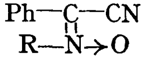
160. N-*Oximino-ethers. Part V. Stereoisomeric* N-*Aryl Ethers of Oximinophenylacetonitrile.*

By F. BARROW and F. J. THORNEYCROFT.

Six pairs of stereoisomeric *N*-aryl ethers of oximinophenylacetonitrile (I and II) have been prepared by the condensation of phenylchloroacetonitrile with aromatic nitroso-compounds. The configurations of the stereoisomerides have been determined from the measurement of their dipole moments.

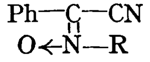
IN Part III (J., 1934, 722) it was shown that phenylchloroacetonitrile condenses with nitrosobenzene, yielding two stereoisomeric *N*-phenyl ethers of oximinophenylacetonitrile, of which the higher-melting α-isomeride, having configuration (I, R = Ph), is thermolabile, being converted at temperatures below its melting point into the stable β-form (II, R = Ph).

(I.)



$$\begin{array}{c}\mathrm{Ph{-}C{-}CN}\\ \|\\ \mathrm{R{-}N{\rightarrow}O}\end{array}$$

(II.)



$$\begin{array}{c}\mathrm{Ph{-}C{-}CN}\\ \|\\ \mathrm{O{\leftarrow}N{-}R}\end{array}$$

In view of the ease with which this condensation takes place, and also of the fact that only four examples of stereoisomeric *N*-oximino-ethers have been described previously, *viz.*, the *N*-methyl ethers of phenyl *p*-tolyl ketone (Semper and Lichtenstadt, *Ber.*, 1918, **51**, 928), *p*-nitrobenzophenone oxime (Brady and Mehta, J., 1924, **125**, 2297), *iso*nitrosomalono-*p*-tolylamide (Plowman and Whiteley, J., 1924, **125**, 587), and 2 : 6-dichloro-3-aminobenzaldoxime (Freudenberg, " Stereochemie," 1932, p. 966), it appeared of interest to extend the reaction to other nitroso-compounds, and the condensation of phenylchloroacetonitrile with the nitrosotoluenes and chloronitrosobenzenes is now described. *p*-Nitrosotoluene readily condenses with phenylchloroacetonitrile in the presence of potassium hydroxide, yielding two stereoisomeric *oximinophenylacetonitrile* N-p-*tolyl ethers*, which differ from the *N*-phenyl ethers in that the more fusible isomeride, m. p. 135°, is thermolabile, being transformed below its melting point into the stable form, m. p. 161°. The configurations of the isomerides have been determined from the measurement of their dipole moments.

It was shown in Part III that the α-*N*-phenyl ether (I), in which the moments of the —CN and —N→O groups augment one another, has a much higher moment than the β-isomeride (II), in which these main dipoles are opposed. In the case of the *N*-*p*-tolyl ethers, the methyl group will have little effect on the total moment, and hence the tolyl ether having configuration (I, R = C_6H_4Me) will have a much higher moment than the stereoisomeric ether (II, R = C_6H_4Me). It was found that the higher melting *N*-*p*-tolyl ether had a small moment, $\mu = 0{\cdot}96$, and therefore has the same configuration (II) as the β-*N*-phenyl ether : the isomeride, m. p. 135°, has a high moment, $\mu = 6{\cdot}42$, and accordingly has the α-configuration (I).

Similar pairs of stereoisomeric N-*ethers* have been obtained by the condensation of phenylchloroacetonitrile with *o*- and *m*-nitrosotoluenes and also with the three chloronitrosobenzenes. Configurations have been assigned to these isomerides from the measurement of their dipole moments, which are given (in Debye units) in Table I, together with the melting points and solubilities in benzene.

TABLE I.

Dipole Moments, Solubilities, and Melting Points of N-*Ethers of Oximinophenylacetonitrile.*

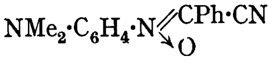
Ether.	α-Form. M. p.	α-Form. Solubility.	α-Form. μ.	β-Form. M. p.	β-Form. Solubility.	β-Form. μ.
Phenyl	170°	1·17 (21°)	$6·3_0$	143°	7·05 (21°)	$1·0_1$
o-Tolyl	158	2·41 (23)	$6·4_2$	117	37·35 (23)	$0·9_6$
m- ,,	134	11·68 (26)	$6·8_3$	126	11·78 (26)	$1·0_6$
p- ,,	135	10·81 (26)	$6·8_4$	161	2·64 (26)	$1·0_5$
o-Chlorophenyl	143	7·45 (19)	$6·9_3$	100	26·21 (19)	$1·2_2$
m- ,,	123	4·31 (19)	$6·2_2$	156	2·95 (19)	$1·7_8$
p- ,,	132	13·76 (26)	$5·6_3$	142	8·58 (26)	$1·5_3$

The values in columns 3 and 6 represent the weight of solute contained in 100 c.c. of a saturated solution at the temperature given in parentheses.

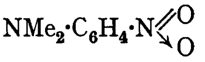
It will be observed that there is no constant relationship between the configuration of the isomerides and their melting points and solubilities. The *o*-compounds resemble the phenyl ethers in that the β-forms have a lower melting point and a higher solubility than the α-isomerides, but with the *p*-compounds and also with the *m*-chlorophenyl ethers this relationship is reversed: the isomeric *m*-tolyl ethers show little difference in solubility and melting point. These results furnish an excellent example of the futility of attempting to assign configurations to geometrical isomerides of even closely related constitution from a comparison of their melting points or solubilities. The α-forms (I) of the stereoisomeric ethers are, in all cases, thermolabile and undergo complete conversion, at temperatures in the neighbourhood of their melting points, into the stable β-forms (II).

In Part III it was shown that the *N*-oximino-ethers resulting from the condensation of phenylchloroacetonitrile with the *p*-nitroso-derivatives of the mono- and di-alkylanilines occur in only one form, which probably has the β-configuration. This view has been confirmed from the measurement of the dipole moment of the *N*-*p*-dimethylaminophenyl ether. The *N*-oximino-ethers are closely related in their constitution to the nitro-compounds, and it would therefore be anticipated that the moments of the *N*-phenyl and *N*-*p*-dimethylaminophenyl (III) ethers, having the same configuration, would show a relationship similar to that of the moments of nitrobenzene and its *p*-dimethylamino-derivative (IV).

(III.)



$$NMe_2\cdot C_6H_4\cdot N{\nearrow\!\!\!\!\!\!=\,CPh\cdot CN \atop \searrow O}$$



$$NMe_2\cdot C_6H_4\cdot N{\nearrow\!\!\!\!\!\!=\,O \atop \searrow O}$$

(IV.)

The introduction of the dimethylamino-group into the *p*-position of nitrobenzene raises the moment from 3·94 to 6·89 (Marsden and Sutton, J., 1936, 599): the moments of the α- and the β-*N*-phenyl ether of oximinophenylacetonitrile are 6·3 and 1·07 respectively. If the *N*-*p*-dimethylaminophenyl ether has the α-configuration, and the dimethylamino-group exercises the same effect in the case of the *N*-oximino-ethers as with the nitro-compounds, the ether should have a moment of *ca.* 9·2. The moment found for the *N*-*p*-dimethylaminophenyl ether in benzene solution had a much lower value, *viz.*, 2·94, and the ether accordingly has the β-configuration.

EXPERIMENTAL.

The melting points of the α-isomerides vary according to the rate of heating, owing to transformation into the β-forms. The values recorded below were determined by noting the temperature at which complete fusion occurred in 15 seconds when the ethers, contained in a capillary tube, were plunged into a previously heated bath.

Preparation of Nitroso-compounds.—Many of the methods described in the literature were investigated, but the following general method was found to give satisfactory results and can be rapidly carried out. Zinc dust (250 g.) is added in one portion to a vigorously stirred mixture of the nitro-compound (1 g.-mol.), alcohol (700 c.c.), water (200 c.c.), and ammonium chloride (40 g.). The temperature rises rapidly, and during the initial stages of the reaction is maintained at *ca.* 70° by occasional external cooling. Stirring is continued until the temperature falls to 55°; the solution is then filtered and the zinc residues are washed twice with hot aqueous alcohol (300 c.c. of 50%). The combined filtrates are distilled until a pronounced turbidity is produced, cooled to 40°, and shaken with light petroleum (800 c.c.; b. p. 60—80°). In the case of the *p*-compounds the hydroxylamine derivative crystallises and is freed from any unchanged nitro-compound by a further extraction with light petroleum (200 c.c.). The *o*- and *m*-hydroxylamines separate as oils below the intermediate aqueous layer; the two lower layers are separated and again extracted with light petroleum (200 c.c.). Oxidation to the nitroso-compounds is effected by slowly adding the hydroxylamine, dissolved in the minimum amount of alcohol, to an aqueous solution of commercial hydrated ferric chloride (680 g. in 2 l.), the mixture being mechanically stirred, and the temperature maintained between 0° and 5° by the addition of ice. After 1 hour, the nitroso-compound is filtered off, washed with water, and distilled in steam. The yield varies from 24 to 45%, being greatest in the case of the *p*-compounds.

Condensations of Phenylchloroacetonitrile.—(a) *With* o-*nitrosotoluene.* An aqueous solution of potassium hydroxide (12 g. in 200 c.c.) was added dropwise to a mechanically stirred solution of the nitrile (29 g.) and *o*-nitrosotoluene (26·7 g.) in acetone (500 c.c.) and water (100 c.c.). The addition of the alkali produces an evanescent orange-red coloration, which becomes permanent when the condensation is complete. After being filtered off and washed with water, the solid (21·5 g.) which separated was crystallised twice from alcohol and furnished *oximinophenylacetonitrile* α-N-o-*tolyl ether* in stout yellow prisms, m. p. 158° (Found: N, 12·1. $C_{15}H_{12}ON_2$ requires N, 11·9%). The aqueous acetone solution, from which the α-ether had been separated, gave, on dilution with water, a crop (14 g.) consisting mainly of the β-N-o-*tolyl ether*, which was successively crystallised from light petroleum (b. p. 60—80°) and alcohol and obtained in small, pale yellow needles, m. p. 117°, much more readily soluble in the common solvents than the α-isomeride (Found: N, 12·0%).

(b) *With* m-*nitrosotoluene.* The condensation of the nitrile (45 g.) and the nitroso-compound (37·5 g.) was carried out in aqueous acetone solution (800 c.c.) in the same manner as described for the *o*-compound. After being washed with water and dried, the solid (45 g.) which separated was boiled with light petroleum (2 l., b. p. 60—80°) and the portion remaining undissolved was crystallised twice from alcohol, *oximinophenylacetonitrile* α-N-m-*tolyl ether* being obtained in small yellow prisms, m. p. 134° (Found: N, 12·0. $C_{15}H_{12}ON_2$ requires N, 11·9%).

The β-N-p-*tolyl ether* was obtained as a white crystalline powder, m. p. 126°, by evaporating the petroleum extract and crystallising the residue from alcohol (Found: N, 11·9%).

(c) *With* p-*nitrosotoluene.* The crop (6·3 g.) resulting from the condensation of the nitroso-compound (13·5 g.) and the nitrile (16·1 g.) in aqueous alcohol (500 c.c.) by means of potassium hydroxide (6 g. in 100 c.c. of water) furnished, on crystallisation from alcohol, *oximinophenylacetonitrile* β-N-p-*tolyl ether*, which formed slender cream-coloured needles, m. p. 161°, much less soluble in the usual solvents than the α-isomeride (Found: N, 12·2. $C_{15}H_{12}ON_2$ requires N, 11·9%).

The α-N-p-*tolyl ether* was obtained in bright yellow needles, m. p. 135°, by diluting the original aqueous solution with water and crystallising the resulting solid from alcohol. When slowly heated in a capillary tube, it melted at 123—124°, then solidified at *ca.* 134°, owing to transformation into the β-form, which then melted at 161°.

(d) *With* o-*chloronitrosobenzene.* Aqueous potassium hydroxide (8·5 g. in 200 c.c.) was added slowly to the nitrile (22·5 g.) and the nitroso-compound (22·5 g.), dissolved in acetone (600 c.c.) and water (100 c.c.). The first crop (12·5 g.) consisted mainly of *oximinophenylacetonitrile* α-N-o-*chlorophenyl ether*, which, after two crystallisations from alcohol, formed stout cream prisms, m. p. 143° (Found: N, 11·0. $C_{14}H_9ON_2Cl$ requires N, 10·9%). Dilution of the acetone filtrate furnished a solid, from which the β-N-o-*chlorophenyl ether* was obtained in deep yellow needles, m. p. 100°, by repeated crystallisation from light petroleum (b. p. 60—80°) (Found: N, 11·0%).

(e) *With* m-*chloronitrosobenzene.* The same relative proportions were employed as in the preceding condensation: crystallisation (twice) of the first crop from alcohol gave *oximinophenylacetonitrile* β-N-m-*chlorophenyl ether* as a white crystalline powder, m. p. 156° (Found: N, 11·1. $C_{14}H_9ON_2Cl$ requires N, 10·9%). The α-N-m-*chlorophenyl ether* was obtained in small yellow prisms, m. p. 125°, by the addition of water to the acetone filtrate and crystallisation of the resulting solid from benzene–light petroleum (Found: N, 10·8%).

(f) *With* p-*chloronitrosobenzene.* The chloronitrile (29·6 g.) and the nitroso-compound (27·7 g.), dissolved in acetone (1 l.) and water (400 c.c.), were condensed in the usual manner by the addition of aqueous potassium hydroxide (12 g. in 200 c.c.). The crop (12·5 g.) which separated was crystallised from alcohol and furnished *oximinophenylacetonitrile* β-N-p-*chlorophenyl ether* in lustrous, colourless needles, m. p. 142° (Found: N, 11·2. $C_{14}H_9ON_2Cl$ requires N, 10·9%). The α-N-p-*chlorophenyl ether* was isolated from the acetone filtrate and obtained in a pure condition after several crystallisations from benzene–light petroleum and finally from methyl alcohol (Found : N, 10·7%). It formed slender yellow needles, m. p. 132°, but when slowly heated in a capillary tube it melted at 114—116° and then resolidified at *ca.* 123° owing to conversion into the β-form.

Determination of Dipole Moments.—The dielectric constants of benzene solutions of the *N*-oximino-ethers were determined at 25° by a resonance method, the apparatus described by Sugden (J., 1933, 768) being used. The results are in Table II, where *w* represents the weight

TABLE II.

N-*Ethers of Oximinophenylacetonitrile.*

α-*N*-*o*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·8143	0·8743	2·435	0·3700	915
1·5776	0·8763	2·585	0·3949	877
2·3828	0·8783	2·749	0·4196	854

$P_{2\infty}$ = 938 c.c.; P_E = 75·9 c.c.;
$P_{2\infty} - P_E$ = 862 c.c.; μ = 6·42.

α-*N*-*m*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·9641	0·8748	2·482	0·3781	981
1·7132	0·8765	2·640	0·4034	936
3·0577	0·8795	2·917	0·4440	868
4·4421	0·8827	3·222	0·4821	828

$P_{2\infty}$ = 1050 c.c.; P_E = 76·6 c.c.;
$P_{2\infty} - P_E$ = 973 c.c.; μ = 6·83.

α-*N*-*p*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·4349	0·8730	2·368	0·3588	1036
1·0544	0·8747	2·505	0·3818	989
1·5326	0·8756	2·607	0·3988	960
2·1045	0·8772	2·730	0·4170	931

$P_{2\infty}$ = 1055 c.c.; P_E = 76·3 c.c.
$P_{2\infty} - P_E$ = 979 c.c.; μ = 6·84.

α-*N*-*o*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·9731	0·8753	2·482	0·3778	1047
1·9728	0·8782	2·698	0·4118	1002
3·8874	0·8839	3·108	0·4669	916

$P_{2\infty}$ = 1082 c.c.; P_E = 76·5 c.c.;
$P_{2\infty} - P_E$ = 1006 c.c.; μ = 6·93.

α-*N*-*m*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·5809	0·8727	2·368	0·3589	861
1·5108	0·8766	2·517	0·3832	798
2·2914	0·8793	2·641	0·4023	769

$P_{2\infty}$ = 886 c.c.; P_E = 76·9 c.c.;
$P_{2\infty} - P_E$ = 809 c.c.; μ = 6·22.

α-*N*-*p*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·6570	0·8739	2·360	0·3570	700
1·0481	0·8751	2·410	0·3654	679
1·9795	0·8780	2·528	0·3843	646

$P_{2\infty}$ = 722 c.c.; P_E = 75·9 c.c.;
$P_{2\infty} - P_E$ = 646 c.c.; μ = 5·57.

β-*N*-*o*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8730	2·272	0·3411	—
1·2854	0·8756	2·282	0·3419	95·5
1·7064	0·8769	2·285	0·3420	93·9
3·3414	0·8804	2·296	0·3427	91·6

$P_{2\infty}$ = 97·2 c.c.; P_E = 75·3 c.c.;
$P_{2\infty} - P_E$ = 21·9 c.c.; μ = 0·96.

β-*N*-*m*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
2·2120	0·8775	2·292	0·3429	101·1
4·1485	0·8820	2·308	0·3444	97·6
7·1123	0·8888	2·330	0·3457	94·8

$P_{2\infty}$ = 103·0 c.c.; P_E = 75·8 c.c.;
$P_{2\infty} - P_E$ = 27·2 c.c.; μ = 1·06.

β-*N*-*p*-Tolyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
2·2120	0·8761	2·288	0·3430	103·8
4·1485	0·8774	2·294	0·3437	103·4
7·1123	0·8775	2·293	0·3433	104·5

$P_{2\infty}$ = 103·8 c.c.; P_E = 77·1 c.c.;
$P_{2\infty} - P_E$ = 26·7 c.c.; μ = 1·05.

β-*N*-*o*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
2·2662	0·8790	2·297	0·3436	112·7
4·1665	0·8844	2·319	0·3454	112·5
6·0808	0·8899	2·342	0·3474	113·0

$P_{2\infty}$ = 112·7 c.c.; P_E = 77·8 c.c.;
$P_{2\infty} - P_E$ = 34·9 c.c.; μ = 1·22.

β-*N*-*m*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8730	2·272	0·3411	—
1·5794	0·8775	2·298	0·3442	138·6
1·6168	0·8776	2·299	0·3444	139·8
3·2033	0·8822	2·324	0·3470	135·1
3·5181	0·8828	2·324	0·3475	134·3

$P_{2\infty}$ = 143·4 c.c.; P_E = 74·1 c.c.;
$P_{2\infty} - P_E$ = 69·3 c.c.; μ = 1·78.

β-*N*-*p*-Chlorophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8730	2·272	0·3411	—
1·7799	0·8782	2·299	0·3441	130·4
3·2771	0·8827	2·322	0·3464	129·2
4·4274	0·8861	2·340	0·3484	129·8

$P_{2\infty}$ = 129·8 c.c.; P_E = 77·3 c.c.;
$P_{2\infty} - P_E$ = 52·5 c.c.; μ = 1·53.

β-*N*-*p*-Dimethylaminophenyl ether.

100*w*.	$d_{4^\circ}^{25^\circ}$.	ϵ_{25°.	p_{12}.	P_2.
0·0000	0·8726	2·272	0·3412	—
0·5082	0·8741	2·294	0·3447	269·7
1·1256	0·8756	2·321	0·3491	267·2

$P_{2\infty}$ = 271·7 c.c.; P_E (calc.) = 87·6 c.c.; $P_{2\infty} - P_E$ = 184·1 c.c.; μ = 2·94.

fraction of the solute, $d_{4°}^{25°}$ the density of the solution, $\epsilon_{25°}$ its dielectric constant, p_{12} its specific polarisation, and P_2 the total polarisation of the solute. In calculating the dipole moments, it has been assumed that the atom polarisation is 5% of P_E (cf. Sugden, *Trans. Faraday Soc.*, 1934, **30**, 734) when P_E is calculated from the refractive index of the Na-D line.

The value for P_E of the β-*N*-*p*-dimethylaminophenyl ether was calculated from that of the β-*N*-phenyl ether and the usual refractive constants for the Na-D line. The other values for P_E given in Table II were determined from the refractive indices, $n_D^{t°}$, of benzene solutions at the ordinary temperature. In Table III the densities of the solutions and of the benzene used are given in columns 5 and 6 respectively; the temperature at which the observations were made is recorded in column 3.

TABLE III.

N-Ether.	100w.	t.	$n_D^{t°}$.	$d_{4°}^{t°}$.	$d_{4°}^{t°}$.
α-*o*-Tolyl	2·285	16·5°	1·5085	0·8843	0·8791
β-*o*- ,,	9·728	16·5	1·5166	0·8984	0·8791
α-*m*-Tolyl	6·812	22·0	1·5117	0·8897	0·8736
β-*m*- ,,	7·867	22·0	1·5121	0·8918	0·8736
α-*p*-Tolyl	5·320	19·1	1·5103	0·8894	0·8764
β-*p*- ,,	1·992	19·1	1·5066	0·8813	0·8764
α-*o*-Chlorophenyl	4·490	19·9	1·5090	0·8908	0·8758
β-*o*- ,,	9·620	19·9	1·5146	0·9039	0·8758
α-*m*-Chlorophenyl	4·051	21·7	1·5076	0·8862	0·8739
β-*m*- ,,	2·407	21·7	1·5049	0·8812	0·8739
α-*p*-Chlorophenyl	9·191	22·0	1·5139	0·9010	0·8736
β-*p*- ,,	6·837	22·0	1·5116	0·8940	0·8736

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