THE THERMAL REVERSIBILITY OF THE MICHAEL REACTION I. NITRILES¹

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ABSTRACT

Michael adducts of nitriles and α,β -unsaturated ketones have been found generally to undergo two or more kinds of thermal reversibility upon being heated to moderate temperatures. When the products are those from which the adduct was prepared, the dissociation is termed "normal," whereas the "abnormal" route gives an α,β -unsaturated nitrile and a methyl ketone. The scope and generality of the reversibility are described in three papers. The first deals with 31 ketonic nitriles, the second with nitroketones, and the last with diketones and acidic derivatives.

Allowing the materials to decompose thermally in the heated inlet of a mass spectrometer permits a direct study of thermal reaction mixtures and it affords data the interpretation of which gives an indication of the products present, many of which may not have been previously expected. Identification of products is confirmed by comparison of the mass spectra with those of reference compounds. Under favorable conditions, such products can be isolated from independent decomposition reactions and their identities further confirmed by classical chemical methods. Both operations have been done often enough to show the general application of the mass spectrometer for this purpose. Thus laborious laboratory separations may be avoided. In two instances the four major products from both paths were isolated, identified, and quantitatively determined.

Forty years ago, the senior author of this paper found that γ -benzoyl- α,β -diphenylbutyronitrile (I) (1), the adduct from benzyl cyanide and benzalacetophenone, dissociated on attempted distillation, and its components were identified in the distillate.

 $\begin{array}{ccc} C_{6}H_{5}CHCH_{2}COC_{6}H_{5} & C_{6}H_{5}CH=CHCOC_{6}H_{5} \\ \downarrow & \rightleftharpoons & + \\ C_{6}H_{5}CHCN & C_{6}H_{5}CH_{2}CN \\ I \end{array}$

Twenty years later, β , γ -diphenyl- γ -nitrobutyrophenone (II) was found to decompose when heated above its melting point; the products identified were benzalacetophenone, benzaldehyde, and nitric oxide (2).

 $\begin{array}{ccc} C_6H_5CHCH_2COC_6H_5 & C_6H_5CH=CHCOC_6H_5 \\ | & \rightarrow & + \\ C_6H_5CHNO_2 & C_6H_5CHO + NO + ? \\ II & II \end{array}$

Although the reversibility of the Michael reaction in the presence of alkaline reagents is well known (3), there are very few recorded instances of the effect of heat upon the adducts. Those few described are all dicarbonyl compounds (see Part III). It seemed

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advisable to postpone a study of the thermal reversibility of the Michael reaction until relatively simple but rapid qualitative and quantitative methods were available. Such tools have been employed in these Laboratories for some years in the form of the mass spectrometer and the gas chromatograph.

Summarizing the present work in three papers, it has been found that the thermal reversibility is dependent upon the number and kind of groups present. The degree of substitution, which has been varied from one to three aryl groups, has considerable effect. Cleavage, which is greatest and may occur in two ways when there are three aryl groups along the chain, is not detectable when there is but one such substituent; the results are intermediate with two aryls. In a given class, the nature of the functional groups is very important. For instance, 1,5-diketones (Part III) and delta ketonic nitriles (this paper) cleave the most easily and follow both paths; keto esters go both ways but less easily. γ -Nitroketones are thermally more stable; they can even be distilled with partial cleavage, which goes only one (normal) way. Cyano esters and diesters are relatively stable; the latter show slight decomposition, but not dissociation, on distillation. Ketonic acids are subject to a competing reaction—any Michael reversal is often undetectable by classical chemical methods.

The mass spectrometer is especially well suited for studying reaction mixtures from thermal decompositions because it furnishes mass numbers from which one can speculate usefully about the identity of the cleavage products, and which can provide positive identification when reference spectra are available. This paper discusses the behavior of nitriles, in particular, those of type I, of which a considerable variety are available.

Approximately 1 milligram of each substance studied was allowed to decompose in the glass and metal heated inlet (230°) system (9) of a mass spectrometer over a period of an hour while several spectra were recorded. Many of the reactions were rapid and there was little change in the spectral pattern during this time, indicating that an equilibrium state had been reached before making the first observation. The pattern changes during the hour were sufficient, however, to indicate that the spectra were those of mixtures. Careful measurement showed that the cracking patterns of the components, as identified, remained constant while the ratios of the several components changed with respect to each other during the period of observation. Factors such as rates of reaction, of volatilization, and of effusion through the leak, may account for the changes. For some slower decompositions, decrease in peak size for the original molecule was observed, accompanied by an increase in the pattern size of the products. Mass-spectral peaks which were judged to be probable parent peaks of undissociated molecule-ions formed the initial basis of speculation concerning the identity of components. Identifications were verified by subsequently comparing the entire spectral pattern with those of known reference compounds. Some of the identifications made by mass spectrometry were further confirmed by carrying out independent decompositions on a larger scale in the laboratory, followed by separation and identification by chemical means as well as by infrared and mass spectrometry.

The quantitative aspects of mass spectrometry are well known and might be applied to these studies. Since this work involved substances of widely different vapor pressures, it would have been necessary to establish the limits within which each substance would yield a linear relationship between amount present and peak intensity under the conditions of operation. The scope of the mass-spectrometric work was limited, therefore, to the qualitative identification of the reaction products, thereby establishing the modes of decomposition of the compounds studied. Once the identity of certain of the products was established by mass spectrometry, it was relatively simple to make quantitative

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measurements on these components by gas chromatography on some of the reaction mixtures from decompositions carried out under laboratory conditions.

Both isomers of adduct I, when decomposed in the heated inlet of the mass spectrometer, yielded not only the expected chalcone and benzyl cyanide (1), but also α -phenylcinnamonitrile (III) and acetophenone, the products of a second mode of decomposition.

$C_6H_5CHCH_2COC_6H_5$ \downarrow C_6H_5CHCN	\rightarrow	C ₆ H₅CH ∥ C ₆ H₅CCN	+	CH₃COC ₆ H₅
Ι		III		

The mass spectra also showed the presence of smaller amounts of other materials which we were unable to identify from the spectral peaks. There was no peak for the parent molecule-ion of either diastereomer of I. However, in a subsequent examination of the adducts, using an all-glass heated inlet to minimize thermal degradation, the mass spectra contained the peaks of the products plus the peaks of the undecomposed molecule, including a prominent peak at the mass of the parent molecule-ion. This finding shows that in the examination of these adducts under the original conditions, where no parent peaks of the adducts were found, the mass spectra represented only the reaction products.

Although the mass-spectrometric identifications were confirmed by comparison with reference spectra of known compounds, further proof was obtained to show that the adducts undergo thermal decomposition to yield the identical products. From an independent decomposition, carried out in the laboratory, the four reaction products were isolated and identified by classical methods.

In this paper the re-formation of the original components is called the "normal" reaction and the second mode of retrogression is termed "abnormal." Although presumably reversible, up to now it has not been possible to isolate any of the adduct I from the attempted Michael addition of these abnormal cleavage products, although from the infrared spectrum a small amount might be present.

It now became important to demonstrate the effect of the glass and metal surfaces of the mass spectrometer upon the reversibility of the Michael reaction at the temperature, 230°, of the heated inlet. Series of experiments in which the decompositions were carried out under several conditions in the laboratory were devised to clarify these and other points, using mainly adduct I. The amounts of benzyl cyanide and acetophenone were determined by gas chromatography, the total being taken as a measure of the retrogression. The results are collected in Table I. Quartz and steamed-out soft glass behaved essentially alike at 230°, giving the lowest value, which was used as the standard. At this temperature only normal dissociation occurred; but at 250° the abnormal reaction occurred. The latter was small in quartz, being only 1/10th that taking place in soft glass; hence it must be concluded that the abnormal retrogression is catalyzed to a much greater extent by the alkali present in the glass. This assumption is supported by the results in untreated soft glass at 250°; the normal reaction is of the same order, but the abnormal is doubled. This behavior also accounts for the failure to effect the synthesis of the Michael adduct from the products of the abnormal cleavage (the rate of the latter reaction must be greater than the rate of adduct formation). Retrogression in steamed-out Pyrex glass was, surprisingly, greater than that in soft glass, and approached that shown by metals (lead in the glass?). The metals tested were copper, stainless steel, Kovar alloy, and silver solder; all these are present in the heated inlet. The steel and Kovar were equal, but the silver solder was four times more effective. In the presence of copper, the

SubstanceTotal, $\%$ Normal, $\%C_{\theta}H_{\delta}CH_{2}CN$ Abnormal, $\%CH_{\delta}COC_{\theta}H_{\delta}$ Total, $\%CH_{\delta}COC_{\theta}H_{\delta}CH_{2}CN$ Normal, $\%C_{\theta}H_{\delta}CH_{2}CN$ Abnormal, $\%C_{\theta}H_{\delta}CH_{2}CN$ Formation in the second			At 230° C, 20 minutes			At 250° C, 20 minutes			
I, 109° Isomer1.31.00.35.25.2I, 118° Isomer7.2(*)7.217.611.56.1I, 118° Isomer10.1(*)10.00.111.56.1I, 118° Isomer10.1(*)10.00.118.010.97.1I, 118° Isomer111118.010.97.1I, 118° Isomer111112.85.3**I, 118° Isomer12.612.50.122.410.312.1I, 118° Isomer25.2214.24.210.312.1I, 118° Isomer28.425.03.44.211.511.54-CH ₂ O derivative32.832.50.318.818.00.84-CH ₂ O derivative26(CNCH CO CH)141414.5	Substance	Total, %	Normal, %C6H₅CH2CN	Abnormal, %CH3COC6	H₅	Total, %	Normal, %C6H₅CH2CN	Abnormal, %CH₃COC6H₅	Foot- notes
I, 118° Isomer7.57.517.611.56.1I, 118° Isomer10.1(*)10.00.1I, 118° Isomer111118.010.97.1I, 118° Isomer111118.112.85.3I, 118° Isomer12.612.50.122.410.312.1I, 118° Isomer25.2214.24.210.312.1I, 118° Isomer25.2214.210.312.111I, 118° Isomer25.2213.44.Chloro derivative28.425.03.44-Chloro derivative32.832.50.318.818.00.884-CH_3O derivative11.511.511.511.511.511.5	I, 109° Isomer I, 118° Isomer	$1.3 \\ 7.2(*)$	1.0 7.2	0.3		5.2	5.2		+
I, 118° Isomer111118.010.97.1I, 118° Isomer11111118.112.85.3I, 118° Isomer12.612.50.122.410.312.1I, 118° Isomer25.2214.24.2 4.2 4.2 4.Chloro derivative29.929.50.4 4.2 4.2 4.Chloro derivative28.425.03.4 4.2 4.Chloro derivative32.832.50.3 18.8 18.00.84.CH ₈ O derivative11.511.511.5 11.5 11.5	I, 118° Isomer I, 118° Isomer	7.5 10.1(*)	$\begin{array}{c} 7.5\\10.0\end{array}$	0.1		17.6	11.5	6.1	* \$
1, 113111118.112.8 5.3 **I, 113Isomer12.612.50.1 22.4 10.312.1 11 I, 118° Isomer25.2214.210.312.1 11 I, 118° Isomer29.929.50.414.210.312.1 11 4-Chloro derivative28.425.03.414.214.214.24-Chl ₂ O derivative32.832.50.318.818.00.8 8 4-CH ₂ O derivative11.511.511.5 11.5 11.5 11.5 11.5	I, 118° Isomer	11	11			18.0	10.9	7.1	۹.
I, 118° Isomer 25.2 21 4.2 10.0 12.1 11.1 4-Chloro derivative 29.9 29.5 0.4 4-Chloro derivative 28.4 25.0 3.4 4-Chloro derivative 32.8 32.5 0.3 4-CH ₂ O derivative 18.8 18.0 0.8 4-CH ₂ O derivative 11.5 11.5	I, 118° Isomer	$11 \\ 12.6$	$11 \\ 12.5$	0.1		$ 18.1 \\ 22.4 $	$12.8 \\ 10.3$	5.3 12.1	** ++
4-Chloro derivative 29.9 29.5 0.4 4 -Chloro derivative 28.4 25.0 3.4 4 -Chloro derivative 32.8 32.5 0.3 4 -CH ₄ O derivative 18.8 18.0 0.8 4 -CH ₄ O derivative 11.5 11.5 11.5	I, 118° Isomer	25.2	21	4.2			10.0	12.1	<u>‡</u> ‡
4-Chloro derivative 32.8 32.5 0.3 4-CH ₂ O derivative 18.8 18.0 0.8 4-CH ₂ O derivative 11.5 11.5 11.5	4-Chloro derivative	29.9	29.5 25.0	0.4	3	1			11.11
4-CH ₃ O derivative 18.8 18.0 0.8 3 4-CH ₃ O derivative 11.5 <t< td=""><td>4-Chloro derivative</td><td>32.8</td><td>32.5</td><td>0.3</td><td></td><td></td><td></td><td></td><td>§. §§</td></t<>	4-Chloro derivative	32.8	32.5	0.3					§. §§
Fortry UI 26 (CNCH CO CU) 14 11.0 11.0	4-CH ₃ O derivative		· .		*	18.8	18.0	0.8	Ş,
$\frac{12}{12}$	Ester, VI	26	$(\text{CNCH}_{2}\text{CO}_{2}\text{CH}_{3})$ 12	14		11.5	11.0		§, ¶¶
	\$Steamed-out soft glass only \$Steamed-out Pyrex glass. \$Stainless steel. **Kovar alloy.								

TABLE I Reversal shown by *b*-ketonic nitriles*, †

*Steamed-out soft glass used except in †Gas chromatography data, ± 0.5%. ‡In quartz. \$Steamed-out soft glass only. \$Steinless steel.
**Kovar alloy.
**Kovar alloy.
*TNew, unwashed soft glass.
‡Silver solder.
\$Effect of doubling time, 40 min.
With a condenser.
¶ At 195-215°.

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retrogression started 20° lower and took only two-thirds as long to run to completion. Doubling the time of heating gave only 4% more products, while raising the temperature by 20° increased them by 2.5 times. The reversal could be made complete by allowing the volatile products (nitrile and ketone) to distill (Table II). Quite surprisingly, the lower-

Adduct from:	Total, %	Normal nitrile, %	Abnormal ketone, %	Time, minutes	Decomp. began at ° C
Benzyl cyanide, 109° isomer (I)	99.6	94.5	5.1	19	270
Benzyl cyanide, 118° isomer (I)	100	56	44	24	259
Benzyl cyanide, 118° isomer (I)	92	48	44	14	240
4-Chlorobenzyl cvanide (IV)	99	28	71	15	252^{+}
Methyl cyano- acetate (VI)	84	36	48	20	196

TABLE II Volatiles distilled, Pyrex glass; final bath temperature, $345^{\circ}\pm 5^{\circ}$ C*

*Values determined by gas chromatography. †Acetophenone, the lowest-boiling component, distilled, upsetting the equilibrium.

melting form was much less (one-sixth at 230°, one-fourth at 250°) active. However, the relative proportion of volatile products on distillation was considerably different, the abnormal component (acetophenone) being considerably less. It is concluded from these experiments that the materials used in constructing the heated inlet of the mass spectrometer do affect the rate of the decomposition reactions of these Michael adducts. In all cases the qualitative mass-spectrometric identifications were substantiated.

The thermal decomposition of 22 delta ketonic nitriles were studied in like manner, by allowing them to decompose in the heated inlet of the mass spectrometer. All identifications were confirmed by comparison with reference spectra, and most were further substantiated by classical methods. In addition to the product identification listed in Table III, in many instances there were other products not identified by their peaks in the spectra.

The effect of substitution was determined in a few instances. Nitrile adducts bearing substituents (IV: X, Z = H; Y = 4-Cl, 4-CH₃O, 3-NO₂, 4-NO₂, 4-NH₂) were selected. They all decomposed both normally and abnormally. In the confirming independent laboratory decompositions, gas-chromatographic analysis of the products showed that there was more retrogression of the first two than of the unsubstituted adduct. One type of adduct (IV: $X = CH_3O$; Y, Z = H) gave only the normal products (benzyl cyanide and 4'-methoxychalcone) from the confirming laboratory decomposition at 250°, yet in the mass spectrometer it showed some evidence of a small amount of abnormal dissociation. The mass spectrum of the phenyl analogue (IV: $X = C_6H_5$; Y, Z = H) showed only normal retrogression. The pair of diastereomers (IV: X, Z = H; Y = 4-NO₂) decomposed so badly in a large-scale laboratory decomposition that no useful quantitative results were obtained by gas chromatography.



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Thermal decomposition products identified by mass spectrometer and masses of parent ions, helpful in establishing identification

Substance	Products
I, Both diastereomers	(208) Chalcone; (205) α -phenylcinnamonitrile (Ia); (120) aceto-
IV, X, $Z = H; Y = F$	phenone; (117) benzyl cyanide (223) 4-Fluoro-I <i>a</i> ; (208) chalcone; (135) 4-fluorobenzyl cyanide; (120)
IV, X, Z = H; Y = Cl IV, X, Z = H; Y = 4 -CH ₃ O IV, X, Z = H; Y = 3 -NO ₂	 (239) 4-Chloro-Ia; (208) chalcone; (151) 4-chlorobenzyl cyanide (235) 4-Methoxy-Ia; (208) chalcone; (147) 4-methoxybenzyl cyanide (250) 3-Nitro-Ia; (208) chalcone; (162) 3-nitrobenzyl cyanide; (30) nitric oxide*
IV, X, $Z = H$; $Y = 4$ -NO ₂ (both diastereomers) IV, X, $Z = H$; $Y = 4$ -NH ₂	 (250) 4-Nitro-Ia; (208) chalcone; (162) 4-nitrobenzyl cyanide; (30) nitric oxide* (220) 4-Amino-Ia; (208) chalcone: (132) 4-aminobenzyl cyanide:
(both diastereomers) $V_{x} = CH_{x} + 2 V_{x}$	(120) acetophenone (250) 4 -Nitro I_a : (238) $4'$ -methoxychalcone: (162) 4 -nitrobenzyl
Z = H IV, X = CH ₃ O; Y, Z = H	 (236) 4-Infloria, (203) 4-Infloria (205) 4-Inflo
IV, $X = C_6 H_5$; Y, Z = H Amides of type IV	(284) 4-Phenylchalcone; (117) benzyl cyanide
$X = OCH_3; Y, Z = H$ X, Z = H; Y = 4-NO ₂ V	 (238) 4'-Methoxychalcone; (135) phenylacetamide (208) Chalcone; (137) unidentified (284) Benzaldesoxybenzoin; (205) α-phenylcinnamonitrile; (117) benzyl cyanide
VI, X = H VI, X = Cl	 (208) Chalcone; (187) methyl α-cyanocinnamate; (120) acetophenone (242) 4'-Chlorochalcone; (187) methyl α-cyanocinnamate; (154) 4-chloroacetophenone
VII VIII	(249) UM;† (208) chalcone; (129) cinnamonitrile; (120) acetophenone (173) UM
IX, $Ar' = C_6H_5$ IX, $Ar' = mesityl$ IV, X, Y = H; Z = Br	 (235) UM; (208) chalcone (257) UM; (250) benzalacetomesitylene (208) Chalcone; (205) α-phenylcinnamonitrile; (117) benzyl cyanide
(both diastereomers) IV, $X = H$; $Y = NO_2$; $Z = Br$ XI, $Ar = H$	(208) Chalcone; (162) 4-nitrobenzyl cyanide; (30) nitric oxide* (208) Chalcone; (205) α -phenylcinnamonitrile; (120) acetophenone; (117) hongyl gyanide
XI, $Ar = 4$ -CH ₃ O XI, $Ar = F$	(235) 4-Methoxy-Ia; (208) chalcone; (120) acetophenone (223) 4-Fluoro-Ia; (208) chalcone; (135) 4-fluorobenzyl cyanide; (120) acetophenone
XII (three)	(132) Phenyl vinyl ketone

*Unconfirmed. †Undecomposed molecule.

Both diastereomeric amides (adducts from *p*-nitrophenylacetamide) corresponding to IV $(X, Z = H; Y = 4-NO_2; CONH_2 \text{ for } CN)$ gave only normal retrogression as would be expected; this is due to the relative inactivity of the CONH₂ as compared to the CN in a Michael reaction.

From these very limited data it may be concluded that the nature of the addendum is the most important single factor in the thermal reversal. This conclusion is borne out by quantitatively observing the behavior of one of the methyl cyanoacetate adducts (VI) (4)—retrogression was 26% at a much lower temperature (195–215°) (Table I). The more highly substituted delta ketonic nitrile (V) (5) falls into line (5) since it gives both the normal products (benzaldesoxybenzoin and benzyl cyanide) and one abnormal product (α -phenylcinnamonitrile) in the mass spectrometer decomposition.

 $\begin{array}{ccc} C_6H_5CHCH_2COC_6H_4X-4 & C_6H_5CHCH_2COC_6H_5 \\ & & & & \\ HC(CN)COOCH_8 & CH_2CN \\ VI & VII \end{array}$

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In order to learn the effect of fewer substituents along the chain, other ketonic nitriles were examined. γ -Benzoyl- β -phenylbutyronitrile (VII) (3) gave a parent peak of the undecomposed compound, as well as the normal product (chalcone) formed by loss of acetonitrile, and the abnormal products, cinnamonitrile and acetophenone. γ -Benzoylbutyronitrile (VIII) (6), having no substituents, shows no retrogression at all; this is in agreement with the fact that it distills unchanged. The mass spectrum appeared to be consistent with the structure of the undecomposed molecule, containing a parent peak at m/e 173 and a fragment ion peak at m/e 119 from cleavage of the bond β to the carbonyl. The largest peak was at m/e 105, the C₆H₅ CO⁺ ion. Two gamma ketonic nitriles (IX) which cannot give abnormal products were also examined; undecomposed molecules and chalcones were

CH ₂ CH ₂ COC ₆ H ₅	ArCHCH ₂ COAr'
∣ CH₂CN	ĊN
VIII	IX

found. In none of these last instances could the nitrile be identified because of undetermined contributions to the useful mass-spectral peaks by other components.

Two diastereomeric bromo derivatives (IV: X, Y = H; Z = Br) were also examined. The unsaturated compounds (chalcone, α -phenylcinnamonitrile), formed by both types of retrogression, were found. Benzyl cyanide was also identified, but there was no evidence as to the fate of the bromine. From the decomposition of the nitro derivative (IV: X = H; $Y = NO_2$; Z = Br), chalcone and *p*-nitrobenzyl cyanide, formed by normal retrogression only, were found. There was evidence for the liberation of nitric oxide also, but there were no products of abnormal decomposition. The identification of nitric oxide could not be confirmed in the mass spectrometer because of other possible sources of an NO⁺ ion.

The trimolecular products, which are usually formed in small amounts in the preparation of Michael adducts from chalcones and nitriles, from their infrared absorption in the solid state, are now known to exist in the form of highly substituted cyclohexanols (X) (7). They are easily reversible by heat. The open-chain form (XI) (XI: $Ar = C_6H_5$, 4-CH₃OC₆H₄, 4-FC₆H₄) is obviously a Michael adduct, and is likewise reversible. The laboratory experiments again confirmed the mass-spectrometric identifications (1). The



only recognizable decomposition product from three non-cyclic trimolecular molecules of the type XII (8) was phenyl vinyl ketone, a normal retrogression product.

 $RR'C(CH_2CH_2COC_6H_5)_2$ $R = CN, R' = CN, CONH_2, COOCH_3$

EXPERIMENTAL

Mass Spectrometry

XII

The instrument was a 60° sector type, equipped with a 230° heated inlet system designed to accept readily samples of liquids or solids. The heated inlet (9) is constructed principally of Pyrex glass with some smaller exposed surfaces of stainless steel, Teflon, Kovar metal, silver solder, and platinum. Relatively large samples were introduced resulting, at least in some instances, in excess non-volatilized material, a condition which precludes quantitative treatment of the data.

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Gas Chromatography

The gas-chromatographic separations were carried out in an 8 ft \times 0.25 in. column packed with 25%, by weight, General Electric silicone gum rubber SE-30, on 80–100 mesh Celite 545. The column was thermostatted with boiling *p*-cymene and the flow rate was 50 ml of helium per minute. A Gow-Mac thermoconductivity cell, Model 9285, was used as the detector. The retention times observed were: methyl cyanoacetate, 2.23 minutes; acetophenone, 6.26 minutes; benzyl cyanide, 7.80 minutes; 4-chlorobenzyl cyanide, 18.8 minutes; 4-methoxybenzyl cyanide, 21.7 minutes; 4-methoxyacetophenone, 22.8 minutes.

Thermolyses

The specimens for gas chromatography were prepared as follows. One-gram samples of the adducts in vials were heated simultaneously in an oil bath at two temperatures $(230^\circ, 250^\circ)$ for 20 minutes. Metal "catalysts" were included, as has been mentioned; the silver solder had the composition: 50% silver, 18% cadmium, 15.5% copper, and 10.5% zinc. The decomposition products were introduced into the chromatograph as ethyl acetate solutions; chalcone was not estimated since its amount would be equivalent to the benzyl cyanide.

The new soft-glass vials received a hot trisodium phosphate wash, followed by five rinses (in one instance, hydrochloric acid was used as a rinse, but the result was unchanged) and drying at 110°. Vials, steamed out for 10 minutes and dried at 110°, likewise gave a comparable result. In the instances in which all the volatiles were distilled, 5 g of adduct in a 25-ml Pyrex distilling flask was heated in an oil bath as long as distillate collected (Table I). The main features of the findings have already been mentioned.

Reagents and Chemical Reactions

The reagents used were Eastman chemicals except p-fluorobenzyl cyanide (10) and 4-aminobenzyl cyanide. The fluoro compound was quite acidic, requiring considerable sodium methoxide in the addition reaction before an alkaline test in moist litmus was obtained. Since Pschorr's procedure (11) (reduction of p-nitrobenzyl cyanide by tin and hydrochloric acid) gives a very pure aminonitrile in a high yield, this was followed. Selective catalytic reduction, using 10% palladium on charcoal, gave a very complex mixture.

Many of the adducts and reference compounds required in this and in the following papers were available from previous work. New 4-substituted- α -phenylcinnamonitriles were synthesized by the usual procedure using sodium methoxide, except for the 4-nitro, in which case Triton B was employed. For example, a mixture of 1.5 g of *p*-nitrobenzyl cyanide, 1 ml of benzaldehyde, and 10 ml of alcohol was heated to dissolve the solid, and five drops of Triton B were added. The initial magenta color quickly became greenish, the solvent boiled, and the solid product crystallized shortly. The yield was quantitative. The buff solid, m.p. 177-178°, was rinsed with methanol to remove most of the green color, and recrystallized from propyl alcohol.

The new delta ketonic nitriles of type I were prepared either in the continuous reactor (12), which gives more of the higher-melting isomer, or batchwise, using only a small amount of sodium methoxide as catalyst. The yield of crystalline mixed adduct was 85–87%; the sticky residue that did not crystallize appeared to be mainly the same adducts, according to infrared spectrometry. Only one of the two possible diastereomeric forms of the new adducts (IV: X, Z = H; 4-Y = F, Cl, OCH₃, 3-NO₂; Y, Z = H; X = C₆H₅) was isolated. Mixtures tended to oil out; the anisyl adduct crystallized readily from solutions if the latter were seeded with a little previously prepared sample. The 4-fluoro derivative did not separate from the oil for a month. Tedious fractional crystallizations from petroleum ether and also from methanol afforded no separation; in the previous instances it had been fortuitous with I, but very easy with IV (X, Z = H; Y = NO₂). The various since the differences were of degree rather than in kind, it was unnecessary to have both pure forms. A little trimolecular product (X) was separated during the first recrystallization of each of the adducts except the amino derivatives.

Both 4-amino adducts were obtained, however, one by addition and the other by selective catalytic reduction of the corresponding nitro adducts (13). The addition takes place (6 hours) at room temperature, after this mixture had been warmed enough to produce complete solution. Prolonged heating gives a complex mixture from which an impure amine can be isolated only with difficulty. In the catalytic reduction procedure, both adducts (m.p. 126° and 143°) gave 50% yields of the same amine, isomeric with the one produced on addition. The remainder of the product was an intractable yellow pitch. A solution of 32.5 g of nitro adduct in 370 ml of dioxane, containing 1 g of 10% palladium on charcoal, was shaken at room temperature and 60 p.s.i. of hydrogen until the theoretical amount was absorbed (24 hours). Most of the solvent was distilled. The residue was a sticky pitch in which a white solid had formed after 3 weeks. Methanol was added to facilitate manipulation, the solid was collected on a filter, and recrystallized.

The properties of the new substances are listed in Table IV.

All attempts to bring about formation of the Michael adducts (I) from the products of the abnormal dissociation (acetophenone and α -phenylcinnamonitrile) have so far been fruitless; conditions employed included changes in time, catalyst, and solvent. Either the cinnamonitrile, which crystallizes well from mixtures, or a sticky glue resulted. Occurrence of addition would have been indicated by the presence of the known adducts, detectable by infrared spectrometry, or the easily isolable trimolecular product (X),

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TABLE IV Properties of new substances

C	'N	Analyses						
C ₆ H ₅ CH=C	с—С ₆ Н ₄ Х-4	α -(4X-Phenyl)	•	Calc.			Found	
X	M.p., ° C	emp. formula	С	Н	N	C	Н	N
F Cl NO ₂ CH ₃ O	107^{*} 115–116† 179–180‡ 96–97†	$\begin{array}{c} C_{15}H_{10}FN\\ C_{15}H_{10}ClN\\ C_{15}H_{10}N_2O_2\\ C_{16}H_{13}NO \end{array}$	$80.7 \\ 75.2 \\ 72.0 \\ 81.7$	$\begin{array}{c} 4.5 \\ 4.2 \\ 4.0 \\ 5.5 \end{array}$	$6.3 \\ 14.8 \\ 11.2 \\ 6.0$	$80.5 \\ 75.0 \\ 72.0 \\ 82.0$	$4.6 \\ 3.9 \\ 3.9 \\ 5.5$	$6.2 \\ 14.8 \\ 11.6 \\ 5.6$
Michael add C ₆ H ₅ 4-F 4-Cl its DNPH 4-CH ₃ O 3-NO ₂ 4-NH ₂	ucts (IV) $Y =$ 116‡ 94–95* 128–129* 96 124–125* 134–135‡ 163‡, **	$\begin{array}{c} : H \\ C_{29}H_{23}NO \\ C_{23}H_{18}FNO \\ C_{23}H_{15}CINO \\ C_{29}H_{22}CIN_5O_4 \\ C_{24}H_{21}NO_2 \\ C_{24}H_{18}N_2O_3 \\ C_{23}H_{20}N_2O \end{array}$	$86.8 \\ 80.5 \\ 76.3 \\ 81.1 \\ 74.6 \\ 81.2$	$5.7 \\ 5.3 \\ 5.0 \\ 6.5 \\ 5.9 \\ 4.9 \\ 5.9 $	3.5 4.1 9.9 13.0 3.9 7.6 8.2	$87.1 \\ 80.2 \\ 76.2 \\ 81.0 \\ 74.9 \\ 80.8 \\$	5.6 - 5.6 - 5.6 - 5.6 - 5.9 - 5.9 - 5.9 - 5.9 - 5.0	3.1 4.1 9.8 12.8 3.6 7.3 8.6

*From methanol. †From ethanol. ‡From propanol. §% chlorine. ||By reduction. *By addition. *Mixed melting point, 141–143°.

or the known 2-oxo-1,2,3,4-tetrahydro-3,4,6-triphenylpyridine (1) which has a very brilliant blue fluorescence when exposed to ultraviolet light. The uncrystallizable glue from these attempts (as well as the residual oil from the normal preparation) always shows a blue fluorescence, but there was insufficient adduct to be isolated or detected by infrared spectrometry.

Tetrahydropyridine formation from delta ketonic nitriles under alkaline conditions (14) was successful with the latter only if they were not highly substituted. The triphenyl derivative (I), when treated in the same way, gives the trimolecular product (X) as previously determined (1) and now reconfirmed; the accompanying uncrystallizable portion does show a similar blue fluorescence.

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