CLXXXIII.—*Aromatic Amides and Imides of Camphoric Acid.*

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THE derivatives of camphoric acid described in this communication were prepared with the object of obtaining an amino-compound, which, while displaying the stability and reactivity of an aromatic amine, should at the same time exhibit the optical properties usually associated with the presence of a camphor nucleus. It was thought that such a compound might prove useful in the study of certain racemic aldehydes, the resolution of which the author desires to effect.

Since camphorylphenylhydrazide, an optically active and readily accessible substance, might be supposed to yield nitro-derivatives, and consequently aromatic amines, the action of nitric acid on this compound was first studied. It was found that the products of nitration were more complex than was at first supposed, the action of nitric

acid (sp. gr. 1.42) leading to the formation of a mixture of substances from which a new nitroamine, *N-nitrocampophorylphenylhydrazide*,

was isolated. It was incidentally discovered that the substance obtained by the action of nitrous acid on campophorylphenylhydrazide is *N-nitrosocampophorylphenylhydrazide*, and not a nitro-compound as stated by E. M. Chaplin (*Ber.*, 1892, 25, 2565). Similar pairs of *N*-nitro- and *N*-nitroso-compounds have been obtained from two new bromo-derivatives of campophorylphenylhydrazide.

The *N*-nitro-compounds appear to exhibit the property, characteristic of nitroamines in the aromatic series, of passing readily into isomeric *C*-nitro-compounds. Thus, when boiled with solvents or simply heated to fusion, the nitro-group migrates from the aminic group to one of the carbon atoms in the benzene nucleus :

A mixture of isomeric *C*-nitro-compounds is probably produced, and it is intended to continue the study of this transformation.

The nitroso-derivatives in this series are very pale yellow, the corresponding *N*-nitro-derivatives are colourless, whilst the *C*-nitro-compounds have a yellow colour. The nitroso-compounds become colourless when cooled to the temperature of liquid air.

The complexity of this nitration has up to the present precluded the possibility of obtaining an aromatic amino-derivative of campophorylphenylhydrazide in a state of purity. It has been found, however, that, by condensing together camphoric anhydride and *p*-bromoaniline, an anilide is obtained ; this, on nitration and subsequent reduction, yields a well-defined amino-compound which, in alcoholic solution, shows $[\alpha]_D$ 40.7°. The behaviour of this base towards aldehydes will be described in a further communication.

Attempts to prepare 4-amino- and 3-amino-phenyl- α -camphoramic acids through the condensation of camphoric anhydride with the *p*- and *m*-nitroanilines respectively were unsuccessful, owing to the difficulty with which these substances react. The 4-amino-compound was, however, ultimately obtained by the reduction of 4-*benzeneazo*-phenyl- α -camphoramic acid, $\text{CO}_2\text{H} \cdot \text{C}_8\text{H}_{14} \cdot \text{CO} \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_5$, a substance which is interesting as being one of the few recorded instances of optically active aromatic azo-compounds.

EXPERIMENTAL.

N-Nitrosocamphorylphenylhydrazide, $C_8H_{14} \begin{smallmatrix} \diagup CO \diagdown \\ \diagdown CO \diagup \end{smallmatrix} N \cdot N(NO) \cdot C_6H_5$.

This substance is most conveniently prepared by treating camphorylphenylhydrazide dissolved in glacial acetic acid with the requisite quantity of sodium nitrite in 20 per cent. aqueous solution. The compound is precipitated by the addition of water and recrystallised from alcohol, from which it separates in yellow needles melting without decomposition at 157° . Repeated crystallisation from various solvents failed to remove the colour of the substance. A specimen prepared by Chaplin's method was found to melt at 157° , and not to depress the melting point of the preceding preparation :

0.1179 gave 0.2722 CO_2 and 0.0663 H_2O . $C = 62.97$; $H = 6.25$.

0.1014 „ 0.2369 CO_2 and 0.0531 H_2O . $C = 63.69$; $H = 5.82$.

0.2318 „ 27.6 c.c. nitrogen at 15° and 755 mm. $N = 13.85$.

$C_{16}H_{19}O_3N_3$ requires $C = 63.79$; $H = 6.31$; $N = 13.95$ per cent.

0.4330 in 25 c.c. of chloroform in a 2-dcm. tube gave α_D 0.49° , whence $[\alpha]_D$ 14.1° .

This nitroso-compound gives the Liebermann reaction with intense colorations in all its phases. Reduction with aluminium amalgam in moist ethereal solution leads to the formation of camphorylphenylhydrazide and ammonia.

N-Nitrocamphorylphenylhydrazide, $C_8H_{14} \begin{smallmatrix} \diagup CO \diagdown \\ \diagdown CO \diagup \end{smallmatrix} N \cdot N(NO_2) \cdot C_6H_5$.

This was prepared by dissolving 10 grams of camphorylphenylhydrazide in 20 c.c. of glacial acetic acid and 10 c.c. of acetic anhydride. The solution was cooled in ice and treated with a mixture of 2 c.c. of nitric acid (sp. gr. 1.5) and 2 c.c. of acetic anhydride. After thirty minutes, the nitro-compound was precipitated by the cautious addition of water. By recrystallisation from carbon disulphide or chloroform, in which the compound is very soluble, it was obtained in large, colourless prisms melting at $115-116^\circ$ to a deep red liquid. The compound is soluble in alcohol or in glacial acetic acid, but if boiled with these solvents decomposition takes place :

0.0888 gave 0.1978 CO_2 and 0.0463 H_2O . $C = 60.75$; $H = 5.80$.

$C_{16}H_{19}O_4N_3$ requires $C = 60.56$; $H = 5.99$ per cent.

0.3594 in 20 c.c. of chloroform in a 2-dcm. tube gave α_D 0.58° , whence $[\alpha]_D$ 16.1° .

The fact that camphorylphenylhydrazide and ammonia are produced when this compound is reduced indicates that the nitro-group is not attached to one of the carbon atoms in the benzene nucleus.

Camphoryl-4-bromophenylhydrazide, $C_8H_{14} \begin{smallmatrix} \diagup CO \\ \diagdown CO \end{smallmatrix} N \cdot NH \cdot C_6H_4Br$.

This derivative was obtained, in the first instance, by treating camphorylphenylhydrazide (1 mol.) in glacial acetic acid solution with bromine (1 mol.). The product did not attain a constant melting point until it had been crystallised four times from glacial acetic acid and five times from alcohol, when it was obtained in colourless, lath-like crystals melting at 182—183°. It would appear that a small quantity of an isomeride is produced in this bromination, probably 2-bromocamphorylphenylhydrazide :

0.2492 gave 17 c.c. of nitrogen at 20° and 762 mm. $N = 7.83$.

0.2468 „ 0.1300 AgBr. $Br = 22.42$.

$C_{16}H_{19}O_2N_2Br$ requires $N = 7.98$; $Br = 22.79$ per cent.

0.2454 in 20 c.c. of absolute alcohol in a 2-dcm. tube gave α_D 0.66°, whence $[\alpha]_D$ 26.9°.

When boiled for some hours with 10 per cent. aqueous potassium hydroxide, potassium camphorate, phenol, bromobenzene, and ammonia are produced.

The orientation of the bromine atom was accomplished by condensing camphoric anhydride with *p*-bromophenylhydrazine. When these were heated together in molecular proportions at 130—150°, a vigorous action ensued. The brown, glassy mass obtained on cooling was recrystallised from alcohol, when colourless needles, melting at 182—183°, were obtained which were identical with the product of the foregoing bromination, inasmuch as they did not depress the melting point of the first preparation.

N-Nitrosocamphoryl-4-bromophenylhydrazide,

separated as a crystalline precipitate when sodium nitrite in aqueous solution was added to a glacial acetic acid solution of camphoryl-4-bromophenylhydrazide. When recrystallised successively from alcohol and carbon disulphide, it formed fine, pale yellow needles melting without decomposition at 154—155°:

0.1135 gave 0.2100 CO_2 and 0.0506 H_2O . $C = 50.46$; $H = 4.95$.

0.2110 „ 20.7 c.c. of nitrogen at 16° and 756 mm. $N = 11.36$.

$C_{16}H_{18}O_3N_3Br$ requires $C = 50.53$; $H = 4.71$; $N = 11.05$ per cent.

0.3868 in 20 c.c. of chloroform in a 2-dcm. tube gave α_D 0.70°, whence $[\alpha]_D$ 18.1°.

N-Nitrocamphoryl-4-bromophenylhydrazide,

was formed when a mixture of acetic anhydride and nitric acid (sp. gr. 1.5) was slowly added to a solution of camphoryl-4-bromophenylhydrazide in glacial acetic acid. The white, crystalline precipitate was washed successively with glacial acetic acid, acetone, and ether; it was thus obtained in the pure state and quite colourless. It is only sparingly soluble in the usual organic solvents:

0.1069 gave 0.1923 CO₂ and 0.0462 H₂O. C = 49.05; H = 4.80.

0.2283 „ 21.0 c.c. of nitrogen at 16° and 755 mm. N = 10.65.

C₁₆H₁₈O₄N₃Br requires C = 48.48; H = 4.55; N = 10.60 per cent.

0.3432 in 20 c.c. of chloroform in a 2-dcm. tube gave α_D 0.48°, whence [α]_D 14.0°.

When slowly heated, this compound becomes yellow at about 130°, and on further heating melts very indefinitely. If, however, the substance contained in a capillary tube is placed in a bath at 155°, it melts sharply to a dark red liquid at 159–160°. The original nitro-derivative is only sparingly soluble in alcoholic potash, giving a colourless solution; after fusion, however, the product is freely soluble in this reagent, the solution being blood-red at first, but becoming purple when diluted with water and allowed to remain for several hours. When the *N*-nitro-compound is boiled for a few minutes with glacial acetic acid, it passes into solution, the liquid gradually becoming yellow. The addition of water occasions the formation of a yellow precipitate, from which, however, no definite crystallisable substance has yet been isolated. Like the product of fusion, this precipitate is readily soluble in alcoholic potash to a deep red solution; unlike the original *N*-nitro-compound, it is freely soluble in the usual organic solvents. These facts are explicable on the supposition that through the action of heat the nitro-group has wandered from the amino-group to the benzene nucleus, where its proximity to the aminic hydrogen atom has conferred sufficient acidity on the compound to enable it to form soluble salts when treated with potassium or sodium hydroxide. This is confirmed by the behaviour of the yellow substance on reduction, when an almost colourless basic product is obtained. This can be diazotised; the diazo-solution gives a red coloration when added to alkaline β-naphthol, thus indicating the formation of an azo-compound.

The *N*-nitro-derivative on reduction yields camphoryl-4-bromophenylhydrazide and ammonia.

Camphoryldibromophenylhydrazide, C₈H₁₄ < $\begin{smallmatrix} \text{CO} \\ \text{CO} \end{smallmatrix}$ > N·NH·C₆H₃Br₂.—

Camphorylphenylhydrazide (1 mol.) was dissolved in glacial acetic acid and treated with bromine (2 mols.). After twelve hours, the greater part of the dibromo-derivative had separated in glistening

needles. When recrystallised from glacial acetic acid, it melted at 198—199° :

0·3229 gave 18·1 c.c. of nitrogen at 17° and 765 mm. $N = 6·47$.

0·2649 „ 0·2299 AgBr. $Br = 36·93$.

$C_{16}H_{18}O_2N_2Br_2$ requires $N = 6·51$; $Br = 37·21$ per cent.

N-Nitrosocamphoryldibromophenylhydrazide,

separated from hot alcohol in small, heavy, pale yellow, rhombic prisms melting at 147—148° :

0·2502 gave 19·8 c.c. of nitrogen at 15° and 755 mm. $N = 9·20$.

0·2287 „ 0·1870 AgBr. $Br = 34·79$.

$C_{16}H_{17}O_3N_3Br_2$ requires $N = 9·15$; $Br = 34·85$ per cent.

0·2776 in 15 c.c. of chloroform in a 2-dcm. tube gave $\alpha_D 0·70^\circ$, whence $[\alpha]_D 19·0^\circ$.

N-Nitrocamphoryldibromophenylhydrazide,

prepared in a similar manner to the corresponding monobromo-derivative, crystallised from a mixture of acetone and alcohol in glistening, colourless, rhombic prisms melting at 140—142° with decomposition :

0·2333 gave 0·1834 AgBr. $Br = 33·46$.

$C_{16}H_{17}O_4N_3Br_2$ requires $Br = 33·68$ per cent.

0·3142 in 15 c.c. of chloroform in a 2-dcm. tube gave $\alpha_D 0·46^\circ$, whence $[\alpha]_D 10·9^\circ$.

Derivatives of α -Camphoramic Acid.

4-Bromophenyl- α -camphoramic acid, $CO_2H \cdot C_8H_{14} \cdot CO \cdot NH \cdot C_6H_4Br$.

When camphoric anhydride and *p*-bromoaniline are heated together in molecular proportions at 120°, combination takes place with considerable evolution of heat. The molten material rapidly sets to a brittle, crystalline mass, which, when crystallised two or three times from dilute alcohol, forms thin, brilliant prisms melting at 206—207°

0·1534 gave 0·0811 AgBr. $Br = 22·51$.

$C_{16}H_{20}O_3NBr$ requires $Br = 22·60$ per cent.

0·6912 in 25 c.c. of absolute alcohol in a 2-dcm. tube gave $\alpha_D 2·60^\circ$, whence $[\alpha]_D 47·0^\circ$.

This acid is freely soluble in acetone or alcohol, sparingly so in benzene, and insoluble in water or light petroleum. It is readily soluble in aqueous solutions of alkalis or alkali carbonates.

The *sodium* salt was obtained as a bulky, gelatinous mass, possessing an extremely nauseous taste.

The *silver* salt is sparingly soluble in hot water, from which, on cooling, it separates in minute leaflets.

4-Bromo-3-nitrophenyl- α -camphoramic acid,

To a mixture of 30 c.c. of nitric acid (sp. gr. 1.5) and 24 c.c. of glacial acetic acid are added, in small portions at a time, 10 grams of 4-bromophenyl- α -camphoramic acid. After thirty minutes, the clear solution is poured on to ice, when the nitro-compound separates as a yellow precipitate. After recrystallisation from alcohol, in which it is only moderately soluble, it is obtained in bright yellow, hexagonal plates melting at 204—206°:

0.1900 gave 0.0900 AgBr. Br = 20.16.

$\text{C}_{16}\text{H}_{19}\text{O}_5\text{N}_2\text{Br}$ requires Br = 20.05 per cent.

0.2996 in 20 c.c. of absolute alcohol in a 2-dcm. tube gave $\alpha_D - 1.45^\circ$, whence $[\alpha]_D - 48.4^\circ$.

The *sodium* salt of this acid forms yellow leaflets readily soluble in water. When boiled with sodium hydroxide, it is hydrolysed with formation of sodium camphorate and 4-bromo-3-nitroaniline. The latter substance after recrystallisation was found to melt at 112° (Hübner gives 111°).

4-Bromo-3-aminophenyl- α -camphoramic acid,

is most conveniently prepared by dissolving 1 part of the foregoing nitro-acid in excess of aqueous ammonia and adding 4 parts of ferrous sulphate dissolved in water in small portions at a time. When the ferrous hydroxide at first precipitated has completely changed into ferric hydroxide, the mixture is heated on the water-bath for a short time with frequent stirring and then filtered by the aid of the pump. On neutralising the filtrate with acetic acid, the amino-compound separates as a bulky, white precipitate. The yield approximates to 75 per cent. of the theoretical. By recrystallisation from dilute alcohol, the substance is obtained in stellate clusters of colourless needles melting at 207—208°:

0.2194 gave 14.4 c.c. of nitrogen at 20° and 758 mm. N = 7.49.

0.2824 „ 0.1414 AgBr. Br = 21.31.

$\text{C}_{16}\text{H}_{21}\text{O}_3\text{N}_2\text{Br}$ requires N = 7.59; Br = 21.68 per cent.

0.4878 in 25 c.c. of absolute alcohol in a 2-dcm. tube gave $\alpha_D 1.59^\circ$, whence $[\alpha]_D 40.7^\circ$.

This amino-acid is readily soluble in aqueous alkalis and alkali carbonates, but less so in concentrated hydrochloric acid. The

hydrochloride is obtained as a white, amorphous precipitate by passing hydrogen chloride into a solution of the base in acetone. When submitted to the action of nitrous acid, the hydrochloride appears to yield a colourless, insoluble diazo-anhydride.

The *acetyl* derivative is freely soluble in aqueous alkalis, and separates from dilute alcohol in iridescent leaflets melting at 217—219°.

4-Benzeneazophenyl- α -camphoramic acid,

This compound results when equimolecular weights of camphoric anhydride and aminoazobenzene are heated together for a short time at 150—180°. It is separated from unchanged material by extraction with aqueous ammonia, reprecipitated from the ammoniacal solution by the addition of acid, and crystallised several times from alcohol. The compound is thus obtained in beautiful orange-red needles melting at 223—224°:

0.2030 gave 20.0 c.c. of nitrogen at 23° and 760 mm. $N = 11.10$.

$\text{C}_{22}\text{H}_{25}\text{O}_3\text{N}_3$ requires $N = 11.08$ per cent.

0.1483 in 25 c.c. of absolute alcohol in a 2-dcm. tube gave α_D 1.04°, whence $[\alpha]_D$ 87.7°.

This compound dissolves in concentrated sulphuric acid to a deep yellow solution. The alkali salts are yellow and soluble in water. The *calcium* salt, however, is excessively insoluble; it is precipitated in fine yellow needles when a few drops of hard water are added to a solution of one of the alkali salts. Reduction of an alcoholic solution of the acid by means of stannous chloride results in the formation of aniline and 4-aminophenyl- α -camphoramic acid

This somewhat unstable substance was obtained as a white or light grey, amorphous powder, readily soluble in alcohol, acetone, or chloroform, and in solutions of sodium hydroxide or sodium carbonate, but insoluble in water or light petroleum. From solutions, however, it separated in a resinous condition, and became solid only when left for several days; it could not be obtained crystalline:

0.2292 gave 20.4 c.c. of nitrogen at 23° and 752 mm. $N = 9.92$.

$\text{C}_{16}\text{H}_{22}\text{O}_3\text{N}_2$ requires $N = 9.66$ per cent.

On attempting to acetylate this base, it underwent decomposition. The *acetyl* derivative, however, was ultimately obtained by heating together camphoric anhydride and 4-aminoacetanilide either alone or with a solvent. From dilute acetic acid, the compound crystallises in glistening leaflets melting at 233—234°. An attempt to prepare the

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foregoing base by the fractional hydrolysis of this acetyl derivative was unsuccessful, only *p*-phenylenediamine and its oxidation products being obtained.

Derivatives of N-Phenylcamphorimide.

The 4-bromo-derivative, $C_8H_{14} \begin{smallmatrix} \diagup CO \\ \diagdown CO \end{smallmatrix} N \cdot C_6H_4Br$, is produced when 4-bromophenyl- α -camphoramidic acid is heated for an hour with glacial acetic acid and acetic anhydride. Unchanged bromo-acid is removed by extraction with aqueous ammonia. The new imide forms prisms, sparingly soluble in hot alcohol and melting at $180-181^\circ$:

0.1939 gave 0.1074 AgBr. Br = 23.57.

$C_{16}H_{18}O_2NBr$ requires Br = 23.80 per cent.

The 4-bromo-3-nitro-derivative, $C_8H_{14} \begin{smallmatrix} \diagup CO \\ \diagdown CO \end{smallmatrix} N \cdot C_6H_3Br \cdot NO_2$, is readily prepared in quantitative yield when the preceding compound is dissolved in cold nitric acid (sp. gr. 1.5). From hot alcohol, it crystallises in clusters of short, pale yellow needles which melt at $171-172^\circ$. When treated with tin and hydrochloric acid in alcoholic solution, reduction to the corresponding amino-compound is effected:

0.1397 gave 8.7 c.c. of nitrogen at 19° and 754 mm. N = 7.10.

$C_{16}H_{17}O_4N_2Br$ requires N = 7.35 per cent.

The 4-bromo-3-amino-derivative, $C_8H_{14} \begin{smallmatrix} \diagup CO \\ \diagdown CO \end{smallmatrix} N \cdot C_6H_3Br \cdot NH_2$, a somewhat ill-defined base, dissolving freely in alcohol, acetone, or chloroform, is deposited on cooling the warm solutions as a colourless oil which on trituration is converted into a white, microcrystalline solid melting at about 130° :

0.1257 gave 8.6 c.c. of nitrogen at 25° and 762 mm. N = 7.66.

$C_{16}H_{19}O_2N_2Br$ requires N = 7.98 per cent.

A solution of this base in acetone is feebly dextrorotatory.

The *hydrochloride* is decomposed by water; on diazotisation, it forms a clear solution which, when added to alkaline β -naphthol, yields a scarlet azo-compound.

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