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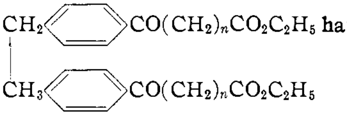
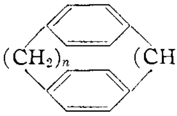
Carbocycles Containing *p*-Phenylene Units. I. Acyloins[1]

BY REYNOLD C. FUSON AND GEORGE P. SPERANZA

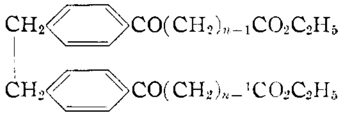
Bibenzyl and a number of higher diphenylalkanes have been converted by the Friedel–Crafts method to the corresponding *p,p'*-dibenzoyl derivatives. *p,p'*-Diacetylbibenzyl has been transformed into the corresponding dicarboxylic acid by the Willgerodt method. The ethyl ester has been made from the acid and also from the corresponding nitrile. A number of keto esters of the type  have been prepared and reduced to the corresponding desoxy esters. The desoxy esters (III) in which n = 3, 5 and 9 have been converted to the corresponding cyclic acyloins.

Carbocycles containing *p*-phenylene units are of particular interest for the stereochemical problems involved, one of which is the possibility of imposing conditions that will prevent free rotation of the aromatic rings. Cycles of type I seem particularly suitable for a study of this question, especially since it appears certain that even in the larger members the benzene rings could be fixed in position by attachment of side chains of suitable blocking power. Although examples of this type of compound have been reported, no synthetic method has been developed for the systematic preparation of the members of the series.

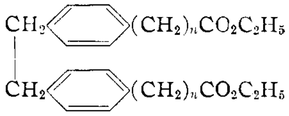
The problem of bridging the para-positions of the benzene ring has been solved in special cases. For example, a chain of eight methylene groups serves to join the two oxygen atoms of hydroquinone.[2] The biphenyl system, being coplanar and coaxial, appears to require a very long chain for bridging; a chain of ten methylene groups fails to connect the oxygen atoms in *p,p'*-dihydroxybiphenyl.[3] On the other hand a bridge of eight methylene groups joins the oxygen atoms of di-(*p*-hydroxyphenyl)-methane.[4] It has been reported that pyrolysis of *p*-xylene yields the compound corresponding to I in which n = 2.[5] However, no example of type I has yet been made by ordinary procedures. This paper reports the results of experiments designed for the development of such a synthesis.



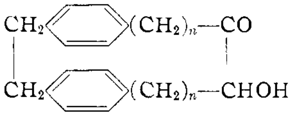
I



II



III



IV

The general procedure that was adopted in this work involves synthesizing esters of type III and subjecting them to the acyloin ring closure.[6,7]

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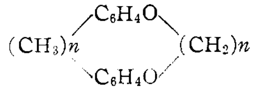
[1] NOTE ADDED IN PROOF.—The experiments reported in this paper are recorded in a thesis presented to the Graduate College of the University of Illinois in June, 1951, by George P. Speranza in partial fulfillment of the requirements for the Ph.D. degree. While this paper was in press an artcile by Cram and Steinberg appeared in which several hydrocarbons of type I are described [D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951)]. Inasmuch as these authors contemplate objectives similar to our own, we have abandoned those phases of our work dealing with the hydrocarbons (paracyclophanes). We are continuing our study of the series



which offers special advantages in the matter of controlled introduction of certain nuclear substituents.

[2] A. Lüttringhaus, *Ann.*, **528**, 181 (1937).

[3] A. Lüttringhaus, *ibid.*, **528**, 211 (1937).

[4] A. Lüttringhaus and R. Kohlhaas, *Ber.*, **72**, 907 (1939); A. Lüttringhaus and K. Buchholz, *ibid.*, **72**, 2057 (1939).

[5] C. J. Brown and A. C. Farthing, *Nature*, **164**, 915 (1949).

[6] M. Stoll and J. Hulstkamp, *Helv. Chim. Acta*, **30**, 1815 (1947).

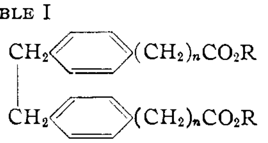
[7] V. Prelog, L. Frenkiel, M. Kobelt and P. Barman, *ibid.*, **30**, 1741 (1947).

The preparation of the esters (III) was effected by the condensation of bibenzyl with acid chlorides of the appropriate half esters and reduction of the resulting keto esters (II) by the Clemmensen and Wolff–Kishner procedures.

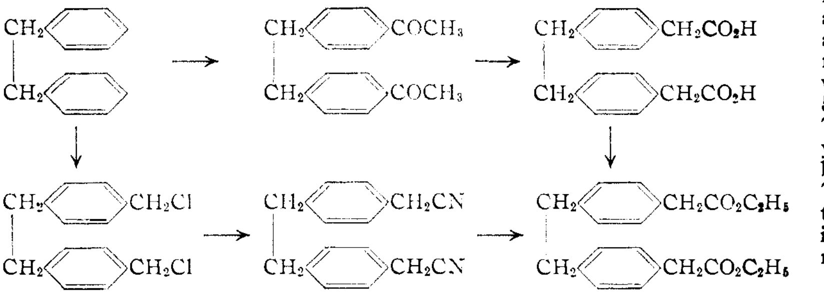
In this way esters of type III have been prepared in which $n = 3, 5$ and 9. Data for these esters and for the acids in which $n = 3$ and 5 are given in Table I. The member in which $n = 1$ was made from the corresponding diacetyl compound, the Willgerodt procedure serving to convert the diketone to the dicarboxylic acid. This ester was synthesized also from the corresponding nitrile, which in turn was made by way of the chloromethyl derivative. The two synthetic routes are indicated in the following chart.

TABLE I

ACIDS AND ESTERS OF TYPE



n	R	M.p., °C.	Formula	Carbon, % Found	Carbon, % Calcd.	Hydrogen, % Found	Hydrogen, % Calcd.
9	C_2H_5	57	$C_{38}H_{55}O_4$	78.77	78.85	10.27	10.10
5	H	148.5	$C_{26}H_{34}O_4$	75.78	76.06	8.40	8.35
5	C_2H_5	69.5	$C_{30}H_{42}O_4$	77.13	77.21	9.07	9.07
3	H	183	$C_{22}H_{26}O_4$	74.75	74.55	7.67	7.40
1	C_2H_5	91	$C_{22}H_{26}O_4$	74.48	74.55	7.64	7.40



In preliminary work a number of diphenylalkanes were condensed with benzoyl chloride to explore further the generality of diacylation by the Friedel–Crafts reaction in such bicyclic compounds. Data concerning the dibenzoyl compounds and the keto esters are collected in Table II.[8]

TABLE II

DIKETONES AND KETO ESTERS

Compound	Yield, %	Solvent	M.p. °C.	Formula	Carbon, % Found	Carbon, % Calcd.	Hydrogen, % Found	Hydrogen, % Calcd.
$[-(CH_2)_5C_6H_4COC_6H_5]_2$	20	Nitrobenzene	75	$C_{36}H_{38}O_2$	86.05	86.01	7.83	7.62
$[-(CH_2)_3C_6H_4COC_6H_5]_2$	43	Nitrobenzene	104	$C_{32}H_{30}O_2$	86.21	86.06	6.92	6.77
$[-(CH_2)_2C_6H_4COC_6H_5]_2$	75	Carbon disulfide	152	$C_{30}H_{26}O_2$	85.85	86.09	6.46	6.26
$[-CH_2C_6H_4COC_6H_5]_2$	64[a]	Carbon disulfide	177[9]					
$[-CH_2C_6H_4COCH_3]_2$	74	Carbon disulfide	168					
$[-CH_2C_6H_4CO(CH_2)_2CO_2C_2H_5]_2$	55	Carbon disulfide	129	$C_{26}H_{30}O_6$	71.50	71.21	6.91	6.90
$[-CH_2C_6H_4CO(CH_2)_4CO_2C_2H_5]_2$	70[b]	Nitrobenzene	94	$C_{30}H_{38}O_6$	72.78	72.85	7.70	7.74
$[-CH_2C_6H_4CO(CH_2)_2CO_2C_2H_5]_2$	79	Carbon disulfide	91	$C_{38}H_{54}O_6$	75.47	75.21	9.10	8.97

[a] When no solvent was employed the yield was 45%. [b] When the solvent was carbon disulfide or tetrachloroethane the yields were 41 and 67%, respectively.

The ring closure was successful with the esters in which $n = 3, 5$ and 9. With the simplest example ($n = 1$) three substances were obtained: the diacid, a brown polymeric appearing material and a white compound which melted about 115–117°. The latter compound had a must, woody odor and the infrared absorption spectrum showed para-phenyl, hydroxyl and carbonyl groups.

Experimental

Preparation of Diphenylalkanes.—The diphenylalkanes were prepared by the Wurtz–Fittig procedure as utilized by Van Alphen.[10] Bibenzyl was purchased from Eastman Organic Chemicals. 1,4-Diphenylbutane was obtained from bromobenzene and 1,4-dibromobutane with sodium in ether in a 54% yield. Diphenylhexane was prepared in a yield of 57% from bromobenzene and 1,6-dibromohexane. Similarly, 1,10-diphenyldecane was obtained in 33% yield from bromobenzene and 1,10-dibromodecane.

The Friedel–Craft Reactions.—The ester-acid chlorides were prepared by the action of thionyl chloride on the acid-esters.[11] In the diacylations, about 2.1 moles of ester-acid chloride and 4.3 moles of aluminum chloride were used for each mole of hydrocarbon. The aluminum chloride was added slowly, with vigorous stirring, to a cold solution of the chloride. With 0.1–0.2 mole of bibenzyl about 500 ml. of carbon disulfide was necessary, since the precipitated complex made stirring difficult when lesser volumes of solvent were used. The choice of solvent affected the yields considerably. When carbon disulfide and high-boiling petroleum ether were used as diluents diphenylhexane and benzoyl chloride gave no diketone. The cleavage of alkyl groups by aluminum chloride can be minimized by employing a complexing solvent.

Reduction of the Carbonyl Groups.—The carbonyl groups of the keto esters were reduced by the Clemmensen method[12] and the Wolff–Kishner method as modified by Huang-Minlon.[13] Acetic acid served as the solvent in the Clemmensen reaction and the refluxing period was about 48 hours. The yields were 50–60% by either method of reduction. The diacids were esterified in excellent yields with ethanol, sulfuric acid or dry hydrogen chloride serving as the catalyst. The esters of type III were solids at room temperature with the exception of that in which $n = 3$; it boiled at 235° (0.3 mm.).

Acyloin Condensation of *sym*-Di-(*p*-carbethoxytrimethylenephenyl)-ethane.—A 2-l., three-necked, creased flask was fitted with a stainless steel stirrer attached to a 10,000 r.p.m. motor controlled by a variac and a high dilution apparatus consisting of a stillhead for distillation of xylene and two reflux condensers for its condensation.[14] A side-arm was attached to a separatory funnel, through which a xylene solu-

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[8] Microanalyses by Miss Emily Davis, Mrs. Jean Fortney and Mrs. K. Pih.

[9] G. Wittig and N. Lee, *Ber.*, **61**, 854 (1928).

[10] J. Van Alphen, *Rec. trav. chim.*, **59**, 580 (1940).

[11] D. Papa, E. Schwenk and N. Hankin, THIS JOURNAL, **69**, 3018 (1947).

[12] E. L. Martin, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 155.

[13] Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

[14] K. Ziegler, H. Eberle and H. Ohlinger, *Ann.*, **504**, 94 (1933).

tion of the ester could be added over a specified period. The apparatus was dried in an oven before use and was protected with drying tubes. An atmosphere of purified nitrogen was maintained until the sodium salt of the acyloin was decomposed. To 800 ml. of distilled xylene (b.p. 137–140°) was added 3 g. (0.13 g. atom) of clean sodium. The xylene was heated to boiling and the mixture was stirred rapidly for 15 minutes. The addition of 12.6 g. (0.0314 mole) of ester, dissolved in 150 ml. of xylene, was started at a very slow rate. The addition was completed in 19 hours, and heating and stirring was continued for 5 additional hours. The solution was cooled to 10° and decomposed with 8 g. of acetic acid. After the addition of acetic acid 200 ml. of 20% sulfuric acid was added. The xylene layer was washed with water four times, once with 10% sodium bicarbonate and again with water. About 0.8 g. of an organic compound which was removed by filtration was found to be soluble in dilute sodium hydroxide solution; it was probably the diacid. The xylene was removed by distillation at 15 mm. pressure and, when the volume was about 30 ml., the contents were transferred to a smaller flask. After all the xylene had been removed 7.93 g. of a light brown oil remained. It was dissolved in high-boiling petroleum ether and, after two days in the ice-box, the solution deposited a white solid. The characteristic absorption[15] for carbonyl (1704 cm.$^{-1}$) and hydroxyl (3424 cm.$^{-1}$) were observed along with absorption for *p*-phenyl substitution (1513 cm.$^{-1}$). There was obtained 5.82 g. (57.5%) of the pure acyloin melting at 95–96°.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 81.95; H, 8.12; mol. wt., 322. Found: C, 82.02; H, 8.39; mol. wt. (ebullioscopic), 327, 318.

2,4-Dinitrophenylhydrazone.—To 0.4 g. of 2,4-dinitrophenylhydrazine was added 2 ml. of concentrated sulfuric acid; 3 ml. of water was added slowly until solution was complete; and to the warm solution was added 10 ml. of 95% ethanol. The acyloin (0.5 g.) was dissolved in 200 ml. of 95% ethanol and added to the solution containing the reagent. A precipitate appeared immediately, and after one hour 0.75 g. of the 2,4-dinitrophenylhydrazone was isolated and recrystallized from ethanol; m.p. 197°.

Anal. Calcd. for $C_{28}H_{30}O_5N_4$: C, 66.91; H, 6.02. Found: C, 66.81; H, 6.25.

2,4-Dinitrophenylosazone from the Acyloin.—2,4-Dinitrophenylhydrazine (1.2 g.) was dissolved in 6 ml. of concentrated sulfuric acid and 4 ml. of water, and 30 ml. of 95% ethanol was added. The resulting solution was filtered and added to a solution of 0.32 g. of acyloin in 20 ml. of 95% ethanol. The mixture was heated in a nitrogen atmosphere for 2 hours. The orange precipitate was collected on a filter. Its infrared spectrum showed complete absence of the carbonyl and hydroxyl groups and corresponded to that expected for the osazone. The osazone was heated under reflux with ethanol several times before being dried for analysis; it decomposes at 286°.

Anal. Calcd. for $C_{34}H_{32}N_8O_8$: C, 59.99; H, 4.74; N, 16.46. Found: C, 60.47; H, 4.91; N, 16.56.

Reaction of *sym*-Di-(*p*-carbethoxynonamethylenephenyl)-ethane with Sodium.—The addition of 26 g. of ester, dissolved in 200 ml. of xylene, to 4.3 g. of sodium sand in 850 ml. of xylene was completed in 36 hours. The mixture was cooled with an ice-bath and 12 g. of acetic acid was added. The organic layer was light yellow and after all the xylene was removed 18 g. of a light red oil remained. The oil was dissolved in 100 ml. of high-boiling petroleum ether. Only 5.2 g. of white solid was obtained, but enough of the oil remained to indicate that the yield in this reaction was good; m.p. 57–57.5°. The infrared spectrum showed the presence of a hydroxyl (3483 cm.$^{-1}$) and a carbonyl group (1703 cm.$^{-1}$).

Anal. Calcd. for $C_{34}H_{50}O_2$: C, 83.21; H, 10.27. Found: C, 83.46; H, 10.02.

2,4-Dinitrophenylosazone.—The procedure previously described yielded the osazone melting at 176–178°.

Anal. Calcd. for $C_{46}H_{56}O_8N_8$: C, 65.07; H, 6.65; N, 13.20. Found: C, 65.37; H, 6.86; N, 13.20.

Reaction of *sym*-Di-(*p*-carbethoxypentamethylenephenyl)-ethane with Sodium.—The addition of 14 g. (0.031 mole) of ester, dissolved in 200 ml. of xylene, to 3 g. of sodium sand (0.13 g. atom) took place over a period of 43 hours. The solution was cooled and 8 g. of acetic acid was added. The xylene layer was washed with dilute sulfuric acid, with water several times, with sodium bicarbonate and again with water. About 3.7 g. of white solid was obtained which, after being refluxed with ethanol and acid, gave the original ester. Apparently some diacid is obtained in each acyloin reaction. When the xylene layer was distilled at reduced pressure 8.2 g. of light brown oil was obtained, which failed to crystallize in an alcohol or high-boiling petroleum ether solution. The oil was distilled at 200–205° (0.05 mm.) and gave about 6 g. of clear, yellow, viscous oil which showed *p*-phenyl (1514 cm.$^{-1}$) and carbonyl absorption (1710 cm.$^{-1}$) but poor hydroxyl absorption (3477 cm.$^{-1}$).

Anal. Calcd. for $C_{26}H_{34}O_2$: C, 82.49; H, 9.06. Found: C, 82.49; H, 9.24.

When this acyloin was heated under reflux with 2-4-dinitrophenylhydrazine a 2,4-dinitrophenylosazone was formed; m.p. 216°.

Anal. Calcd. for $C_{38}H_{40}O_8N_8$: C, 61.95; H, 5.47; N, 15.20. Found: C, 61.81; H, 5.70; N, 15.04.

***sym*-Di-(*p*-carbethoxymethylphenyl)-ethane.**—A mixture of 87 g. of *p*,*p*′-diacetylbibenzyl and 32 g. of sulfur was heated under reflux for 16 hours, and the resulting black solution was poured into hot ethanol. A mixture of the crude morpholide, 400 ml. of acetic acid, 120 ml. of concentrated sulfuric acid and 100 ml. of water was heated for 12 hours under reflux and poured into 3 l. of water. After 8 hours the organic acid was removed by filtration. It was dissolved in potassium hydroxide solution and precipitated by addition of hydrochloric acid. After being dissolved and precipitated a second time in this manner the crude acid was converted to the ethyl ester by heating with 250 ml. of ethanol and 10 ml. of concentrated sulfuric acid. It was recrystallized from ethanol; yield 32 g.; m.p. 90–91° (cor.).

This ester was prepared by an independent route. Bibenzyl was chloromethylated according to the procedure of Reichstein and Oppenauer.[16] A mixture of the chloromethyl compound (4 g.), sodium cyanide (2 g.) and 95% ethanol (40 ml.) was heated under reflux. A solution of the dinitrile (3.3 g.) in 30 ml. of ethanol, containing sulfuric acid as a catalyst, was heated under reflux for 4 hours. The pure ester melted at 90–91°, and a mixture with that obtained from the diacetylbiphenyl showed no depression in melting point.

URBANA, ILLINOIS

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[15] Infrared data and interpretation by Miss Elizabeth Petersen.

[16] T. Reichstein and R. Oppenauer, *Helv. Chim. Acta*, **16**, 1373 (1933).