157. N-*Oximino-ethers. Part III. Condensation of Phenylchloroacetonitrile with Nitroso-compounds. Stereoisomeric* N-*Phenyl Ethers of Oximinophenylacetonitrile.*

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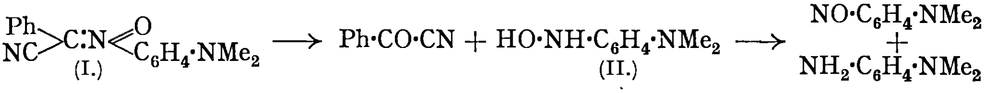
IT has been found previously (J., 1921, **119**, 212; 1922, **121**, 1713) that *p*-nitro-substituted benzyl halides readily condense with aromatic nitroso-compounds, yielding *N*-aryl ethers of the corresponding benzaldoximes. A similar behaviour is shown by the halogen derivatives of other compounds containing an active methylene group (compare Bergmann and Hervey, *Ber.*, 1929, **62**, 893), and the reaction with phenylchloroacetonitrile is now described.

p-Nitrosodimethylaniline condenses with phenylchloroacetonitrile, under the influence of alcoholic potassium hydroxide, even more readily than with the nitrobenzyl halides, yielding *oximinophenylacetonitrile* N-p-*dimethylaminophenyl ether* (I), the constitution of which has been established from its behaviour on hydrolysis; when heated with concentrated hydrochloric acid, it is rapidly converted into benzoyl cyanide, *p*-nitrosodimethylaniline, and *p*-aminodimethylaniline:



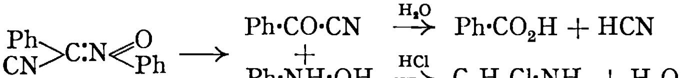
$$\underset{\text{(I.)}}{{}^{Ph}_{NC}{>}C{:}N{<}^{O}_{C_6H_4\cdot NMe_2}} \longrightarrow Ph\cdot CO\cdot CN + \underset{\text{(II.)}}{HO\cdot NH\cdot C_6H_4\cdot NMe_2} \longrightarrow \begin{matrix}NO\cdot C_6H_4\cdot NMe_2\\ +\\ NH_2\cdot C_6H_4\cdot NMe_2\end{matrix}$$

The *p*-dimethylamino-β-phenylhydroxylamine (II) intermediately formed in the hydrolysis is apparently unstable and at once undergoes simultaneous oxidation and reduction to the *p*-nitroso- and the *p*-amino-derivative of dimethylaniline respectively. Similar oximino-ethers have been prepared by the interaction of phenylchloroacetonitrile with *p*-nitrosoaniline and its *N*-methyl, ethyl, phenyl, diethyl, and benzylethyl derivatives.

In view of the occurrence of isomeric *N*-methyl ethers of phenyl *p*-tolyl ketoxime (Semper and Lichtenstadt, *Ber.*, 1918, **51**, 928), *p*-nitrobenzophenoneoxime (Brady and Mehta, J., 1924, **125**, 2297), and *iso*nitrosomalonomono-*p*-tolylamide (Plowman and Whiteley, J., 1924, **125**, 587), the condensations with the mono- and the di-methyl- and -ethyl derivatives were carried out under various conditions in the presence of sodium ethoxide, alcoholic potassium hydroxide, and sodium carbonate; in no instance, however, was any evidence obtained of the existence of a second isomeride.

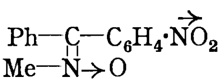
The condensation of nitrosobenzene with phenylchloroacetonitrile produced two stereoisomeric *N*-phenyl ethers (III), which were readily separated by means of their markedly different solubilities in benzene. The more sparingly soluble isomeride, which will be referred to as the *α-ether*, crystallises in pale yellow needles, m. p. 170°. It is thermolabile and is slowly transformed at temperatures considerably below its m. p. into the more soluble stable *β-ether*, which crystallises in stout prisms, m. p. 143°, and has a paler yellow colour than the α-form. The separate and the combined effects of the two compounds in depressing the freezing point of benzene (compare Sidgwick, J., 1915, **107**, 672) show that they are isomeric and not dimorphous. Both isomerides are reduced by zinc dust and ammonium chloride in aqueous-alcoholic solution to α-phenyliminophenylacetonitrile, $PhN{:}CPh\cdot CN$, and on hydrolysis with concentrated hydrochloric acid yield benzoic acid, hydrogen cyanide, and *p*-chloroaniline:

(III.)



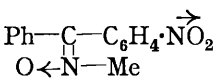
$$\text{(III.)}\quad {}^{Ph}_{CN}{>}C{:}N{<}^{O}_{Ph} \longrightarrow \begin{matrix} Ph\cdot CO\cdot CN & \xrightarrow{H_2O} & Ph\cdot CO_2H + HCN\\ + & & \\ Ph\cdot NH\cdot OH & \xrightarrow{HCl} & C_6H_4Cl\cdot NH_2 + H_2O\end{matrix}$$

The stereochemical configurations of the two isomerides have been determined from measurements of their electric dipole moments. Sutton and Taylor (J., 1931, 2190), who applied the method to the *N*-methyl ethers of *p*-nitrobenzophenoneoxime, pointed out that the —N→O group should have a moment comparable with that of the nitro-group, and hence the moment of the ether having configuration (IV) will be large, whilst that of the stereoisomeric ether (V) will be small: the α-ether gave $\mu = 6{\cdot}6 \times 10^{-18}$ e.s.u. and therefore has configuration (IV); the β-ether had $\mu = 1{\cdot}09 \times 10^{-18}$ e.s.u. and must accordingly be represented by (V).



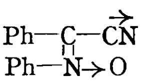
$$\begin{array}{l} Ph-C-C_6H_4\cdot\overrightarrow{NO_2}\\ \quad\;\;\, \| \\ Me-N\rightarrow O\end{array}$$

(IV.)
$\mu = 6{\cdot}60.$



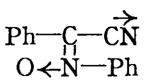
$$\begin{array}{l} Ph-C-C_6H_4\cdot\overrightarrow{NO_2}\\ \quad\;\;\, \| \\ O\leftarrow N-Me\end{array}$$

(V.)
1·09.



$$\begin{array}{l} Ph-C-\overrightarrow{CN}\\ \quad\;\;\, \| \\ Ph-N\rightarrow O\end{array}$$

(VI.)
6·3.



$$\begin{array}{l} Ph-C-\overrightarrow{CN}\\ \quad\;\;\, \| \\ O\leftarrow N-Ph\end{array}$$

(VII.)
$1{\cdot}07 \times 10^{-18}$ c.s.u.

The cyano-group in the isomeric *N*-phenyl ethers of oximinophenylacetonitrile has a large moment, the negative pole being nearer the nitrogen atom, and hence the ether (VI) will have a large moment, whilst in the other (VII) the moment will be small.

We are much indebted to Prof. S. Sugden for undertaking the measurement of the dipole moments of the two isomerides. He found that the α-ether had $\mu = 6{\cdot}3 \times 10^{-18}$ e.s.u. and the β-ether, $\mu = 1{\cdot}07 \times 10^{-18}$ e.s.u. From these results there can be no doubt that the α-ether has the configuration (VI), whilst the β-ether is represented by (VII). The *N*-phenyl ethers of oximinophenylacetonitrile possess moments of almost the same magnitude as those of the corresponding *N*-methyl ethers of *p*-nitrobenzophenoneoxime—a result which would be anticipated in view of the fact that the moments of the nitro- and the cyano-group are almost identical.

EXPERIMENTAL.

Phenylchloroacetonitrile is more conveniently prepared by the action of thionyl chloride on mandelonitrile than by the method of Michael and Jeanpêtre (*Ber.*, 1892, **25**, 1679), who used phosphorus pentachloride. Mandelonitrile (400 g.) in dry ether (400 c.c.) was added slowly to thionyl chloride (400 g.), and the mixture refluxed until the evolution of hydrogen chloride ceased. After filtration and removal of the ether, the chloro-nitrile (200 g.) had b. p. 108—110°/5 mm. The nitroso-compounds were all prepared by the methods given in the literature.

Oximinophenylacetonitrile N-p-*Dimethylaminophenyl Ether.*—Methyl-alcoholic potassium hydroxide (6·2 g. in 40 c.c.) was added during 10 minutes with constant stirring to a solution of *p*-nitrosodimethylaniline (15 g.) and phenylchloroacetonitrile (15·1 g.) in ethyl alcohol (150 c.c.). Rise of temperature occurred and the mixture became red. After 1 hour, the *ether* was collected, washed with water to remove potassium chloride, and crystallised from alcohol, forming stout red prisms (21·5 g.), m. p. 185° (Found: N, 15·5. $C_{16}H_{15}ON_3$ requires N, 15·8%).

Hydrolysis. The ether (2 g.) was heated with hydrochloric acid (15 c.c. of 25%) on the steam-bath until it dissolved and a colourless oil separated. The mixture was cooled in ice, the liquid filtered, and the yellow solid extracted with ether. The colourless oil obtained by evaporating the dried ethereal solution readily solidified and crystallised from light petroleum in leaflets of benzoyl cyanide, m. p. 32°, which was converted into benzanilide (m. p. and mixed m. p. 162°) when heated with aniline. The yellow solid remaining after the ether extraction consisted of *p*-nitrosodimethylaniline hydrochloride, from which the free base (m. p. and mixed m. p. 85°) was isolated. The acid solution after the hydrolysis was basified with sodium carbonate and shaken with *p*-nitrobenzoyl chloride (1·5 g.) in benzene (20 c.c.), and the dark brown solid obtained was washed with hot alcohol and crystallised from pyridine–alcohol, p-*nitrobenzo*-p′-*dimethylaminoanilide*, $NO_2{\cdot}C_6H_4{\cdot}CO{\cdot}NH{\cdot}C_6H_4{\cdot}NMe_2$, separating in lustrous, dark bronze leaflets, m. p. 258° (either alone or when mixed with a specimen prepared directly from *p*-nitrobenzoyl chloride and *p*-aminodimethylaniline in a similar manner) (Found: N, 14·8. $C_{15}H_{15}O_3N_3$ requires N, 14·7%).

Oximinophenylacetonitrile N-p-*Methylaminophenyl Ether.*—This was prepared by the addition of potassium hydroxide (3·1 g.), dissolved in methyl alcohol (20 c.c.), to a solution of *p*-nitrosomethylaniline (7·8 g.) and phenylchloroacetonitrile (7·5 g.) in ethyl alcohol (50 c.c.). After being washed with water and crystallised from acetone, it formed slender yellow needles, m. p. 193° (Found: N, 16·8. $C_{15}H_{13}ON_3$ requires N, 16·7%).

The N-p-*diethylaminophenyl ether*, obtained from *p*-nitrosodiethylaniline in a similar manner, crystallised from acetone in stout, bright red prisms, m. p. 153° (Found: N, 14·5. $C_{18}H_{19}ON_3$ requires N, 14·3%); and the N-p-*ethylaminophenyl ether*, from *p*-nitrosoethylaniline, in slender, orange-red needles, m. p. 185° (Found: N, 15·9. $C_{16}H_{15}ON_3$ requires N, 15·8%). The following ethers were prepared by using sodium ethoxide as a condensing agent: N-p-*Benzylethylaminophenyl ether.* To *p*-nitrosobenzylethylaniline (12 g.) and phenylchloroacetonitrile (7·5 g.), dissolved in alcohol (150 c.c.), was added gradually at room temperature, with constant stirring, a solution of sodium (1·15 g.) in alcohol (20 c.c.); the solid which separated was washed with water and crystallised from alcohol, forming bright red needles, m. p. 142° (Found: N, 12·0. $C_{23}H_{21}ON_3$ requires N, 11·8%). The N-p-*phenylaminophenyl ether*, prepared from *p*-nitrosodiphenylamine, separated from chloroform in golden-brown needles, m. p. 154° (Found: N, 13·2. $C_{20}H_{15}ON_3$ requires N, 13·4%); and the N-p-*aminophenyl ether*, from *p*-nitrosoaniline, in lustrous golden-yellow plates, m. p. 195° (Found: N, 17·5. $C_{14}H_{11}ON_3$ requires N, 17·7%).

Isomeric N-*Phenyl Ethers of Oximinophenylacetonitrile*.—Aqueous potassium hydroxide (28 g. in 100 c.c.) was added during 45 minutes to a mechanically stirred solution of nitrosobenzene (53 g.) and phenylchloroacetonitrile (71 g.) in alcohol (250 c.c.), the temperature being maintained at *ca*. 30° by external cooling. The solution was then diluted with water (1000 c.c.) and the solid which separated was collected and washed with a little cold alcohol. The yield of mixed ethers amounted to 85 g., but this was diminished considerably if the addition of the alkali was made too rapidly, or the temperature was maintained too low during the condensation. Separation was effected by shaking the mixture with benzene (600 c.c.) at room temperature. The solution, filtered from the undissolved α-ether, on evaporation deposited the β-N-*phenyl ether*, which was obtained in a pure condition after two crystallisations from alcohol (yield, 22 g.). It separates in stout, pale yellow prisms, m. p. 143°, which slowly turn brown on exposure to light, and are readily soluble in acetone and benzene, moderately so in alcohol, and only very sparingly soluble in light petroleum and *cyclo*hexane: 100 c.c. of the saturated solution in benzene at 21° contain 7·05 g. (Found: C, 75·4; H, 4·7; N, 12·7; *M*, cryoscopic in benzene, 216, 229. $C_{14}H_{10}ON_2$ requires C, 75·7; H, 4·5; N, 12·6%; *M*, 222).

Hydrolysis of the β-*ether*. The ether (2 g.) was heated with concentrated hydrochloric acid (100 c.c.) on the steam-bath for 1 hour, and the solution cooled and filtered from the benzoic acid which separated. After concentration and basification with sodium hydroxide, the mixture was cooled in ice and shaken with acetic anhydride; *p*-chloroacetanilide (m. p. and mixed m. p. 178°) was then obtained.

Reduction of the β-*ether*. A mixture of the ether (8·5 g.), ammonium chloride (2 g.), zinc dust (8 g.), alcohol (120 c.c.), and water (20 c.c.) was mechanically stirred at 60° for 45 minutes, alcohol being added at intervals to replace that lost by evaporation. After filtration the solution was diluted with water and the precipitate obtained was crystallised from alcohol (80%). It formed bright yellow leaflets, m. p. 71°, either alone or when mixed with α-phenyliminophenylacetonitrile prepared according to Sachs and Bry (*Ber*., 1901, **34**, 501).

The α-*phenyl ether*, remaining undissolved after extraction of the β-ether from the original condensation product with benzene, crystallised from benzene or acetone in lustrous, pale yellow needles (23 g.), m. p. 170°, much less soluble in the common solvents than the β-isomeride: 100 c.c. of the saturated solution in benzene at 21° contain 1·17 g. (Found: C, 75·5; H, 4·7; N, 12·8%; *M*, cryoscopic in benzene, 207).

The depressions of the freezing point of benzene produced by saturation with the two isomerides were:

Depression produced by saturation with the β-ether	1·245°
Depression after addition of the α-ether also	1·390°

The α-ether undergoes transformation into the β-isomeride at temperatures far below that at which fusion occurs. The melting point was therefore taken as the temperature, 170°, at which complete melting took place in 15 seconds when the ether, contained in a capillary tube, was plunged in a previously heated bath. If the temperature is raised slowly, the melting point recorded is 142° owing to complete transformation into the β-form. The two ethers form a eutectic mixture which melts at 126° and then resolidifies to the β-isomeride at a slightly higher temperature (*ca*. 130°).

On hydrolysis with concentrated hydrochloric acid the α-ether yielded benzoic acid and *p*-chloroaniline, which were isolated and identified in the manner described previously in the case of the β-isomeride. The reduction was effected by heating the α-ether (3·5 g.) with zinc dust (6 g.) and ammonium chloride (2 g.) in boiling aqueous alcohol (300 c.c. of 75%) for 2 hours (mechanical stirring): the α-phenyliminophenylacetonitrile obtained by the addition of water to the filtered solution had m. p. and mixed m. p. 71°.

Measurement of Electric Dipole Moments (By S. Sugden).

These were measured in benzene at 25°, the dielectric constants being determined by the method previously described (Sugden, J., 1933, 768). The results are tabulated below, where f_2 is the molar fraction of the solute, d the density of the solution, ε its dielectric constant, n its refractive index, p_{12} its specific polarisation, P_2 the total polarisation of the solute, and P_E the electron polarisation calculated from the refractive index.

f_2.	$d^{25°}$.	$\epsilon_{25°}$.	p_{12}.	P_2.	$n_D^{18°}$.	P_E.
*Oximinophenylacetonitrile β-*N*-phenyl ether.*						
0	0·8726	2·273	0·3414	—	1·5037	—
0·006262	0·8767	2·289	0·3430	95·9	—	—
0·012521	0·8807	2·303	0·3438	91·1	1·5086	74·4
0·020213	0·8859	2·318	0·3446	88·6	1·5111	74·4

P_2 at infinite dilution = 98·3; $P\mu = P_2 - P_E = 23·9$ cm.^{3}: $\mu = 1·07 \times 10^{-18}$ e.s.u.

*Oximinophenylacetonitrile α-*N*-phenyl ether.*				
0	0·8729	2·273	0·3413	—
0·000874	0·8735	2·323	0·3504	900
0·001765	0·8742	2·375	0·3593	886

P_E could not be determined from the refractive index of the solutions owing to the sparing solubility of the substance. It was therefore assumed to have the same value as the β-isomeride, *viz.*, 74·4. P_2 at infinite dilution = 915; $P\mu = P_2 - P_E = 841$ cm.^{3}: $\mu = 6·3 \pm 0·1 \times 10^{-18}$ e.s.u.

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