139. Neighboring-Group Participation in the Gas Phase

Loss of Benzaldehyde from [(Benzyloxy)methyl]dialkylsilyl-Substituted 1,3-Dithianes

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Dedicated to Prof. Dr. *M. Hesse* on the occasion of his 60th birthday

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[(Benzyloxy)methyl]dialkylsilyl-substituted 1,3-dithianes show in CI-MS an abundant loss of benzaldehyde from the $[M + H]^+$ quasi-molecular ion. The fragmentation is explained with an intramolecular redox process, where a hydride is proposed to be transferred from the benzyl position to a neighboring thionium ion. This would form a particle that could readily lose benzaldehyde as a neutral fragment. The CI-MS results provide an explanation for the unusual instability of (benzyloxy)methyl-substituted silanes towards acids. In fact, the formation of benzaldehyde was established in the decomposition of a (benzyloxy)methyl-substituted acylsilane in the presence of *Lewis* or *Brønsted* acids and ethanethiol. The CI-MS study, therefore, represents a useful method to recognize unusual reactions that are – or might be – important in solution.

Introduction. – Chemical ionization (CI) is widely used in mass spectrometry (MS) as a 'soft' ionization method [1] [2]. Usually, a reactant ion (HX^+) simply protonates a functionalized sample molecule M to give the quasi-molecular ion $[M + H]^+$, or it forms with M a cluster ion of the type $[M + H + X]^+$. Little or no fragmentation is generally observed with low-molecular-weight compounds, and the CI-MS method is, therefore, quite reliable for determining the relative mass of a sample compound. Only in special cases, fragmentation becomes more important. Most of these fragmentations, however, are easily explained by simple elimination or substitution reactions, but, as we have shown earlier, fragmentations that follow more elaborate mechanisms are also possible [3] [4]. The latter become particularly interesting with molecules that permit the facile expulsion of neutral fragments by a reaction involving neighboring-group participation.

In solution chemistry, it is at times difficult *a priori* to recognize neighboring-group-facilitated reactions or structural features that allow them. At first, a compound can simply exhibit a rather undesired or unexpected reactivity which migh be later explained – knowing more about, *e.g.*, product structures – by the effect of a proximate functional group. In molecules, however, where neighboring-group participation leads mainly to decomposition, the recognition of such processes as well as the localization and characterization of the responsible structure moieties might present a serious problem.

Since ionic gas-phase fragmentations in CI-MS and acid-catalyzed reactions in solution possibly start from similar intermediates, analogous reactions might be detected in

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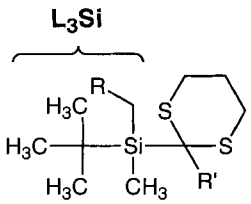
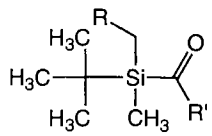
the gas phase and in solution. In cases where the gas-phase reactions are easier to follow, the careful study of CI-MS fragmentation can efficiently help to solve problems of the above kind, as we report in this paper.

Results and Discussion. – In connection with our investigations of Si-based chiral auxiliaries [5] [6], we have encountered that some (benzyloxy)methyl-substituted silanes exhibit a different behavior than their (alkoxymethyl)dialkylsilyl- or simple trialkylsilyl-substituted analogs: *e.g.* the hydrolysis of (benzyloxy)methyl-substituted thioacetals of the type **1** ($HgCl_2$, $CdCO_3$, H_2O/toluene/acetone; reflux) involved considerable side reactions, but the deprotection of (2-methoxyethoxy)methyl- and the Me-substituted analogs **2** and **3** was unproblematic. Likewise, the treatment of acylsilanes **4** with organometallic species or silyl enol ethers in presence of strong *Lewis* acids led to complete decomposition of the starting material [7]; the corresponding acylsilanes **5** and **6**, on the other hand, afforded the desired addition products in reasonable yields. Analogously, *Brønsted*-acid-catalyzed reaction of **5** and **6** with 1,2-diols gave the corresponding acetals in good yields, whereas the acetalization of **4** was slow and affluently accompanied by side reactions.





1 R = $PhCH_2O$
R': see the *Table*

2 R = $CH_3OCH_2CH_2O$
R': see the *Table*

3 R = H
R': see the *Table*

4 R = $PhCH_2O$
R': see the *Table*

5 R = $CH_3OCH_2CH_2O$
R': see the *Table*

6 R = H
R': see the *Table*

Evidently, the unique reactivity of the compounds **1** and **4** is connected to the $PhCH_2O$ moiety. How the $PhCH_2O$ groups promote decomposition, however, and what kind of transformations are involved in the decay were first of all unknown. From previous experiences with $PhCH_2O$ substituted silanes [3], we suspected intramolecular redox reactions as a possibility and expected mass spectrometry to provide more information. In fact, the CI-MS and ESI-CAD-MS (electrospray-ionization collision-activated-decomposition mass spectrometry) studies on dithiane derivatives **1** – in comparison to those of the analogs **2** and **3** – gave evidence for an intramolecular hydride shift.

The results of our MS investigations are summarized in the *Table*; representative spectra for compounds of the type **1** (CI-MS of **1a** with NH_3 and ND_3 as the reactant gases and the corresponding ESI-CAD-MS) are shown in *Fig. 1*. The CI-MS of silyl-substituted dithianes **1** exhibit the trivial signals for the quasi-molecular ions $[M + H]^+$ and

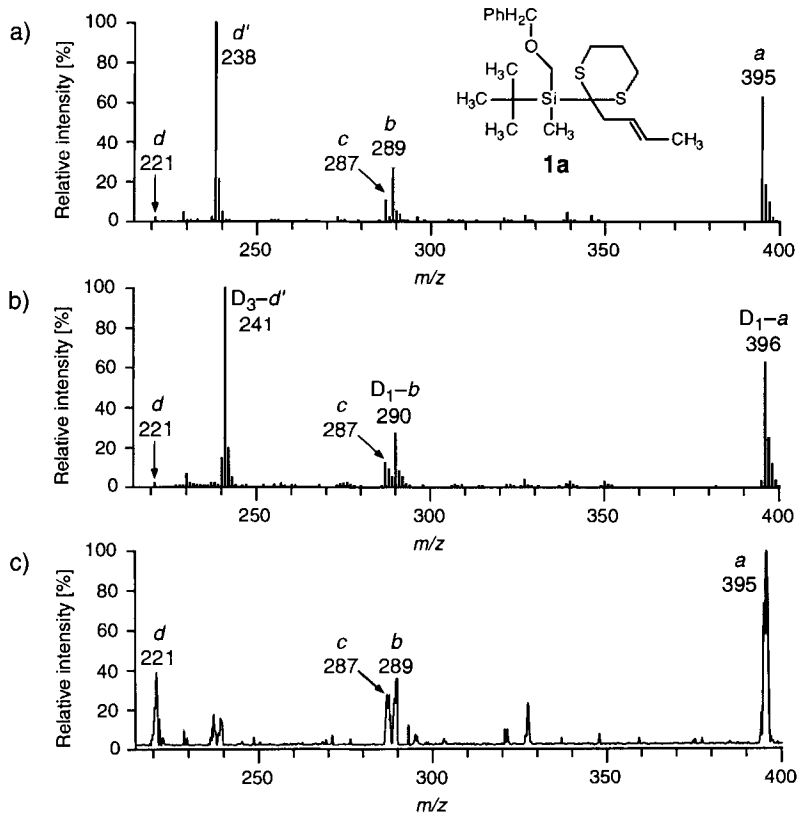


Fig. 1. *MS of* **1a**. *a*) CI-MS with NH_3 as reactant gas; *b*) CI-MS with ND_3 as reactant gas; *c*) ESI-CAD-MS of the $[M + H]^+$ ions (*m/z* 395) at $E_{coff} = 10$ eV. Focus is given on the ions of the type $a = [M + H]^+$, $b = [M + H - PhCHO]^+$, $c = [M + H - RH]^+$, $d = [L_3Si]^+$, and $d' = [L_3SiNH_3]^+$.

for the Si-containing cations $[L_3Si]^+$ and/or $[L_3SiNH_3]^+$[2]) (signals *a*, *d*, and *d'*, resp., in spectrum a of compound **1a**; *Fig. 1* and *Table*). Such ions are ubiquitously detected with most types of silanes and are, therefore, not too informative; for their formation, the most polarized Si–C bond is cleaved heterolytically. Additionally, abundant signals for particles of the type $[M + H - PhCH_2OH]^+$ (signals *c*) and $[M + H - 106]^+$ (signals *b*) are observed. Signals *c* arise most probably by elimination or substitution of $PhCH_2OH$; the (2-methoxyethoxy)methyl-substituted analog **2d** loses likewise 2-methoxyethanol (*Table*). Signals *b*, which are unique for (benzyloxy)methyl-substituted compounds of the type **1**, and which are equally found in ESI-CAD-MS[3]), could be formed by the loss of

[2]) Interestingly, the parent quasi-molecular ions of the type $[M + NH_4]^+$ are not observed (< 1 rel. %) for most of the compounds given in the *Table*.

[3]) The ESI-CAD spectrum shows besides the quasi-molecular ion *a* and the fragment ions *b*, *c*, and *d* some further signals that are not observed in CI-MS. Evidently, additional fragmentation reactions are important in CAD-MS. We assume, however, that the fragments *b* and *c* arise in CAD-MS on a similar path as in CI-MS. A parent-ion scan of *b* or *c* cannot give more information about the fragmentation paths, since solely the $[M + H]^+$ and $[M + Na]^+$ signals were observed in the ESI-MS.

Table. *MS Results Obtained with Compounds* **1–7**

Sample Molecule			Ionization method (reactant gas)	Fragments (relative intensities in %)					
No.	R	R′		*a* $[M+H]^+$	*a′* $[M+NH_4]^+$	*b* $[M+H–PhCHO]^+$	*c* $[M+H-RH]^+$	*d* $[L_3Si]^+$	*d′* $[L_3SiNH_3]^+$
1a	$PhCH_2O$	$MeCH=CHCH_2$	CI (NH_3)	62	0	*27*	10	2	100
1a	$PhCH_2O$	$MeCH=CHCH_2$	CI (ND_3)	62[a])	0	*27*	12	2	100[b])
1a	$PhCH_2O$	$MeCH=CHCH_2$	CI (i-Bu)	54	0	*30*	27	100	–
1a	$PhCH_2O$	$MeCH=CHCH_2$	ESI-CAD	100	–	*35*	25	38	–
1b	$PhCH_2O$	$CH_2=CHCH_2$	CI (NH_3)	44	0	*100*	43	3	95
1b	$PhCH_2O$	$CH_2=CHCH_2$	CI (ND_3)	39[a])	0	*100*	44	3	84[b])
1c	$PhCH_2O$	$PhCH_2$	CI (NH_3)	51	0	*100*	42	2	75
1c	$PhCH_2O$	$PhCH_2$	CI (ND_3)	39[a])	0	*100*	46	1	81[b])
1d	$PhCH_2O$	Ph	CI (NH_3)	33	0	*100*	15	4	29
2d	$MeOCH_2CH_2O$	Ph	CI (NH_3)	36	0	*0*[c])	100	0	0
3a	H	$MeCH=CHCH_2$	CI (NH_3)	100	0	–	–	0	0
3a	H	$MeCH=CHCH_2$	CI (ND_3)	100[a])	0	–	–	0	0
3a	H	$MeCH=CHCH_2$	CI (i-Bu)	100	0	–	–	5	0
3b	H	$CH_2=CHCH_2$	CI (NH_3)	100	0	–	–	0	0
3b	H	$CH_2=CHCH_2$	CI (ND_3)	100[a])	0	–	–	0	0
3c	H	$PhCH_2$	CI (NH_3)	100	0	–	–	0	0
3c	H	$PhCH_2$	CI (ND_3)	100[a])	0	–	–	0	0
4b	$PhCH_2O$	$CH_2=CHCH_2$	CI (NH_3)	71	100	*0*	0	4	45
4c	$PhCH_2O$	$PhCH_2$	CI (NH_3)	57	24	*0*	0	8	100
4d	$PhCH_2O$	Ph	CI (NH_3)	100	0	*0*	0	0	0
4e	$PhCH_2O$	Me	CI (NH_3)	100	34	*0*	0	0	8
5d	$MeOCH_2CH_2O$	Ph	CI (i-Bu)	100	0	*0*[c])	0	6	–
5e	$MeOCH_2CH_2O$	Me	CI (i-Bu)	100	0	*0*[c])	7	100	–
6b	H	$PhCH_2$	CI (NH_3)	27	100	–	–	0	24
6e	H	Me	CI (NH_3)	35	100	–	–	0	7
7a	Et	H	CI (i-Bu)	49	0	*100*	–	8	0
7b	Me_3Si	H	CI (NH_3)	95	0	*100*	–	0	7
7c	Me	$CH_2=CH$	Ci (NH_3)	100	0	*5*	–	0	27

[a]) $[M+D]^+$. [b]) $[L_3SiND_3]^+$. [c]) $[M+H-CH_3OCH_2CHO]^+$.

PhCHO from the protonated sample molecule. A fragmentation involving the loss of PhCHO from the quasi-molecular ion is most reasonable, since the fragment ion has directly to be related to the $PhCH_2O$ group of the molecule, and since a fragmentation path involving the expulsion of particles of the composition $C_3H_6S_2$ (106 a.m.u.) could be excluded due to the isotopic patterns of the signals *b* (see *Fig. 2*).

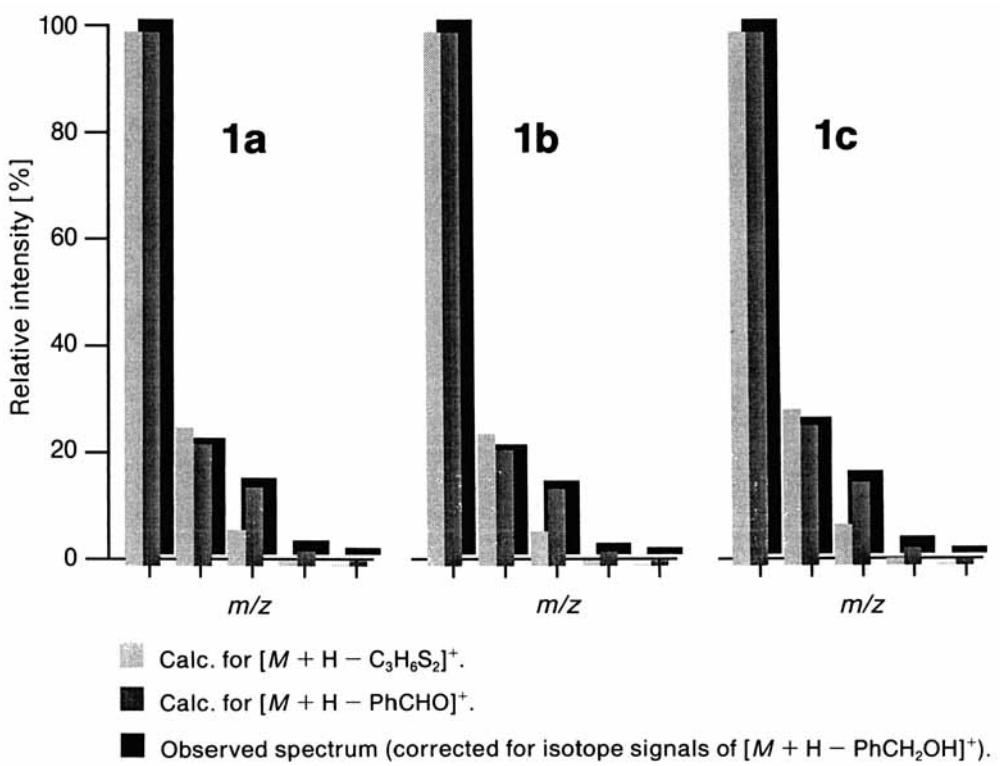
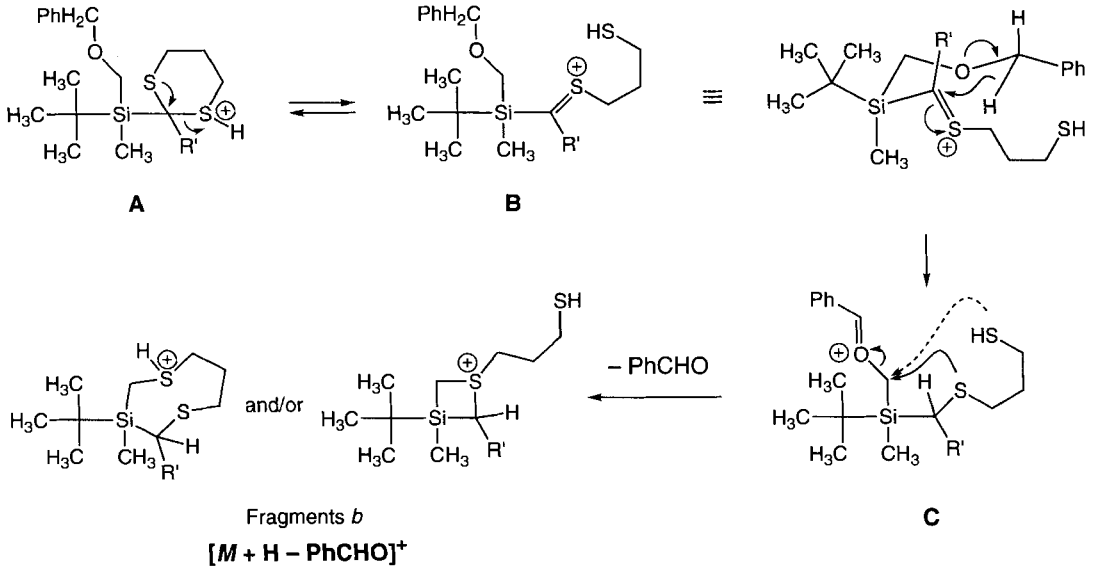


Fig. 2. *Isotopic patterns of the* b *fragments of* **1a–1c**

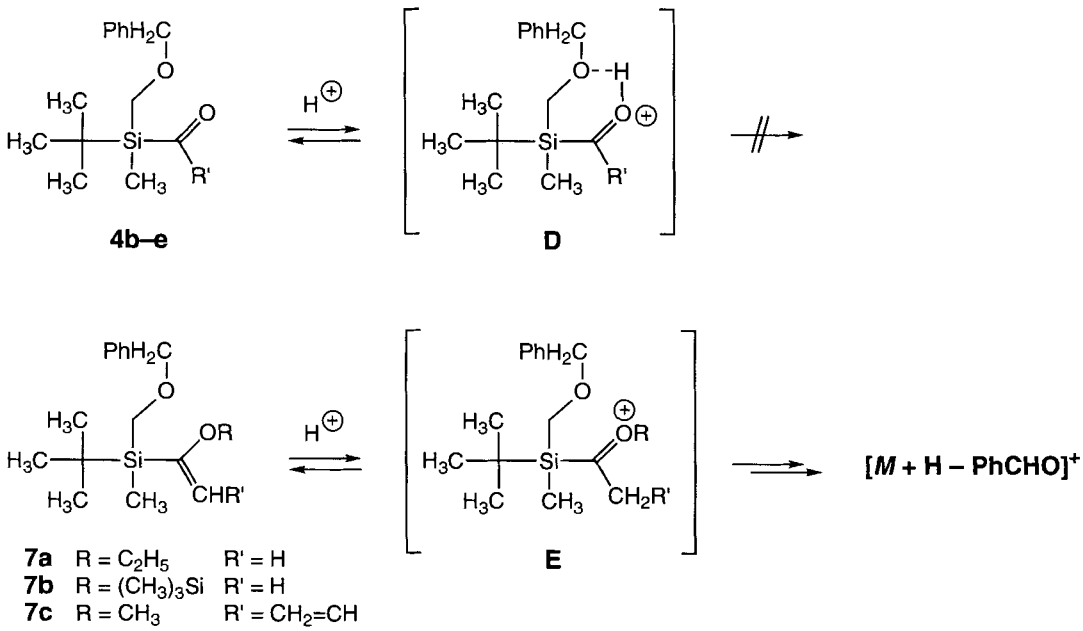
For the loss of PhCHO from the quasi-molecular ion of a $PhCH_2O$-group-containing molecule, which would indicate an intramolecular redox process, we propose the mechanism outlined in *Scheme 1*. After protonation of a S-atom by the reactant ion, the dithiane ring of intermediate **A** would reversibly open to form a thionium species of the type **B**. Under the influence of the electron-donating effect of the O-atom, a benzylic H-atom could be transferred as a hydride *via* the six-membered transition state to the neighboring electrophilic C-center leading irreversibly to a species of the type **C**. An analogous process was already described earlier [3]. The species **C**, in turn, could lose PhCHO either spontaneously or, which is more likely, by an intramolecular substitution, again supported by a neighboring S-atom.

The proposed mechanism is in agreement with the CI-MS results obtained with ND_3 as the reactant gas: the fragment ions *b* (see *e.g.* spectrum *b* in *Fig. 1*, or the *Table*) still

Scheme 1



Scheme 2

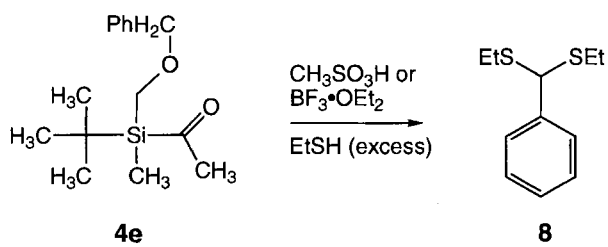


possess the D-atoms that were transferred from the reactant gas by chemical ionization of the sample. This is, as expected, not the case for, *e.g.*, the fragments *c* that arise from $[M + D]^+$ by intramolecular substitution or elimination of $PhCH_2OD$.

Since the fragmentation of (benzyloxy)methyl-substituted dithiane derivatives is assumed to proceed *via* thionium species of the type **B**, it is rather astonishing that acylsilanes **4** do not show a similar loss of a fragment with the mass 106 a.m.u. from quasi-molecular ion in CI-MS (for fragmentation pattern, see the *Table*). It would be expected that protonation of an acylsilane could lead to an oxonium ion that should be equally amenable for a hydride transfer as a thionium cation, and finally should lead to the expulsion of PhCHO. We assume, however, that the H-atom in such an oxonium species is primarily located inbetween the two O-atoms as shown with **D** (*Scheme 2*). This would not only decrease the reduction power of the benzyl-ether moiety, but also prevent the molecule to attain the ideal conformation for a hydride transfer. In fact, oxonium ions, in which this kind of deactivation does not happen, lose 106 a.m.u. in CI-MS, too: *e.g.* enol ethers **7** are protonated to produce O-substituted oxonium ions, which are close relatives of the thionium intermediates proposed above. Intramolecular hydride transfer should be possible with these species and PhCHO (106 a.m.u.) could be lost (see the *Table*).

The loss of PhCHO from (benzyloxy)methyl-substituted silanes is not unequivocally established by the MS investigation discussed above. However, the fragmentation observed in MS seems not to be restricted to the gas-phase alone: *e.g.* the reaction of **4e** with ethanethiol in CH_2Cl_2 and in presence of $BF_3 \cdot OEt_2$ or $MeSO_3H$ afforded thioacetal **8** in 85 or 69% yields, respectively (*Scheme 3*). This reaction gives evidence for the proposed

Scheme 3



4e **8**

facile loss of PhCHO from $PhCH_2O$-substituted silanes. The decomposition of **4e** is also assumed to proceed *via* a thionium ion by intramolecular hydride transfer and expulsion of PhCHO. Subsequently, the liberated PhCHO is trapped and transferred to the thioacetal. To successfully detect PhCHO, it is crucial to perform the degradation experiment in presence of a thiol. The treatment of acylsilanes **4** (or of dithianes **1**) with *Lewis* or *Brønsted* acid alone gave complete decomposition of the starting compounds. No PhCHO could be detected by GC analysis and spectroscopic means.

Conclusion. – We have shown with our investigation that the study of CI-MS and ESI-CAD-MS fragmentations, particularly the analysis of unusual decomposition pathways, is important. The profound knowledge of such fragmentation paths does not only

prevent misinterpretations of mass spectra, but the study of gas-phase reactions allows also the acquisition of information concerning the reactivity of a certain molecule. In our case, the interpretation of the CI-MS and ESI-CAD-MS of [(benzyloxy)methyl]dialkylsilyl-substituted 1,3 dithiane derivatives gave the clue for the understanding of the instability of a whole class of compounds towards acids.

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Experimental Part

Instrumental. The CI-MS experiments were carried out on a *Finnigan MAT-90* mass spectrometer. Standard conditions: ion-source pressure, 10^{-4} mbar (isobutane, NH_3, or ND_3); temp. 220°; emission current, 0.2 mA, 150 eV ($[C_4H_9]^+/[C_3H_7]^+ = 5.6$ or $[NH_4]^+/[NH_4NH_3]^+ = 3.0$); scan low mass m/z 60; sample inlet, crucible in crucible holder on a 'direct introduction sample rod' at 40°. The RICs ($m/z > 60$; corresponds to sample fragment ions) were 7.6 (± 3)% of the TICs or 8.2 (± 3)% of the RICs ($m/z < 60$; corresponds to reactant ions). The spectra were reproducible within ± 5% of the resp. rel.% intensities. No time dependence of the spectra could be recognized after constant conditions in the source were reached. EI-MS: *Finnigan MAT-90* mass spectrometer; ion-source temp., 220°; emission current, 0.8 mA, 70 eV; scan low mass m/z 30.

ESI-CAD-MS were obtained on a *Finnigan TSQ 700* triple quadrupole mass spectrometer (San Jose, CA, USA). Samples were continuously introduced through the electrospray interface (N_2 drying gas at 110°) at a rate of 2 µl/min and with the capillary held at 3.5–3.6 kV. Only the $[M + H]^+$ ions were selected in the first quadrupole (Q_1) and passed through the collision cell (Q_2) with an Ar pressure of 3.0–3.5 mTorr. The collision activation energy (E_{coff}) was set to 10 eV to obtain optimized fragment-to-noise ratios and best reproducibility of the spectra. The product ions were detected by scanning the third quadrupole (Q_3) in the range of m/z 40 to 450 over 3 s, and 20 scans were averaged to obtain representative spectra.

The abundance of the ions in the CI-MS and ESI-CAD-MS are reported in % relative to the base peak.

Samples. The sample compounds [8] were chromatographed, distilled, and characterized by ^{1}H-NMR, ^{13}C-NMR, IR, and elemental analysis. No neutral loss of mass 106 a.m.u. is detected in the EI-MS, showing that not (partial) EI-MS conditions in the source are responsible for the formation of the corresponding fragments in CI-MS. For the ESI-CAD-MS experiments, the samples were dissolved in a 0.3% soln. of CF_3CO_2H in CH_2Cl_2/MeOH (2:1) to give a 10^{-4} M soln.

REFERENCES

[1] F.H. Field, 'Chemical Ionization Mass Spectrometry', Butterworths, London, 1972, Vol. 1.
[2] F.H. Field, 'Ionization Methods in Mass Spectrometry', John Wiley & Sons, Chichester, 1985, Vol. 10, Part A.
[3] N. Bild, A. Chapeaurouge, S. Gfeller, S. Bienz, *Org. Mass Spectrom.* **1992,** *27,* 896.
[4] S. Matile, A. Janowitz, S. Ghirlanda, A. Lorenzi-Riatsch, A. Horni, A. Moricz, S. Bienz, N. Bild, W.-D. Woggon, M. Hesse, *Helv. Chim. Acta* **1993,** *76,* 1305.
[5] S. Bienz, A. Chapeaurouge, *Helv. Chim. Acta* **1991,** *74,* 1477.
[6] A. Chapeaurouge, S. Bienz, *Helv. Chim. Acta* **1993,** *76,* 1876.
[7] V. Enev, A. Chapeaurouge, S. Bienz, unpublished results.
[8] P. Huber, J. Fässler, S. Bienz, in preparation.