Mass Spectra of Dicyanomethylene Derivatives of Benzophenone Analogs

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The dicyanomethylene derivative of a benzophenone analog significantly alters the fragmentation pattern observed during electron impact ionization of the underivatized parent compound. A double bond connecting the dicyanomethylene moiety to the parent compound is cleaved during a major fragmentation pathway for many of these compounds. A mechanism involving rearrangement of two hydrogen atoms is proposed to rationalize cleavage of this double bond. Conventional mass spectra as well as collisionally activated dissociation mass spectra of selected ions of several model compounds are reported and described in support of a proposed fragmentation mechanism.

INTRODUCTION

In the course of characterizing the dicyanomethylene (DCM) derivatives (1) of ketogenic compounds by mass spectrometry, it was observed that many of the benzophenone DCM derivatives undergo cleavage of the double bond connecting the parent structure and the DCM moiety. This report focuses on a possible mechanism to rationalize cleavage of this double bond by an intramolecular rearrangement involving migration of two hydrogen atoms. The mass spectra of several model compounds including stable-isotopelabelled analogs are reported to support the suggestion that many of these compounds undergo decomposition to a fluorene-like fragment ion of mass 165. A triple quadrupole mass spectrometer was used to obtain identical collisionally activated dissociation (CAD) mass spectra of the putative fluorene-like fragment ion from each of several related compounds.

The dicyanomethylene (DCM) derivative (1) of ketogenic compounds results from condensation of malononitrile with the carbonyl moiety^{1,2} as indicated in Scheme 1.



EXPERIMENTAL

Electron impact (EI) ionization mass spectra were obtained either with a Hewlett–Packard 5985A GC-MS-DS or with a Finnigan 4000 GC-MS-DS. Samples were introduced through a 3% OV-1 or 3% SP-2100 GLC column $(2 \text{ m} \times 2 \text{ mm})$ at temperatures in the range 150–200 °C. Exact mass measurements were performed by peak matching on a Varian-MAT CH-5 double focusing instrument with sample introduction by direct probe. Collisionally activated dissociation

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(CAD) mass spectra were obtained with an Extranuclear Laboratories triple quadrupole mass spectrometer with sample introduction by direct probe. In all cases, the ionizing voltage was 70 eV and the ion source temperature was 200 °C. The CAD spectra were obtained with a pressure of 1×10^{-2} Torr of argon in the collision cell (second quadrupole).

The dicyanomethylene (DCM) derivative was prepared by condensing the ketone with malononitrile in the presence of a buffer consisting of ammonium acetate and acetic acid in ethyl acetate. This mixture was then refluxed for approximately 4 hours. Yields varied from 10 to 90%; no attempts were made to optimize DCM derivative production. Frequently, the reaction product would be accompanied by dark colored by-products (polymer of malononitrile?) which were readily separated by TLC.

Most of the model compounds were prepared from benzophenone analogs which were commercially available. Pentadeuterobenzophenone was synthesized from hexadeuterobenzene and benzoyl chloride by conventional methods. The DCM 2,4-dimethylbenzophenone was prepared from bromobenzene and 2,4-dimethylbenzonitrile.³ 9-Dicyanomethylfluorene (**3**) was prepared by reduction of compound **2** (condensation product of 9-fluorenone and malononitrile) by LiAlH₄.

RESULTS AND DISCUSSION

The mass spectrum of the DCM derivative of benzophenone (1; $R = R' = C_6H_5$) is presented in Fig. 1. The base peak at m/z 165 ($[M-65]^+$) corresponds to the loss of 'CH(CN)₂ from the molecular ion (confirmed by exact mass measurement at 165.0696 compared to calculated value of 165.0704 for $C_{13}H_9$); this elimination requires cleavage of a double bond. The proposed mechanism for this elimination is shown in Scheme 2.

This mechanism suggests that the molecular ion of the DCM derivative of benzophenone (1; $R = R' = C_6H_5$) which undergoes this elimination rearranges to

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Figure 1. Mass spectrum of dicyanomethylene derivative of benzophenone (1; $R = R' = C_6H_5$).



Scheme 2

a fluorene-like structure upon electron impact. To assess this possibility, authentic 9-dicyanomethylfluorene (3) was prepared by reduction of 9dicyanomethylenefluorene (2) according to the method of Collins and Hobbs.⁴ The mass spectrum of 9dicyanomethylfluorene (3) is presented in Fig. 2; note that it too is characterized by a base peak at m/z 165 corresponding to loss of 'CH(CN)₂ from the molecular ion (confirmed by exact mass measurement of 165.0699 compared to 165.0704 calculated for $C_{13}H_9$).



To obtain direct evidence that the ion of mass 165 in the mass spectra of the DCM derivative of benzophenone $(\mathbf{1}; \mathbf{R} = \mathbf{R}' = \mathbf{C}_6 \mathbf{H}_5)$, 9-dicyanomethylfluorene (3), fluorene (4; R = H) and 9-bromofluorene (4; R = Br) have comparable structural features, this ion from each compound during EI was subjected to collisionally activated dissociation (CAD). The relative importance of this ion of mass 165 in the EI mass spectrum of each compound can be seen in Fig. 1 and Table 1. The results of CAD analysis of m/z 165 using a triple quadrupole mass spectrometer are shown in graphical form in Fig. 3 and in tabular form in Table 2. The most prominent daughter ions appear to result from loss of hydrogen, elements of acetylene and 1.3-butadiene from the parent ion $(m/z \ 165)$ to produce peaks at m/z 164, 139 and 115, respectively. The



Figure 2. Mass spectrum of 9-dicyanomethylfluorene (3).

Table 1. Abbreviated tabular EI mass spectra of fluorene derivatives							
Compound name	Relative abundance						
	M	m/z 165					
9-Dicyano-		100%					
methylfluorene (3)	m/z 230(13%)	[M-CH(CN) ₂] ⁺					
Fluorene (4; R = H)	m/z 166(100%)	90%					
		[M-H]+					
9-Bromofluorene	m/z 244(7%)	100%					
(4; R = Br)		[M-Br]+					

data are normalized to the ion current at m/z 164, the most abundant daughter ion. The abundance of the parent ion $(m/z \ 165)$ was 2-3 times greater than that of m/z 164 during replicate CAD analyses of m/z 165 from' these four compounds. The daughter ion mass spectra of m/z 165 from these four compounds are identical within experimental error. These CAD data provide convincing evidence that the ion of m/z 165, produced by fragmentation of any one of these four compounds, has a fluorene-like structure.

The mass spectrum of the DCM derivative of 9fluorene (2) indicates no peak corresponding to loss of 'CH(CN)₂ from $[M]^{+}$. This result is consistent with the theme represented in Scheme 2; following electron impact ionization, compound 2 would have no driving force to undergo this rearrangement because 2 already has the fluorene-like stable structure. Otherwise, the mass spectrum of 2 is characterized by a base peak representing $[M]^{+}$. (m/z 228) and another peak, one tenth as intense, representing $[M-HCN]^{+}$; no other significant peaks appear in the mass spectrum.

The mass spectrum of the DCM derivative of benzophenone (Fig. 1) also exhibits an intense peak corresponding to loss of a hydrogen from the molecular ion. Although other mechanisms exist, this elimination could also be rationalized through a molecular rearrangement leading to a substituted fluorene-like species as illustrated in the Scheme 3 (which assumes the molecular ion in the form of ion a in Scheme 2).

Additional evidence for the rearrangement in

Table 2.	2. Daughter ion CAD mass spectra of mass 165 from EI of the DCM derivative of benzophenone (A), 9-							
	aicyanon bromoflu (D)	iorene ((C) and	fluorene				
	Compound							
m/z	Α	в	С	D				
164	100%	100%	100%	100%				
163	72%	69%	68%	77%				
139	72%	75%	77%	75%				
126	6%	6%	6%	6%				
115	83%	88%	95%	88%				
113	6%	6%	6%	7%				
91	15%	18%	25%	15%				
89	19%	21%	30%	18%				
87	10%	17%	16%	9%				
65	13%	11%	15%	6%				
63	16%	16%	28%	15%				



Scheme 2 is provided in Table 3 which is a summary of mass spectra of the DCM derivatives of some benzophenone analogs (5). In nearly every case, a



significant peak was observed for an ion corresponding to [M-65].⁺ As expected, the loss of HCN from [M]⁺ was frequently observed^{6,7} and in cases of the chlorinated analogs, the loss of 'Cl from [M]+' was a dominant process. Fragmentation of the bond between the dicyanoethylene and (substituted) phenyl moieties was found very rarely; apparently only a small fraction of the molecular ions retain the benzophenone-like structure which would permit them to generate an ion representing the (substituted) phenyl moiety. The mass spectrum of benzophenone (and underivatized analogs) often exhibit a significant peak at m/z 77 as well as at a m/z value corresponding to loss of the phenyl moiety from the molecular ion. That is, the C-C bond between the carbonyl and phenyl moieties of the (underivatized) benzophenones can be easily cleaved.5

Other corroborative evidence for the characteristic proposed rearrangement as illustrated by Scheme 2 is provided by the mass spectra of the DCM derivatives 6 and 7. The spectrum of the pentadeutero compound



exhibits approximately equal ion abundance for the loss of $CD(CN)_2$ and $CH(CN)_2$, which is consistent with the symmetry of available hydrogens in Scheme 2. Incidentally, the spectrum of 6 also indicates approximately equal ion abundance for $[M-H]^+$ and $[M-D]^+$. The experiment involving compound 7 was designed to preclude the pathway illustrated in Scheme 2 because compound 7 does not contain a hydrogen to donate from one of the phenyl groups. However, the mass spectrum of 7 exhibits some ion current corresponding to the elimination represented in Scheme 2; the fact that both hydrogen and fluorine participate in this rearrangement may reflect the similar bond strengths of C-F and C-H. The essence of the mass spectrum of compound 7 is as follows: [M]⁺⁻ (100%), $[M-F]^+$ (26%), $[M-HF]^+$ (36%), $[M-HCN]^+$ (16%), $[M-CH(CN)_2]^+$ (18%) and $[M-CF(CN)_2]^+$ (3%). The loss of HF from **7** is consistent



Figure 3. Daughter ion (CAD) mass spectra of the ion of mass 165 produced upon El for each of the indicated compounds: A: DCM derivative of benzophenone (1; $R = R' = C_6H_5$); B: 9-dicyanomethylfluorene (3); C: 9-bromo-fluorene (4; R = Br); D: fluorene (4; R = H).

resented by	5						
Name	[M] ⁺ '	[M-HCN]+*	$[M-CH(CN)_2]^+$	[M-R'] ⁺	$[M - (R' + R^2)]^+$		
DCM-2,4-dimethyl-	258 (100)	231 (57.3)	193 (8.6)	243 (16.2)			
benzophenone 2 $R^1 = CH_2, R^2 = H$							
DCM-4,4'-dimethoxy-	290 (100)	263 (0.9)	225 (7.2)	259 (8.7)	228 (1.1)		
$R^1 = R^2 = OCH_3$							
DCM-4,4'-dimethyl-	258 (100)	231 (7.6)	193 (20.3)	243 (86.9)	228 (16.7)		
benzophenone $R^1 = R^2 = CH_3$							
DCM-4,4'-dichloro-	298 (73.8)	271 (2.7)	233 (10.1)	263 (86.8)	228 (100)		
benzophenoné $R^1 = R^2 = CI$							
DCM-4-chloro-	264 (68)	237 (4.0)	199 (11)	229 (100)			
benzophenone $B^1 = CL B^2 = H$							
DCM-4,4'-bis-	316 (100)	289 (0.6)	251 (2.0)	272 (3.3)	228 (4.4)		
(N,N-dimethylamine)							
benzophenone							
$\mathbf{R}' = \mathbf{R}^2 = \mathbf{N}(\mathbf{C}\mathbf{H}_3)_2$ $\mathbf{D}\mathbf{C}\mathbf{M} \ge \mathbf{A} \text{ disblore}$	209 (52 0)	271 (6 1)	222 (14 7)	263 (100)	228 (70)		
benzophenone	230 (00.3)	271 (0.1)	233 (14.7)	203 (100)	220(10)		
$2 R^1 = CI, R^2 = H$							
^a The <i>m/z</i> value is reported together with the relative abundance of the ion (in parentheses).							

Table 3. Abbreviated tabular mass spectra of DCM-benzophenone analogs represented by structure 5^s

with the tendency of these compounds to form the fluorene-like structure in Scheme 2.

Williams et $al.^6$ and Reichert⁷ have reported that the mass spectra of benzolmalononitriles (1; R' = C_6H_5 ; R = H, CH₃, etc.) exhibit a peak representing the elements of the corresponding benzonitriles as formed via intramolecular rearrangement. In the mass spectra of the DCM derivatives of the benzophenone analogs, there are no such peaks. The absence of benzonitrile fragments in these spectra is consistent with the proposed rearrangement (Scheme 2) of these molecules to form a more rigid structure (fluorene-like species) upon electron impact ionization.

The electron impact mass spectrum of the DCM derivative of benzophenone has been reported by Reichert⁷ but with no explanation for the major peak corresponding to $[M-65]^+$. Collins and Hobbs⁴ also reported the mass spectrum of 9-dicyanomethylfluorene, but in that case, the $[M-65]^+$ $(m/z \ 165)$ peak was apparently misassigned the value of m/z163.

This fragmentation study of model compounds suggests a fundamental mechanism by which to

rationalize the principal bond cleavages observed during the mass spectrometry of the DCM derivatives of benzophenone analogs. The driving force for this mechanism, involving cleavage of a double bond, is apparently provided by the formation of a stable fragment ion having a putative fluorene-like structure. Collisionally activated dissociation (CAD) mass spectra of this fragment ion generated from several fluorene analogs and the DCM-benzophene derivative during EI indicate nearly identical fragmentation patterns. The CAD data together with conventional mass spectra provide evidence for the formation of a common ion of fluorene-like structure. These results should facilitate interpretation of the mass spectra of similar derivatives of other benzophenone analogs.

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