Fragmentation of Trimethylsilyl Derivatives of 2-Alkoxyphenols: a Further Violation of the 'Even-electron Rule'

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The mass spectra of trimethylsilyl (TMS) ethers of 2-methoxyphenols show abundant $[M-30]^+$ ions originating from consecutive loss of two methyl radicals. This is illustrated by comparison of the accurate mass-measured and linked-scan spectra of the TMS derivatives of 2-methoxyphenol (guaiacol), 4-hydroxy-3-methoxybenzaldehyde (vanillin) and 3-(4-hydroxy-3-methoxyphenyl)-2-propenoic acid methyl ester (ferulic acid methyl ester) with those of the TMS derivatives of phenol, 4-hydroxybenzaldehyde, 3-(4-hydroxy-phenyl)-2-propenoic acid methyl ester (*p*-coumaric acid methyl ester), 3-methoxyphenol and 4-methoxyphenol. This distinctive ortho effect is valuable in the identification of isomeric phenolic compounds. In the spectra of the TMS derivatives of 2-ethoxyphenol and 2-propoxyphenol the sequential loss of two radicals is less pronounced, because elimination of the side-chain and a methyl group with rearrangement and hydrogen migration is competitive.

INTRODUCTION

With the advent of the coupling of gas chromatography and mass spectrometry as a routine method in the analytical laboratory, the separation and identification of natural polar compounds as their trimethylsilyl (TMS) derivatives, has become a well-established procedure. However, since the silyl group migrates as readily as the hydrogen atom, the mass spectra of TMS derivatives are marked by intramolecular rearrangements, as shown by numerous detailed investigations.¹⁻⁴ Because of this the interpretation of spectra of unknown compounds has been difficult. Moreover intermolecular transfer of TMS groups may occur,⁵⁻⁷ and incorporation^{8,9} and displacement¹⁰⁻¹² reactions during silylation must be taken into account. The complexity is increased when overlapping spectra of mixtures have to be evaluated.

In this situation accurate mass measurement is the most convincing support, because even the electron bookkeeping guide, generally known as the evenelectron rule, is violated,^{13,14} as we report in this investigation.

RESULTS AND DISCUSSION

Comparing the mass spectra of the TMS ethers of phenol (1) and guaiacol (2) in Fig. 1 one may assume that 2 loses formaldehyde under electron impact (EI) to yield a radical cation which corresponds to the molecular ion of 1. The agreement in nominal masses below m/z 166 in the two spectra seems to confirm this assumption, but the differences in the abundances of the ions are not to be neglected. Accurate mass † Author to whom correspondence should be addressed.

measurement, however, reveals an elemental composition of $C_8H_{10}O_2Si$ for ion m/z 166 in the spectrum of 2 without any detectable amount of $C_9H_{14}OSi$, a surprising violation of the even-electron rule, which is verified by linked-scan measurements B/E of the ions m/z 196 and m/z 181 as well as B^2/E of ion m/z 166 in the spectrum of 2 (Table 1).

The same conditions are encountered when comparing the spectra of the TMS ethers of 4hydroxybenzaldehyde (3) and of vanillin (4) in Fig. 2. The ions m/z 194 to be compared in the two spectra have different elemental compositions. The molecular ion of 4 eliminates two methyl radicals to yield m/z 194 with the elemental composition C₉H₁₀O₃Si. Ion m/z 194 $[C_{10}H_{14}O_2Si]^{+}$, is not detectable. The B/E scan of m/z 224 and m/z 209 and the B^2/E scan m/z 194 verify the fragmentation pathway of suggested (Table 2).

In an examination of the literature we found that data were already available for this type of fragmentation. In 1972 Horman and Viani, for example, reported on metastable ions for the consecutive loss of two methyl radicals from the molecular ion of the TMS derivative of ferulic acid methyl ester (5).¹⁵ We were able to confirm the suggested mechanism by mass measurement, which accurate proved $C_{12}H_{14}O_4Si$ to be the elemental composition of ion m/z 250, the base peak in the spectrum of 5, without any detectable quantity of $[C_{13}H_{18}O_3Si]^+$. The work of Horman and Viani and of McCloskey¹⁶ provided further examples which demonstrated that consecutive loss of two methyl radicals is possible under electron impact with compounds which have the methoxy and the TMS group in the 1,2-positions on the aromatic ring and do not possess any other fragmentationdirecting groups. This is the case with 3-(3,5-dimethoxy-4-trimethylsilyloxyphenyl)-2-propenoic acid

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Figure 1. EIMS of phenol-TMS and guaiacol-TMS.

methyl ester (6), 3-methoxy-4-trimethylsilyloxybenzoic acid methyl ester (7) and 3-methoxy-4-trimethylsilyloxyphenylacetic acid methyl ester (8). In the spectrum of the TMS derivative of α -hydroxy-4hydroxy-3-methoxybenzeneacetic acid methyl ester (9) an α -cleavage is favoured over the sequential radical elimination as illustrated in Table 3. With the methoxy and the trimethylsilyloxy group in 1,3- or 1,4-positions on the ring, *ortho* interaction is no longer possible and the sequential loss of two methyl radicals is suppressed



Figure 2. EIMS of 4-hydroxybenzaldehyde-TMS and vanillin-TMS.

ORGANIC MASS SPECTROMETRY, VOL. 20, NO. 10, 1985 615



[M-30] spectra	intensity of ions in the of 6–9			
Compound	Rel. int. (%)			
6	100			
7	100			
8	52			
9	0			



Scheme 1

as illustrated in Fig. 3, which shows the spectra of 1methoxy-3-trimethylsilyloxybenzene (10) and of 1methoxy-4-trimethylsilyloxybenzene (11). This pronounced *ortho* effect is valuable in the interpretation of unknown phenolic compounds.

The driving force for the expulsion of the second radical in aromatic 1-methoxy-2-trimethylsilyloxy compounds is the stability of the silicon-oxygen bond, which leads to the formation of a stable cyclic radical cation. To give further proof for this mechanism, we synthesized 1-methoxy- d_3 -2-trimethylsilyloxybenzene (**12**) and found elimination of a methyl group in the first step, and of the trideuteromethyl group in the second step exclusively, as shown in Scheme 1.

To corroborate the conclusions drawn from the experimental findings, we examined the corresponding



Figure 3. EIMS of 3-methoxyphenol-TMS and 4-methoxyphenol-TMS.

⁶¹⁶ ORGANIC MASS SPECTROMETRY, VOL. 20, NO. 10, 1985



Scheme 2

energetics by applying MNDO-UHF calculations^{17,18} to the possible equilibrium structures on the potential energy surface. Since the individual structural parameters of the species were not known, we optimized all geometrical parameters with respect to the theoretical heats of formation. An overall view of the obtained results is summarized in Scheme 2. Evidently, the calculations predict that a primary fragmentation of a methyl group originating from the 2-methoxydimethylsilylbenzene cation would involve a highly endothermic reaction step. A primary cyclization of the reactant is predicted to be energetically much more favourable. As seen from the scheme, the consecutive loss of a second methyl radical is predicted to take place at the methoxy group of the parent species, because the amount of internal vibronic energy (= 171 kJ mol⁻¹) does not allow for the alternative route to be followed.

Elimination of a third or even a fourth methyl radical to give a 1,3-dioxa-2-silainden radical cation is possible¹⁹ (Scheme 1).

Examination of the spectra of TMS derivatives of 2ethoxyphenol (13), 2-propoxyphenol (14), 2-(1methylethoxy)phenol (15) and 2-butoxyphenol (16) showed that pronounced consecutive loss of two alkyl radicals is limited to 1-methoxy-2-trimethylsilyloxy compounds. According to the spectra of 13-16 loss of a methyl group together with the side-chain leads under rearrangement and hydrogen migration to a common base peak at m/z 167 [C₈H₁₁O₂Si]⁺, while consecutive loss of an alkyl radical from [M-15]⁺ to m/z 166 is only a minor pathway (Table 4). The linked-scan spectrum B/E of the molecular ion of 16 revealed a direct genetic relationship between ion m/z 167 and the molecular ion. Furthermore a B/E scan of ion m/z 167 gave loss of a hydrogen atom as a second reaction channel for the genesis of ion m/z 166.

CONCLUSION

In summary successive loss of stable radicals is frequent in the fragmentation of *ortho*-substituted trimethylsilyl ethers of phenols. The first step in this type of fragmentation is usually loss of a methyl radical from the molecular ion, the second a loss of a stable radical from the *ortho* position.^{20,21}

EXPERIMENTAL

The phenolic compounds were obtained from commercial sources or synthesized according to wellknown procedures.²² Their purity was confirmed by b.p., n_D^{25} and ¹H-NMR spectra.

Iodomethan- d_3 was prepared in 91% yield from methanol- d_4 . The isotopic purity of 1-methoxy- d_3 -2hydroxybenzene was approximately 99.5 atomic % D (¹H-NMR).

Esterification was performed with methanol and dry HCl.

TMS derivatives were obtained by silulation with N,O-bis(trimethylsilul)acetamide (BSA, Aldrich) in concentrations of 10 mg phenolic compound in 1 cm³ dry CCl₄.

All mass spectra were recorded on a VG ZAB mass spectrometer connected to a data system VG Multispec and to a Carlo Erba Fractovap 2900 Gas Chromatograph (GC). Inlet was either GC or direct. The ionization energy was 70 eV, the trap current $200 \,\mu$ A and the source temperature $200 \,^{\circ}$ C. Accurate mass measurement was made with the data system at a dynamic resolution of 4000 and by variation of the acceleration voltage at a static resolution of 15 000. PFK was used as reference.

Typical GC conditions were: column 3% OV 101, 2 m; temperature program, 60–200 °C, 4°/min; injector, 225 °C; interface, 170 °C; 22 cm³ He/min.

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	Table 4	. Partial	mass	spectra	of	compounds 13–16
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Compound	[M]*'	[M CH ₃]+	[C ₈ H ₁₁ O₂Si] ⁺	Rel. int. (%) [C ₈ H ₁₀ O₂Si] ^{+∵}	[C ₇ H ₇ O₂Si] ⁺	[C ₆ H₄O₂Si] ^{+∙}	[C ₇ H ₇]⁺
13	50	5	100	58	35	17	7
14	51	1	100	48	40	14	7
15	40	1	100	81	65	14	12
16	43	0.3	100	64	42	11	7

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