Studies in Mass Spectrometry. X.[1] High-Resolution Mass Spectra of Cyanoacetates. Alkyl Migrations upon Electron Impact

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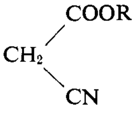
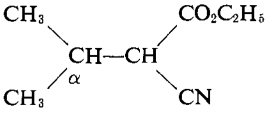
Abstract: The mass spectra of a number of methyl and ethyl cyanoacetates have been determined and interpreted by means of high-resolution measurements and deuterium labeling. Important fragmentation paths upon electron impact occur by elimination of the elements of CO_2 from the ester group with an associated methyl or ethyl migration.

The fragmentation reactions of aliphatic cyanides upon electron impact are relatively complicated.[4-6] A study of cyanoacetates has now been undertaken to see if these compounds behave in a simple manner analogous to other active methylene compounds (β-keto esters,[7] diethyl malonates,[8] and β-diketones[9]), or if the complex behavior of aliphatic cyanides is exhibited.

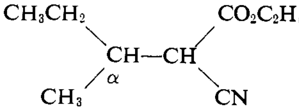
The mass spectra of methyl cyanoacetate (I), ethyl cyanoacetate (II), and the alkyl derivatives III–VII have been determined and are illustrated in Figures 1–7. Generally speaking, these spectra contain low-abundance molecular ions and frequently appreciable M + 2 peaks, in contrast to alkyl cyanides, which exhibit M − 1 and M + 1 peaks in their mass spectra.[4-6]



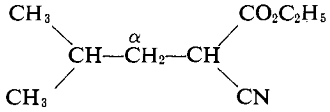
I, R = CH_3
II, R = C_2H_5



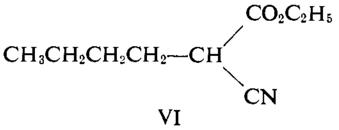
III



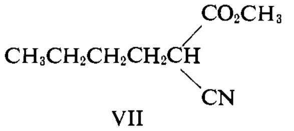
IV



V

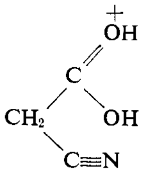


VI

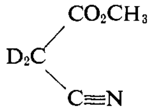


VII

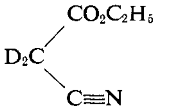
Conventional fragmentation processes which are evident in the mass spectra (Figures 1 and 2) of methyl cyanoacetate (I) and ethyl cyanoacetate (II) are summarised in the figures;[10] the elimination of C_2H_3 from the ethyl group of II can occur with the formation of the protonated acid ion a.[11] However, high-resolution measurements uncover two very unusual features in these spectra, namely, that I can decompose by loss of CO_2 to *m/e* 55 ($C_3H_5N^+$) (and hence by loss of a hydrogen radical to *m/e* 54 ($C_3H_4N^+$)), while II can eliminate HCO_2 to afford *m/e* 68 ($C_4H_6N^+$ (10% of the base peak intensity), the remaining 90% of this peak arising *via* elimination of the ethoxyl group to give $C_3H_2NO^+$). These processes necessitate interesting alkyl migrations of a methyl group and an ethyl group (or ethylene or its equivalent), respectively, upon electron impact. All the fragmentation reactions proposed for I and II are supported by the spectra of the partially deuterated derivatives Ia and IIa, which were obtained by introduction of the esters into the inlet system of the spectrometer with deuterium oxide.[12]



a, *m/e* 86



Ia, d_0 = 43%
d_1 = 36%
d_2 = 21%



IIa, d_0 = 20%
d_1 = 41%
d_2 = 39%

Fragmentation processes which necessitate the elimination of CO_2 with an associated alkyl migration[13] are extremely important in the spectra of ethyl isopropylcyanoacetate (III, Figure 3a), the isomeric butyl derivatives IV, V, and VI (Figures 4, 5, and 6), and of methyl *n*-butylcyanoacetate (VII, Figure 7). The compositions of the fragment ions associated with many of the intense peaks in these spectra have been determined by exact mass measurements and are summarized in Table I. A list of relevant metastable ions occurring in the spectra of III–VII is given in Table II, which gives both observed and calculated values.

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[1] Part IX: see ref 9.

[2] University Chemical Laboratory, Cambridge, England.

[3] Department of Organic Chemistry, Aarhus University, Aarhus, Denmark.

[4] F. W. McLafferty, *Anal. Chem.*, **34**, 26 (1962).

[5] R. Beugelmans, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 1386 (1964).

[6] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964.

[7] J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Am. Chem. Soc.*, **87**, 5742 (1965).

[8] J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Org. Chem.*, in press.

[9] J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *ibid.*, in press.

[10] Throughout this paper, transitions supported by an appropriate metastable peak are indicated by an asterisk (*).

[11] See, for example, A. G. Harrison and E. G. Jones, *Can. J. Chem.*, **43**, 960 (1965).

[12] J. S. Shannon, *Australian J. Chem.*, **15**, 265 (1962).

[13] For additional examples of the decomposition of esters by elimination of CO_2 upon electron impact, see J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson, and G. Schroll, *Chem. Commun.* (London), 403 (1965), and P. Natalis and J. L. Franklin, *J. Phys. Chem.*, **69**, 2943 (1965).

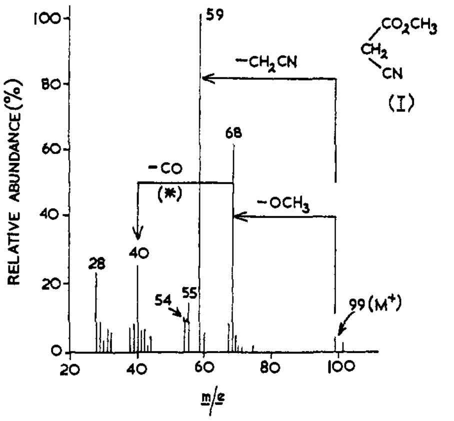


Figure 1. Mass spectrum of methyl cyanoacetate (I).

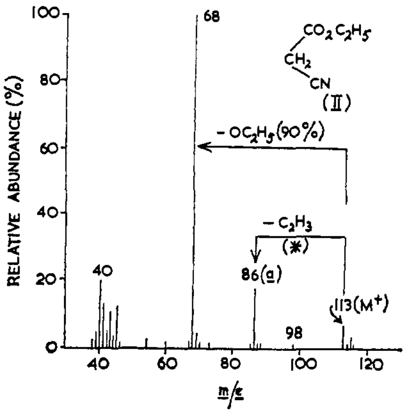


Figure 2. Mass spectrum of ethyl cyanoacetate (II).

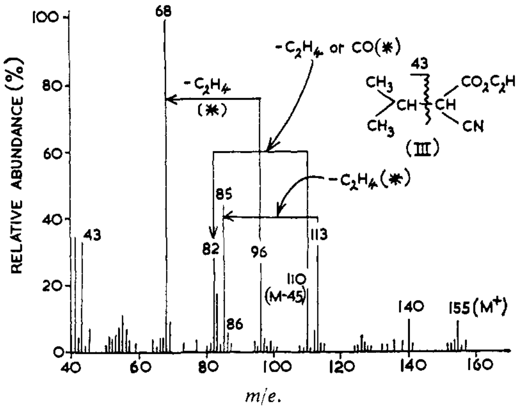


Figure 3a. Mass spectrum of ethyl isopropylcyanoacetate (III).

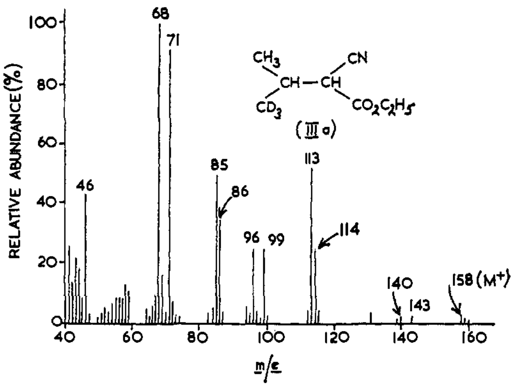


Figure 3b. Mass spectrum of ethyl d_3-isopropylcyanoacetate (IIIa).

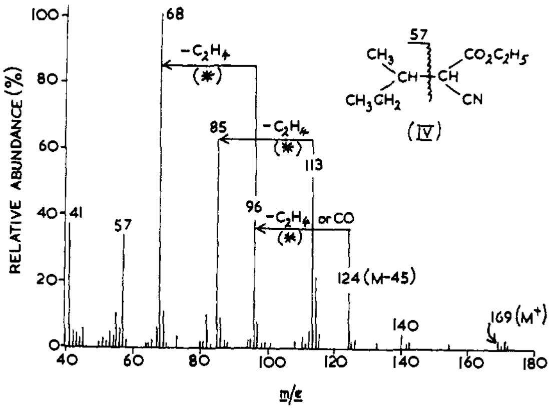


Figure 4. Mass spectrum of ethyl *sec*-butylcyanoacetate (IV).

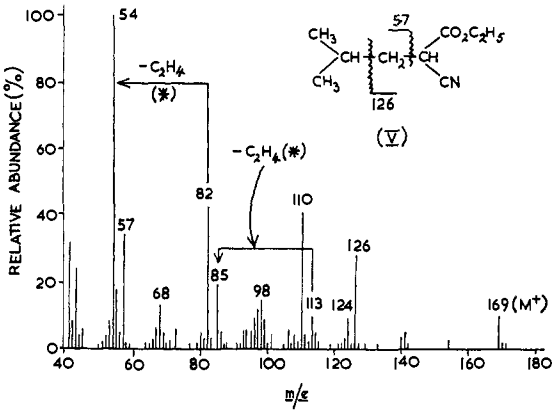


Figure 5. Mass spectrum of ethyl isobutylcyanoacetate (V).

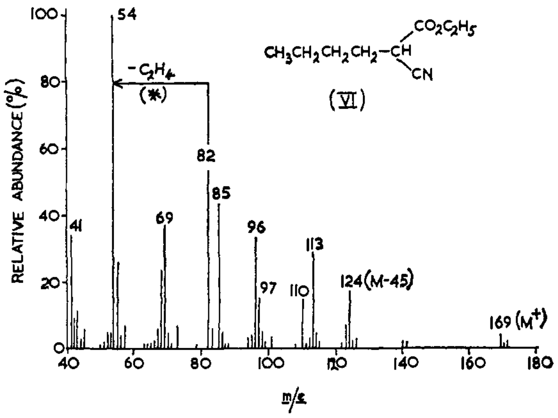


Figure 6. Mass spectrum of ethyl *n*-butylcyanoacetate (VI).

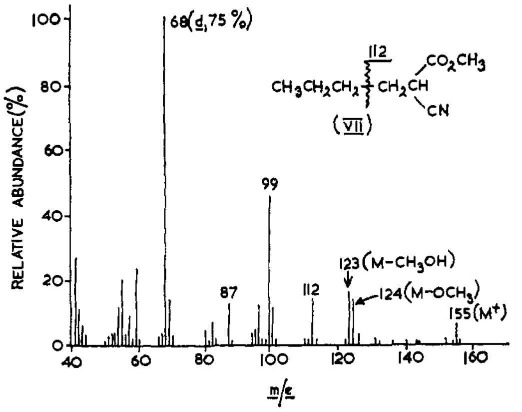


Figure 7. Mass spectrum of methyl *n*-butylcyanoacetate (VII).

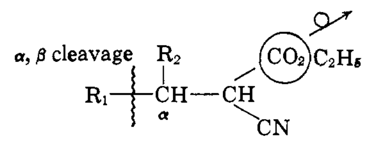
Table I. Compositions of Some of the Major Fragment Ions in the Mass Spectra of the Cyanoacetates III–VII

m/e values	Compound, % III	IV	V	VI	VII
54			C_3H_4N	C_3H_4N	
57		C_4H_9	C_4H_9		
68	C_4H_6N, 80 C_3H_2NO, 20	C_4H_6N	C_3H_2NO, 65 C_4H_6N, 35	C_4H_6N, 65 C_3H_2NO, 35	C_4H_6N, 75 C_3H_2NO, 25
69				C_4H_7N, 60 C_5H_9, 40	
82	C_5H_8N		C_5H_8N	C_5H_8N	
85	$C_3H_3NO_2$	$C_3H_3NO_2$	$C_3H_3NO_2$	$C_3H_3NO_2$	
87					$C_4H_7O_2$
96	$C_6H_{10}N$	$C_6H_{10}N$	$C_6H_{10}N$	$C_6H_{10}N$	
97			$C_6H_{11}N$, 80 C_6H_9O, 20		
98			$C_4H_4NO_2$		
99					$C_4H_5NO_2$
110	C_6H_8NO, 65 $C_7H_{12}N$, 35		$C_7H_{12}N$	$C_7H_{12}N$	
112					$C_5H_6NO_2$
113	$C_5H_7NO_2$	$C_5H_7NO_2$			
123					C_7H_9NO
124		$C_7H_{10}NO$, 80 $C_8H_{14}N$, 20		$C_7H_{10}NO$, 83 $C_8H_{14}N$, 17	

Table II. Some Metastable Ions (Calculated and Observed Values) Found in the Spectra of III–VII

Compd	Obsd	Calcd	Transition
III	64.0	63.9	113 → 85
	61.2	61.1	110 → 82
	48.1	48.2	96 → 68
IV	74.5	74.5	124 → 96
	64.0	63.9	113 → 85
	48.1	48.2	96 → 68
V	76.1	76.2	126 → 98
	64.0	63.9	113 → 85
	35.5	35.6	82 → 54
VI	35.5	35.6	82 → 54
VII	73.5	73.4	123 → 95

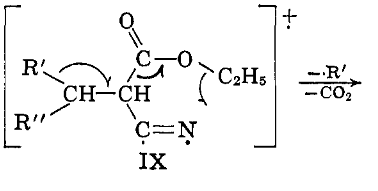
The most outstanding difference between the spectra (Figures 3–6) of the substituted ethyl cyanoacetates (III–VI) is that V and VI, which have no α branching in the alkyl substituent, give rise to base peaks at *m/e* 54 ($C_3H_4N^+$), while III and IV, which are α branched (with a methyl substituent at the branched α position), afford base peaks at *m/e* 68 ($C_4H_6N^+$ (80%) and $C_4H_6N^+$ (100%) from III and IV, respectively). Metastable peaks at 35.5 in the spectra of V and VI indicate that the $C_3H_4N^+$ ions (*m/e* 54) are formed by elimination of ethylene from a $C_5H_8N^+$ species (*m/e* 82), whereas metastable peaks at 48.1 in the spectra of III and IV likewise establish the formation of the $C_4H_6N^+$ ions (*m/e* 68) from $C_6H_{10}N^+$ ions (*m/e* 96), again by elimination of ethylene (see Figures 3–6). Evidently, the most pronounced decomposition pathway of V and VI upon electron impact is *via* the over-all elimination of C_3H_7 and CO_2 to *m/e* 82 ($C_5H_8N^+$) (and hence by loss of ethylene to *m/e* 54), whereas III and IV prefer to eliminate (CH_3 + CO_2) and (C_2H_5 + CO_2), respectively, to give *m/e* 96 ($C_6H_{10}N^+$) and subsequently *m/e* 68 by loss of ethylene. Hence, it may be seen that the spectra can only be interpreted in a self-consistent manner if the major fragmentation mainly involves the loss of CO_2 from the ester group (with an accompanying ethyl migration) and associated cleavage of the C(α)–C(β) bond in the alkyl substituent to eliminate the larger available radical (see VIII).



VIII

III, $R_1 = R_2 = CH_3$
IV, $R_1 = C_2H_5$; $R_2 = CH_3$
V, $R_1 = i\text{-}C_3H_7$; $R_2 = H$
VI, $R_1 = n\text{-}C_3H_7$; $R_2 = H$

The apparent occurrence of such remarkable rearrangement processes requires supporting evidence. It should be pointed out that the formation of a $C_6H_{10}N^+$ ion (*m/e* 96, M − CH_3CO_2) in the spectrum (Figure 3a) of III demands some kind of alkyl migration from the ethyl group of the ester. The spectrum (Figure 3b) of the trideuterio derivative of III (IIIa) establishes that the intact ethyl group migrates and that a terminal methyl group is lost from the isopropyl substituent. The observation that the *m/e* 68 and *m/e* 96 peaks of Figure 3a are both split into *m/e* 68/71 and *m/e* 96/99 doublets in Figure 3b indicates that in the transition *m/e* 96 → *m/e* 68 ethylene is expelled from the ethyl group which was originally part of the ester. While any mechanistic proposals concerning these migrations must be regarded as speculative, it seems very reasonable to implicate the cyano group in the rearrangement step, since such processes have not been noted in the spectra of simple esters. One possibility is that the energy of the electron bombardment is sufficient to uncouple a pair of π electrons of the cyano group, and then the elimination of an alkyl radical R′ and CO_2



IX

$$R''{-}CH{=}CH{-}C{\equiv}\overset{+}{N}C_2H_5 \xrightarrow[*]{-C_2H_4} R''{-}CH{=}CH{-}C{\equiv}\overset{+}{N}H$$

b, $R'' = CH_3$; *m/e* 96
$R'' = H$; *m/e* 82

c, $R'' = CH_3$; *m/e* 68
$R'' = H$; *m/e* 54

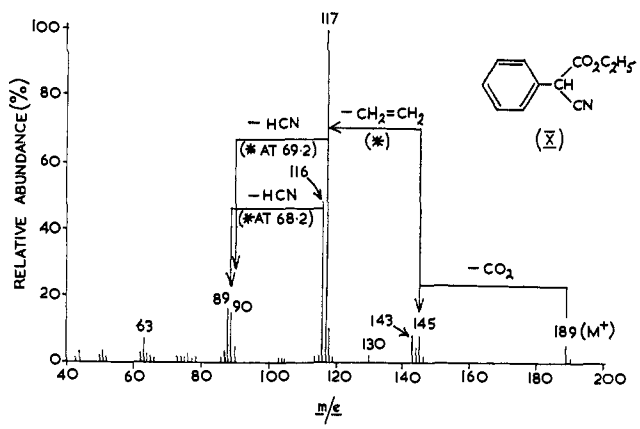
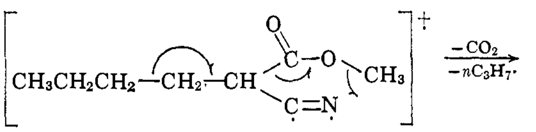


Figure 8. Mass spectrum of ethyl phenylcyanoacetate (X).

can occur with associated ethyl migration to nitrogen (IX → b); subsequent loss of ethylene may then afford c. Hence *m/e* 96 and *m/e* 68 will result when R″ = CH_3 (from III and IV), and *m/e* 82 and *m/e* 54 when R″ = H (from V and VI).

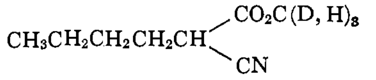
Additional evidence for this type of rearrangement has been sought in the mass spectrum (Figure 7) of methyl *n*-butylcyanoacetate (VII). On the basis of the spectrum (Figure 6) of the corresponding ethyl ester (VI), the base peak in the spectrum of VII should be anticipated at *m/e* 68 ($C_4H_6N^+$) perhaps corresponding to structure d. It should be noted that d is not, of course, able to eliminate ethylene and, in addition, no loss of methylene from d is anticipated since this is known to be an energetically unfavorable process.[14] In fact, *m/e* 68 is the base peak of Figure 7 and has been shown by exact mass measurements to correspond to the extent of 75% to $C_4H_6N^+$ (see Table I). Moreover, in the spectrum of the partially deuterated ester VIIa, prepared by esterification of the acid with diazomethane in the presence of deuterium oxide,[15] the $C_4H_6N^+$ ion retains the isotopic label, thus unequivocally establishing the methyl migration.



VII

$CH_2{=}CH{-}C{\equiv}\overset{+}{N}CH_3$

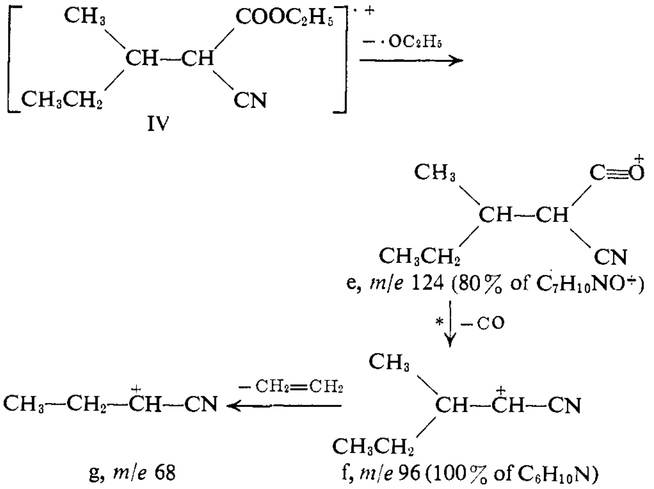
d, *m/e* 68



$CH_3CH_2CH_2CH_2CH(CO_2C(D,H)_3)(CN)$

VIIa, d_0 = 38%; d_1 = 38%; d_2 = 20%; d_3 = 4%

However, there is no definite evidence that the formation of the ions represented by b and d occurs in a one-step process. Indeed, in the spectrum (Figure 4) of IV there is some evidence that ions corresponding to b *in composition* cannot arise completely *via* a one-step process. In this case (Figure 4), a metastable peak indicates that *m/e* 96 ($C_6H_{10}N^+$) can arise, at least in part, by elision of ethylene from $C_8H_{14}N^+$ (20% of *m/e* 124, M − CO_2H) or loss of carbon monoxide from $C_7H_{10}NO^+$ (80% of *m/e* 124, M − OC_2H_5). It is therefore possible that in the spectrum of IV some portion of the *m/e* 68 ion is formed by the more conventional sequence IV → e → f → g.



IV

e, *m/e* 124 (80% of $C_7H_{10}NO^+$)

f, *m/e* 96 (100% of $C_6H_{10}N$)

g, *m/e* 68

In the spectra (Figures 3a, 4, and 5) of III, IV, and V the M − 45 ions were of sufficient abundance to warrant investigation by exact mass measurements. The results (Table I) establish that in all three spectra extremely unusual M − HCO_2 ions accompany the anticipated M − OC_2H_5 fragments; the formation of the former group again requires an ethyl (or ethylene) migration from the ester, perhaps in a manner similar to that discussed previously. Finally the *m/e* 110 ions ($C_7H_{12}N^+$; M − CH_3CO_2) furnished by V and VI are presumably formed by related rearrangement processes (perhaps loss of carbon dioxide and a terminal methyl group in each case).

More conventional fragmentation processes which are evident from the spectra of these cyanoacetates merit brief comment. The spectra of all the substituted ethyl esters (III–VI) contain fairly abundant *m/e* 113 ions, shown by representative exact mass measurements (Table I) to arise through the elimination of the alkyl substituent (presumably as the olefin) with hydrogen rearrangement. The hydrogen atom involved in the rearrangement originates from the β-carbon atom of the alkyl group in the spectrum (Figure 3a) of III, as may be seen on examination of Figure 3b.[16] Probably a McLafferty rearrangement is operative (see III → h), although hydrogen rearrangement to nitrogen cannot be excluded. However, hydrogen rearrangement to carbon (see III → i) to give the ethyl cyanoacetate molecular ion is untenable, because the *m/e* 113 ions decompose by explusion of ethylene to an *m/e* 85 species ($C_3H_3NO_2^+$, see Table I and Figures 3a, 4, and 5), in contrast to the behavior of the ethyl cyanoacetate molecular ion which eliminates C_2H_3 to afford *m/e* 86 (see Figure 2). A plausible representation for the *m/e* 85 ions is j, although it should be noted that they do not show any marked tendency to eliminate water (contrast the decomposition of analogous ions from β-keto esters[7] and diethyl malonates[8]).

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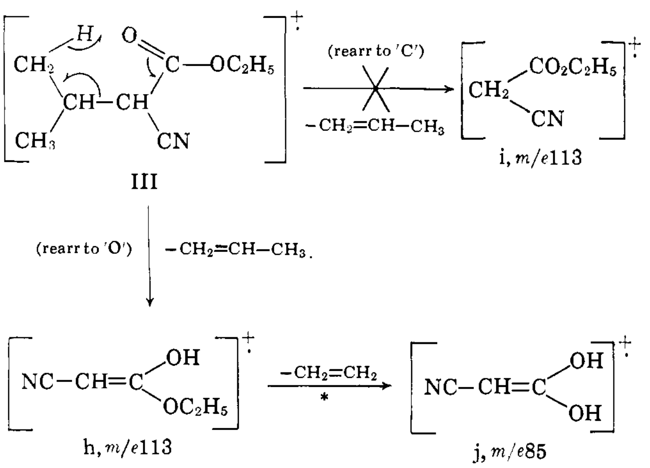
(14) For a summary of the isolated examples of loss of CH_2 from the parent ion of a hydrocarbon, see S. Meyerson, *J. Am. Chem. Soc.*, **85**, 3340 (1963).

(15) K. J. van der Merwe, P. S. Steyn and S. H. Eggers, *Tetrahedron Letters*, 3923 (1964).

(16) The shifts which can be discerned on comparison of Figures 3a and 3b are *m/e* 110 → *m/e* 113 and *m/e* 113 → *m/e* 114 (~50%), while approximately 50% of *m/e* 113 is not shifted, because either a CH_3 or CD_3 group may participate in the rearrangement process.



The mass spectrum (Figure 8) of ethyl phenylcyanoacetate (X) has been briefly mentioned in an earlier communication.[17] The *m*/*e* 145 ion is formed by elimination of CO_2 from the molecular ion and can then lose a methyl radical or ethylene (from the ethyl group at its new site of attachment) to give *m*/*e* 130 and *m*/*e* 117, respectively. However, there is no evidence for additional rearrangement ions in this spectrum, the *m*/*e* 143 and *m*/*e* 144 ions arising by simple loss of ethanol and an ethoxyl radical, respectively. It is of course possible for the *m*/*e* 117 ion ($M - CO_2C_2H_4$) to arise in part other than *via* a skeletal rearrangement pathway, but, regardless of its mode of formation, a portion of this $C_8H_7N^+$ ion does have the structure of the benzyl cyanide molecular ion, as evidenced by the very similar spectra of the two compounds below *m*/*e* 117 and identical metastable peaks at *m*/*e* 88.5, *m*/*e* 69.2, and *m*/*e* 68.2.

Experimental Section

All mass spectra were obtained on an AEI MS 9 mass spectrometer operating at 70 ev. Samples were introduced into the ion chamber through a heated inlet system operating at approximately 150°.

Exact mass measurements were performed either against reference masses in the spectrum of heptacosafluorotributylamine or against ions of previously established composition in the spectrum of the cyanoacetate itself. The measurements were performed at a resolving power of approximately 15,000 (10% valley definition) and calculated and observed values were always in agreement within 15 ppm, thus rigorously excluding alternative compositions.

Methyl cyanoacetate (I) and ethyl cyanoacetate (II) were commercial samples. Known procedures were employed for the preparation of ethyl propylcyanoacetate (III),[18] ethyl *sec*-butylcyanoacetate (IV),[19] ethyl isobutylcyanoacetate (V),[20] ethyl *n*-butylcyanoacetate (VI),[20] and ethyl phenylcyanoacetate (X).[21] Ethyl (3-trideuteriomethyl)ethylcyanoacetate (IIIa, bp 95.5–96.5° (12 mm), n^{25}D 1.4215) was prepared by a Grignard reaction, using the addition of trideuteriomethylmagnesium iodide to ethyl ethylidenecyanoacetate.

Methyl *n*-butylcyanoacetate (VII, bp 111° (11 mm), n^{20}D 1.4281) was available by alkylation of methyl cyanoacetate in methanol. *Anal.* Calcd for $C_8H_{13}NO_2$: C, 61.95; H, 8.44; N, 9.03. Found: C, 61.74; H, 8.55; N, 8.98.

All compounds were distilled at least twice and their purities were checked by nuclear magnetic resonance, infrared, and mass spectroscopy, and also by vapor phase chromatography. The analysis was performed by Alfred Bernhardt, Mülheim (Ruhr), Germany.

Acknowledgment. One of us (J. H. B.) is grateful for the award of an ICI Postdoctoral Fellowhsip.

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[17] See the first reference quoted in footnote 13.

[18] E. Fischer and E. Flatau, *Chem. Ber.*, **42**, 2981 (1909).

[19] P. E. Gagnow, U. Savard, R. Gaudry, and E. M. Richardson, *Can. J. Res.*, **25**, 30 (1947).

[20] J. C. Hessler and W. F. Henderson, *J. Am. Chem. Soc.*, **43**, 672 (1921).

[21] S. Widequist, *Arkiv Kemi Mineral Geol.*, **24B**(14) (1947).