[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

On 1,2- and 1,4-Addition. I. The 1,4-Addition of Potassium Isocyanide[1]

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The synthesis of β-cyano ketones, esters and nitriles through the action of potassium isocyanide on the corresponding α,β-ethylenic ketones, esters and nitriles is a general reaction.[2] It has been and is assumed that it proceeds by addition of liberated hydrocyanic acid to the α,β-ethylenic carbons, analogously to the addition of strong mineral acids,[3] or primarily by the union of the cyano ion to the β-carbon.[2i] However, hydrogen cyanide[4] functions very weakly acidic ($k^{25}_{\mathrm{HCN}} = 7.2 \times 10^{-10}$), and the facility with which an acid adds to an ethylene group is in direct relation to the strength of the acid.[5] Obviously, so weak an acid as hydrogen cyanide cannot add to ethylenic carbons. Further, the supposed addition of hydrogen cyanide occurs only in the presence of alkali isocyanide and to compounds containing an ethylenic group conjugated with a carbonyl, carbalkoxyl, nitro or nitrile group. The synthesis of pyrotartaric dinitrile from an allyl halide, or allyl cyanide, and isocyanide may seem an exception. However, the reactions were carried out in a partially aqueous medium,[2a,6] in which alkali isocyanides show strongly alkaline properties. Such conditions favor the allyl into propylene shift and allyl cyanide undoubtedly first undergoes a change to crotononitrile. That the formation of pyrotartaric dinitrile proceeds in this manner was proved by the recovery of considerable unchanged allyl cyanide after protracted boiling with isocyanide in absolute methyl alcoholic solution and that no dinitrile was formed under these conditions. Bredt and Kallen[2c] attributed the function of the isocyanide to the formation of *nascent* hydrogen cyanide; but its greater reactivity could be connected only with a greater heat of reaction and hydrogen cyanide does not add even at higher temperatures. Lapworth[2g] believed the reaction proceeds primarily through the —CN ion of a complex salt, formed from hydrogen cyanide and isocyanide, and that it proceeds analogously to Thiele's view, by union of hydrogen with carbonyl oxygen and a cyano group with the β-Δ-carbon; although Thiele[2d] accepted 1,2-addition and his 1,4-viewpoint had been shown untenable.[7a] Lapworth[2i] also thought that the addition may occur to an unconjugated ethylene group, since an analogous addendum, sodium acid sulfite, unites with the α,β-Δ-carbons of cinnamyl alcohol. If the sulfite, $NaSO_2OH$,[7b] added as $NaSO_2O$— and H— a poorly neutralized sulfite derivative would be formed, but, if the H— joins the α-Δ-carbon, with migration of sodium to its place, and the sulfur radical the β-Δ-carbon, then in the well-neutralized sodium sulfonate the maximum possible energy degradation is attained. Obviously, no connection exists between the mechanisms of the two addenda. Recently, Ingold[8] compared the hydrogen cyanide addition to α,β-Δ-esters to that of enolates; the latter and isocyanide providing the anions and the cations uniting with the carbonyl oxygen. This comparison is not tenable; the additivity of malonic ester depends upon the free chemical energy in the ethylenic group,[9] and the pure sodium enolate adds instantaneously in organic solvents with low dielectric and dissociating constants; further the addition does not depend upon an imagined dissociation of the addenda, but upon the possible formation of a new, chemically better neutralized, system.[10] The

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(1) The correct, scientific name and structure of "potassium cyanide" is used in this paper. See *Ann.*, **364**, 64 (1908), for literature.

(2) (a) Claus, *Ann.*, **191**, 33 (1878); (b) Rupe and Schneide, *Ber.*, **28**, 960 (1895); (c) Bredt and Kallen, *Ann.*, **293**, 342 (1896); (d) Thiele and Meisenheimer, *ibid.*, **306**, 247 (1899); (e) Ruhemann and Watson, *J. Chem. Soc.*, **85**, 1454 (1904); Lapworth and coworkers, *ibid.*, (f) **85**, 1065, 1284, 1355 (1904); (g) **83**, 995 (1903); (h) **89**, 1868 (1906); (i) **121**, 49 (1922); (j) **127**, 560 (1925); (k) Hope, *ibid.*, **121**, 2223 (1922).

(3) Michael and Carlson, THIS JOURNAL, **57**, 1268 (1935); Michael and Weiner, *ibid.*, **58**, 294 (1936).

(4) According to Michael [*Ber.*, **34**, 4030, footnote 3 (1901)], hydrogen cyanide contains an extremely small content of the corresponding isocyanide (HNC), in reversible equilibrium with the nitrilic form. E. H. Usherwood [*J. Chem. Soc.*, **121**, 1604 (1922)] concluded from specific heat measurements that gaseous hydrogen cyanide contains several tenths of one per cent. of the acidic form. K. H. Meyer [*Ber.*, **54**, 1709 (1921)], apparently under the belief that an appreciable proportion of the latter is present, endeavored, unsuccessfully, to isolate it by fractionation. The formation of hydroxynitriles from aldehydes and aqueous hydrogen cyanide should proceed through the more energetic acidic form and the addition forms a nitrile because of the greater affinity of the formyl carbon for the C than for the N of HNC and that this course leads to the maximum degradation of energy.

(5) Michael and Brunel, *Am. Chem. J.*, **41**, 118 (1909).

(6) Wislicenus and Euler, *Ber.*, **28**, 2952 (1895); Pomeranz, *Ann.*, **351**, 357 (1907).

(7) Michael, *J. prakt. Chem.*, (a) **60, 467**, (b) 305 (1899).

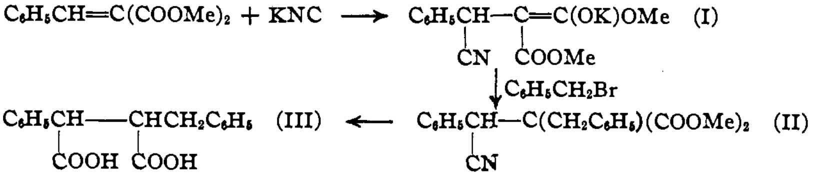
(8) Ingold and Bloom, *J. Chem. Soc.*, 2765 (1931).

(9) Michael, *J. prakt. Chem.*, **36**, 114 (1887).

(10) Michael, *Ber.*, **37**, 22 (1904); Michael and Cobb, *Ann.*. **363**, 64 (1908).

theoretical importance of 1,2-addition of hydrogen cyanide has long been and is still emphasized as proving that no relation exists between 1,4-addition and structure; for example, Hinrichsen[11] in 1902 and Hückel[12] in 1934. However, the following experimental results prove conclusively that hydrogen cyanide is not essential for, nor does it enter into, these reactions, and that they take place exclusively by 1,4-addition, through the isocyanide; thus invalidating all the above speculations.

Previous investigators of the isocyanide reaction used aqueous ethyl alcohol, as the salt is sparingly soluble in absolute alcohol. Under these conditions it seemed possible that primarily formed intermediates may be decomposed by the action of water. Bredt and Kallen[2c] found that a mixture of aqueous potassium isocyanide and an alcoholic solution of benzalmalonic ester, followed by hydrochloric acid, gave β-cyanobenzylmalonic ester and the ester in alcoholic solution with an aqueous solution of isocyanide at 60° gave β-cyanophenylpropionic ester. These results were explained when absolute methanol was used as a solvent. The addition of isocyanide to ester proceeds so rapidly that the salt, suspended in a small volume of absolute methanol, dissolves almost immediately upon addition of ester and a good yield of potassium compound quickly separates, which represents an equimolecular addition product of isocyanide and ester. Acidification of this potassium derivative yielded β-cyanobenzylmalonic ester (IV), identical with the compound prepared according to Bredt and Kallen,[2c] but in far better yield. The potassium compound (I) is an enolate; it reacts with benzyl bromide to give the α-benzyl derivative (II), the structure of which is established by hydrolysis to α-benzyl-β-phenylsuccinic acid (III):

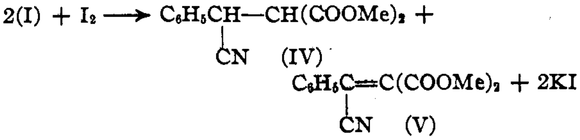


$$C_6H_5CH{=}C(COOMe)_2 + KNC \longrightarrow \underset{\displaystyle CN}{C_6H_5CH}\text{—}\underset{\displaystyle COOMe}{C}{=}C(OK)OMe \quad (\mathrm{I})$$

$$\downarrow C_6H_5CH_2Br$$

$$\underset{\displaystyle COOH}{C_6H_5CH}\text{——}\underset{\displaystyle COOH}{CHCH_2C_6H_5} \quad (\mathrm{III}) \longleftarrow \underset{\displaystyle CN}{C_6H_5CH}\text{—}C(CH_2C_6H_5)(COOMe)_2 \quad (\mathrm{II})$$

With iodine, instead of the usual C-copulation, equivalent amounts of β-cyanobenzylmalonic ester (IV) and β-cyanobenzalmalonic ester (V) are formed



$$2(\mathrm{I}) + I_2 \longrightarrow \underset{\displaystyle CN}{C_6H_5CH}\text{—}CH(COOMe)_2 + \quad (\mathrm{IV})$$

$$\underset{\displaystyle CN}{C_6H_5C}{=}C(COOMe)_2 + 2KI \quad (\mathrm{V})$$

The reaction follows in the first stage the mechanism suggested for the coupling of enolates,[13] which postulates the intermediate formation of an α-iodo compound and its interaction with unchanged enolate. However, the α-iodo compound, $C_6H_5CH(CN)CI(COOMe)_2$ (VI), contains the halogen in the β-position to the nitrile group and belongs to a class of β-derivatives from which halogen hydride is separated with great ease. As (VI) is formed, hydrogen iodide is eliminated by unchanged enolate and (IV) and (V) therefore appear in equal amounts.

Since the addition of potassium isocyanide to benzalmalonic ester is very rapid[14] and the primary product is an enolate, the explanation of Bredt and Kallen's results is apparent. In the experiment with aqueous alcohol at 60°, the enolate was formed practically at once and was changed upon heating into $C_6H_5CH(CN)CH(COOK)COOEt$, which upon further heating, analogously to similarly structured compounds,[15] broke up into potassium bicarbonate and β-cyanophenylpropionic ester. In the reaction at room temperature, the enolate had formed before the addition of mineral acid, which simply set free a poor yield of the corresponding enolic derivative.

The above reaction is an ideal illustration of the interpretation of 1,4-addition from Michael's standpoint.[16] Benzalmalonic ester contains a malonic ester group, without the essential α-hydrogen necessary to yield an enolate; the carbonyl oxygen of a carbmethoxy group has, however, a

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[11] Hinrichsen, *Ann.*, **320**, 60 (1902).

[12] "Hückel, Theoretische Grundlagen der organischen Chemie," 1934, pp. 347, 351.

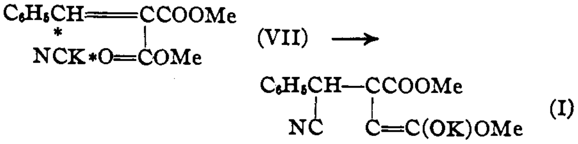
[13] Michael, *J. prakt. Chem.*, **60**, 286 (1899).

[14] So rapid, that an attempt to measure the rate of disappearance of potassium isocyanide by titration was unsuccessful; more than 50% of the isocyanide had disappeared before the first titration could be carried out.

[15] Michael, *J. prakt. Chem.*, **72**, 544 (1906).

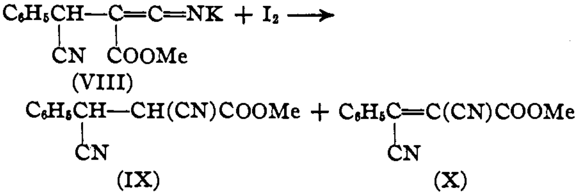
[16] Michael, *J. prakt. Chem.*, **60**, 299, 467, 470, 481 (1899); **68**, 512, 521 (1903); **79**, 418 (1909). A theoretical development of 1,4-addition, based upon the chemical affinity and the chemical energy of the atoms involved in the reacting chemical systems, and a theoretical and exper imental refutation of Thiele's [*Ann.*, **306**, 89 (1899)] mechanical speculations. Straus [*Ber.*, **42**, 2866 (1909)] took exception to the implication of the affinity factor, since he found that Br_2 added 1,2 and Wieland [*Ann.*, **360**, 311 (1908)] that nitrogen tetroxide added NO_2 in 1,4-position to 1,4-diphenylbutadiene. However, Wieland's conclusion is based upon inconclusive experimental results and the more important experiments could not be repeated in this Laboratory.

developed affinity for the slightly neutralized potassium atom of the isocyanide and a strong attraction exists between it and the respective, unsaturated oxygen. Further, the β-Δ-carbon of the ester shows the necessary free chemical energy and affinity, *i. e.*, the chemical potential,[17] to unite with the cyano group. The first formed, cyclic, polymolecule[18] (VII) passes over into the β-cyano enolate (I)



$$\underset{\text{NCK}*\text{O}=\text{COMe}}{\overset{*}{C_6H_5CH}=CCOOMe}\ \text{(VII)} \longrightarrow \underset{\text{NC}\quad \text{C}=\text{C(OK)OMe}}{C_6H_5CH-CCOOMe}\ \text{(I)}$$

For, the β-Δ-carbon has a far more developed affinity for the carbon than the nitrogen of the addendum and the introduction of the decidedly negative cyano group leads to a far better neutralized enolate (I) than would the basic isocyano group. The combination of the ester molecule, loaded with free, negative chemical energy at Δ-oxygens and Δ-carbons, and the isocyanide, with free, positive, chemical energy in large excess, to form the almost neutral enolate molecule, represents the possible maximum degradation of energy of the original chemical system and, therefore, the inevitable course of the chemical change. The above considerations apply also to the reaction between benzalcyanoacetic ester and isocyanide. This facile reaction leads to the iminolate of β-cyanobenzylcyanoacetic ester (VIII),[19] which with iodine gives equimolecular amounts of β-cyanobenzylcyanoacetic ester (IX) and β-cyanobenzalcyanoacetic ester (X)



$$\underset{\text{CN}\quad \text{COOMe}}{C_6H_5CH-C=C=NK} + I_2 \longrightarrow$$

(VIII)

$$\underset{\text{CN}}{C_6H_5CH}-CH(CN)COOMe + \underset{\text{CN}}{C_6H_5C}=C(CN)COOMe$$

(IX) (X)

To confirm these views further, the reaction between fumaric ester and potassium isocyanide was examined under varied conditions. In 90% methanol reaction occurs readily at room temperature; after acidification, 1-cyano-2,3,4-carbmethoxybutane (XV), along with considerable acid fumaric ester, were obtained. In absolute methanol at room temperature, after acidification, the products were methoxysuccinic ester and 2-cyano-3,4,5-carbmethoxycyclopentanone (XVII), the relative proportions depending on the time, the methoxy ester disappearing for the cyclopentanone derivative (XVII) on longer standing. Finally, in boiling absolute methanol, only the cyclopentanone derivative (XVII) was formed in appreciable yield. These relations support the proposed 1,4-mechanism. In methyl alcohol, potassium isocyanide is undoubtedly in equilibrium with potassium methylate and the presence of the methylate brings about reversible formation of methoxysuccinic ester.[20] The reaction is, therefore, competitive between isocyanide and methanol for addition to fumaric ester. Without water, enolate (XI) should mainly rearrange to the much better neutralized iminolate (XII) with some of the corresponding enolate (XIII), which undergo the enolate addition[21] with unchanged fumaric ester, to form the potassium derivative of 1-cyano-1,2,3,4-carbmethoxybutane (XIV).[22] In absolute methanol the new potassium derivative undergoes a Dieckmann condensation and the iminolate (XVI) yields with mineral acid the cyclopentanone derivative (XVII).[23] In the presence of water, however, even at room temperature, the iminolate ester (XIV) is partially saponified and, in the subsequent manipulation, it is decarboxylated to (XV).

When the metal is insufficiently neutralized in the KNC addition product, the following phase of the reaction should, as it does, proceed slowly and, under such conditions, the product behaves exactly like other imperfectly neutralized enolates toward compounds of the type RCH=CHCOOR. The formation of the more complex addition products in the isocyanide reactions is, therefore, experimental proof that, in the first phase, they add normally to form enolates and the addition reaction is experimental evidence that the isocyanide has the iminolate structure, *i. e.*, KNC.

Michael and Schulthess[24] showed that sodium malonic enolate added to citraconic ester in ether solution and gave the expected addition product;

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(17) Michael, *Ann.*, **363**, 21 (1908); THIS JOURNAL, **32**, 990 (1910).

(18) Michael and Carlson, *ibid.*, **57**, 160 (1935), for use of asterisk and graphic illustrations.

(19) There can be no doubt that the metal is attached mainly to nitrogen. The term iminolate is suggested for a compound containing the =C=Nmetal group.

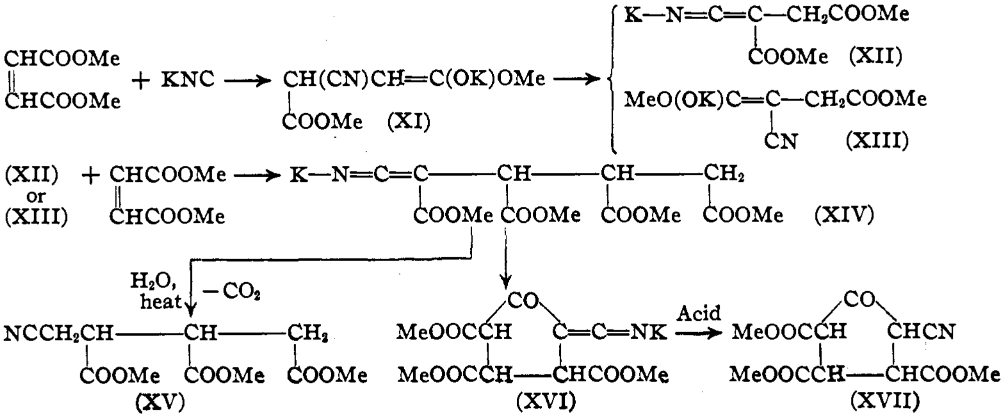
(20) Purdie and Marshall, *J. Chem. Soc.*, **59**, 469 (1886).

(21) See Michael and Ross, THIS JOURNAL, **53**, 1150 (1931), for literature.

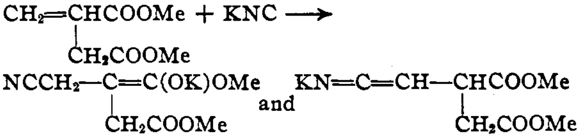
(22) V. Auwers and Jacob, *Ber.*, **27**, 1114 (1894).

(23) V. Auwers, *ibid.*, **26**, 364 (1893).

(24) Michael and Schulthess, *J. prakt. Chem.*, **45**, 55 (1892).



but in alcoholic solution[25] a condensation occurred with loss of alcohol and the enolate of a cyclic ketone derivative was formed. Hope[26] proved that citraconic ester first isomerized to itaconic ester and that the ketone was a cyclopentanone derivative. In absolute methanol, at room temperature, citraconic methyl ester and isocyanide gave, after acidification, two products; one by addition of methyl alcohol and a second with the empirical constitution $C_7H_9O_4N$, their relative proportions depending on time; $C_7H_9O_4N$ being formed with disappearance of the methoxy ester. In boiling methanol only $C_7H_9O_4N$ could be isolated. After heating with acid, or base, it yielded tricarballylic acid, or its salt, which showed that citraconic ester must have rearranged to itaconic ester, before the addition of isocyanide.

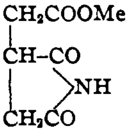


$$CH_2{=}\underset{\displaystyle CH_2COOMe}{C}HCOOMe + KNC \longrightarrow$$

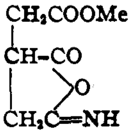
$$NCCH_2{-}\underset{\displaystyle CH_2COOMe}{C}{=}C(OK)OMe \quad \text{and} \quad KN{=}C{=}CH{-}\underset{\displaystyle CH_2COOMe}{C}HCOOMe$$

(XVIIIa) (XVIIIb)

The resulting product (XVIIIa, b) underwent rearrangement and condensation to give an imidic (XIX) or imidolactonic (XX) derivative

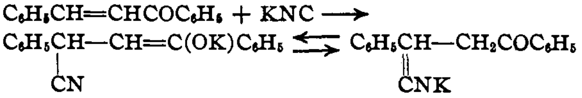


(XIX)



(XX)

β-Cyanobenzylacetophenone (XXI) has been prepared by the action of the isocyanide on benzalacetophenone under varied conditions[2b,27] Hann and Lapworth[27a] treated the ketone, in 92% alcohol, with two equivalents of potassium isocyanide and one equivalent of diluted acetic acid. Along with (XXI) a small yield of compound, $C_{31}H_{23}ON$,[27a] was obtained; it was also formed by condensation of benzalacetophenone with (XXI) by strong alkali. In boiling absolute methanol, benzalacetophenone reacts with isocyanide to give, directly, $C_{31}H_{25}O_2N$, which, with alkali or acid, lost water and gives Hann and Lapworth's $C_{31}H_{23}ON$. The first stage of the reaction evidently results in enolate (XXII), in which the metal is poorly neutralized and which should rearrange to a mixture containing, largely, the still imperfectly neutralized iminolate (XXIII)

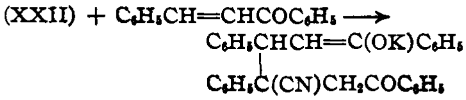


$$C_6H_5CH{=}CHCOC_6H_5 + KNC \longrightarrow$$

$$C_6H_5\underset{\displaystyle CN}{C}H{-}CH{=}C(OK)C_6H_5 \rightleftarrows C_6H_5CH{-}CH_2COC_6H_5 \atop \underset{\displaystyle CNK}{\|}$$

(XXII) (XXIII)

The potassium enolate (XXII) can attain a better neutralization by reacting with another molecule of benzalacetophenone, but iminolate (XXIII) cannot do so. The reaction, therefore, proceeds through enolate (XXII), which is reformed as it disappears in the addition process



$$(XXII) + C_6H_5CH{=}CHCOC_6H_5 \longrightarrow \begin{array}{l} C_6H_5CHCH{=}C(OK)C_6H_5 \\ \quad | \\ C_6H_5C(CN)CH_2COC_6H_5 \end{array} \qquad (XXIV)$$

This formula (XXIV) is the enolate of the structure suggested by Hann and Lapworth for the hitherto unisolated, second phase of the addition process. Since the cyclic intramolecular condensation product is formed from $C_{31}H_{25}O_2N$ in alkaline solution, *i. e.*, from the enolate, the reaction can proceed in one direction, not in two, as Hann and Lapworth assume. However, two isomeric compounds of the formula $C_{31}H_{23}ON$ may be formed, through aldolization, with ring

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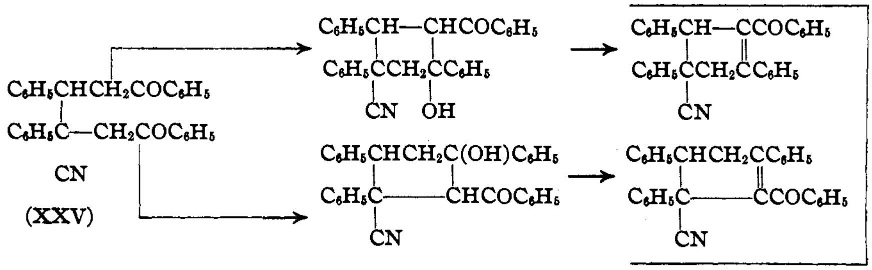
[25] Michael, *Ber.*, **33**, 3757 (1900).

[26] Hope, *J. Chem. Soc.*, **101**, 902 (1912).

[27] (a) Hann and Lapworth, *ibid.*, **85**, 1358 (1904); (b) Lapworth and Wechsler, *ibid.*, **97**, 38 (1910).

formation and elimination of water, of the corresponding free compound



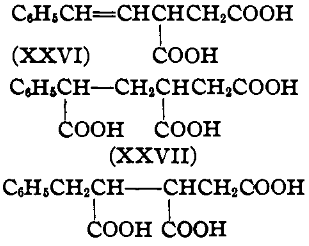
(XXV)

$$C_6H_5CHCH_2COC_6H_5 ;\ C_6H_5\underset{CN}{C}\text{—}CH_2COC_6H_5\ (XXV) \rightarrow C_6H_5CH\text{—}CHCOC_6H_5 ;\ C_6H_5\underset{CN}{C}CH_2\underset{OH}{C}C_6H_5 \rightarrow C_6H_5CH\text{—}CCOC_6H_5 ;\ C_6H_5\underset{CN}{C}CH_2\overset{\|}{C}C_6H_5$$

$$(XXV) \rightarrow C_6H_5CHCH_2C(OH)C_6H_5 ;\ C_6H_5\underset{CN}{C}\text{——}CHCOC_6H_5 \rightarrow C_6H_5CHCH_2CC_6H_5 ;\ C_6H_5\underset{CN}{C}\text{——}\overset{\|}{C}COC_6H_5$$

We attempted, without success, to prove definitely the structures of $C_{31}H_{25}O_2N$ and $C_{31}H_{23}ON$. The first compound resists hydrolysis with concentrated acid and alkali, but is dehydrated to $C_{31}H_{23}ON$, which is, as stated above, probably a ring compound. Hydrolysis in sealed tubes with concentrated hydrochloric acid, at temperatures from 140 to 200°, gave only intractable tars, and treatment with chromic anhydride in glacial acetic acid, or potassium permanganate in acetone, brought about dehydration to $C_{31}H_{23}ON$. In agreement with Hann and Lapworth, we found the latter compound very resistant to hydrolysis or oxidation, reaction taking place under very drastic conditions and giving nothing more significant than benzoic acid or acetophenone. Suspended in glacial acetic acid, $C_{31}H_{25}O_2N$ gave $C_{31}H_{22}ONBr$ with bromine, by substitution of one of the hydrogens for bromine and elimination of water. This compound is apparently not directly related to $C_{31}H_{23}ON$ since it could not be produced by bromination of that compound. The bromination product lost hydrogen bromide by the action of sodium methylate and gave a bright yellow compound $C_{31}H_{21}ON$. This was oxidized by chromic acid to give a poor yield of $C_{24}H_{17}ON$.

Cinnamalmalonic ester and isocyanide reacted in absolute methanol at room temperature and gave, after acidification, $C_{29}H_{29}O_8N$, formed by union of the primary β-cyano enolate with unchanged ester. In aqueous alcohol, with isocyanide and ester in molecular proportions, by subsequent hydrolysis, Thiele and Meisenheimer[2d] obtained styrylsuccinic acid (XXVI). With three moles of isocyanide to one of ester a product was obtained which on hydrolysis gave tribasic acid (XXVII).



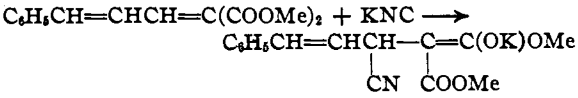
(XXVI) (XXVII) (XXVIII)

$$C_6H_5CH{=}CH\underset{COOH}{C}HCH_2COOH\ (XXVI)$$

$$C_6H_5\underset{COOH}{C}H\text{—}CH_2\underset{COOH}{C}HCH_2COOH\ (XXVII)$$

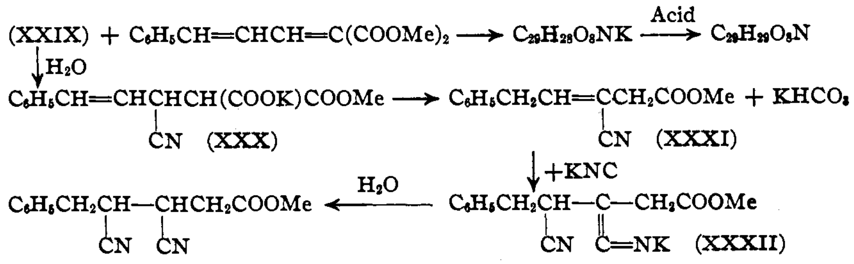
$$C_6H_5CH_2\underset{COOH}{C}H\text{——}\underset{COOH}{C}HCH_2COOH\ (XXVIII)$$

Thiele and Meisenheimer assumed that the reaction leading to (XXVI) was 1,2-addition of hydrogen cyanide, and to (XXVII), first 1,4- and then 1,2-addition. Duff and Ingold[28] proved the correct structure, (XXVIII), the formation of which was explained by assuming α,β-addition to give $C_6H_5CH{=}CHCH(CN)CH(COOR)_2$, which rearranged to $C_6H_5CH_2CH{=}C(CN)CH(COOR)_2$, and which by a second β,γ-addition of hydrogen cyanide yielded the dinitrile $C_6H_5CH_2CH(CN)CH(CN)CH(COOR)_2$ corresponding to (XXVIII). Since hydrogen cyanide does not add, the primary product must be enolate (XXIX), which under the first experimental conditions gave potassium salt (XXX). With excess of isocyanide (XXX) rearranges to (XXXI), which by 1,4-addition of isocyanide forms iminolate (XXXII). Without water, enolate (XXIX) is stable and adds to unchanged ester, forming $C_{29}H_{28}O_8NK$.



(XXIX)

$$C_6H_5CH{=}CHCH{=}C(COOMe)_2 + KNC \longrightarrow C_6H_5CH{=}CH\underset{CN}{C}H\text{—}\underset{COOMe}{C}{=}C(OK)OMe\ (XXIX)$$



$$(XXIX) + C_6H_5CH{=}CHCH{=}C(COOMe)_2 \longrightarrow C_{29}H_{28}O_8NK \xrightarrow{\text{Acid}} C_{29}H_{29}O_8N$$

$$(XXIX) \xrightarrow{H_2O} C_6H_5CH{=}CH\underset{CN}{C}HCH(COOK)COOMe\ (XXX) \longrightarrow C_6H_5CH_2CH{=}\underset{CN}{C}CH_2COOMe + KHCO_3\ (XXXI)$$

$$(XXXI) \xrightarrow{+KNC} C_6H_5CH_2\underset{CN}{C}H\text{—}\underset{C=NK}{\overset{}{C}}\text{—}CH_2COOMe\ (XXXII) \xrightarrow{H_2O} C_6H_5CH_2\underset{CN}{C}H\text{—}\underset{CN}{C}HCH_2COOMe$$

In absolute methanol, isocyanide acts slowly and incompletely on crotonic ester, giving enolates of complex, high boiling esters, probably formed by interaction of primarily formed enolates with unchanged ester. In the presence of water, the enolate is hydrolyzed to the corresponding salt, thus preventing secondary reactions, and by hydrolysis pyrotartaric acid was obtained.[2i]

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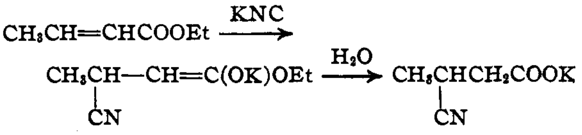
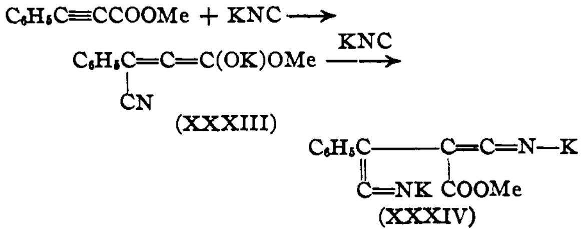
[28] Duff and Ingold, *J. Chem. Soc.*, 87 (1934).



$$CH_3CH{=}CHCOOEt \xrightarrow{KNC} \underset{\displaystyle CN}{CH_3CH}{-}CH{=}C(OK)OEt \xrightarrow{H_2O} \underset{\displaystyle CN}{CH_3CHCH_2COOK}$$

Cobb[29] heated phenylpropiolic ester, isocyanide and aqueous alcohol and isolated $C_6H_5CH(CN)$-CH_2CN with potassium bicarbonate obviously formed by decomposition of $C_6H_5CH(CN)$-$C(CN){=}C(OK)OEt$. In boiling absolute methyl alcohol, phenylpropiolic methyl ester reacts with isocyanide to give after acidification, mainly a mixture of β-methoxycinnamic ester and benzoylacetic ester and about 20% of β-cyanobenzylcyanoacetic ester (IX). The first-formed β-methoxycinnamic ester undoubtedly adds a second molecule of alcohol to form $C_6H_5C(OCH_3)_2CH_2$-$COOMe$,[30] which is converted by isocyanide into benzoylacetic ester enolate. In aqueous alcohol, at room temperature, the addition of methanol is suppressed in favor of isocyanide, and a better yield of (IX) is obtained by the way of the enolate (XXIII) and the diiminolate (XXXIV).



$$C_6H_5C{\equiv}CCOOMe + KNC \longrightarrow \underset{\displaystyle CN}{C_6H_5C}{=}C{=}C(OK)OMe \xrightarrow{KNC}$$

(XXXIII)

$$\underset{\displaystyle \overset{\|}{C}{=}NK}{C_6H_5C}\text{———}\underset{\displaystyle COOMe}{C}{=}C{=}N{-}K$$

(XXXIV)

The di-iminolate (XXXIV) contains two potassium atoms in different states of neutralization; that at the cyanoacetic ester grouping is better neutralized than that attached to the β-cyano group, and the latter yields, with water, the free nitrile group and potassium hydroxide which saponifies unchanged phenylpropiolic ester.

Malonic enolates add to monobasic α,β-acetylenic esters, with migration of the metal from the malonic to the mono-carbmethoxy group;[31] to this new type of stable enolates belongs (XXXIII), which also derived from an α,β-Δ-ester through enolization of the α-Δ-CH group. Earlier attempts to prepare such enolates directly from esters and sodium[32] led to the formation of enolates of depolymerized esters; in recent experiments, using a solution of sodium in liquid ammonia, we obtained analogous results.

Experimental

Action of Potassium Isocyanide on Allyl Cyanide.—The allyl cyanide (6.7 g.), b. p. 117.5–119°, was added to a suspension of 6.5 g. of potassium isocyanide in 50 cc. of absolute methanol and boiled. At the end of four hours the solution started to turn yellow and at the end of twenty-four, when the reaction was stopped, the solution had become dark brown. The solvent was removed as completely as possible on the water-bath and the residue diluted with 100 cc. of dry ether. The precipitate was filtered and the filtrate was concentrated, leaving a residue of 6.0 g. This was distilled and yielded 5.5 g. of allyl cyanide, b. p. 115–120°.

β-Cyanobenzylmalonic Dimethyl Ester, (I) and (IV), (a).—Benzalmalonic dimethyl ester (5.5 g.) was added to a suspension of 1.63 g. of potassium isocyanide in 20 cc. of boiling absolute methanol. The salt dissolved immediately; one-half of the solvent was distilled off, which resulted in the separation of a voluminous, white, crystalline potassium compound. One hundred cc. of dry ether was added and the mixture cooled in an ice-bath. The solid was filtered, washed repeatedly with ether and dried *in vacuo* at 100°; yield 7.0 g. (100%).

Anal. Calcd. for $C_{13}H_{12}O_4NK$ (I): K, 13.7. Found: K, 13.4.

The potassium compound was suspended in ether, dilute acid added and the mixture shaken until solution was complete. The dried solution was freed of ether and the colorless residual oil was dissolved in an equal volume of methanol and cooled to −20°, when it completely solidified; yield 6.0 g. (100%). The compound was recrystallized by dissolving in the minimum volume of methanol at room temperature and cooling in a freezing mixture; it separated in rosets of needles, m. p. 47.5–48.5°.

Anal. Calcd. for $C_{13}H_{13}O_4N$ (IV): C, 63.16; H, 5.26. Found: C, 63.25; H, 5.43.

(b).—Benzalmalonic dimethyl ester (5.5 g.) was dissolved in 50 cc. of methanol and a solution of 1.65 g. of potassium isocyanide in 20 cc. of water was added. The solution stood ten minutes, 3 cc. of concentrated hydrochloric acid was added, and then allowed to stand for twenty-four hours. It was diluted with sufficient water to cause precipitation of an oil, which was extracted with ether and the residue from the dried ether solution was dissolved in methanol. By seeding and cooling to −20°, 3 g. of a solid separated, identical with the β-cyanobenzylmalonic ester (IV) obtained above.

α-Benzyl-β-cyanobenzylmalonic Dimethyl Ester (II).—Potassium enol β-cyanobenzylmalonic ester (I), (12.2 g.), was suspended in 75 cc. of dry toluene and boiled with 7.3 g. of benzyl bromide for three hours. The solid was separated by centrifuging and was washed repeatedly with ether; weight 10.2 g. (theoretical for potassium bromide, 5.1 g.). The solid was suspended in ether, shaken with dilute acid, and the dried ether solution yielded, on concentration, 5.5 g. of β-cyanobenzylmalonic ester (IV). The ether–toluene solution was concentrated *in vacuo* and the residue taken up in ether. Dilution with petroleum ether and cooling to −20° yielded 4 g. of crystalline solid, which, after recrystallization from ether–petroleum ether, melted at 117.5–118°.

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[29] Cobb, *Am. Chem. J.*, **45**, 604 (1910).

[30] See Michael and Bucher, *Ber.*, **29**, 1793 (1896).

[31] Gidvani, Kon and Wright, *J. Chem. Soc.*, 1027 (1932); Gidvani and Kon, *ibid.*, 2443; Farmer, Ghosal and Kon, *ibid.*, 1804 (1936).

[32] Michael, *Ber.*, **33**, 3766 (1900).

Anal. Calcd. for $C_{21}H_{19}O_4N$ (II): C, 71.22; H, 5.64. Found: C, 70.90; H, 5.56.

α-Benzyl-β-phenylsuccinic Acid (III).—One gram of (II) was heated in a sealed tube with 25 cc. of concentrated hydrochloric acid at 200° for five hours. The resulting solution was extracted with ether and the ether washed with saturated sodium bicarbonate solution. Acidification of the washings, extraction with ether and concentration of the dried ether solution yielded 0.6 g. of acid, which, after recrystallization from 30% methanol, melted at 175–176° and had a neutral equivalent of 144. Calcd. for $C_{17}H_{16}O_4$: (dibasic) 142. It is therefore α-benzyl-β-phenylsuccinic acid.[33]

β-Cyanobenzalmalonic Dimethyl Ester (V).—Potassium enol β-cyanobenzylmalonic ester (I), (10.5 g.) was suspended in 75 cc. of boiling toluene and a solution of 4.6 g. of iodine in 25 cc. of toluene was added dropwise. The iodine was decolorized immediately until the last drop, which colored the supernatant liquor faintly pink. The potassium iodide was separated by centrifuging and was washed repeatedly with ether; weight 6.1 g. (theoret.). The solution and washings were concentrated *in vacuo*, the residue was dissolved in ether, diluted with petroleum ether and cooled to −20°. A small amount of solid crystallized out and repeated concentration of the mother liquor and cooling finally yielded 3.85 g. of this compound, leaving 4.25 g. of brown oil. The solid was recrystallized from ether–petroleum ether, giving flat needles, m. p. 74°.

Anal. Calcd. for $C_{13}H_{11}O_4N$ (V); C, 63.67; H, 4.47; mol. wt., 245. Found: C, 64.17, 63.81; H, 4.36, 5.02; mol. wt. (Pirsch, camphor), 247, 250.

One gram of this compound was shaken with hydrogen in the presence of 0.05 g. of Adams catalyst and absorbed 120 cc. (one mole) in four minutes. The filtered solution yielded β-cyanobenzylmalonic ester (IV).

The residual brown oil from the iodine reaction was freed of ether and dissolved in an equal volume of methanol and cooled to −20°. Inoculation with a seed crystal caused separation of 4 g. of β-cyanobenzylmalonic ester (IV).

β-Cyanobenzylcyanoacetic Methyl Ester, (VIII) and (IX).—Benzalcyanoacetic methyl ester (9.35 g.) was added to a suspension of 3.25 g. of potassium isocyanide in 25 cc. of absolute methanol. The salt disappeared almost immediately after warming the mixture but no solid separated when half the solvent was distilled off. The residual solution, cooled and diluted with 100 cc. of dry ether, gave a crystalline potassium compound. This was filtered, washed repeatedly with ether and dried *in vacuo* at 100°; yield 12 g. (100%).

Anal. Calcd. for $C_{12}H_9O_2N_2K$ (VIII): K, 15.5. Found: K, 14.7.

The potassium compound was suspended in ether and shaken with dilute acid until completely decomposed. The resulting compound was only sparingly soluble in ether and was filtered, washed with ether and cold methanol. The washings were combined with the ether layer, dried and concentrated, yielding a small additional quantity of the compound; yield 10.5 g. (100%). After recrystallization from benzene it melted at 107–108°.

Anal. Calcd. for $C_{12}H_{10}O_2N_2$ (IX): C, 67.30; H, 4.67. Found: C, 67.21; H, 4.89.

β-Cyanobenzalcyanoacetic Methyl Ester (X).—Potassium enol β-cyanobenzylcyanoacetic ester (VIII), (12.6 g.), was suspended in 50 cc. of dry toluene and a solution of 6.3 g. of iodine in 50 cc. of toluene was added dropwise to the boiling mixture. When the addition was completed the hot solution was filtered and the salt washed with hot benzene. The combined filtrate and washings was washed with sodium thiosulfate solution, dried and concentrated to about 10 cc. Dilution with ether and petroleum ether gave 7.0 g. of solid and concentration of the mother liquor yielded an additional gram. The solid was extracted several times with ether, leaving undissolved 3.8 g. of β-cyanobenzylcyanoacetic ester (IX). The ether was concentrated, and, after 0.2 g. of (IX) was obtained, dilution with petroleum ether gave 3.8 g. of a new substance. This was recrystallized from ether–petroleum ether and melted at 87–88°.

Anal. Calcd. for $C_{12}H_8O_2N_2$ (X): C, 67.93; H, 3.77. Found: C, 67.91; H, 4.36.

Catalytic reduction of this compound gave a quantitative yield of β-cyanobenzylcyanoacetic ester (IX).

1 - Cyano - 2,3,4 - carbmethoxybutane (XV).—Fumaric methyl ester (7.2 g.) was suspended in a solution of 3.25 g. of potassium isocyanide in 5 cc. of water and 50 cc. of methanol. Solution of the ester was complete at the end of two hours, but the mixture stood for forty-eight hours. It was then neutralized with an equivalent of hydrochloric acid, diluted with 50 cc. of ether, and the potassium chloride filtered. The solution was concentrated and the residue fractionated at reduced pressure, yielding (1) 1 g., b. p. 85–100° (2 mm.); (2) 3.9 g. CH(COOMe)=CH-COOH, b. p. 145–155° (2 mm.), m. p. 143°; (3) 2.5 g. of viscous oil, b. p. 190–200° (3 mm.). Fraction I was identified as methoxysuccinic ester, as described below. Fraction 3 was redistilled and boiled at 178–180° (3 mm.).

Anal. Calcd. for $C_{11}H_{15}O_6N$ (XV): C, 51.37; H, 5.83; N, 5.45; OCH_3, 36.19. Found: C, 51.0, 50.83; H, 5.63, 6.03; N, 5.1; OCH_3, 36.86.

Three and four-tenths grams of this compound was heated in a sealed tube at 200° with 10 cc. of concentrated hydrochloric acid for four hours. The resulting solution was evaporated to dryness on the water-bath, and the crystalline residue dissolved in 15 cc. of boiling acetic anhydride, which on cooling deposited an anhydride that melted at 245–248°. This anhydride was dissolved in boiling water, the solution concentrated and the acid allowed to crystallize. This acid melted at 185–188°. These are, therefore, the lower melting butane-1,2,3,4-tetracarboxylic acid and its anhydride, described by v. Auwers and Jacob.[22]

2 - Cyano - 3,4,5 - carbmethoxycyclopentanone (XVII), (a), and Methoxysuccinic Ester.—Fumaric methyl ester (14.4 g.) was added to a suspension of 6.5 g. of potassium isocyanide in 50 cc. of absolute methanol, which stood at room temperature for four days. The undissolved potassium isocyanide was filtered, washed with ether and, when dry, weighed 3.0 g. The filtrate was neutralized with a

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(33) Avery and Upson, *Am. Chem. J.*, **30**, 600 (1902).

solution of dry hydrochloric acid in absolute methanol and the potassium chloride filtered. The solvent was removed at room temperature under reduced pressure, leaving a residue of 16.3 g. This was fractionated into (1) 5.5 g., b. p. 75–85° (2 mm.); and (2) 5.4 g., b. p. 196–205° (2 mm.).

When the same quantities of reagents stood for six days and the mixture was worked up as above, the same weight of isocyanide was recovered. There was a residue of 14.7 g. which was fractionated into (1) 3.0 g. and (2) 6.6 g. The combined low boiling fractions boiled completely at 119° (21 mm.), and was identified as methoxysuccinic ester by saponification to methoxysuccinic acid,[20] m. p. 107–108°. Fraction 2 of both experiments was identified as the cyclopentanone derivative (XVII), obtained also in the following experiment, by its boiling point, brilliant coloration with ferric chloride and complete solubility in sodium bicarbonate solution.

(b).—A solution of 14.4 g. of fumaric methyl ester in 150 cc. of absolute methanol was boiled for two hours with 3.25 g. of potassium isocyanide. The solvent was then removed completely, the gummy residue suspended in ether and shaken with acid until completely dissolved. The residue from the dried ether extract weighed 10.8 g. and boiled at 190–200° (4 mm.). On redistillation it was obtained as a colorless, extremely viscous liquid, b. p. 196° (4 mm.). The substance is completely soluble in sodium bicarbonate solution and is recovered unchanged on acidification of that solution. With ferric chloride it gives a brilliant scarlet coloration.

Anal. Calcd. for $C_{12}H_{13}O_7N$ (XVII): C, 50.89; H, 4.59; N, 4.95; OCH_3, 32.86. Found: C, 50.72; H, 4.67; N, 5.4; OCH_3, 32.08.

Six grams of this viscous liquid was boiled for two hours with 50 cc. of concentrated hydrochloric acid. The solution was evaporated to dryness, leaving a crystalline residue which was absolutely insoluble in organic solvents, nor did it melt below 300°, but charred and sublimed. This was not investigated further, but was boiled with concentrated hydrochloric acid and amyl nitrite. The dark solution was concentrated to about 5 cc., and diluted with 100 cc. of acetone to precipitate any unaltered infusible substance, which was filtered. The filtrate was decolorized with charcoal and concentrated, yielding a crystalline acid, which after recrystallization from acetone–ether melted at 188° with decomposition. This was suspended in ether and treated with excess of diazomethane, giving a clear solution, from which was obtained an ester, crystallizing from petroleum ether in needles, m. p. 63–64°. This fixes the acid as cyclopentanone-3,4-dicarboxylic acid,[23] and establishes the structure of the cyclopentanone derivative (XVII). The infusible compound is undoubtedly an amide sufficiently stable to withstand hydrolysis with acids.

Action of Potassium Isocyanide on Citraconic Methyl Ester, (a), at Room Temperature.—Citraconic methyl ester (15.8 g.) was added to a suspension of 6.5 g. of potassium isocyanide in 50 cc. of absolute methanol, which then stood at room temperature for four days. The undissolved salt, when filtered, washed with ether and dried, weighed 3.5 g. The filtrate was neutralized with a solution of dry methyl alcoholic hydrochloric acid, the potassium chloride filtered, and the solution concentrated to a solvent-free residue of 17.8 g. This was fractionated into (1) 10 g., b. p. 120–135° (20 mm.); and (2) 4.6 g. of viscous liquid, b. p. 167–175° (1 mm.), which solidified on standing.

When the same quantities of reagents were allowed to stand for six days and worked up in the same manner, 2.6 g. of isocyanide was recovered, and 17.2 g. of oil was obtained, which was fractionated into (1) 7 g., and (2) 6.5 g. The solid (fraction 2) was recrystallized from acetone–petroleum ether and ether–petroleum ether and melted at 80–81°.

Anal. Calcd. for $C_7H_9O_4N$, (XIX) or (XX): C, 49.12; H, 5.26; N, 8.19; OCH_3, 18.13; mol. wt., 171. Found: C, 48.87, 48.93; H, 5.32, 5.51; N, 8.34; OCH_3, 17.93; mol. wt. (b. p. of acetone), 173, 174, 178.

The compound is very soluble in water, reacting neutral to litmus and sodium carbonate solution. When boiled with 50% hydrochloric acid, or excess of 20% caustic soda followed by acidification, the solution evaporated to dryness, the resulting acid, extracted from the residue with acetone, was tricarballylic acid, identified by m. p. and mixed m. p. with an authentic sample.

(b), In Boiling Methanol.—Citraconic methyl ester (15.8 g.) was boiled with 6.5 g. of potassium isocyanide in 100 cc. of absolute methanol for four hours, when all the potassium cyanide had dissolved. The solution was cooled and neutralized with dry methyl alcoholic hydrochloric acid. The solution was diluted with ether, the potassium chloride separated by centrifuging, and the solution concentrated at reduced pressure. The residue was distilled at reduced pressure and gave 7.0 g. of $C_7H_9O_4N$, (XIX) or (XX).

1,2-Dicarbmethoxy-3-methoxypropane.—Fraction 1 of the above room temperature reactions was distilled through a Fenske column, and, after removal of a trace of starting material, boiled at 80.5° (1 mm.) and had n^{22}_D 1.4294.

Anal. Calcd. for $C_8H_{14}O_5$: C, 50.56; H, 7.37. Found: C, 49.88, 50.10; H, 7.20, 7.42.

Saponification of this ester yielded an acid, which, after recrystallization from ether–petroleum ether, melted at 102–103°. Hope[26] gave a m. p. of 92° for $CH_3OCH_2CH(COOH)CH_2COOH$, prepared from the diethyl ester. To check this, the methoxy ester was prepared by an unequivocal procedure. Citraconic methyl ester (15.8 g.) was added to a solution of 0.2 g. of sodium in 50 cc. of absolute methanol and allowed to stand at room temperature for four days. The solution was neutralized and concentrated. The residue was dissolved in ether and a small amount of gelatinous material removed by filtration. The ether-free residue was distilled in a Fenske column and yielded 1.4 g. of starting material and 14.1 g., b. p. 82° (1.5 mm.), n^{22}_D 1.4292. and, therefore, identical with the product obtained in the citraconic ester–potassium isocyanide reaction. The acid obtained from this ester melted at 102–103° and did not depress the m. p. of the acid obtained in the previous reaction. Therefore, Hope's acid of m. p. 92° was impure, or the figure given is a typographical error.

Action of Potassium Isocyanide on Benzalacetophenone, $C_{31}H_{25}O_2N$, (XXV).—Benzalacetophenone (10.4 g.) was added to a boiling suspension of 3.3 g. of potassium isocyanide in 50 cc. of absolute methanol. The salt dissolved and, after an hour, a voluminous solid separated. This was filtered from the cooled solution, and when washed colorless with ether and dried it weighed 7.4 g. An additional gram was obtained by concentration of the mother liquor. It is sparingly soluble in all solvents, hot or cold, except hot alcohol and benzene. Recrystallized from the latter solvent, it melted at 237°.

Anal. Calcd. for $C_{31}H_{25}O_2N$ (XXV): C, 83.95; H, 5.64; N, 3.16; mol. wt., 443. Found: C, 84.00; H, 5.75; N, 3.48; mol. wt. (camphor), 418.

In an attempt to oxidize (XXV), 2 g. was added to a solution of 1.1 g. of chromic anhydride in 10 cc. of glacial acetic acid. The mixture was warmed on the water-bath and turned green in about five minutes. The solution was poured into water, and the resulting precipitate separated by filtration. When dry it weighed 1.8 g., and after recrystallization from benzene was identified as $C_{31}H_{23}ON$[27a] by m. p. and mixed m. p. with an authentic sample.

In an attempt to hydrolyze or cleave $C_{31}H_{25}O_2N$ (XXV), 1 g. was treated with a solution of 5 g. of sodium hydroxide in 25 cc. of 50% alcohol at 100° for eighteen hours. The undissolved solid was filtered and dried; weight 0.8 g. After recrystallization, it was identified as $C_{31}H_{23}ON$.

Action of Br_2 on $C_{31}H_{25}O_2N$, (XXV); $C_{31}H_{22}ONBr$.—Five grams of $C_{31}H_{25}O_2N$ (XXV) was suspended in 50 cc. of glacial acetic acid containing 2 g. of bromine. The solution was boiled for ten minutes before the evolution of hydrogen bromide started, but the reaction then proceeded rapidly resulting in a clear pale yellow solution. The cooled solution was poured into water and the precipitated yellow solid separated by filtration. This was dissolved in cold benzene, the water layer drawn off and the benzene dried. Concentration of the benzene solution, and dilution with petroleum ether gave 4.5 g. of colorless solid, which after repeated crystallization from benzene–petroleum ether, melted at 188–189°.

Anal. Calcd. for $C_{31}H_{22}ONBr$: C, 73.81; H, 4.36; Br, 15.85. Found: C, 74.35; H, 4.47; Br, 16.21.

Action of Br_2 on $C_{31}H_{23}ON$.—Eleven grams of $C_{31}H_{23}ON$ was suspended in 100 cc. of glacial acetic acid containing 4 g. of bromine and the mixture boiled. The solid dissolved with evolution of hydrogen bromide and gave a deep red solution. This was poured into water, the water extracted with benzene, which was washed with sodium bicarbonate solution, dried and concentrated, leaving a deep red oil from which no solid could be isolated.

Action of Sodium Methylate on $C_{31}H_{22}ONBr$; $C_{31}H_{21}ON$.—Four grams of $C_{31}H_{22}ONBr$ was suspended in a solution of 0.2 g. of sodium in 50 cc. of absolute methanol and boiled for an hour, during which time the white solid dissolved and a yellow solid crystallized, the solution becoming transitorily pink, and finally yellow. The solution was concentrated to 25 cc., and the solid filtered from the cooled solution; weight, 3.2 g. It crystallized from methanol as lemon-yellow needles, m. p. 188°.

Anal. Calcd. for $C_{31}H_{21}ON$: C, 87.94; H, 4.96. Found: C, 87.41; H, 4.70.

Oxidation of $C_{31}H_{21}ON$, $CH_{24}O_{17}N$.—Two grams of $C_{31}H_{21}ON$ was dissolved in 10 cc. of boiling glacial acetic acid and a solution of 1 g. of chromic anhydride in 5 cc. of glacial acetic acid was added dropwise until the red color was no longer discharged immediately. The solution was poured into water and extracted with benzene, which was washed with water and sodium bicarbonate solution. The acidified sodium bicarbonate solution yielded no solid acid. The dried benzene solution was concentrated and 0.5 g. of white crystalline compound separated. This was recrystallized from benzene and melted at 235–237° with decomposition.

Anal. Calcd. for $C_{24}H_{17}ON$: C, 85.97; H, 5.07. Found: C, 85.93; H, 5.17.

Action of Potassium Isocyanide on Cinnamalmalonic Ester.—Five grams of cinnamalmalonic methyl ester was dissolved in 50 cc. of absolute methanol containing 1.3 g of potassium isocyanide. The solution stood at room temperature for three hours and was then neutralized with an equivalent of concentrated hydrochloric acid. The precipitated solid was filtered and washed with water, leaving, when dry, 1 g. of white solid. The filtrate was concentrated and yielded an additional 1.5 g. of the same solid. It crystallized from methanol as needles, m. p. 143–144°.

Anal. Calcd. for $C_{29}H_{29}O_8N$: C, 67.05; H, 5.59; N, 2.70; mol. wt., 519. Found: C, 67.35, 67.26; H, 5.76, 5.49; N, 3.5; mol. wt. (boiling acetone), 559, 500, 518.

Action of Potassium Isocyanide on Crotonic Ester.—Twenty grams of crotonic methyl ester was treated with 13 g. of potassium isocyanide in 100 cc. of boiling absolute methanol for forty hours. The dark brown solution was concentrated to 50 cc. and cooled, causing crystallization of 7.0 g. of potassium isocyanide. This was removed by filtration and the filtrate concentrated further. The gummy residue was suspended in ether and shaken with dilute acid until completely decomposed. The dried ether solution was concentrated and the residue fractionated into (1) 4.4 g. of crotonic ester, b. p. 58–70° (25 mm.): (2) 2 g., b. p. 135–145° (4 mm.); and (3) 1.4 g. of viscous liquid, b. p. 190–200° (4 mm.). There was a large tarry residue.

Action of Potassium Isocyanide on Phenylpropiolic Ester, (a) in Absolute Methanol.—Eight grams of phenylpropiolic methyl ester was boiled with a suspension of 6.5 g. of potassium isocyanide in 25 cc. of absolute methanol. The solution turned yellow immediately and, finally, at the end of thirty minutes, dark brown. Since the potassium isocyanide did not seem to be dissolving, the mixture was cooled in an ice-bath and the isocyanide filtered, washed with ether and dried; weight 3.7 g. The filtrate was diluted with 50 cc. of dry ether and neutralized by bubbling in gaseous hydrogen chloride. The potassium chloride was filtered and the filtrate concentrated to a solvent-free residue of 9.9 g. This was fractionated into (1) 6.5 g., b. p. 109–120° (2 mm.), and (2) 2.0 g. of β-cyanobenzylcyanoacetic ester (IX), which distilled when the bath was raised to 240°. Fraction 1 was redistilled and boiled completely at 138–139° (8 mm.). This material gave a ferric chloride test, and, so, 1 g. was treated with excess of saturated cupric acetate solution, thus giving 0.3 g. of a copper derivative that was identified as that of benzoylacetic methyl ester by m. p. (200°) and mixed m. p. The distillate had n^{25}D 1.5455; v. Auwers[34] gives

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[34] Von Auwers, *Ann.*, **413**, 274 (1916); **415**, 230 (1918).

the indices of refraction ($n^{25}\mathrm{D}$) of benzoylacetic methyl ester and β-methoxycinnamic methyl ester, respectively, as 1.537 and 1.550. Thus the yield of copper derivative shows a benzoylacetic ester content of 30%, while the index of refraction checks this approximation with benzoylacetic ester content of 35%.

(b). **In Aqueous Methanol.**—Eight grams of phenylpropiolic methyl ester was added to a solution of 6.5 g. of potassium isocyanide in 10 cc. of water and 50 cc. of methanol and allowed to stand at room temperature for four hours and, then, for an additional twenty hours in a bath at −20°. One gram of crystallized potassium salt was filtered and the solution was diluted with 500 cc. of ether, yielding an additional 5.8 g. of potassium salt. The combined potassium salts was suspended in ether and shaken with dilute acid. The dried ether solution yielded 3.5 g. of phenylpropiolic acid. The filtrate from the salt was shaken with dilute acid, changing from deep orange to pale yellow. The dried ether solution was concentrated and left 5 g. of solid, which was extracted repeatedly with petroleum ether, thus leaving 4 g. of pure β-cyanobenzylcyanoacetic ester (IX). The petroleum ether extracts yielded 1 g. of phenyl propiolic acid.

Summary

1. The formation of pyrotartaric dinitrile from potassium isocyanide and allyl cyanide proceeds primarily through rearrangement of allyl cyanide to crotononitrile.

2. The mechanisms hitherto proposed for the syntheses of β-cyano-ketones, -esters and -nitriles from the corresponding α,β-Δ-ketones, -esters and -nitriles, which was assumed to proceed by addition of hydrocyanic acid or through a complex salt with potassium isocyanide to the Δ-carbons of the Δ-compounds has been shown to be impossible.

3. The formation of β-cyano-ketones, -esters and -nitriles from the corresponding α,β-ethylenic compounds proceeds through the formation of enolates, or iminolates, by 1,4-addition of potassium isocyanide to the conjugated groups of the unsaturated compounds, the metal uniting with carbonyl oxygen or cyano nitrogen.

4. When the reaction products from potassium isocyanide and the α,β,Δ-esters are poorly neutralized enolates, in the absence of water, they realize a better intramolecular neutralization by addition to unchanged ester.

5. The action of potassium isocyanide upon fumaric methyl ester proceeds primarily by 1,4-addition; under certain conditions, the enolate adds to unchanged fumaric ester and the addition product condenses to a cyclopentanone derivative. With citraconic methyl ester, the first phase consists in rearrangement to the itaconic ester, which undergoes the 1,4-addition with the isocyanide and is then changed to a cyclic nitrogen derivative.

6. According to the experimental conditions, phenylpropiolic ester unites by 1,4-addition with one and then with a second molecule of isocyanide. The first addition product is an enolate of the structure $C_6H_5C(CN){=}C{=}C(OK)OMe$; a type of enolate involving the enolization of an unsaturated α-CH group of an α,β,Δ-ester.

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[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES CHEMICAL LABORATORIES, UNIVERSITY OF CHICAGO]

The Catalytic Hydrogenation and Esterification of C_4-Saccharinic Acid Lactones and the Hydrogenation of Butyl Erythronate[1]

BY J. W. E. GLATTFELD AND ANNE M. STACK

Various reduction methods have been studied in these Laboratories with the object of finding a practical method for the reduction of the C_4-saccharinic acids to the corresponding aldehydes and alcohols and for the reduction of erythronic lactone to erythrose. Low pressure catalytic reduction of aldonic acids was studied by Glattfeld and Shaver[2] and by Glattfeld and Schimpff.[3] The work reported in this paper is a continuation of these experiments and includes a study of the catalytic hydrogenation, under pressures of 2–136 atmospheres, of 2,3-dihydroxybutyric acid lactone and one of its derivatives, of 1,3-dihydroxybutyric acid lactone, and of the butyl ester of *dl*-erythronic acid. The last named compound was first prepared in these Laboratories by Snoddy.[4] His method of preparation was followed in general but, as a few changes were made, the procedure is given in some detail in the Experimental Part. (Hereinafter the 2,3- and 1,3-dihydroxybutyric

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(2) Glattfeld and Shaver, THIS JOURNAL, **49**, 2305 (1927).

(3) Glattfeld and Schimpff, *ibid.*, **57**, 2204 (1935).

(4) J. A. Snoddy, S.M. Dissertation, University of Chicago, 1934.