

XCVI.—*Reactions involving the Addition of Hydrogen Cyanide to Carbon Compounds.*

By ARTHUR LAPWORTH.

It is probably a general experience that in preparing cyanohydrins by the addition of the elements of hydrogen cyanide to ketones and aldehydes, the speed of the reaction and the yield of cyanohydrin obtained may vary in an extraordinary manner, even when the experimental conditions are apparently constant. Hitherto, no systematic attempts seem to have been made to discover the cause of the variation, but amongst the records as to the effects of impurities or of slight alterations of the method adopted, the following points appear very significant.

In preparing the cyanohydrins of the aldoses and ketoses, Kiliani found that the addition of a drop of ammonia to the anhydrous hydrogen cyanide was of great assistance (*Ber.*, 1888, 21, 916; and 1889, 22, 370). This effect, however, might have been the result of the usual influence of alkalis in accelerating desmotropic change, and in this case, possibly, the base assisted in the necessary initial formation of the carbonyl modification of the sugar (compare Lowry, *Trans.*, 1899, 75, 214).

Again, it is frequently noticed that hydrogen cyanide is more reactive when it is being produced in presence of the unsaturated compound, and the statement is occasionally made to the effect that only by the use of this process can the addition products be obtained (compare Bredt and Kallen, *Annalen*, 1896, 293, 340). The use of the term "nascent" as applied to such a case, namely, where an electrolyte is being formed by an ordinary double decomposition, is open to serious objection, and, from the standpoint of the electrolytic dissociation hypothesis, is meaningless, for, when once formed in this way, the substance is still nascent in precisely the same sense, that is to say, is being continuously regenerated from its ions.

The whole question being in this unsatisfactory condition, it seemed very desirable that the matter should be more closely examined, attention being particularly directed to the effect produced by small quantities of agents which might not improbably influence the speed of the reactions. There are many difficulties in the way of devising any fairly precise method for the quantitative measurement of the quantities of ketone and aldehyde cyanohydrins formed within definite periods of time, for, owing to the fact that these compounds are undoubtedly dissociated to some extent in solution, any attempt to separate completely the free hydrocyanic acid might lead to the

destruction of a part of the cyanohydrin itself, and the use of silver nitrate or of alkalis is consequently altogether excluded.

It was therefore decided to resort to a method of investigation in which the speed of reaction could be roughly gauged by means of a colour change, and for this purpose, advantage was taken of the fact that camphorquinone has a bright yellow colour, which is perceptible even in very dilute solutions, whilst its cyanohydrin is almost, if not quite, colourless. The use of this substance appeared particularly likely to lead to definite results, as in the original experiments in which the cyanohydrin was prepared in quantity (Trans., 1901, 79, 382) the time of reaction and the yields obtained had been found to vary in an inexplicable manner.

It was anticipated that small quantities of acids, bases, cyanides, and other electrolytes would be likely to produce some noteworthy influence on the velocity of reaction, and the effect of these in particular was investigated, although other possibilities were also tested.

*The Effect of Catalytic Agents on the Velocity of Formation of Camphorquinone Cyanohydrin.*

The quinone was generally used in dilute alcoholic or aqueous solution; excess of freshly distilled hydrocyanic acid was added, and portions of the resulting yellow solution were then transferred to well-stoppered glass vessels; into these were then introduced varying quantities of the agent the effect of which it was desired to ascertain, a record of the time taken for the disappearance of the visible yellow colour being made in each case. With the dilutions usually employed, the colour of the solutions in the absence of foreign substances disappeared in about 8—10 hours.

Mineral acids in small quantities were found to prolong the time occupied to a very marked extent, and with one drop of ordinary hydrochloric acid in 10 c.c. of the solution no noticeable diminution in colour had taken place at the end of 14 days. Small quantities of acetic acid and other weak acids produced a less marked retardation. With large quantities of mineral acids, also, a very great retardation was observed, and no evidence could be obtained after 3 weeks that any cyanohydrin had been formed; this result did not necessarily follow from the similar effect of smaller quantities.

Small quantities of bases, on the other hand, produced a very great acceleration, and one drop of 15 per cent. aqueous potassium hydroxide in 100 c.c. of the yellow solution caused a disappearance of the colour within the space of a few seconds; with a corresponding quantity of ammonia, a less marked effect was noticed, but even here the duration of the action was measured in minutes instead of in hours; the same

remark applies to organic bases like the fatty amines, whether primary, secondary, or tertiary; with the weaker organic bases, such as pyridine, the results again were quite appreciable when comparatively large quantities were used, and they were of the same nature.

With small quantities of neutral salts, such as sodium nitrate or chloride, the effects were very doubtful, but sodium sulphate in large quantity appeared to cause a slight acceleration. With the sodium or potassium salts of weak acids, on the other hand, a marked acceleration was noticed, and substances like borax or sodium phosphate behaved in much the same way as alkalis.

Potassium cyanide produces a great acceleration, but this in itself might be attributed to the effect of the alkaline nature of its solutions. If, however, a solution of camphorquinone cyanohydrin at  $60^{\circ}$  is rendered alkaline by the addition of potassium hydroxide until a faint yellow colour appears, indicating that the cyanohydrin is partially decomposed, and a little powdered potassium cyanide is then introduced, the solution again becomes colourless. Thus, whilst a large concentration of alkali causes the reversal of the reaction, with potassium cyanide this is not the case.

The conclusion to be drawn from the experiments seemed obvious; basic substances act in virtue of the fact that they diminish the concentration of the hydrogen ions, which themselves retard the change. When small quantities of bases or potassium cyanide are present, the concentration of the cyanogen ions must increase, whereas it diminishes in presence of hydrogen ions. It was probable, therefore, that the reaction velocity depended mainly on the concentration of the cyanogen ions, and all subsequent experiments have only served to confirm this view.

The value of the so-called "nascent" as compared with "free" hydrogen cyanide is thus clearly understood; in the latter instance, until the theoretical quantity of strong acid has been added, potassium cyanide is present, and the effect of this would be most marked in cases where the salt is entirely dissolved in the solution containing the unsaturated substance. Doubtless, too, the varying yields obtained in many cases depend on the precise amount of acid introduced; if a little less than the amount required to entirely decompose the cyanide is used, the reaction will continue rapidly; if more, then the velocity will be greatly diminished.

Experiments on other substances have been made in order to test more closely the validity of the above view. The following examples will serve to show that the principle is a fairly general one.

*Condensation of Benzylidenebenzyl Cyanide with Hydrogen Cyanide.*

With the object of preparing considerable quantities of symmetrical diphenylsuccinonitrile, the author, in conjunction with Mr. A. W. Harvey, made a considerable number of attempts to bring about the condensation of hydrogen cyanide with benzylidenebenzyl cyanide in the manner represented by the equation  $\text{CHPh}\cdot\text{CPh}\cdot\text{CN} + \text{HCN} = \text{CHPh}(\text{CN})\cdot\text{CHPh}\cdot\text{CN}$ .

The experiments were performed under a great variety of conditions and at varying temperatures, but without success, and the work was temporarily abandoned. With the knowledge gained in the above investigation of the camphorquinone condensation, the attempt was repeated in the following manner.

Five grams of benzylidenebenzyl cyanide were dissolved in 100 c.c. of alcohol containing 1 molecular proportion of dilute hydrocyanic acid, and the whole heated in a stoppered bottle at  $100^\circ$ ; at the end of 2 hours there was no evidence that any reaction had occurred. A solution of 4 grams of potassium cyanide in 15 c.c. of water was then added, and the heating recommenced; in 5 minutes, rapid separation of a crystalline material commenced, and at the end of half an hour the bottle was cooled, and the solid material collected, washed with alcohol, and finally with ether, which readily dissolves the unaltered benzylidene compound. The crude product presented the appearance of a colourless, crystalline powder, and when dry weighed 2.5 grams; it was found to be a mixture of the  $\alpha$ - and  $\beta$ -diphenylsuccinonitriles, which was analysed without further purification:

0.3021 gave 0.9183  $\text{CO}_2$  and 0.1481  $\text{H}_2\text{O}$ . C = 82.6; H = 5.4.

$\text{C}_{16}\text{H}_{12}\text{N}_2$  requires C = 82.8; H = 5.2 per cent.

$\text{C}_{15}\text{H}_{11}\text{N}$  „ C = 87.8; H = 5.4 „

It is interesting to notice that the same mixture of diphenylsuccinonitriles was made by Challanay and Knoevenagel (*Ber.*, 1892, 25, 289) by warming mandelonitrile with benzyl cyanide and potassium cyanide on the water-bath. Doubtless, this process takes place in the following stages: (1) the reversible decomposition of the mandelic nitrile into benzaldehyde and hydrocyanic acid, (2) the condensation of the benzaldehyde and the benzyl cyanide in the alkaline solution to form benzylidenebenzyl cyanide, (3) the condensation of the latter with the hydrogen cyanide, in presence of the potassium cyanide, to form the dinitrile. Thus, the two methods are in reality the same, but whilst the process of Challanay and Knoevenagel requires 18 hours, when the condensation is carried out in the way above described, it does not occupy more than one hour.

*Condensation of Phorone with Hydrogen Cyanide.*

Anschütz (*Ber.*, 1893, 26, 827) prepared phoronitrile from the unsaturated ketone by first saturating the latter with hydrogen chloride and then boiling the dihydrochloride with potassium cyanide in dilute alcohol. He found that it was necessary to heat the mixture for 18 hours, and that the yield obtained was very uncertain. The following experiments show that no advantage is gained by first preparing the dihydrochloride.

A solution of 10 grams of phorone in alcohol containing 1 molecular proportion of hydrogen cyanide was warmed for an hour at 100°, as in the foregoing experiment, at the end of which time the solution was quite clear. The bottle was therefore cooled, and 1 molecular proportion of potassium cyanide dissolved in a little water was introduced, and the heating then recommenced. A well-defined, crystalline material began to separate within 10 minutes, and increased rapidly in amount; at the end of an hour it was removed, washed with alcohol, and dried. The product, which was nearly pure phoronitrile, weighed 6 grams, and a further quantity was obtained from the mother liquor:

0·3128 gave 0·7170 CO<sub>2</sub> and 0·2337 H<sub>2</sub>O. C = 62·5; H = 8·3.

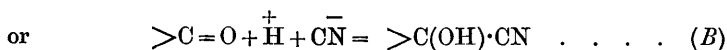
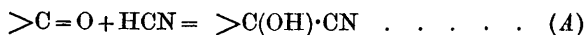
C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>N<sub>2</sub> requires C = 62·9; H = 8·6 per cent.

The methods above described are not those recommended for the preparation of diphenylsuccinonitrile and phoronitrile, but were made for the purpose of showing that the rapid condensation is not dependent on "nascent" hydrogen cyanide but on the presence of potassium cyanide. It is much more convenient to warm an alcoholic solution of these compounds on the water-bath with an excess of potassium cyanide (1·25—1·5 mols.) dissolved in several times its own weight of water, gradually introducing at the bottom of the mixture 1 molecular proportion of hydrochloric acid by means of a thistle funnel with a very small terminal aperture.

In connection with this method, it should be mentioned that Brett and Kallen (*Annalen*, 1896, 293, 350) prepared the hydrogen cyanide addition product of ethyl benzylidenemalonate by adding hydrochloric acid to a cold alcoholic solution of the unsaturated ester in presence of potassium cyanide; they also made a number of β-cyano-acids by warming solutions of the esters of alkylidenemalonic acids with potassium cyanide, the cyano-esters being hydrolysed in the process. The esters did not react under other conditions, but the activity of the hydrogen cyanide was erroneously attributed to the circumstance that it was present "*in statu nascendi*."

*The Mechanism of the Hydrogen Cyanide Addition Process.*

The foregoing observations appear to be of considerable value in connection with the theory of the mechanism of the process of the formation of cyanohydrins. The most natural way of expressing the reaction as a whole is



according as it is the hydrocyanic acid itself or its ions which are really concerned.

The extraordinary effect of the cyanide ions at once renders (A) highly improbable, because the hydrogen cyanide being a weak electrolyte is usually present almost entirely in the undissociated form; its amount is increased only to a very slight extent by the addition of small quantities of either strong acids or cyanides, both, it should be observed, decreasing its dissociation. The equation (B) represents a change the velocity of which would be proportional to the product of the concentrations of the ions of the hydrocyanic acid, and this again, in accordance with the general law, is unaltered by the addition of small quantities of acids, bases, or cyanides. Neither view, therefore, can correctly represent the mechanism.

There appears to be only one suggestion which is of any real assistance in this case, and this is one which was made by the author (Trans., 1901, 79, 1267), to account for the commoner types of change among carbon compounds. The suggestion was simply a proposal to extend to carbon compounds the well-known principle\* that ions, and particularly weak ones, frequently unite with neutral components which possess "residual affinity," thus forming complex ions, the process being frequently, if not invariably, a reversible one (compare Abegg and Bodländer, *Zeit. anorg. Chem.*, 1899, 20, 453).

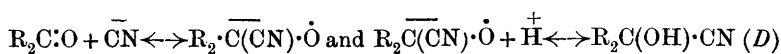
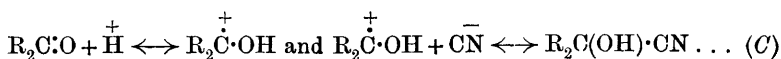
\* The main features of the principle of "complex ions" advanced by Abegg and Bodländer (*loc. cit.*) may be briefly summarised in the following words:

Ions, and more particularly weak ones, may unite with neutral components which possess some form of residual affinity, thus forming complex ions. These appear to have a greater affinity for the electric charge than the simple ions, since it is the latter which, during electrolysis, are liberated at the electrodes in their neutral state, providing, of course, that the concentration of the liquid or the current density is not too great to admit of the sufficiently rapid regeneration of the simple from the complex ions.

In explanation of the greater "electro-affinity" of the complex ion, it is pointed out (*ibid.*, p. 475) that by the distribution of the charge on the simple ion over the larger surface of the former, its potential will naturally be diminished, and therefore the ease with which it is held should now be greater.

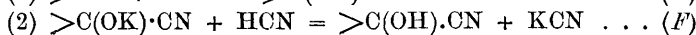
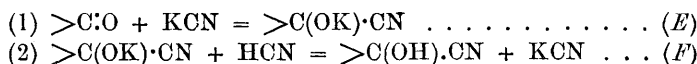
At the present time, it seems more probable than ever that this process may be one of the most important factors in the reactions of carbon compounds, and has been employed in isolated cases by other workers (compare Hantzsch and Schümann, *Ber.*, 1899, 32, 1691).

On this assumption, two possibilities at once present themselves, namely (*C*) that complex ions are formed by the hydrogen ions by union with the ketone or aldehyde, followed by a union of these complex ions with the cyanogen ions, or (*D*) that it is the cyanogen ions which form the initial complex, the two processes being represented by the following diagrams :



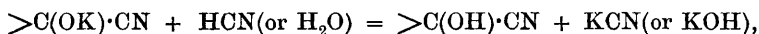
It is easy to show that the law of mass action when applied to the case of (*C*) would predict no acceleration by the addition of a base, but rather the reverse, and this is true whatever may be the relative reaction-velocities of the two stages. In the case of (*D*), however, the predicted results would be precisely those obtained in practice, namely, acceleration by bases and by cyanides of the alkali metals and retardation by acids; if the second stage is very rapid in comparison with the first, it may readily be seen that the velocity will be proportional to the concentration of the cyanogen ions present.

If objection is taken to any ionic view of the change, it may be suggested that the formation of cyanohydrins in presence of potassium cyanide will be represented most satisfactorily as follows :



although it should be noticed that this hypothesis does not embrace the whole series of observations described above, as is the case with the explanation previously advanced.

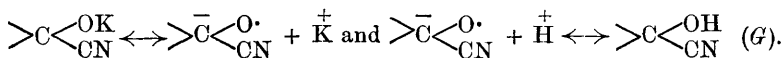
Even if it is admitted that the ions of the cyanide are directly concerned in the change, the view might be held that the reactions could be represented in a simpler manner by supposing that the ionised salt acts in the following way,  $>C:O + \overset{+}{K} + \overset{-}{CN} = >C(OK)\cdot CN$ , but this mode of representing the change would render it necessary to assume the subsequent hydrolysis of this substance, either as in (*F*),



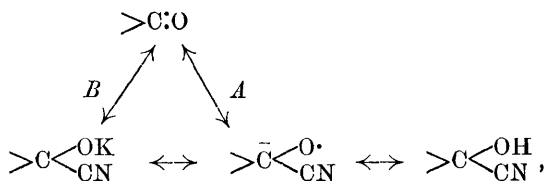
or, in order that this view may possess any claim whatever to recognition as a consistent explanation, the last process must be represented

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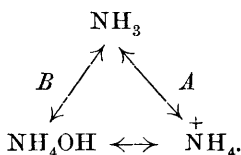
in the usual way as the hydrolysis or double decomposition of the salt of a weak acid,



This hypothesis, which is not less complicated than that put forward above, is one in which the formation of the complex ion is again necessarily assumed. Moreover, this view supplies no clue whatever to the retarding influence exerted by the addition of small quantities of acids, but requires that they should produce no effect. The real difference between the two ionic views is exhibited in the following diagram :



where the reversible reaction, *A*, is assumed in the one case, and *B* in the other. The views differ in the same way as those which may be taken of the formation of an ammonium ion from, say, ammonia and water, namely,



The experiments, therefore, make it appear probable that the formation of cyanohydrins is to be represented as a comparatively slow union of the negative cyanide ions with the carbonyl compound, followed by the almost instantaneous combination of the complexes with hydrogen ions. This was *a priori* the most probable mode of viewing the mechanism, as had been previously pointed out (Trans., 1901, 79, 1268), where the exactly inverse process was suggested in alluding to the disruption of acetone cyanohydrin by alkalis.

If, then, hydrogen cyanide addition reactions are thus to be explained, it should follow, where the addition product is not easily decomposed by alkali, that, in the presence of water to provide the hydrogen ions, potassium cyanide itself in sufficiently concentrated solution should be capable of effecting the conversion.

The following experiments were therefore made in order to test this conclusion.



*Action of Potassium Cyanide on Aldehydes, Ketones, and  $\alpha\beta$ -Unsaturated Ketones and Nitriles.*

(a) *Camphorquinone*.—The quinone (5 grams) was dissolved in ether and shaken with a moderately strong cold solution of potassium cyanide (10 grams). The yellow colour rapidly diminished in intensity, and when no further alteration was apparent, the ethereal solution was removed, washed repeatedly with water, dried over calcium chloride, and evaporated by means of a current of air, the residual yellow mass being treated with fuming sulphuric acid in the method recommended in a previous paper (Trans., 1901, 79, 382). The colourless, microcrystalline, crude product, which, when dry, weighed about 1.5 grams, had all the properties of a mixture of the amides of the  $\alpha$ -hydroxycamphorcarboxylic acids, and on crystallisation from acetone gave the pure amide melting at 235—240°:

0.2802 gave 0.6419 CO<sub>2</sub> and 0.2105 H<sub>2</sub>O. C = 62.3; H = 8.3.

C<sub>11</sub>H<sub>17</sub>O<sub>3</sub>N requires C = 62.6; H = 8.1 per cent.

(b) *Benzaldehyde*.—Twenty grams of the aldehyde were shaken with 20 c.c. of water containing phenolphthalein, and sodium hydroxide was added until the water showed a permanent alkaline reaction. A solution containing 45 grams of potassium cyanide in 150 c.c. of water was then added, and the shaking continued for 2 minutes; after this the whole was left until a separation into two layers occurred, when the clear oil was removed and shaken repeatedly with large quantities of water rendered faintly alkaline with sodium hydroxide, when it was removed, dissolved in ether, and dried over calcium chloride. The product thus obtained was boiled with strong hydrochloric acid and worked up for mandelic acid in the usual way. The acid, recrystallised from benzene, weighed 3 grams and melted at 116—117° (pure mandelic acid melts at 118°). A larger quantity could probably have been obtained, as a considerable amount of material was rejected during the purification.

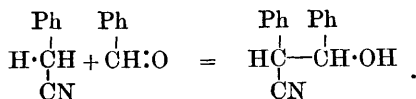
(c) *Benzylidenebenzyl Cyanide*.—Five grams of benzylidenebenzyl cyanide dissolved in dilute alcohol containing 5 grams of potassium cyanide gave 1.8 grams of the mixed diphenylsuccinonitriles after 20 minutes' heating on the water-bath.

(d) *Phorone*.—Five grams of phorone warmed on the water-bath with 10 grams of potassium cyanide dissolved in dilute alcohol gave 3.9 grams of the pure nitrile after 45 minutes.

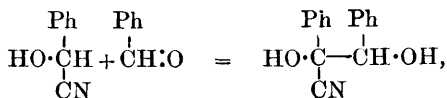
Although it is impossible to bring potassium cyanide and water together without producing some free hydrocyanic acid, it was, nevertheless, thought necessary to make the above experiments.

*The Benzoin Reaction.*

It is now generally accepted that the condensation of ketones and aldehydes with compounds such as ethyl malonate, acetoacetate, benzyl cyanide, and in general such substances as contain the grouping  $>CH \cdot R$  (where  $\cdot R = \cdot CO \cdot, \cdot NO_2, \cdot CN, \cdot SO_2 \cdot$ ) is the result of an additive process in which a hydroxy-compound is produced, as, for example :



Now it has been shown that the first product of the action of potassium cyanide on benzaldehyde is mandelonitrile (=hydroxybenzyl cyanide). The former, like benzyl cyanide itself, has a labile  $\alpha$ -hydrogen atom and in the alkaline solution would condense with benzaldehyde as follows :



which is simply the unstable cyanohydrin of benzoin,  $\begin{array}{c} \text{Ph} \quad \text{Ph} \\ | \quad | \\ \text{O} : \text{C} - \text{C} \cdot \text{H} \cdot \text{OH} \end{array}$ ; this would break up, reversibly, into benzoin and hydrogen cyanide, which would then be available for a further conversion of the benzaldehyde.

To test this latter view, 10 grams of benzaldehyde were converted into mandelonitrile in the usual way, and washed with water repeatedly; the oil was then mixed with 10 grams of freshly distilled benzaldehyde, and 3 grams of tripropylamine were added to the mixture. After remaining at the temperature of the laboratory for 20 days, the material, which had been converted into a semi-solid, yellow mass and had evolved hydrocyanic acid continuously, was triturated in a mortar with dilute alcohol containing hydrochloric acid in order to remove the base, and was then washed repeatedly with water and dissolved in a small quantity of alcohol. A yellow, crystalline material separated; this weighed 4 grams, and was easily identified as benzoin by its melting point, crystalline form, and behaviour with pure benzil and alcoholic potassium hydroxide (Bamberger and Scholl, *Ber.*, 1899, 32, 1809) :

0.3018 gave 0.8733  $\text{CO}_2$  and 0.1589  $\text{H}_2\text{O}$ . C = 78.9; H = 5.8.

$\text{C}_{14}\text{H}_{12}\text{O}_2$  requires C = 79.2; H = 5.7 per cent.

In conclusion, it may be pointed out that the additive reactions of

hydrogen cyanide occur under the same condition as those of ethyl malonate, ethyl acetoacetate, and similar compounds. The mechanism is doubtless much the same in all these cases, and of course affords no clue to the constitution either of the free compounds or of their metallic derivatives. Moreover, in connection with this point, the experiments described in the preceding pages do not exclude the possibility that in certain circumstances, particularly in the absence of much water, or in solvents such as ether or benzene, the additive reactions might occur under the influence of powerful acids, but in such cases, doubtless, the mechanism is of a different character.

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