chem.*, 1949, *14*, 1036).

Ethyl alcohol and diethyl malonate were purified as previously described for malonic ester synthesis (see p.10)

32.5g. (2.0 mol.) freshly cut sodium were added to 600 ml. dry ethyl alcohol in a 2l. two-necked flask fitted with a dropping funnel and reflux condenser, each sealed with calcium chloride traps. 128g. (1.2 mol.) diethyl malonate were added after the sodium had finished reacting with the alcohol. The flask was warmed on a water-bath until the sodio-derivative of the ester had dissolved, and then 134g. (1.0 mol.) 1:3-dibromopropane were added dropwise from the funnel. A vigorous reaction took place and sodium bromide was precipitated. The reaction mixture was heated under reflux for three hours, and a large quantity of alcohol was then removed under vacuum. The remaining mixture was poured into water and a heavy orange oil separated out. The product was salted out with sodium chloride, and extracted with ether. The combined extracts were dried over ahhydrous potassium carbonate. The ether was removed by distillation, and the fraction of the extract, b.p. 190-240°, was transferred to a vacuum distillation apparatus fitted with an 8" fractionating column packed with Fenske helices.

Fraction	Range	Weight	n_D^{20}
1	46-52°/3mm.	15.0g.	1.3791
2	52-58° "	59.0	1.4159
3	58-64° "	22.0	1.4196
4	64-66° "	19.0	1.4255
5	66-69° "	24.3	1.4349
6	69°	26.0	1.4360
7	69-72° "	29.7	1.4359
8	72° "	20.9	1.4359
9	74-80° "	5.0	1.4354

Analyses.

Fraction (6 + 7 + 8) Found: C, 60.2; H, 8.1

Fraction 5 Found: C, 60.0; H, 8.2

Calculated for $C_{10}H_{16}O_4$: C, 60.0; H, 8.05%

Yield of 1:1-dicarbethoxycyclobutane (6+7+8) 76.6g. (58%)

(c) Hydrolysis of 1:1-dicarbethoxycyclobutane.

5G. ester were heated under reflux with 30 ml. 10% alcoholic potassium hydroxide solution for thirty minutes. Most of the alcohol was then removed under reduced pressure, and the potassium salt was dissolved in water. The aqueous solution was acidified with concentrated hydrochloric acid, and the precipitated acid was extracted with ether and dried over calcium sulphate. After two recrystallisations from ethyl acetate the 1:1-*cyclo*butane dicarboxylic acid had a melting point of 158°. Recorded melting points for this acid vary between 154° (Farmer and Wallis, *J.*, 1933, 1304), and 158° (Jeffery and Vogel, *J.*, 1948, 1804).

(d) Preparation of 1:1-bis(hydroxymethyl) *cyclo*butane.

60G. (1.0 mol.) 1:1-dicarbethoxy*cyclo*butane diluted with 50ml. anhydrous ether were added dropwise to a mixture of 13.5g. (1.2 mol.) lithium aluminium hydride and 500ml. dry ether, at such a rate as to maintain steady boiling of the ether. When the addition was complete the mixture was heated under reflux for one hour on the water-bath. The excess of lithium aluminium hydride was decomposed by the addition of water. 100G. crushed ice were added to the mixture, and 5% v/v sulphuric acid solution was added until the aqueous layer became clear. The ether layer was isolated and the aqueous layer was extracted several times with ether. The combined extracts were dried over anhydrous potassium carbonate, and after the ether had been removed by distillation, a pale yellow liquid remained which was distilled under reduced pressure.

Fraction	Range	Weight	n_D^{25}	
1	80-82°/5mm.	4.7g.	1.4659	Pale yellow liquid which darkens on standing.
2	112°/5mm.	18.8g.	1.4788	Colourless, viscous liquid, with sweet smell.

Analysis. 1:1-bis (hydroxymethyl) *cyclo*butane.

Fraction 2. Found: C, 62.3; H, 10.55

$C_6H_{12}O_2$ requires: C, 62.0; H, 10.5%

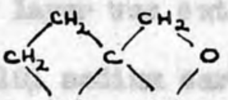
Yield of 1:1-bis(hydroxymethyl) cyclobutane 18.8g. (54%). This compound is very soluble in alcohol, ether, and benzene, but is immiscible with water.

The low yield of the diol was thought to have been due to the formation of the cyclic ether by dehydration, thus giving the low fraction of boiling point 82°/5mm. The analysis however, shows that this is not the case.

Analysis.

Fraction 1 Found: C, 65.0 ; H, 9.0

$C_6H_{10}O$ requires: C, 73.4 ; H, 10.2%



$C_6H_{10}O$

(e) Attempts to prepare 1:1-bis(bromomethyl) cyclobutane.

(i) 1.0G. (1.0 mol.) diol was heated under reflux for thirty minutes with 10g. (6.0 mol.) 48% hydrobromic acid solution at 90° on a water-bath. A black, charred solid was formed, from which it was not possible to extract any product.

The experiment was repeated using a more dilute solution of hydrobromic acid, but this too, was unsuccessful.

(ii) 6.2G. (1.0 mol.) phosphorus tribromide were added dropwise to 2.0g. (1.0 mol.) ice-cooled 1:1-bis(hydroxymethyl)-cyclobutane. At first no reaction took place, but after stirring for a few moments, a violent reaction occurred and hydrogen bromide was evolved. An orange-black gum was formed. The excess of reagent was decomposed by the addition of ice, and attempts were made to extract the product with ether, petroleum ether, alcohol and benzene, but only a trace of pungent smelling liquid,

n_D^{25} 1.5176, was obtained. The theoretical yield of the dibromide was 4g.

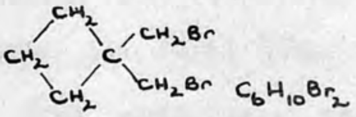
This experiment was repeated on a larger scale, but the product which contained bromine represented less than a 10% yield.

(iii) 4.0G. (1.0 mol.) diol were dissolved in 20g. dry benzene and 12.5g. (1.7 mol.) phosphorus tribromide were added dropwise to the ice-cooled solution. The temperature of the reaction mixture was slowly raised to 80°, and heated for one hour on a water-bath. The excess of phosphorus tribromide was decomposed by stirring the mixture with crushed ice. The pale yellow benzene layer was removed, and the aqueous layer was extracted with benzene. The combined extracts were washed with 10% sodium carbonate solution, water, and then dried over calcium chloride. The benzene was removed by distillation, and the pale yellow oil which remained represented a yield of only 18%.

Molecular weight of the product in benzene.

Found: 228.5 ; 265.0

$C_6H_{10}Br_2$ requires: 242.



(f) Attempt to prepare 1:1-bis(chloromethyl) cyclobutane.

2.0G. (1.0 mol.) 1:1-bis(hydroxymethyl) cyclobutane dissolved in 5g. ethanol were shaken with 2.0g. (2.5 mol.) concentrated hydrochloric acid in a stoppered flask for thirty minutes. No reaction took place. The mixture was gently warmed on a water-bath, and rapid darkening of the solution occurred. The mixture was poured into water, and the product was extracted with ether and washed with 10% sodium carbonate solution and then with water. The extract was dried over calcium chloride. The ether was evaporated off, leaving some of the unchanged diol together with its charred decomposition products.

2.0G. (1.0 mol.) diol were heated under reflux for one hour with 7.0g. (4.5 mol.) acetyl chloride. The excess of reagent was decomposed with water, and the product was extracted with ether, and the extract was treated as described above. After removal of the ether, a colourless, mobile, pungent smelling liquid remained which was distilled at atmospheric pressure. Yield 1.8g., b.p. 238-242°, n_D^{25} 1.4483.

Analysis.

Lassaigne test; chlorine absent.

Found: C, 60.2 ; H, 8.2

$C_{10}H_{16}O_4$ (1:1-bis(hydroxymethyl)cyclobutane acetate) requires: C, 60.0; H, 8.1.%

III The Synthesis of Spiro(5:2)octane.

(a) Preparation of 1:5-dibromopentane.

Benzoyl piperidine was prepared by the method of Marvel and Lazier, (Org. Synth., 1929, 9, 18).

A solution of 210g. sodium hydroxide in 1600ml. water was added to 340g. (1.0 mol.) piperidine contained in a 3l. three-necked flask fitted with a mechanical stirrer, dropping -funnel, and air-condenser. 560G. (1.0 mol.) benzoyl chloride were added dropwise from the funnel, and the reaction mixture was continuously stirred, and cooled by standing the flask in a bath of cold running water.

When the addition was complete, two layers of emulsion were formed which were broken up by the addition of 100ml. saturated solution of sodium hydroxide. The product was extracted with benzene, and the extracts were washed several times with water, and then dried over anhydrous sodium sulphate. The benzene was distilled from the product under reduced pressure, and the distillation was continued; the first 20ml. of the distillate which were red were discarded. 690G. pale yellow viscous liquid, b.p. 152-154°/6mm., were collected, and some crystals of benzoyl piperidine, m.p. 45°, were deposited in the condenser.

Yield 91%. Recorded yield 77-81%.

1:5-dibromopentane was prepared from benzoyl piperidine by the method of Dox and Yoder, (J. Amer. Chem. Soc., 1921, 43, 1367) which is a modification of the method of von Braun, (Ber., 1904, 37, 3210-13).

331G. (0.9 mol.) phosphorus tribromide were slowly added to 230g. (1.0 mol.) benzoyl piperidine contained in a litre distillation flask.

Each addition was followed by a vigorous reaction. The syrupy mixture was shaken and cooled, and 186g. (0.9 mol.) bromine were added. The flask was connected to a vacuum distillation apparatus and gently heated. At first there was a rapid evolution of gas, after which a pale yellow liquid distilled at, b.p. 70°/20mm. As the distillation proceeded, off-white crystals formed in the condenser and finally blocked the apparatus. The distillate was poured on to a large quantity of crushed ice, and vigorously stirred for thirty minutes in a flask fitted with a reflux-condenser, in order to decompose the phosphorus oxybromide. A dense, orange, oil separated out which was transferred to a litre flask and boiled under reflux for three hours with 350ml. 48% hydrobromic acid solution to hydrolyse the benzonitrile to benzoic acid. A black oil was formed which was isolated and steam-distilled, using an air-condenser between the distillation flask and the receiver; the latter was fitted with a reflux-condenser, thus avoiding blockage of the primary condenser with benzoic acid. A colourless, oil separated out in the aqueous distillate. This oil was isolated, washed with 5% sodium carbonate solution, and dried over calcium chloride. The crude product was distilled under vacuum and yielded 115g. (39%), b.p. 104°/18mm., 1:5-dibromopentane.

(b) Preparation of 1:1-dicarbethoxycyclohexane.

Purification of starting materials.

Ethyl alcohol was dried by heating under reflux a mixture of 1 litre 95% alcohol, 7g. sodium, and 27.5g. diethyl phthalate for two hours. The alcohol was distilled into a dry flask after the first 25ml. had been discarded.

Diethyl malonate was dried over calcium sulphate and distilled under vacuum. Fraction, b.p. 89-90°/13mm., was used in the preparation.

The method used for the preparation of 1:1-dicarbethoxy*cyclo*hexane was similar to that of Dox and Yoder, (*idem, loc.*).

8G. (2.0 mol.) freshly cut sodium were added to 100g. dry ethyl alcohol contained in a 2l. two-necked flask fitted with a dropping-funnel and reflux-condenser, each equipped with a calcium chloride trap. When the reaction had ceased, the solution was cooled and 28g. (1.0 mol.) diethyl malonate were added dropwise. A gelatinous precipitate of sodio-diethyl malonate was formed which was dissolved by gently warming the flask on a water-bath. 40g. (1.0 mol.) 1:5-dibromopentane were then added slowly, and a precipitate of sodium bromide began to form immediately. The reaction became vigorous and caused the alcohol to boil. When all the bromo-compound had been added, the reaction mixture was heated under reflux for two and a half hours. A buff-coloured mixture pH 7 was formed, and the alcohol was removed from this by distillation under reduced pressure. The remaining liquid and solid were poured into water, and a light brown oil was salted out with sodium chloride and extracted several times with ether. The combined extracts were washed with water and then dried over anhydrous potassium carbonate. The ether was removed by distillation, and the oil was distilled under reduced pressure.

1	90-125°/11mm.	15.3g.	n_D^{25} 1.4379	Odour of malonic ester.
2	125-150° "	16.8g.	1.4441	Colourless liquid.
3	150-210° "	7.9g.	1.4428	Pale yellow liquid.

Rapid decomposition occurred during the final stages of the distillation.

Fractions 1 and 2 were combined and redistilled using an 8" electrically heated column packed with Fenske helices.

A	60-75°/5mm.	1.0g.	n_D^{25} 1.4289
B	75-90° "	1.7g.	1.4422
C	120° "	19.0g.	1.4452

Residue 1.5g. dark brown liquid.

Analysis of fraction C.

Found: C, 62.25 ; H, 8.85.

Calculated for $C_{12}H_{20}O_4$: C, 63.1 ; H, 8.8%

Yield of 1:1-dicarbethoxycyclohexane 19g. (48%), b.p. 120°/5mm., n_D^{25} 1.4452.

Fraction 3 of the first distillation presumably contained some 1:1:7:7-tetracarbethoxyheptane; this was investigated by hydrolysing some of the distillate with alcoholic potassium hydroxide solution. The mixture was heated under reflux for six hours, and then the alcohol was distilled from the solution of the potassium salt. More water was added to dissolve all the solid, and the solution was acidified with concentrated hydrochloric acid and extracted with ether. The extract was dried over calcium sulphate, and after the ether had been evaporated off, a pale yellow viscous liquid remained which was soluble in ethanol, benzene, toluene, hot water, and insoluble in petroleum ether. Attempts to crystallise the product from these solvents were unsuccessful. The viscous liquid was then heated in a flask at 140° for one hour. Rapid evolution of carbon dioxide was observed. The product was decolourised with activated charcoal and recrystallised from ethyl alcohol, m.p. 104°.

Analysis.

Found: C, 57.3 ; H, 8.6.

Calculated for $C_9H_{16}O_4$ (azelaic acid); C, 57.4; H, 8.6.%

(c) Hydrolysis of 1:1-dicarbethoxycyclohexane.

5.0G. ester were heated under reflux for one hour with 50ml. 20% alcoholic potassium hydroxide solution. The solid potassium salt was dissolved by the addition of water, and the solution was acidified with concentrated hydrochloric acid. The precipitated acid was extracted with ether and the extract was dried over calcium sulphate. Purification and crystallisation of the product was rather difficult. After it had been decolourised with charcoal, an alcoholic solution of the acid yielded a white emulsion which solidified only on the addition of light petroleum (b.p. 60-80°.). Colourless, crystals m.p. 166° (decomp.) were obtained which after two recrystallisations from a 50:50 mixture of ether and light petroleum had a m.p. 176° (decomp.).

Analysis.

Found: C, 56.0; H, 7.1.

Calculated for $C_8H_{12}O_4$: C, 55.8 ; H, 7.0%

Several melting-points have been recorded for 1:1-cyclohexanedicarboxylic acid varying from 176° (decomp.) (Wightman, J., 1926, 2543) to 207° (Ingold and Thorpe, J., 1919, 115, 376).

Preparation of the anilide.

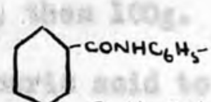
1G. 1:1-cyclohexane dicarboxylic acid and 2g. aniline were heated together in a test-tube fitted with a short air-condenser. The temperature was gradually raised to 130° and maintained at 130-140° for two hours.

The product was extracted with 50ml. ether and washed with 30ml. 10% hydrochloric acid solution, followed by 20ml. 10% sodium hydroxide solution. The ether was distilled from the extract, and the residue was decolourised with charcoal and recrystallised from a 50:50 mixture of water and alcohol. Colourless needles were obtained, m.p. 140°.

Analysis

Found: C, 76.2 ; H, 8.4 ; N, 7.1.

Calculated for $C_{13}H_{17}ON$: C, 76.8 ; H, 8.4 ; N, 7.0%.



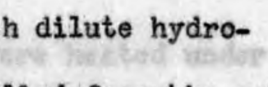
The analysis obtained corresponds to the anilide of cyclohexane carboxylic acid $C_{13}H_{17}NO$, it is therefore obvious that the dicarboxylic acid must have undergone decarboxylation during the heat treatment at 130°. This anilide is described by Edson, (J. Soc. Chem. Ind., 1934, 53, 138), m.p. 141°.

0.5G. dry powdered 1:1-cyclohexane dicarboxylic acid was heated under reflux with 10ml. thionyl chloride on a water-bath for thirty minutes. The excess of thionyl chloride was removed by distillation, and the remaining liquid was shaken with 5ml. ether. 4G. aniline in 50ml. ether were added to the ethereal solution, and a white precipitate sparingly soluble in ether was immediately formed. The mixture was shaken with dilute hydrochloric acid and washed with water. The ether was distilled from the solid product, and the latter was recrystallised from 50% aqueous alcohol. Colourless needles, m.p. 228°, were obtained.

Analysis.

Found: C, 74.2 ; H, 6.8 ; N, 8.8

$C_{20}H_{22}O_2N_2$ requires: C, 74.5 ; H, 6.8 ; N, 8.7%



The product was therefore the dianilide of 1:1-cyclohexane dicarboxylic acid.

(d) Preparation of 1:1-bis(hydroxymethyl) cyclohexane.

A reducing mixture was prepared of 8.2g. (1.2 mol.) lithium aluminium hydride in 400ml. dry ether. To this was added 40g. (1.0 mol.) 1:1-dicarbethoxy*cyclo*hexane in 50 ml. dry ether at such a rate as to maintain steady boiling of the ether. The reaction mixture was stirred continuously. When the addition of the ester was complete, the reaction mixture was heated under reflux for one hour on a water-bath. The excess of reducing agent was decomposed by the addition of water, then 100g. crushed ice were added followed by sufficient 5% v/v sulphuric acid to render the mixture clear. The ethereal layer was isolated and the aqueous layer was extracted twice with ether. The combined extracts were dried over anhydrous potassium carbonate, and then the ether was removed by distillation. A solid, m.p. 94°, remained which after three recrystallisations from ethanol yielded a crop of prisms of 1:1-*bis*(hydroxymethyl)-*cyclo*hexane, m.p. 98.5°. Yield 20.8g. (84%)

(e) Preparation of 1:1-bis(bromomethyl)cyclohexane.

Several attempts were made to prepare the dibromide before a successful method was found.

1) 2.0G. (1.0 mol.) 1:1-*bis*(hydroxymethyl)*cyclo*hexane were heated under reflux with 6g. (4.0 mol. hydrogen bromide) 48% hydrobromic acid solution for one hour on a water-bath. The excess of reagent was decomposed with water, and the aqueous solution was extracted with ether. The extract was washed with water, 10% sodium carbonate solution, and then dried over calcium chloride. The ether was evaporated off, and a crystalline solid, m.p. 96°, remained, which proved to be unchanged diol.

2) 4.0g. (1.0 mol.) 1:1-*bis*(hydroxymethyl)*cyclo*hexane were heated under

reflux with a mixture of 12g. (3.5 mol hydrogen bromide) 48% hydrobromic acid solution and 3.6g. (2.0 mol.) concentrated sulphuric acid, for three hours. Water was added to decompose excess of hydrobromic acid, and the reaction mixture was extracted with ether. The extract was washed in turn with concentrated sulphuric acid, 10% sodium carbonate solution, and water, and finally dried over calcium chloride. After the ether had been distilled from the extract, 2g. brown liquid remained; a Lassaigne test on this proved that bromine was absent.

This experiment was repeated, and the reaction mixture was heated under reflux for twelve hours, but again no successful result was obtained.

3) Hydrogen bromide was prepared by bubbling sulphur dioxide into bromine water. The gas produced was passed through a tube of damp red phosphorus and glass wool to remove bromine and finally into a bottle containing a weighed amount of glacial acetic acid. 27g. (4.5 mol.) acetic acid absorbed 21.5g. (2.7 mol.) hydrogen bromide. 16G. of this reagent were transferred to a litre flask together with 5.0g. 1:1-bis(hydroxymethyl) cyclo-hexane. The stopper of the flask was wired on, and the flask was slowly warmed up in a water-bath, and left in boiling water for eight hours. The reaction mixture was poured into water, and the heavy orange oil which separated out was isolated, and then steam-distilled. 8g. pale yellow oil separated from the aqueous distillate; this oil was removed and dried over calcium chloride. A Lassaigne test proved that bromine was present in the product. The oil was distilled under vacuum using a semi-micro distillation apparatus with an 8" vacuum jacketed Vigreux column.

1	148-150/23mm.	0.7g.	n_D^{25} 1.4783	Pale yellow liquid.
2	150-152° "	3.0g.	1.4770	Colourless liquid.
3	152-152.5° "	0.5g.	1.4743	" "
4	153-154° "	2.3g.	1.4707	" "
5	154° "	0.5g.	1.4683	Pale yellow liquid.

Analyses.

Fraction 2. Found: C, 53.7 ; H, 7.8 ; Br, 21.3.

Fraction 3. Found: C, 55.2 ; H, 7.1; Br, 15.1.

Calculated for $C_8H_{14}Br_2$ (1:1-bis(bromomethyl)cyclohexane):
C, 35.6; H, 5.2 ; Br, 59.2.%

4) The method finally used to prepare 1:1-bis(bromomethyl)-cyclohexane combines the methods of Backer and Winter, (Rec. trav. chim., 1937, 56, 492) and Shortbridge, Craig, Greenlee, Derfer, and Boord, (J. Amer.Chem. Soc., 1948, 70, 946) in which phosphorus tribromide is employed.

3G. (1.0 mol.) 1:1-bis(hydroxymethyl)cyclohexane were weighed into a Pyrex combustion tube. The tube was stood in a beaker of water at 70°, and 6.6g. (2.0 mol.) freshly distilled phosphorus tribromide were added dropwise to the solid. A vigorous reaction took place and hydrogen bromide was evolved. When the effervescence had subsided, the tube was sealed in an oxygen flame, and then heated in a Carius oven for twelve hours at 140-150°. This reaction was repeated on 40g. diol, and it was found that by reducing the heating period to eight hours, there was no appreciable reduction in the yield of the dibromide.

The tube was opened, and the vivid orange viscous product was poured into water. The aqueous mixture was distilled with superheated steam, and the heavy, colourless oil which separated out in the aqueous distillate was extracted with ether and dried over calcium chloride. After the ether had been removed, the remaining liquid was distilled under reduced pressure using a Vigreux column of approximately 10-plate efficiency. Low boiling-point liquid 30°/5.5mm. was first removed.

A	112-113°/5mm.	1.8g.	n_D^{20} 1.5273
B	113°/5.5mm.	2.0g.	1.5335
C	113-113.5° "	22.0g.	1.5337
D	113.5-114° "	20.6g.	1.5335
E	114° "	1.0g.	1.5296

Total yield of 1:1-bis(bromomethyl)cyclohexane B+C+D= 44.6g.(55%)

Analysis.

Found: C, 35.9 ; H, 5.2 ; Br, 59.9.

Calculated for $C_8H_{14}Br_2$: C, 35.6 ; H, 5.2 ; Br, 59.2.%

The figures quoted in the literature for this experiment are:

Yield 48%. b.p. 139. 5/17mm. (Backer and Winter, Rec. trav. chim., 1937, 56, 492); Yield 27% b.p. 117°/6mm. n_D^{20}1.5390 (Shortbridge et al., J. Amer. Chem. Soc., 1948, 70, 946)

(f) Preparation of spiro (5:2)octane.

The method used for the cyclisation of the dibromide was a modification of the method of Gustavson, (J. prakt. chim., 1887, 36, 300) given by Shortbridge et al., (idem, loc. cit.)

A mixture of 65ml. 95% ethyl alcohol and 6.5ml. distilled water was poured into a 500ml. three-necked flask fitted with a mechanical stirrer sealed with a polythene gland, a dropping-funnel, and a reflux-condenser. 36.6g. (4.0 mol.) zinc dust were added to the aqueous solution and the mixture was rapidly stirred to prevent coagulation of the zinc. The flask was heated in an isomantle until gentle refluxing commenced, and then 40g.

(1.0 mol.) 1:1-bis(bromomethyl)-cyclohexane were added dropwise from the funnel. The reaction mixture was heated under reflux for twenty-four hours with continuous stirring, after which time the product was distilled from the flask with the aqueous alcohol. The distillate was diluted to three times its volume with distilled water, and the colourless upper layer which separated out was isolated and dried in turn over calcium chloride, and sodium wire.

The liquid was filtered, and distilled from a 25ml. flask using a 4" electrically heated column packed with Fenske helices.

A	129-129.5°	1.8g.	n_D^{20} 1.4480	Barometer 759mm.
B	129.5-130°	7.3g.	1.4483	
C	130-131°	1.7g.	1.4487	
D	131°	2.7g.	1.4497	
E	131	1.2g.	1.4498	

Fractions A,B and C were combined and redistilled using a semi-micro distillation apparatus fitted with a 6" vacuum jacketed Vigreux column.

1	125.5°	1.6g.	n_D^{20} 1.4477	Barometer 764mm.
2	125.5-126°	1.4g.	1.4480	
3	126-126.5°	1.4g.	1.4481	
4	127°	1.2g.	1.4481	
5	127°	2.2g.	1.4484	
6	130-131°	1.5g.	1.4498	

Fractions 5 and 6 were combined and redistilled.

1'	125-126°	0.3g.	n_D^{20} 1.4482	Barometer 758mm.
2'	127°	0.4g.	1.4492	
3'	127°	0.6g.	1.4493	
4'	129-130°	0.9g.	1.4504	

Yield of crude spiro(5:2)octane - 14.7g. (89%).

Yield of hydrocarbon n_D^{20}1.4480- n_D^{20}1.4481, = 4.0g. - volatile, liquid with typical hydrocarbon odour.

The physical properties of spiro(5:2)octane were determined on the combined fractions 2, 3 and 4.

Refractive index - n_D^{20} 1.44800, determined with a Pulfrich refractometer.

Density - determined with respect to benzene sample n_D^{20} 1.50099 and freshly boiled distilled water n_D^{20} 0.33252.

d_4^{20} 0.82332 $d_{20}^{C_6H_6}$ 0.82243.

Analysis.

Found; C, 87.2 ; H, 12.9.

Calculated for C_8H_{14} : C, 87.2 ; H, 12.8.%

The following physical constants have been recorded for spiro-(5:2)-octane by Shortbridge et al., (J. Amer. Chem. Soc., 1948, 70, 948), b.p. 125.5°/760mm., d_4^{20} 0.8282, n_D^{20} 1.4476.

IV The Synthesis of Spiro(4:2)heptane.

(a) Preparation of 1:4-dibromobutane.

1:4-dibromobutane was prepared by the method of Steele, (J. Amer. Chem. Soc., 1931, 53, 283).

100G. (1.0 mol.) tetramethylene glycol were added slowly, with cooling, to a mixture of 455g. (2.5 mol. hydrogen bromide) 48% hydrobromic acid solution and 137.2g. (1.3 mol.) concentrated sulphuric acid contained in a 2l. flask. 221.5g. (2.1 mol.) concentrated sulphuric acid were gradually added, each addition was followed by a vigorous reaction. The mixture was heated under reflux for eight hours and then distilled. An oil separated out in the aqueous distillate; to complete the distillation of the oil, water was added to the mixture in the distillation flask. The layer of oil was isolated and washed in turn with water, 10ml. concentrated sulphuric acid, and finally 10% sodium carbonate solution. The product was dried over calcium chloride and then distilled under reduced pressure. 219.5g. (92%) liquid distilled between 92-93°/25mm. Recorded yield 70%.

(b) Preparation of 1:1-dicarbethoxycyclopentane.

The ethyl alcohol and diethyl malonate used in this preparation were purified as previously described on p. 21-22

The reaction was carried out in a similar manner to that described for the synthesis of 1:1-dicarbethoxycyclohexane (see p. 22) using 34.5g. (1.5 mol.) sodium, 240g. (1.5 mol.) diethyl malonate, 216g. (1.0 mol.) 1:4-dibromobutane in 800ml. ethyl alcohol. After the ether had been removed from the dried extract, the remaining liquid was distilled under vacuum using a 24" Vigreux column.

1	64-66°/1.5mm.	29g.	n_D^{20} 1.4285
2	67-68° "	66g.	1.4230
3	68-70° "	31.5g.	1.4192
4	70-77° "	13.5g.	1.4222
5	82-87° "	15.5g.	1.4369
6	87° "	58g.	1.4415
7	87-88° "	55g.	1.4416
8	88-89° "	24g.	1.4416
9	90-114° "	14g.	1.4346
10	114° "	5g.	1.4343
11	114-118° "	2g.	1.4365

Yield of 1:1-dicarbethoxycyclopentane (Fractions 6 + 7 + 8) = 137g.(64%)

Analysis.

Found: C, 61.5 ; H, 8.3

Calculated for $C_{11}H_{18}O_4$: C, 61.6 ; H, 8.5.%

Some of the literature values given for the physical properties of 1:1-dicarbethoxycyclopentane are as follows: b.p. 115°/16mm. (Vogel, J., 1929, 1490)

b.p. 97.5°/4mm. n_D^{25}1.44203 (Farmer and Wallis, J., 1933, 1308).

b.p. 97-98°/3mm. n_D^{25}1.4390 (Skinner, Limperos, and Pettebone, J.Amer. Chem. Soc., 1950, 72, 1649).

(c) Hydrolysis of 1:1-dicarbethoxycyclopentane.

6G. 1:1-dicarbethoxycyclopentane were hydrolysed with 80ml. 20% alcoholic potassium hydroxide solution as described for 1:1-dicarbethoxycyclohexane on p.24. The acid product was rather difficult to crystallise. Finally, it was dissolved in a mixture of equal parts of ether, benzene, and light petroleum (b.p. 40-60°), and then granular, crystals of 1:1-cyclopentane dicarboxylic acid were formed m.p. 194°(decomp.). A wide range of melting-points have been recorded for this acid. m.p. 170-180° (Advani and Sudborough, J. Indian Inst. Sci., 1923, 6, 53).

m.p. 190° (decomp.) (Vogel, J., 1929, 1490).
m.p. 186° (Farmer and Wallis, J., 1933, 1308).
m.p. 184-5° (Skinner, Limperos, and Pettebone, J. Amer. Chem. Soc., 1950, 72, 1648).

Analysis.

Found: C, 53.4 ; H, 6.5.

Calculated for $C_7H_{10}O_4$: C, 53.2 ; H, 6.4.%

Preparation of the anilide.

The dianilide of 1:1-cyclopentane dicarboxylic was prepared by the method described on p.25 for the preparation of the dianilide of 1:1-cyclohexane dicarboxylic acid. The product was recrystallised from 50% aqueous alcohol, and needles, m.p. 227°, were obtained.

Analysis. Dianilide of 1:1-cyclopentane dicarboxylic acid.

Found: C, 73.8; H, 6.4; N, 9.3.

$C_{19}H_{20}N_2O_2$ requires: C, 74.1; H, 6.5 ; N, 9.1.%

Hydrolysis of 3g. of the high boiling fraction 10 obtained from the distillation of the crude 1:1-dicarbethoxycyclopentane (p.33) produced an oil, which after decarboxylation yielded a specimen of suberic acid, m.p. 142°.

(d) Preparation of 1:1-bis(hydroxymethyl)cyclopentane.

136G. (1.0 mol.) 1:1-dicarbethoxycyclopentane diluted with 100ml. dry ether were added dropwise to a mixture of 29.5g (1.2 mol.) lithium aluminium hydride in 1400 ml. dry ether, at such a rate as to maintain steady boiling of the ether. The usual precautions were taken to exclude moisture from the reaction mixture. After the ester had been added, the reaction mixture was heated under reflux on a water-bath for two hours. The excess of lithium aluminium hydride was decomposed with water, then 100g. crushed ice were added, followed by sufficient 5% v/v sulphuric acid to decompose the solid complex and hydroxides. The ethereal layer was isolated, and the aqueous layer was extracted twice with ether. The combined extracts were dried over anhydrous potassium carbonate, and after the solvent had been distilled off, a white solid, m.p. 87°, remained. The product was recrystallised from acetone and gave 78g. (94%) plates of 1:1-bis(hydroxymethyl)cyclopentane, m.p. 91°.

Analysis. 1:1-bis(hydroxymethyl)cyclopentane.

Found: C, 64.45 ; H, 10.8.

$C_7H_{14}O_2$ requires: C, 64.6 ; H, 10.85%

(e) Preparation of 1:1-bis(bromomethyl)cyclopentane.

Similar difficulties were encountered in the attempts to prepare 1:1-bis(bromomethyl)cyclopentane as were in the preparation of 1:1-bis(bromomethyl)cyclohexane (see p.26-28). 48% Hydrobromic acid solution and hydrogen bromide in acetic acid were not satisfactory reagents, and therefore phosphorus tribromide was used.

14G. (1.7 mol.) freshly distilled phosphorus tribromide were added dropwise to 5g. (1.0 mol.) 1:1-bis(hydroxymethyl)cyclopentane in a Pyrex combustion tube standing in a water-bath at 50°. When the vigorous reaction had subsided and the evolution of hydrogen bromide had ceased, the tube was sealed and heated in a Carius oven at 120-130° for ten hours. (This was repeated on 76g. diol.). The tube was opened and the pale yellow liquid was poured into water and steam-distilled. An oil separated in the aqueous distillate; this oil was isolated and dried over calcium chloride, it was then distilled under reduced pressure.

A	40-90°/20mm.	7.2g.	n_D^{25} 1.4616
B	90-126° "	12.1g.	1.5170
C	126-130° "	30.1g.	1.5297

Fractions B and C were combined and redistilled.

1	80-120/20mm	5.5g.	n_D^{25} 1.5003
2	123-123.5° "	16.3g.	1.5359
3	123.5-124° "	14.7g.	1.5359
4	124-126° "	2.0g.	1.5239
5	126-128° "	0.8g.	1.5250

Residue in distillation flask identified as unchanged diol.

Fraction 1 was redistilled.

1'	80-100°/20mm.	1.1g.	n_D^{25} 1.4614
2'	118-120° "	3.0g.	1.5065

Analysis. Combined Fractions 2 and 3. *1:1*-bis(*bromomethyl)*cyclo*pentane.*
Found: Br, 60.8.
$C_7H_{12}Br_2$ requires: Br, 61.5.%

Yield of 1:1-*bis*(bromomethyl)*cyclo*pentane, b.p. 123-124°/20mm. = 31g. (21%).

Physical constants determined for 1:1-*bis*(bromomethyl)*cyclo*pentane.

Refractive index - n_D^{25} 1.5359

Density - d_4^{20} 1.6403.

(e) *Preparation of* spiro(*4:2)heptane*.

The method used for the preparation of the *spiro*hydrocarbon from 1:1-*bis*(bromomethyl)*cyclo*pentane was similar to that described on p. 29 for the formation of *spiro*(5:2)-octane from 1:1-*bis*(bromomethyl)*cyclo*hexane.

The quantities used were 31.4g. (4.0 mol.) zinc dust, 55ml. absolute alcohol, 3ml. distilled water, 30g. (1.0 mol.) 1:1-bis(bromomethyl)*cyclo*pentane. About 10g. crude product were obtained after it had been dried over calcium chloride. The volatile, liquid was distilled from sodium.

1	90-92°	0.7g.	n_D^{20} 1.4277	Barometer 762mm.
2	92-93°	2.7g.	1.4280	
3	93-94°	5.1g.	1.4282	
4	94°	0.4g.	1.4296	

Fractions B and C were combined and redistilled.

A	90.5-92°	0.5g.	n_D^{20} 1.4277	Barometer 762mm.
B	92-93°	0.9g.	1.4280	
C	93-93.5°	2.1g.	1.4282	
D	93.5-94°	1.8g.	1.4282	
E	94°	0.6g.	1.4285	

Yield of crude spiro(4:2)heptane -10g. (89%).

Yield of hydrocarbon n_D^{20} 1.4282 -3.9g. volatile, liquid.

Density was determined on the combined fractions C + D, with respect to freshly boiled distilled water. d_4^{20} 0.79044.

Analysis. Spiro(4:2)heptane.

Found: C, 87.4 ; H, 12.4

C_7H_{12} requires: C, 87.4 ; H, 12.6.%

Section I

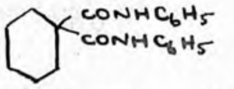
Discussion.

The results of the experimental work are not entirely in agreement with the theories on the stability of the four-, five-, and six-membered alicyclic compounds, e.g. the cyclisation reaction between the alkyl halides and malonic ester, produced 1:1-dicarbethoxy-esters in the following yields,

1:1-dicarbethoxy*cyclo*butane - 58%
" " " " pentane - 64%
" " " " hexane - 48%

i.e. $C_5>C_4>C_6$. It has been previously mentioned (see p. 2) that Perkin obtained yields which approximately corresponded to predictions based on the assumption that the tendency for ring formation is governed by the degree of strain it possesses, which according to the Baeyer Strain Theory was $C_5>C_6>C_4$. It should be born in mind that relative stability of ring systems is not the sole criterion for ease of formation. In the malonic ester synthesis under consideration, when a short chain separates the halogen atoms, the reaction leading to ring closure is preferred to that leading to the extension of the chain to a greater extent than when a long chain separates the halogen atoms. It was found that 1:4-dibromobutane and 1:5-dibromopentane differ markedly in their behaviour towards diethyl malonate. The former reacts to give the cyclic compound with only a trace of the straight-chain addition product, whereas 1:5-dibromopentane reacts with diethyl malonate to form both cyclic and straight-chain compounds, sometimes in equal proportions. The great tendency for the stable five-membered ring to be formed is evident.

By way of interest, the 1:1-dicarbethoxy-esters of *cyclo*-pentane and *cyclo*hexane were hydrolysed, and the new anilides of the dicarboxylic acids were prepared.



m.p. 228°

m.p. 226°

Some of the high boiling fractions obtained from the synthesis of the five-membered and six-membered rings were also hydrolysed, to yield samples of suberic, and azelaic acids.

The reduction of the 1:1-dicarbethoxy-esters with lithium aluminium hydride to give 1:1-*bis*(hydroxymethyl)-compounds was accomplished without difficulty; the products obtained were,

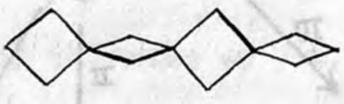
	% Yield.			
1:1-*bis*(hydroxymethyl)*cyclo*butane	54	b.p.	112°/5mm.	n_D^{25} 1.4788
" " " pentane	94	m.p.	91°	plates.
" " " hexane	84	m.p.	98.5°	prisms.

The first two members of this series have not previously been prepared.

The next stage of the synthesis, i.e. the preparation of the 1:1-*bis*-(bromomethyl)-compounds was difficult. In the *cyclo*butane series, the synthesis did not progress beyond this stage since all attempts to prepare the gem-dihalogeno-methyl compound from 1:1-*bis*(hydroxymethyl)*cyclo*butane using quite mild conditions, resulted in the decomposition of the diol, presumably by rupturing the *cyclo*butane ring.

The diols, 1:1-*bis*(hydroxymethyl)*cyclo*pentane and 1:1-*bis*-(hydroxymethyl)-*cyclo*hexane were in contrast very stable to reagents such as 48% hydrobromic acid solution, and a saturated solution of hydrogen bromide in glacial acetic acid. The method of heating the diol with phosphorus tribromide in a sealed tube had to be used for the preparation of the bromo-compounds. 1:1-*bis*-(hydroxymethyl)*cyclo*pentane was more resistant to this treatment than the corresponding cyclohexane compound, since after heating with phosphorus tribromide, some of the diol was recovered from the reaction mixture. The yields of 1:1-bis(bromomethyl)cyclohexane and 1:1-bis(bromomethyl)cyclopentane were 55% and 21% respectively; the latter compound has not been prepared before.

The final reaction between the dibromo-compounds and zinc to form the spirohydrocarbons was satisfactory in that yields of 89% of the crude product were obtained in both cases. The compounds were purified by distillations in semi-micro apparatus, and the two spiranes spiro(2:4) heptane, and spiro(5:2)octane, were thus produced. The former compound, b.p. 93-94°, n_D^{25}1.4282, d_4^{20}0.79044, has not previously been prepared.

It has been mentioned already (see p. 5) that the scheme to synthesise 'stick' spiro-compounds of the type  from 1:1:5:5-tetracarbethoxyspiroheptane was abandoned because of the failure to isolate the pure ester produced in the malonic ester synthesis; the oil could not be distilled without decomposition. The reduction of the impure ester with lithium aluminium hydride gave a liquid having a composition which did not correspond to that of 1:1:5:5-tetra(hydroxymethyl)-spiroheptane, therefore the scheme was not further studied.

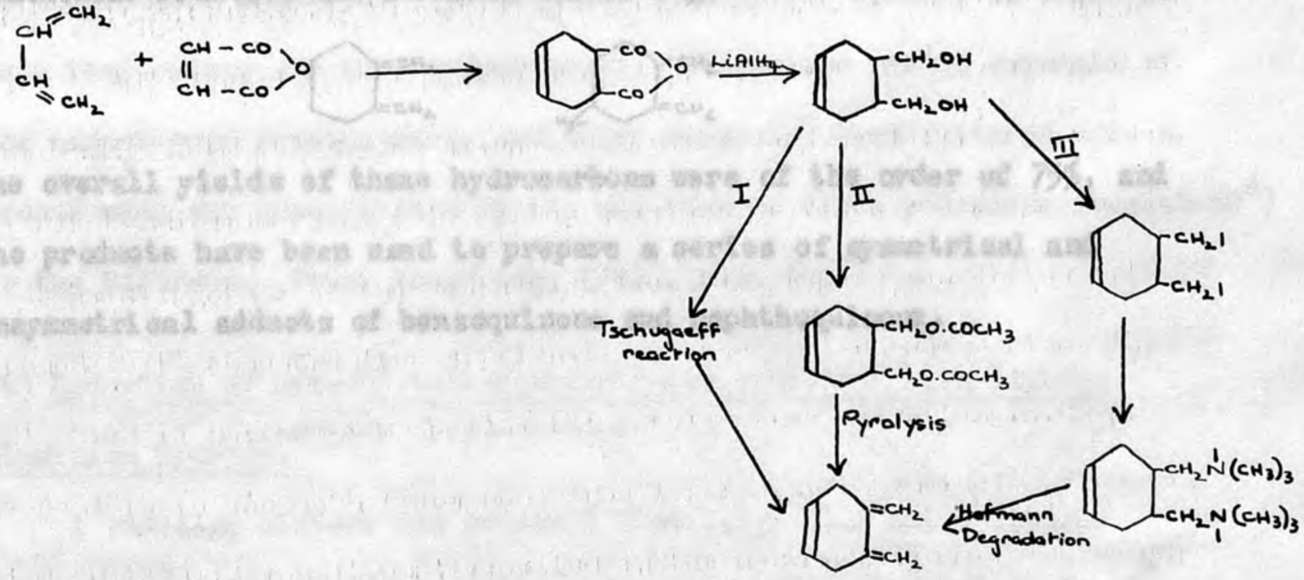
Section II.

The Formation of o-Xylene through 4:5-Dimethylenecyclohexene.

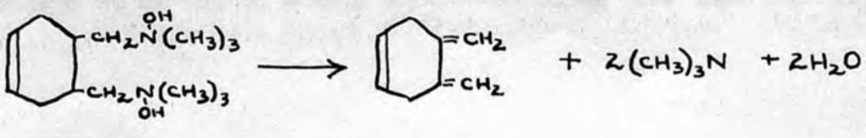
Introduction.

A study of the syntheses and properties of dimethylene-cyclohexene compounds has not been investigated before. This section deals with the possible methods of preparation of 4:5-dimethylenecyclohexene with a view to studying its chemical behaviour, and its interconversion to form o-xylene.

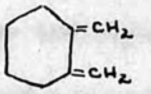
The three schemes of synthesis considered were as follows:

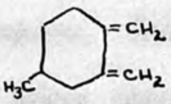


Schemes I and III were attempted. The Tschugaeff reaction was favoured as it has been used successfully to prepare olefines from the corresponding alcohols without causing any rearrangement in the molecule. The third scheme although somewhat lengthy was thought not to be condusive to any intramolecular rearrangement: this scheme involves the process of degradation of a quaternary ammonium compound to give an olefine, water, and trimethylamine,



a reaction which is the basis of the important Hofmann degradation so often used for the investigation of the structure of compounds of unknown constitution. The standard method of pyrolysis of an acetate to produce an olefine in scheme II was considered to be rather drastic for the production of 4:5-dimethylene*cyclo*hexene, a compound which was so likely to isomerise to form the corresponding aromatic compound. This method has, however, been very successfully employed by Bailey, Rosenberg, and Young, (*J. Amer. Chem. Soc.*, 1953, *75*, 4780; 1954, *76*, 1940; 2251), to synthesise reactive and strained dienes e.g.





The overall yields of these hydrocarbons were of the order of 75%, and the products have been used to prepare a series of symmetrical and unsymmetrical adducts of benzoquinone and naphthoquinone.

Section II

Experimental.

(a) Preparation of cis-$\triangle^4$-tetrahydrophthalic anhydride.

180G. (1.0 mol.) 1:3-butylene glycol were heated with 70g. (0.2 mol.) p-toluene sulphonic acid to 180° on a metal-bath. The dehydration products were passed through a vertical air-condenser, an inclined water-condenser fitted with a distillate receiver, an ice-trap, and finally, through a train of three Drechsel bottles, the first being empty and the next two containing weighed quantities of benzene. After three hours the dissolved butadiene was weighed, (26g. 24% yield), and the corresponding molecular quantity of finely powdered maleic anhydride (47g.) was added to the benzene solution. The reaction mixture was allowed to stand at room temperature for twenty-four hours. Colourless needle crystals of the adduct were precipitated, and after these had been filtered off, a second crop was precipitated by the addition of light petroleum (b.p.40-60°) to the filtrate. Total yield 68g. (93%), m.p. 102°.

(b) Reduction of cis-$\triangle^4$-tetrahydrophthalic anhydride with lithium aluminium hydride.

A reducing mixture was prepared from 7.5g. (1.2 mol.) lithium aluminium hydride in 500ml. anhydrous ether. 25G. (1.0 mol.) cis-$\triangle^4$-tetrahydrophthalic anhydride were slowly added to the mixture by extraction from a thimble in a Sohxlet apparatus. The reaction mixture was heated on a water-bath for an hour after the extraction was complete. The excess of lithium aluminium hydride was decomposed by the addition of water, and 5% v/v sulphuric acid was added until the mixture became clear. The ether layer combined with three ether extracts from the aqueous layer, were dried over anhydrous potassium carbonate. The ether was removed by distillation, and the pale yellow, viscous, liquid which remained was distilled under reduced pressure.

10G. colourless, viscous, liquid, b.p. 169-170°/11mm., n_D^{25}1.5092, were collected, which could not be solidified. After the product had stood for several weeks at 0° a few crystals separated out. Another 4g. of product were obtained by continuously extracting the aqueous layer with ether for twenty-four hours. Total yield 14g. (61%).

Analysis. cis-4:5-bis(hydroxymethyl)cyclohexene.

Found: C, 67.6 ; H, 10.2.

$C_8H_{14}O_2$ requires : C, 67.6 ; H, 9.9%

(c) Preparation of methyl cis-cyclohexene-4:5-dicarboxylate.

A mixture of 48g. cis-Δ^4-tetrahydrophthalic anhydride, 500ml. methyl alcohol, and 20ml. concentrated sulphuric acid, was heated under reflux for seven hours on a water-bath. Most of the alcohol was distilled off, and the remaining liquid was poured into twice its volume of water and neutralised by the addition of solid sodium bicarbonate. A colourless, sweet-smelling oil was precipitated which was extracted with ether. The combined extracts were dried over anhydrous magnesium sulphate. The ether was removed by distillation, and the remaining oil was distilled under reduced pressure. 56.5G. (93%) liquid, b.p. 116-117°/5.5mm., n_D^{25}1.4726, were collected.

The method used above for the preparation of the dimethyl ester is less complicated than the procedure given by Cope and Herrick, (J.Amer.Chem. Soc., 1950, 72, 985) in which the anhydride, the alcohol, and p-toluene sulphonic acid monohydrate are heated under reflux for 16 hours. Toluene is then added and the azeotropic mixture of methanol, water and toluene is distilled off at 75-78° until the distillation temperature begins to drop. More methanol is then added, and the procedure of refluxing and azeotropic distillation is repeated. The remaining toluene and methanol are removed under reduced pressure, and the residue is extracted with ether. Yield 80%, b.p. 120-122°/5mm., n_D^{25} 1.4700.

(d) Reduction of methyl cis-cyclohexene-4:5-dicarboxylate with lithium aluminium hydride.

55G. (1.0 mol.) methyl cis-cyclohexene-4:5-dicarboxylate in 100ml. anhydrous ether, were added dropwise to a reducing mixture of 13.5g. (1.3 mol.) lithium aluminium hydride in 400ml. anhydrous ether, at such a rate as to maintain steady boiling of the ether. After the addition was complete, the reaction mixture was allowed to stand for one hour, after which time water was added to decompose any excess of lithium aluminium hydride. Dilute hydrochloric acid was added until the mixture was clear. The ether layer was isolated, and the aqueous layer was extracted continuously for 24 hours. The combined extracts were dried over anhydrous potassium carbonate. After the ether had been removed by distillation 33.5g. pale yellow liquid remained; distillation under reduced pressure of the product gave 30g. (76%) cis-4:5-bis(hydroxymethyl)cyclohexene, b.p. 168-170°/11mm.

(e) Preparation of the di-p-toluenesulphonyl derivative of cis-4:5-bis(hydroxymethyl)cyclohexene.

An ice-cold solution of 110g. (2.1 mol.) p-toluene sulphonyl chloride in 350ml. dry pyridine was added slowly to a cool solution of 37.7g. (1.0 mol.) cis-4:5-bis(hydroxymethyl)-cyclohexene in 100ml. dry pyridine. The mixture was allowed to stand overnight at 0°, and then poured into an excess of dilute hydrochloric acid. An oil was precipitated which solidified on cooling. The precipitate was filtered off and dissolved in chloroform. The solution was washed with 10% sodium bicarbonate solution, then water, and finally dried over anhydrous magnesium sulphate. The chloroform was removed by distillation, and the remaining oil was crystallised from methanol. The product was 23g. (19%) colourless needles, m.p. 94.5°.

~~Analysis. Di-p-toluenesulphonyl derivative of cis-4:5-bis(hydroxymethyl) cyclohexene.~~

~~An ice-cold solution of 110g. (2.1 mol.) p-toluene sulphonyl chloride in 350ml. dry pyridine was added slowly to a cool solution of 37.7g. (1.0 mol.) cis-4:5-bis(hydroxymethyl)-cyclohexene in 100ml. dry pyridine. The mixture was allowed to stand overnight at 0°, and then poured into an excess of dilute hydrochloric acid. An oil was precipitated which solidified on cooling. The precipitate was filtered off and dissolved in chloroform. The solution was washed with 10% sodium bicarbonate solution, then water, and finally dried over anhydrous magnesium sulphate. The chloroform was removed by distillation, and the remaining oil was crystallised from methanol. The product was 23g. (19%) colourless needles, m.p. 94.5°.~~

Analysis. Di-p-toluenesulphonyl derivative of cis-4:5-bis(hydroxymethyl)-cyclohexene.

Found: C, 58.7; H, 5.5 ; S, 14.6

$C_{22}H_{26}O_6S_2$ requires: C, 58.6 ; H, 5.8 ; S, 14.2%

The experiment was repeated several times and it was found that the yield of the ditoluene sulphonate was considerably decreased when the pyridine was distilled off under reduced pressure before pouring the reaction mixture into dilute hydrochloric acid.

(e) Preparation of cis-4:5-bis(iodomethyl)cyclohexene.

A mixture of 23g. (1.0 mol.) sulphonic ester and 33g. (4.4 mol.) sodium iodide in 360ml. dry acetone was boiled under reflux on a water-bath for sixteen hours. The precipitated sodium p-toluene sulphonate was filtered off and weighed 19.3g. (theoretical yield 19.9g). The acetone was removed from the filtrate under reduced pressure. Addition of water to the residue precipitated a heavy oil which was dissolved in chloroform and washed with 5% sodium thiosulphate solution and then with water. The solution was dried over anhydrous magnesium sulphate, and the chloroform was removed under vacuum. The product was 17.5g. (95%) pale yellow oil.

(g) Reaction between cis-4:5-bis(iodomethyl)cyclohexene and trimethylamine.

The gas produced by heating 150ml. 21% aqueous trimethylamine solution was passed through a spiral water-condenser, and then dried by passing through a column of soda-lime. It was finally dissolved in 60ml. cool, dry acetone.

17.5g. (1.0 mol) cis-4:5-bis(iodomethyl)cyclohexene dissolved in 50ml. dry acetone were added dropwise to the gently refluxing solution of trimethylamine in acetone. The reaction mixture was heated under reflux until no trimethylamine could be detected at the top of the condenser; this was approximately three hours. The acetone was removed by distillation, and some pale yellow liquid, and a white solid remained. More solid was precipitated when anhydrous ether was added to the mixture. The solid was filtered off, and recrystallised from 95% ethyl alcohol. Yield 0.8g., m.p. 158-160°(decomp.).

Analysis. cis-4:5-bis(dimethylaminomethyl)cyclohexene dimethiodide.

Found: I, 52.6 ; 52.2

$C_{14}H_{30}N_2I_2$ requires: I, 52.9%

Ether was distilled from the filtrate leaving 14g. liquid which proved to be the starting material.

Reaction under pressure.

1.5g. cis-4:5-bis(iodomethyl)cyclohexene were heated with 2g. trimethylamine in 6ml. dry acetone at 100° for two hours in a sealed glass tube. A considerable quantity of solid separated out which was filtered off, and more solid was precipitated in the filtrate with anhydrous ether; this too was isolated by filtration. The product was recrystallised from 95% ethyl alcohol. Yield 0.8 g. (40%).

This experiment was repeated many times and almost quantitative yields were obtained.

(h) Formation and decomposition of the quaternary ammonium hydroxide.

Silver oxide was prepared from 40g. silver nitrate and 20g. potassium hydroxide. The precipitated oxide was thoroughly washed with water by decantation. 21g. quaternary ammonium iodide were added to the moist oxide, and the mixture was shaken for two hours. The rapid formation of silver iodide was observed. The reaction mixture was filtered, and the residue was washed several times with water. The washings and the filtrate were combined and distilled. The rate of distillation was slow, and the liberation of trimethylamine was detected. When only 20ml. liquid remained in the distillation flask, a colourless oil commenced to distil over with the water. This continued until the flask was heated to dryness. The layer of oil which formed the upper layer of the aqueous distillate was extracted with a small quantity of ether. The extracts were dried over anhydrous magnesium sulphate, and the ether was removed under vacuum. About 4ml. liquid remained which was distilled from sodium. The distillation flask was heated in an oil-bath at 180°, and 2g. liquid, b.p. 143°, n_D^{25} 1.5017, were collected. This product did not decolourise a solution of bromine in carbon tetrachloride.

(i) Preparation of the sulphonamide of o-xylene.

The method given by Huntress and Autenrieth, (*J. Amer. Chem. Soc.*, 1941, *63*, 3446) and Huntress and Carten, (*J. Amer. Chem. Soc.*, 1940, *62*, 511) was used.

5 ml. chlorosulphonic acid were added dropwise with continuous stirring to an ice-cold solution of 1.0g. pure *o*-xylene in 5ml. chloroform. When the addition was complete, stirring was continued for 45 minutes. The reaction mixture was then allowed to come to room temperature, and after standing for twenty minutes it was poured into a 50ml. beaker containing crushed ice. The chloroform layer was isolated and washed several times with water and then dried over anhydrous magnesium sulphate. The chloroform was evaporated off, and the pale yellow oil which remained was dissolved in warm light petroleum (b.p. 40-60°) and left to crystallise. Colourless needles, m.p. 52°, were formed. These crystals were

thoroughly mixed with 2g. powdered ammonium carbonate and heated in a water-bath at 100° for thirty minutes. 10ml. water were added and the mixture was filtered; the residue was washed several times with 10ml. portions of water, and then transferred to a beaker containing warm dilute sodium hydroxide solution when most of the solid dissolved. The solution was filtered, and the filtrate was acidified with 6N sulphuric acid. Colourless plates were precipitated which were filtered off and recrystallised from ethyl alcohol, m.p. 144-145°.

(j) Preparation of the sulphonamide of the synthesised compound.

The procedure was exactly as described above, and the following results were obtained:
m.p. of the sulphonyl chloride 51-52°.
m.p. of the sulphonamide 143-144°.
Mixed m.p. of the sulphonamides prepared in experiments (i) and (j) 143-145°.

(k) Dehydration of cis-4:5-bis(hydroxymethyl)cyclohexene.

20G. (1.0 mol.) diol were distilled from 3g. 2-naphthalene sulphonic acid. A pale yellow liquid separated out as the upper layer in the aqueous distillate. The product was salted out with sodium chloride and isolated. After the liquid had been dried over anhydrous sodium carbonate it was distilled again from 2-naphthalene sulphonic acid, and the process of extraction was repeated. Distillation of the final product from a semi-micro distillation apparatus with an 8" vacuum-jacketed Vigreux column gave the following fractions:

1	170-174°	n_D^{25} 1.4857	0.3g.
2	174-176°	1.4928	0.7g.
3	176-178°	1.4887	0.5g.
4	178-179°	1.4888	3.8g.

Fraction 4, was a colourless, mobile liquid having a strong odour.

Analysis cis-1':4':2:3:4:5-hexahydro-3:4-benzofuran.

Found: C, 77.6 ; H, 9.6

$C_8H_{12}O$ requires: C, 77.4 ; H, 9.7%

(1) Attempt to rupture the ring of the cis-cyclic ether

5g. cis-cyclic ether were heated under reflux for six hours in 400ml. saturated hydrobromic acid solution. The mixture was cooled and poured into water, when a dark brown oil was precipitated. The oil was extracted with ether, and the combined extracts were washed with 5% sodium carbonate solution and finally with water. This ethereal solution was dried over calcium chloride, and after the ether had been removed under reduced pressure, the remaining oil was distilled from a semi-micro distillation apparatus. Three fractions were collected.

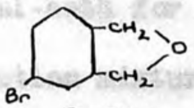
1	160-164°/25mm.	2.5g.	n_D^{25} 1.5263
2	165-167°	2.0g.	1.5267
3	167-170°	0.5g.	1.5480

Some decomposition of the product occurred during distillation, this was accompanied by the evolution of hydrogen bromide. All the fractions rapidly darkened in colour on standing, although they were sealed up immediately after distillation.

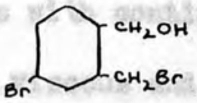
Analysis. Fraction 1. Test for unsaturation was negative.

Found: Br, 40.0%

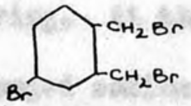
The following compounds are possible products of the reaction:



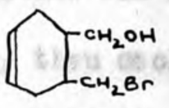
Br 39.2



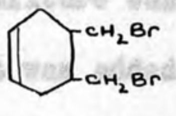
Br 56.0



Br 69.0



Br 39.2



Br 60.0

(m) Attempted Tschugaeff reaction on cis-4:5-bis(hydroxymethyl)-cyclohexene.

The method used was similar to the original preparation introduced by Tschugaeff for the synthesis of an olefine from the corresponding alcohol, (Tschugaeff, Ber., 1899, 32, 3332; 1900, 33, 735, 3118: 1901, 34, 2276; 1904, 37, 1481; 1901, 42, 4631).

Purification of reagents.

Toluene-this was dried over sodium and then distilled. The fraction with, b.p. 110.6°, was collected.

Carbon disulphide-this was dried over calcium chloride and then distilled. The fraction with, b.p. 46.3°, was collected.

A solution of 20g. (1.0 mol.) cis-4:5-bis(hydroxymethyl)-cyclohexene in 15g. toluene was heated to boiling on an oil-bath, and 6.6g. freshly cut sodium was slowly added in about 0.5g. quantities. At first a vigorous reaction occurred accompanied by the separation of the solid sodio-compound. The reaction subsided as additions of sodium were continued. The mixture was heated under reflux and stirred vigorously for one hour on an oil-bath at 170-180°, and then heated strongly on a metal-bath for eight hours with continuous stirring. At this stage the reaction mixture was very viscous and some unchanged sodium was visible. The solid was washed with toluene into a mixture of 250ml. dry ether and 26g. (2.4 mol.) carbon disulphide contained in a litre flask. Immediately a yellow precipitate was formed. The mixture was heated for thirty minutes on a water-bath, then cooled, and to it was added 60g. (3.0 mol.) methyl iodide. No immediate reaction was observed, but as the mixture was heated under reflux on a water-bath the yellow precipitate was replaced by a fine white powder, which was presumably sodium iodide. The solid was filtered off, and the yellow filtrate was dried over anhydrous magnesium sulphate. The solvents were removed under reduced pressure, and the pale yellow oil which remained could not be solidified. A drop of this oil gave a positive test for unsaturation with a solution of bromine in carbon tetrachloride thus indicating the presence of the cyclohexene

skeleton. The oil was distilled from a metal-bath, and a fraction, b.p. 180-184°, was collected when the distillation flask was heated to 230°. This fraction was a pale yellow, foul-smelling liquid which was redistilled. The three fractions collected,

1	b.p. 178-180°	1.7g.
2	b.p. 180-186°	1.3g.
3	b.p. 186-187°	3.2g.

indicated that no further change had occurred during the second distillation.

The modified Tschugaeff reaction of Whitmore and Simpson,

(J. Amer. Chem. Soc., 1933, 55, 3810) was tried on *cis*-4:5-*bis*(hydroxymethyl)-*cyclo*hexene. The first stage involves the reaction between finely powdered sodium hydroxide and the diol in a mixture of ether and carbon tetrachloride. This was also unsuccessful as a method of producing the required olefine, 4:5-dimethylene*cyclo*hexene.

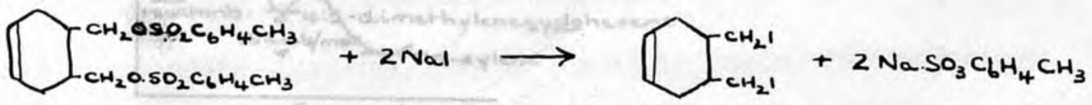
Section II

Discussion.

cis-Δ^4- Tetrahydrophthalic anhydride was prepared in good yield by the Diels Alder reaction between butadiene and maleic anhydride; the procedure of leaving the reactants standing in benzene solution for twenty-four hours at room temperature gives yields as high as those obtained in the older methods which involved heating the reaction mixture to 100°(Diels and Alder, *Annalen*,1927, *459*, 113).

cis-4:5-*Bis*(hydroxymethyl)*cyclo*hexene was produced in two ways, (a) by reduction of the anhydride with lithium aluminium hydride in a Sohxlet apparatus, and (b) by reduction of the ether soluble methyl *cis*-*cyclo*hexene-4:5-dicarboxylate with lithium aluminium hydride. It was found in this reduction that the intramolcular formation of the cyclic ether was caused by decomposing the reduction complex with 20% sulphuric acid solution, it was also produced when the diol was distilled at high pressures. The best yield of diol was obtained by reducing the dimethyl ester, and using dilute hydrochloric acid to decompose the complex. Haggis and Owen (*J.*, 1953, 389) established the stereo-specificity of this method in their studies of the reduction by lithium aluminium hydride of dimethyl-*trans*-hexahydrophthalate, *cis*-hexahydrophthalic anhydride, and *cis*-diethyl hexahydrophthalate.

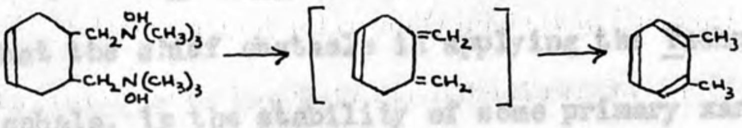
The basis of the method of preparation of the di-*p*-toluenesulphonyl derivative of *cis*-4:5-*bis*(iodomethyl)*cyclo*hexene was obtained from the paper by Haggis and Owen (idem. ibid., p.394) on Alicyclic Glycols Part VIII, in which they study the reactions of 1:2-*bis*(hydroxymethyl)*cyclo*hexane. The yield of *cis*-sulphonic ester obtained was not good (see p.46) but this is attributed to the simultaneous formation of the cyclic oxide which was identified in the products. The cis-4:5-bis (iodomethyl)cyclohexene prepared from the cis-sulphonic ester was not purified by distillation, as the only attempt to do this caused severe decomposition of the compound, this is probably because a pressure below 1.5 mm. could not be obtained. The conditions given for the distillation of a similar type of compound, cis-1:2-bis(iodomethyl)cyclohexane, by Haggis and Owen, (idem.ibid., p. 395) are b.p. 100°(bath)/0.002mm. The almost theoretical yield of sodium toluene-p-sulphonate produced in the reaction



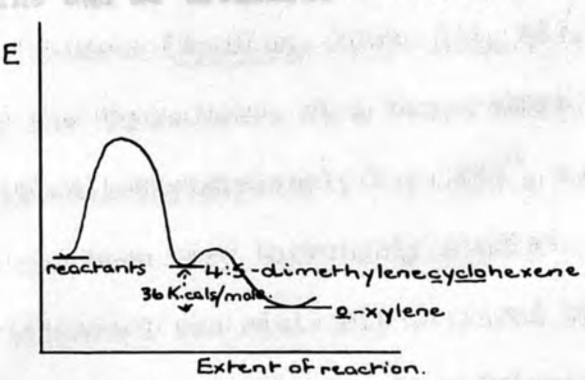
may be an indication of the purity of the di-iodide obtained.

The Hofmann degradation was successful, but the failure to isolate 4:5-dimethylene cyclohexene seems to indicate that the isomerisation to form o-xylene must occur during the final distillations. Tests for unsaturation on samples of the distillate obtained from the degradation of the quaternary ammonium hydroxide did not prove conclusively that 4:5-dimethylenecyclohexene was present. The product obtained from the distillation of the crude hydrocarbon (see p. 49) gave a negative test for unsaturation. The physical properties recorded for this product were, b.p. 143°, n_D^{25} 1.5019, which compare favourably with those of o-xylene. Literature values given for the boiling-point of o-xylene vary between 142°, and 144.7°; Egloff, (Physical Constants of Hydrocarbons, 1946, III, 65) quotes, b.p. 144.18°, and n_D^{25} 1.50516, as accepted physical constants.

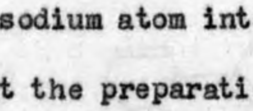
On consideration of the energetics of the system,



it is not surprising that o-xylene is formed in preference to 4:5-dimethylenecyclohexene, since o-xylene is more stable to the extent of the resonance energy of the benzene ring system.



The lack of success in the attempt to carry out the Tschugaeff reaction on cis-4:5-bis(hydroxymethyl)cyclohexene is attributed to the failure to form the di-sodio derivative of the diol. There is no doubt that the sodium and the diol did react together, but the mono-sodio derivative was precipitated immediately on formation, and therefore, the introduction of another sodium atom into the molecule becomes very difficult. Assuming that the preparation proceeded as far as to form the mono-methyl xanthate ester, the distillation of this compound did not cause any decomposition to produce 4-hydroxymethyl-5-methylene-cyclohexene. The yellow liquid obtained (see p.53) contained sulphur, and was thought to be,



Whitmore and Simpson, (J. Amer. Chem. Soc., 1933, 55, 3810), have pointed out that the chief obstacle in applying the Tschugaeff reaction to primary alcohols, is the stability of some primary xanthates towards heat. Some can be distilled *in vacuo*, and even when boiled at atmospheric pressure their decomposition is slow and incomplete, so that little or no yield of olefine can be obtained.

Section III. Part 1.

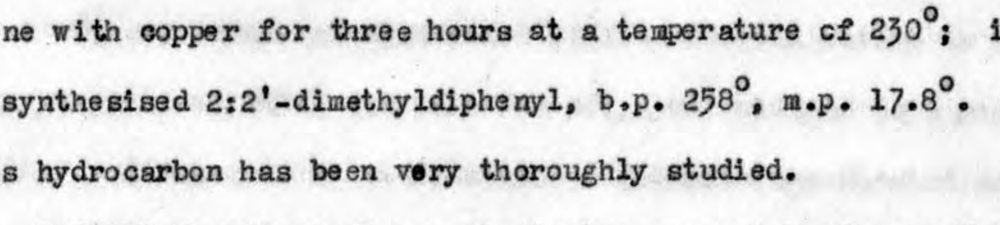
Anomalous Reductionsof 2:2'-diacetyldiphenyl.

Introduction.

Only two compounds in the 2:2'-dialkyldiphenyl series have been prepared, these are 2:2'-dimethyl- and 2:2'-diethyl-diphenyl. The former was prepared as early as 1867 by Fittig, (Annalen, 1867, 138, 178) from the reaction between sodium and *o*-bromotoluene. This method was later improved by Ullmann (Annalen, 1904, 332, 42), who heated *o*-iodotoluene with copper for three hours at a temperature cf 230°; in this way he synthesised 2:2'-dimethyldiphenyl, b.p. 258°, m.p. 17.8°. Since then this hydrocarbon has been very thoroughly studied.

2:2'-Diethyldiphenyl was similarly prepared by Mascarelli and Longo (Gazzetta., 1941, 71, 289), in the reaction between *o*-iodo-ethylbenzene and copper at 250°; the hydrocarbon, b.p. 147°/14-15mm., was produced, and no other data were recorded for this compound.

An attempt was made to synthesis 2:2'-diethyldiphenyl and some new higher members of the 2:2'-dialkyldiphenyl series using the following possible four-stage synthesis:



This was adopted since the preparation of some of the *o*-iodo-alkylbenzenes for the Ullmann reaction would be difficult, and it was probable that with increased chain-length of the alkyl group the yields of the Ullmann products would be poor.

The experimental work that follows shows how the anomalous result of the Clemmensen reduction on 2:2'-diacetyldiphenyl led to an investigation of the reduction of this compound by the Huang Minlon, Meerwein-Ponndorf-Verley methods, and with lithium aluminium hydride.

Section III. Part I.

Experimental.

Preparation of 9:10-phenanthraquinone.

The method of Linstead and Levine, (J. Amer. Chem. Soc., 1942, 64, 2023) was used. 300G. (2.0 mol.) potassium dichromate were added in small quantities to a stirred hot mixture of 100g. (1.0 mol.) commercial phenanthrene in 500 ml. concentrated sulphuric acid and 1.5 l. water. When the addition was complete, stirring and heating were continued for one hour, and water was then added to increase the volume to about 4 litres. The precipitated solid was filtered off, and returned to a beaker for further oxidation in a hot solution of 250 ml. concentrated sulphuric acid and 650 ml. water, with 175g. (1.0 mol.) potassium dichromate. The crude quinone was isolated as before, and then heated with 3 l. water, and 2 kg. sodium bisulphite until all the quinone had reacted. The solid sodium bisulphite addition compound was separated by filtration (this stage separates the product from anthraquinone which forms a soluble addition compound), and treated with concentrated sodium hydroxide solution to regenerate the phenanthraquinone. The product was filtered off, thoroughly washed with water, and then recrystallised from glacial acetic acid after heating the solution under reflux for ten minutes with decolourising charcoal. 56G. (48%) phenanthraquinone, m.p. 205-206°, were obtained.

This preparation was repeated using phenanthrene (Puriss) which gave after the second oxidation a product having a melting-point of 208-209°. After the formation and decomposition of the bisulphite compound, followed by recrystallisation from glacial acetic acid, the melting point was 209°. In later preparations of phenanthraquinone, therefore, the formation of the bisulphite compound was omitted. Linstead and Levine (<u>ibid.</u>, p.2024) quote a melting-point of 205-207°.

<u>Preparation of 9:10-dihydroxy-9:10-dimethylphenanthrene.</u>

This preparation was carried out according to the method of Zincke and Tropp, (<u>Annalen,</u>1908, <u>362,</u> 242) using methyl iodide instead of methyl bromide for the preparation of the Grignard reagent.

A Grignard reagent was prepared from 4.6g. magnesium and 30g. (3.0 mol.) methyl iodide in 300 ml. anhydrous ether. To it was added slowly with vigorous stirring 15g. (1.0 mol.) finely powdered phenanthraquinone. A bluish-green mixture was formed. After the addition was complete, the reaction mixture was warmed on a water-bath for one hour, and then most of the ether was removed by distillation. The residue was heated under reflux for two hours with 690 ml. dry benzene. The benzene solution was allowed to cool, and poured into ice-water and decomposed with dilute sulphuric acid solution, when the colour changed from green to orange. The benzene-ether layer was isolated and combined with two ether extracts from the aqueous layer. Most of the ether was distilled from the extract, and the remaining solution was heated under reflux with decolourising charcoal and a few copper turnings for fifteen minutes. The solution was filtered, and the solvent was evaporated off until a pale yellow solid commenced to separate out. When the solution had cooled, the solid was filtered off and recrystallised from chloroform. 12G. 9:10-dihydroxy-9:10-dimethylphenanthrene, m.p. 161-163°, were produced.

Preparation of 2:2'-diacetyldiphenyl.

The method of Zincke and Tropp (Annalen, 1908, 363, 302) was used for this preparation.

40G. 9:10-dihydroxy-9:10-dimethylphenanthrene were dissolved in 400 ml. hot glacial acetic acid, and to this was slowly added with stirring, 11.1g. chromium trioxide dissolved in 110 ml. water. The reaction mixture was allowed to cool, and the diketone separated out; more was precipitated by diluting the solution with water. The pale yellow solid was filtered off and recrystallised from aqueous alcohol, m.p. 86-87°. Further recrystallisation from *cyclo*hexane and then aqueous alcohol raised the melting-point to 92°.

Zincke and Tropp give m.p. 84°.

A yield of 28g. (70%) of 2:2'-diacetyldiphenyl was obtained.

Attempted Clemmensen reduction on 2:2'-diacetyl diphenyl.

Preparation of zinc amalgam.

A mixture of 150g. zinc wool, 11.5g. mercuric chloride, 7.5 ml. concentrated hydrochloric acid, and 187.5 ml. water was shaken for five minutes, and the liquid was then removed by decantation.

Clemmensen reduction.

A mixture of 114 ml. water, and 150 ml. concentrated hydrochloric acid was added to the amalgam, immediately followed by the addition of 28g. 2:2'-diacetyl-diphenyl. The mixture was warmed on a water-bath for fifteen minutes, and then heated under reflux for six hours, adding 15 ml. concentrated hydrochloric acid at the end of every two hours. The reaction mixture was allowed to stand overnight. The liquid was separated by decantation from the unchanged zinc, and salted out with sodium chloride, but only a trace of oil was formed on the liquid surface. The unchanged zinc in the reaction flask appeared to be coated with a white solid which was extracted repeatedly with boiling ether. The extracts were combined and dried over anhydrous magnesium sulphate. The ether was removed by distillation leaving 24.5g. pale yellow solid slightly contaminated with a sweet smelling oil. The melting-point of the crude material was 138-140°, and one recrystallisation from ethyl alcohol produced needle crystals, m.p. 142-144°, and this was subsequently raised to 144°.

Investigation of product.

The crystalline product was tested for the presence of carbonyl groups with 2:4-dinitrophenylhydrazine, for unsaturation with bromine in carbon tetrachloride and potassium permanganate, and for carbinol groups with α-naphthyl isocyanate. All these tests gave negative results. The compound was insoluble in alkaline solutions, charred on standing in concentrated sulphuric acid, and was extremely soluble in benzene. Analysis showed that it was a hydrocarbon,

Found: C, 92.8 ; H, 7.0.

The picrate was prepared, and the orange product was recrystallised from ethyl alcohol to give fine needles, m.p. 192-193°.

These results are in agreement with the melting-points given for 9:10-dimethylphenanthrene, and its picrate, i.e. 144°, and 192°, (Rimmer, Christiansen, Brown and Sandin, *J. Amer. Chem. Soc.*, 1950, *72*, 2298).

Calculated for $C_{14}H_{10}$ (9:10-dimethylphenanthrene) C, 93.2 ; H, 6.8.%

Reduction of 2:2'-diacetyldiphenyl with lithium aluminium hydride.

A reducing mixture was prepared from 1.5g. (5.0 mol.) lithium aluminium hydride and 70 ml. anhydrous ether. 2.0g. (1.0 mol.) 2:2'-diacetyldiphenyl dissolved in dry ether were added dropwise to the mixture at such a rate as to maintain steady boiling of the ether. When the addition was complete, the reaction mixture was allowed to stand for thirty minutes before decomposing the excess of lithium aluminium hydride with ice-water. 2% v/v sulphuric acid solution was added until the mixture became clear, and the ethereal layer was isolated. The aqueous layer was extracted twice with ether, and the combined ether extracts were dried over anhydrous sodium sulphate. The ether was distilled off, leaving 1.85g. crystalline solid, m.p. 130-146°. The product was soluble in ethyl alcohol but came down as an oil, it was sparingly soluble in light petroleum (b.p. 80-100°). Three recrystallisations from benzene raised the melting-point to 146-148°. Recrystallisation from aqueous alcohol did not alter the melting-point. The mixed melting-point given on admixture with 9:10-dimethylphenanthrene (m.p. 144°) was 124-132°.

Found: C, 79.3 ; H, 7.5.

$C_{16}H_{18}O_2$ (2:2'-bis(α-hydroxyethyl)-diphenyl) requires, C, 79.3, H, 7.5.%

There appeared to be two compounds present in the crude product, one, m.p. 146-148°, (prisms) 2:2'-bis(α-hydroxyethyl)diphenyl which was less soluble in benzene than a very small quantity of 2:7-dihydro-2:7-

dimethyl-3:4-5:6-dibenzoxepin present in the form of needles. The latter caused the depression in melting-point in the early stages of the purification of the product.

Dehydration of 2:2'-bis(α-hydroxyethyl)-diphenyl.

2G. powdered diol were heated on a water-bath for one hour with 30 ml. 20% sulphuric acid solution. A pale yellow oily layer, having a pleasant odour was formed, and some needle crystals sublimed on to the sides of the flask. The product was extracted with ether and dried over anhydrous magnesium sulphate. The solvent was evaporated off, and the residual oil was recrystallised from ethyl alcohol. Needles. m.p.78°, were obtained.

Found: C, 85.9 ; H, 7.3.

$C_{16}H_{16}O$ (2:7-dihydro-2:7-dimethyl-3:4-5:6-dibenzoxepin)
requires, C, 85.7 ; H, 7.2.%

Attempted Huang Minlon reduction on 2:2'-diacetyldiphenyl.

A mixture of 20g. 2:2'-diacetyldiphenyl, 14g. sodium hydroxide, and 20 ml. 85% hydrazine hydrate solution in 200 ml. triethylene glycol, was heated under reflux for two hours. The reaction mixture was distilled free of water and excess of hydrazine hydrate, until its temperature rose to 195°. It was then heated under reflux for a further four hours. The viscous mass produced, and the aqueous distillate, were extracted with ether several times. The extracts were combined, washed with water, and dried over anhydrous magnesium sulphate. After the ether had been removed, about 20 ml. pale brown oil remained which was distilled under reduced pressure. The following fractions were obtained.

A	156-158°/6mm.	6.8g.	Very viscous liquid.
B	158-163° "	2.8g.	Pale yellow liquid.

Heating was continued, but although the temperature rose rapidly to 190°, no distillate came over, and decomposition was observed to be taking place in the distillation flask. At this stage heating was stopped. As the apparatus cooled, needle crystals separated out in the condenser and in the distillation flask; these were extracted with, and recrystallised from ethyl alcohol. The product, m.p. 143-144° formed a picrate, m.p. 193°. The mixed melting-point obtained with the picrate of authentic 9:10-dimethylphenanthrene was unchanged, it therefore may be concluded that 9:10-dimethylphenanthrene is one of the products of the Huang Minlon reduction on 2:2'diacetyldiphenyl.

Fraction A, partly solidified on standing to form a waxy, solid, m.p. 42-44°. Complete solidification of the product was achieved by cooling to 0°, and after recrystallisation from ethyl alcohol, a solid, m.p. 46-48°, was produced. This compound gave a negative test for the presence of a carbonyl group, but a positive test for unsaturation with bromine in carbon tetrachloride, and with potassium permanganate.

Found: C, 92.8 ; H, 7.0.%

The analysis shows that the compound is an unsaturated hydrocarbon. An estimation of double bonds with bromine in carbon tetrachloride, indicated the presence of one double bond.

Fraction B, deposited some needle crystals which were identified as 9:10-dimethylphenanthrene, and the remaining pale yellow liquid was found to contain some of the unsaturated hydrocarbon isolated in fraction A.

Part of the brown glassy residue in the distillation flask was dissolved in hot glacial acetic acid, and on cooling, a pale yellow solid was isolated which melted over a very wide range of temperature. Further treatment with <u>cyclo</u>-hexane did not purify the product; it was considered to be a hydrocarbon mixture, as apart from glacial acetic acid it was soluble only in hydrocarbon solvents, e.g. benzene, toluene, <u>cyclo</u>hexane.

<u>Hydrogenation of unsaturated hydrocarbon.</u>

1.0G hydrocarbon in 125 ml. glacial acetic acid was hydrogenated over platinum oxide catalyst for one and a half hours at a pressure of 64 lbs./sq.inch. 120 ml. solvent were distilled off, and the remaining liquid was poured into a large volume of water, and the precipitated oil was extracted with ether. The extract was washed in turn with 10% sodium carbonate solution and water, and dried over anhydrous magnesium sulphate. The ether was distilled off, leaving 0.7g. sweet-smelling oil.

<u>Tests for unsaturation.</u>

The product was tested with bromine in tetrachloride, and the solution was decolourised very slowly in the cold, but when heated, it decolourised rapidly with vigorous evolution of hydrogen bromide.

Baeyer Test. A drop of the product was dissolved in ethyl alcohol and two drops of 1% potassium permanganate solution were added; no brown colouration or precipitate were formed. This shows that the unsaturated hydrocarbon had been successfully hydrogenated.

Attempt to oxidise hydrogenation product.

0.4G. saturated hydrocarbon was heated under reflux with 2g. potassium permanganate, and 5g. potassium hydroxide in 50 ml. water for two days. After this treatment, the excess of permanganate was reduced with sulphur dioxide, and the original hydrocarbon was obtained.

Attempt to oxidise unsaturated hydrocarbon.

0.5G. unsaturated hydrocarbon was heated under reflux with 1.5g. nitrobenzene, and 2g. sodium hydroxide in 20 ml. water. Investigation of the product proved that no reaction had taken place.

Reaction between 2:2'-diacetyldiphenyl and hydrazine.

A mixture of 2.0g. 2:2'-diacetyldiphenyl and 1.0g. 85% hydrazine hydrate solution was dissolved in ethyl alcohol, and the solution was warmed on a water-bath for five minutes. Water was added dropwise until an oil was precipitated, and the mixture was allowed to stand overnight at 0°. Some crystals separated out, and the remaining oil was crystallised by vigorously stirring the mixture. The solid product was filtered off, and recrystallised twice from aqueous ethyl alcohol, and twice from absolute alcohol. Prisms, m.p. 167-168°, were obtained. Found: C, 82.0 ; H, 6.2 ; N, 11.8.% A negative test for unsaturation was obtained with this compound and a solution of bromine in carbon tetrachloride.

A mixture of 0.3g. of the above nitrogen containing compound, and 0.2g. sodium hydroxide in 5 ml. triethylene glycol was heated on a metal-bath for three hours at 220-240°. The reaction mixture was allowed to cool, extracted with ether, washed with water, and dried over anhydrous sodium sulphate. The ether was evaporated off, leaving about 0.2g. pale yellow needle crystals. After recrystallisation from ethyl alcohol, colourless, needles, m.p. 144.5° were produced. A melting-point of 144°, was obtained when a sample of the product was mixed with authentic 9:10-dimethylphenanthrene. A picrate, m.p. 193.5°, was prepared from the product.

It is evident that 9:10-dimethylphenanthrene is the product of decomposition of the compound obtained from the reaction between 2:2'-diacetyldiphenyl and hydrazine.

Reaction between 2:2'-diacetyldiphenyl and sodium hydroxide.

3.0G. 2:2'-diacetyldiphenyl were heated with 2.1g. sodium hydroxide in 30 ml. triethylene glycol to a temperature of 220°. A vigorous reaction was observed to take place. The mixture was allowed to cool to 150°, and was maintained at this temperature for two hours. The product was extracted with ether, washed with water, and dried over anhydrous magnesium sulphate. The ether was evaporated off, and the yellow oil which remained formed a glassy solid on standing. A sample of the product gave a positive test for unsaturation with bromine in carbon tetrachloride. The solid was sparingly soluble in alcohol and light petroleum, but readily soluble in benzene, cyclohexane, and other hydro-carbon solvents. An attempt to purify the product from cyclohexane produced a light brown solid having a melting-point which covered a wide range of temperature.

Attempted Meerwein-Ponndorf-Verley reduction on 2:2'-diacetyl-diphenyl.

Preparation of aluminium *iso*propoxide.

13.5G. aluminium foil were washed in turn with dilute sodium hydroxide solution, water, acetone, and then dried. The foil was cut into small pieces and added to 150 ml. dry isopropyl alcohol, (distilled from freshly prepared calcium oxide), and 0.25g. mercuric chloride. The mixture was heated to boiling, and 2 ml. carbon tetrachloride, which acts as a catalyst for the reaction between aluminium and dry alcohols, were added. Heating under reflux was continued for four hours. The excess of *iso*propyl alcohol was removed under reduced pressure of 20mm. by heating the flask in an oil-bath at 90°. The condenser was removed, and a receiver was attached directly to the distillation flask. The temperature of the bath was raised to 170°, and 59.9g. viscous aluminium *iso*propoxide, b.p. 135-$145^{\circ}/10$mm. were collected.

Meerwein-Ponndorf-Verley reaction.

10.0G. (1.0 mol.) 2:2'-diacetyldiphenyl, 51g. (19.0 mol.) aluminium *iso*propoxide, and 210 ml. dry *iso*propyl alcohol were heated on a water-bath. The vapour was passed through a vertical double-surface condenser (without water flowing) and then through an inclined double-surface condenser (with water flowing). The first five drops of distillate gave a positive test for the presence of acetone with 0.1% 2:4-dinitrophenylhydrazine solution in dilute hydrochloric acid. The distillation was continued at the rate of eight drops per minute for one and a half hours, testing for acetone at regular intervals. When a negative test was obtained at the end of this period, cold water was passed through the vertical condenser, and the reaction mixture was heated under reflux for fifteen minutes. The distillation was restarted, and the test for acetone in the distillate was negative, thus showing that the reaction had finished.

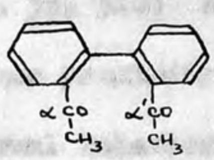
Most of the solvent was removed under reduced pressure, and the residual slurry was treated with dilute hydrochloric acid solution (70 ml. concentrated hydrochloric acid in 250 ml. water). An oily white product was formed which was extracted with ether and dried over anhydrous sodium sulphate. The solvent was distilled off, and a pale yellow viscous liquid remained which became cloudy after standing for twenty-four hours at 0°. The product appeared to be a mixture, and all attempts to isolate pure compounds were unsuccessful.

Section III. Part I.

Discussion.

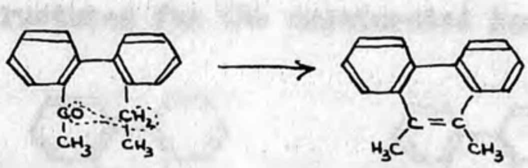
The preparation of 2:2'-diacetyldiphenyl was accomplished without difficulty, and the melting-point of this compound, (see p. 63) and of the intermediate product phenanthraquinone, (see p. 62) were considerably higher than recorded literature values.

Clemmensen reduction of 2:2'-diacetyldiphenyl produced an almost quantitative yield of 9:10-dimethylphenanthrene instead of the expected 2:2'-diethyldiphenyl. This anomalous reaction can be attributed to the close proximity of the α, α' carbon atoms of the acetyl groups in the diketone.



The mechanism of the Clemmensen reduction is not clearly understood, and in this particular case it is evident that a carbinol is not formed as an intermediate in the reaction since under the existing conditions, the cyclic ether would be the ultimate product.

It is possible, however, that one carbonyl group is reduced first, and that 9:10-dimethylphenanthrene is then formed by the elimination of water.



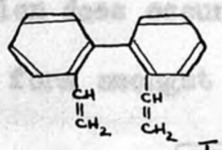
Some other anomalous Clemmensen reductions on aliphatic-aromatic ketones have been observed, e.g. in the preparation of ethylbenzene from acetophenone side reactions occurred to produce styrene, styrene polymers, and the pinacolone of acetophenone (Steinkopf and Wolfram, Annalen, 1923, 430, 113).

The only diacetyldiphenyl reported to have been reduced by the Clemmensen reaction is 4:4'-diacetyldiphenyl ether, (Tomita, J. Pharm. Soc. Japan., 1938, 58, 510) and this gave a normal product, which is to be expected if close proximity of carbonyl groups is responsible for the departure from normal behaviour of 2:2'-diacetyldiphenyl.

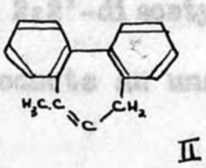
The Huang Minlon modification of the Wolff-Kishner reduction (J. Amer. Chem. Soc., 1946, 68, 2487) was attempted on 2:2'-diacetyldiphenyl. The procedure consists of heating under reflux a mixture of carbonyl compound, 85% hydrazine hydrate solution, and about three equivalents of sodium hydroxide in triethylene glycol. After an hour, water and excess of hydrazine hydrate are distilled off, and the mixture is heated under reflux for a further three hours. This method has been used to prepare diphenylmethane, n-propylbenzene, and cyclohexane, from the corresponding ketones in excellent yield.

The two products identified from the Huang Minlon reduction on 2:2'-diacetyldiphenyl were an unsaturated hydrocarbon having an analysis corresponding to $C_{16}H_{14}$, and 9:10-dimethylphenanthrene.

Possible structures for the unsaturated compound are,

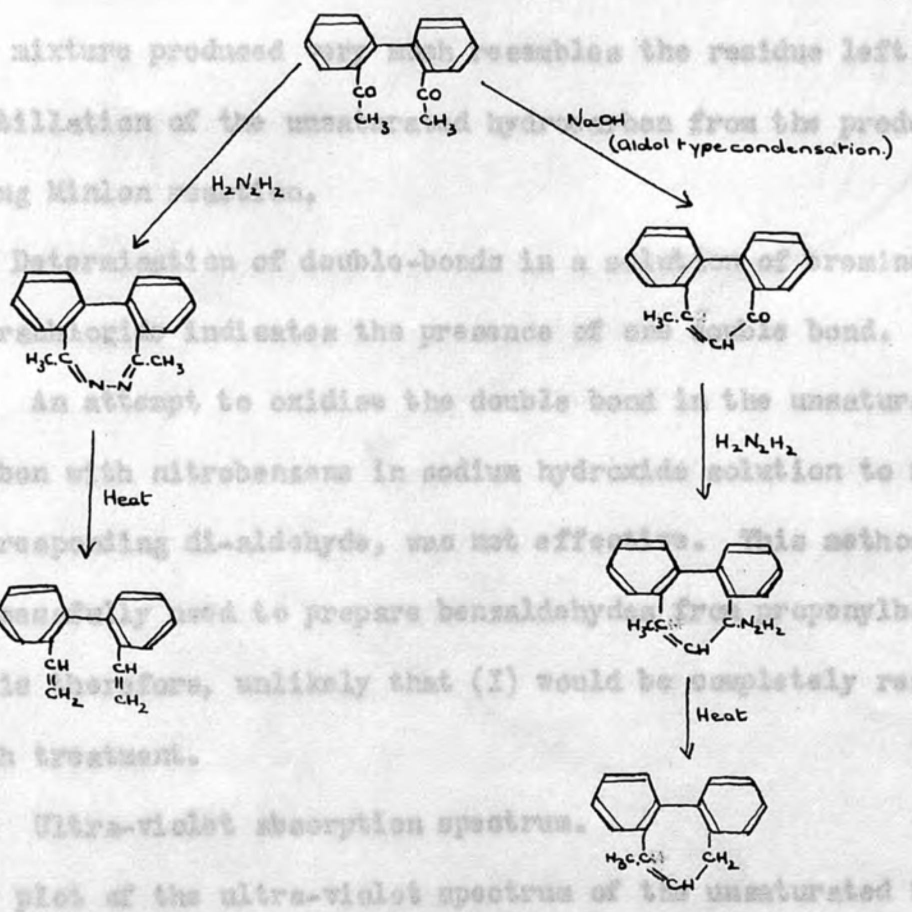


I



II

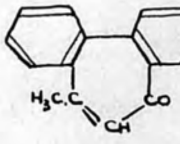
and these could have been formed in the following manner,



but the evidence obtained in subsequent experiments favoured structure II.

(a) The compound was hydrogenated, and the saturated product could not be oxidised with strong alkaline permanganate solution; there is no doubt that the side chains of the hydrogenation product of (I) i.e. 2:2'-diethyldiphenyl, would oxidise to give some diphenic acid, and the corresponding decomposition products.

(b) A reaction does occur between 2:2'-diacetyldiphenyl and sodium hydroxide to form amongst other products an unsaturated compound, possibly



The mixture produced very much resembles the residue left after distillation of the unsaturated hydrocarbon from the products of the Huang Minlon reaction.

(c) Determination of double-bonds in a solution of bromine in carbon tetrachloride indicates the presence of one double bond.

(d) An attempt to oxidise the double bond in the unsaturated hydrocarbon with nitrobenzene in sodium hydroxide solution to form the corresponding di-aldehyde, was not effective. This method has been successfully used to prepare benzaldehydes from propenylbenzene compounds. It is therefore, unlikely that (I) would be completely resistant to such treatment.

(e) Ultra-violet absorption spectrum.

The plot of the ultra-violet spectrum of the unsaturated hydrocarbon $C_{16}H_{14}$ is shown in fig. II. In the short-wave band the values ϵ_{max}36,500, λ_{max}2340, and ϵ_{min}20,000, λ_{min}2,180, with an inflexion at λ 2,550 are obtained. It is obvious that this curve bears no resemblance to that shown for 2:2'-dimethyl-diphenyl, which is typical of 2:2'-substituted diphenyls in failing to show the characteristic intense diphenyl band in the region 2400-2700°A.

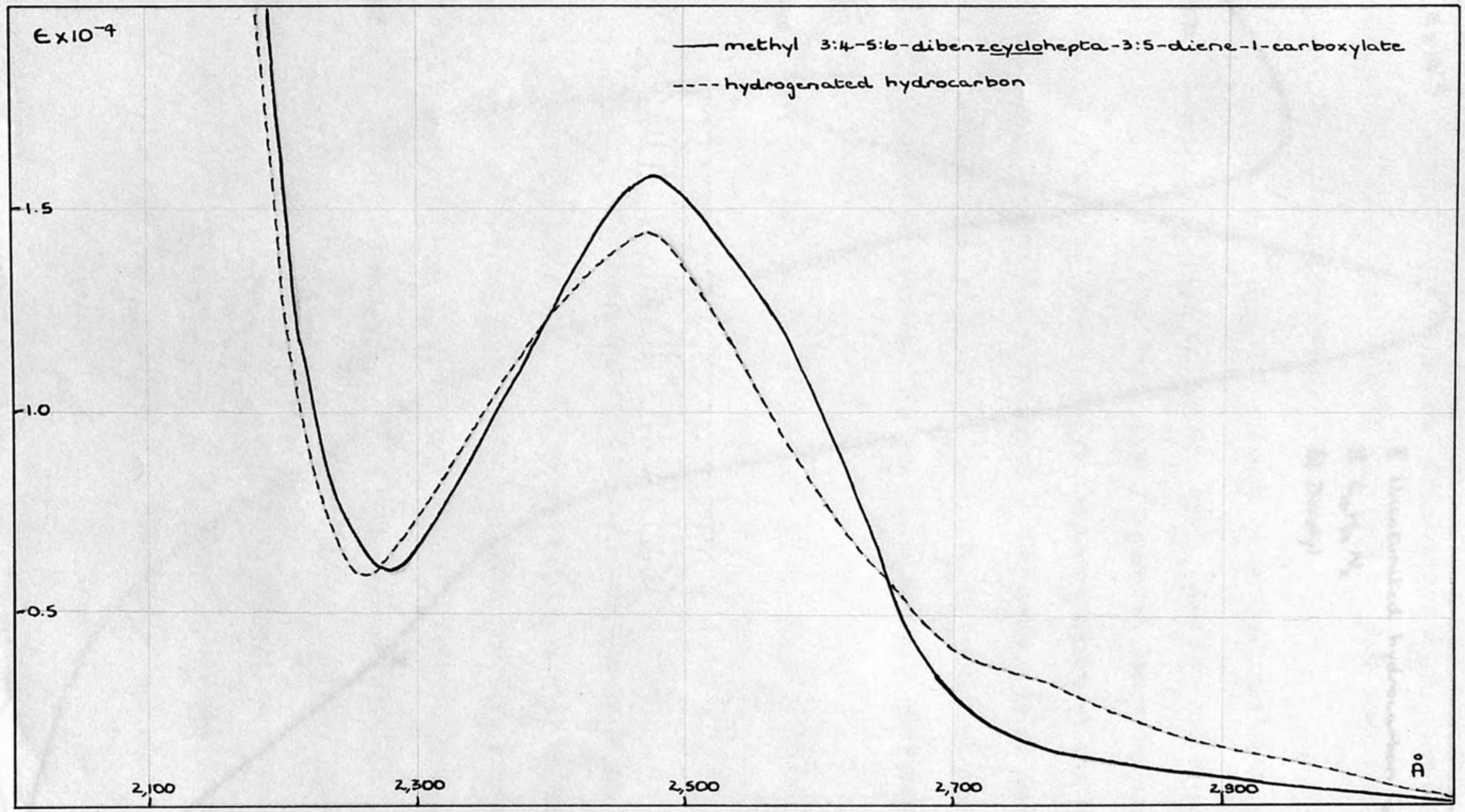

ε x 10⁻⁴
methyl 3:4-5:6-dibenzcyclohepta-3:5-diene-1-carboxylate
hydrogenated hydrocarbon
1.5
1.0
0.5
2,100
2,300
2,500
2,700
2,900
Å

Fig. I

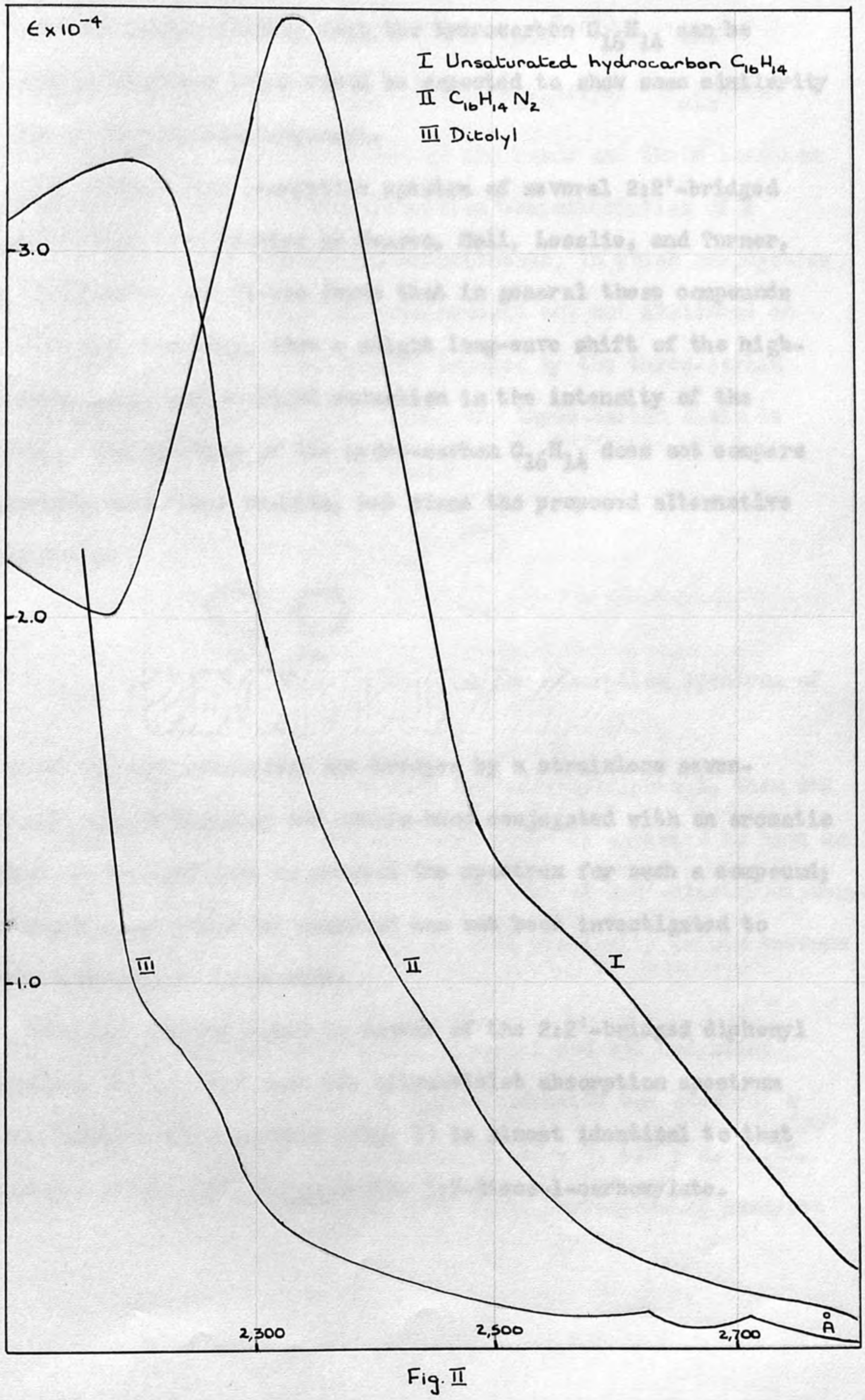
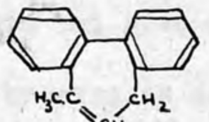

ε x 10⁻⁴
I Unsaturated hydrocarbon C₁₆H₁₄
II C₁₆H₁₄N₂
III Ditolyl
3.0
2.0
1.0
III
II
I
2,300
2,500
2,700
Å

Fig. II

It therefore seems unlikely that the hydrocarbon $C_{16}H_{14}$ can be 2:2'-divinyldiphenyl which would be expected to show some similarity to that of 2:2'-dimethyldiphenyl.

The ultra-violet absorption spectra of several 2:2'-bridged diphenyls have been studied by Beaven, Hall, Lesslie, and Turner, (J., 1952, 854), and it was found that in general these compounds compared with diphenyl, show a slight long-wave shift of the high-intensity band, and a slight reduction in the intensity of the maximum. The spectrum of the hydro-carbon $C_{16}H_{14}$ does not compare favourably with these results, but since the proposed alternative structure is

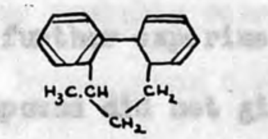


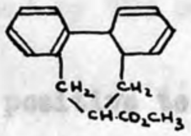
in which the 2:2'-positions are bridged by a strainless seven-membered ring containing one double-bond conjugated with an aromatic system, it is difficult to predict the spectrum for such a compound; the spectrum of a similar compound has not been investigated to enable comparisons to be made.

However, another point in favour of the 2:2'-bridged diphenyl structure, is the fact that the ultra-violet absorption spectrum of the hydrogenation product (fig. I) is almost identical to that of methyl 3:4-5:6-dibenzcyclohepta- 3:5-diene-1-carboxylate.

Ester	ϵ_{max} 15,900	λ_{max} 2,480	ϵ_{min} 5,750	λ_{min} 2,275
Hydrocarbon	ϵ_{max} 14,500	λ_{max} 2,475	ϵ_{min} 5,750	λ_{min} 2,265

In both these curves, the intensities of the bands and their location are consistent with the expected absorption characteristics of a diphenyl not containing auxochromic substituents, in which conjugation between the two benzene rings has been reduced but not abolished as a result of departure from coplanarity imposed by the three-carbon chain joining the 2:2'-positions. Since the three-carbon chain is saturated, the substituents in the rings

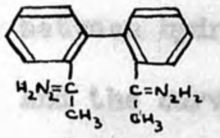




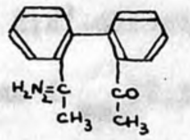
would be expected to have little effect on the absorption spectrum of the conjugated system.

If the hydrocarbon $C_{16}H_{14}$ had been 2:2'-divinyldiphenyl, then the hydrogenation product 2:2'-diethyldiphenyl would be expected to have an ultra-violet absorption spectrum resembling that of 2:2'-dimethyldiphenyl in fig. II. It is quite obvious that no such similarity exists between them.

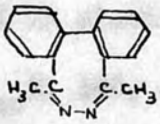
The reaction between 2:2'-diacetyldiphenyl and 85% hydrazine hydrate solution, in the absence of sodium hydroxide was studied; a crystalline compound having the analysis, C, 82.0; H, 6.2 ; N, 11.8%, was obtained. The possible products with their corresponding analyses are as follows:



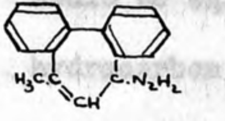
(a) N 21.0



(b) C, 76.2
H, 6.4
N, 11.1



(c) C, 82.1
H, 6.1
N, 11.96



(d) C, 82.1
H, 6.1
N, 11.96

Structures (c) and (d) have analyses in close agreement with that of the unknown compound, but evidence favouring structure (c) was obtained in further experiments.

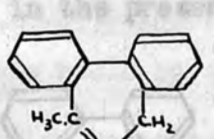
(i) The compound did not give a positive test for unsaturation with a solution of bromine in carbon tetrachloride; a negative result would be expected of (c) but not of (d).

(ii) When the compound was heated with sodium hydroxide in triethylene glycol under conditions similar to those in the Huang Minlon reaction, a complete rearrangement of the molecule to form 9:10-dimethylphenanthrene occurred. Such a change seems feasible with the loss of nitrogen in (c), but an unlikely intramolecular rearrangement would have to take place in (d) in order to form this hydrocarbon.

(iii) It is improbable that an internal condensation of the diketone to form (d) would take place in an alcoholic solution of hydrazine.

(iv) Ultra-violet absorption spectrum.

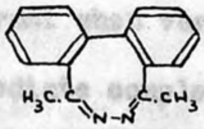
The ultra-violet absorption of the compound produced in the reaction between hydrazine and 2:2'-diacetyldiphenyl is plotted in fig. II., and the curve which has ϵ_{max} 32,500 at λ_{max} 2, 190, does not show any features which are characteristic of absorption spectra of diphenyls. If the compound $C_{16}H_{14}N_2$ had the structure (d), it would be expected to have a spectrum very similar to that of the hydrocarbon



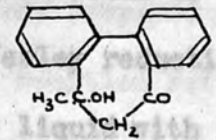
which is very probably represented by the curve given for the unsaturated hydrocarbon $C_{16}H_{14}$ in fig. II.

The spectrum of a diphenyl bridged across the 2:2'-positions by a conjugated eight-membered ring has not been investigated. Therefore, it is not possible to compare the spectrum obtained for $C_{16}H_{14}N_2$ with that for such a system in order to decide if structure (c) is favoured. However, the two compounds (c) and (d) are the only possible products from the reaction between hydrazine and 2:2'-diacetyldiphenyl which have analyses in agreement with those obtained, and since the spectrum is not in favour of (d), it seems likely that $C_{16}H_{14}N_2$ is 1:2-diaza-4:5-6:7-dibenz-3:8-dimethyl<u>cyclo</u>-octa-2:4:6:8-tetraene.

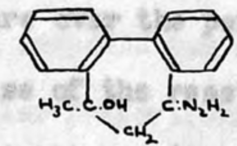
In view of the results discussed, it is possible to propose a mechanism for the anomalous Huang Minlon reduction on 2:2'-diacetyldiphenyl. When the mixture of dicarbonyl compound, hydrazine hydrate, and sodium hydroxide in triethylene glycol is heated two major reactions occur, one between the carbonyl groups and hydrazine to form,



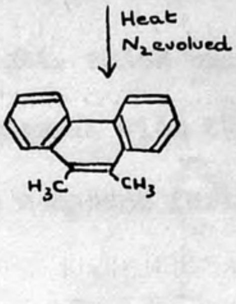
and the other a type of intramolcular Aldol condensation of the dicarbonyl compound in the presence of alkali to form,

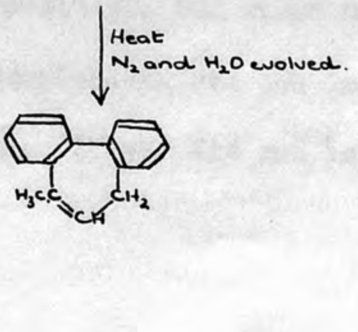


which reacts further with hydrazine to give,



It can be seen that strong heating of these products for several hours after the removal of water and excess of hydrazine hydrate will produce the two products isolated from the reaction mixture (see p. 67).





The reduction of 2:2'-diacetyldiphenyl with lithium aluminium hydride was quite normal when very dilute sulphuric acid was used to decompose the intermediate complex. The product 2:2'-*bis*(α;α'-dihydroxydiethyl)diphenyl was readily dehydrated by warming with 20% dilute sulphuric acid. In this way 2:7-dihydro-2:7-dimethyl-3:4-5:6-dibenz-oxepin was prepared.

No pure compounds could be isolated from the product of the Meerwein-Ponndorf-Verley reduction on 2:2'-diacetyldiphenyl. Attempts to seed the viscous liquid with 2:2'-*bis*(α:α'-dihydroxydiethyl) diphenyl and its dehydration product did not initiate solidification. That reaction did occur, is shown by the distillation of acetone from the reaction mixture over the period of an hour. It is difficult to postulate the course of the reaction in this instance as it has previously been established (Lund, *Ber.*, 1937, *7*^{0}, 1520,; *Kem. Maanedsblad.*, 1936, *17*, 169; *Chem. Zentr.*, 1937, *1*, 3480), that reduction of carbonyl groups in the Meerwein-Ponndorf-Verley reaction does not stop at an intermediate stage; no pinacol formation has been observed, and pinacols are not reduced further by aluminium alkoxides.

Section III. Part 2.

Introduction.

Condensation Reactions with 2:2'-Bis(bromomethyl)diphenyl.

The ease of formation and the stability of ring compounds derived from 2:2'-bis(bromomethyl)diphenyl were first investigated by Kenner and Turner (J., 1911, 96, 2101; 1913, 103, 613). They prepared 9:10-dihydrophenanthrene in 26% yield from the reaction between the dibromo-compound and sodium, and later attempted the synthesis of a seven-membered cyclic compound using diethyl malonate as the condensing agent. Kenner found that the tendency to form the seven-membered ring compound was so great, that even in the presence of two molecular proportions of diethyl malonate the reaction takes the same course, and one half of the reagent is recovered. The dicarbethoxyester produced was hydrolysed, and the acid obtained was partly decarboxylated to give 3:5-dibenzo-$\Delta^{3:5}$-cycloheptadiene-1-carboxylic acid. Attempts were also made to synthesise derivatives of dibenzo-cyclooctadiene. A reaction was carried out between 2:2'-bis(bromomethyl)diphenyl and 1:1:2:2-tetracarbethoxyethane, and a product was isolated having the expected percentage composition, but whose molecular weight, which was determined cryoscopically, was not in agreement with the calculated value. Kenner did not investigate the compound further.

In the experimental section that follows, the reactions between 2:2'-*bis*(bromomethyl)diphenyl and 1:1:2:2-tetra-carbethoxyethane, 1:1:3:3-tetracarbethoxypropane, and diethyl methylmalonate were studied. Structural models of the expected products in the first two condensations, showed that eight-, and nine-membered ring compounds of diphenyl would be of considerable spectroscopic interest in the study of the conjugation of diphenyl.

Section III. Part 2.

Experimental.

Preparation of dimethyl diphenate.

Method 1.

Preparation of diphenic acid.

The method is a modification of the methods of Vorlander and Meyer (Annalen., 1902, 320, 122), Atkinson, Lawler, Heath, Kimball, and Read (J. Amer. Chem. Soc., 1941, 63, 730), and Professor E.E. Turner (private communication).

25G. anthranilic acid in 75ml. water and 75ml. concentrated hydrochloric acid, were diazotised between 0° and 5° with 12g. sodium nitrite. The solution of the diazonium salt was filtered.

88g. copper sulphate crystals were dissolved in 500ml. water, and 100ml. ammonia (d. 0.880) were added; the solution was cooled to 10°. 200g. sodium bisulphite were slowly added, followed by 200ml. ammonia (d. 0.880). This catalytic solution was maintained at a temperature between 10° and 15°, and stirred mechanically while the solution of the diazonium salt was added below the surface of the liquid from a burette at the approximate rate of 5ml. per minute. Stirring was continued for a further thirty minutes after the addition was completed.

A solution of 130g. anhydrous ferric chloride in 200ml. water and 650ml. concentrated hydrochloric acid was poured slowly into the reaction mixture. The mixture was allowed to stand overnight, and then filtered. The buff-coloured precipitate was thoroughly washed with water, and then crystallised from glacial acetic acid. The yields of diphenic acid obtained in several experiments varied between 61% and 75%, m.p. 228°.

Preparation of dimethyl diphenate.

A mixture of 75g. (0.3 mol.) diphenic acid, 75g. concentrated sulphuric acid, and 750g. (23 mol.) methyl alcohol, was heated under reflux for six hours. 600ml. of the alcohol were removed by distillation, and the remaining liquid was poured into twice its volume of water and thoroughly stirred. A light brown precipitate was formed, which was filtered off and washed with dilute sodium bicarbonate solution, and then with water. The product was purified by one treatment with decolourising charcoal and crystallisation from methyl alcohol. 73g. (88%) colourless prisms, m.p. 74°, were obtained.

Method 2.

Preparation of o-iodobenzoic acid.

219.2G. anthranilic acid were dissolved in 2160ml. hot 10% sulphuric acid, then cooled and diazotised below 5° with 110g. sodium nitrite in 160ml. water. The solution of the diazonium salt was slowly added with vigorous stirring to a cool solution of 400g. potassium iodide in 480ml. 10% sulphuric acid solution and 240ml. water. The reaction mixture was allowed to stand at room temperature for one hour, and was then heated on a water-bath with occasional stirring for two hours. A few grams of sodium metabisulphite were finally added to remove any free iodine. The heavy precipitate was filtered off, and thoroughly washed with water. Yield of crude acid 386g. (97%).

Esterification of o-iodobenzoic acid.

A solution of 175g. (0.7 mol.) o-iodobenzoic acid in 2.2l. (55 mol.) methyl alcohol and 87.4g. concentrated sulphuric acid was heated under reflux for six hours. Most of the methyl alcohol was then removed by distillation and the rest of the liquid was poured into a large volume of water. The mixture was neutralised by the addition of solid sodium bicarbonate, and the precipitated oil was extracted with ether. The extract was dried over anhydrous magnesium sulphate, and after the ether had been removed by distillation, the remaining oil was distilled under reduced pressure. 143G. methyl o-iodobenzoate b.p. 128-129°/4mm. were obtained. Yield 77%.

Preparation of dimethyl diphenate (Ullmann method).

55g. (0.21 mol) methyl o-iodobenzoate were heated in a Pyrex boiling-tube in a metal-bath to a steady temperature of 250°. 40G. copper bronze were added in small quantities. Each addition was followed by a rapid increase in temperature, and this was counteracted by cooling the reaction mixture down to 250° in a metal-bath at 100° before a further addition of copper bronze was made. After the addition was completed, the reaction mixture was maintained between 250° and 260° for thirty minutes, and then allowed to cool. The product was extracted with hot *o*-dichlorbenzene; each hot extract was filtered through a fine sintered-glass funnel to remove suspended copper-bronze. The solvent was removed from the filtrate under vacuum, and the remaining viscous, green oil solidified immediately on cooling. The product was purified by treatment with decolourising charcoal, and crystallisation from methyl alcohol. 41G. (80%) dimethyl diphenate, m.p. 74°, were obtained.

Preparation of 2:2'-bis(hydroxymethyl)diphenyl.

The method of Hall, Lesslie and Turner (*J.*, 1950, 711) was used for the reduction of dimethyl diphenate with lithium aluminium hydride.

A reducing mixture was prepared from 14.5g. (2.0 mol.) lithium aluminium hydride in 600 ml. anhydrous ether. A solution of 64.7g. (1.0 mol.) dimethyl diphenate in 690 ml. anhydrous ether was added dropwise to the mixture at such a rate as to maintain steady boiling ofthe ether. After the addition of the ester was completed, the reaction mixture was allowed to stand fifteen minutes before decomposing the excess of lithium aluminium hydride with water. Dilute sulphuric acid (approximately 3% v/v), was added until two clear layers were obtained. The ether layer was isolated, and the solvent was removed by distillation. A solid remained which was dried and crystallised from benzene. 46G. (90%) 2:2'-bis(hydroxymethyl)diphenyl, m.p. 111-112°, were obtained.

Preparation of 2:2'-bis(bromomethyl)diphenyl.

800 ml. 48% hydrobromic acid solution were heated to 90° on a water-bath, and 15g. 2:2'-bis(hydroxymethyl)-diphenyl were slowly added. The reaction mixture was heated under reflux for twenty minutes, and then poured into a large excess of water, and allowed to cool. A light brown solid was filtered off, and allowed to stand overnight in a vacuum dessicator containing potassium hydroxide pellets. The product was treated with decolourising charcoal in light petroleum (b.p. 60-80°). This yielded 21g. (88%) 2:2'-bis(bromomethyl)diphenyl, m.p. 92°.

A study of the reaction between 1:1:2:2-tetracarbethoxyethane and 2:2'-bis(bromomethyl)diphenyl.

a) Preparation of 1:1:2:2-tetracarbethoxyethane.

The method of Bischoff and Rach, (Ber., 1894, 17, 2781) was used.

160G. (1 mol.) diethyl malonate in 150 ml. anhydrous ether was added to a solution of sodium ethoxide prepared from 23g. (1 atom) freshly cut sodium in 400 ml. dry ethyl alcohol. The sodio-derivative of malonic ester was precipitated, and after gently warming the mixture on a water-bath, 127g. (1 atom) iodine was gradually added with thorough shaking after each addition. When the addition of iodine was completed, water was added to dissolve the precipitated sodium iodide. The ethereal layer was separated and shaken with 10% sodium thiosulphate solution, and dried over anhydrous magnesium sulphate. The ether was removed by distillation, leaving a pale yellow solid, which after recrystallisation from ethyl alcohol yielded 135g. (84%) prisms, m.p. 78°.

b) Reaction between 1:1:2:2-tetracarbethoxyethane and 2:2'-bis (bromomethyl)diphenyl.

A solution of sodium ethoxide was prepared from 4.0g. (2.0 mol.) freshly cut sodium in 150 ml. dry alcohol. To this was added 28g. (1.0 mol.) 1:1:2:2-tetracarbethoxyethane, and the mixture was heated under reflux for one hour. 30G. (1.0 mol.) finely powdered 2:2'-bis(bromomethyl)diphenyl were added, and the mixture was heated under reflux for a further twenty hours. Most of the alcohol was distilled off, and the remaining slurry was poured into water. The oil and crystals which were precipitated were extracted with ether and dried over anhydrous magnesium sulphate. The ether was distilled off, and the pale yellow viscous oil which remained partly solidified on standing and cooling to 0°. The solid (23g.) was filtered off and after one recrystallisation from light petroleum (b.p. 40-60°) gave a product melting over a large range of temperature, 80-102°. This solid was extracted twice with 10 ml. portions of boiling light petroleum (b.p.40-60°), and the residual solid (9.0g) formed crystalline plates, m.p. 108.5-109°, after one recrystallisation from light petroleum (b.p. 60-80°).

Found: C, 67.7 ; H, 6.19.

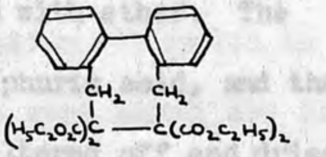
Calculated for $C_{28}H_{32}O_8$: C, 67.7 ; H, 6.5.%

Molecular weight. Cryoscopic method.

Found: 363 ; 391 ; 384. (In dry benzene)

446 ; 464. (In damp benzene).

Calculated for $C_{28}H_{32}O_8$: 496.



$C_{28}H_{32}O_8$

The light petroleum (b.p. 40-60°) extract was allowed to evaporate, and about 9g. crystalline solid, m.p. 78°, remained which was identified as unchanged 1:1:2:2-tetracarbethoxy-ethane.

The oil isolated after the removal of the solid product was distilled under reduced pressure. 6.6g. viscous liquid were collected between 150° and 160°/10mm., after which there was a temperature rise to 200°, and rapid decomposition occurred in the distillation flask. The distillate partly solidified on standing to give crystals, m.p. 75° (starting material). The remaining liquid could not be identified.

5G. solid product, m.p. 108.5-109°, were heated under reflux with 60 ml. saturated alcoholic solution of potassium hydroxide for twelve hours; milder conditions of hydrolysis were found to be ineffective. After removal of the alcohol, the potassium salt was dissolved in water, and the solution was extracted with ether to remove any unchanged ester. The aqueous solution was acidified with 2% sulphuric acid solution, and the waxy solid precipitate, m.p. 110°(decomp.) was filtered off, washed with water and dried. The product was heated to 150° in a metal-bath for thirty minutes, and the evolution of carbon dioxide and water was observed. Hot, 20% sodium carbonate solution was used to extract the product; the extract was washed with ether. The aqueous solution was acidified with dilute sulphuric acid, and the fine white precipitate which was formed was filtered off and dried. It was difficult to find a suitable solvent for the purification of the acid produced. Recrystallisation from glacial acetic acid, and acetonitrile, gave several specimens for which consistent melting-points and analyses could not be obtained. The values determined were:

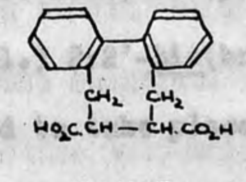
m.p. 196° (decomp.) Found: C, 72.4 ; H, 5.7.

m.p. 200° (decomp.) Found: C, 71.8 ; H, 5.4.

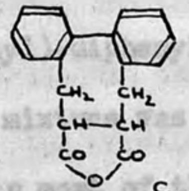
m.p. 203° (decomp.) Found: C, 70.8 ; H, 5.5

$C_{18}H_{16}O_4$ requires C, 72.9 ; H, 5.4.

$C_{18}H_{14}O_3$ requires C, 77.7 ; H, 5.0. %



$C_{18}H_{16}O_4$



$C_{18}H_{14}O_3$

A study of the reaction between 1:1:3:3-tetracarbethoxypropane and 2:2'-bis(bromomethyl)diphenyl.

a) Preparation of 1:1:3:3-tetracarbethoxypropane.

The method of Knoevenagel (Ber., 1914, 27, 2346) was used for this preparation.

A mixture of 96g. (1.0 mol.) diethyl malonate and 24g. (0.5 mol. formaldehyde) 40% formaldehyde solution was cooled in ice-water, and 1.5g. (0.03 mol.) diethylamine were added; the flask was stoppered, and the reaction mixture was allowed to stand overnight at room temperature. The reaction was completed by heating the mixture under reflux for six hours, and the upper layer of water which separated out was removed. The pale yellow oil was distilled under reduced pressure, and 72g. (36%) 1:1:3:3-tetracarbethoxypropane, b.p. 201-204°/18mm. were collected.

b) Reaction between 1:1:3:3-tetracarbethoxypropane and 2:2'-bis(bromomethyl)diphenyl.

A solution of sodium ethoxide was prepared from 2.7g. (2.0 atom) freshly cut sodium in 125 ml. dry ethyl alcohol. To this was added 20g. (1.0 mol.) 1:1:3:3-tetracarbethoxypropane followed by 20g. (1.0 mol.) 2:2'-bis(bromomethyl)-diphenyl; immediate reaction was observed to take place. The mixture was heated under reflux on a water-bath for ten hours, then most of the alcohol was distilled off, and the remaining slurry was poured into water. The oily product was extracted with ether, and the combined extracts were dried over magnesium sulphate. After the ether had been distilled off, the residual oil which did not solidify on standing for several days, was distilled under reduced pressure. About 5g. unchanged ester were collected in the first fraction, and then the following two fractions were obtained:

A	215-218°/5mm.	5.6g.	Viscous liquid
B	218-22°/5mm.	8.3g.	" "

Both fractions were free of bromine.

After fraction B had been collected, the remaining liquid in the distillation flask boiled with considerable decomposition. At this stage the distillation was stopped.

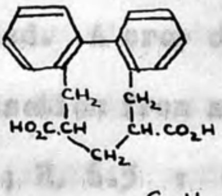
Hydrolysis of fraction A.

Fraction A was heated under reflux for six hours with 50 ml. 20% alcoholic potassium hydroxide solution. The potassium salt was isolated and dissolved in water; the solution was filtered through a No. 4 sintered glass crucible to remove some suspended solid. The filtrate was acidified with 2% sulphuric acid. The precipitated tetracarboxylic acid was filtered off, washed with water, and dried, m.p. 200° (decomp.). The product was partly decarboxylated by heating to 210° in a metal-bath, and then extracted with 10% sodium carbonate solution. The extract was washed with ether, and acidified with dilute sulphuric acid; the precipitated acid was filtered off and purified. Recrystallisation from benzene yielded needles, m.p. 160°, and purification using aqueous ethyl alcohol as solvent produced similar crystals, m.p. 160-161°.

Several analyses were carried out on the acid product, but these did not agree with the analysis required for the expected product.

Found: C, 80.3 ; H, 5.7. : C, 80.6 ; H, 6.1 : C, 80.1 ; H, 6.1.

$C_{19}H_{18}O_4$ requires C, 73.55 ; H, 5.9. %



$C_{19}H_{18}O_4$

For further investigation of the product its molecular weight and equivalent were determined.

Molecular weight. Found: 460, 480, 530.

Equivalent weight. Found: 247.

The ultra-violet spectrum was also studied, (see fig. III) and the following figures were obtained from the absorption curve.

ϵ_{max} 30,810 λ_{max} 2,493.

ϵ_{min} 11,200 λ_{min} 2,278

Hydrolysis of fraction B gave a similar acid product, m.p. 161°.

Esterification of the acid product.

A mixture of 1g. acid, 10 ml. methyl alcohol, and 0.6 ml. concentrated sulphuric acid was heated under reflux on a water-bath for five hours. Some of the alcohol was distilled off, and the remaining liquid was poured into twice its volume of water, and the mixture was neutralised by the addition of solid sodium bicarbonate. The precipitated oil was extracted with ether, and the extract was dried over anhydrous magnesium sulphate. The solvent was evaporated off, and the residual oily product was allowed to stand overnight at 0°, after which treatment it was easily solidified. A crop of prisms, m.p. 44-46°, were obtained after crystallisation from aqueous alcohol.

Found: C, 80.9 ; H, 6.5 : C, 80.8 ; H, 6.5. %

Some of the ester was hydrolysed with alcoholic potassium hydroxide solution, and the original acid, m.p. 160-161°, was obtained. This proved that esterification was the only reaction that had occurred.

A study of the reaction between diethyl methylmalonate and 2:2'-bis(bromomethyl)diphenyl.

a) Preparation of diethyl methylmalonate.

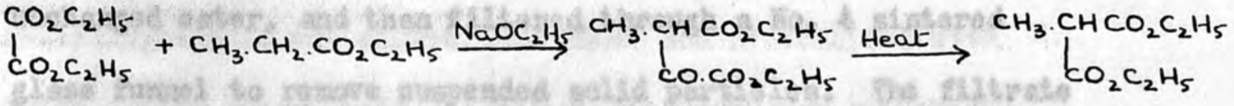
The method of Cox and McElvain, (Org. Synth., 1943, Coll. Vol. II,272) was used.

34.5G. (1.5 mol.) freshly cut sodium were heated under reflux in 500 ml. boiling xylene, and the mixture was vigorously stirred. The xylene was decanted from the finely divided sodium, and the latter was repeatedly washed with anhydrous ether, and then added to 500 ml. dry ethyl alcohol. The mixture was stirred, and 87.5 ml. anhydrous ether were added dropwise over two hours. When no unchanged sodium could be seen, the solution was cooled in ice-water, and a mixture of 145.5g.

(1.4 mol.) ethyl propionate and 208g. (1.4 mol.) ethyl oxalate was added slowly at a rate such that the ether did not boil. When all the ester mixture had been added, the ether and alcohol were removed by distillation. The distillation was stopped when a yellow scum formed on the surface of the liquid in the distillation flask. The solution was cooled, and the sodium derivative which crystallised with considerable increase in volume, was treated with 400 ml. cold 33% acetic acid solution, and allowed to stand for several hours with frequent shaking. The product was extracted with ether, and the combined extracts were washed in turn with 500 ml. water, 500 ml. 10% sodium bicarbonate solution, and finally with 500 ml. water. The extract was dried over anhydrous sodium sulphate. The ether was distilled off, and the remaining liquid was distilled under reduced pressure using a 12" electrically heated column packed with Fenske helices. 158G. ethyl ethoxalylpropionate, b.p. 100-102°/2mm. were obtained.

The ethyl ethoxalylpropionate was heated to 150-160° in a flask fitted with a reflux condenser, and when the liberation of carbon monoxide subsided, the temperature of the liquid was raised until it began to reflux steadily. The liquid was heated under reflux for thirty minutes and then distilled.

A yield of 126g. (overall yield 37%) diethyl methylmalonate, b.p. 197-199° was obtained.



$$\underset{CO_2C_2H_5}{\overset{CO_2C_2H_5}{|}} + CH_3.CH_2.CO_2C_2H_5 \xrightarrow{NaOC_2H_5} CH_3.\underset{CO.CO_2C_2H_5}{\underset{|}{C}}H\,CO_2C_2H_5 \xrightarrow{Heat} CH_3.\underset{CO_2C_2H_5}{\underset{|}{C}}H\,CO_2C_2H_5$$

b) Reaction between diethyl methylmalonate and 2:2'-bis(bromomethyl) diphenyl.

A solution of sodium ethoxide was prepared from 2.8g. (2.0 mol.) freshly cut sodium and 150 ml. dry ethyl alcohol. 20.5G. (2.0 mol.) diethyl methylmalonate were added, followed by 20g. (1.0 mol.) finely powdered 2:2'-*bis*(bromomethyl)-diphenyl. Reaction occurred immediately, accompanied by the separation of a fine precipitate of sodium bromide. The mixture was heated under reflux for three hours, then 75 ml. alcohol were distilled off and the remaining slurry was poured into water. A waxy solid was precipitated, and this was filtered off and recrystallised from ethyl alcohol. 25G. fine needle crystals, m.p. 107°, (89%) were obtained.

Found: C, 68.5 ; H, 7.3.

$C_{30}H_{38}O_8$ (2:2'-bis(ββ dicarbethoxy-n-propyl)diphenyl)

requires, C, 68.4 ; H, 7.3.%

Hydrolysis of the ester.

25G. ester were heated under reflux for five hours with 150 ml. alcoholic potassium hydroxide solution (30%). The alcohol was distilled off, and the remaining solid was dissolved in water.

The aqueous solution was extracted with ether to remove any unchanged ester, and then filtered through a No. 4 sintered glass funnel to remove suspended solid particles. The filtrate was acidified with 2% sulphuric acid solution. A heavy precipitate separated out, which was filtered off, thoroughly washed with water, and dried. 17.5g. rectangular plates, m.p. 200° (decomp.) were obtained.

Decarboxylation of tetracarboxylic acid.

The acid was heated in a metal-bath at 220° for thirty minutes. The light brown solid product was extracted with 10% sodium carbonate solution, and the extract was washed with ether. The alkaline solution was acidified by the addition of 2% sulphuric acid solution, and the precipitated oily, solid was filtered off, washed with light petroleum (b.p. 60-80°) and then crystallised from benzene. Prisms, m.p. 154-155°, of 2:2'-bis-(β-carboxy-n-propyl)diphenyl.

Found: C, 73.8 ; H, 6.7.

$C_{20}H_{22}O_4$ (2:2'-bis(β-carboxy~~l~~-n-propyl)diphenyl)
requires, C, 73.6 ; H, 6.8.%

Esterification of 2:2'-bis(β-carboxy-n-propyl)diphenyl.

Diethyl ester.

A mixture of 5g. acid, 63 ml. ethyl alcohol. and 2.8 ml. concentrated sulphuric acid was heated under reflux for five hours.

Most of the alcohol was removed by distillation, and the remaining liquid was poured into water and neutralised with solid sodium bicarbonate. A yellow oil separated out which could not be solidified; it was extracted with ether, and the extract was dried over anhydrous magnesium sulphate. The ether was evaporated off, and the residual oil was distilled under reduced pressure. 3G. liquid, b.p. 194-196°/3mm., were collected. n_D^{25} 1.5248.

Found: C, 75.3 ; H, 7.6.

$C_{24}H_{30}O_4$ (2:2'-bis(β-ethoxycarbonyl-n-propyl)diphenyl.) requires, C, 75.3 ; H, 7.9.%

Dimethyl ester.

The method used was the same as that described for the diethyl ester.

A viscous liquid, b.p. 186-188°/3.5mm., was obtained, which slowly crystallised on standing. Recrystallisation from aqueous alcohol produced rectangular plates, m.p. 68°.

Found: C, 74.5 ; H, 7.7.

$C_{22}H_{26}O_4$ (2:2'-bis(β-methoxycarbonyl-n-propyl)diphenyl.) requires, C, 74.5 ; H, 7.4.%

Section III   Part 2.

Discussion.

The reaction between 2:2'-bis(bromomethyl)diphenyl and 1:1:2:2-tetracarbethoxyethane was carried out under somewhat different conditions from those used by Kenner (J., 1913, 103, 626), who heated the mixture of the dibromide, tetraethyl ester, and sodium in absolute alcohol at 120-140° under pressure for five hours, and obtained a yield of 24%. Instead, the reaction mixture was heated under reflux for twenty hours under atmospheric pressure, and the condensation product was formed in 21% yield. The analysis for this compound was in agreement with the calculated value. The molecular weight was determined by the cryoscopic method in benzene, and it was found that when dried benzene was used as solvent, results were obtained which agreed with those published by Kenner.

Found: 363 ; 391 ; 384.

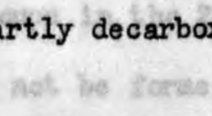
(Kenner) 364 ; 387.

When however, benzene was used which had been allowed to stand for an hour in an open vessel in order to come to equilibrium with the atmosphere, the values for the molecular weight were 446 and 464, which are nearer the calculated value of 496. This suggests that the molecular weights determined for Kenner, were made in dry benzene.

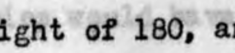
The acidic product obtained from the hydrolysis of the tetracarbethoxy-ester, and partial decarboxylation of the resultant acid could not be identified since the analyses carried out on the specimens having different melting-points (see p. 92) were not in close agreement with the calculated values for the expected dicarboxylic acid. It is evident that the discrepancy is not due to the formation of the corresponding anhydride as this would cause percentages of carbon to be higher rather than lower than the calculated value for the acid.

The compound produced in the condensation between 2:2'-bis-(bromomethyl)diphenyl and 1:1:3:3-tetracarbethoxypropane was not identified. There is no doubt that all the dibromide had reacted since there was a quantitative yield of sodium bromide, and also the crude product was free of bromine. As some unchanged 1:1:3:3-tetracarbethoxypropane was recovered it is obvious that a simple condensation between one molecule of dibromide and one molecule of ester, had not taken place.

The product was hydrolysed, and the mean molecular weight determined on the partly decarboxylated acid was 490. Since the skeleton structure



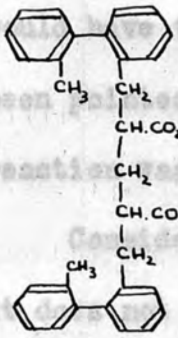
has a 'molecular' weight of 180, and the grouping



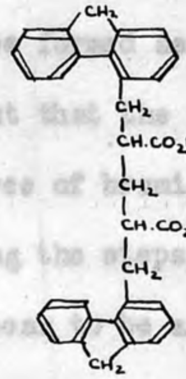
$$\underset{CO_2H}{-CH}-CH_2-\underset{CO_2H}{CH}-$$

has a 'molecular' weight of 130, it rather indicates that two diphenyl units are present in the product. This is supported by the fact that the equivalent weight of the acid is 247, which shows that it is only dibasic. The chemical analyses obtained give the acid the empirical formula, $C_{33}H_{28}O_4$.

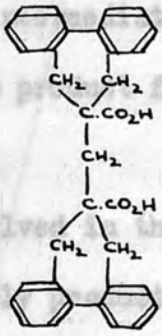
Five dibasic acids almost fitting these requirements were considered as possible products,



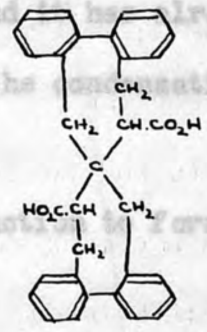
I
$C_{33}H_{32}O_4$



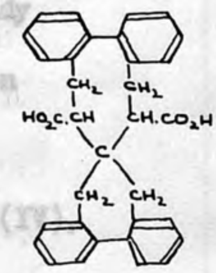
II
$C_{33}H_{30}O_4$



III
$C_{33}H_{28}O_4$



IV
$C_{33}H_{28}O_4$



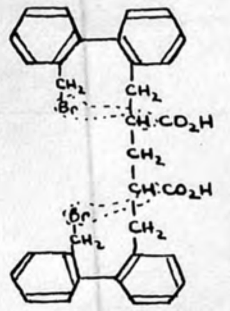
V
$C_{33}H_{28}O_4$

but chemical evidence and the study of the ultra-violet absorption spectrum did not favour all these.

The methyl groups in the 2-position of diphenyl in compound (I) could not be formed by the elimination of bromine from the bromomethyl groups in a solution of sodium ethoxide; and since the condensation product was free of bromine, the replacement of bromine would have to occur during this stage. This renders structure (I) as an impossible product.

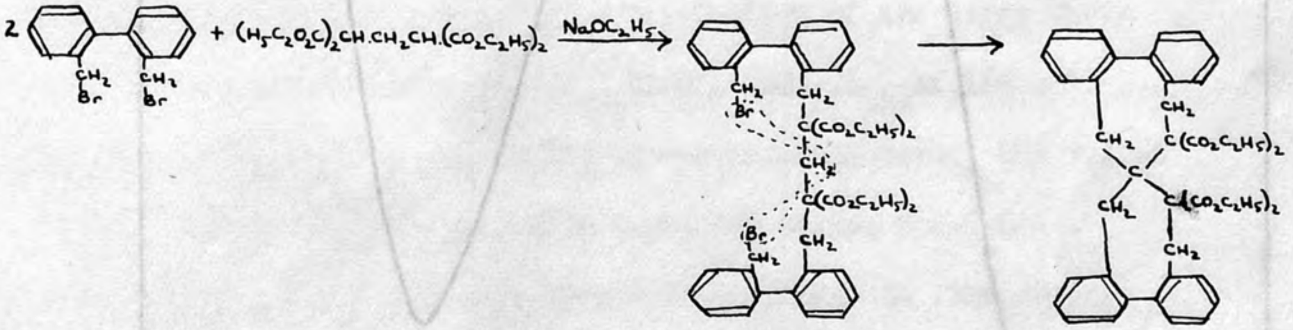
Compound (II) is favoured chemically, but the ultra-violet spectrum rules it out completely.

The ultra-violet spectrum is, however, in excellent agreement with (III), but its formation is chemically impossible since the compound

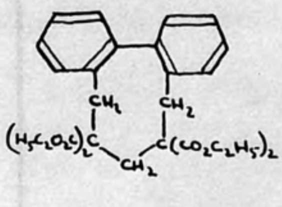


would have to be formed as an intermediate, and it has already been pointed out that the crude product from the condensation reaction was free of bromine.

Considering the steps involved in the reaction to form (IV), it does not appear to be a likely product.



Compound (V) would also have to be produced by a two-stage mechanism i.e. a condensation between the dibromide and ester to form



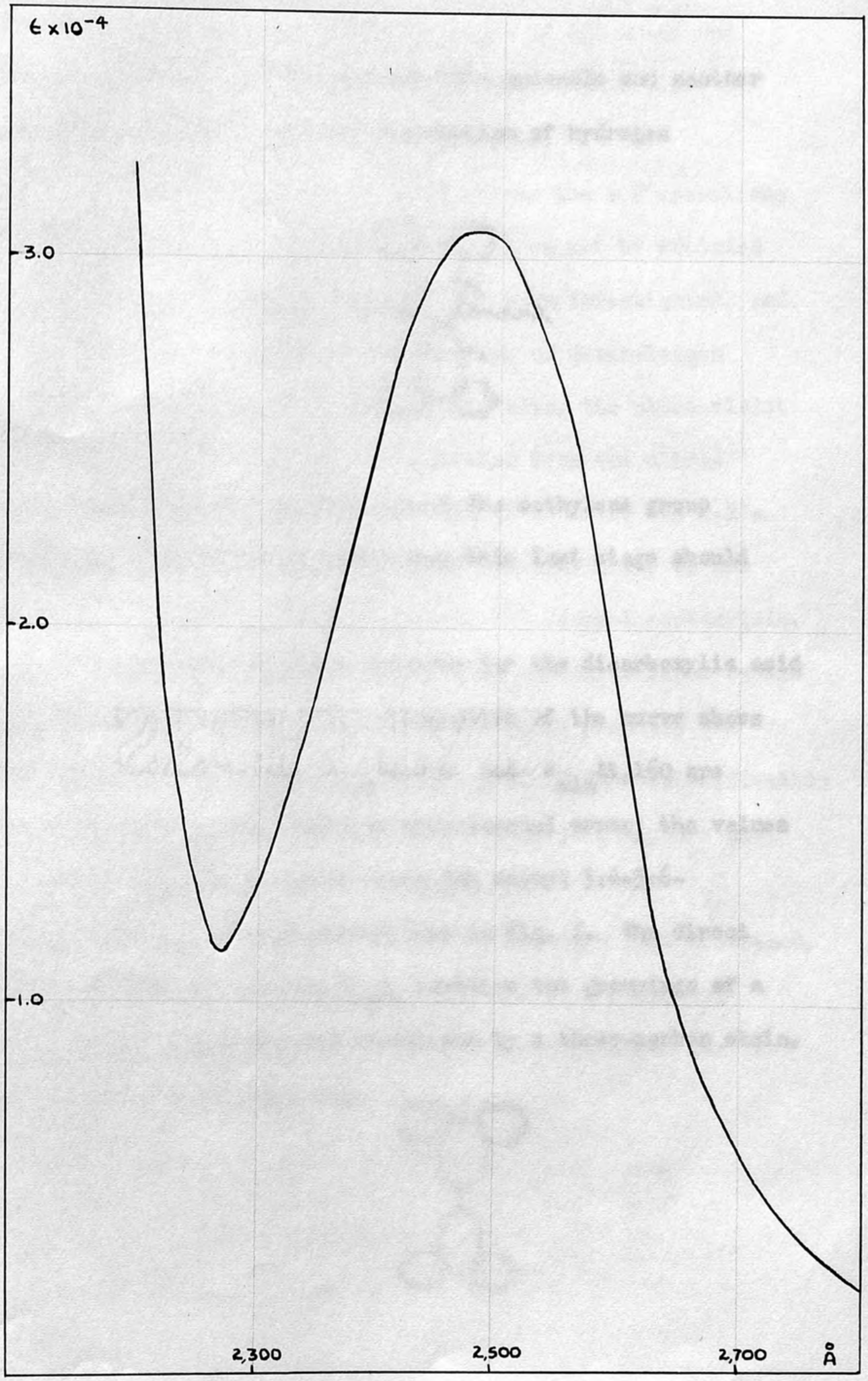
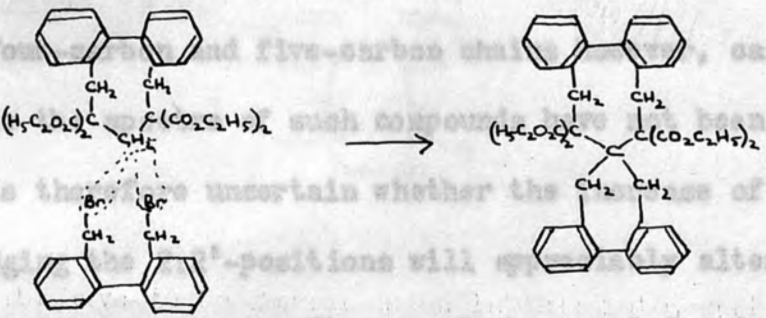


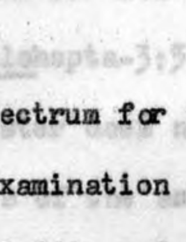
Fig. III

followed by a further reaction between this molecule and another molecule of the dibromide with the elimination of hydrogen bromide.



It is not known, however, to what extent the methylene group would have to be activated in order that this last stage should occur.

The ultra-violet absorption spectrum for the dicarboxylic acid $C_{33}H_{28}O_4$ is plotted in fig. III. Examination of the curve shows that the values obtained for ϵ_{max} 30,800 and ϵ_{min} 11,160 are exactly twice (within the limits of experimental error) the values for ϵ_{max} and ϵ_{min} on the curve drawn for methyl 3:4-5:6-dibenz*cyclo*hepta-3:5-diene-1-carboxylate in fig. I. The direct conclusion is that the acid $C_{33}H_{28}O_4$ contains two groupings of a diphenyl bridged across the 2:2'-positions by a three-carbon chain, in some way linked together, e.g.



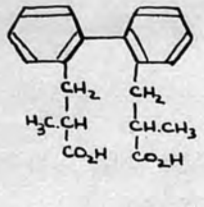
This is in agreement with the molecular weight of 490 which was determined for the acid, since this also indicates that two 'diphenyl groupings' are present in the molecule.

The possibility of diphenyls bridged across the 2:2'-positions by four-carbon and five-carbon chains however, cannot be excluded since the spectra of such compounds have not been investigated, and it is therefore uncertain whether the increase of chain-length bridging the 2:2'-positions will appreciably alter the ultra-violet absorption spectrum. It can only be concluded from the ultra-violet absorption spectrum of $C_{33}H_{28}O_4$ that it contains two 2:2'-bridged diphenyl groups, which account for its similarity to the spectrum of methyl 3:4-5:6-dibenz*cyclo*hepta-3:5-diene-1-carboxylate.

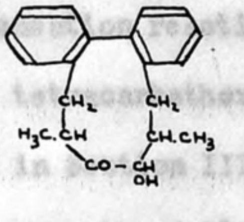
The preparation of the methyl ester does not throw light on the problem, but the fact that hydrolysis of the ester produces the original acid does indicate that no reaction other than esterification takes place when the acid is heated under reflux in a mixture of methyl alcohol and concentrated sulphuric acid.

In contrast to the complex condensation reaction just discussed, the reaction between 2:2'-*bis*(bromomethyl)diphenyl and diethyl methylmalonate proceeded normally. The new ester produced and its acid derivatives, gave satisfactory analyses.

The methyl and ethyl esters of the acid



were easily prepared, and are of interest in that it should be possible to use them as starting compounds in the Acyloin reaction for the preparation of derivatives of dibenzo<u>cyclo</u>-decadiene. e.g.

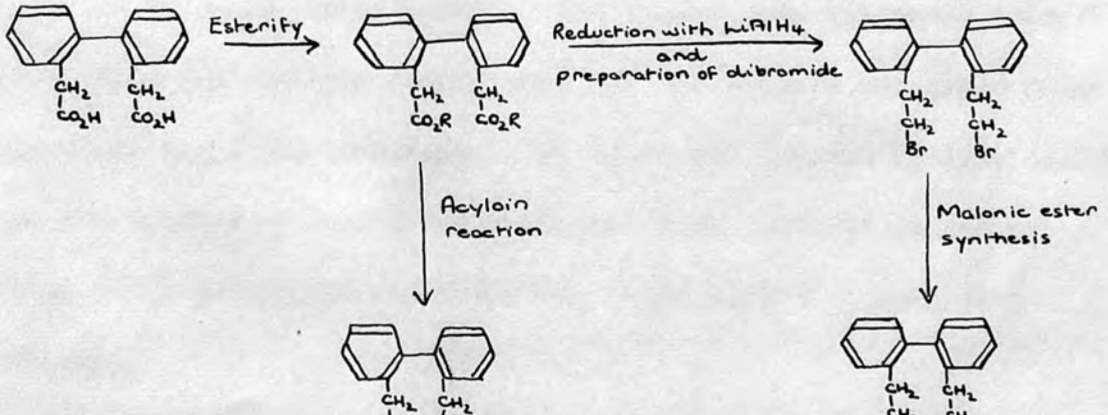


Section III Part 3.

Methods of Preparation of 2:2'-Diphenyl diacetic acid.

Introduction.

Since the condensation reactions between 2:2'-*bis*(bromomethyl)diphenyl and tetracarbethoxyethane and tetracarbethoxypropane, (described in Section III, Part II), to produce diphenyls bridged across the 2:2'-positions by four, and five carbon-chains were not successful, it was decided to investigate possible methods of preparing 2:2'-diphenyl diacetic acid which would be used as a starting compound in other possible syntheses of these large ring compounds, e.g.



Only one method of preparation of 2:2'-diphenyl diacetic acid appears in the literature, (Kenner and Turner, *J.*, 1911, *99*, 2109), and here the yields are not recorded for each stage of the synthesis. Kenner's work was repeated, and attempts were also made to prepare the acid by the Ullmann reaction on methyl *o*-bromo- and methyl *o*-iodophenyl acetate, and by the Arndt Eistert reaction on the dichloride of diphenic acid.

Preparation of methyl o-bromobenzoate.

A mixture of 154g. copper sulphate ($5H_2O$), 440g. (3.0 mol.) sodium bromide, 81 ml. concentrated sulphuric acid, 132g. copper turnings, and 1520 ml. water, was boiled until the solution became colourless. 220g. (1.0 mol.) methyl anthranilate were added, and the mixture was cooled below 10°. The ester solution was diazotised between 5-7° with 97g. sodium nitrite dissolved in the minimum amount of water. The diazotised solution was allowed to stand overnight, and the dense brown oil which separated out was isolated by steam-distillation. The product was extracted with ether from the aqueous distillate, and the extract was dried over anhydrous magnesium sulphate. The ether was removed by distillation, and the remaining liquid was distilled under reduced pressure. 212g. (67%) methyl o-bromobenzoate, b.p. 96-99°/3.5mm. were obtained.

Preparation of o-bromobenzyl alcohol.

165g. (1.0 mol.) methyl o-bromobenzoate diluted with 100 ml. dry ether were added dropwise to a refluxing mixture of 20g. (0.6 mol.) lithium aluminium hydride in 500 ml. anhydrous ether. After the addition was complete, the reaction mixture was allowed to stand

Section III Part 3

Experimental.

Preparation of methyl o-bromobenzoate.

A mixture of 154g. copper sulphate ($5H_2O$), 440g. (3.0 mol.) sodium bromide, 81 ml. concentrated sulphuric acid, 132g. copper turnings, and 1320 ml. water, was boiled until the solution became colourless. 220g. (1.0 mol.) methyl anthranilate were added, and the mixture was cooled below 10°. The ester solution was diazotised between 5-7° with 97g. sodium nitrite dissolved in the minimum amount of water. The diazotised solution was allowed to stand overnight, and the dense brown oil which separated out was isolated by steam-distillation. The product was extracted with ether from the aqueous distillate, and the extract was dried over anhydrous magnesium sulphate. The ether was removed by distillation, and the remaining liquid was distilled under reduced pressure. 212g. (67%) methyl o-bromobenzoate, b.p. 96-99°/ 3.5mm. were obtained.

Preparation of o-bromobenzyl alcohol.

165g. (1.0 mol.) methyl o-bromobenzoate diluted with 100 ml. dry ether were added dropwise to a reducing mixture of 20g. (0.6 mol.) lithium aluminium hydride in 500 ml. anhydrous ether. After the addition was complete, the reaction mixture was allowed to stand for one hour. The excess of lithium aluminium hydride was decomposed with water, and dilute sulphuric acid solution was added until the mixture became clear. The ethereal solution was isolated, and the aqueous layer was extracted with ether. The combined extracts were dried over anhydrous sodium sulphate. 131.2g. (91%) pale, orange crystals, m.p. 70-72°, remained after the ether had been distilled from the product. Crystallisation of the product from ethyl alcohol, gave a crop of needle crystals, m.p. 79-80°.

Preparation of o-bromobenzyl bromide.

65G. *o*-bromobenzyl alcohol were heated under reflux with 500 ml. 48% hydrobromic acid solution for one hour. The reaction mixture was allowed to cool, and the light brown oil which separated out was carefully extracted with ether and dried over anhydrous magnesium sulphate. The solvent was distilled off in the fume-cupboard as *o*-bromobenzyl bromide is extremely lachrymatory. A yield of 125.5g. (75%) light brown oil was obtained which solidified when cooled in ice to give crystals, m.p. 28-31°. Further purification of this compound was not attempted.

Preparation of o-bromobenzyl cyanide.

A mixture of 30g. (1.2 mol.) sodium cyanide and 27 ml. water was heated on a water-bath to dissolve the solid, and then 125g. (1.0 mol.) *o*-bromobenzyl bromide dissolved in 125 ml. absolute alcohol were added slowly through a funnel over thirty minutes. The mixture was heated under reflux for three hours, then cooled and filtered under suction to remove the precipitated sodium bromide. The bulk of the alcohol was distilled from the filtrate, and the residual liquid was distilled under reduced pressure. 86g. (88%) o-bromobenzyl cyanide, b.p. 138-140°/10mm. were obtained.

Preparation of o-bromophenylacetic acid.

A mixture of 86g. o-bromobenzyl cyanide, 65 ml. concentrated sulphuric acid, 65 ml. glacial acetic acid, and 65 ml. water, was heated under reflux for one hour. The mixture was cooled, and poured into a large volume of water; the o-bromophenylacetic acid which was immediately precipitated was filtered off. 90G. of the crude acid, m.p. 96-98°, were obtained. After recrystallisation from ethyl alcohol, the melting-point of the product was raised to 103°. Yield 94%.

Preparation of methyl o-bromophenylacetate.

48 G. o-bromophenylacetic acid, 27 ml. concentrated sulphuric acid, and 95 ml. methyl alcohol, were heated together under reflux for two hours. The reaction mixture was allowed to cool before pouring it into twice its volume of water. The mixture was neutralised by the addition of solid sodium bicarbonate, and the pale yellow sweet-smelling oil which separated out was extracted with ether, and dried over anhydrous sodium sulphate. The ether was distilled off, and the residual liquid was distilled under reduced

pressure. 35.4G. (70%) methyl o-bromophenylacetate, b.p. 121-123°/7mm., n_D^{25} 1.5427, were produced.

Found: C, 48.9; H, 4.1 ; Br. 35.5

$C_9H_9BrO_2$ (methyl o-bromophenylacetate) requires, C, 47.2 ; H, 4.0 ; Br, 34.8.

Attempted Ullmann reaction on methyl o-bromophenylacetate.

A small quantity of copper bronze was added at 10° intervals of temperature to 10g. heated methyl o-bromophenylacetate contained in a Pyrex boiling-tube. The addition was started at 190°, and was continued until a temperature of 250° was reached. No reaction was observed to take place. A crystal of iodine was added to activate the mixture, which after the addition of a further 6g. copper bronze was maintained at a temperature of 250° for thirty minutes. After cooling, the product was extracted several times with hot methyl alcohol, and filtered. The alcohol was distilled from the filtrate, and distillation of the residual liquid yielded 8.6g. unchanged ester.

A further attempt was made to carry out the Ullmann reaction on methyl o-bromophenylacetate by heating a mixture of 10g. ester, and 8g. copper bronze under reflux for eight hours. The mixture was extracted as before, and 3.3g. dark brown viscous liquid were isolated which did deposit a few crystals after standing for

Preparation of *o*-iodobenzoic acid.

several days. An attempt was made to purify this product, but the pale brown solid obtained did not give a good analysis, and an attempt to hydrolyse the product was not satisfactory.

The method of preparation of *o*-iodobenzoic acid has already been described (see p. 86).

Preparation of *o*-iodobenzoyl chloride.

For this preparation 30 ml. thionyl chloride were distilled and the fraction, b.p. 77°, was collected.

70g. (1.0 mol.) finely powdered *o*-iodobenzoic acid were mixed with 42g. (1.3 mol.) thionyl chloride in a 500 ml. flask, and heated on a water-bath with occasional shaking for about one hour until the evolution of hydrogen chloride had ceased. The excess of thionyl chloride was distilled off, and the distillation of *o*-iodobenzoyl chloride was carried out under reduced pressure. Two fractions were collected.

155°/25mm. 30g. pale yellow solid, m.p. 30-31°.

155-158°/25mm. 7g. yellow solid, m.p. 29-30°.

Preparation of diazomethyl-*o*-iodophenyl ketone.

The method used was similar to that employed by Fieser and Kilmer (*J. Amer. Chem. Soc.*, 1940, *62*, 1356), for the preparation of diazomethyl-*o*-bromophenyl ketone.

Diazomethane was prepared by dropping 55ml. N-nitroso-methyl urethane in 55 ml. dry ether into 60 ml. saturated solution of potassium hydroxide in absolute alcohol, covered with 20 ml. dry ether. The gas was passed through a vertical spiral condenser, and then dissolved in cold anhydrous ether. After complete absorption of the yellow gas, the ethereal solution was diluted to 800 ml.

Preparation of o-iodobenzoic acid.

The method of preparation of o-iodobenzoic acid has already been described (see p. 86).

Preparation of o-iodobenzoyl chloride.

For this preparation 50 ml. thionyl chloride were distilled and the fraction, b.p. 77°, was collected.

70G. (1.0 mol.) finely powdered o-iodobenzoic acid were mixed with 42g. (1.3 mol.) thionyl chloride in a 500 ml. flask, and heated on a water-bath with occasional shaking for about one hour until the evolution of hydrogen chloride had ceased. The excess of thionyl chloride was distilled off, and the distillation of e-iodobenzoyl chloride was carried out under reduced pressure. Two fractions were collected.

155°/25mm. 50g. pale yellow solid, m.p. 30-31°.

155-158°/25mm. 7g. yellow solid, m.p. 29-30°.

Preparation of diazomethyl-o-iodophenyl ketone.

The method used was similar to that employed by Fieser and Kilmer (J.Amer. Chem. Soc., 1940, 62, 1356), for the preparation of diazomethyl-o-bromophenyl ketone.

Diazomethane was prepared by dropping 55ml. N-nitroso-methyl urethane in 55 ml. dry ether into 60 ml. saturated solution of potassium hydroxide in absolute alcohol, covered with 20 ml. dry ether. The gas was passed through a vertical spiral condenser, and then dissolved in cold anhydrous ether. After complete absorption of the yellow gas, the ethereal solution was diluted to 800 ml.

with cold dry ether, and 26.5g. o-iodobenzoyl chloride dissolved in dry ether were added dropwise with stirring, at 0° over one hour. After standing overnight at room temperature a slight precipitate had formed which was removed by filtration. The ether was distilled from the filtrate under reduced pressure, leaving 29g. brownish oil which solidified on cooling, m.p. 54-60°. The product was extracted with hot cyclohexane, and the solution was allowed to cool very slowly with vigorous stirring. In this way two crops of yellow prisms were obtained, 16g., m.p. 59-60°, and 8.1g., m.p. 57-59°. Yield 90%.

Found: I, 46.2.

$C_8H_5ON_2I$ (diazomethyl-o-iodophenyl ketone) requires, I, 46.65%

Preparation of o-iodophenylacetic acid.

A solution of 24g. diazomethyl-o-iodophenyl ketone in technical dioxan was added dropwise to a suspension of 32g. silver oxide (precipitated from silver nitrate solution with potassium hydroxide) in a solution of 40g. sodium thiosulphate in 800 ml. water at 60-65°. The addition took thirty minutes to complete, and the mixture was vigorously stirred throughout. After leaving for an hour, the evolution of nitrogen had ceased,; the mixture was made alkaline with 10% sodium hydroxide solution, and filtered. The filtrate was washed twice with benzene, acidified with dilute nitric acid solution, and extracted with ether. The extract was dried over anhydrous magnesium sulphate and the ether was distilled off leaving a pale yellow oil. This oil was dissolved in 5% sodium carbonate solution and the solution was acidified with 2% nitric acid solution. A pale yellow solid was precipitated which was washed and dried. 18.8g. (81.5%) o-iodophenylacetic acid, m.p. 108-110°, were obtained.

Preparation of methyl o-iodophenylacetate

A mixture of 18.5g. o-iodophenylacetic acid, 200 ml. methyl alcohol, and 9 ml. concentrated sulphuric acid were heated under reflux for five hours on a water-bath. About 100 ml. alcohol were distilled off, and the remaining liquid was poured into twice its volume of water, and the mixture was neutralised by the addition of solid sodium bicarbonate. The precipitated oil was extracted with ether and the extract was dried over anhydrous potassium carbonate. The ether was removed by distillation and the residual liquid was distilled under reduced pressure. The following fractions were collected.

		n_D^{25}	
1	117°/3mm.	1.5801	0.55g.
2	117-119°/3mm.	1.5831	3.9g.
3	119-120°/3mm.	1.5834	4.3g.
4	120°/3mm.	1.5835	4.1g.
5	120-121°/3mm.	1.5835	3.7g.

Yield 12.1g. (62%) methyl o-iodophenylacetate. (Found: C, 39.2; H, 3.1 ; I, 45.2. $C_9H_9O_2\,1$ (methyl o-iodophenylacetate) requires, C, 39.2 ; H, 3.2 ; 1, 45.9)

Ullmann on methyl o-iodophenyl acetate.

10g. methyl *o*-iodophenylacetate were heated in a Pyrex boiling-tube to 170° in a metal-bath. About 0.5g. copper bronze was added, and no temperature rise due to reaction taking place was observed. The same quantity of copper bronze was added to the mixture after each 10° rise in temperature, and after the addition at 220° a rapid increase up to 250° was observed. The reaction mixture was then maintained at 220°, and 4g. more of copper bronze were added in small portions; the reaction mixture was then maintained at 200-220° for one hour. The mixture was allowed to cool, and the product was repeatedly extracted with hot *o*-dichlorbenzene, and filtered through a sintered glass funnel to remove suspended copper bronze particles. Most of the solvent was distilled off at atmospheric pressure, and the remainder was removed under reduced pressure. About 0.5g. unchanged ester was collected, and the remaining brown viscous liquid partly solidified on cooling, but did not crystallise. Many attempts were made to purify this product using various solvents and treatment with decolourising charcoal. A yellow solid was obtained, m.p. 140-145°, from *cyclo*hexane solution, this solid did not give a satisfactory analysis.

3g. of the brown viscous Ullmann product were hydrolysed with 20% alcoholic potassium hydroxide solution, but only *o*-iodophenylacetic acid was recovered.

Preparation of the dichloride of diphenic acid.

The method of Underwood and Kochmann, (J. Amer. Chem. Soc., 1924, 46, 2072) was used.

A mixture of 15g. (1.0 mol.) diphenic acid and 27g. (2.0 mol.) phosphorus pentachloride was heated in an oil-bath at 190-195° for thirty-minutes. The temperature was allowed to fall to 150° and maintained at this for one hour; air was frequently blown through the neck of the flask to remove phosphorus oxychloride. The reaction mixture was then allowed to cool, and the dichloride was extracted with benzene. A yield of 11.8g. (61%), m.p. 95-97°, was obtained.

An attempt was made to prepare the dichloride using thionyl chloride instead of phosphorus pentachloride, but this was unsatisfactory since the bulk of the product was diphenic acid anhydride. The anhydride could, however, be separated from the dichloride since it is practically insoluble in ether, whereas the dichloride is readily soluble.

Arndt-Eistert reaction on the dichloride of diphenic acid.

Preparation of 2:2'-diazomethyl diphenyl diketone.

A solution of diazomethane in ether was prepared from 80 ml. N-nitrosomethyl urethane in the manner described on p. 115

14G. dichloride dissolved in ether, were added dropwise with mechanical stirring to the solution of diazomethane at 0°. After standing overnight at room temperature the solution was filtered, and the solvent was removed from the filtrate under reduced pressure. 10.6g. yellow oil remained, some of which rapidly crystallised. The solid was filtered off, and crystallised from toluene. 6.6g. fine yellow prisms which darkened at 116° on heating but melted at 131° with decomposition, were produced.

Found: C, 66.2 ; H, 3.8 ; N, 19.1.

$C_{16}H_{16}O_2N_4$ requires, (2:2'-diazomethyl diphenyl diketone);

C, 66.2 ; H, 3.5 ; N, 19.3%.

Preparation of diphenyldiacetic acid.

A solution of 5.4g. 2:2'-diazomethyl diphenyl diketone in technical dioxan was added dropwise with vigorous stirring to a suspension of 22g. silver oxide in a solution of 32g. sodium thiousulphate in 1460ml. water at 65°. The mixture was left for an hour during which time the evolution of nitrogen was observed. The mixture was made alkaline by addition of 10% sodium hydroxide solution, and filtered under suction. The filtrate was washed with benzene, acidified with dilute nitric acid, and extracted with ether. The ether was evaporated off, and the remaining oil was dissolved in 5% sodium carbonate solution, and the solution was acidified with 2% nitric acid solution. The product was extracted continuously with ether for several hours, and 0.4g. prisms were obtained which after crystallisation from water had, m.p. 151-152°.

Found: C, 70.7 ; H, 5.1

Calculated for $C_{16}H_{14}O_4$: C, 71.1 ; H, 5.2.%

Preparation of 2:2'-diphenyldiacetonitrile.

The method used was that given by Kenner and Turner (J., 1911, 99, 2109).

A saturated aqueous solution of 5.2g. potassium cyanide was mixed with three times its volume of ethyl alcohol. The mixture was heated under reflux, and to it was added in small quantities 12g. powdered 2:2'-bis(bromomethyl)diphenyl. The reaction mixture was maintained at a temperature between 50° and 60° for five hours, and then poured into water. A light brown oil was precipitated which solidified on standing. The solid was filtered off and crystallised from ethyl alcohol. 6.6g. (81%) cubic crystals, m.p. 77-78°, were obtained.

Preparation of 2:2'-diphenyldiacetamide.

The reaction was carried out according to the method of Kenner and Turner (loc, cit.).

A solution of 6.6g. dinitrile in 18.4ml. concentrated sulphuric acid was allowed to stand at room temperature for twenty-four hours. The solution was poured into water and made alkaline by the addition of ammonia. A pale yellow solid was precipitated which was filtered off and recrystallised from ethyl alcohol. 2.9g. needles, m.p. 215-216°, were obtained. Kenner and Turner give, m.p. 210-211°.

Preparation of 2:2'-diphenyldiacetic acid.

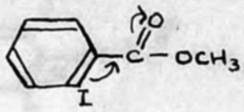
The conditions used for the hydrolysis of the amide were those given by Kenner and Turner, (loc. cit.).

2.9G. amide were heated under reflux with 30ml. 10% potassium hydroxide solution until the test for the evolution of ammonia was negative (14 hours). The mixture was acidified with dilute sulphuric acid solution, and immediately a buff-coloured precipitate was formed. The solid was filtered off, giving a yield of 2.4g., m.p. 151-152°. After treatment with decolourising charcoal, and crystallisation from water, colourless prisms, m.p. 153°, were produced. Kenner and Turner record a melting-point of 152°.

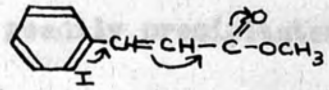
Section III Part 3.

Discussion.

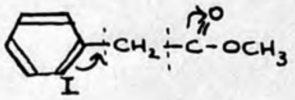
The success of the Ullmann reaction is dependent upon the nature of the aromatic halide used. Certain negative groups in the ortho- and para-positions with respect to the halogen atom activate the latter through the operation of the -T effect, which leaves the carbon atom to which the halogen is attached with a residual positive charge. An ortho-carbalkoxyl group has been shown to have a marked activating effect on the halide, e.g.



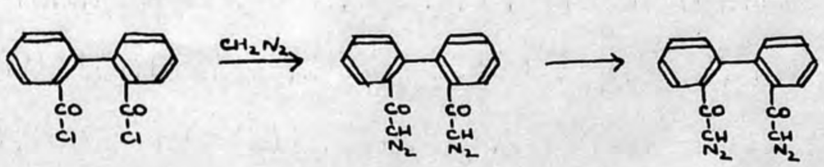
Ullmann reactions have been carried out on methyl o-iodobenzoate, o-iodo-β : β-dimethoxybenzene, and methyl o-iodocinnamate. In the first case a yield of 82% was obtained, (Ullmann, *Annalen*, 1904, 332, 70), and in the second the yield was 82% (Weitzenbock, *Monatsh.*, 1913, 34, 193), but methyl o-iodo cinnamate (*idem*, *loc. cit.*)gave only a poor yield. It is difficult to explain the last result, however, if the -T effect is the main factor concerned in the activation of the o-halogen atom, since it would be expected that the effect of the carbalkoxyl group would still be transmitted,



The Ullmann reaction on methyl o-bromo- and o-iodophenylacetate was unsuccessful; a temperature increase was observed with the iodo-compound indicating that reaction had taken place, but no identifiable product could be isolated. Comparison of this with the Ullmann reaction on methyl o-iodobenzoate in which the yield is over 80% leads to the conclusion that the methylene group interposed between the carbalkoxyl-group and the nucleus nullifies the activating (-T) effect on the molecule,



The preparation of 2:2'-diphenyldiacetic acid from the Arndt Eistert reaction on the dichloride of diphenic acid was successful. This method of synthesis is not lengthy, and although it involves the use of diazomethane, each stage proceeds without difficulty.



Kenner's method of preparing 2:2'-diphenyldiacetic acid gave an overall yield of 25%, starting with 2:2'-bis(bromo-methyl) diphenyl. In the final stage of the synthesis it was not found necessary to continuously extract the acid with ether, as described by Kenner, since the acidification of the alkaline hydrolysis product readily precipitated the acid in almost quantitative yield.