Journal of Fluorine Chemistry, 46 (1990) 393–406

Received: March 24, 1989; accepted: September 11, 1989

PHOTOCHEMICAL BROMINATION OF ARENES. 2. FLUOROBENZENE DERIVATIVES[1]

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ABSTRACT

Photochemically induced reaction of fluorobenzene and a range of polyfluorobenzenes, both in an excess of the arene and with fluorotrichloromethane as solvent, gave isolable adducts only with fluorobenzene, the isomeric difluorobenzenes, and in very small yield with 1,3,5-trifluorobenzene. These adducts were identified by combustion analysis, mass spectrometry, and n.m.r. techniques (^{1}H, ^{13}C, ^{19}F). In every case, the expected substitution products accompanied these adducts, and in the more fully fluorinated benzene derivatives substitution was the only process observed.

Fluorotrichloromethane encouraged the formation of adducts, but the concurrent formation of substantial amounts of substitution products suggested that adducts are not the necessary precursors of the substitution products, in contrast with other systems.

0022-1139/90/$3.50

INTRODUCTION

Our study of the products of photochemical bromination of benzene and its simple derivatives [1] led us to conclude that direct photochemical bromodeprotiation (eqn. 1)

$$ArH + Br^{\cdot} = ArBr + H^{\cdot} \qquad (1)$$

was at best a minor contributor, and that the orientation of substitution which was found [1,2] in photochemical bromination of arenes arose from the various decomposition pathways available to the first-formed adducts.

The number of adducts isolated during photochemical bromination is small. 'Benzene hexabromide' (1,2,3,4,5,6-hexabromocyclohexane) has been reported by a number of workers [1-4]. It acts as a source of bromine under photochemical conditions [5], perhaps because the addition of halogen to 3,4,5,6-tetrahalogenocyclohexenes is reported [6] to be reversible. The existence of other bromine-containing analogues seems to rest almost entirely upon van der Linden's report [3] of 1-chloro-1,2,3,4,5,6-hexabromocyclohexane (from chlorobenzene and bromine in the presence of light) and of three products of reaction of fluorobenzene. A monofluoroheptabromocyclohexane, thought to arise from addition to *p*-fluorobromobenzene, was obtained along with two isomers of 1-fluoro-1,2,3,4,5,6-hexabromocyclohexane.

This report deals with the isolation of new adducts and an assessment of the earlier work in a study of the photochemical reaction of some polyfluorobenzenes with bromine.

DISCUSSION

The previous studies [1,2] had been carried out using an excess of the arene as solvent or, in the case of solid substrates such as biphenyl or naphthalene, using tetrachloromethane as solvent. Under such conditions the removal of the solvent after photochemical reaction was often difficult, and these difficulties implied that at least part of the decomposition of the adducts might have thermal rather than photochemical origins. We found that fluorotrichloromethane was an excellent solvent for these reactions, although they proceed a little more slowly than in the arene.

The crude products left after removal of the solvent were complex mixtures; for example, the ^{19}F-n.m.r. spectrum of the product from fluorobenzene showed at least ten separate peaks, of which addition products accounted for about 30%. Steam distillation removed a mixture of unreacted starting material and variously brominated derivatives; again, fluorobenzene provided a mixture in which *o*- (δ, -107.6: 13%) and *p*-bromofluorobenzene (δ, -115.8 ppm: 45%), 2,4-dibromofluorobenzene (δ, -97.0 ppm; *J*, 9 Hz: 32%) and 2,4,6-tribromofluorobenzene (δ, -92.3 ppm: 3%) were identified (^{19}F n.m.r.) along with a little pentabromofluorobenzene and some fluorobenzene. The non-steam volatile residue in each case contained hexabromocyclohexane derivatives along with polybrominated substitution products; crystallisation from ethanol separated the adducts, but with some loss.

(i) Fluorobenzene

The addition products from fluorobenzene could be compared with those earlier reported by van der Linden although the conditions of their preparation were not identical. In the earlier work, mixtures of bromine and arene were sealed in glass and exposed to summer sunlight for some weeks or months before opening the vials and examining the contents. In a number of instances van der Linden reported a vigorous evolution of hydrogen bromide upon mixing the reagents; this was allowed to slacken before sealing the tube and exposing it to light [3]. We observed no such evidence of a rapid substitution process on mixing solutions of arene and bromine, whether alone or in fluorotrichloromethane. Correspondingly, we found no evidence of a monofluoroheptabromocyclohexane and we believe this to have followed an uncontrolled substitution and not to have come from the direct photochemical bromination of fluorobenzene.

The solid from 16 hours'photochemical bromination of fluorobenzene analysed as $C_6H_5FBr_6$ (combustion) and showed an exemplary e.i. mass spectrum in which the regular fragmentation of the six bromine substituents was marked by the appropriate fall in mass of the ion fragment and the corresponding change in complexity of the isotope pattern. A similar series of peaks of lesser intensity arose from the initial loss of fluorine and the further loss of up to six bromine atoms from the derived species. The sharp m.p. suggested a single compound but the ^{19}F-n.m.r. spectrum showed three sets of peaks. Two of these were large, a singlet at δ, -88.6 ppm and a triplet at δ, -113.7 ppm (*J*, 24 Hz), with a small doublet at δ, -98.4 ppm (*J*, 24 Hz) of about one tenth of the intensity of the singlet (All chemical shifts refer to $CFCl_3$ = 0). The singlet may be associated with an equatorial fluorine substituent, since the small coupling constants (*J*, 3-4 Hz [7]) found between such a substituent and axial adjacent hydrogen substituents may well be lost under our spectroscopic conditions. The triplet corresponds to an axial fluorine substituent, flanked by two identically situated axial hydrogen substituents.

These adducts were the major components of all photochemical bromination mixtures from fluorobenzene. When the excess of arene and the substitution products were removed by steam distillation from the adducts, another compound was apparently present since bromine (colour; reaction with $Na_2S_2O_3$) was swiftly formed as the aqueous reaction mixture reached boiling point. This bromine could not have arisen from the three adducts which we have so far identified in the ^{19}F-nmr spectrum and suggests the presence of a fourth. We have only been partly successful in attempts to separate the three stable adducts whether by crystallisation from a range of solvent mixtures, or by column chromatography, or by selective extraction by solvents. However, the three components are apparently a mixture and not part of a dynamic equilibrium of conformers.

(ii) *p*-Difluorobenzene

The steam-volatile material apparently contained 2-bromo-1,4-difluorobenzene (δ, -112.9 and -117.4 ppm: 22%), 2,5-dibromo-1,4-difluorobenzene (δ, -111.2 and -115.7 ppm; 20%), 1,3-dibromo-2,5-difluorobenzene (δ, -104.9 and -105.8 ppm: 20%), 2,3,5-tribromo-1,4-difluorobenzene (δ, -96.7 and -103.5 ppm: 35%) and 2,3,5,6-tetrabromo-1,4-difluorobenzene (δ, -89.0 ppm: 3%) as judged by ^{19}F-n.m.r. Only one adduct was isolated from the *p*-difluorobenzene bromination, and this was used as the key in the analysis of the n.m.r. spectra of the various isolated adducts. The compound analysed well for the structure $C_6H_4F_2Br_6$ and showed the expected e.i. mass spectrum with the regular fragmentation of bromine isotopes from the original molecular ion. Two peaks of equal intensity appeared in the ^{19}F-n.m.r. spectrum, an equatorial fluorine showing δ, -86.2 ppm and an axial fluorine appearing at δ, -112.9 ppm. The axial fluorine showed a triplet arising from interactions (*J*, 26 Hz) with adjacent hydrogen atoms (H_2, H_6) whereas the equatorial fluorine showed no such interactions.

The ^{13}C-n.m.r. spectrum (Fig. 1) showed two doublets at δ, -105.0 and -101.0 ppm respectively, each with $J(C_1\text{-}F)$ of 285 Hz and corresponding to the carbon atoms bearing the axial and the equatorial fluorine atoms respectively. Two doublets centred at δ, -59.4 and -53.3 ppm corresponded to the two pairs of identical carbon atoms. Carbon-fluorine couplings between equatorial fluorine and the second ($J(C_2\text{-}F_e)$, 101.7 Hz) and the third ($J(C_3\text{-}F_e)$, 20.7 Hz) ring carbon atoms, and the corresponding interactions between the axial fluorine and the second ($J(C_2\text{-}F_a)$, 254 Hz) and the third ($J(C_3\text{-}F_a)$, 20.7 Hz) ring carbons atoms were clearly identified. Finally, the ^{1}H-n.m.r. spectrum (Fig. 2) showed couplings between axial hydrogen and axial fluorine in two cases. The set of four peaks in the region δ, 4.56-4.70 ppm showed $J(H_a\text{-}F_a)$, 22 Hz and $J(H_a\text{-}H_a)$, 10 Hz and evidently correspond to a hydrogen atom (H_2) in the least electronegative environment in the system and adjacent to an axial fluorine and an axial hydrogen atom. The second proton showing $J(H_a\text{-}F_a)$, 24 Hz was located in the most electronegative region of the molecule (δ, 5.20-5.30 ppm) and showed interaction with an adjacent equatorial proton ($J(H_a\text{-}H_e)$, 4.1 Hz); it must therefore be H_6. The proton with which H_6 interacted must therefore be H_5, the doublet at δ, 5.07 ppm, and the proton at δ, 4.82-4.88 ppm must similarly be H_3, interacting with the adjacent equatorial fluorine group ($J(H_a\text{-}F_e)$, 3 Hz) and the axial proton at C_2 ($J(H_a\text{-}H_a)$, 10 Hz). Other possible proton interactions were not found.

Such a structure (**1**) suggested that *trans*-addition of bromine had taken place exclusively so that the orientation of halogen addition paralleled that found in benzene itself. As addition to give **1** must be a multi-stage process conformational rearrangements during addition

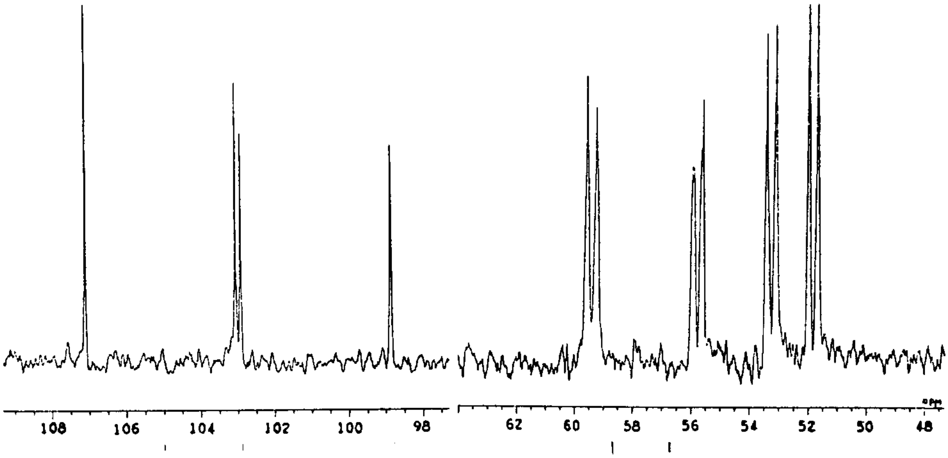


Fig. 1. ^{13}C-NMR Spectrum of hexabromo-adduct of *p*-difluorobenzene.

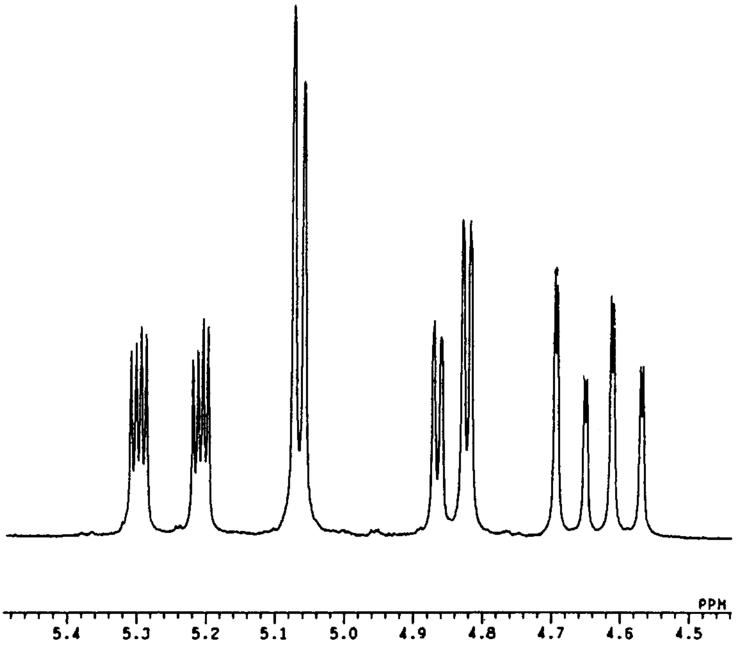
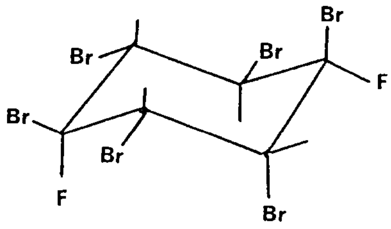


Fig. 2. ^{1}H-NMR Spectrum of hexabromo-adduct of *p*-difluorobenzene.

cannot be excluded and the apparent orientation of addition may be a consequence of a number of energetic interactions.



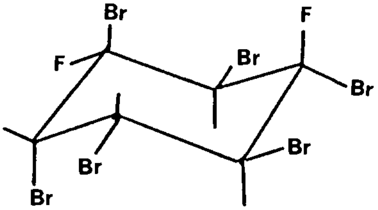
(1)

<u>(iii) *m*-Difluorobenzene</u>

The steam volatile materials from this difluorobenzene apparently contained 2-bromo-1,3-difluorobenzene (δ, -107.7 ppm: 7%) and the 4- (δ, -104.6 and -105.0 ppm: 3%) and 5- (δ, -109.5 ppm: 19%) isomers, along with 2,5-dibromo-1,3-difluorobenzene (δ, -12.3 ppm: 26%), 2,4,5-tribromo-1,3-difluorobenzene (δ, -94.9 and -95.5 ppm: 13%), 2,4,5,6-tetrabromo-1,3-difluorobenzene (δ, -88.1 ppm: 4%) and some recovered difluorobenzene (28%).

The ^{19}F-nmr spectrum of the adduct showed two peaks of equal intensity at δ, -87.3 (singlet) and -115.7 (triplet) ppm corresponding to an equatorial and an axial fluorine group respectively, the latter coupling (*J*, 23 Hz) to two adjacent axial hydrogen atoms. The ^{13}C-nmr spectrum (Fig. 3) showed the presence of these two fluorine atoms clearly in two doublets (*J*, 271 Hz) centred at -101.0 and -100.0 ppm. The second doublet showed fine coupling representing interaction between the carbon atom and the equatorial fluorine group two atoms away, and confirms the orientation of these halogen atoms. Of the four remaining carbon atoms, the system between the two fluorine substituents was readily identified (a) as the carbon atom (C_2) at the highest field (δ,

-61.5 ppm) in the ^{13}C-nmr spectrum and (b) as the hydrogen (H_2) in the ^{1}H-nmr spectrum (δ, 5.3 ppm; doublet of doublets {$J(H_a$-$F_a)$, 22.3 Hz; $J(H_a$-$H_e)$, 5 Hz}; these couplings were reflected in the ^{19}F-nmr spectrum) evidently adjacent to fluorine and, according to the C-H correlation spectrum, attached to C_2. The assignments of C_4 (δ, -57.5 ppm), C_6 (δ, -58.0 ppm), and C_5 (δ, -47.3 ppm) followed from their distances away from the fluorine substituents and their correlation with the complex proton peaks at δ, 4.86 (H_4), 5.18 (H_6) and 4.78 (H_5) ppm respectively. The structure 2 was therefore assigned to this adduct.



(2)

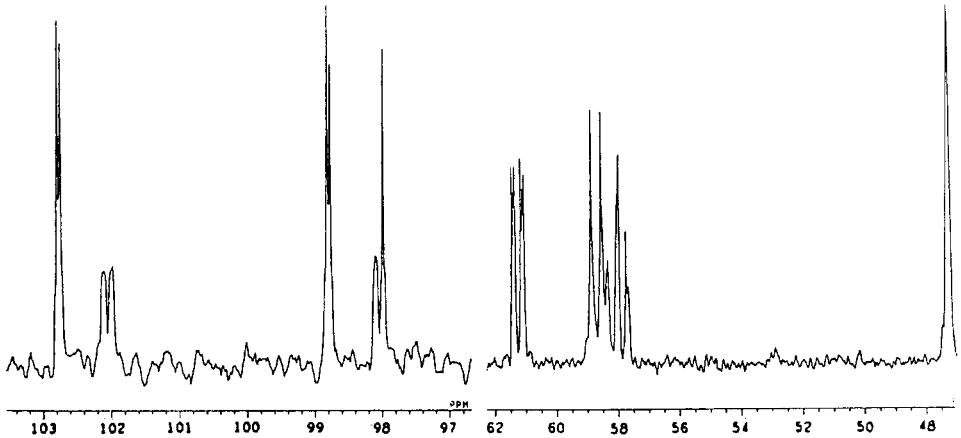
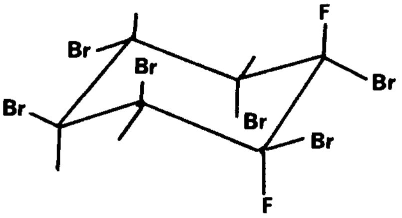


Fig. 3. ^{13}C-NMR Spectrum of hexabromo-adduct of *m*-difluorobenzene.

(iv) *o*-Difluorobenzene

^{19}F-n.m.r. spectroscopy showed the steam-volatile component of the reaction product to contain 4-bromo-1,2-difluorobenzene (δ, -131.0 and -135.4 ppm: 13%) and 1,2-difluoro-4,5-dibromobenzene (δ, -134.4 ppm: 48%) along with unreacted *o*-difluorobenzene.

The ^{19}F-nmr spectrum of the adduct showed a single peak at δ, -98.3 ppm. The ^{13}C-nmr spectrum was remarkably simple, showing (i) a doublet of doublets (*J*, 286 Hz and *J*, 23 Hz) centred at δ, -105.8 ppm and evidently reflecting carbon atoms bearing fluorine, (ii) a triplet (*J*, 100 Hz) centred at δ, -56.4 ppm, and (iii) a broad singlet at δ, -54.3 ppm. These absorbances corresponded to the carbon atoms bearing fluorine, and those which are one and two bonds away from these. The ^{1}H-nmr spectrum was similarly simple, comprising of two peaks at δ, 4.24 and 4.69 ppm, each peak showing a small splitting of 4 Hz. We therefore propose the structure 3 for the 1,2-difluoro-1,2,3,4,5,6-hexabromocyclohexane formed from *o*-difluorobenzene.



(3)

(v) 1,3,5-Trifluorobenzene

The crude reaction mixture contained two identifiable materials, both formed in small amount; one was

1,3,5-trifluoro-2,4,6-tribromobenzene, whose ^{19}F-nmr absorbance at δ, -95.4 ppm agreed with that of authentic material [8]. The second compound was very difficult to separate completely from the mixture, and was obtained in only minute amounts. However, this compound was the major component of the crude reaction product. The ^{19}F-nmr spectrum showed a single sharp peak at δ, -102.35 ppm, suggesting that all three fluorine were in identical environments. The ^{13}C-nmr spectrum showed a triplet of triplets about δ, 101.03 ppm with coupling constants of 175 ($J(C_1-F)$) and 25 ($J(C_2-F)$) Hz, and a second triplet at δ, 58.9 ppm (J, 25 Hz). We associate the first with the carbon atoms bearing fluorine and the second with the carbon atoms bearing only hydrogen and bromine in a very symmetrical molecule; we also found absorbances about δ, 5.2 ppm in the proton nmr spectrum which were consistent with the -CHBr- fragment of the system. Finally, the mass spectrum of the isolated material showed clearly the series of peaks at M/Z 606-618 consistent with the structure $C_6H_3F_3Br_6$. The peaks corresponding to the fragmentation of this ion, through the successive loss of the six bromine atoms, were easily seen. We therefore suggest that the compound may be a,a,a-1,3,5-trifluoro-e,a,e,a,e,a-1,2,3,4,5,6- hexabromocyclohexane, although the configuration about the carbon atoms is open to discussion.

The corresponding attempted photobromination of 1,2,3,4-tetrafluorobenzene and of 1,2,4,5-tetrafluorobenzene was unsuccessful, as judged by ^{19}F-nmr.

EXPERIMENTAL

A Hanovia medium pressure 100-watt mercury lamp was used to irradiate the mixtures of fluoroarene and bromine. The nmr analyses were carried out using two JEOL machines at 90 MHz and 270 MHz with $CDCl_3$ as solvent;

^{19}F-nmr measurements were taken at 84.26 MHz, ^{13}C-nmr at 67.80 MHz and ^{1}H-nmr at 270.05 MHz. Mass spectra (70 eV; e.i.) were obtained using the University of London ULIRS service at the School of Pharmacy; combustion analyses were by Medac (School of Chemistry, Brunel University, Uxbridge).

Synthesis of hexabromocyclohexanes

1-Fluoro-1,2,3,4,5,6-hexabromocyclohexane

A mixture of bromine (0.15 mol), fluorobenzene (0.053 mol) and fluorotrichloromethane (75 cm^3) was irradiated for 42 hours. The cooled mixture was washed with aqueous sodium metabisulphite to remove bromine, evaporated to dryness, and steam-distilled to remove a liquid volatile fraction from the semi-solid residue. Recrystallisation from ethanol gave 1-fluoro-1,2,3,4,5,6-hexabromocyclohexane (4.0 g., 13%. m.p. 121.5-123.0° (lit., 126-7° [3]). (Found: C, 12.48; H, 0.75; Br, 83.09% $C_6H_5FBr_6$ requires C, 12.52; H, 0.88; Br, 83.30%) Mass spectrum (70 eV; E.I.) showed M/Z 570, 572, 574, 576, 578, 580, 582 (1:6:15:20:15:6:1), 491,493, 495, 497, 499, 501 (1:5:10:10:5:1), 412, 414, 416, 418, 420 (1:4:6:4:1), 333, 335, 337, 339 (1:3:3:1), 254, 256, 258 (1:2:1), 175, 177 (1:1) and 96, and a second series beginning at M/Z 551-63 (septet), and proceeding through groups at M/Z, 472-482 (sextet), 393-401 (quintet), 314-320 (quartet), 235-9 (triplet) and ending at 156-8 (1:1) in which fluorine loss preceded bromine abstraction. Column chromatography of the product changed the composition of the mixture and showed that the three fluorine environments arose from different compounds in admixture.

Difluorohexabromocyclohexanes

Under analogous conditions, *o*-difluorobenzene gave 1,2-difluoro-1,2,3,4,5,6,hexabromocyclohexane, m.p. 112-3.5° (1.3 g., 4%. Found, C, 12.27; H, 0.61; Br, 80.88%. $C_6H_4F_2Br_6$ requires C, 12.14; H, 0.61; Br, 80.78%) while *m*-difluorobenzene gave 1,3-difluoro-1,2,3,4,5,6-hexabromocyclohexane m.p. 137-8° (2.01 g, 11%. Found: C, 12.15; H, 0.61; Br, 80.95%) and *p*-difluorobenzene gave 1,4-difluoro-1,2,3,4,5,6-hexabromocyclohexane m.p. 110-111° (0.9 g., 3.1%. Found: C, 12.25; H, 0.66; Br, 80.59%). Each product showed similar mass spectra, with M/Z values of 588-600 (1:6:15:20:15:6:1) for the parent ion and the regular loss of bromine from intermediate ions until M/Z 114 corresponding to the original difluorobenzene.

The corresponding treatment of 1,3,5-trifluorobenzene gave a semi-solid product whose mass spectrum and ^{19}F-nmr (δ, -102.35 ppm) showed the presence of the hexabromo-adduct (M/Z, 606-618, 527-537, 448-456, and 369-375 blurred by the presence of 1,3,5-trifluoro-2,4,6-tribromobenzene at 366-372.) Continuous crystallisation gave the impure adduct (1 mg) which was identified by mass spectrometry. 1,2,3,4- and 1,2,4,5-Tetrafluorobenzene showed no evidence of attack by bromine under photochemical bromination conditions.

ACKNOWLEDGEMENTS

A generous grant for chemicals from the Associated Octel Company, Ellesmere Port, South Wirral is gratefully acknowledged. The authors also wish to thank Dr L H Sutcliffe for his considerable help in the interpretation of the n.m.r. spectra.

Lastly, we are most grateful to the Astra Neuroscience Research Unit for permission to use their 270 MHz JEOL instrument, without which the identification of the adducts would have been severely hampered.

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