CHAPTER IV

SYNTHESIS OF SOME C-ACYL DERIVATIVES OF BIPHENYLS

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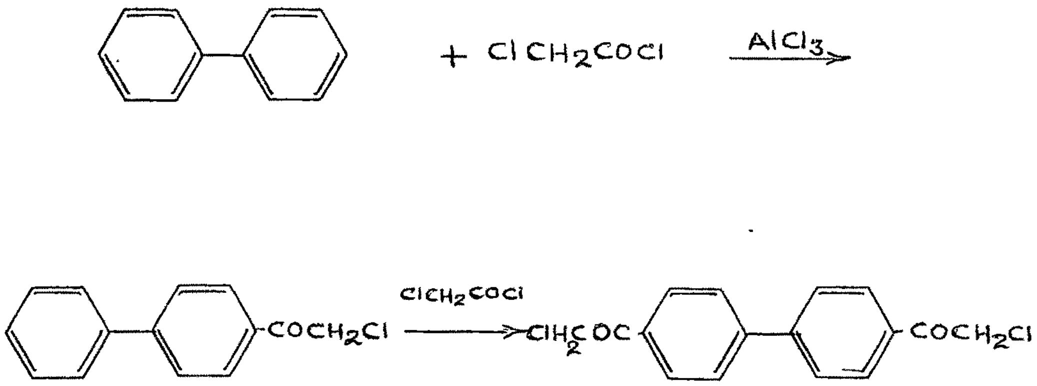
Synthesis of some C-acyl derivatives of biphenyls:

Friedel-Crafts and Fries reactions are well known reactions for the synthesis of C-acyl derivatives of phenolic substances. The different types of Friedel-Crafts reactions including Fries rearrangement have been comprehensively reviewed in a recent monograph[1]. As the present work deals with the acetylation of biphenyl derivatives the previous work in this field is briefly reviewed here.

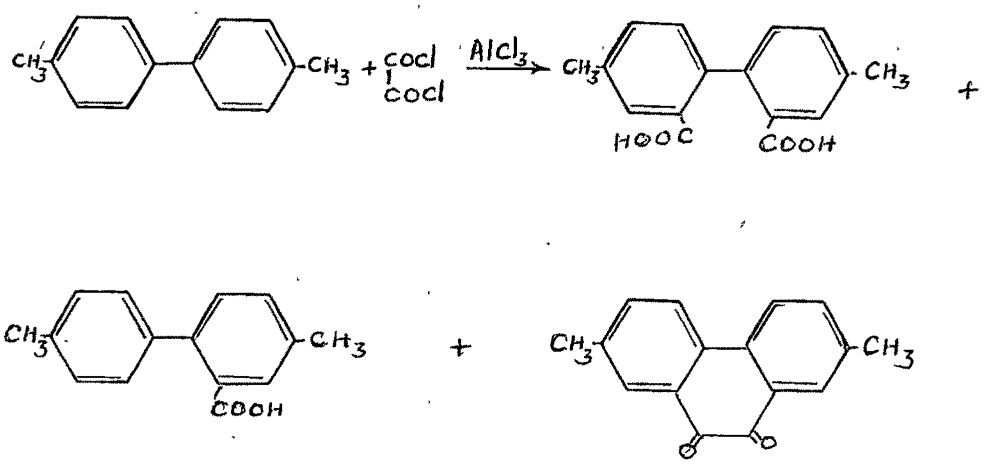
Phosgene and biphenyl react in the presence of anhydrous aluminium chloride to give 4,4'-biphenyl ketone[2].

$$COCl_2 + 2C_6H_5C_6H_5 \longrightarrow (C_6H_5-C_6H_4)_2CO + 2HCl$$

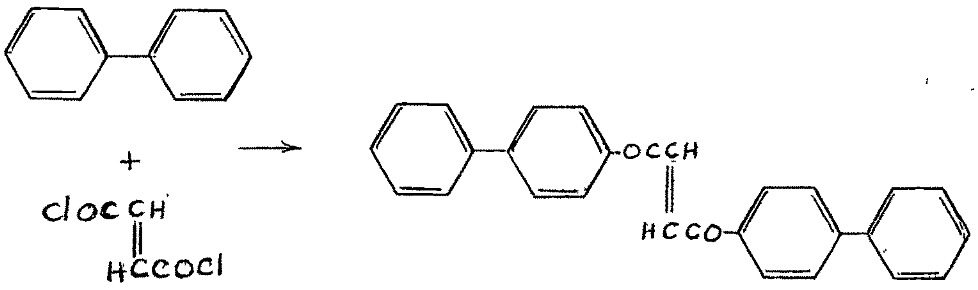
Adam[3] reported that acetyl chloride and biphenyl readily undergo Friedel-Crafts reaction to yield 4-acetylbiphenyl. However, Silver and Lowy[4] found that the product obtained was 4,4'-diacetylbiphenyl. 4-Chloroacetylbiphenyl[5] was obtained when Friedel-Crafts reaction was carried out on biphenyl with chloroacetyl chloride and anhydrous aluminium chloride. Silver and Lowy[4] prepared 4,4'-di(chloroacetyl)-biphenyl in 35 per cent yield by reacting excess of chloroacetyl chloride with biphenyl in the presence of excess of anhydrous aluminium chloride.



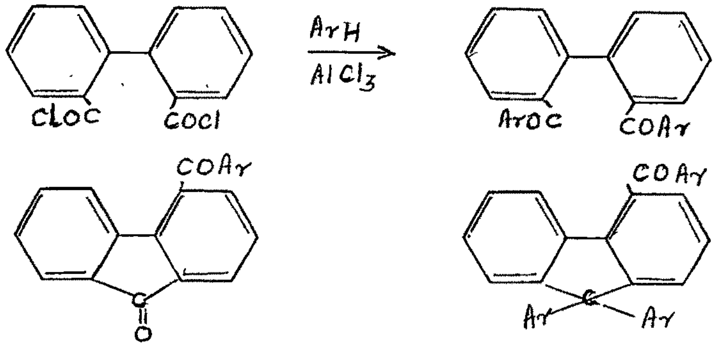
Willgerodt and Scholtz[6] reacted equimolecular quantities of biphenyl and propionyl chloride in carbon disulphide in the presence of anhydrous aluminium chloride and reported the formation of *m*-propionylbiphenyl. Machlis and Blachard[7] however, reported the formation of *p*-propionylbiphenyl when propionyl chloride was reacted with biphenyl. Biphenyl or substituted biphenyls have been reacted with stearoyl chloride and other higher fatty acid chlorides and alkyl ketones obtained[8]. Oxalyl chloride on reaction with biphenyl in the presence of anhydrous aluminium chloride and carbon disulphide gave *p*-biphenyl carboxylic acid in 75 per cent yield. Biphenyl and oxalyl chloride easily yield the mono carboxylic acid, while *p*,*p*'-dimethylbiphenyl gives mainly the 2,2'-dicarboxylic acid with a small amount of mono carboxylic acid and a large amount of *p*,*p*'-dimethyl phenanthrene quinone.



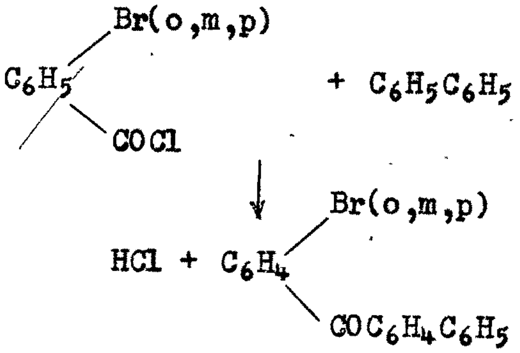
Biphenyl with fumaryl chloride and anhydrous aluminium chloride in benzene solution gives bis (*p*-phenylbenzoyl) ethylene[9]



The chloride of biphenyl 2,2′-dicarboxylic acid exists in two types of products in Friedel-Crafts reactions. One type comprises 2,2′-diaroylbiphenyls and the other 4-aroyl fluorenones and the 4-aroyl-9,9-diaryl fluorenes derived from them[10].



Wolf[11] reacted biphenyl with benzoyl chloride in the presence of aluminium chloride and obtained 4,4′-dibenzoylbiphenyl. Gomberg and Bailar[12] prepared 4-bromo-4′-phenyl-,3-bromo-4′-phenyl-and 2-bromo-4′-phenyl-benzophenone according to the reaction



$$C_6H_5\begin{matrix}Br(o,m,p)\\COCl\end{matrix} + C_6H_5C_6H_5 \downarrow HCl + C_6H_4\begin{matrix}Br(o,m,p)\\COC_6H_4C_6H_5\end{matrix}$$

4/

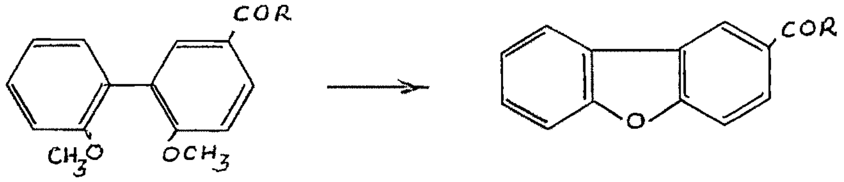
Cinnamoyl chloride reacts with biphenyl to give 4-phenyl chalcone[13].

$$C_6H_5CH = CHCOCl + C_6H_5C_6H_5 \longrightarrow$$
$$C_6H_5CH = CHCOC_6H_4C_6H_5 + HCl$$

Scholl and Seer[14] obtained p-xenyl 1-naphthyl ketone in 48 % yield when naphthoyl chloride was reacted with biphenyl in the presence of aluminium chloride. The condensation of biphenyl with 2-methyl-1-naphthoyl chloride led to the formation of 1-(4-phenylbenzoyl) 2-methyl naphthalene together with some corresponding di-ketone[15]. Schlonk and Brauns[16] reported the formation of 1,4-bis(4-phenylbenzoyl)benzene from terephthaloyl chloride and biphenyl. Phthaloyl chloride with biphenyl afforded dixenylphthalide[17]. p-Xenylsulphonyl chloride and biphenyl yielded di-p-xenylsulphone[18]. 4-Ethyl-4′-acetyl-, 4-methyl-4′-acetyl- and 4-methyl-4′-benzoyl- biphenyls were prepared from 4-ethyl- and 4-methyl-biphenyls using acetyl chloride or benzoyl chloride with aluminium chloride in the presence of carbon disulphide[19]. 4-Ethyl-4′-butyroyl-, 4-ethyl-4′-benzoyl-, 4-ethyl-4′-(phenylacetyl)-, 4-ethyl-4′-caproyl-, 4-ethyl-4′-anisoyl- biphenyls were obtained when 4-ethyl biphenyl was reacted with butyryl chloride, benzoyl chloride, benzylchloride, hexyl chloride and p-methoxybenzoyl chloride respectively. 4-Benzoylbiphenyl with acetyl chloride and aluminium chloride gave 4-benzoyl-4′-acetyl biphenyl[20]. Friedel-Crafts acylation of 3,4-Cl(MeO)C_6H_3Ph with aliphatic and aromatic acid chlorides were shown to give p-$\left[3,4\text{-Cl(MeO)}\ C_6H_3\right]$ C_6H_4COR[21]

Recently, Friedel-Crafts alkylation and acylation on 2,2′-dimethoxybiphenyl have been carried out by Buu-Hoi and co-workers[22] with different molecular proportions of alkyl and acyl chlorides and they obtained 5-alkyl and

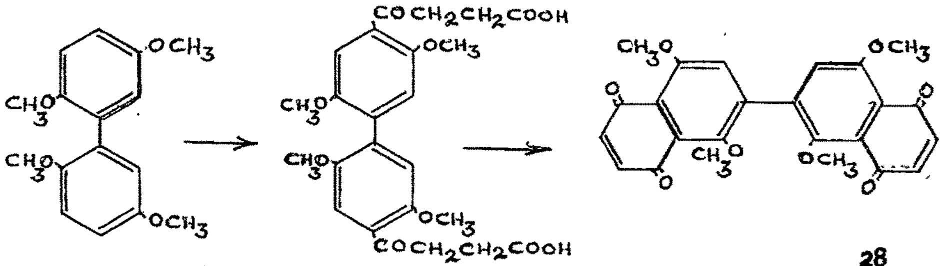
5-acyl derivatives. These alkyl and acyl 2,2′-dimethoxybiphenyls on demethylation with pyridine hydrochloride gave the substituted dibenzofurans.



van Arendonk et al.[23] obtained the 3,3′-diacetyl derivative when the Friedel-Crafts acetylation of 2,2′,6,6′-tetramethoxybiphenyl was carried out with acetyl chloride in carbon disulphide using anhydrous ferric chloride as the catalyst, whereas they isolated the 3,3′,5,5′-tetra-acetyl derivative when the acetylation was done with acetic anhydride in presence of aluminium bromide.

Friedel-Crafts reaction has been carried out with one mole of succinic anhydride or its derivatives on 2,2′- and 4,4′-dimethoxybiphenyls by Baddar et al.[24] and they obtained the 5 and 3-substituted products respectively. Similarly Friedel-Crafts phthaloylation of 4,4′-dihydroxybiphenyl and 4,4′-dimethoxybiphenyl have been reported by Scholl and Seer[25] and they obtained the mono and disubstituted products depending upon the conditions, but they could isolate only the demethylated product in the case of 4,4′-dimethoxybiphenyl. 2,2′,4,4′-Tetramethoxybiphenyl with succinic anhydride and aluminium chloride in nitrobenzene gave 2,2′,4,4′-tetramethoxy 5,5′-di(β-carboxypropionyl)biphenyl[26]. Brockmann and co-workers[27] carried out the succinoylation of

2,2',5,5'-tetramethoxybiphenyl and the 2,2',5,5'-tetramethoxy-4,4'-bis(3-carboxypropionyl)biphenyl formed was cyclised to binaphthazarin, *using aluminium chloride and sodium chloride mixture.*



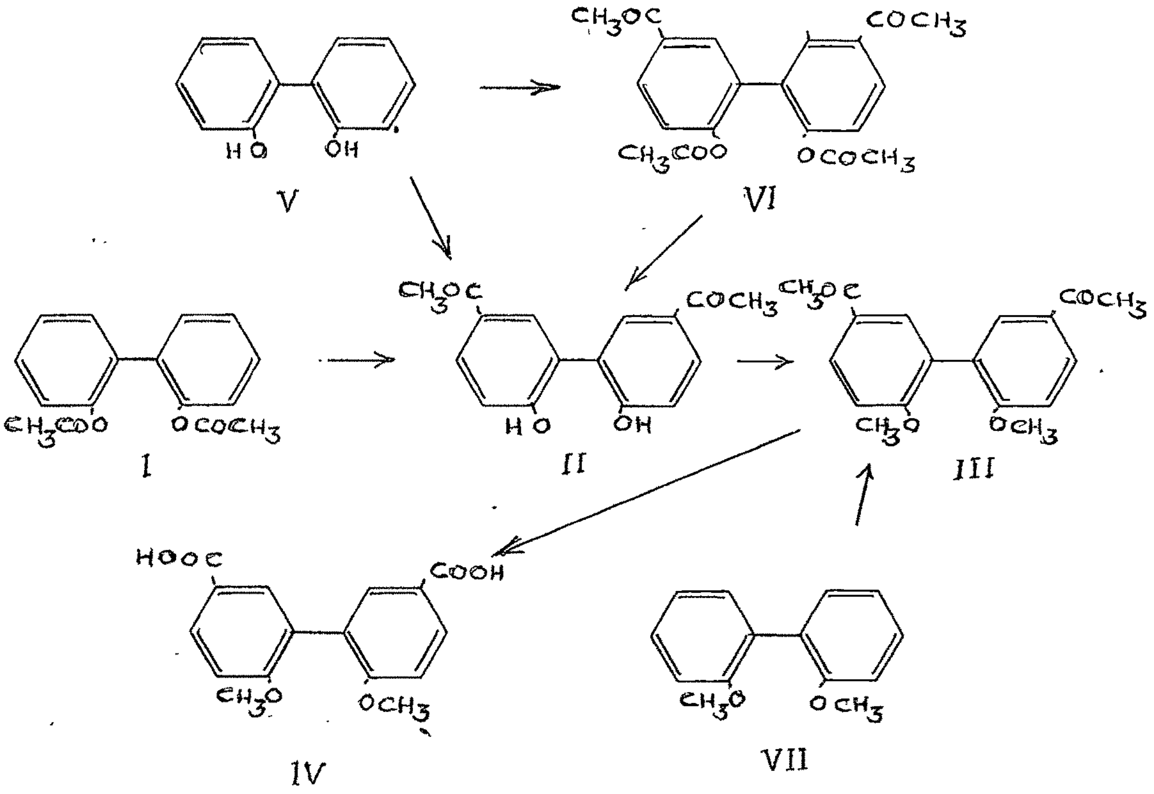
In this laboratory Mathai and Sethna[28] have studied the succinoylation of 2,2'-and 4,4'-dimethoxybiphenyl with excess of succinic anhydride in the presence of anhydrous aluminium chloride in nitrobenzene medium and obtained the 2,2'-dimethoxybiphenyl-5,5'-bis-γ-ketobutyric acid and 4,4'-dimethoxybiphenyl-3,3'-bis-γ-ketobutyric acid respectively. They have also studied the phthaloylation of 2,2'-dimethoxybiphenyl with phthalic anhydride in presence of anhydrous aluminium chloride in nitrobenzene and obtained 2,2'-dimethoxy-5,5'-bis-(o-carboxybenzoyl)biphenyl.

Stoughton et al[29] have prepared the esters of 4,4'-dihydroxybiphenyl with various acid chlorides and then subjected them to Fries rearrangement. Boon-Long[30] has also prepared the 4,4'-dihydroxy-3,3'-diacetylbiphenyl by the same method. He prepared the biphenol dilaurates which were then subjected to Fries rearrangement. 4,4'-Biphenyl dilaurate on Fries rearrangement gave the 3,3'-derivative while 2,2'-biphenyl dilaurate failed to undergo Fries reaction under the same condition. 4-Acetoxybiphenyl with aluminium chloride in tetrachloroethane at 140° gave 4-hydroxy-3-acetylbiphenyl[31] whereas 4-benzoyloxybiphenyl gave 4-hydroxy-4'-benzoylbiphenyl[32].

The present work deals with the Fries rearrangement of 2,2′-diacetoxy and 2,2′,4,4′-tetraacetoxy biphenyl and the Friedel-Crafts acylation of 2,2′-dihydroxy-2,2′,4,4′-tetrahydroxy-, 2,2′- and 4,4′-dimethoxy-, 2,2′,4,4′- and 2,2′,5,5′-tetramethoxybiphenyls with a view to study the pattern of these reactions in the biphenyl series but and also with a view to get C-acylbiphenyl derivatives as intermediates for other studies.

Fries rearrangement of 2,2′-diacetoxybiphenyl :

2,2′-Diacetoxybiphenyl (I)[33] on Fries migration with anhydrous aluminium chloride at 110-20° gave 2,2′-dihydroxy-5,5′-diacetylbiphenyl (II) which on methylation gave the dimethyl ether (III). The dimethyl ether on



oxidation with alkaline potassium permanganate gave 2,2′-dimethoxybiphenyl 5,5′-dicarboxylic acid (IV) which was identical with the product obtained on oxidation of 2,2′-dimethoxy-5,5′-di(chloromethyl)biphenyl[34] as seen by direct comparison.

The above ketones are characterised by the preparation of its di-(2,4-dinitrophenylhydrazone).

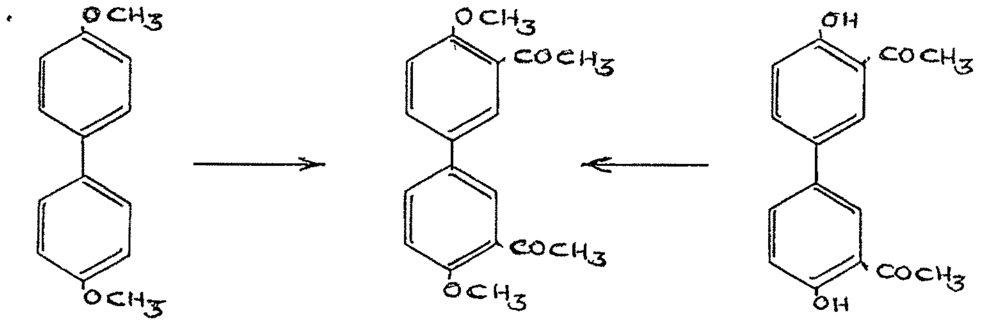
Friedel-Crafts acetylation of 2,2′-dihydroxybiphenyl and its dimethyl ether :

2,2′-Dihydroxybiphenyl (V) on Friedel-Crafts acetylation with acetyl chloride at 120° in the presence of anhydrous aluminium chloride gave 2,2′-dihydroxy-5,5′-diacetylbiphenyl (II) as seen by direct comparison with the product obtained above on Fries migration of 2,2′-diacetoxybiphenyl. An alkali insoluble ketone was also isolated from the reaction mixture which was 2,2′-diacetoxy-5,5′-diacetylbiphenyl (VI). On hydrolysis with 10 % sodium hydroxide it gave 2,2′-dihydroxy-5,5′-diacetylbiphenyl (II).

2,2′-Dimethoxybiphenyl (VII) on Friedel-Crafts acetylation with acetyl chloride in the presence of anhydrous aluminium chloride gave 2,2′-dimethoxy-5,5′-diacetylbiphenyl (III) which was identical with the product obtained on methylation of 2,2′-dihydroxy-5,5′-diacetylbiphenyl (II) as seen by direct comparison .

Friedel-Crafts acetylation of 4,4′-dimethoxybiphenyl :

4,4′-Dimethoxybiphenyl (VIII) on Friedel-Crafts



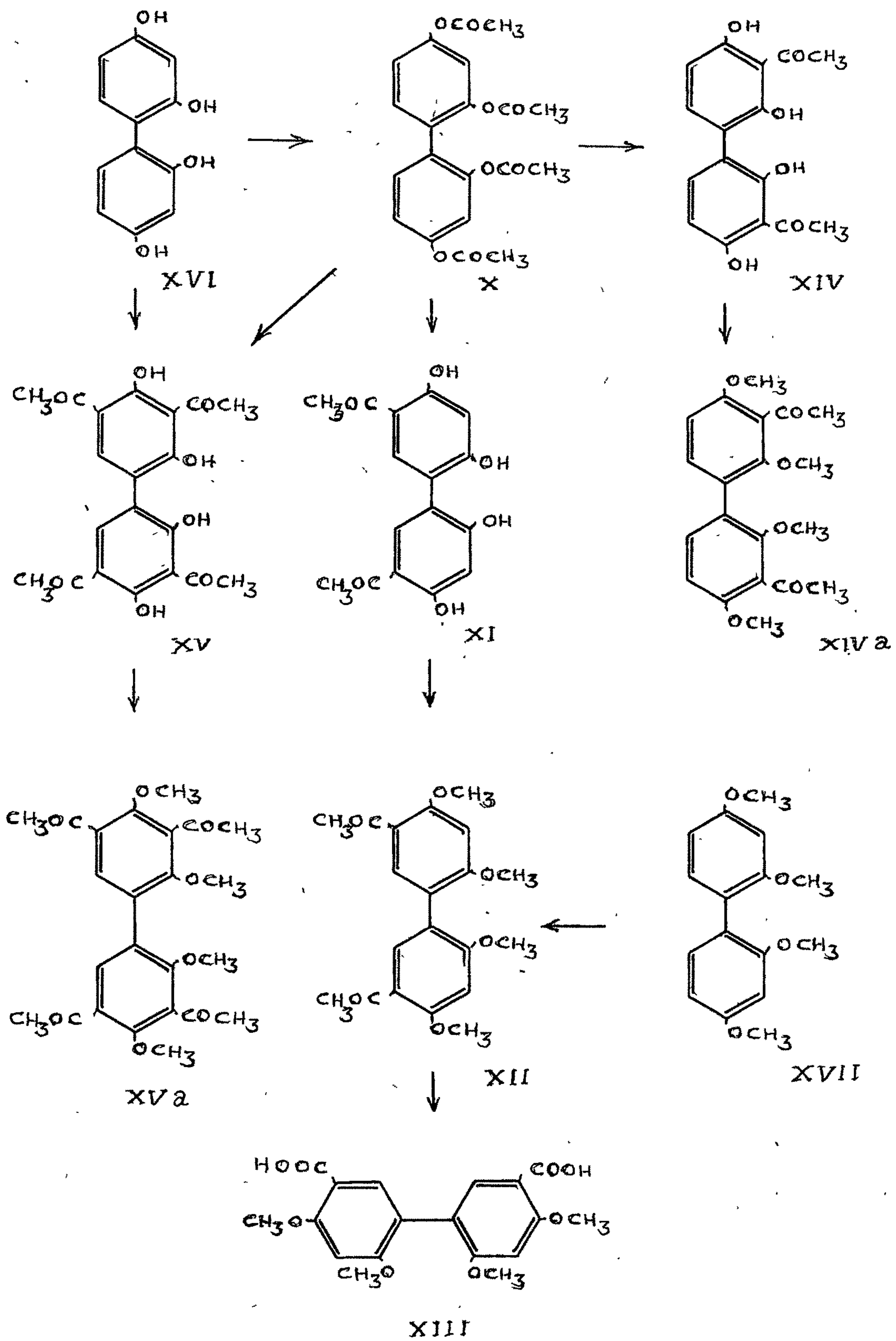
VIII IX

acetylation afforded the 3,3′-diacetyl derivative (IX) which was identical with the product obtained on methylation of 3,3′-diacetyl-4,4′-dihydroxybiphenyl prepared by the Fries migration of 4,4′-diacetoxybiphenyl according to Boon-Long[30] as seen by direct comparison.

The di-(2,4-dinitrophenylhydrazone) of the above diacetyl derivative was also prepared.

Fries rearrangement of 2,2′,4,4′-tetraacetoxybiphenyl :

2,2′,4,4′-Tetraacetoxybiphenyl [35](X) on Fries migration with anhydrous aluminium chloride at 130-40° afforded 2,2′,4,4′-tetrahydroxy-5,5′-diacetylbiphenyl (XI) which on methylation gave the tetramethyl ether (XII). This on oxidation with alkaline potassium permanganate afforded 2,2′,4,4′-tetramethoxybiphenyl-5,5′-dicarboxylic acid (XIII) as seen by direct comparison with the product obtained on oxidation of 2,2′,4,4′-tetramethoxy-5,5′-di-(chloromethyl)biphenyl.


OH
OH
OH
OH
XVI
OCOCH3
OCOCH3
OCOCH3
OCOCH3
X
OH
COCH3
OH
OH
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OH
XIV
CH3OC
OH
COCH3
OH
OH
CH3OC
COCH3
OH
XV
CH3OC
OH
OH
OH
CH3OC
OH
XI
OCH3
COCH3
OCH3
OCH3
COCH3
OCH3
XIV a
CH3OC
OCH3
COCH3
OCH3
OCH3
CH3OC
COCH3
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XV a
CH3OC
OCH3
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OCH3
CH3OC
OCH3
XII
OCH3
OCH3
OCH3
OCH3
XVII
HOOC
COOH
CH3O
OCH3
CH3O
OCH3
XIII

The di-(2,4-dinitrophenylhydrazone) of the above diacetyl derivatives was prepared.

An isomeric product isolated from the reaction mixture has been tentatively assigned the 3,3′-diacetyl structure (XIV) as the m.p. of this product is in close aggrement with the same product obtained by Apsimon et al[36]. by a different method. This on methylation gave the tetramethyl ether (XIVa).

A tetraacetyl derivative was also isolated to which the 2,2′,4,4′-tetrahydroxy-3,3′,5,5′-tetraacetylbiphenyl (XV) structure has been tentatively assigned. On methylation it gave the tetramethyl ether (XVa).

Fries migration of 2,2′,4,4′-tetraacetoxybiphenyl (X) at room temperature with aluminium chloride in nitrobenzene gave the same three products as described above.

Friedel-Crafts acetylation of 2,2′,4,4′-tetrahydroxybiphenyl and its tetramethyl ether

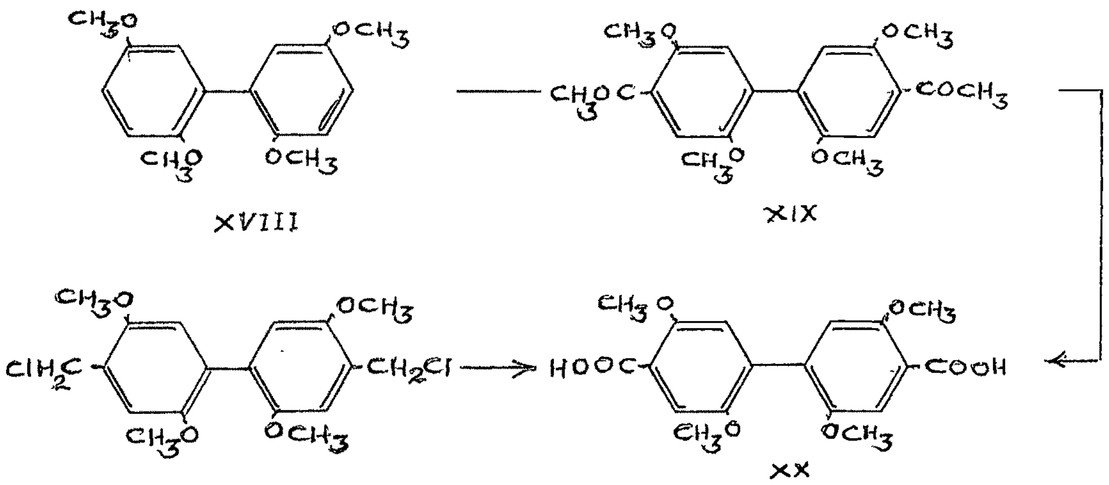
2,2′,4,4′-Tetrahydroxybiphenyl (XVI) on Friedel-Crafts acetylation with acetyl chloride at 110-20° in the presence of anhydrous aluminium chloride gave a tetraacetyl derivative same as described above to which 2,2′,4,4′-tetrahydroxy-3,3′,5,5′-tetraacetylbiphenyl (XV) structure has been tentatively assigned.

It was characterised by the preparation of its tetra-(oxime)

2,2′,4,4′-Tetramethoxybiphenyl (XVII) on Friedel-Crafts acetylation with acetyl chloride at 10° in the presence of anhydrous aluminium chloride gave 2,2′,4,4′-tetramethoxy-5,5′-diacetylbiphenyl (XII) as seen by direct comparison with the product obtained on methylation of 2,2',4,4-tetrahydroxy-5,5'-diacetylbiphenyl (XI) described before.

Friedel-Crafts acetylation of 2,2',5,5'-tetramethoxybiphenyl :

2,2',5,5'-Tetramethoxybiphenyl (XVIII) on Friedel-Crafts acetylation with acetyl chloride in presence of anhydrous aluminium chloride gave 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl (XIX) which on oxidation with alkaline potassium permanganate furnished 2,2',5,5'-tetramethoxybiphenyl-4,4'-dicarboxylic acid (XX) as seen by direct comparison with the product obtained on oxidation of 2,2',5,5'-tetramethoxy-4,4'-dichloromethylbiphenyl.



The di(2,4-dinitrophenylhydrazone) of the above acetyl derivative was also prepared.

EXPERIMENTAL

2,2′-Dihydroxy-5,5′-diacetylbiphenyl :

(a) Fries rearrangement of 2,2′-diacetoxybiphenyl :

2,2′-Diacetoxybiphenyl (2 g ; 0.01 M) was mixed with anhydrous aluminium chloride (5.3 g. ; 0.04 M) and heated in an oil bath at 110-20° for 4 hours. The reaction mixture was cooled and ice cold hydrochloric acid was added. The product obtained crystallised from acetic acid, m.p. 275°. Yield 1.4 g.

Analysis	: Found	: C, 70.6 % ; H, 5.3 %.
$C_{16}H_{14}O_4$	requires	: C, 71.1 % ; H, 5.2 %.

(b) Friedel-Crafts acetylation of 2,2′-dihydroxybiphenyl :

A mixture of 2,2′-dihydroxybiphenyl (1.86 g.; 0.01 M), acetyl chloride (3.12 g. ; 0.04 M) and anhydrous aluminium chloride (5.3 g. ; 0.04 M) was heated in an oil bath at 110-20°. Ice-cold hydrochloric acid (1 : 1) was added to the reaction mixture and the product obtained was extracted with sodium hydroxide. The alkali soluble product was reprecipitated by the addition of hydrochloric acid and crystallised from acetic acid. Mixed m.p. with 2,2′-dihydroxy-5,5′-diacetylbiphenyl obtained in the Fries rearrangement of 2,2′-diacetoxybiphenyl as described above was not depressed.

2,2′-Diacetoxy-5,5′-diacetylbiphenyl :

The alkali insoluble product from the above reaction mixture was crystallised from benzene in white needles, m.p. 150°.

Analysis : Found : C,67.6 % ; H,5.3 %.
$C_{20}H_{18}O_6$ requires : C,67.8 % ; H,5.1 %.

Hydrolysis : 2,2'-Diacetoxy-5,5'-diacetylbiphenyl (0.5 g.) was heated on a steam bath with sodium hydroxide (10 ml.; 10 %) for 2 hours. The product obtained on acidification crystallised from acetic acid, m.p.275°. Mixed m.p. with 2,2'-dihydroxy-5,5'-diacetylbiphenyl described above was not depressed.

2,2'-Diacetoxy-5,5'-diacetylbiphenyl was also prepared as follows : 2,2'-Dihydroxy-5,5'-diacetylbiphenyl (0.5 g.) was mixed with acetic anhydride (5 ml.) and freshly fused sodium acetate (1 g.) . The mixture was heated on a steam bath for 2 hours and then poured into water. The product crystallised from benzene, m.p.275° Mixed m.p. with the above product was not depressed.

The di-(2,4-dinitrophenyl hydrazone) of 2,2'-dihydroxy-5,5'-diacetylbiphenyl :

2,2'-Dihydroxy-5,5'-diacetylbiphenyl (0.5 g.) was dissolved in minimum quantity of alcohol and 2,4-dinitrophenylhydrazine hydrochloride in alcohol was added. The mixture was refluxed on a steam bath for 30 minutes and the product obtained on cooling the reaction mixture was crystallised from nitrobenzene, m.p.300°.

Analysis : Found : N, 17.8 %.
$C_{28}H_{22}O_{10}N_8$ requires : N, 17.8 %.

2,2′-Dimethoxy-5,5′-diacetylbiphenyl :

(a) Methylation of 2,2′-dihydroxy-5,5′-diacetylbiphenyl :

2,2′-Dihydroxy-5,5′-diacetylbiphenyl (1 g.) was refluxed in acetone (50 ml.) with dimethyl sulphate (2 g.) and anhydrous potassium carbonate (10 g.) for 8 hours on a steam bath. The product obtained on removal of acetone and addition of water crystallised from benzene-petroleum ether, m.p. 163°.

Analysis : Found : C, 72.8 % ; H, 6.1 %.

$C_{18}H_{18}O_4$ requires : C, 72.5 % ; H, 6.0 %.

(b) Friedel-Crafts acetylation of 2,2′-dimethoxybiphenyl :

2,2′-Dimethoxybiphenyl (2.1 g. ; 0.01 M) was dissolved in carbon disulphide and acetyl chloride (3.1 g.; 0.04 M) and anhydrous aluminium chloride (5.3 g. ; 0.04 M) was added. The reaction mixture was kept below 10° for 1 hour and then decomposed with ice-cold hydrochloric acid. The product obtained was washed with alkali to remove the demethylated product if any and then crystallised from benzene-petroleum ether. M.P. and mixed m.p. with 2,2′-dimethoxy-5,5′-diacetylbiphenyl described above was 163°.

The di-(2,4-dinitrophenylhydrazone) : Prepared as before and crystallised from nitrobenzene, m.p. 310°.

Analysis : Found : N, 16.8 %.

$C_{30}H_{26}N_8O_{10}$ requires : N, 17.0 %.

Oxidation of 2,2'-dimethoxy-5,5'-diacetylbiphenyl :

The above dimethoxy diacetyl derivative (0.5 g.) was suspended in sodium hydroxide (10 g. ; 10 ml. water) and heated on a steam bath with potassium permanganate (1 g.) for 2 hours. The reaction mixture was then filtered and the filtrate acidified with hydrochloric acid. The acid obtained was purified through bicarbonate treatment and crystallised from acetic acid, m.p. 340°. Mixed m.p. with the 2,2'-dimethoxybiphenyl-5,5'-dicarboxylic acid obtained according to Mathai and Sethna[34] was not depressed.

Friedel-Crafts acetylation of 4,4'-dimethoxybiphenyl :

3,3'-Diacetyl-4,4'-dimethoxybiphenyl :

4,4'-Dimethoxybiphenyl (2.1 g. ; 0.01 M) in carbon disulphide (30 ml.) was mixed with acetyl chloride (3.1 g. ; 0.04 M) and the reaction mixture was cooled in ice. Anhydrous aluminium chloride (3.1 g. ; 0.04 M) was added and the reaction mixture stirred till a pasty mass was formed. It was kept for 1 hour in ice and ice-cold hydrochloric acid was then added. The product obtained was washed with sodium hydroxide to remove the demethylated product if any and crystallised from alcohol, m.p. 148°. Yield 1.8 g. Mixed m.p. with the product obtained on methylation of 3,3'-diacetyl-4,4'-dihydroxybiphenyl, prepared according to Boon-Long[30], was not depressed.

The di-(2,4-dinitrophenylhydrazone) : Prepared as before and crystallised from nitrobenzene -xylene, m.p. 302°.

Analysis : Found : N, 16.7 %.
$C_{30}H_{26}O_{10}N_8$:requires : N, 17.0 %.

Fries rearrangement of 2,2′,4,4′-tetraacetoxybiphenyl :

(a) 2,2′,4,4′-Tetrahydroxy-5,5′-diacetylbiphenyl :

An intimate mixture of 2,2′,4,4′-tetraacetoxybiphenyl (3 g. ; 0.01 M) and anhydrous aluminium chloride (5.3 g. ; 0.04 M) was heated in an oil bath at 130-40° for 4 hours. The reaction mixture was cooled and then treated with ice and hydrochloric acid. The product obtained was extracted with ether. The etheraal layer was extracted repeatedly with alkali. The product obtained on acidification of the alkaline extracts crystallised from alcohol, m.p. 236°. Yield 0.9 g.

Analysis : Found : C, 63.4 % ; H, 5.0 %.
$C_{16}H_{14}O_6$ requires : C, 63.5 % ; H, 4.6 %.

(b) 2,2′,4,4′-Tetrahydroxy-3,3′-diacetylbiphenyl :

After separating the 2,2′,4,4′-tetrahydroxy-5,5′-diacetylbiphenyl through ether extraction the product insouble in ether was crystallised from xylene, m.p. 245° Yield 0.8 g. Mixed m.p with the above product was depressed by 15°.

Analysis : Found : C, 63.8 % ; H, 4.5 %.
$C_{16}H_{14}O_6$ requires : C, 63.5 % ; H, 4.6 %.

Apsimon et al.[36] who prepared the same compound by a different method reported m.p. 248-49°.

(c) 2,2',4,4'-Tetrahydroxy-3,3',5,5'-tetraacetylbiphenyl :

After separating the two diacetyl derivatives from the Fries reaction mixture, a product insoluble in xylene was obtained which crystallised from diphenyl ether, m.p. 302°. Yield 0.6 g.

Analysis : Found : C, 62.4 % ; H, 4.4 %.
$C_{20}H_{18}O_8$ requires : C, 62.2 % ; H, 4.7 %.

The same three products were isolated when the reaction was carried out in nitrobenzene solution as follows :

2,2',4,4'-Tetraacetoxybiphenyl (3 g. ; 0.01 M) was dissolved in nitrobenzene (20 ml.) and anhydrous aluminium chloride (5.3 g. ; 0.04 M) in nitrobenzene (20 ml.) was added. The reaction mixture was kept at room temperature for 48 hours. Ice cold hydrochloric acid was then added and the product obtained on removal of nitrobenzene gave 2,2',4,4'-tetrahydroxy-5,5'-diacetylbiphenyl, 2,2',4,4'-tetrahydroxy-3,3'-diacetylbiphenyl and 2,2',4,4'-tetrahydroxy-3,3',5,5'-tetraacetylbiphenyl. Mixed m.ps. with the products described above were not depressed.

2,2',4,4'-Tetramethoxy-5,5'-diacetylbiphenyl :

(a) By methylation of 2,2',4,4'-tetrahydroxy-5,5'-diacetylbiphenyl :

2,2',4,4'-Tetrahydroxy-5,5'-diacetylbiphenyl (0.5 g.) was dissolved in dry acetone (50 ml.) and refluxed with dimethyl sulphate (1 g.) and anhydrous potassium carbonate (5 g.) for 8 hours. The white solid obtained on working up the reaction mixture as before crystallised from benzene in white needles, m.p. 214°.

Analysis : Found : C, 67.0 % ; H, 6.1 %.

$C_{20}H_{22}O_6$ requires : C, 67.0 % ; H, 6.1 %.

(b) Friedel-Crafts acetylation of 2,2',4,4'-tetramethoxybiphenyl :

A solution of 2,2',4,4'-tetramethoxybiphenyl (2.7 g. ; 0.01 M) and acetyl chloride (3.1 g. ; 0.04 M) in carbon disulphide (30 ml.) was cooled in ice. Anhydrous aluminium chloride (5.3 g. ; 0.04 M) was added and the reaction mixture stirred till a pasty mass was formed. After keeping for 1 hour below 10° the carbon disulphide was removed by decantation and ice cold hydrochloric acid was added. The solid obtained was washed with sodium hydroxide to remove the demethylated product if any and crystallised from benzene, m.p. 214°. Mixed m.p. with the dimethyl ether described above was not depressed.

The di-(2,4-dinitrophenylhydrozone): Prepared as before and crystallised from nitrobenzene gave m.p. 301°.

Analysis : Found : N, 15.2 %.

$C_{32}H_{30}O_{12}N_8$ requires : N, 15.6 %.

Oxidation of 2,2′,4,4′-tetramethoxy-5,5′-diacetylbiphenyl :

2,2′,4,4′-Tetramethoxy-5,5′-diacetylbiphenyl (0.5 g.) was suspended in sodium hydroxide (10 g. in 10 ml. water), potassium permanganate (2 g.) was added and the reaction mixture heated for 2 hours. on a steam bath. The product obtained on working up as before crystallised from alcohol. Mixed m.p. with 2,2′,4,4′-tetramethoxy-5,5′-dicarboxylic acid obtained by the oxidation of 2,2′,4,4′-tetramethoxy-5,5′-dichloromethyl derivative as described in Chapter II was not depressed.

2,2′,4,4′-Tetramethoxy-3,3′-diacetylbiphenyl :

Prepared by refluxing the dihydroxy diacetylbiphenyl (0.5 g.), described above, in acetone (50 ml.) with dimethyl sulphate (3 g.) and anhydrous potassium carbonate (15 g.) for 8 hours on a steam bath. The product obtained on working up as usual crystallised from benzene-petroleum ether in white needles, m.p. 144°.

Analysis : Found : C, 66.6 % ; H, 5.9 %.
$C_{22}H_{22}O_6$ requires : C, 67.0 % ; H, 6.1 %.

Apsimon et al.[36] who prepared this compound by a different method gave m.p. 136°.

Friedel-Crafts acetylation of 2,2′,4,4′-tetrahydroxybiphenyl :

2,2′,4,4′-Tetrahydroxy-3,3′,5,5′-tetraacetylbiphenyl:

2,2′,4,4′-Tetrahydroxybiphenyl (2.2 g. ; 0.01 M), acetyl chloride (3.1 g. ; 0.04 M) and anhydrous aluminium chloride (9.3 g. ; 0.07 M) was heated in an oil bath at 120° for 2 hours. The product obtained on addition of ice and hydrochloric acid was extracted with sodium hydroxide. The alkaline solution was acidified with hydrochloric acid and the product obtained crystallised from diphenyl ether. Mixed m.p. with 2,2',4,4'-tetrahydroxy-3,3',5,5'-tetraacetylbiphenyl described before was not depressed.

2,2',4,4'-Tetramethoxy-3,3',5,5'-tetraacetylbiphenyl :

Prepared by refluxing the above tetrahydroxybiphenyl derivative (0.5 g.) in acetone (25 ml.) with dimethyl sulphate (2 g.) and anhydrous potassium carbonate (8 g.) for 8 hours on a steam bath and the product obtained on working up as usual crystallised from petroleum ether in white cubes, gave m.p. 95°.

Analysis : Found : C, 65.2 % ; H, 6.0 %.
$C_{24}H_{26}O_8$ requires : C, 65.1 % ; H, 5.8 %.

The tetra-(oxime) : The tetramethyl ether (0.5 g.) was dissolved in alcohol and refluxed with hydroxylamine hydrochloride (1 g.) in water and ~~neutralised with~~ potassium hydroxide (0.5 g.) on a steam bath for 2 hours. Alcohol was distilled off and the product obtained on cooling crystallised from alcohol, m.p. 150°.

Analysis : Found : N, 10.8 %.
$C_{24}H_{30}N_4O_8$ requires : N, 11.1 %.

Friedel-Crafts acetylation of 2,2′,5,5′-tetramethoxybiphenyl :

2,2′,5,5′-Tetramethoxy-4,4′-diacetylbiphenyl :

A mixture of 2,2′,5,5′-tetramethoxybiphenyl (2.7 g.; 0.01 M) and acetyl chloride (3.1 g. ; 0.04 M) in carbon disulphide (30 ml.) was cooled in ice. Anhydrous aluminium chloride (5.3 g. ; 0.04 M) was added and the reaction mixture stirred till a pasty mass was formed. The product obtained on addition of ice cold hydrochloric acid was washed with sodium hydroxide to remove the demethylated product and crystallised from xylene in white needles, m.p. 197°.

Analysis : Found : C, 67.3 % ; H, 6.4 %.

$C_{20}H_{22}O_6$ requires : C, 67.0 % ; H, 6.1 %.

The di-(2,4-dinitrophenylhydrazone): Prepared as usual and crystallised from nitrobenzene gave m.p.299°.

Analysis : Found : N, 15.7 %.

$C_{32}H_{30}N_8O_{12}$ requires : N, 15.6 %.

Oxidation of 2,2′,5,5′-tetramethoxy-4,4′-diacetylbiphenyl :

2,2′,5,5′-Tetramethoxy-4,4-diacetylbiphenyl(0.5 g.) was suspended in sodium hydroxide (10 g. ; 10 ml. water), potassium permanganate (2 g.) was added and the reaction mixture heated on a steam bath for 2 hours. The reaction mixture was worked up as before and the product obtained crystallised from alcohol, m.p.255°. Mixed m.p.with the acid obtained on oxidation of 2,2′,5,5′-tetramethoxy-4,4′-di-(chloromethyl) biphenyl as described in Chapter II was not depressed.

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