

## II.—*Cyanocarone.*

By REGINALD WILLIAM LANE CLARKE and ARTHUR LAPWORTH.

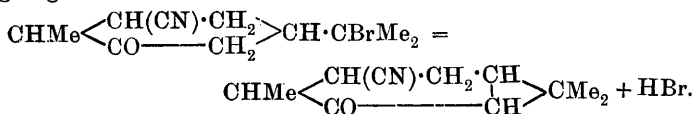
ALTHOUGH carvone and its dihydro-derivative only differ inasmuch as the six-carbon ring in the former contains an ethylenic linking, the products which their hydrobromides yield by loss of hydrogen bromide under the influence of alkalis are quite different in structure, as carone contains a three-carbon and a six-carbon ring, whilst neither nucleus is present in eucarvone, which appears to contain only one seven-membered ring (Wallach, *Annalen*, 1905, **339**, 94, *et seq.*).

The explanation of the formation of eucarvone which most naturally suggests itself is the one indicated by Wallach, namely, that in the first stage of the action of potassium hydroxide on carvone hydrobromide, halogen hydride is removed in the same manner as in the case of dihydrocarvone hydrobromide, but that the molecule of the resulting compound is less stable than that of carone, owing to the additional strain produced by the ethylenic linking, and consequently the *cyclopropane* ring is at once resolved, but between the two carbon atoms which previously formed part of the six-ring of the carvone hydrobromide; hitherto, however, no direct evidence confirming this idea has been forthcoming Had it

been possible to remove two hydrogen atoms from carone, or to separate two groups from adjacent carbon atoms in a substitution product of carone, in such a way as to produce an ethylenic linking at the position where this is found in the hypothetical intermediate compound, it would have been possible to ascertain whether this at once resulted in the formation of eucarvone, and thus to confirm the view referred to, but no substituted derivatives of carone yet appear to have been obtained either by direct substitution or by preparing them from substituted dihydrocarvones.

The investigation of the action of alkalis on cyanodihydrocarvone seemed likely to lead to the formation of such a substituted carvone, and since it has been shown by one of us that  $\beta$ -cyano-derivatives of ketones are frequently convertible into  $\alpha\beta$ -unsaturated ketones by the action of alkalis in presence of ferrous hydroxide, a possible mode of attacking this question was promised.

After many unsuccessful attempts, pure cyanocarone was obtained by a method similar to that used in preparing carone from dihydrocarvone, and under certain conditions it was found that cyanodihydrocarvone hydrobromide might be converted nearly quantitatively into the new substance, only traces of cyanodihydrocarvone being regenerated :

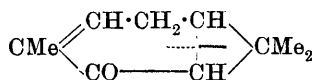


A mixture of isodynamic forms is doubtless produced in the first instance, but in presence of the alkali, which acts as equilibrator, these, during the process of solidification, change with such ease that only one isomeride remains, the equilibrium mixture being saturated with respect to one form.

The product, when nearly pure, crystallises in massive, transparent forms, and has the properties which it might be anticipated a substance having the above constitution would possess. By the action of mineral acids, the *cyclopropane* complex is attacked in all cases before the cyano-group is affected, and with halogen hydrides the first product appears invariably to be the compound of the acid with cyanodihydrocarvone, the reaction above represented taking place in the reverse sense.

The nitrile is saturated in character, and is attacked by cold permanganate solution only with great difficulty, but at the water-bath temperature it is oxidised in alkaline solution, yielding caronic acid, the presence of the dimethyl*cyclopropane* nucleus thus being confirmed. With acid permanganate, another acid, apparently isomeric with caronic acid, but not yet described, is produced.

By the action of alkalis, however, the substance loses the elements of hydrogen cyanide, and if hot dilute aqueous alkali is used in presence of ferrous hydroxide to facilitate this reaction, the volatile product being allowed to pass away at once in the steam, eucarvone is obtained. The product which cyanocarone should normally yield by the action of alkali is the  $\alpha\beta$ -unsaturated ketone:

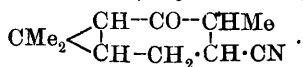


or the hypothetical intermediate product in the preparation of eucarvone from carvone hydrobromide. It follows, therefore, that at  $100^\circ$ , even in presence of quite dilute aqueous alkali, this substance is unstable, and is at once converted into eucarvone. As the cyanocarone certainly contains the *cyclopropane* ring, which is not stable to alkali, it seems certain that the presence of the ethylenic linking in the six-carbon ring to which the *cyclopropane* nucleus is attached does in fact render the molecule unstable, and leads mainly to the opening of the three-carbon ring at the point indicated by the dotted line.

The matter is of further general interest, too, in contrasting the mode in which the *cyclopropane* nucleus breaks down under varying conditions. It would not appear reasonable to suggest that the complex  $\cdot\text{CMe}_2\cdot\text{CH}\cdot$  is less stable than  $\cdot\text{CH}\cdot\text{CH}\cdot$ , as under the influence of halogen hydride it is the former which is resolved. Nor can it be maintained that either is in such a position with reference to the keto- or cyano-group as would render it more liable to attack on this account. It would rather appear that when the carbon ring is saturated there is the less strain when the ring is composed of six atoms, but when there is an ethylenic linking in the nucleus, at least in certain positions, then the reverse obtains, and the smaller ring is the less stable one.

#### EXPERIMENTAL.

##### *Formation of Cyanocarone,*



The hydrobromide of cyanodihydrocarvone, prepared as described by Lapworth (*Trans.*, 1906, **89**, 1826), was rapidly crystallised from alcohol, and treated in the following manner. The hydrobromide (160 grams) was suspended in methyl alcohol (300 c.c.), cooled to  $0^\circ$ , and to the pasty mixture an ice-cold solution of potassium hydroxide (36 grams) in methyl alcohol (150 c.c.) was added gradually with frequent agitation. The resulting liquid

was kept for some hours, while it gradually assumed a violet colour, potassium bromide being deposited. The whole was then saturated with carbon dioxide, and the precipitated potassium bromide and bicarbonate separated by filtration; the methyl alcohol was removed by distillation, and the volatile material expelled with the aid of a rapid current of steam. In some experiments the oil remaining in the distillation flask solidified on cooling, but it was found to be advantageous, as a rule, to shake the semi-solid material for some time with an ice-cold solution of potassium permanganate, added gradually until the colour of the latter was no longer discharged, the excess of permanganate and the precipitated manganese dioxide being subsequently removed by sulphur dioxide. The crude cyanocarone, which solidified on again cooling the liquid, was collected, and crystallised several times from alcohol:

0.2158 gave 0.589 CO<sub>2</sub> and 0.166 H<sub>2</sub>O. C=74.4; H=8.55.

0.2206 „ 0.606 CO<sub>2</sub> „ 0.172 H<sub>2</sub>O. C=74.9; H=8.66.

0.1264 „ 9.0 c.c. N<sub>2</sub> (moist) at 19° and 757 mm. N=8.15.

C<sub>11</sub>H<sub>15</sub>ON requires C=74.6; H=8.47; N=7.92 per cent.

*Cyanocarone* is very soluble in ethyl and methyl alcohols, ether, acetone, benzene, or ethyl bromide, fairly so in light petroleum, and almost insoluble in water. It crystallises with great readiness from its alcoholic solution in large, colourless, six-sided, transparent crystals, which melt sharply at 54–55°. When strongly heated, cyanocarone boils and distils with some decomposition above 300°.

0.201, made up to 25.05 c.c. with absolute alcohol, at 18° gave, in a 2-dcm. tube,  $\alpha_D + 4.79^\circ$ , whence  $[\alpha]_D + 298^\circ$ .

0.2306, made up to 25.1 c.c. with absolute alcohol, at 20° gave, in a 2-dcm. tube,  $\alpha_D + 5.45^\circ$ , whence  $[\alpha]_D + 297^\circ$ .

Cyanocarone is only very slowly attacked by a cold aqueous solution of potassium permanganate, or by a solution of the same salt in acetone at the boiling point of the solvent. It does not decolorise a solution of bromine in glacial acetic acid in presence of sodium acetate.

The *semicarbazide*, C<sub>11</sub>H<sub>15</sub>N:N<sub>2</sub>H·CO·NH<sub>2</sub>, crystallises from alcohol in thin, flat, rectangular plates, which melt rather indefinitely, and decompose slightly at 218–221°:

0.1526 gave 31.6 c.c. N<sub>2</sub> (moist) at 15° and 758 mm. N=24.18.

C<sub>12</sub>H<sub>18</sub>ON<sub>4</sub> requires N=23.93 per cent.

Cyanocarone also yields an oxime, but this could not be obtained in crystalline form.

*Action of Alkali and Ferrous Hydroxide on Cyanocarone.*

On boiling cyanocarone with a 10 per cent. sodium hydroxide solution, an oil with a peppermint-like odour is produced, and the aqueous solution gives the reactions of a cyanide. The removal of hydrogen cyanide appears to take place more readily in presence of ferrous hydroxide, and for the investigation of this decomposition the following conditions were employed. Twenty grams of cyanocarone, 12 grams of potassium hydroxide, 4 grams of ferrous chloride, and 150 c.c. of water were gently heated in a flask attached to a condenser, and the water which distilled over, carrying with it the odorous oil, was replaced by gradually adding water to the flask. The process was continued until the aqueous distillate no longer contained an appreciable quantity of oil. The distillate was then saturated with common salt, and the oil extracted with ether. On fractionation, 4.4 grams of liquid boiling between  $205^{\circ}$  and  $208^{\circ}$ , and 1.1 grams boiling between  $208^{\circ}$  and  $215^{\circ}$  were obtained, a small amount of residue, which underwent decomposition on further heating, remaining in the distilling flask.

The oil thus obtained readily decolorised a solution of bromine, and gave a reddish-violet colour on boiling with methyl-alcoholic potash. It yielded an easily crystallisable semicarbazide, which, on recrystallisation from alcohol, melted at  $183-184^{\circ}$ :

0.1978 gave 35.5 c.c.  $N_2$  (moist) at  $19^{\circ}$  and 751 mm.  $N=20.38$ .

$C_{11}H_{17}ON_3$  requires  $N=20.29$  per cent.

On mixing this semicarbazide with eucarvone semicarbazide, prepared as described by Wallach and Löhr (*Annalen*, 1899, **305**, 237), the mixture melted at  $183-184^{\circ}$ ; the product, after repeated crystallisation from methyl and ethyl alcohols, was optically inactive. The conversion of cyanocarone into eucarvone by the above process is not quantitative, and a considerable amount of a white substance crystallises out of the aqueous residue. This was isolated by diluting the residual liquid in the flask with water, heating to boiling, and filtering, when, on cooling, the substance separated, and was purified by recrystallisation from water, and finally from alcohol:

0.2278 gave 0.5630  $CO_2$  and 0.1786  $H_2O$ .  $C=67.43$ ;  $H=8.72$ .

0.203 „ 13.3 c.c.  $N_2$  (moist) at  $20^{\circ}$  and 756 mm.  $N=7.45$ .

$C_{11}H_{17}O_2N$  requires  $C=67.69$ ;  $H=8.72$ ;  $N=7.18$  per cent.

The substance has the properties of a saturated lactam or anhydramide, it is unaffected by a cold potassium permanganate solution, or by boiling aqueous or alcoholic potassium hydroxide

solutions, and is only slowly changed by fusion with potassium hydroxide and a few drops of water. It crystallises from water or alcohol in square plates or cubes, melting at 210—212°.

*Action of Hydrogen Halides on Cyanocarone.*

When heated with concentrated hydrochloric acid on the water-bath, cyanocarone yielded an acidic substance, which appeared to be a mixture of the stereoisomeric dihydrocarvonecarboxylic acids (Trans., 1906, **89**, 1823); from this after repeated crystallisation from carbon tetrachloride and finally ethyl acetate, an unsaturated acid melting at 141—142° was obtained, which was identified by the mixed melting-point method as  $\beta$ -dihydrocarvonecarboxylic acid. With a cold saturated solution of hydrogen chloride, cyanocarone is first converted into a hydrogen chloride additive product identical with that obtained from cyanodihydrocarvone, the cyclopropane ring undergoing fission. This substance on further treatment with hydrochloric acid loses the elements of hydrogen chloride, and the  $\cdot\text{CN}$  group is converted into the  $\text{CO}\cdot\text{NH}_2$  group, the amide of the unsaturated dihydrocarvonecarboxylic acid being formed. Twenty grams of cyanocarone were suspended in 100 c.c. of concentrated hydrochloric acid, and the mixture was saturated with hydrogen chloride in the cold. The cyanocarone dissolved, and after a short time a white, crystalline substance separated, which was purified by crystallisation from alcohol:

0.3035, after being heated with fuming nitric acid and 0.325 of silver nitrate, required 4.5 c.c. of 0.112*N*-thiocyanate.  
Cl = 16.5.

$\text{C}_{11}\text{H}_{16}\text{ONCl}$  requires Cl = 16.6 per cent.

The substance crystallised from alcohol in flattened, prismatic needles, melting at 69°, and when mixed with cyanodihydrocarvone hydrochloride its melting point was unaltered.

0.402, made up to 25 c.c. with absolute alcohol, at 18°, gave, in a 2-dcm. tube,  $\alpha_D + 0.82^\circ$ , whence  $[\alpha]_D + 25.6^\circ$ . Cyanodihydrocarvone hydrochloride has  $[\alpha]_D + 25.3^\circ$  at 18° (Trans., 1906, **89**, 1826).

When cyanocarone is dissolved in a saturated solution of hydrogen bromide in glacial acetic acid, and kept for some time, a crystalline substance separates, of which a further amount can be obtained by diluting the acetic acid solution with water; this was collected and crystallised from alcohol:

0.2964, after being heated with fuming nitric acid and 0.2478 of silver nitrate, required 2.68 c.c. of 0.112*N*-thiocyanate.  
Br = 30.7.

$\text{C}_{11}\text{H}_{16}\text{ONBr}$  requires Br = 31.0 per cent.

The substance crystallised from alcohol in flattened needles, melting at  $85^{\circ}$ , and on mixing it with cyanodihydrocarvone hydrobromide, its melting point was unaltered:

0.3546, made up to 25.1 c.c. with absolute alcohol, at  $14^{\circ}$ , gave, in a 2-dcm. tube,  $\alpha_D + 0.72^{\circ}$ , whence  $[\alpha]_D + 25.5^{\circ}$ .

0.3208 of cyanodihydrocarvone hydrobromide, made up to 24.9 c.c. with absolute alcohol, at  $14^{\circ}$ , gave, in a 2-dcm. tube,  $\alpha_D + 0.665^{\circ}$ , whence  $[\alpha]_D + 25.8^{\circ}$ .

*Unsaturated Amide.*—When cyanocarone is allowed to remain with saturated aqueous hydrogen chloride for some hours, the hydrochloride at first formed slowly dissolves. When the liquid no longer gave the reactions of a nitrile, it was diluted with twice its volume of water, and rendered alkaline with strong ammonia. After cooling, the separated solid was collected and crystallised several times from water:

0.2055 gave 0.5120  $\text{CO}_2$  and 0.1648  $\text{H}_2\text{O}$ .  $\text{C} = 68.0$ ;  $\text{H} = 8.91$ .

0.2022 „ 12.8 c.c.  $\text{N}_2$  (moist) at  $18^{\circ}$  and 751 mm.  $\text{N} = 7.22$ .

$\text{C}_{11}\text{H}_{17}\text{O}_2\text{N}$  requires  $\text{C} = 67.7$ ;  $\text{H} = 8.72$ ;  $\text{N} = 7.18$  per cent.

0.2335, made up to 25 c.c. with absolute alcohol, at  $18.5^{\circ}$ , gave, in a 2-dcm. tube,  $\alpha_D + 1.33^{\circ}$ , whence  $[\alpha]_D + 71.2^{\circ}$ .

The amide is readily soluble in hot water or benzene, very soluble in alcohol, acetone, chloroform, or ethyl acetate, and sparingly so in cold water or light petroleum. It crystallises from alcohol or water in small, flattened, white needles, melting at  $130^{\circ}$ .

It evolves ammonia when boiled with 10 per cent. aqueous sodium hydroxide, reduces permanganate solution immediately in the cold, and decolorises a solution of bromine in acetic acid in presence of sodium acetate.

When heated on the water-bath with concentrated hydrochloric acid, the amide was converted into an acidic substance, which, on dilution, was precipitated as an oil; this was collected, and finally obtained as a solid, which was recrystallised several times from ethyl acetate. It melted at  $141$ — $142^{\circ}$ , and when mixed with  $\beta$ -dihydrocarvonecarboxylic acid its melting point was unaltered. The amide was therefore in all probability an isomeride of the dihydrocarvonecarboxylic amide previously described (Trans., 1906, 89, 958).

#### *Oxidation of Cyanocarone.*

An aqueous solution of potassium permanganate oxidises cyanocarone fairly rapidly when heated with it on the water-bath. A solution of 140 grams of potassium permanganate in 3500 c.c. of water was added gradually to a mixture of 20 grams of cyanocarone and 200 c.c. of water. The liquid was filtered from the

precipitated manganese dioxide, evaporated to small bulk, saturated with salt, and extracted with ether twice to remove any unchanged cyanocarone or other neutral material. The liquid was then acidified with hydrochloric acid, and extracted twelve times with ether. The extracted material was freed from volatile material in the usual manner, and was finally obtained as a dark semi-solid mass. This was purified by triturating it with chloroform, and crystallising from a relatively small quantity of chloroform, using a Soxhlet extractor, as it is sparingly soluble in this solvent. After a subsequent crystallisation from water, it was dried at  $100^{\circ}$ :

0.2065 gave 0.4012  $\text{CO}_2$  and 0.1168  $\text{H}_2\text{O}$ .  $\text{C}=52.98$ ;  $\text{H}=6.28$ .

$\text{C}_7\text{H}_{10}\text{O}_4$  requires  $\text{C}=53.16$ ;  $\text{H}=6.33$  per cent.

0.1075 required 13.5 c.c. of  $N/10$ -sodium hydroxide at  $-5^{\circ}$  for neutralisation, using phenolphthalein as indicator, whence the equivalent = 79.6. A dibasic acid,  $\text{C}_7\text{H}_{10}\text{O}_4$ , requires equivalent = 79.

The acid crystallised from water in small, white masses, melting at  $173$ – $174^{\circ}$ . The anhydride, prepared from the acid by means of acetyl chloride, was crystallised from light petroleum, and was found to melt at  $55^{\circ}$ .

The properties of the acid prove it to be identical with the *cis*-caronic acid prepared by Baeyer and Ipatieff from carone (*Ber.*, 1896, **29**, 2796), and synthesised by Perkin and Thorpe (*Trans.*, 1899, **75**, 48).

The first experiment on the oxidation of cyanocarone was carried out with an aqueous solution of potassium permanganate containing rather more sulphuric acid than that required to combine with the potassium hydroxide which is formed during the oxidation. In this instance, an acid similar in solubility to caronic acid was isolated, which melted, however, at  $204^{\circ}$ . On titration with sodium hydroxide solution, 0.104 required 6.15 c.c. of 0.1075  $N$ -alkali for neutralisation, using phenolphthalein as indicator, whence equivalent = 157.3. On adding a further 7 c.c. of the alkali and heating for one hour on the water-bath, the excess of alkali required 0.9 c.c. of 0.1003  $N$ -hydrochloric acid for neutralisation, whence the equivalent calculated from the total amount of alkali neutralised = 79.

The data indicate that the substance is the lactone of a saturated hydroxydicarboxylic acid, and probably isomeric with terebic acid.

GOLDSMITHS' COLLEGE, NEW CROSS.

THE UNIVERSITY,  
MANCHESTER.