Original research paper

Proximity Effects in Mass Spectra of Benzanilides

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Abstract

The analytical value of peaks arising by a proximity effect in the electron ionization mass spectra of benzanilides has been established by examining the spectra of numerous examples of general structure $XC_6H_4NHCOC_6H_4Y$. Significant $[M-X]^+$ signals are observed only when $X = Cl$, Br, I or CH_3O in the 2-position. The presence of strong $[M-X]^+$ signals, but negligibly weak $[M-Y]^+$ peaks, even when the C-Y bond would be expected to break more readily than the C-X bond, indicates that these diagnostically useful signals do not arise by simple cleavage. Similarly, the presence of an appreciable $[M-Cl]^+$ signal, but no $[M-Br]^+$ signal, in the spectra of representative examples of $4-Br-2ClC_6H_3NHCOC_6H_4Y$, reveals that loss of a substituent from the 2-position occurs much more rapidly than fission of a weaker bond to a substituent in the 4-position. These trends are interpreted in terms of cyclization of the ionized 2-substituted benzanilide, followed by elimination of the substituent originally in the 2-position, to form a protonated 2-arylbenzoxazole.

Keywords

benzanilides, proximity effect, rearrangement, cyclization, simple cleavage

Introduction

Benzanilides of general structure $Ar^1NHCOAr^2$ have been prepared and utilised in organic chemistry for over a century. Prior to the development of spectroscopic methods, one standard technique for characterising amines, many of which are liquids or oils, was to convert them into highly crystalline derivatives such as amides, which were then identified from their melting point and mixed melting point with authentic samples. Amides derived from benzoyl chloride were especially useful in this context because they were easy to prepare and had well-defined melting points.[1] Aromatic amines, particularly anilines, were immensely important industrial intermediates; consequently, benzanilides were useful in confirming the structure and purity of these materials.

More recently, benzanilides have been found to have medicinal and pharmaceutical properties, as illustrated by papers describing their synthesis by novel methods and their biological activity.[2–6] Developing and refining sensitive and specific spectroscopic methods for establishing the structure of benzanilides is, therefore, important.

Although mass spectrometry is increasingly being used primarily as a detection method, the fragmentation of ionized substrates by characteristic pathways frequently reveals a great deal of structural information that would be difficult or impossible to acquire by other means.[7] Rearrangements are often especially useful, as illustrated

by the seminal discovery of the McLafferty rearrangement of ionized carbonyl compounds.[8,9] A related, but less well known, category of rearrangements that are analytically valuable is ortho effects, in which elimination of a neutral species derived by interaction of adjacent substituents on an aromatic ring sometimes permits ortho disubstituted substrates to be distinguished from their meta and para isomers.[7] Another class of useful rearrangements are "proximity effects", in which the interaction of two parts of an ionized molecule leads to the formation of a new ring, thus allowing a substituent to be eliminated to form an especially stable product ion. The archetypal example involved formation of a benzopyrylium cation, **2**, by cyclization and elimination of a hydrogen atom from the ortho position of the original aromatic ring in ionized cinnamaldehyde, benzylidineacetone, cinnamic acid, chalcone or related species, $1^{+\cdot}$, Figure 1.[10] Subsequent studies confirmed the structure of the product ion[11] and revealed that similar processes occur in a wide

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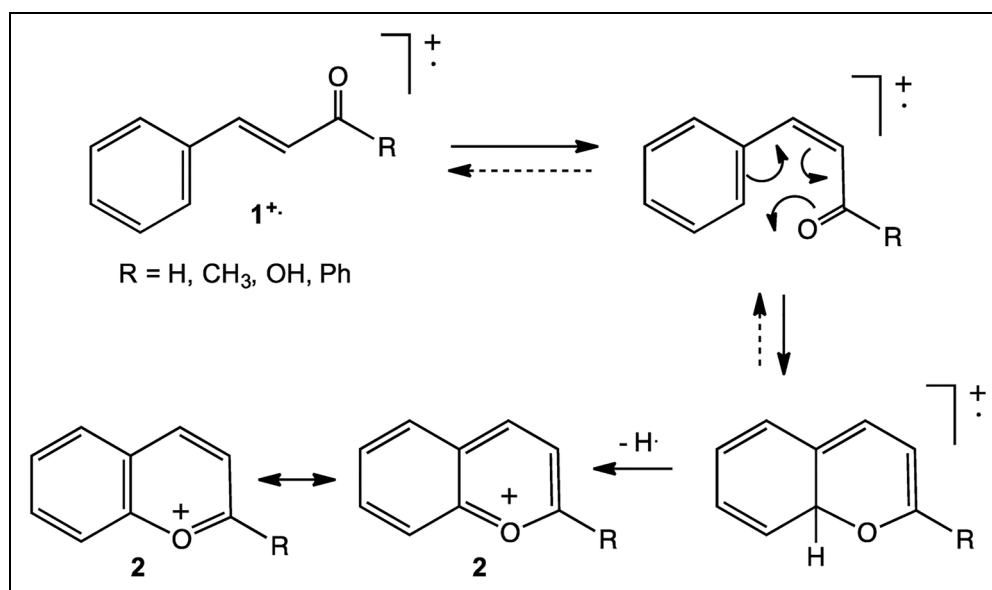
Figure 1. Mechanism of formation of [M-H]$^+$ from $C_6H_5CH=CHCOR^{+\cdot}$ via the proximity effect.

range of radical-cations, including ionized aurones[12,13] and other natural products. An important review[14] highlighted the analogy between these proximity effects in electron ionization, EI, mass spectra and aromatic substitution.

More recent work has shown that [M-H]$^+$ and [M-X]$^+$ (X = F, Cl, Br, CH$_3$ and CH$_3$O) signals are sometimes extraordinarily strong in the EI spectra of substrates such as 2-substituted benzazoles in which cyclization is followed by elimination of a substituent originally attached to the 2-position of a pendant aromatic ring.[15,16] In these systems, the polycyclic aromatic product ion, **4**, is exceptionally stable, Figure 2.

The base peak in the EI spectrum of 2-(2-fluorostyryl)benzimidazole (**3**, Z = NH, X = F)

corresponds to [M-F]$^+$. In contrast, the relative intensity, RI, of the [M-F]$^+$ signal in both 2-(3-fluorostyryl)benzimidazole and 2-(4-fluorostyryl)benzimidazole is less than 1%.[15] Parallel trends that permit 2 substituted derivatives to be distinguished from their 3 and 4 substituted isomers were observed in the spectra of isomeric styrylbenzoxazoles (Z = O), styrylbenzothiazoles (Z = S) and related heterocycles.[15,16] In view of the analytical value of the proximity effect in the fragmentation of these ionized heterocycles and the importance of benzanilides in various contexts, establishing the circumstances in which similar rearrangements give rise to useful signals in the mass spectra of benzanilides is of interest
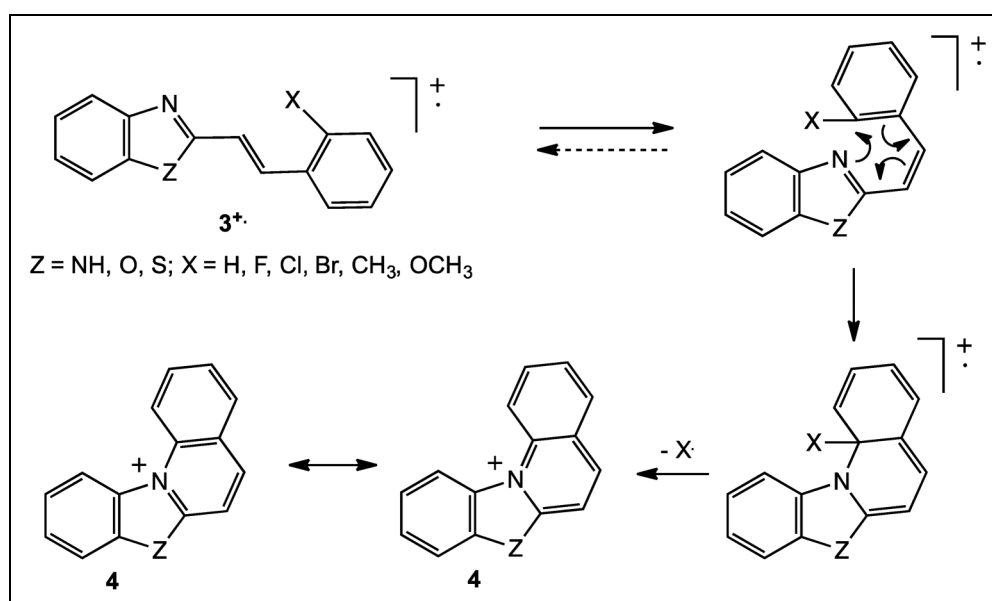
Figure 2. Mechanism of formation of [M-X]$^+$ from $C_6H_4NZCCH=CHC_6H_4X^{+\cdot}$ via the proximity effect.

Experimental

Synthesis. Most benzanilides of general structure ArNHCOPh were obtained by treatment of the requisite substituted aniline, $ArNH_2$, with excess benzoyl chloride, PhCOCl, in the presence of sodium hydroxide solution at 0° C under standard Shotten-Baumann conditions.[1] Isolation of the solid from the alkaline solution by filtration, followed by recrystallization from ethanol/water, gave pure product.

The following method was devised to prepare $Ar^1NHCOAr^2$ when the substituted aniline, Ar^1NH_2, or substituted benzoyl chloride, Ar^2COCl, was expensive. A solution of ~1 equivalent of Ar^2COCl in dichloromethane was added dropwise under a nitrogen atmosphere to a magnetically stirred solution of ~1 equivalent of Ar^1NH_2 in dichloromethane solution containing 1.5-2 equivalents of triethylamine or pyridine. The cheaper reactant was used in slight excess (5–10%). After stirring overnight, the solution was poured into cold water and the dichloromethane layer was separated. The aqueous phase was extracted with dichloromethane. The combined organic phases were washed sequentially with aqueous sodium carbonate solution (10% w/v) and dilute hydrochloric acid, dried (magnesium sulphate) and rotary evaporated to constant mass to give crude product (generally a solid) that was recrystallized from ethanol/water. Crude yields obtained by this method were usually at least 90%; yields of recrystallized benzanilides, $Ar^1NHCOAr^2$, were in the range 65–80%. An illustrative example of this procedure is given in the supplemental information, together with a list of all the benzanilides studied in this work.

Mass spectrometry. Two different instruments were used to record representative electron ionization, EI, mass spectra by complementary methods in order to ensure reproducibility of the data.

A Shimadzu QP-2010 quadrupole MS system, fitted with a heated solids probe and controlled by 'GCMS solutions' software, version 2.0 (Shimadzu UK Ltd, Milton Keynes, UK) was used to record spectra by direct probe insertion. The sample in a disposable glass vial was placed in the solids probe and admitted into the mass spectrometer ion source via a vacuum lock. The probe was then heated from ambient temperature to 320 °C during 10 min. Ionization of the thermally desorbed sample was achieved with 70 eV electrons; data were acquired over the *m/z* range 50–600 at a scan speed of 1250 *m/z* units s^{-1} at unit mass resolution.

Admission of the samples though a 7890 gas chromatograph attached to a 5975 EI Inert MSD (Agilent Technologies, USA) was found to be more convenient in practice because it was easier to automate. Gas chromatography was achieved with a 30 m × 0.25 mm 5% diphenyl low-polarity fused-silica capillary column, using helium as the carrier gas at a flow rate of 1.2 mL min^{-1}. Ionization was effected with electrons having a nominal energy of 70 eV. The temperature of the source and quadrupole was 230 and 150 °C, respectively. The initial temperature of the GC was 100 °C, increasing linearly at 25 °C min^{-1} to 350 °C, where it was maintained for 2 min. Data were acquired over the m/z range 50–600. No significant impurities were detected, thus establishing that the benzanilides were pure and were not affected by the temperatures in the GC column or the source. The spectra recorded by the two methods were in excellent qualitative agreement.

Results and discussion

In order to facilitate the discussion, the following system of abbreviation is used to describe the benzanilides. The core "BZ" denotes "benzanilide; a prefix indicates the position of any substituent(s) in the aromatic ring (A) derived from Ar^1NH_2; a suffix defines the position of any substituent in the ring (B) originating from Ar^2COCl. For example, "2BrBZ4CH$_3$" represents $2\text{-BrC}_6H_4NHCOC_6H_4(4'\text{-CH}_3)$.

The representative spectra shown in Figures 3 and 4, obtained by direct probe insertion, show that loss of a chlorine or bromine atom from ionized XBZ or XBZ4CH$_3$ (X = Cl or Br, respectively) occurs to a significant extent only when the halogeno substituent is in the 2-position. Parallel information was obtained using the GCMS methodology, as illustrated by the comparison of data for the three isomeric ClBZs, Table 1. More fragmentation was generally observed when the sample was admitted through the GC system, presumably because of the higher thermal energy imparted to the molecule prior to ionization. In the following discussion, the data quoted were acquired by the GCMS methodology. The formation of m/z 196 from 2ClBZ may be explained as a proximity effect: cyclization of **5$^{+\cdot}$** forms **6**, which loses X$^\cdot$ to give protonated 2-phenylbenzoxazole, **7**, Figure 5. In contrast, the spectra of 3ClBZ and 4ClBZ instead contain strong signals at m/z 105, 77 and 51, corresponding to $[C_6H_5CO]^+$, $[C_6H_5]^+$ and $[C_4H_3]^+$, respectively, Figure 3. Parallel behaviour is observed for the three BrBZ4CH$_3$ cases: the spectrum of 2BrBZ4CH$_3$ is unique in showing a significant [M-Br]$^+$ signal, Figure 4. The spectra of the other two isomers are dominated by peaks at m/z 119, 91 and 65, corresponding to $[CH_3C_6H_4CO]^+$, $[C_7H_7]^+$ and $[C_5H_5]^+$, respectively. Other sets of isomeric ClBZY and BrBZY show the same trends in their spectra.

The importance of the proximity effect in the spectra of 2XBZ and 2XBZY reported in this paper depends critically on the nature of X, Table 2. When X = H, CH$_3$ or F, [M-X]$^+$ is of negligible RI. Each of these spectra is dominated by the alternative σ-cleavage to give the familiar pattern of peaks at m/z 105, 77 and 51, which are attributed to $[C_6H_5CO]^+$, $[C_6H_5]^+$ and $[C_4H_3]^+$, respectively. However, when X = CH$_3$O, Cl, Br or I, loss of X$^\cdot$ to give a signal at m/z 196 generally increases in importance relative to the peak at m/z 105 for $[C_6H_5CO]^+$. In the halogeno series, the ratio of RI of the [M-X]$^+$ signal to the $[C_6H_5CO]^+$ signal rises from
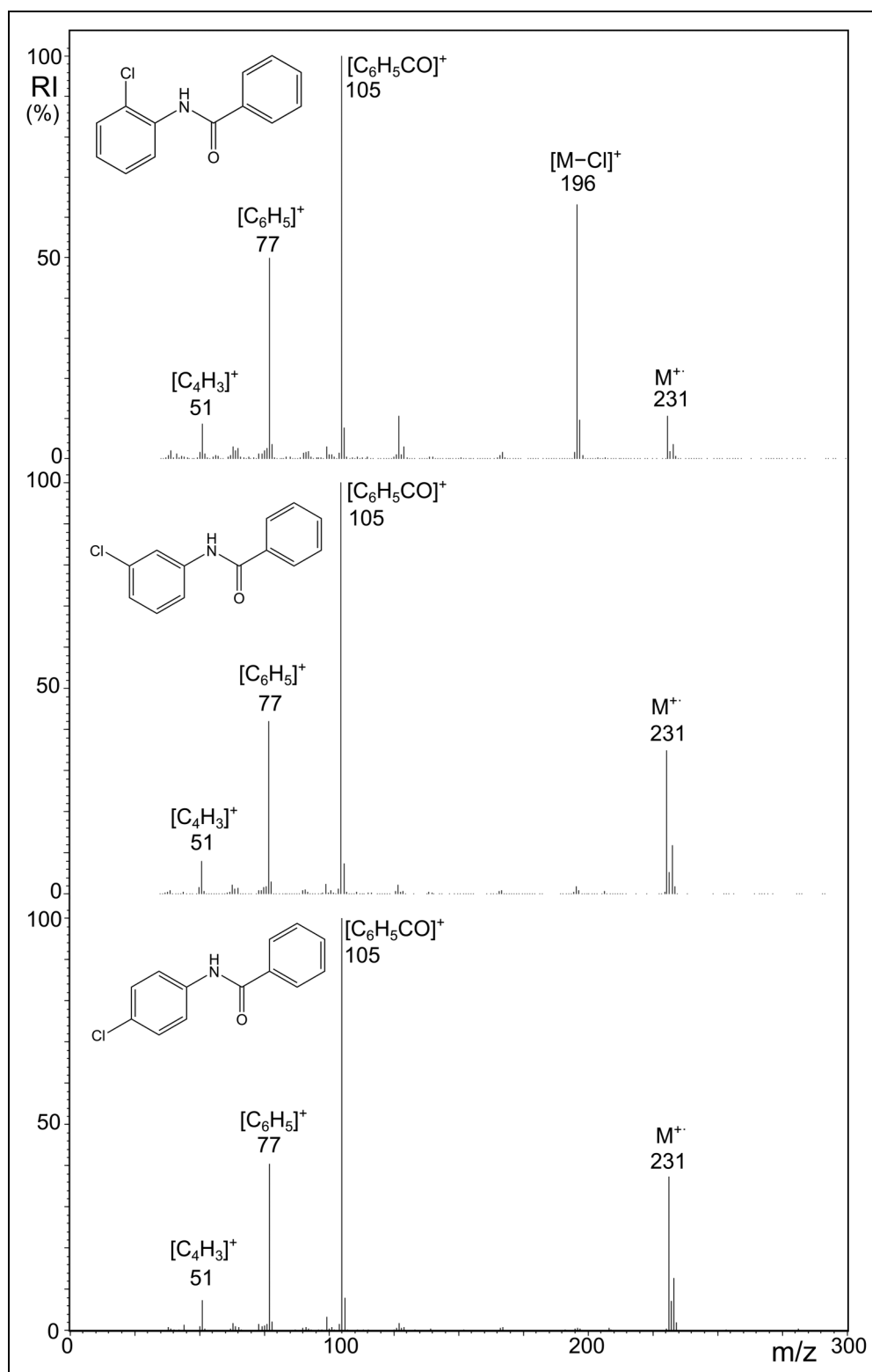
Figure 3. Mass spectra of isomeric $ClC_6H_4NHCOC_6H_5$ recorded by direct probe insertion.

0.67:1 for $X = Cl$, to 0.84:1 when $X = Br$, to 1.15:1 when $X = I$.

Early work on the formation of benzoyl cations from various precursors,[17–20] including ionized benzanilides, indicated that this process may sometimes be more complicated than appears at first sight, especially at low internal energies.[19,20] However, these caveats do not in any way affect the central arguments presented below about the competition between loss of $X^.$ by the proximity effect and simple cleavage to form a substituted benzoyl cation.

The observation that $[M-X]^+$ signals formed by the proximity effect are significant in the spectra of
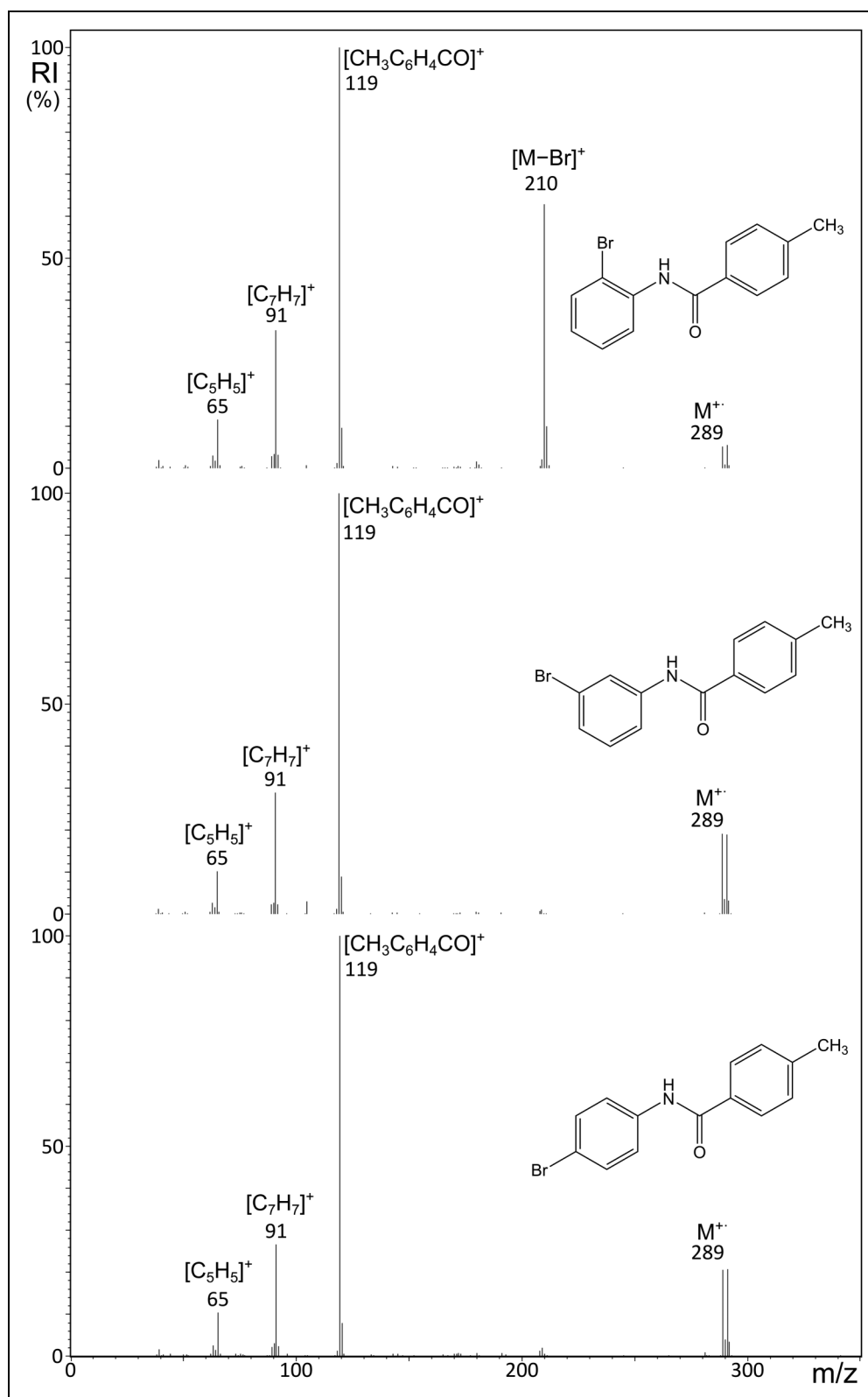
Figure 4. Mass spectra of isomeric $BrC_6H_4NHCOC_6H_4CH_3$, recorded by direct probe insertion.

substituted benzanilides only when $X = CH_3O$, Cl, Br or I, but not when $X = H$, CH_3 or F, is in sharp contrast with the facile loss of $X^.$ from all the ionized styrylbenzimidazoles investigated in previous work.[15] This divergent behaviour reflects two main factors. Firstly, although **7**

is a stable product ion, it is not so extensively stabilized as **4**. Secondly, there is no obvious σ-cleavage of ionized 2-styrylbenzazoles to form a stable product ion; consequently, loss of $X^.$ from these species is not in competition with a favourable alternative fragmentation. In

Table 1. Summary of electron ionisation mass spectra of $ClC_6H_4NHCOC_6H_5$.

m/z	2ClBZ RI[b,c,d]	2ClBZ RI[b,c,e]	3ClBZ RI[b,c,d]	3ClBZ RI[b,c,e]	4ClBZ RI[b,c,d]	4ClBZ RI[b,c,e]	Interpretation[a]
234	0.5	<0.5	1.5	0.7	1.5	1	^{13}C satellite of $[M+2]^{+\cdot}$
233	3.5	4	11.5	5	12	7	$[M+2]^{+\cdot}$
232	1.5	2	4.5	2	4.5	3	^{13}C satellite of $M^{+\cdot}$
231	10.5	12	34.5	15	37	21	$M^{+\cdot}$
197	8	11					^{13}C satellite of $[M-X]^+$
196	63	67					$[M-X]^+$
106	8	10	8	8	8	8	^{13}C satellite of $[C_6H_5CO]^+$
105	100	100	100	100	100	100	$[C_6H_5CO]^+$
78	3	5	2.5	7	2.5	5	^{13}C satellite of $[C_6H_5]^+$
77	48	63	42	97	40	63	$[C_6H_5]^+$
52	0.5	2	0.5	5	0.5	2	^{13}C satellite of $[C_4H_3]^+$
51	8	15	7.5	39	7.5	20	$[C_4H_3]^+$

[a]The data in this table are arranged so that the m/z values of ions in each row correspond to a common interpretation.
[b]RI measured by peak height and normalised to a value of 100 units for the base peak.
[c]Blank entries indicate that the requisite signal was too weak to be detected.
[d]Data obtained from direct probe insertion.
[e]Data obtained by automated GCMS.

contrast, ionized 2XBZ species may undergo σ-cleavage to form the highly stable benzoyl cation, which normally pre-empts the proximity effect when X = H, CH_3 or F.

This explanation for the variation in RI of $[M-X]^+$ may be tested by examining the influence of a substituent, Y, on the fragmentation of $2XC_6H_4NHCOC_6H_4Y^+$. If Y is an electron-donating group, which stabilizes $[YC_6H_4CO]^+$, the proximity effect should compete less effectively with σ-cleavage. Conversely, when Y is electron-withdrawing, it would be expected to destabilize $[YC_6H_4CO]^+$ and favour the proximity effect. Relevant data for two illustrative series, with Y = CH_3O and NO_2, which are strongly electron-donating and

electron-withdrawing, respectively, by the + M or −M mesomeric effect of the substituent in the 4 position, are shown in Tables 3 and 4.

In the spectra of the $2XBZOCH_3$ series, the RI of $[M-X]^+$ is greatly reduced compared to that in the spectra of the corresponding 2XBZ analogues. Even in the most favourable case, where X = I, the ratio of RI of $[M-I]^+$:$[CH_3OC_6H_4CO]^+$ is only 0.34:1, compared to a ratio of 1.15:1 for $[M-I]^+$:$[C_6H_5CO]^+$ in the spectrum of IBZ. The opposite effect is observed in the $2XBZNO_2$ series: the RI of $[M-X]^+$ is substantially increased. Indeed, the powerful −M effect of the nitro group exerts such a strong influence that an observable $[M-CH_3]^+$
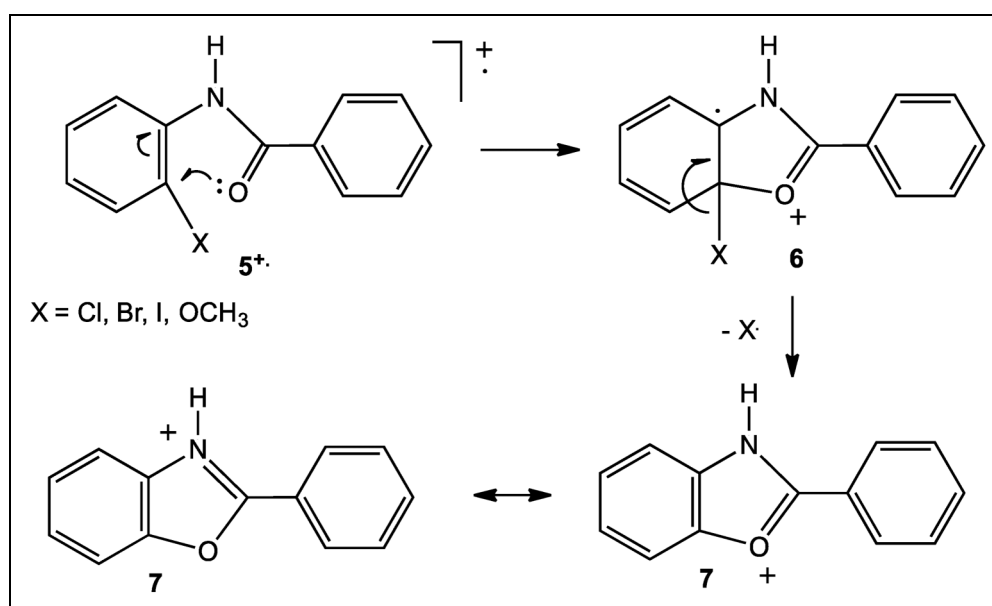
Figure 5. Mechanism of formation of $[M-X]^+$ from $XC_6H_4NHCOC_6H_5^{+\cdot}$ via the proximity effect.

Table 2. Important signals in electron ionisation mass spectra of 2-$XC_6H_4NHCOC_6H_5$.

	M^+		$[M-X]^+$		$[C_6H_5CO]^+$		$[C_6H_5]^+$		$[C_4H_3]^+$	
X	m/z	RI[a,b]	m/z	RI[a,b]	m/z	RI[a,b]	m/z	RI[a,b]	m/z	RI[a,b]
H	197	49	196		105	100	77	58	51	14
CH_3	211	49	196		105	100	77	57	51	12
CH_3O	227	66	196	8	105	100	77	59	51	13
F	215	44	196		105	100	77	55	51	13
Cl^c	231	12	196	67	105	100	77	52	51	10
Br^c	275	7	196	84	105	100	77	63	51	15
I	323	8	196	100	105	87	77	53	51	11

[a]RI = Relative Intensity, measured by peak height and normalised to a value of 100 units for the most intense signal in spectra obtained by GCMS methodology.
[b]Blank entries indicate that the requisite signal was too weak to be detected.
[c]Data are shown only for the more abundant (^{35}Cl and ^{79}Br, respectively) isotope signals; the ^{37}Cl and ^{81}Br satellites were present at 33% and 99% relative intensity.

signal with RI = 2% appears in the spectrum of $2CH_3BZNO_2$.

Further support for the mechanism of Figure 5 is provided by the fragmentation of $2XBZY^{+\cdot}$ in which loss of Y from ring B might be expected to dominate or pre-empt elimination of X from ring A, Table 5. Thus, when X = Cl and Y = Br, the RI of $[M-Cl]^+$ is 71% and 52%, respectively, in the spectrum of ClBZ3Br and ClBZ4Br, but that of $[M-Br]^+$ is below 0.5%. If elimination of a halogen atom occurred by σ-cleavage, as is often the case, fission of the weaker C-Br bond would take place preferentially or exclusively. Similarly, a bromine atom is lost from $2BrBZI^+$ to form m/z 322 (RI 100% or 71%, respectively), rather than an iodine atom to give m/z 274 (RI<0.5%) irrespective of whether the iodo substituent is in the 3 or 4 position in ring B. Moreover, $2ClBZI^+$ expels a chlorine atom (RI of m/z 322 = 79 or 62%), rather than an iodine atom (RI<0.5% for m/z 230), regardless of whether the iodo substituent in ring B is in the 3 or 4 position. The cleavage of the stronger C-Cl bond, instead of the much weaker C-I bond, in these cases is compelling evidence that loss of a chlorine atom occurs by a facile rearrangement that gives rise to a far more stable product ion than would be formed by σ-cleavage. Indeed, in the 2XBZI spectra recorded in this work, appreciable $[M-I]^+$ signals are observed only if X = I, when an iodine atom can be lost by the proximity effect, rather than by σ-cleavage.

The data of Table 5 reveal three other trends. Firstly, as noted previously, loss of $H^{\cdot}$, $F^{\cdot}$ or CH_3 from ring A usually is of negligible importance; it is pre-empted by σ-cleavage to form an iodobenzoyl cation (or smaller fragment ions that may be derived from that acylium ion). Secondly, the proximity effect becomes increasingly favourable on progressing down the halogen series: it is not observed to a significant extent when X = F; it is progressively more important when X = Cl and Br; and it supersedes σ-cleavage when X = I. The same trend is evident in the spectra summarized in Tables 3 and 4. For example, the ratio of $[M-X]^+$:$[O_2NC_6H_4CO]^+$ increases dramatically from 0.26 when X = CH_3O to 2.70 when X = I. Thirdly, when X = OCH_3, Cl, Br or I, the proximity effect competes more effectively with σ-cleavage if the iodo substituent in ring B is in the 3 position, presumably because $[3\text{-}IC_6H_4CO]^+$ is less stable than $[4\text{-}IC_6H_4CO]^+$. This order of stability of the isomeric $[IC_6H_4CO]^+$ cations is consistent with the combined influence of the inductive and mesomeric effect of the iodo substituent, as summarized by the Hammett σ constant (0.35 and 0.18, respectively, for an iodo substituent the 3 and 4 position).[21,22]

Table 3. Important signals in electron ionisation mass spectra of 2-$XC_6H_4NHCOC_6H_4OCH_3$.

	$M^{+\cdot}$		$[M-X]^+$		$[CH_3OC_6H_4CO]^+$		226/135
X	m/z	RI[a,b]	m/z	RI[a,b]	m/z	RI[a,b]	
H	227	20	226		135	100	0
CH_3	241	28	226		135	100	0
CH_3O	257	39	226	1	135	100	0.01
F	245	21	226		135	100	0
Cl^c	261	10	226	22	135	100	0.22
Br^c	305	5	226	32	135	100	0.32
I	353	4	226	34	135	100	0.34

[a]RI = Relative Intensity, measured by peak height and normalised to a value of 100 units for the most intense signal in spectra obtained by GCMS methodology.
[b]Blank entries indicate that the requisite signal was too weak to be detected.
[c]Data are shown only for the more abundant (^{35}Cl and ^{79}Br, respectively) isotope signals; the ^{37}Cl and ^{81}Br satellites were present at 33% and 99% relative intensity.

Table 4. Important signals in electron ionisation mass spectra of $2\text{-}XC_6H_4NHCOC_6H_4NO_2$.

	$M^{+\cdot}$		$[M\text{-}X]^+$		$[O_2NC_6H_4CO]^+$		241/150
X	m/z	RI[a,b]	m/z	RI[a,b]	m/z	RI[a,b]	
H	242	59	241		150	100	0
CH_3	256	59	241	2	150	100	0.02
CH_3O	272	100	241	22	150	84	0.26
F	260	55	241		150	100	0
Cl[c]	276	13	241	100	150	70	1.43
Br[c]	320	7	241	100	150	52	1.92
I	368	9	241	100	150	37	2.70

[a]RI = Relative Intensity, measured by peak height and normalised to a value of 100 units for the most intense signal in spectra obtained by GCMS methodology.
[b]Blank entries indicate that the requisite signal was too weak to be detected.
[c]Data are shown only for the more abundant (^{35}Cl and ^{79}Br, respectively) isotope signals; the ^{37}Cl and ^{781}Br satellites were present at 33% and 99% relative intensity.

A more positive σ constant reflects a greater electron-withdrawing and destabilizing influence of the substituent.

The spectra of a limited set of X^1X^2BZY species with halogeno substituents in positions 2 and 4 of ring A provide additional support for the interpretation of Figure 5. The spectra of 4Br2ClBZY (Y = H, CH_3O or NO_2) show sizeable $[M\text{-}Cl]^+$ peaks, but no appreciable $[M\text{-}Br]^+$ signals, Figure 6. In contrast, the spectra of the corresponding 2Br4ClBZY isomers display strong $[M\text{-}Br]^+$ signals, but no significant $[M\text{-}Cl]^+$ peaks. The divergent behaviour of these isomeric pairs of BrClBZY compounds is easily and logically interpreted in terms of a proximity effect, which leads to specific elimination of a substituent from the 2-position of ring A, but it is impossible to rationalize on the basis of σ-cleavage of a carbon halogen bond in the ionized molecule. Moreover, the spectra of Figure 4 further illustrate the influence of the 4-substituent in ring B on the competition between simple cleavage and the proximity effect. When Y = CH_3O, the proximity effect occurs to only a minor extent (though specific elimination of the substituent in the 2-position on ring A is still observed). In contrast, when Y = NO_2, the proximity effect, leading to specific elimination of the Cl- or Br- from position 2 of ring A, occurs to a far greater extent.

Table 5. Important signals in electron ionisation mass spectra of $2\text{-}XC_6H_4NHCOC_6H_4Y$.

		$M^{+\cdot}$		$[M\text{-}X]^+$		$[M\text{-}Y]^+$		$[YC_6H_4CO]^+$		$[YC_6H_4]^+$	
X	Y	m/z	RI[a]	m/z	RI[a]	m/z	RI[a]	m/z	RI[a]	m/z	RI[a]
H	3-I	323	68	322		196	<1	231	100	203	37
	4-I	323	47	322		196	<0.2	231	100	203	35
CH_3	3-I	337	38	322		210	<0.2	231	100	203	37
	4-I	337	50	322		210	<0.2	231	100	203	30
CH_3O	3-I	353	72	322	8	226	<0.2	231	100	203	37
	4-I	353	64	322	6	226	<0.2	231	100	203	29
F	3-I	341	57	322	7[d]	214	<0.2	231	100	203	41
	4-I	341	44	322	7[d]	214	<0.5	231	100	203	31
Cl[c]	3-I	357	26	322	79	230	<0.5	231	100	203	39
	4-I	357	12	322	62	230	<0.3	231	100	203	32
Br[c]	3-I	401	6	322	100	274	<0.5	231	96	203	42
	4-I	401	5	322	71	274	<0.5	231	100	203	33
I	3-I	449	6	322	100	322	100[e]	231	62	203	35
	4-I	449	6	322	100	322	100[e]	231	78	203	33
Cl[c]	3-Br	309	9	274	71	220	<0.2	183	100	155	45
	4-Br	309	8	274	52	220	<0.2	183	100	155	37

[a]RI = Relative Intensity, measured by peak height and normalised to a value of 100 units for the most intense signal in spectra obtained by GCMS methodology.
[b]Blank entries indicate that the requisite signal was too weak to be detected.
[c]Data are shown only for the more abundant (^{35}Cl and ^{79}Br, respectively) isotope signals; the usual ^{37}Cl and ^{81}Br satellites were present. Inclusion of these isotope satellites would increase the RI of the molecular ion signal in cases where only bromine or chlorine was present. This point explains the apparently anomalous fact that the RI of the molecular ion signal is greater in the $2\text{-}IC_6H_4NHCOC_6H_4I$ series (in which there is no satellite signal for a heavier halogen isotope) compared to those in the $2\text{-}BrC_6H_4NHCOC_6H_4I$ series (in which there is such an isotope satellite).
[d]Explained entirely by ^{13}C satellite of m/z 231.
[e]Essentially all formed by loss of I- from ring A by the proximity effect.
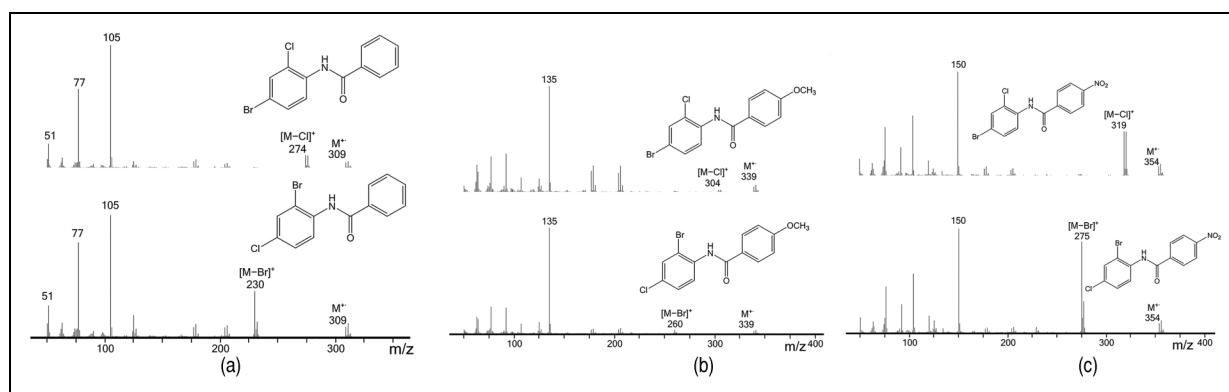
Figure 6. Mass spectra of isomeric pairs of (a) $BrClC_6H_3NHCOC_6H_4CH_3$, (b) $BrClC_6H_3NHCOC_6H_4OCH_3$ and (c) $BrClC_6H_3NHCOC_6H_4NO_2$, recorded by GCMS methodology.

A final point relates to the relatively low RI of $[M-CH_3O]^+$ signals in the spectra of $2\text{-}CH_3OC_6H_4NHCOC_6H_4Y$. This point is at first somewhat surprising. However, it may be understood on the basis of the powerful $+M$ effect of the CH_3O substituent, which will increase the electron density at the 2-position of ring A, thereby making the initial cyclization less favourable.

Conclusions

Loss of a 2-substituent, X, from ionized benzanilides occurs in well-defined circumstances that are analytically useful. It rarely takes place when $X = H$, CH_3 or F; it is significant when $X = CH_3O$; and it becomes increasingly important on progressing through the series of heavier halogeno substituents, $X = Cl$, Br and I, until it rivals or exceeds the competing σ-cleavage to form a (substituted) benzoyl cation. The presence of an electron-donating or electron-withdrawing substituent in the aromatic ring to which the carbonyl group is attached affects the competition between the proximity effect and σ-cleavage. Electron-donating groups stabilize the benzoyl cation, thus discriminating against the proximity effect. In contrast, electron-withdrawing groups favour the proximity effect because they destabilize the benzoyl cation.

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Supplemental material

Supplemental material for this article is available online.

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