

LXIII.—*Synthesis of Imino-ethers. N-Arylbenzimino-ethers.*

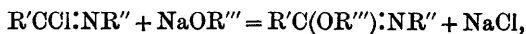
By G. D. LANDER.

ALTHOUGH aryl substituted benzimino-ethers may be prepared from the benzoylated amines by means of silver oxide and alkyl iodides (Trans., 1901, 79, 698), the yields are poor, partly owing to the relatively sparing solubility of the benzoyl compounds. It therefore became desirable to find a more economical process, by which imino-ethers of this class can be prepared in larger quantities for the purpose of

studying some of their properties, and especially a process in which the chance of the simultaneous formation of both N- and O-ethers, which seems to be characteristic of methylation by means of silver oxide, is either absent or at a minimum.

This 'molecular rearrangement in the course of synthesis' of methyl ethers by means of silver oxide and methyl iodide is not so characteristic of the benzoylated as of the acetylated arylamines. Whilst the methylation of aceto-*o*-toluidide by this process leads to the formation of about equal proportions of the isomeric ethers, and that of aceto-*p*-toluidide to the almost exclusive formation of the N-ether, with benz-*o*-toluidide scarcely any N-ether is formed, and with benz-*p*-toluidide about equal amounts of the two isomerides are produced.

The possibility of preparing imino-ethers from imide chlorides and sodium alkylloxides, in accordance with the general reaction,



appeared most promising; moreover, on *a priori* grounds, it was probably a reaction of simple replacement, and consequently one in which molecular rearrangement would not occur. The application of this mode of synthesis is not new. It has been used, among other instances, by Hantzsch (*Ber.*, 1893, 26, 927) in the preparation of N-phenylbenzimidino-phenyl ether, and by Lengfeld and Stieglitz (*Amer. Chem. J.*, 1895, 17, 98) in the formation of ethyl isocarbamilide from carbodiphenylimide monohydrochloride (the imide chloride corresponding to diphenylurea). I have found that the reaction is very well adapted to the synthesis of aryl substituted benzimidino-ethers, and that methyl ethers are obtainable with as great ease as the ethyl derivatives, no isomerisation appearing to take place.

Our knowledge of the imide chlorides is due mainly to Wallach (*Annalen*, 1876, 184, 1), who has shown how they are derived from substituted amides by the action of phosphorus pentachloride, the group $-CO \cdot NH-$ giving first $-CCl_2 \cdot NH-$ and then $-CCl : N-$. The use of imide chlorides derivable from amides, as distinguished from compounds such as $C_6H_5 \cdot N : CCl \cdot NH \cdot C_6H_5$, $C_6H_5 \cdot N : CCl_2$, and $N : C \cdot Br$, which, although belonging to the same category, are not usually prepared directly from an amido-compound, is restricted as a practical method of imino-ether synthesis, apparently, to the benzoylated amines. Its application to the preparation of phenyl, *o*-tolyl, and *p*-tolyl substituted benzimidino-ethers is described in this paper.

Acetanilide imide chloride is difficult to prepare, as it passes at about 50° into the chlorinated base $C_{16}H_{15}N_2Cl$, which is resolved by alcohol into two mols. of acetanilide (Wallach, *loc. cit.*, 86).

In the hope that sodium ethoxide might cause the resolution of this compound into molecular proportions of acetanilide and N-phenyl-

acetimino-ethyl ether, I caused a solution of sodium in ethyl alcohol to act on a benzene solution of the base; the main product was, however, diphenylethenylamidine, probably formed by the conversion of the chlorinated base by the action of the ethoxide into the chlorine-free base $C_{16}H_{14}N_2$, and the subsequent change of this into the amidine (compare Wallach, *loc. cit.*).

The imide chloride of *s*-benzoylphenylhydrazine (Pechmann, *Ber.*, 1894, 27, 322) gave, on treatment in benzene solution with alcoholic sodium ethoxide, a deep brownish-red, tarry substance, possibly a formazyl derivative, which was not further examined.

EXPERIMENTAL.

I. *N*-Phenylbenzimino-ethers.

Formation of N-Phenylbenzimino-ethyl Ether from Benzanilide Imide Chloride

In the earlier experiments on the formation of this imino-ether, the benzanilide imide chloride, prepared as directed by Wallach (*loc. cit.*), was purified by distillation in a vacuum, a procedure subsequently found to be unnecessary. In the first instance, the action of dry sodium ethoxide on a solution of the imide chloride in light petroleum was tried. The liquid acquired a dark brown colour, but after several hours' boiling the reaction was incomplete. Most of the solvent having been distilled off, the residue was extracted with water, and on distillation in a vacuum, a small quantity of a yellowish-brown liquid having all the properties of *N*-phenylbenzimino-ethyl ether was obtained. The employment of an alcoholic solution of the ethoxide leads, however, to the production of imino-ether, both rapidly and in excellent yield. The method of preparation finally adopted may be described.

Fifty grams of benzanilide and 51 grams of phosphorus pentachloride were fused together, warmed gently until the evolution of hydrogen chloride had ceased, and the phosphorus oxychloride distilled off in a vacuum. By extraction of the residue with light petroleum and filtration, a somewhat opalescent but practically pure solution of the imide chloride was obtained.

A solution of 5.5 grams of sodium in the requisite amount of ethyl alcohol was added to this solution, which was cooled, the addition requiring only a few minutes, and the resulting product having an alkaline reaction. The sodium chloride was extracted by water, the petroleum solution filtered from some benzanilide, dried with calcium chloride, and the product distilled in a vacuum. By this means, 41.5 grams of *N*-phenylbenzimino-ethyl ether, boiling at 175—177°

under 16 mm. pressure, was obtained. The boiling point is 172° under 15 mm., $168\text{--}170^{\circ}$ under 14 mm., and $220\text{--}230^{\circ}$ under from 20 to 30 mm. pressure :

0.128 gave 7 c.c. moist nitrogen at 16° and 762 mm. $N = 6.37$.

$C_{15}H_{15}ON$ requires $N = 6.22$ per cent.

The compound showed all the properties of this imino-ether, readily undergoing hydrolysis by dilute mineral acids into aniline and ethyl benzoate, and giving a sticky hydrochloride which evolved ethyl chloride on being warmed or kept, leaving a residue of benzanilide.

A small quantity of a substance of high boiling point was invariably formed in this as in other similar reactions. It remained as a glassy mass after the imino-ether had been distilled. Unless in a state approaching purity, it was exceedingly difficult to crystallise, in spite of its high melting point. The formation of this bye-product was considerably increased at the expense of the imino-ether by adding alcohol drop by drop to a boiling solution of the imide chloride, to which the calculated amount of sodium wire had been added, until the latter was dissolved ; but thus prepared, the substance resisted all attempts at crystallisation. The united residues of several imino-ether preparations were crystallised from a mixture of chloroform and light petroleum, forming dense, pale yellow, prismatic crystals melting at $170\text{--}172^{\circ}$ without decomposition. On analysis :

0.1486 gave 0.4515 CO_2 and 0.0798 H_2O . $C = 82.86$; $H = 5.96$.*

0.1278 „ 0.3874 CO_2 „ 0.0660 H_2O . $C = 82.67$; $H = 5.73$.

0.1560 „ 10 c.c. moist nitrogen at 13° and 768 mm. $N = 7.64$.

0.1330 „ 8.4 c.c. „ 12° „ 768 mm. $N = 7.56$.

A cryoscopic determination of the molecular weight in acetic acid solution gave the value 372.

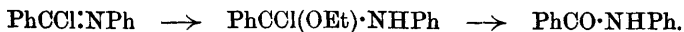
These data agree best with the formula $C_{26}H_{20}ON_2$, which requires $C = 82.97$; $H = 5.32$; $N = 7.44$ per cent.

This is the composition of *benzoyldiphenylbenzenylamidine*, $PhC:NPh \cdot N(COPh)Ph$, with which the substance proved to be identical. By boiling it with moderately concentrated sulphuric acid, it was resolved into benzoic acid and diphenylbenzenylamidine. The benzoyl derivative of the latter compound, prepared either by allowing benzoyl chloride and the base to interact in benzene solution, or by the Schotten-Baumann method, possessed the same crystalline appearance, colour, and melting point as the compound from the imide chloride, and gave $N = 7.56$, instead of the calculated 7.44 per cent.

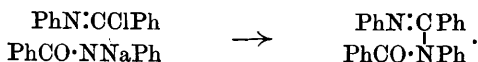
It is exceedingly probable that the formation of benzoylated amidine from imide chloride takes place in the following manner. The

* Analysed by Mr. G. Clarke, A.I.C.

alcohol used as a solvent for the sodium ethoxide causes a partial decomposition of the benzanilide imide chloride into benzanilide,



By the action of the sodium ethoxide, sodiobenzanilide would be formed and yield the benzoylated amidine thus,



N-Phenylbenzimidino-methyl Ether.

By the interaction of a solution of the required amount of sodium in methyl alcohol and a light petroleum solution of benzanilide imide chloride from 25 grams of benzanilide, 18·5 grams of the imino-ether boiling at 157—158° under 12 mm. pressure were obtained :

0·1858 gave 10·8 c.c. moist nitrogen at 18° and 770 mm. $N = 6·79$.

$\text{C}_{14}\text{H}_{13}\text{ON}$ requires $N = 6·63$ per cent.

The compound was resolved by dilute mineral acids into aniline and methyl benzoate, and by anhydrous ethereal hydrogen chloride into benzanilide and methyl chloride.

This imino-ether has been prepared by Wislicenus and Goldschmidt (*Ber.*, 1900, 33, 1471) by an application of Lossen's method (*Annalen*, 1891, 265, 138). They give 145—150° under 8 mm. pressure as its boiling point.

Benzoyldiphenylbenzenylamidine was a bye-product of the synthesis, and in addition a small quantity of diphenylbenzenylamidine, melting at 143—145°, appeared to have been formed.

Methylation of Benzanilide by Methyl Iodide and Silver Oxide.—This methylation was carried out for the purpose of comparison with the process of alkylation of acetylarylamines by the same method. The product obtained from 10 grams of benzanilide, 35 grams of silver oxide, and 42 grams of methyl iodide in 50 c.c. of benzene after 3 hours' boiling, consisted of 5 grams of *N*-phenylbenzimidino-methyl ether boiling at 163° under 11 mm. pressure, and identified in the usual way, some unaltered benzanilide, and between 3 and 4 grams of benzoylmethylaniline. The last named compound was present in the part of the product which boiled between 180° and 190° under 9 mm. pressure, and was not obtained solid. It was freed from imino-ether by steam distillation with dilute hydrochloric acid, the unaltered oil separated, hydrolysed with moderately concentrated sulphuric acid, and the methylaniline thus obtained identified by means of its acetyl derivative.

N-Phenylbenzimidino-propyl Ether.

This compound was prepared by the action of a solution of 3 grams of sodium in *n*-propyl alcohol on the light petroleum extract of the imide chloride from 25 grams of benzanilide. It boiled at 180—182° under 13 mm., and at 177—179° under 11 mm. pressure. After three distillations, 10 grams of the desired product, displaying the usual reactions of an imino-ether, were obtained:

0.1872 gave 9.2 c.c. moist nitrogen at 9° and 760 mm. $N = 5.89$.

$C_{16}H_{17}ON$ requires $N = 5.85$ per cent.

II. *N-o-Tolylbenzimidino-ethers.**N-o-Tolylbenzimidino-ethyl Ether.*

A light petroleum solution of the imide chloride from 20 grams of benz-*o*-toluidide was treated with 3 grams of sodium dissolved in ethyl alcohol in the manner already described. After three distillations, 14 grams of imino-ether boiling at 179—180° under 15 mm. pressure were obtained:

0.2344 gave 11.8 c.c. moist nitrogen at 9° and 749 mm. $N = 5.95$.

$C_{16}H_{17}ON$ requires $N = 5.85$ per cent.

As in the similar reaction between sodium ethoxide and benzanilide imide chloride, a residue of high boiling point remained after distillation of the imino-ether. It displayed, however, less tendency to crystallise, and in view of the very probable similarity between it and the product already dealt with, was not further examined. The same remark is true of the products obtained from the imide chloride of benz-*p*-toluidide.

N-o-Tolylbenzimidino-methyl Ether.

The imide chloride from 20 grams of benz-*o*-toluidide, by interaction with the requisite amount of sodium in methyl alcoholic solution, gave 15 grams of the imino-ether boiling at 173° under 15 mm. pressure:

0.1495 gave 0.4375 CO_2 and 0.0925 H_2O . $C = 79.81$; $H = 6.86$.*

$C_{15}H_{15}ON$ requires $C = 80.00$; $H = 6.66$ per cent.

Methylation of Benz-o-toluidide by Methyl Iodide and Silver Oxide.

—Interaction between 35 grams of silver oxide, 42 grams of methyl iodide, and 15 grams of benz-*o*-toluidide dissolved by the aid of 60 c.c. of benzene, resulted in the formation of 8 grams of *N-o*-tolylbenzimidino-methyl ether boiling at 170—171° under 11 mm. pressure. Nearly all

* Analysed by Mr. G. Clarke, A.I.C.

the remaining product was unaltered toluidide, but after this had been removed as completely as possible by crystallisation from aqueous alcohol, a small quantity of a thick oil remained. After separation, hydrolysis with sulphuric acid and liberation of the base, a sufficient quantity was obtained to give Liebermann's reaction, thus showing that benz-*o*-methyltoluidide was a product of the reaction.

The influence of orientation on the properties of the substituted benzimino-ethers is notably less well defined than in the cases of the analogous substituted acetimino-compounds, indeed, scarcely any influence can be detected by the methods applicable to the latter substances (compare *Trans.*, 1901, **79**, 693). When cold dilute hydrochloric acid is added to the *o*-tolylbenzimino-ethers, solution occurs, but the almost instantaneous appearance of a turbidity indicates the commencement of the characteristic hydrolysis, and a platinichloride cannot be prepared, even by the addition of alcoholic platinic chloride to an alcoholic solution of the base. The hydrochlorides could not be prepared by means of anhydrous ethereal hydrogen chloride.

I take this opportunity of making a correction and addition to the description of the substituted acetimino-ethers formerly described (*loc. cit.*). When freshly distilled acetyl chloride is added to a light petroleum solution of N-*o*-tolylacetimino-ethyl ether, an oil is precipitated, which solidifies on rubbing to colourless needles, fusing with copious evolution of gas at 109–110° and leaving a residue of aceto-*o*-toluidide. These needles are the hydrochloride of the imino-ether in a purer state than the amorphous salt melting at 90–91° previously prepared from the base by means of ethereal hydrogen chloride. On analysis, the crystalline salt gave Cl = 16.42 instead of 16.62 per cent. Moreover, by the same mode of treatment N-phenylacetimino-ethyl ether, the hydrochloride of which I have not formerly prepared, gives that salt in a crystalline state; it melts evolving gas at 100°. This result of the action of acetyl chloride is easily explicable, bearing in mind the difficulty of freeing this substance from traces of hydrochloric acid. The reagent, however, has not proved suitable for the preparation of the hydrochlorides of substituted benzimino-ethers.

The only respect, then, in which orientation seems to influence the formation of the aryl substituted benzimino-ethers is displayed in the extent to which the isomeric N-methyl homologues are formed in methylation by means of silver oxide (*loc. cit.*, 696).

III. N-*p*-Tolylbenzimino-ethers.

N-*p*-Tolylbenzimino-ethyl Ether.

The imide chloride corresponding to 20 grams of benz-*p*-toluidide gave, on treatment with sodium ethoxide and four distillations of the

product in a vacuum, 15 grams of the imino-ether boiling at 178° under 11 mm. pressure :

0.1730 gave 8.3 c.c. moist nitrogen at 10° and 773 mm. $N = 5.83$.
 $C_{16}H_{17}ON$ requires $N = 5.85$ per cent.

The compound possesses the usual properties of the imino-ethers, but appears to be more stable than the corresponding *N-p*-tolylacetimino-ethyl ether.

N-p-Tolylbenziminomethyl Ether.

The imide chloride from 20 grams of benz-*p*-toluidide gave 13.2 grams of imino-ether, boiling after two distillations at 177° under 12 mm. pressure :

0.2470 gave 12.5 c.c. moist nitrogen at 11° and 770 mm. $N = 6.10$.
 $C_{15}H_{15}ON$ requires $N = 6.22$ per cent.

Methylation of Benz-p-toluidide by Methyl Iodide and Silver Oxide.—The product obtained by boiling together 10 grams of benz-*p*-toluidide, 35 grams of silver oxide, 42 grams of methyl iodide, and 50 c.c. of benzene for 4 hours, gave, on distillation, 4 grams of *N-p*-tolylbenziminomethyl ether boiling at 175 — 182° under 11 mm. pressure, a thick oil distilling between 185° and 200° at the same pressure, and a residue of unchanged toluidide. The thick oil was a mixture of imino-ether and benz-*p*-methyltoluidide. After getting rid of the imino-ether by steam distillation with dilute hydrochloric acid, the residue gave on hydrolysis with sulphuric acid a secondary base identified as methyl-*p*-toluidine by acetylation.

Much of the expense incurred in this work was defrayed by a grant made by the Research Fund Committee of the Chemical Society, for which I desire to express my indebtedness.

UNIVERSITY COLLEGE,
 NOTTINGHAM.
