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 XC₆H₄NHCOC₆H₄Y. Significant [M-X]+ signals are observed only when X = Cl, Br, I or CH₃O 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-2ClC₆H₃NHCOC₆H₄Y, 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

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Introduction
Benzanilides of general structure Ar¹NHCOC₂Ar² 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 substituted 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.

Figure 1.10 Subsequent studies confirmed the structure of the product ion¹¹ and revealed that similar processes occur in a wide

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range of radical-cations, including ionized aurones\textsuperscript{12,13} and other natural products. An important review\textsuperscript{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]\textsuperscript{+} and [M-X]\textsuperscript{+} (X = F, Cl, Br, CH\textsubscript{3} and CH\textsubscript{3}O) signals are sometimes extraordinarily strong in the EI spectra of substrates such as 2-substituted benzoazoles in which cyclization is followed by elimination of a substituent originally attached to the 2-position of a pendant aromatic ring.\textsuperscript{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]\textsuperscript{+}. In contrast, the relative intensity, RI, of the [M-F]\textsuperscript{+} signal in both 2-(3-fluorostyryl)benzimidazole and 2-(4-fluorostyryl)benzimidazole is less than 1\%.\textsuperscript{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.\textsuperscript{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.
**Experimental**

**Synthesis.** Most benzanilides of general structure ArNHCOAr' when the substituted aniline, Ar'NH$_2$, or substituted benzoyl chloride, ArCOCl, was expensive. A solution of $\sim$1 equivalent of ArCOCl in dichloromethane was added dropwise under a nitrogen atmosphere to a magnetically stirred solution of $\sim$1 equivalent of Ar'NH$_2$ in dichloromethane solution containing 1.5-2 equivalents of triethylamine or pyridine. The cheaper reactant was used in slight excess (5 equivalent 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 evaporation, followed by recrystallization from ethanol/water, gave pure product.

The following method was devised to prepare Ar'NHCOAr' when the substituted aniline, Ar'NH$_2$, or substituted benzoyl chloride, ArCOCl, was expensive. A solution of $\sim$1 equivalent of ArCOCl in dichloromethane was added dropwise under a nitrogen atmosphere to a magnetically stirred solution of $\sim$1 equivalent of Ar'NH$_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 evaporation, followed by recrystallization from ethanol/water, gave pure product.

**Isolation of the solid from the alkaline solution by filtration, followed by recrystallization from ethanol/water, gave pure product.**

**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 ArNH$_2$; a suffix defines the position of any substituent in the aromatic ring (B) originating from ArCOCl. For example, “2BrBZ4CH$_3$” represents 2-BrC$_6$H$_4$NHCOCH$_3$(4′-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 CIBZs, 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 2CIBZ may be explained as a proximity effect: cyclization of 5$^+$ forms 6, which loses X to give protonated 2-phenylbenzoazole, 7, Figure 5. In contrast, the spectra of 3CIBZ and 4CIBZ instead contain strong signals at m/z 105, 77 and 51, corresponding to [C$_6$H$_5$CO]$, [C$_7$H$_7$]$^+$ and [C$_9$H$_7$]$^+$, 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 [C$_7$H$_6$COHCO]$, [C$_9$H$_7$]$^+$ and [C$_9$H$_7$]$^+$, respectively. Other sets of isomeric CIBZY 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 cleavage to give the familiar pattern of peaks at m/z 105, 77 and 51, which are attributed to [C$_6$H$_5$CO]$, [C$_7$H$_7$]$^+$ and [C$_9$H$_7$]$^+$, respectively. However, when X = CH$_3$O, Cl, Br or I, loss of X to give a signal at m/z 196 generally increases in importance relative to the peak at m/z 105 for [C$_6$H$_5$CO]$. In the halogeno series, the ratio of RI of the [M-X]$^+$ signal to the [C$_8$H$_7$CO]$^+$ signal rises from

**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 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 x 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.
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,\textsuperscript{17–20} including ionized benzanilides, indicated that this process may sometimes be more complicated than appears at first sight, especially at low internal energies.\textsuperscript{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]\textsuperscript{+} signals formed by the proximity effect are significant in the spectra of

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Mass spectra of isomeric ClC\textsubscript{6}H\textsubscript{4}NHCOC\textsubscript{6}H\textsubscript{5} recorded by direct probe insertion.}
\end{figure}
substituted benzanilides only when $X = \text{CH}_3\text{O}, \text{Cl}, \text{Br}$ or $\text{I}$, but not when $X = \text{H}, \text{CH}_3$ or $\text{F}$, is in sharp contrast with the facile loss of $X$ from all the ionized styrylbenzimida-
zoles investigated in previous work. 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 $\sigma$-cleavage of
ionized 2-styrylbenzazoles to form a stable product ion; consequently, loss of $X$ from these species is not in com-
petition with a favourable alternative fragmentation. In

Figure 4. Mass spectra of isomeric $\text{BrC}_6\text{H}_4\text{NHCOC}_6\text{H}_4\text{CH}_3$, recorded by direct probe insertion.
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 \([M-CH_3]^+\)

### Table 1. Summary of electron ionisation mass spectra of ClC\(_2\)H\(_2\)NHCOC\(_6\)H\(_5\).

| m/z | 2ClBZ | 3ClBZ | 4ClBZ |
|-----|-------|-------|-------|
|     | RI\(^{b,c,d}\) | RI\(^{b,c,e}\) | RI\(^{b,c,d}\) | RI\(^{b,c,e}\) | RI\(^{b,c,d}\) | RI\(^{b,c,e}\) |
| 234 | 0.5   | <0.5  | 1.5   | 0.7   | 1.5   | 1     |
| 233 | 3.5   | 4     | 11.5  | 5     | 12    | 7     |
| 232 | 1.5   | 2     | 4.5   | 2     | 4.5   | 3     |
| 231 | 10.5  | 12    | 34.5  | 15    | 37    | 21    |
| 197 | 8     | 11    |       |       |       |       |
| 196 | 63    | 67    |       |       |       |       |
| 106 | 8     | 10    | 8     | 8     | 8     | 8     |
| 105 | 100   | 100   | 100   | 100   | 100   | 100   |
| 78  | 3     | 5     | 2.5   | 7     | 2.5   | 5     |
| 77  | 48    | 63    | 42    | 97    | 40    | 63    |
| 70  | 0.5   | 2     | 0.5   | 5     | 0.5   | 2     |
| 51  | 8     | 15    | 7.5   | 39    | 7.5   | 20    |

\(^a\)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.

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**Figure 5.** Mechanism of formation of \([M-X]^+\) from \(XC_6H_4NHCOC_6H_5^+\) via the proximity effect.
signal with RI = 2% appears in the spectrum of 2CH₃BZNO₂. Further support for the mechanism of Figure 5 is provided by the fragmentation of 2XBZI⁺ 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 2XBZ3Br and 2XBZ4Br, 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, F or CH₃ from ring A is usually 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]+/[O₂NC₆H₄CO]+ increases dramatically from 0.26 when X = CH₃Ot o2 . 7 0 whenX = I. Thirdly, when X = OCH₃, 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-IC₆H₄CO]+ is less stable than [4-IC₆H₄CO]+. This order of stability of the isomeric [IC₆H₄CO]+ 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 in the 3 and 4 position).21,22

Table 2. Important signals in electron ionisation mass spectra of 2-XC₆H₄NHCOC₆H₅.

| X   | 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     |
| CH₃ | 211 | 49     | 196 | 105    | 100| 77     | 57 | 51     |
| CH₃O| 227 | 66     | 196 | 8      | 105| 77     | 59 | 51     |
| F   | 215 | 44     | 196 | 105    | 100| 77     | 55 | 51     |
| Clc | 251 | 12     | 196 | 67     | 105| 77     | 52 | 51     |
| Brc | 275 | 7      | 196 | 84     | 105| 77     | 63 | 51     |
| I   | 323 | 8      | 196 | 100    | 105| 87     | 77 | 53     | 51 |

Table 3. Important signals in electron ionisation mass spectra of 2-XC₆H₄NHCOC₆H₄OCH₃.

| X     | m/z | RI a,b | m/z | RI a,b | m/z | RI a,b | m/z | RI a,b |
|-------|-----|--------|-----|--------|-----|--------|-----|--------|
| H     | 227 | 20     | 226 | 135    | 100| 0      |     | 0      |
| CH₃   | 241 | 28     | 226 | 135    | 100| 0      |     | 0      |
| CH₃O  | 257 | 39     | 226 | 1      | 135| 100    | 0.01|        |
| F     | 265 | 21     | 226 | 135    | 100| 0      |     | 0      |
| Clc   | 261 | 10     | 226 | 22     | 135| 100    | 0.22|        |
| Brc   | 305 | 5      | 226 | 32     | 135| 100    | 0.32|        |
| I     | 353 | 4      | 226 | 34     | 135| 100    | 0.34|        |

Table 4. Important signals in electron ionisation mass spectra of 2-XC₆H₄NHCOC₆H₄OCH₃.

| X     | m/z | RI a,b | m/z | RI a,b | m/z | RI a,b | m/z | RI a,b |
|-------|-----|--------|-----|--------|-----|--------|-----|--------|
| H     | 227 | 20     | 226 | 135    | 100| 0      |     | 0      |
| CH₃   | 241 | 28     | 226 | 135    | 100| 0      |     | 0      |
| CH₃O  | 257 | 39     | 226 | 1      | 135| 100    | 0.01|        |
| F     | 265 | 21     | 226 | 135    | 100| 0      |     | 0      |
| Clc   | 261 | 10     | 226 | 22     | 135| 100    | 0.22|        |
| Brc   | 305 | 5      | 226 | 32     | 135| 100    | 0.32|        |
| I     | 353 | 4      | 226 | 34     | 135| 100    | 0.34|        |

*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.
*Blank entries indicate that the requisite signal was too weak to be detected.
*Data are shown only for the more abundant (35Cl and 79Br, respectively) isotope signals; the 37Cl and 81Br satellites were present at 33% and 99% relative intensity.
A more positive $\sigma$ 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 NO2) show sizeable $[M-Cl]^+$ peaks, but no appreciable $[M-Br]^+$ signals, Figure 6. In contrast, the spectra of the corresponding 2Br4ClBZY isomers display strong $[M-Br]^+$ signals, but no significant $[M-Cl]^+$ peaks. The divergent behavior 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 $\sigma$-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 4. Important signals in electron ionisation mass spectra of 2-XC₆H₄NHCOC₆H₄Y.

| X  | Y   | m/z | RI | [M-X]^+ | m/z | RI | [M-Y]^+ | m/z | RI | [O₂NC₆H₄CO]^+ | 241/150 |
|----|-----|-----|----|---------|-----|----|---------|-----|----|----------------|--------|
|    |     |     |    |         |     |    |         |     |    |                 |        |
| H  | 3-I | 323 | 68 | 322     | 196 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 323 | 47  | 322 | 210    | <0.2 | 231 | 100     | 203 | 35 |
| CH₃| 3-I | 337 | 38  | 332     | 116 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 337 | 50  | 322 | 210    | <0.2 | 231 | 100     | 203 | 37 |
| CH₃O| 3-I| 353 | 72  | 322     | 226 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 353 | 64  | 322 | 226    | <0.2 | 231 | 100     | 203 | 37 |
| F  | 3-I | 361 | 57  | 322     | 214 | 2  | 231     | 100 | 0  |                 | 41     |
| 4-I| 361 | 44  | 322 | 214    | <0.5 | 231 | 100     | 203 | 37 |
| Cl₃| 3-I | 357 | 26  | 322     | 230 | <0.5 | 231     | 100 | 0  |                 | 39     |
| 4-I| 357 | 12  | 322 | 230    | <0.3 | 231 | 100     | 203 | 32 |
| Br₃| 3-I | 401 | 6   | 322     | 274 | <0.5 | 231     | 96  | 33 |
| 4-I| 401 | 5   | 322 | 274    | <0.5 | 231 | 100     | 203 | 33 |
| I  | 3-I | 449 | 6   | 322     | 322 | 100   | 231     | 62  | 35 |
| 4-I| 449 | 6   | 322 | 322    | 100   | 231 | 78      | 203 | 33 |
| Cl₃| 3-Br| 309 | 9   | 274     | 71   | 220 | <0.2    | 183 | 100 |                 | 45     |
| 4-Br| 309| 8   | 274 | 52     | 220 | <0.2 | 183     | 100 | 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 $^{37}$Cl and $^{81}$Br satellites were present at 33% and 99% relative intensity.

Table 5. Important signals in electron ionisation mass spectra of 2-XC₆H₄NHCOC₆H₄Y.

| X  | Y   | m/z | RI | [M-X]^+ | m/z | RI | [M-Y]^+ | m/z | RI | [YC₆H₄CO]^+ | 241/150 |
|----|-----|-----|----|---------|-----|----|---------|-----|----|----------------|--------|
|    |     |     |    |         |     |    |         |     |    |                 |        |
| H  | 3-I | 323 | 68 | 322     | 196 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 323 | 47  | 322 | 210    | <0.2 | 231 | 100     | 203 | 35 |
| CH₃| 3-I | 337 | 38  | 332     | 116 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 337 | 50  | 322 | 210    | <0.2 | 231 | 100     | 203 | 37 |
| CH₃O| 3-I| 353 | 72  | 322     | 226 | 2  | 231     | 100 | 0  |                 | 37     |
| 4-I| 353 | 64  | 322 | 226    | <0.2 | 231 | 100     | 203 | 37 |
| F  | 3-I | 361 | 57  | 322     | 214 | 2  | 231     | 100 | 0  |                 | 41     |
| 4-I| 361 | 44  | 322 | 214    | <0.5 | 231 | 100     | 203 | 37 |
| Cl₃| 3-I | 357 | 26  | 322     | 230 | <0.5 | 231     | 100 | 0  |                 | 39     |
| 4-I| 357 | 12  | 322 | 230    | <0.3 | 231 | 100     | 203 | 32 |
| Br₃| 3-I | 401 | 6   | 322     | 274 | <0.5 | 231     | 96  | 33 |
| 4-I| 401 | 5   | 322 | 274    | <0.5 | 231 | 100     | 203 | 33 |
| I  | 3-I | 449 | 6   | 322     | 322 | 100   | 231     | 62  | 35 |
| 4-I| 449 | 6   | 322 | 322    | 100   | 231 | 78      | 203 | 33 |
| Cl₃| 3-Br| 309 | 9   | 274     | 71   | 220 | <0.2    | 183 | 100 |                 | 45     |
| 4-Br| 309| 8   | 274 | 52     | 220 | <0.2 | 183     | 100 | 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 $^{37}$Cl and $^{81}$Br satellites were present at 33% and 99% relative intensity.

$^d$Essentially all formed by loss of I. from ring A by the proximity effect.

$^e$Essentially all formed by loss of I. from ring A by the proximity effect.
A final point relates to the relatively low RI of \([M-\text{CH}_3\text{O}]^+\) signals in the spectra of 2-\text{CH}_3\text{OC}_6\text{H}_4\text{NHCOC}_6\text{H}_4\text{Y}. This point is at first somewhat surprising. However, it may be understood on the basis of the powerful +M effect of the CH\text{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\text{3} or F; it is significant when X = CH\text{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 \(\sigma\)-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 \(\sigma\)-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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**Figure 6.** Mass spectra of isomeric pairs of (a) BrCl\text{C}_6\text{H}_3\text{NHCOC}_6\text{H}_4\text{CH}_3, (b) BrCl\text{C}_6\text{H}_3\text{NHCOC}_6\text{H}_4\text{OCH}_3 and (c) BrCl\text{C}_6\text{H}_3\text{NHCOC}_6\text{H}_4\text{NO}_2, recorded by GCMS methodology.
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