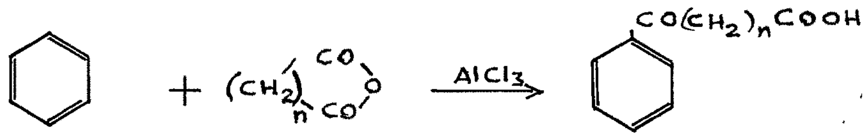
CHAPTER III

FRIEDEL-CRAFTS SUCCINOYLATION AND PHTHALOYLATION OF BIPHENYL DERIVATIVES

CHAPTER III

Friedel-Crafts succinoylation and phthaloylation of biphenyl derivatives. Since the literature concerned with Friedel-Crafts reaction is so vast, it will not be possible to give a general survey of this reaction in a few pages nor is it necessary to do so. The following discussion is primarily concerned with the Friedel-Crafts reaction on aromatic compounds with succinic and phthalic anhydrides, as the present work deals with the succinoylation and phthaloylation of biphenyl derivatives. The different types of Friedel-Crafts reactions have been extensively reviewed in a recent comprehensive monograph[1].

(A) Friedel-Crafts succinoylation :- The Friedel-Crafts reaction between an aliphatic dibasic acid anhydride and an aromatic compound results in the formation of an aroyl fatty acid with the aroyl group situated at the terminal carbon atom of the aliphatic chain.



---

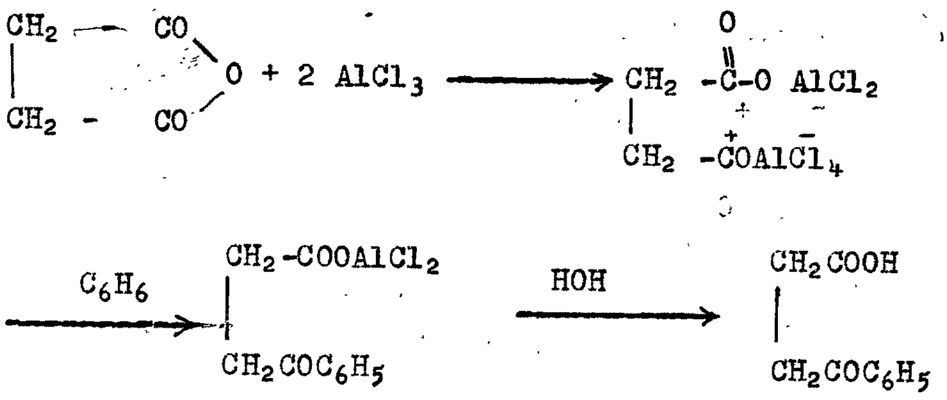
[1] Friedel Crafts and related reactions (Vol.I and II published so far), Edited by G.A.Olah, Inter Science Publishers, New York, 1964.

The importance of this reaction lies in the fact that the B-aroyl propionic acids, obtained from the reaction constitute very important intermediates in the synthesis of aromatic hydrocarbons. The keto acids readily undergo Clemmensen reduction[2] and the reduced acids on cyclization give cyclic ketones[3] which on aromatization give aromatic hydrocarbons. Once the cyclic ketones are formed, further modifications become available through a Grignard reaction.

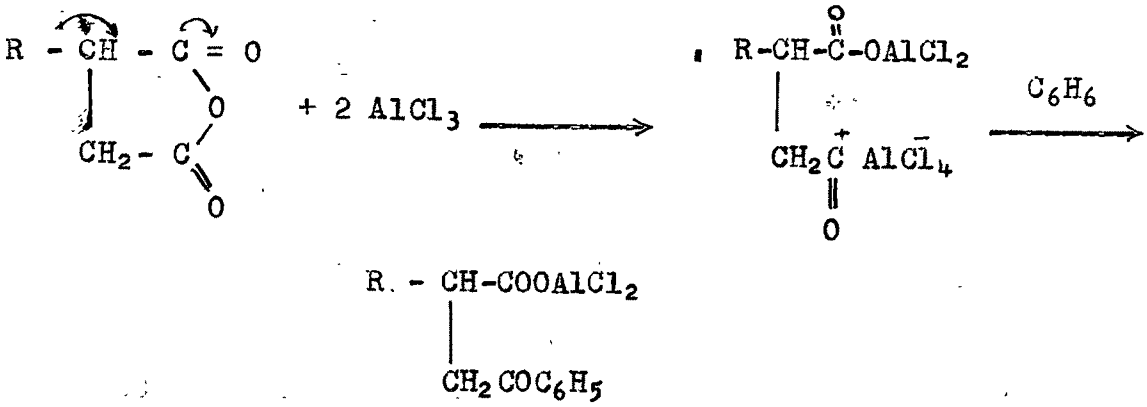
Mechanism :- It is observed that the Friedel-Crafts reaction with an anhydride proceeds with a maximum yield when two moles of aluminium chloride are used per mole of anhydride[4,5]. One mole of catalyst brings about the fission of the anhydride with the formation of the aluminium chloride salt of one carboxyl group and the second mole of aluminium chloride functions as catalyst as in a typical Friedel-Crafts acylation. Therefore the reaction can be visualized as proceeding through the complex (I) which attacks the aromatic ring by virtue of the electrophilic centre on the acyl ion.

---

2. Martin., Organic reaction I., 155, Wiley, New York 1942.
3. Johnson., Organic reaction II., 114, Wiley, New York 1944.
4. Noller and Adams., J.Am.Chem.Soc., 46, 1889 (1924).
5. Groggins and Nagel., Ind.Eng.Chem., 26, 1313 (1934).



The preferentical fission of unsymmetrical anhydrides can be explained if the assumption is made that the electron seeking aluminium chloride opens the anhydride towards the carboxyl group that has the higher electron density.



Scope of Friedel-Crafts succinoylation:- A great number of hydrocarbons such as simple as well as polynuclear aromatic and partially aromatic hydrocarbons, bicyclic compounds and halogen substituted phenyls have been subjected to Friedel-Crafts succinoylation. Migration or isomerisation of large groups which often accompanies Friedel-Crafts acylation has not been observed in Friedel-Crafts succinoylation. Benzene and alkylated benzenes[6],

---

6. Muhr.Ber., 28, 3215 (1895)

Barnelt and Sanders., J.Chem.Soc., 1933, 434.

naphthalene, and its alkyl derivatives[7] phenanthrene[8] anthracene[9], chrysene[10], acenaphthene[7] etc. undergo Friedel-Crafts succinoylation smoothly.

Phenols and phenolic ethers which undergo the succinoylation reaction particularly readily have been extensively studied. Thus anisole[11],cresols and their methyl ethers[12], trimethyl ether of pyrogallol[13] and free resorcinol[14],orcinol[14] etc. have been successfully succinoylated. Diphenyl ether and diphenyl sulphide

---

7. Haworth et al., Ibid., 1932, 1125, 1784, 2248, 2720. Fieser and Peters., J.Am.Chem.Soc., 54, 4347 (1932).
8. Haworth and Mavin., J.Chem.Soc., 1933, 1012.
9. Cook and Robinson., J.Chem.Soc., 1938, 505 ; Bergmann and Weizmann., Ibid., 1938, 1243.
10. Beyer., Ber., 71, 915 (1938) ; Cook and Graham., J. Chem.Soc., 1944, 329.
11. Poppenberg., Ber., 34, 3257 (1901) ; Fieser and Hershberg., J.Am.Chem.Soc., 58, 2314 (1936).
12. Rosenmund and Schapiro., Arch.Pharm., 272, 313 (1934) ; Desai and Wali., Pro.Ind.Acad.Sci., 6A, 144 (1937).
13. Bergellini and Giva.Gazz.Chim.ital., 42I, 197 (1912). Mitter and De., J.Ind.Chem.Soc., 16, 35 (1939).
14. Desai and Shroff., J.Uni.Bombay., 10, pt. 3,97 (1941).

afford the corresponding acids in good yield[15]. Various heterocyclic compounds such as thiophene[16], benzothiophene[17] thiochroman[18] diphenylene oxide[19] etc. etc. undergo Friedel-Crafts succinoylation smoothly.

Orientation of entering groups :- The orientation in the aromatic ring in Friedel-Crafts succinoylation is determined by the group already present in the ring and can be predicted from the rules governing aromatic substitution. Steric hindrance, however, directs the course of substitution to some extent. Succinoyl group, being a bulky group, usully avoids the ortho position. Succinoylation of phenols is exceptional in which ortho substitution predominates[20]. In all other cases like phenolic ethers[11], halogenated benzenes[21], alkylbenzenes[6] etc. the para isomer predominates. When more than one

---

[15] Kipper., Ber., 38, 2490 (1905); Rice., J.Am.Chem.Soc., 48, 269 (1926).

[16] Fieser and Kenelly., J.Am.Chem.Soc., 57, 1611 (1935).

[17] Buu-Hoi and Cagniant., Ber., 76, 1269 (1943).

[18] Cagniant and Deluzarche., Compt.rend., 223, 1012 (1946).

[19] Gilman, Parker, Bailie and Brown., J.Am.Chem.Soc., 61, 2836 (1939).

[20] Raval, Bokil and Nargund., J.Uni.Bomb., 7, pt. 3184(1938).

[21] Skraup and Schwamberger., Ann., 462, 135 (1928).
Fieser and Seligman., J.Am.Chem.Soc.,60, 170 (1938).

group is present in the ring the substitution is directed by the group which has got the stronger directing influence. Thus 2-methyl-5-ethyl anisol on succinoylation gives the 4-anisoyl propionic acid derivative[12]. 4-Methoxy biphenyl, however, gives 4'-and 3-derivatives[22]. In polynuclear hydrocarbons usually two isomeric products are formed. Naphthalene and anthracene give the 1-and 2-isomers[7,9]. The ratio of isomers is influenced sometimes by the solvent and the reaction temperature. When nitrobenzene is used as solvent, positions that are ordinarily subject to steric hindrance are usually avoided. This may be due to the formation of a bulky complex of nitrobenzene, aluminium chloride and the anhydride which finds an easier reaction path in a less blocked position. Thus 2-methoxy naphthalene gives the 6-isomer in succinoylation with nitrobenzene as solvent where as in bromination and nitration the 1-isomer is obtained[23].

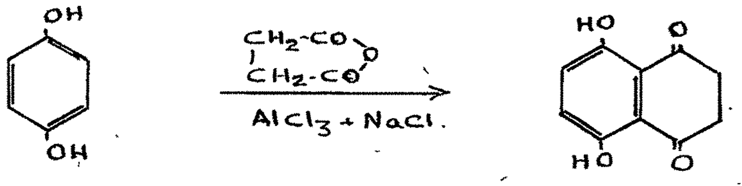
The condensation of succinic acid and its anhydride with aromatic compounds generally gives B-aroyl propionic acid. There are a few cases where the use of an aluminium chloride-sodium chloride melt leads to the formation of a cyclic product. For example, hydroquinone condenses with succinic acid in an aluminium chloride-sodium chloride melt to give 1,2,3,4-tetrahydro-5,8-dihydroxy-

---

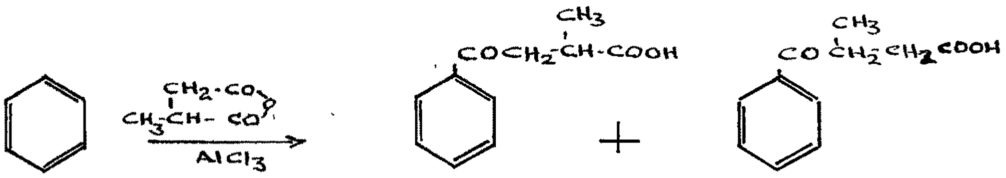
22. Fieser and Bradsher., J.Am.Chem.Soc., 58, 1738 (1936).

23. Ruzicka and Waldmann., Helv.Chem.Acta., 15, 907 (1932).
Short, Stromberg and Wiles., J.Chem.Soc., 1936, 319.

1,4-diketo naphthalene in 25 % yield[23a].



Substituted anhydrides :- Various substituted succinic anhydrides are also used for the Friedel-Crafts reaction. Out of the two types of substituted succinic anhydrides, the monosubstituted succinic anhydride can give rise to isomeric products. Methyl succinic anhydride on condensation with benzene gives rise to α-methyl-β-benzoyl propionic acid and β-methyl-β-benzoyl propionic acid[24].



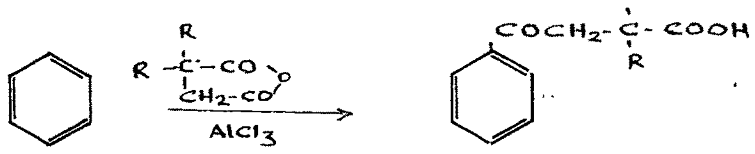
Unsymmetrically substituted succinic anhydrides having two substitutents on the same carbon atom such as α,α-dimethyl or α,α-diethyl succinic anhydride, invariably

---

[23a] Bruce, Sorrie and Thomson., J.Chem.Soc., 2403, 1953.

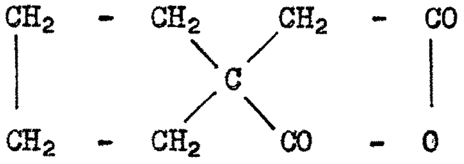
[24] Klobb., Bull.Soc.Chim.France., (3) 23, 511 (1900) Oppenheim., Ber., 34, 4227 (1901).

reacts so as to form the α,α-dialkyl-β-aroyl propionic acid as the sole product.

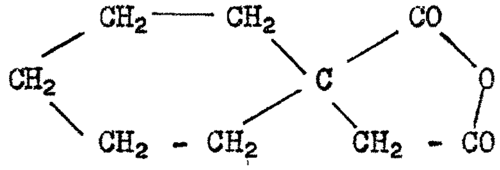


Here the fission of the anhydride always occurs in such a way that the gem-dialkyl group is farthest away from the aromatic ring[25].

Several other substituted succinic anhydrides such as those given below have been subjected to Friedel-Crafts reaction with benzene, hydrindene, naphthalene etc.



;



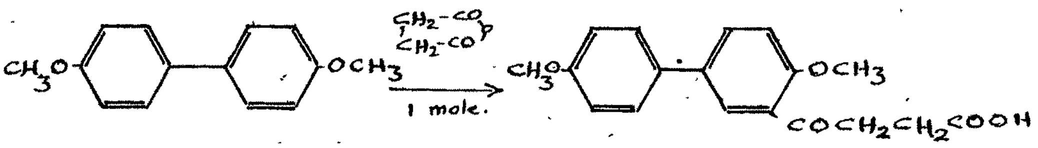
Among the biphenyl and its derivatives, simple biphenyl has been succinoylated and the 4-phenyl benzoyl propionic acid obtained. The succinoylation of 4-methoxy biphenyl has been studied by Fieser and Bradsher[22]. They isolated the 4-methoxy-4'-xenoyl propionic acid and 4-methoxy-3-xenoyl propionic acid[22]. Succinoylation of 2,2'-and 4,4'-dimethoxy biphenyls have been carried out by Baddar and his co-workers[26]. With one mole of succinic

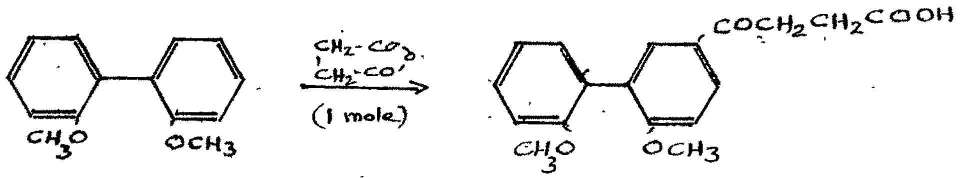
---

25. Sengupta., J.Prakt.Chem., (2) 152, 9 (1939).

26. Baddar, Fahim and Fleifel., J.Chem.Soc., 1955, 2199.

anhydride they isolated the β-2-methoxy-5-p-methoxyphenyl and β-4-methoxy-3-o-methoxyphenyl benzoylpropionic acids respectively. But they failed to reduce the above ketonic acids to γ-ar~~o~~yl butyric acids.





Similarly succinoylation of 2,2'-and 4,4'-dimethoxy biphenyls with one mole of methyl succinic anhydride gave two products in each case ; Ar $COCH_2CHMeCOOH$ and Ar $COCHMeCH_2COOH$ and they have been reduced and cyclized to the tetralone derivatives. They have not reported the succinoylation of the above dimethoxy biphenyls with excess of succinic anhydride or its substituted derivatives. It was thought of interest to see whether the substitution takes place in both the rings simultaneously and to cyclize the di-ketonic acids if obtained to the corresponding bitetralonyls. As we have undertaken in this laboratory the studies of substitution in the biphenyl derivatives it was thought of interest to study systematically the succinoylation of the hydroxy and methoxy biphenyls.

<u>Friedel-Crafts reaction on 2,2'-and 4,4'-dimethoxy biphenyls with succinic anhydride</u> :- 4,4'-Dimethoxy biphenyl (I) on Friedel-Crafts reaction with 2.2 moles of succinic anhydride (II) and anhydrous aluminium chloride in nitrobenzene at room temperature gave a ketonic acid which on oxidation with alkaline potassium permanganate gave the known 4,4'-dimethoxy-biphenyl-3,3'-dicarboxylic acid[27] (IV). The same acid was obtained for comparison by the oxidation of dimethyl ether of 4,4'-dihydroxy-3,3'-diacetyl biphenyl[28] (V) with alkaline potassium permanganate. 4,4'-Dimethoxy biphenyl-3,3'-bis-γ-keto butyric acid (III) structure has therefore been assigned to the product. The above ketonic acid (III) on Clemmensen reduction gave 4,4'-dimethoxy biphenyl-3,3'-bis-butyric acid (VI) which on heating with polyphosphoric acid on a water bath at 80-90°C gave 5,5'-dimethoxy-8,8'-bitetralonyl (VII).

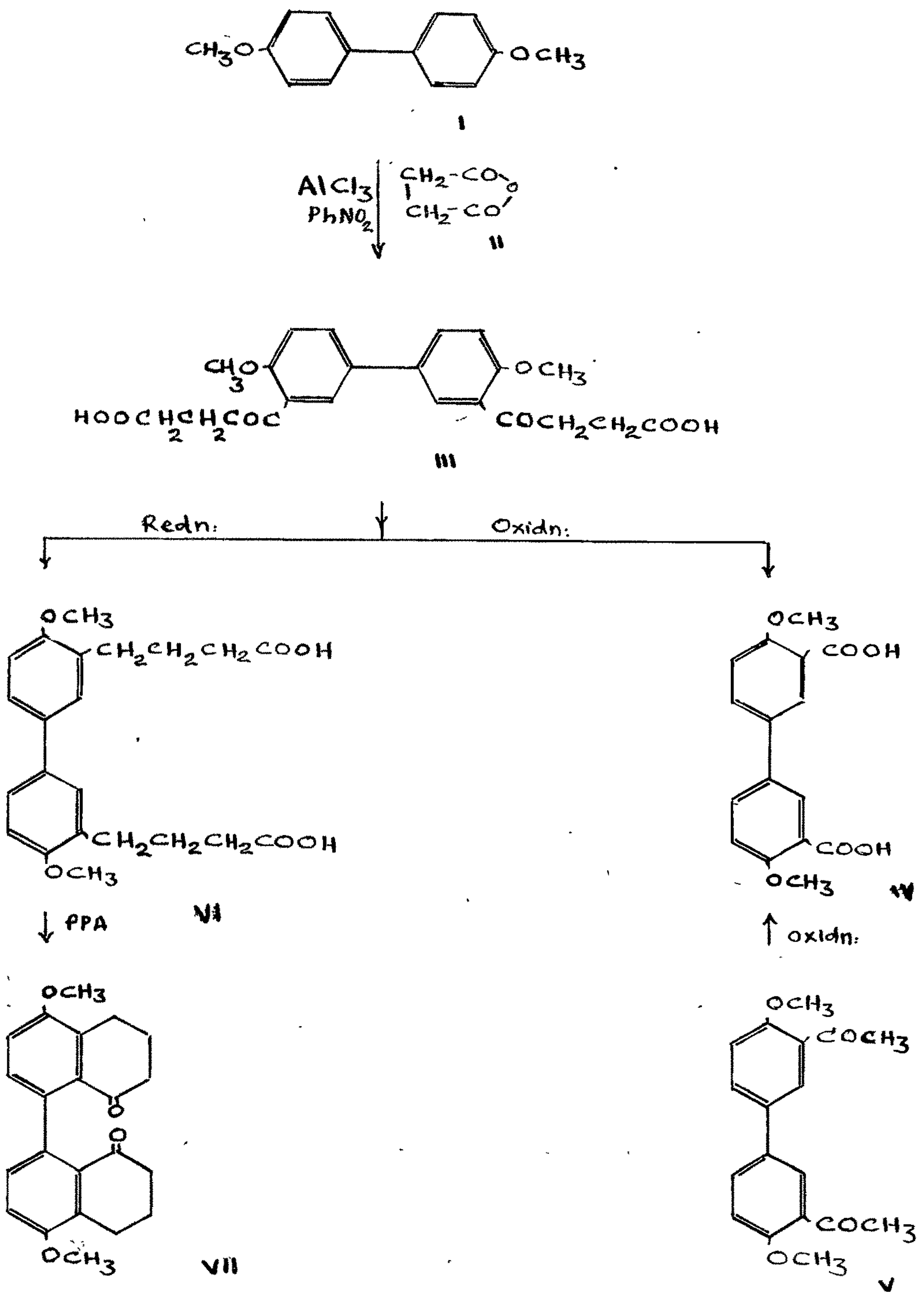
2,2'-Dimethoxy biphenyl (VIII) on Friedel-Crafts succinoylation with excess of succinic anhydride and anhydrous aluminium chloride in nitrobenzene at room temperature gave a bis-ketonic acid derivative which was found to be 2,2'-dimethoxy biphenyl-**5,5'**-bis-γ-keto butyric acid (IX) since it gave the known 2,2'-dimethoxy biphenyl-5,5'-dicarboxylic acid[29] (X) on oxidation with alkaline

---

[27] Mathai and Sethna., J.Ind.Chem.Soc., <u>40</u>, 347 (1963).

[28] Boon-Long., C.A., <u>43</u>, 5018.

[29] Gilman et al., J.Am.Chem.Soc., <u>62</u>, 1963 (1940).


CH3O
OCH3
I
AlCl3
PhNO2
CH2-CO
CH2-CO
O
II
CH3O
OCH3
HOOCH2CH2COC
COCH2CH2COOH
III
Redn.
Oxidn.
OCH3
CH2CH2CH2COOH
CH2CH2CH2COOH
OCH3
VI
PPA
OCH3
O
O
OCH3
VII
OCH3
COOH
COOH
OCH3
IV
oxidn.
OCH3
COCH3
COCH3
OCH3
V

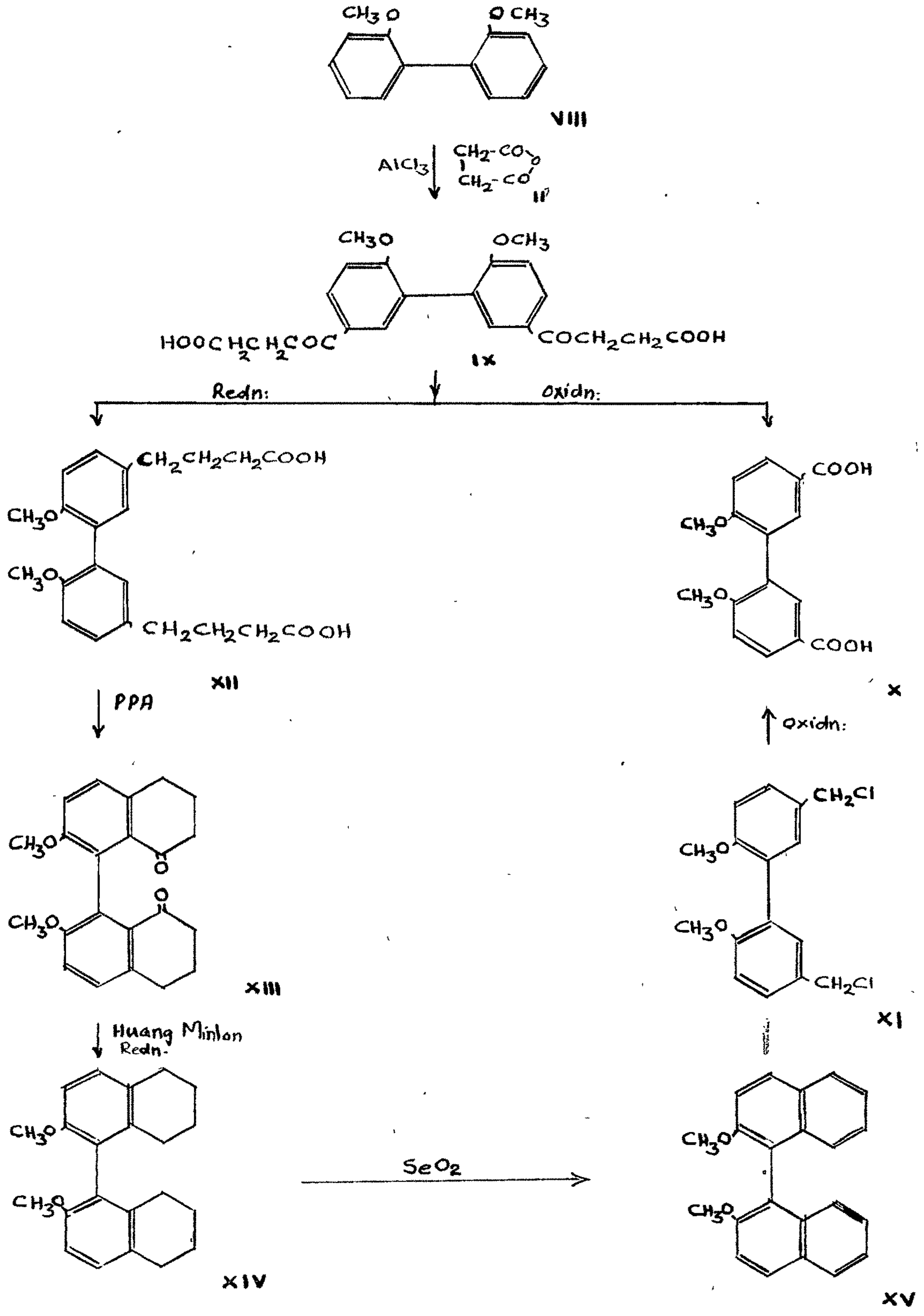
potassium permanganate. This was prepared for comparison by the oxidation of 2,2'-dimethoxy-5,5'-dichloromethyl biphenyl[27] (XI) with alkaline permanganate. The above ketonic acid (IX) on Clemmensen reduction with zinc amalgam and hydrochloric acid in acetic acid gave 2,2'-dimethoxy biphenyl-5,5'-bis-γ-butyric acid (XII). Cyclization of the above butyric acid (XII) can take place at 4,4' or 6,6' or 4,6' positions. It was however found that the cyclization with polyphosphoric acid at 70-80° took place at the 6,6' positions giving rise to 7,7'-dimethoxy-8,8'-bitetralonyl (XIII). The structure of the product was established as follows.

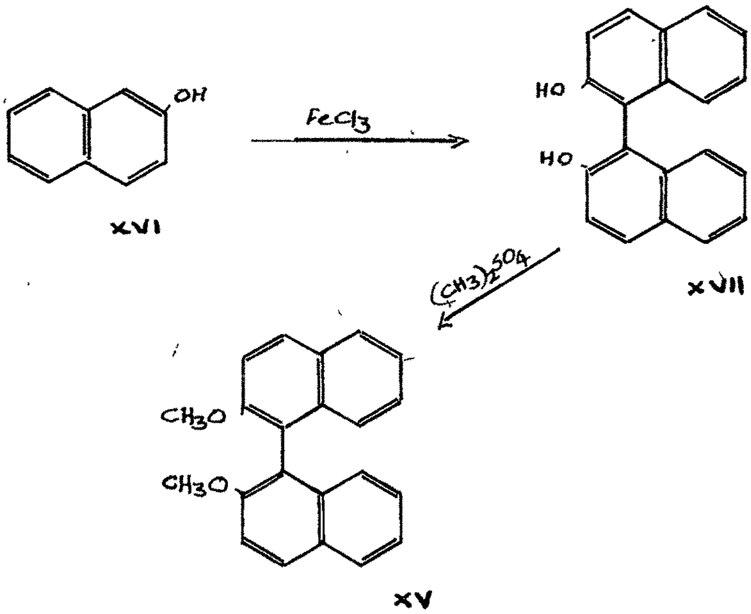
The 7,7'-dimethoxy-8,8'-bitetralonyl (XIII) obtained above on reduction by Huang Minlon method[30] i.e. by refluxing the bitetralonyl derivative (XIII) with alkaline hydrazine hydrate in glycol solvent, gave the 7,7'-dimethoxy-8,8'-bitetralenyl (XIV) which on aromatisation with selenium dioxide gave 2,2'-dimethoxy-1,1'-binaphthyl (XV) identical with the one obtained by the oxidation of β-naphthol (XVI) with ferric chloride and subsequent methylation of the bi-B-naphthol (XVII) formed with dimethyl sulphate.

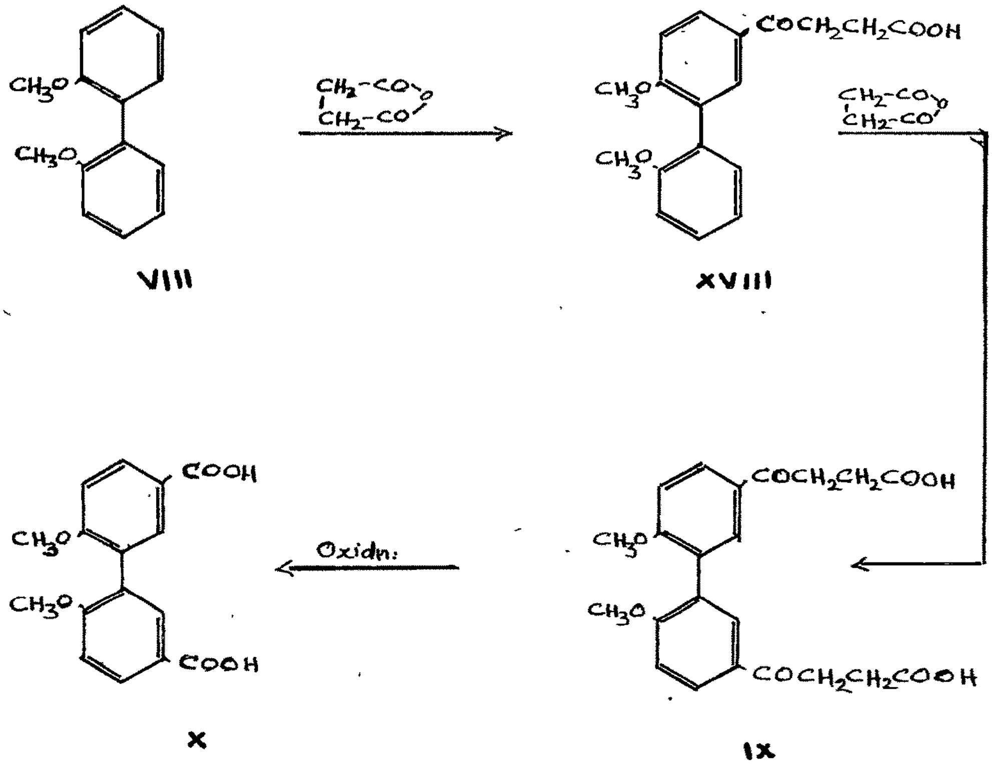
Cyclization of the 2,2'-dimethoxy biphenyl 5,5'-bis-butyric acid (XII) with con.sulphuric acid at room temperature also gave the 7,7'-dimethoxy-8,8'-bitetralonyl (XIII) ; but the yield by the polyphosphoric acid method was better than with sulphuric acid.

---

30. Huang Minlon., J.Am.Chem.Soc., 68, 2487 (1946).


CH3O
OCH3
VIII
AlCl3
CH2-CO
CH2-CO
O
IX
HOOCH2CH2COC
COCH2CH2COOH
Redn:
Oxidn:
CH2CH2CH2COOH
CH2CH2CH2COOH
XII
COOH
COOH
X
PPA
Oxidn:
XIII
CH2Cl
CH2Cl
XI
Huang Minlon Redn.
XIV
SeO2
XV


OH
XVI
FeCl3
HO
HO
XVII
(CH3)2SO4
CH3O
CH3O
XV


CH3O
CH3O
VIII
CH2-CO
CH2-CO O
COCH2CH2COOH
CH3O
CH3O
XVIII
CH2-CO
CH2-CO O
COCH2CH2COOH
CH3O
CH3O
COCH2CH2COOH
IX
Oxidn:
COOH
CH3O
CH3O
COOH
X

2,2'-Dimethoxy biphenyl (VIII) when subjected to Friedel-Crafts succinoylation with one mole of succinic anhydride in the presence of anhydrous aluminium chloride in nitrobenzene at room temperature gave a ketonic acid (A) which on further succinoylation with excess of succinic anhydride gave 2,2'-dimethoxy biphenyl-5,5'-bis-γ-keto butyric acid described above. Hence the acid (A) must be β-4-methoxy-3-(o' methoxy phenyl) benzoyl propionic acid (XVIII).

Baddar et al.[26] have reported the succinoylation of 2,2'-dimethoxy biphenyl with one mole of succinic anhydride in nitrobenzene. They obtained an acid m.p. 229-30° to which they gave the structure - β-(4-methoxy-3-(o-methoxyphenyl)benzoyl) propionic acid. The analysis of the above acid has been stated to agree with one mole of acetic acid of crystallization. They have reported the ethyl ester of the above ketonic acid but no analysis has been given. Oxidation of the above acid with 10 % sodium hypobromite solution has been reported to give 4-methoxy-3-(o-methoxyphenyl)benzoic acid (334-36°) which was prepared for comparison by the crossed Ullmann reaction between methyl-3-iodo-4-methoxybenzoate and o-iodo anisole with copper bronze at 230-35°.

As the author obtained the product 229-30° in the present work which was found to be 2,2'-dimethoxy biphenyl-5,5'-bis-γ-keto butyric acid, it was thought of interest to examine the work of Baddar et al. as the fitting of the analysis with one molecule of acetic acid of crystallization and the formation of 3-(2-methoxy phenyl)-4-methoxybenzoic acid by a crossed Ullmann reaction between 2-iodo anisole and methyl 4-methoxy-3-iodo benzoic acid and subsequent hydrolysis was not very convincing as in the above crossed Ullmann reaction the acid 2,2'-dimethoxy biphenyl-5,5'-dicarboxylic acid can also be formed.

Now it is found that the ketonic acid, m.p. 229-30°, reported by Baddar et al. is not the B-(4-methoxy-3-o-methoxyphenyl benzoyl) propionic acid ; but the 2,2'-dimethoxybiphenyl-5,5'-bis-γ-butyric acid. This on oxidation with alkaline potassium permanganate gave 2,2'-dimethoxy biphenyl-5,5'-dicarboxylic acid, m.p. 335-40°. Gilman[29] has also prepared the same acid by a different method and reported the same melting point. The acid obtained by Baddar et al. through the crossed Ullmann reaction on methyl-3-iodo-4-methoxy benzoate and o-iodoanisole appears to be not the 4-methoxy-3-o-methoxy-phenyl benzoic acid but the 2,2'-dimethoxybiphenyl-5,5'-dicarboxylic acid. The other product of the crossed Ullmann reaction which they isolated was 2,2'-dimethoxy-biphenyl.

EXPERIMENTAL

Succinoylation of 4,4'-dimethoxy biphenyl. 4,4'-Dimethoxy-biphenyl-3,3'-bis-γ-ketobutyric acid :- To a mixture of anhydrous aluminium chloride (5.5 g. ; 0.04 mole) and dry nitrobenzene (50 c.c.) kept below 10°C in a round bottomed flask succinic anhydride (2.2 g. ; 0.021 mole) and finely powdered 4,4'-dimethoxy biphenyl (2.1 g. ; 0.01 mole) were added. The flask was well protected from moisture and kept for 2 days at room temperature with occasional stirring. It was poured into crushed ice containing hydrochloric acid. The mixture was steam distilled to expel all the nitrobenzene. The product obtained after the removal of nitrobenzene was crystallised from ethyl acetate in white needles, m.p.187°C. Yield 2 g. It was soluble in common organic solvents and gave a bluish green colour with alcoholic ferric chloride.

Analysis : 4.480 mg. of the substance gave 10.520 mg. of carbon dioxide and 2.254 mg. of water.

Found : C = 64.1 % ; H = 5.6 %.

$C_{22}H_{22}O_6$ requires : C = 63.8 % ; H = 5.3 %.

4,4'-Dimethoxy biphenyl-3,3'-dicarboxylic acid :- The above acid (1 g.) was mixed with powdered potassium permanganate (5 g.) and sodium hydroxide (20 c.c. 10 %) and the mixture heated over a steam bath for 6 hrs. It was filtered and decolourised with sodium bisulphite. On acidification it gave the 3,3'-dicarboxylic acid derivative which was crystallised from acetic acid in white cubes. M.P. 236°C.

Mixed m.p. with an authentic sample of 4,4'-dimethoxy biphenyl-3,3'-dicarboxylic acid prepared by the oxidation of 4,4'-dimethoxy-3,3'-diacetyl biphenyl with alkaline potassium permanganate was not depressed.

4,4'-Dimethoxy biphenyl-3,3'-bis-—-butyric acid :- 4,4'-Dimethoxy biphenyl-3,3'-bis-γ-ketobutyric acid (1 g.) was dissolved in acetic acid (20 c.c.) and zinc amalgam (10 g.) was added. To this mixture con.hydrochloric acid (20 c.c.) was added portionwise and the reaction mixture heated over a steam bath for 8 hrs. It was filtered hot. On dilution it gave the reduced product which gave colourless needles from dil.acetic acid, m.p. 185°C. It was highly soluble in organic solvents and sparingly soluble in hot water and it did not give any colouration with alcoholic ferric chloride.

Analysis : 4.376 mg. of the substance gave 10.916 mg. of carbon dioxide and 2.670 mg. of water.

Found : C = 68.1 % ; H = 6.8 %.

$C_{22}H_{26}O_6$ requires : C = 68.4 % ; H = 6.7 %.

5,5'-Dimethoxy-8,8'-bitetralonyl :- Polyphosphoric acid (prepared by dissolving 10 g. of phosphorous pentoxide in 6 c.c. of orthophosphoric acid) (10 c.c.) was added to 4,4'-dimethoxy biphenyl-3,3'-bis-butyric acid (1 g.) in a test tube well protected from moisture with a guard tube. The mixture was heated over a water bath at 70-80° for 4 hrs. with occassional stirring. It was cooled and poured into water. The precipitated product was crystallised from acetic acid in colourless cubes, m.p. 211°. It was sparingly soluble in benzene, alcohol etc. but highly soluble in acetic acid. It gave no colouration with alcoholic ferric chloride.

<u>Analysis</u> : 4.494 mg. of the substance gave 12.462 mg. of carbon dioxide and 2.548 mg. of water.

Found : C = 75.7 % ; H = 6.3 %.

$C_{22}H_{22}O_4$ requires : C = 75.4 % ; H = 6.3 %.

<u>4-Methoxy-3-(2-methoxy phenyl) benzoyl propionic acid</u>:- To a mixture of anhydrous aluminium chloride (2.7 g. ; 0.02 mole), 2,2'-dimethoxy biphenyl (2.1 g. ; 0.01 mole) and dry nitrobenzene (50 c.c.) succinic anhydride (1 g. ; 0.01 mole) was added slowly. The reaction mixture was stirred well and kept for two days in a round bottomed flask well protected from moisture. It was mixed with 1:1 hydrochloric acid and steam distilled to remove the nitrobenzene. The residue after filtration gave white needles from alcohol. Yield 1 g. M.P. 162°.

It was soluble in sodium bicarbonate and gave bluish green colour with alcoholic ferric chloride.

Along with this product some 2,2'-dimethoxy biphenyl 5,5'-bis-γ-keto butyric acid derivative was also obtained.

<u>Analysis</u> : 4.600 mg. of the substance gave 11.548 mg. of carbon dioxide and 2.404 mg. of water.

Found : C = 68.5 % ; H = 5.8 %.

$C_{18}H_{18}O_5$ requires : C = 68.8 % ; H = 5.7 %.

2,2'-Dimethoxy biphenyl-5,5'-bis-γ-keto butyric acid :- To a mixture of 4-methoxy-3-(2-methoxyphenyl)benzoyl propionic acid (3.1 g. ; 0.01 mole), anhydrous aluminium chloride (2.7 g. ; 0.02 mole) and nitrobenzene (30 c.c.) succinic anhydride (1.5 g. ; 0.015 mole) was added portion-wise and the mixture was kept overnight. Dilute hydrochloric acid was added. The product after removing nitrobenzene by steam distillation gave white needles from alcohol. M.P. 230°.

It was soluble in sodium bicarbonate and gave bluish green colouration with alcoholic ferric chloride.

Analysis : 4.626 mg. of the substance gave 10.814 mg. of carbon dioxide and 2.124 mg. of water.

Found : C = 63.8 % ; H = 5.1 %.

$C_{22}H_{22}O_8$ requires : C = 63.8 % ; H = 5.3 %.

The same ketonic acid derivative was obtained directly from 2,2'-dimethoxy biphenyl as follows :

Powdered 2,2'-dimethoxy biphenyl (2.1 g. ; 0.01 mole) was added to dry nitrobenzene (50 c.c.) followed by anhydrous aluminium chloride (5.4 g. ; 0.04 mole) and succinic anhydride (2.5 g. ; 0.025 mole). The mixture was kept overnight at room temperature, well protected from moisture. Hydrochloric acid (1:1) was then added and the product obtained after the removal of nitrobenzene by steam distillation was crystallised from alcohol. M.P. and mixed m.p. with 2,2'-dimethoxy biphenyl-5,5'-bis-γ-keto-butyric acid described above was 230°C.

2,2'-Dimethoxy biphenyl-5,5'-dicarboxylic acid :- The above ketonic acid (1 g.) was dissolved in sodium hydroxide (20 c.c. ; 10 %) and powdered potassium permanganate (6 g.) was added. The reaction mixture was heated on a steam bath for 6 hrs. The product obtained on working up as usual gave white crystals from acetic acid. M.P. 266°.

M.P. and mixed m.p. with an authentic sample prepared by the oxidation of 2,2'-dimethoxy-5,5'-dichloromethyl biphenyl with alkaline potassium permanganate was 266°.

2,2'-Dimethoxy biphenyl-5,5'-bis-γ-butyric acid :- 2,2'-Dimethoxy biphenyl-5,5'-bis-γ-keto butyric acid (1 g.) was reduced with zinc amalgam (10 g.) and hydrochloric acid in acetic acid. The product obtained was crystallised from alcohol in white needles. M.P. 155°.

It did not give any colour with alcoholic ferric chloride.

Analysis : 4.094 mg. of the substance gave 10.222 mg. of carbon dioxide and 2.534 mg. of water.

Found : C = 68.4 % ; H = 6.7 %.

$C_{22}H_{26}O_6$ requires : C = 68.1 % ; H = 6.9 %.

7,7'-Dimethoxy-8,8'-bitetralonyl :- 2,2'-Dimethoxy biphenyl-5,5'-bis-γ-butyric acid (1 g.) was mixed with polyphosphoric acid (15 g.) and heated over a water bath at 75-85° for 6 hrs. The reaction mixture was cooled and poured into water. The separated bitetralonyl derivative was crystallised from acetic acid in white needles. M.P. 187°

Analysis : 4.160 mg. of the substance gave 11.510 mg. of carbon dioxide and 2.312 mg. of water.

Found : C = 75.5 % ; H = 6.2 %.

$C_{22}H_{22}O_4$ requires : C = 75.4 % ; H = 6.2 %.

6,6'-Dimethoxy-5,5'-bitetralyl :- 7,7'-Dimethoxy-8,8'-bitetralonyl (1 g.) was dissolved in 30 c.c. of glycol and 10 c.c. of hydrazine hydrate (85 % solution) and powdered potassium hydroxide (10 g.) was added. The mixture was refluxed on a wire gauze with an air condenser for 10 hrs. It was cooled and diluted with water. The precipitated bitetralyl was crystallised from petrol in cubes. M.P.116°.

The same bitetralyl was also obtained by the Clemmensen reduction of the bitetralonyl, but the yield was poorer than that of the former method.

Analysis : 4.188 mg. of the substance gave 12.572 mg. of carbon dioxide and 2.982 mg. of water.

Found : C = 81.9 % ; H = 8.0 %.

$C_{22}H_{26}O_2$ requires : C = 82.0 % ; H = 8.1 %.

2,2'-Dimethoxy-1,1'-binaphthyl :- 6,6'-Dimethoxy-5,5'-bitetralenyl (1 g.) was dissolved in amyl alcohol (15 c.c.) and powdered selenium dioxide was added. The reaction mixture was refluxed in an oil bath for 10 hrs. It was filtered hot and on removal of the solvent gave 2,2'-dimethoxy-1,1'-binaphthyl which was crystallised from acetic acid in white needles. M.P. 195°.

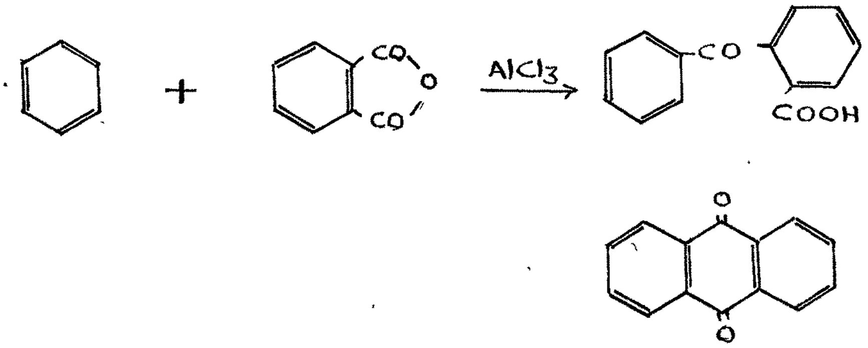
Analysis : 5.076 mg. of the substance gave 15.614 mg. of carbon dioxide and 2.726 mg. of water.

Found : C = 83.9 % ; H = 6.0 %.

$C_{22}H_{18}O_2$ requires : C = 84.1 % ; H = 5.7 %.

The same binaphthyl derivative was also prepared by methylation of bi-B-naphthol with dimethyl sulphate and potassium carbonate in acetone. M.P. and mixed m.p. with the former was 195°.

(B) Friedel-Crafts phthaloylation of biphenyl derivatives :- Friedel-Crafts condensations with anhydrides of aromatic dicarboxylic acids proceed as with succinic anhydride. Reactions of the phthalic anhydride and its derivatives with aromatic hydrocarbons or their derivatives in the presence of aluminium chloride generally yield o-aroyl benzoic acids, which can be smoothly dehydrated to yield an anthraquinone derivative.



It has been found in the reaction of phthaloyl chloride with benzene and aluminium chloride that rapid reaction leads to the formation of diphenyl phthalide whereas the use of low temperature with consequently longer reaction time induces the formation of 2-benzoyl benzoic acid[1]. Aluminium chloride causes the conversion of phthaloyl chloride into its isomer. The following observations are made by Rubidge and Qua[2]. (1) By employing 2 moles of aluminium chloride per mole of phthalic anhydride no

---

[1] Scheiber., Ann., 390, 121 (1912).

[2] Rubidge and Qua., J.Am.Chem.Soc., 36, 732 (1914).

phthalide is formed and a 97 % yield of o-benzoyl benzoic acid is formed. Similar results are also obtained if more than two moles of aluminium chloride are used. (2) Reducing the aluminium chloride to one mole cuts the keto acid yield to 30 % and a small amount of phthalide is foemed ; one half mole of aluminium chloride gives very poor results. (3) Prolonged heating increases phthalide formation. (4) The addition of extra mole of phthalic anhydride to the correct reaction mixture after reaction would normally be complete, causes phthalide formation. (5) The stepwise addition of aluminium chloride during reaction to reach the proper 2:1 ratio does not prevent phthalide formation. Groggins[3] has added the following factors which promotes phthalide formation; (1) too rapid heating of the reaction mixture, (2) inadequate mixing, (3) an excessive reaction temperature.

The keto acids obtained in phthaloylation are of great value as they are the intermediates for the synthesis of anthraquinone derivatives which are of fundamental importance to the dyestuff industry. Phthalic anhydride undergoes reaction with aromatic compounds like hydrocarbons,phenols and phenol ethers, aromatic ketones, carboxylic acid derivatives, nitrogenous compounds and heterocyclic compounds. These reactions though resembling that of benzene with phthalic anhydride, necessarily involve differences in procedure and are subject to orienting and accelerating or retarding influences of

---

3. Groggins., Ind.Eng.Chem., 23, 152 (1931).

the individual substances.

Various alkylated benzenes such as toluene[4] mesitylene[4], hexyl benzene[5] and polynuclear hydrocarbons such as tetralin[4], acenaphthene[6], anthracene[7] and phenanthrene[8] and biphenyl[9] and biphenyl derivatives. S such as o,o'-bitolyl[10] -p,p'-bitolyl[10] have been successfully phthaloylated. Halogenated aromatic hydrocarbons such as chlorotoluenes[4,11,12], fluorotoluene[11] and bromotoluenes[11] undergo Friedel-Crafts phthaloylation smoothly. Iodotoluene however, on Friedel-Crafts phthaloylation gave only a non iodinated product[11].

Phenols,naphthols,hydroxy- anthracenes, and their ethers have also been phthaloylated. Carbon-disulphide, tetrachloroethane, or nitrobenzene are usually used as

---

[4] Underwood and Walsh., J.Am.Chem.Soc., 57, 940 (1935).

[5] Burson U.S.Pat., 1933520, 1934033., J.Am.Chem.Soc., 47, 2357 (1925).

[6] Lorriman., J.Am.Chem.Soc., 47, 211 (1925).

[7] Heller., Ber., 45, 665 (1912).

[8] Clar., Ber., 62, 350)1929).

[9] Scholl and Neovius., Ber., 44, 1075 (1911) ; Groggins ., Ind.Eng.Chem., 22, 620 (1930).

[10] Scholl and Seer., Ber., 44, 1091 (1911).

[11] Mc Mullen., J.Am.Chem.Soc., 43, 1965 (1921).

[12] Elbs., J.Prakt.Chem., (2) 33, 318 (1886).

solvents. A lower temperature always favours the keto acid formation ; but higher temperature favour the anthraquinone formation. Friedel-Crafts phthaloylation of o-cresol is an example[13]. As in other Friedel-Crafts reactions, cleavage of alkoxy groups may occur during the condensation of phenol ethers with phthalic anhydride. Both the keto and carboxyl groups have an inhibiting effect on Friedel-Crafts condensation. The addition of two moles of the anhydride is not so common in the same nucleus. Esters of benzoic acid do not condense with phthalic anhydride ; however, the presence of a hydroxy group in the nucleus of the ester may enable reaction to occur. Ester hydrolysis also occurs in like reactions[14].

Nitro derivatives of hydrocarbons ordinarily undergo Friedel-Crafts reaction only when activating groups are present in the nucleus. While nitrobenzene does not react with phthalic anhydride o-nitro-m-cresol reacts giving 3,5-dimethoxy-2-(4-hydroxy-2-methyl-5-nitrobenzoyl) benzoic acid, in 62 % yield[15].

---

13. Waldman and Sellner., J.Prakt.Chem., 150, 145 (1938).

14. Mitter and Ray., J.Ind.Chem.Soc., 9, 247 (1932).

15. Graves and Adams., J.Am.Chem.Soc., 45, 2439 (1923).

Various aryl amines such as dimethyl aniline[16] p-phenyl aniline[17] and anilides such as 4-acetamido-1,2-dimethyl benzene[18] etc. undergo Friedel-Crafts phthaloylation smoothly.

Ring compounds of nitrogen are generally resistant to Friedel-Crafts reaction. However more highly aromatic ring compounds of nitrogen like phenanthridone[19] and carbazole[20] do react with phthalic anhydride to give the keto acids.

Aromatic sulphur compounds with the hetero atom either in the nucleus or in the side chain undergo Friedel-Crafts phthaloylation . Methyl phenyl sulphide[21], thiophene[22] thianthrene[23], phenothiazine[24] etc. are examples. Oxygen ring compounds such as dibenzofuran undergo Friedel-Crafts phthaloylation smoothly[25].

---

[16] Hallen and Guyot., Compt.rend., 119, 205 (1894).

[17] Kranzlein., Ber., 71, 2328 (1938).

[18] Idem., Ibid., 70, 1952 (1937).

[19] British Patent., 305488 (1929).

[20] Scholl and Neovins., Ber., 44, 1249 (1911).

[21] Halen and Reid., J.Am.Chem.Soc., 46, 1645 (1924).

[22] Steinkopt., Ann., 407, 94 (1914).

[23] Scholl and Seer., Ber., 44, 1249 (1911).

[24] Scholl and Seer., Ber., 44, 1233 (1911).

[25] Stummer Monatsh., 28, 411 (1907).

Various substituted phthalic anhydrides with chloro,bromo,iodo,alkyl,hydroxy,alkoxy and acetyl groups in the nucleus,have been subjected to Friedel-Crafts condensation with various aromatic compounds. In some cases it was found that the substituted phthalic anhydrides react more vigorously ~~/~~than the unsubstituted one ; but in some other cases the reverse was also observed. Nitrobenzene though unreactive to phthalic anhydride gives 2-(nitrobenzoyl) tetrachlorobenzoic acid with tetrachlorophthalic anhydride[26].

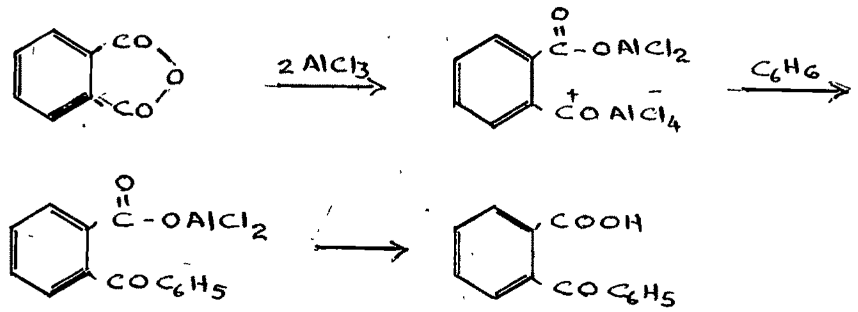
<u>Mechanism</u> :- Rubidge and Qua[26a] observed that the Friedel-Crafts phthaloylation proceeds with a maximum yield when two moles of aluminium chloride are used per mole of anhydride. Variation from this amount gave low yields of the keto acids or high yield of the phthalide. Heller and Schulke[26b], however,suggested that the reaction proceeded through formation of an intermediate compound. One mole of catalyst brings about the fission of the anhydride with the formation of the aluminium chloride salt of one carboxyl group and the second mole of aluminium chloride functions as catalyst. Therefore the reaction may be explained by assuming a preliminary formation of a complex as given below.

---

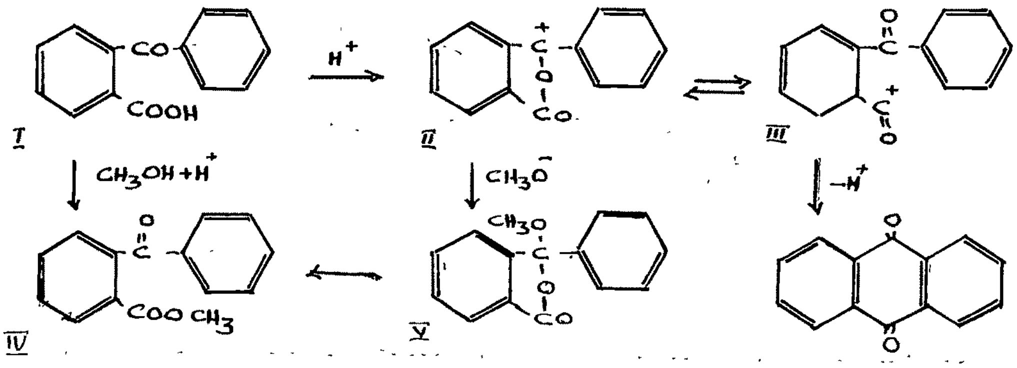
[26] Hofmann Monatsh., 36, 805 (1915).

[26a] Rubidge and Qua., J.Am.Chem.Soc., 36, 732 (1914).

[26b] Heller and Schulke., Ber., 41, 3627 (1908).



Aroyl benzoic acids generally cyclize with ease with con.sulphuric acid or sometimes with aluminium chloride to give anthraquinone derivatives. The intramolecular acylation ortho to a ketonic function is remarkable in view of the fact that ketones do not undergo Friedel-Crafts acylation in a like manner. Newman[26c] suggested that the cyclization proceeds through the carbonium ions II and III and showed that if a cold solution of o-aroyl benzoic acid in 98 % sulphuric acid is poured into methanol the chief product is the pseudo ester V, this is rearranged by sulphuric acid into the normal ester IV.

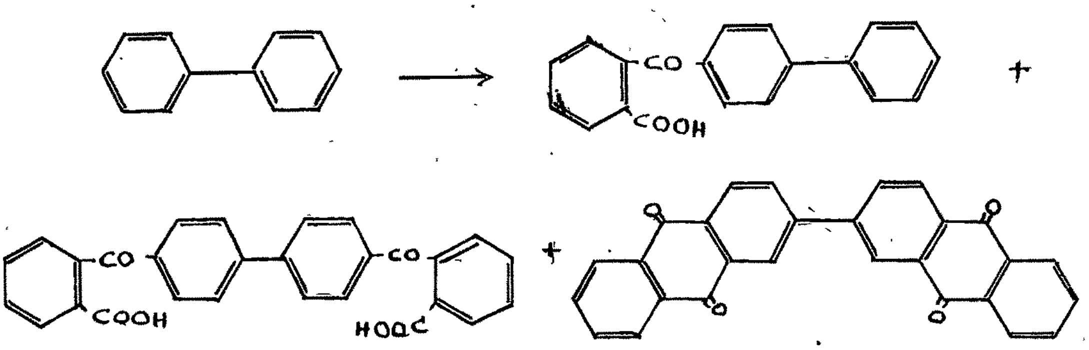


Biphenyl and some of its derivatives have been subjected to Friedel-Crafts phthaloylation. Simple biphenyl

---

[26c] Newman., J.Am.Chem.Soc., 64, 2324 (1942).

on Friedel-Crafts phthaloylation gives 4'-phenyl-2-benzoyl benzoic acid ; but when the reaction is effected by heating to 100° in the presence of a solvent, the products are 2-phenyl anthraquinone, 4,4'-bis(2''-carboxybenzoyl)biphenyl and 4'-(3''-anthraquinonyl)-2-benzoyl benzoic acid with a small amount of 4'-phenyl-2-benzoyl benzoic acid[9].



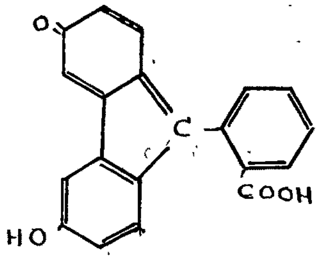
Scholl and Seer[10] observed that o,o'-bitolyl and p,p'-bitolyl on Friedel-Crafts phthaloylation give the disubstituted and the mono substituted compounds. Similarly 2,2,2',4'-tetramethyl biphenyl gives the disubstituted compound[27]. They also observed that p,p'-dihydroxy biphenyl and p,p'-dimethoxy biphenyl both yield 4,4'-dihydroxy-3-(2''-carboxybenzoyl) biphenyl when reacted with phthalic anhydride. On further heating of the reaction mixture to 130-35° 4,4'-dihydroxy-3,3'-bis-(2''-carboxybenzoyl) biphenyl has been obtained. The loss of a methyl group has also been noted with the naphthyl ethers[28]. But 3,3'-dihydroxy biphenyl on Friedel-Crafts

---

[27] Scholl, Liese, Michelson and Gruneewald., Ber., 43, 512 (1910).

[28] Scholl, Seer and Zinke., Monatsh., 41, 583 (1921).

phthaloylation gave the following compound[29].



Thus it is found that the products obtained in Friedel-Crafts phthaloylation of biphenyl derivatives mainly depend upon the conditions under which the reaction is carried out and also on the position of the substitutent groups in the biphenyl nucleus. The present work deals with the study of the Friedel-Crafts phthaloylation of 2,2'-dimethoxy biphenyl.

---

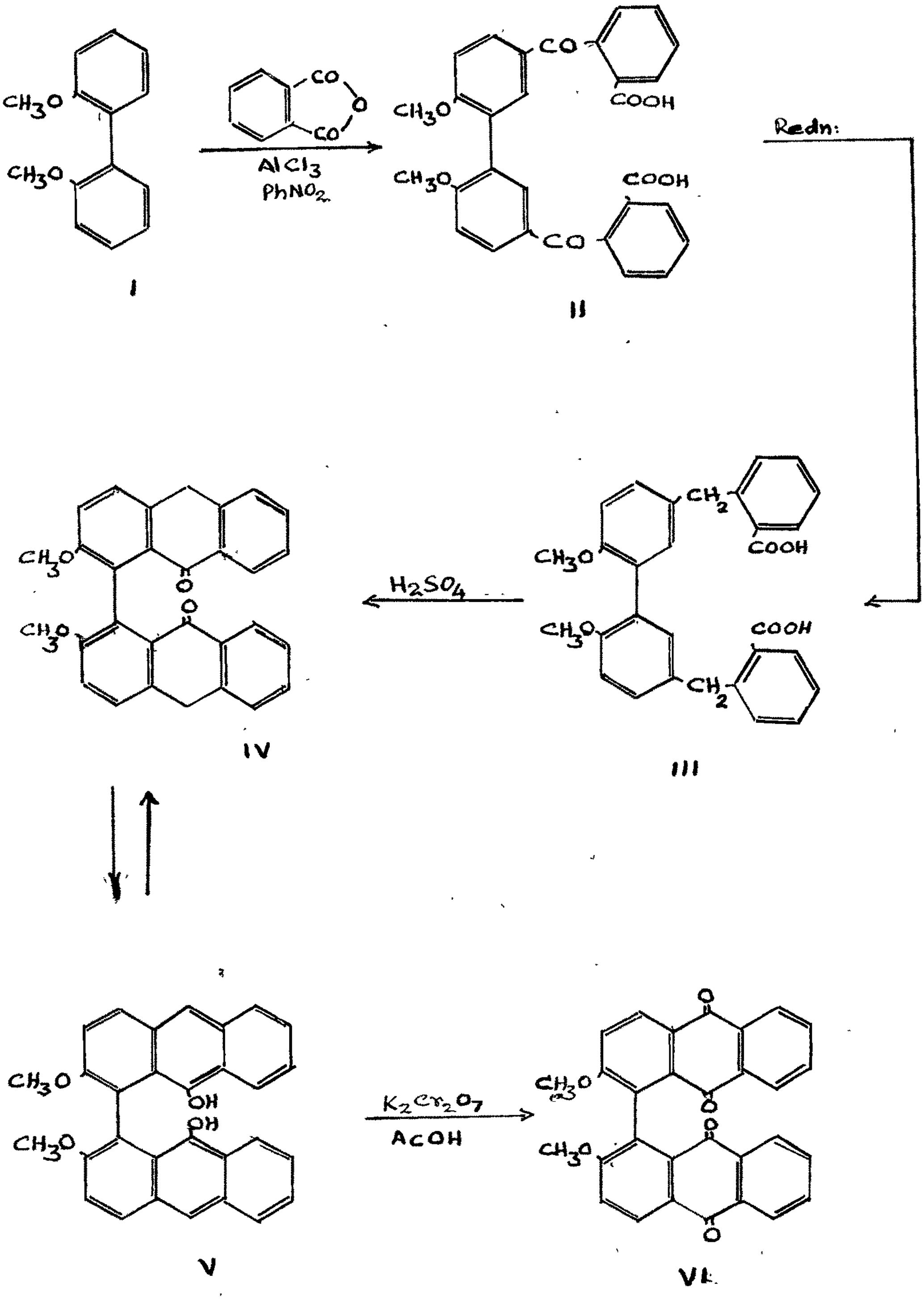
29. S.Dutt., J.Chem.Soc., 1926, 1171.

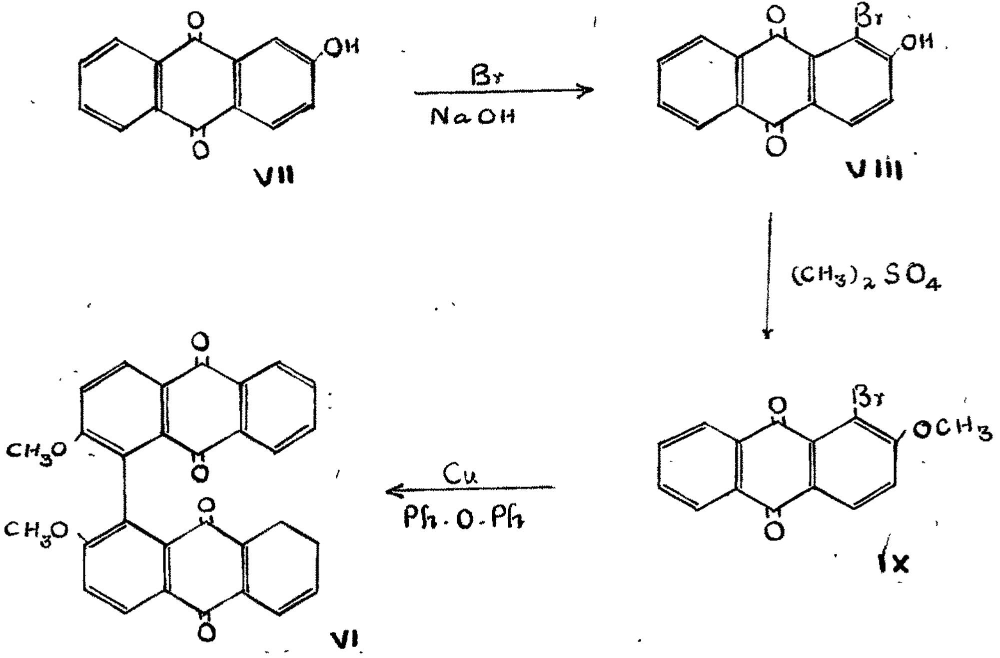
When 2,2'-dimethoxybiphenyl (I) was subjected to Friedel-Crafts phthaloylation with phthalic anhydride and anhydrous aluminium chloride in nitrobenzene at room temperature a product was obtained to which 2,2'-dimethoxy-5,5'-bis-(*o*-carboxybenzoyl) biphenyl (II) structure was assigned from the following reasons. Attempts to cyclize this acid with conc.sulphuric acid or polyphosphoric acid did not succeed. It was therefore decided to try the cyclization after reducing the carbonyl groups. The above ketonic acid (II) on Clemmensen reduction gave a product which was presumed to be the 2,2'-dimethoxy-5,5'-bis-(*o*-carboxybenzyl) biphenyl (III). This on treatment with 95 % sulphuric acid gave a bianthronyl derivative. Oxidation of the above bianthronyl derivative with sodium dichromate in glacial acetic acid gave the known 2,2'-dimethoxy-1,1'-bianthraquinonyl[30] (VI) as seen by direct comparison, thereby eliminating the other two possibilities of cyclization viz. cyclization to the 4,4'-and 4,6'-positions. Therefore 2,2'-dimethoxy-1,1'-bianthronyl (IV) structure has been assigned to the bianthronyl derivative. Since the bianthronyl derivative was found to be soluble in sodium hydroxide giving a red solution, it was concluded that the 2,2'-dimethoxy-1,1'-bianthronyl (IV) exists in tautomeric form with 2,2'-dimethoxy-9,9'-dihydroxy-1,1'-bianthracenyl (V).

2,2'-Dimethoxy-1,1'-bianthraquinonyl (IV) was

---

[30] Haller and Perkin., J.Chem.Soc., **125**, 236


CH₃O
CH₃O
I
CO
O
CO
AlCl₃
PhNO₂
CO
COOH
COOH
CO
II
Redn:
CH₂
COOH
COOH
CH₂
III
H₂SO₄
O
O
IV
OH
OH
V
K₂Cr₂O₇
AcOH
O
O
O
O
VI



prepared according to the method of Haller and Perkin[30] with slight modifications as follows. 2-Hydroxyanthraquinone (VII) was brominated with one mole of bromine in sodium hydroxide and the resulting 2-hydroxy-1-bromo anthraquinone (VIII) on methylation gave 2-methoxy-1-bromo anthraquinone (IX). This on Ullmann reaction by refluxing a mixture of 2-methoxy-1-bromo anthraquinone and copper bronze in diphenyl ether instead of naphthalene gave the 2,2'-dimethoxy-1,1'-bianthraquinonyl (VI) identical with the one obtained by the oxidation of the bianthronyl derivative (IV) with sodium dichromate in acetic acid.

Cyclization of 2,2'-dimethoxy-5,5'-bis-(o-carboxybenzyl) biphenyl (II) with polyphosphoric acid at room temperature was unsuccessful while at higher temperature some charred product was obtained from which no pure product could be isolated.

EXPÈRIMENTAL

Friedel-Crafts reaction on 2,2'-dimethoxy biphenyl with phthalic anhydride : 2,2'-Dimethoxy-5,5'-bis-(o-carboxybenzoyl) biphenyl :- To a mixture of anhydrous aluminium chloride (5.4 g. ; 0.04 mole) and nitrobenzene (50 c.c.) powdered 2,2'-dimethoxy biphenyl (2.1 g. ; 0.01 mole) and phthalic anhydride (3 g. ; 0.02 mole) were added. The reaction mixture was kept overnight in a round bottomed flask well-protected from moisture. It was poured into dil.hydrochloric acid and steam distilled to remove the nitrobenzene. The mixture after the removal of nitrobenzene was filtered hot, and the phthalic acid removed by repeatedly boiling with hot water and decantation. The residue was then dried and washed with a little ethyl acetate. It crystallised from alcohol-ethylacetate mixture in cubes, m.p. 250°.

Analysis : 4.496 mg. of the substance gave 11.600 mg. of carbon dioxide and 1.850 mg. of water.

Found : C = 70.4 % ; H = 4.6 %.

$C_{30}H_{22}O_8$ requires : C = 70.6 % ; H = 4.3 %.

2,2'-Dimethoxy-5,5'-bis-(o-carboxybenzyl)biphenyl :- 2,2'-Dimethoxy-5,5'-bis-(o-carboxybenzoyl)biphenyl was reduced with zinc amalgam as usual and crystallised from alcohol in white needles, m.p. 220°.

Analysis : 4.616 mg. of the substance gave 12.510 mg. of carbon dioxide and 2.244 mg. of water.

Found : C = 74.6 % ; H = 5.4 %.
$C_{30}H_{26}O_6$ requires : C = 74.6 % ; H = 5.4 %.

2,2'-Dimethoxy-1,1'-bianthronyl or 2,2'-dimethoxy- 1,1'-bianthranolyl :- 2,2'-Dimethoxy-5,5'-bis(o-carboxybenzyl) biphenyl (1 g.) was mixed with sulphuric acid (95 % ; 15 c.c.) and kept for 1 hr. It dissolved giving a red solution. It was poured into crushed ice and the precipitated product was crystallised from benzene in pink needles, m.p. 263°.

When experiment was repeated with polyphosphoric acid instead of sulphuric acid the cyclization did not take place and the original product was obtained.

Since the product was insoluble in sodium bicarbonate, but soluble in sodium hydroxide giving a red solution it was concluded that the product exists in two tautomeric forms viz. the ketonic 2,2'-dimethoxy-1,1'-bianthronyl and the enolic 2,2'-dimethoxy-1,1'-bianthranolyl. It gave a bluish green colouration with alcoholic ferric chloride.

Analysis : 4.488 mg. of the substance gave 13.292 mg. of carbon dioxide and 2.012 mg. of water.

Found : C = 80.8 % ; H = 5.0 %.
$C_{30}H_{22}O_4$ requires : C = 80.7 % ; H = 4.9 %.

2,2'-Dimethoxy-1,1'-bianthraquinonyl :-2,2'-Dimethoxy-1,1'-bianthronyl (1 g.) was dissolved in glacial acetic acid (25 c.c.) and powdered sodium dichromate (10 g.) was added and heated over a steam bath for 4 hrs. A red product separated out. The mixture was poured into water and the precipitated product was crystallised from nitrobenzene in long yellow needles, m.p. 345°. It was insoluble in sodium hydroxide and gave no colouration with alcoholic ferric chloride.

<u>Analysis</u> : 4.316 mg. of the substance gave 11.944 mg. of carbon dioxide and 1.460 mg. of water.

Found : C = 75.5 % ; H = 3.8 %.

$C_{30}H_{18}O_6$ requires : C = 75.9 % ; H = 3.8 %.

The same bianthraquinonyl was prepared according to method of Haller and Perkin with slight modifications as follows[30] :

2-Methoxy-1-bromo anthraquinone obtained by the bromination of 2-hydroxy anthraquinone with one mole of bromine in sodium hydroxide and subsequent methylation with dimethyl sulphate, was refluxed with copper powder in diphenyl ether. The mixture was filtered hot and on cooling yellow needles of 2,2'-dimethoxy-1,1'-bianthraquinonyl was obtained. M.P. and mixed m.p. with the former was not depressed.