CHAPTER V

BECKMANN REARRANGEMENT OF THE OXIMES OF SOME C-ACYL DERIVATIVES OF BIPHENYLS

CHAPTER V

Beckmann rearrangement of the oximes of some C-acyl derivatives of biphenyls :

In its most general form the Beckmann rearrangement[1] consists in the transformation of a ketoxime into an acid amide. The rearrangement can be effected by a large number of reagents such as phosphorus pentachloride, phosphorus oxychloride, acetyl chloride, sulphuric acid and polyphosphoric acid.

Phosphorus pentachloride remains the most generally used and most valuable reagent. The rearrangement is carried out in ethereal solution and at a low temperature.

The Beckmann rearrangement was reviewed in 1958 in detail by Popp and Mcewen[2].

Lachmann[3] used hydrochloric acid satisfactorily and Polyphosphoric acid has been found in recent years to be an excellent reagent for this rearrangement[4].

Simple ketoximes undergo rearrangement with polyphosphoric acid in almost quantitative yields. The reactions are satisfactory when applied to the oximes of diarylketones, aryl alkylketones and cyclic ketones as observed by Horning and Stromberg[5]. Under the proper conditions aldoximes ~~will~~ undergo the Beckmann rearrangement to yield amides.

$RCH = NOH \longrightarrow RCONH_2$ and / or $HCONHR$.

It was Meisenheimer's work[6] which led to a better understanding of the Beckmann rearrangement and enhanced its usefulness from a preparative method to a tool for determining the configuration of the oximes.

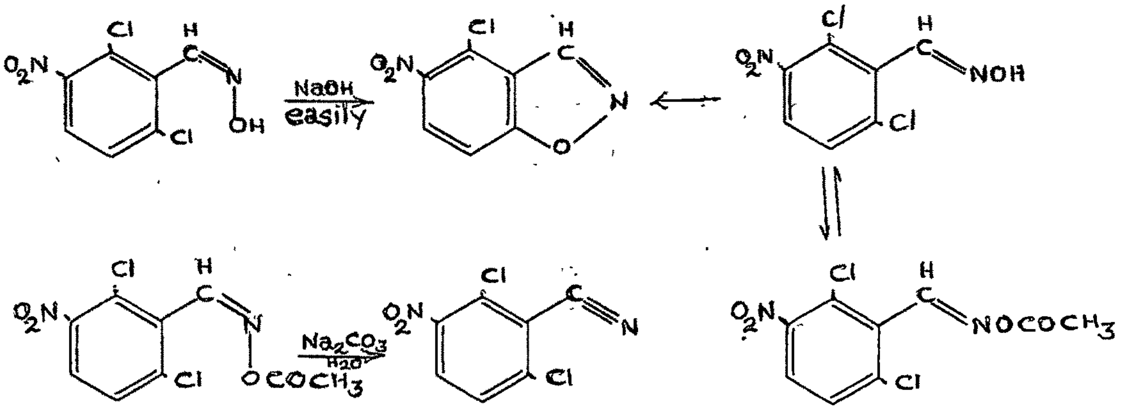
Configuration of isomeric ketoximes

With the discovery that unsymmetrical ketones furnished in many cases isomeric oximes, several theories were advanced to account for the isomerism of these compounds. The one which has received general acceptance is that of Hantzsch and Werner[7].

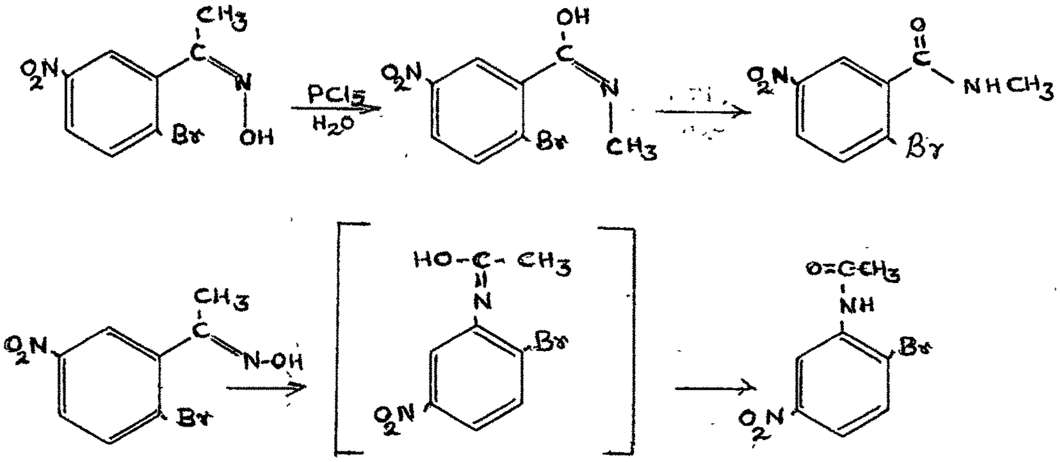
Hantzsch and Werner[7] proposed a stereochemical explanation for the isomerism. They assumed that the three nitrogen valencies are non-planar and that a carbon-nitrogen double bond can give geometrical isomers in the same way as a carbon-carbon double bond. Hantzsch proposed the terms syn and anti for the two forms.

The currently accepted configurations of the isomeric forms were assigned by Meisenheimer[6]. If a reactive halogen atom is ortho to aldoximino group one form of the aldoxime undergoes ring formation easily in presence of alkali whereas the other form gives the same product much more slowly.

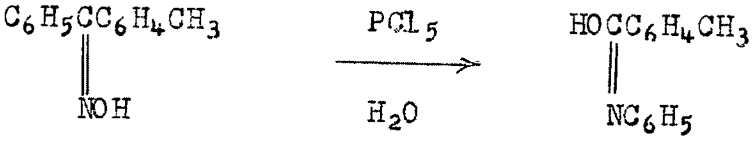
It seems likely therefore that the form undergoing ready cyclisation is the anti-aldoxime and that the syn-aldoxime first must rearrange to the anti-form before cyclisation takes place. Further, the form that undergoes easy ring closure gives an acetate which reacts with alkali to form a nitrile whereas the acetate of the other form regenerates the original oxime.



The syn and anti ketoximes yield different products on Beckmann rearrangement. This is illustrated in the case of bromo nitro acetophenone as shown below.

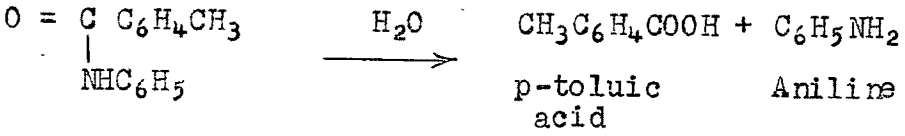


Thus the groups that exchange places in the rearrangement are those that are anti to each other.



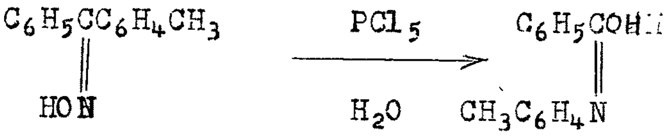
$$\begin{array}{c} C_6H_5CC_6H_4CH_3 \\ \| \\ NOH \end{array} \xrightarrow[H_2O]{PCl_5} \begin{array}{c} HOCC_6H_4CH_3 \\ \| \\ NC_6H_5 \end{array}$$

anti-phenyl-tolyl ketoxime

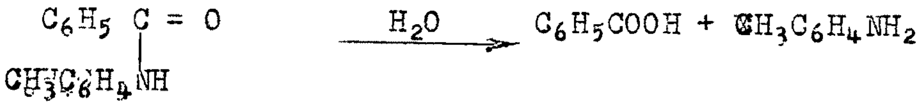


$$\begin{array}{l} O = C\ C_6H_4CH_3 \\ \quad\ | \\ \quad NHC_6H_5 \end{array} \xrightarrow{H_2O} CH_3C_6H_4COOH + C_6H_5NH_2$$

p-toluic acid   Aniline



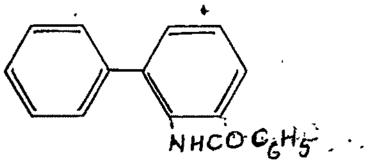
$$\begin{array}{c} C_6H_5CC_6H_4CH_3 \\ \| \\ HON \end{array} \xrightarrow[H_2O]{PCl_5} \begin{array}{c} C_6H_5COH \\ \| \\ CH_3C_6H_4N \end{array}$$

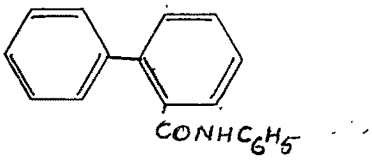


$$\begin{array}{l} C_6H_5\ C = O \\ \qquad | \\ CH_3C_6H_4NH \end{array} \xrightarrow{H_2O} C_6H_5COOH + CH_3C_6H_4NH_2$$

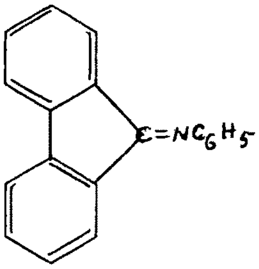
The present work deals with the Beckmann rearrangement of the oximes of C-acyl biphenyl derivatives.

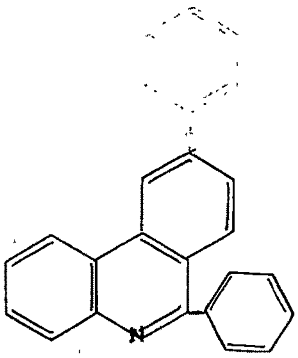
Smith[8] has studied the rearrangement of the oxime of 2-benzoyl biphenyl with phosphorus pentachloride in benzene at room temperature and obtained 2-benzamido-biphenyl and biphenyl anilide in a ratio 70 : 30.





The rearrangement with polyphosphoric acid at 110-30° gave the corresponding cyclization products fluorenone anil and 9-phenyl phenanthridine in a ratio 80 : 20.





There does not appear to be any other reference in the literature on the Beckmann rearrangement in the biphenyl series.

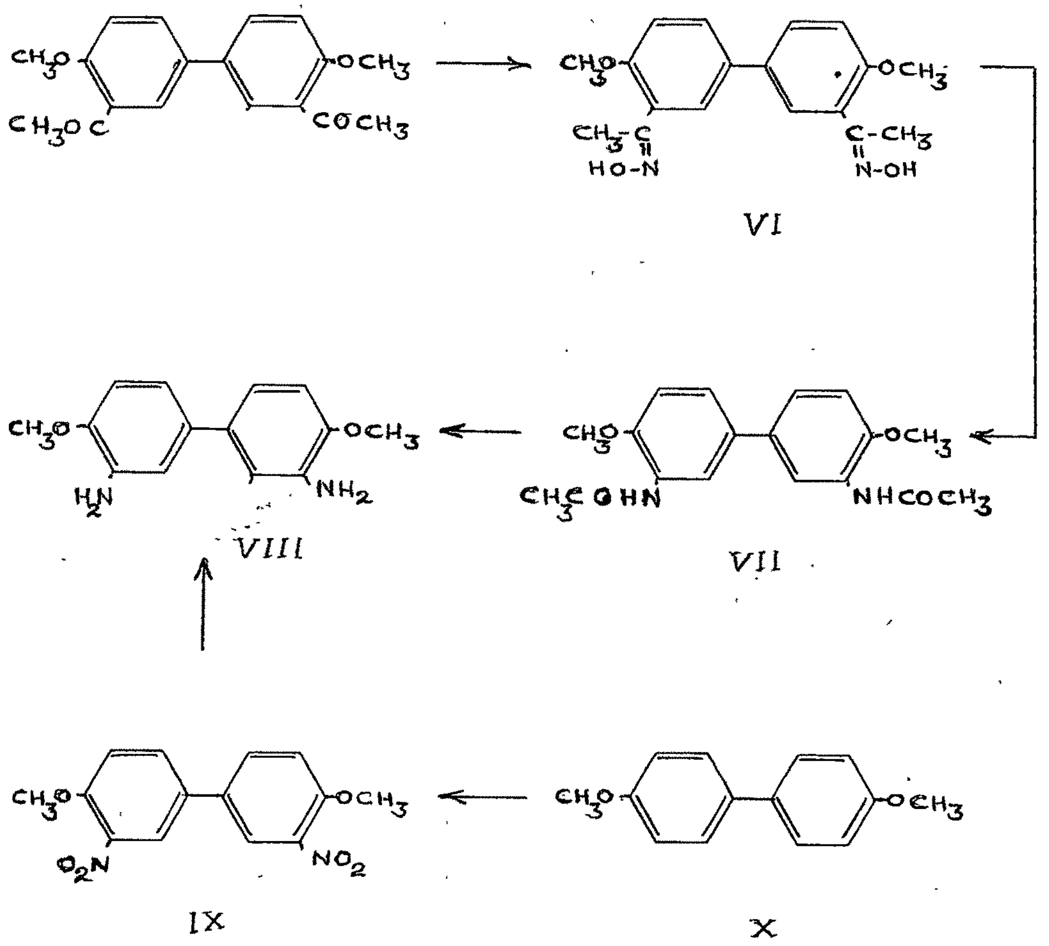
In the present work the Beckmann rearrangement of the di-oximes of (a) 2,2'-dimethoxy-5,5'-diacetyl biphenyl ; (b) 4,4'-dimethoxy-3,3'-diacetylbiphenyl ; (c) 2,2',4,4'-tetramethoxy-5,5'-diacetylbiphenyl and (d) 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl have been carried out to see if the rearrangement occurs simultaneously in both the phenyl rings and to see the nature of the products formed.

Beckmann rearrangement of the di-oxime of 2,2'-dimethoxy-5,5'-diacetylbiphenyl

The di-oxime of 2,2'-dimethoxy-5,5'-diacetyl of 2,2'-dimethoxy biphenyl (V) according to Borsche and Scholten[9].

Rearrangement of the di-oxime of 4,4'-dimethoxy-3,3'-diacetyl biphenyl

The di-oxime of 4,4'-dimethoxy-3,3'-diacetyl biphenyl (VI) when subjected to Beckmann rearrangement with polyphosphoric acid gave 4,4'-dimethoxy-3,3'-diacetamido biphenyl[10] (VII) . The diacetamido derivative



VI

VIII

VII

IX

X

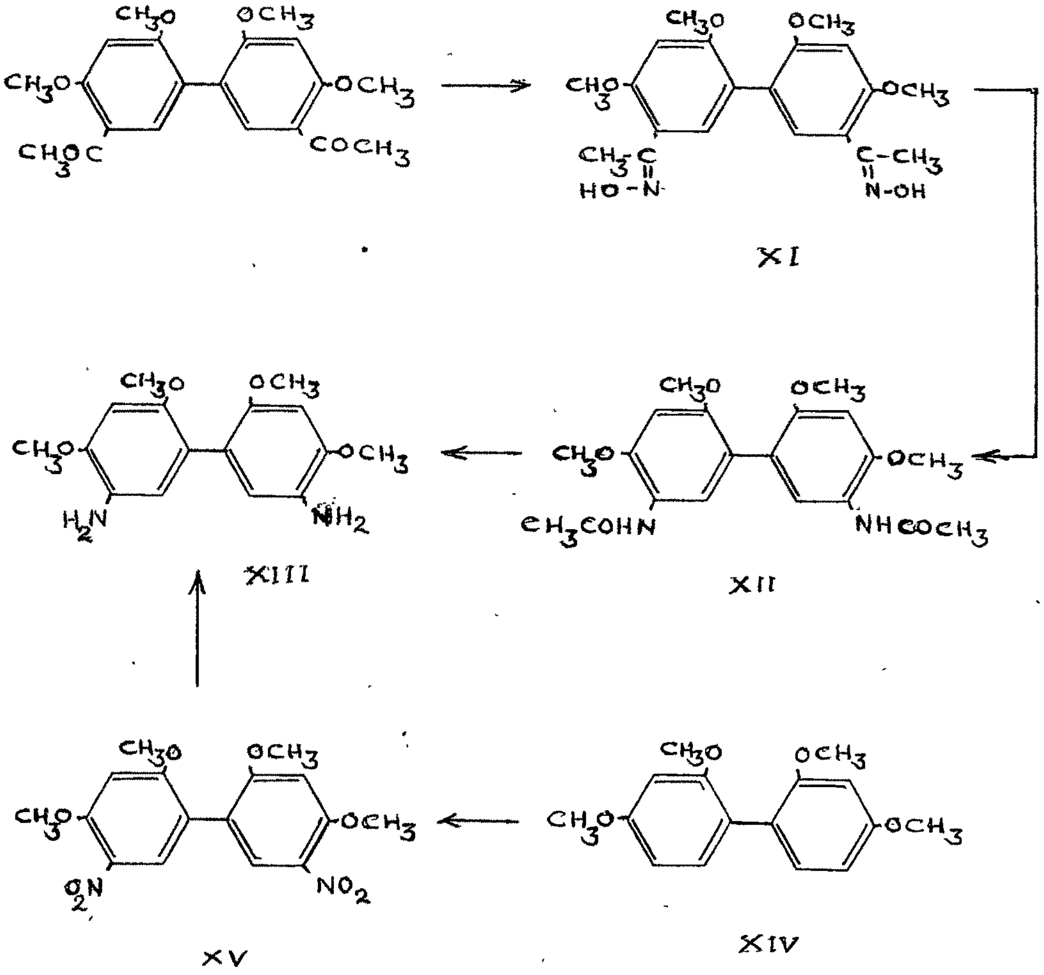
on hydrolysis with concentrated hydrochloric acid gave the known 4,4'-dimethoxy-3,3'-diamino biphenyl[10] (VIII). It was directly compared with the product obtained by the reduction of 4,4'-dimethoxy-3,3'-dinitro biphenyl (IX) prepared by the nitration of 4,4'-dimethoxy biphenyl (X) according to Herbert, Hodgson and Holt[10].

Rearrangement of the di-oxime of 2,2',4,4'-tetramethoxy-5,5'-diacetyl biphenyl

The di-oxime of 2,2',4,4'-tetramethoxy-5,5'-diacetylbiphenyl (XI) on Beckmann rearrangement with polyphosphoric acid gave 2,2',4,4'-tetramethoxy-5,5'-diacetamidobiphenyl (XII) which on hydrolysis with conc. hydrochloric acid gave 2,2',4,4'-tetramethoxy-5,5'-diaminobiphenyl (XIII).

The same amino compound was also prepared as follows : 2,2',4,4'-tetramethoxybiphenyl (XIV) on nitration gave a dinitro derivative (XV) which on reduction with stannous chloride and hydrochloric acid gave the diamino derivative (XIII) which was found to be identical with the 5,5'-diamino derivative (XIII) obtained above, thereby confirming the structure of the nitro compound as the 2,2',4,4'-tetramethoxy-5,5'-dinitrobiphenyl.

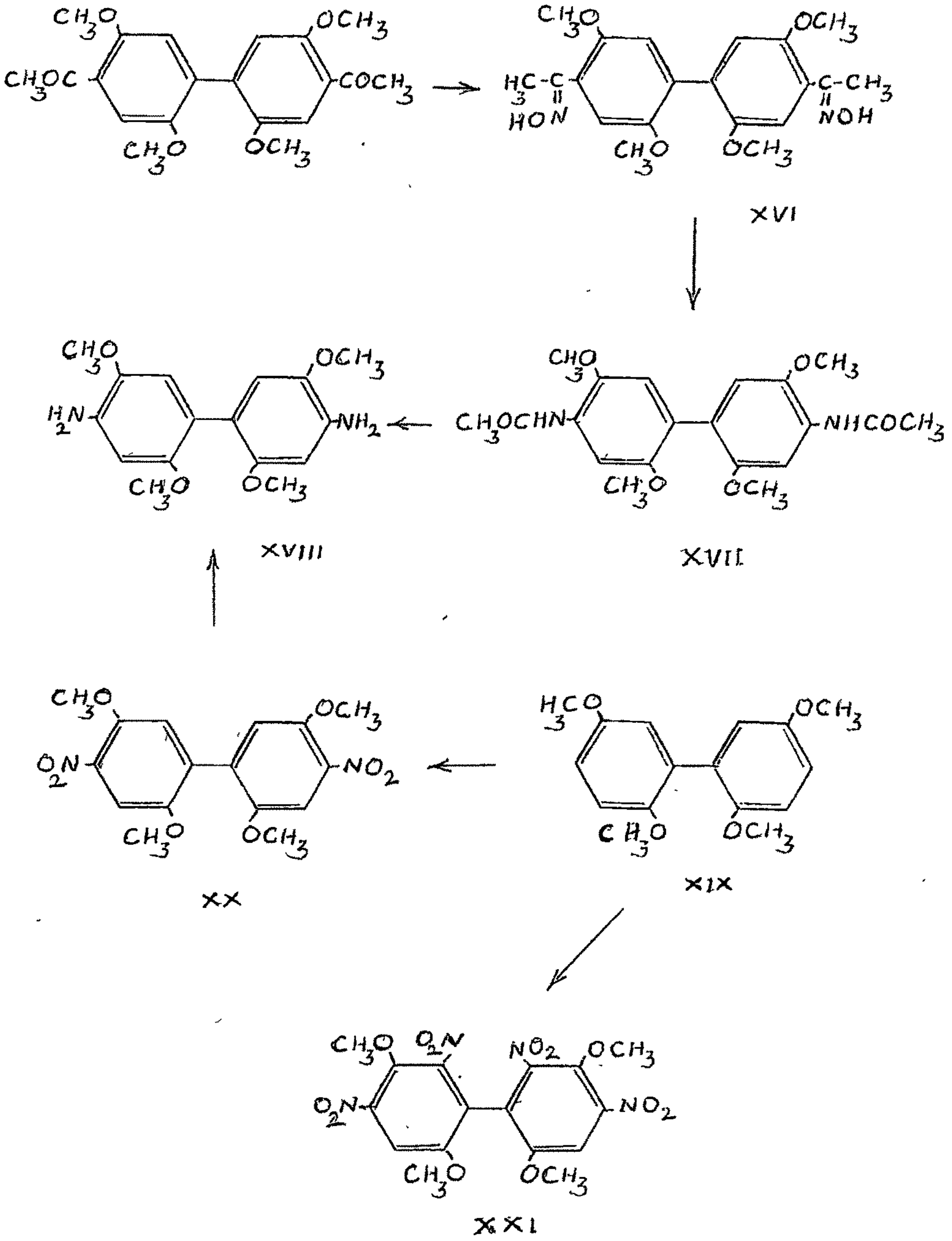
Schiemann and Roselius[11] claimed to have prepared the above dinitro derivative by boiling the 2,4,4'-trifluoro-5-nitrobiphenyl for 33 hours with 2 moles of potassium



hydroxide in methyl alcohol and reported m.p. 182-83[9], but the present author obtained m.p. 288°.

Beckmann rearrangement of the di-oxime of 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl

The di-oxime of 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl (XVI) when subjected to Beckmann rearrangement afforded 2,2',5,5'-tetramethoxy-4,4'-


XVI
XVII
XVIII
XIX
XX
XXI

diacetamidobiphenyl (XVII) which on hydrolysis with conc.hydrochloric acid gave 2,2',5,5'-tetramethoxy-4,4'-diaminobiphenyl[12] (XVIII).

The same diamino derivative was also prepared as follows : 2,2',5,5'-tetramethoxybiphenyl (XIX) on nitration with conc.nitric acid at 0° gave a dinitro derivative (XX) which on reduction with stannous chloride and hydrochloric acid furnished the diamino derivative (XVIII) which was found to be identical with the 4,4'-diamino derivative (XVIII) obtained above, there by the structure of the dinitro derivative is confirmed as the 2,2',5,5'-tetramethoxy-4,4'-dinitrobiphenyl (XX).

When fuming nitric acid was used instead of conc.nitric acid for nitration, a tetranitro derivative (XXI) was obtained which is tentatively assigned the 4,4',6,6'-tetranitro structure as the dinitro derivative has the 4,4'-dinitro structure and the other likely positions for the entry of the nitro group would be the 6,6'-positions which are ortho to the methoxyl groups in 5 and 5'-positions and meta to the nitro groups in 4 and 4'-positions.

Attempted Beckmann rearrangement of the di-oxime of 2,2',6,6'-tetramethoxy-3,3'-diacetylbiphenyl[13]

The Beckmann rearrangement of the di-oxime of 2,2',6,6'-tetramethoxy-3,3'-diacetylbiphenyl was tried with polyphosphoric acid. But no pure product could be isolated.

EXPERIMENTAL

The di-oxime of 2,2'-dimethoxy-5,5'-diacetylbiphenyl

2,2'-Dimethoxy-5,5'-diacetylbiphenyl (2 g.) in alcohol was added to a mixture of hydroxylamine hydrochloride (2 g.) and potassium hydroxide (1 g.). The reaction mixture was refluxed on a steam bath for 2 hours. The product obtained after removing the alcohol crystallised from acetic acid, m.p. 269°.

Analysis : Found : C,66.0 % ; H,6.3 % ; N,8.2 %.
$C_{18}H_{22}N_2O_4$ requires : C,65.9 % ; H,6.1 % ; N,8.5 %.

2,2'-Dimethoxy-5,5'-diacetamidobiphenyl

The above dioxime (0.5 g.) was added to polyphosphoric acid (20 g. phosphorus pentoxide and 12 ml. of ortho phosphoric acid) . The reaction mixture protected from moisture was heated on a steam bath for 3 hours. Ice cold water was then added and the product separated was thoroughly washed with water and crystallised from alcohol, m.p. 247°.

Analysis : Found : C,65.5 % ; H,6.0 % ; N,8.7 %.
$C_{18}H_{20}N_2O_4$ requires : C,65.9 % ; H,6.1 % ; N,8.5 %.

2,2'-Dimethoxy-5,5'-diaminobiphenyl

The diacetamido derivative (0.2 g.) was heated with hydrochloric acid (1 : 1 ; 5 ml.) for 3 hours on a steam bath. It was neutrallised with sodium hydroxide and the product obtained crystallised from toluene, m.p. 162°.

Analysis : Found : C,68.8 % ; H,6.6 % ; N,10.9 %.

$C_{14}H_{16}N_2O_2$ requires : C,68.8 % ; H,6.5 % ; N,11.4 %.

The same di-amino compound was synthesised for comparison by the reduction of 2,2'-dimethoxy-5,5'-dinitrobiphenyl prepared according to Borsche and Scholten[9]. The dinitrobiphenyl derivative (0.5 g.) was dissolved in glacial acetic acid and stannous chloride (1 g.) in glacial acetic acid (2 ml.) with 2 drops of hydrochloric acid was added to the above mixture. Hydrogen chloride gas was passed till the amine hydrochloride was precipitated. It was filtered, dissolved in water and neutralised with sodium hydroxide. The precipitated amino compound was extracted with ether and crystallised from benzene. Mixed m.p. with the diamino derivative described above was not depressed.

The di-oxime of 4,4'-dimethoxy-3,3'-diacetylbiphenyl

4,4'-Dimethoxy-3,3'-diacetylbiphenyl (1 g.) in alcohol, hydroxylamine hydrochloride (1 g.) and potassium hydroxide (0.5 g.) were refluxed on a steam bath for 2 hours. The product obtained on removal of alcohol was crystallised from alcohol, m.p. 225°.

Analysis : Found : C,66.0 % ; H,6.2 % ; N,8.7 %.

$C_{18}H_{20}N_2O_4$ requires : C,65.9 % ; H,6.1 % ; N,8.5 %.

4,4'-Dimethoxy-3,3'-diacetamidobiphenyl

The di-oxime (0.5 g.) was mixed with polyphosphoric acid (40 g.) and heated on a steam bath for 2 hours. It was diluted with water and the product obtained crystallised from glacial acetic acid, m.p. 340°.

Analysis	: Found	: C,65.7 % ; H,6.0 % ; N,8.6 %.
$C_{18}H_{20}N_2O_4$	requires	: C,65.9 % ; H,6.1 % ; N,8.5 %.

The same diacetamidobiphenyl was prepared by Herbert et al.[10] by the acetylation of 4,4'-dimethoxy-3,3'-diaminobiphenyl. They gave m.p. 330°.

Hydrolysis : The above diacetamido derivative (0.2 g.) was heated with conc. hydrochloric acid (5 ml.) on a steam bath for 2 hours. The amine hydrochloride obtained was neutralised with sodium hydroxide and the free base obtained was crystallised from alcohol, m.p. 193°.

The same amino compound was prepared by Herbert et al.[10] by the reduction of 4,4'-dimethoxy-3,3'-dinitrobiphenyl using iron powder and glacial acetic acid. They gave m.p. 195°. The present author used stannous chloride and hydrochloric acid for this reduction. Mixed m.p. with the diamino derivative described above was not depressed.

The di-oxime of 2,2',4,4'-tetramethoxy-5,5'-diacetylbiphenyl

It was prepared by refluxing an alcoholic solution of 2,2',4,4'-tetramethoxy-5,5'-diacetylbiphenyl (1 g.),hydroxylamine hydrochloride (1 g.) and potassium hydroxide (0.5 g.) on a steam bath for 2 hours. The product obtained on removal of alcohol crystallised from acetic acid, m.p. 238°.

Analysis : Found : C,62.0 % ; H,6.5 % ; N,7.6 %.
$C_{20}H_{24}N_2O_6$ requires : C,61.9 % ; H,6.2 % ; N,7.2 %.

2,2',4,4'-Tetramethoxy-5,5'-diacetamidobiphenyl

The above di-oxime (0.5 g.) was mixed with polyphosphoric acid (40 g.) and heated on a steam bath for 2 hours. Ice cold water was added and the product obtained was filtered, washed with water and crystallised from alcohol,m.p. 220°.

Analysis : Found : C,61.7 % ; H,6.3 % ; N,7.1 %.
$C_{20}H_{24}N_2O_6$ requires : C,61.9 % ; H,6.2 % ; N,7.2 %.

2,2',4,4'-Tetramethoxy-5,5'-diaminobiphenyl

The diacetamido derivative (0.5 g.) was heated with hydrochloric acid (1 : 1 ; 5 ml.) for 2 hours on a steam bath. The mixture was neutrallised with sodium hydroxide and the diamino compound obtained crystallised from benzene in white needles, m.p. 150°.

Analysis : Found : C,63.5 % ; H,6.6 % ; N,9.1 %.
$C_{16}H_{20}N_2O_4$ requires : C,63.2 % ; H,6.2 % ; N.9.2 %.

The same diamino compound was obtained by the nitration of 2,2',4,4'-tetramethoxybiphenyl and subsequent reduction of the dinitro derivative formed.

2,2',4,4'-Tetramethoxy-5,5'-dinitrobiphenyl

2,2',4,4'-Tetramethoxybiphenyl (1 g.) was dissolved in glacial acetic acid and the solution added to cold conc.nitric acid (5 ml.) in glacial acetic acid (5 ml.). The mixture was kept for 30 minutes and the product obtained on pouring into water crystallised from xylene, m.p. 288°.

Analysis : Found : C,53.0 % ; H,4.7 % ; N,7.4 %.
$C_{16}H_{16}N_2O_8$ requires : C,52.7 % ; H,4.4 % ; N,7.7 %.

Schiemann and Roselius[11] prepared the above dinitro derivative by a different method and reported m.p. 182-83°.

Reduction : The above dinitro derivative (0.5 g.) was added to stannous chloride (1 g.) in glacial acetic acid (2 ml.) with two drops of conc.hydrochloric acid and hydrogen chloride gas was passed. The amine hydrochloride precipitated was filtered and then neutralised with sodium hydroxide. The diamino derivative crystallised from benzene, m.p. 150°. Mixed m.p. with the product obtained from the hydrolysis of diacetamido biphenyl as described above was not depressed.

The di-oxime of 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl

A mixture of 2,2',5,5'-tetramethoxy-4,4'-diacetylbiphenyl (1 g.) in alcohol, hydroxyamine hydrochloride (1 g.) and potassium hydroxide (0.5 g.) was refluxed for 2 hours on a steam bath. The product obtained on removal of alcohol crystallised from acetic acid, m.p. 288°.

Analysis : Found : C,61.6 % ; H,6.0 % ; N,7.2 %.
$C_{20}H_{24}N_2O_6$ requires : C,61.9 % ; H,6.2 % ; N,7.2 %.

2,2',5,5'-Tetramethoxy-4,4'-diacetamidobiphenyl

The above oxime (0.5 g.) mixed with polyphosphoric acid (30 g.) was heated on a steam bath for 2hours. Ice cold water was added and the product crystallised from dil.acetic acid in white needles, m.p. 252°.

Analysis : Found : C,62.1 % ; H,6.5 % ; N,7.6 %.
$C_{20}H_{24}N_2O_6$ requires : C,61.9 % ; H,6.2 % ; N,7.2 %.

2,2',5,5'-Tetramethoxy-4,4'-diaminobiphenyl

The above diacetamido derivative (0.5 g.) was heated on a steam bath for 2 hours with hydrochloric acid (1 : 1 ; 5 ml.) sodium hydroxide was then added to neutralise and the product taken up in ether. The product obtained on removal of ether crystallised from alcohol in white needles, m.p. 210°.

Analysis : Found : C,63.6 % ; H,6.4 % ; N,9.0 %.
$C_{16}H_{20}N_2O_4$ requires : C,63.2 % ; H,6.2 % ; N,9.2 %.

Baessler[12] prepared the same diamino compound by a different method and gave m.p. 210°.

The same diamino compound was also prepared by the nitration of 2,2',5,5'-tetramethoxybiphenyl and subsequent reduction of the dinitro derivative obtained.

2,2',5,5'-Tetramethoxy-4,4'-dinitrobiphenyl

2,2',5,5'-Tetramethoxybiphenyl (0.5 g.) was dissolved in acetic anhydride and the reaction mixture was cooled in ice. Conc.nitric acid (2 ml.) in acetic anhydride (5 ml.) was slowly added by stirring. It was kept for 30 minutes in ice and then poured in water. The product obtained crystallised from xylene,m.p.277°.

Analysis : Found : C, 52.4 % ; H, 4.6 % ; N, 7.2 %.
$C_{16}H_{16}N_2O_8$ requires : C, 52.7 % ; H, 4.4 % ; N, 7.7 %.

2,2',5,5'-Tetramethoxy-4,4',6,6'-tetranitrobiphenyl

2,2',5,5'-Tetramethoxybiphenyl (0.5 g.) was dissolved in acetic anhydride and the reaction mixture was cooled in ice. Fumming nitric acid (4 ml.) in acetic anhydride (5 ml.) was slowly added by stirring. It was kept for 2 hours and then poured in water. The product obtained crystallised from acetic acid,m.p.221°.

Analysis : Found : C,42.5 % ; H,3.5 % ; N,12.4 %.
$C_{16}H_{14}N_4O_{12}$ requires : C,42.3 % ; H,3.1 % ; N,12.3 %.

Reduction of 4,4'-dinitro derivative

The 4,4'-dinitrobiphenyl (0.5 g.) was dissolved in glacial acetic acid and added to stannour chloride (1 g.) in acetic acid (2 ml.) with two drops of conc.hydrochloric acid. Hydrogen chloride gas was passed and the amino hydrochloride precipitated on working up as usual crystallised from alcohol. Mixed m.p. with the diamino derivative obtained above was not depressed.

The di-oxime of 2,2',6,6'-tetramethoxy-3,3'-diacetylbiphenyl

A mixture of 2,2',6,6'-tetramethoxy-3,3'-diacetylbiphenyl (1 g.) was dissolved in alcohol and hydroxylamine hydrochloride (1 g.) and potassium hydroxide (0.5 g.) was added. The reaction mixture was refluxed for 2 hours on a steam bath. The product obtained on removal of alcohol crystallised from acetic acid, m.p. 262°.

Analysis	: Found	: C,61.8 % ; H,6.4 % ; N,7.7 %.
$C_{20}H_{24}N_2O_6$	requires	: C,61.9 % ; H,6.2 % ; N,7.2 %.

Attempted Beckmann rearrangement of the di-oxime of 2,2',6,6'-tetramethoxy-3,3'-diacetylbiphenyl

The above oxime (0.5 g.) was heated with polyphosphoric acid (30 g.) on a steam bath for 2 hours. No pure product could be obtained on adding ice cold water to the above reaction mixture.

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