

Intramolecular benzyl–benzyl interactions in protonated benzyl diethers in the gas phase. Effects of internal hydrogen bonding



Marina Edelson-Averbukh, Alexander Etinger and Asher Mandelbaum*

Department of Chemistry, Technion - Israel Institute of Technology, Haifa, Israel

Received (in Cambridge) 10th March 1999, Accepted 6th April 1999

Protonated molecules of a variety of benzyl diethers, produced by chemical ionization (CI), undergo a unique rearrangement yielding relatively abundant m/z 181 $C_{14}H_{13}^+$ ions, both in the ion source and under collision-induced dissociation (CID) conditions. This highly general rearrangement involves an intramolecular C–C bond formation between the two benzyl groups, and the resulting $C_{14}H_{13}^+$ ions have been shown by the analysis of their CID spectra to be an almost equimolar mixture of isomeric α -*o*-tolylbenzyl, α -*p*-tolylbenzyl and *p*-benzylbenzyl cation structures in all cases. This structural information suggests that this process may be viewed as gas-phase aromatic substitution of the non-charged benzyloxy group by the benzyl cation originating from the protonated ether function involving a series of π - (and/or ion–neutral) and σ -complexes. The extent of this fragmentation in alkane benzyl diethers $PhCH_2O(CH_2)_nOCH_2Ph$ ($n = 2–10, 12$) is strongly affected by the alkane chain length. Stereoisomeric benzyl diethers display an unusual steric effect: the *trans*-isomers give rise to more abundant $C_{14}H_{13}^+$ ions than their *cis*-counterparts. The latter two effects are explained in terms of intramolecular hydrogen bonding between the two alkoxy groups. Bis(benzyloxy)benzenes and -naphthalenes exhibit very low abundance $C_{14}H_{13}^+$ ions in contrast to the aliphatic analogues. This behavior is attributed to competing intramolecular benzylation involving the aromatic skeletons of these compounds.

Introduction

Rearrangement processes of organic ions in the gas phase have been the subject of continuous interest since the early days of organic mass spectrometry. They represent the most fascinating kind of gas phase interactions leading, sometimes, to totally unexpected fragmentation products. In many cases remarkably good correlations have been found for gas phase reactions under chemical ionization (CI) conditions with well known acid catalyzed molecular rearrangements in solution.^{1–4} Besides its fundamental value in gas phase ion chemistry, the study of the rearrangements in CI mass spectrometry can thus be of considerable importance for the solution chemistry.

The behavior of alkyl diethers under chemical ionization conditions has been studied in detail by several groups.^{5–8} Our group has been interested for a long time in the intramolecular interactions between alkoxy groups leading to stereochemical effects in gas phase protonated diethers.^{9–13} It was demonstrated that the major fragment ions in CI mass spectra of various diethers are formed by the elimination of one or two alcohol molecules from the protonated compounds. In analogy to other difunctional systems,¹⁴ the mass spectral behavior of protonated diethers strongly depends on the spatial arrangement of the functional groups in the corresponding molecules. In fact, protonated diethers with geometry allowing an intramolecular proton chelation by the two polar ether functions give rise to more abundant MH^+ ions and lower $[MH - ROH]^+$ and $[MH - 2ROH]^+$ ions, relative to their analogues in which proton bridging stabilization is not possible (the trend of such non-stabilized MH^+ ions to lose an alcohol is similar to the behavior of protonated monofunctional ethers). If the configuration of the diether molecule satisfies the requirements of the anchimeric assistance mechanism¹⁵ then the alcohol elimination reaction may be facilitated by an internal back-side attack of the second functional group.^{10,5c}

In the present work we show that the main decomposition mode of the majority of the examined protonated *benzyl* diethers is not the alcohol elimination, but rather a rearrangement process yielding m/z 181 $C_{14}H_{13}^+$ fragment ions. This

novel rearrangement reaction involves an intramolecular benzyl–benzyl interaction resulting in a C–C bond formation between the two benzyl groups of the diethers.

The literature contains several examples of rearrangement processes (upon CI and electron ionization conditions) leading to $C_{14}H_{13}^+$ ion formation. We have recently reported on the occurrence of a highly efficient process of such a type in CI and collision-induced dissociation (CID) fragmentation of protonated benzyl diesters.¹⁶ The m/z 181 ion formation has also been observed in protonated dibenzyl ether.¹⁷ The results of high-pressure CI mass spectral measurements of benzyl acetate indicated generation of the $C_{14}H_{13}^+$ ion as well.¹⁸ In the latter case the m/z 181 ion formation has been interpreted in terms of an ion–molecule reaction resulting in a protonated dimer of benzyl acetate, which undergoes a skeletal rearrangement, to form the benzyl–benzyl C–C bond. The $C_{14}H_{13}^+$ ions have been detected for the first time under electron impact (EI) conditions in the mass spectrum of tribenzylamine.¹⁹ The m/z 181 ions were also observed in the EI mass spectra of *N*-nitrosodibenzylamine²⁰ and *o*- and *m*-bis(benzyloxy)benzenes.²¹

In the course of the present work we have found that, contrary to many rearrangement reactions known in the gas phase organic chemistry, the formation of the $C_{14}H_{13}^+$ ions is not only surprisingly general in protonated molecules containing two benzyloxy groups, but is also extraordinarily efficient for the majority of these compounds. This rearrangement may be of analytical value due to the importance of benzyl derivatives of diols in synthetic organic chemistry.²²

The objective of this work was to explore the generality of this process, determine the structure of the resulting $C_{14}H_{13}^+$ ion(s), propose a mechanism for this fragmentation and study the effect of the spatial separation of the two ether groups on the facility of this rearrangement.

Results and discussion

General considerations

The most abundant peak in the isobutane-CI mass spectra of

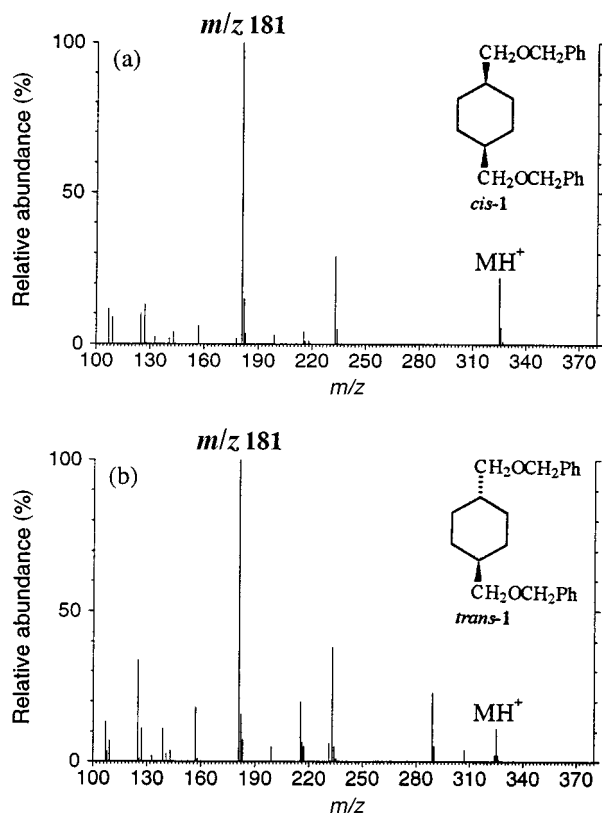


Fig. 1 Isobutane-CI mass spectra of (a) *cis*- and (b) *trans*-1,4-bis(benzyloxymethyl)cyclohexanes (*cis*-1 and *trans*-1).

cis- and *trans*-1,4-bis(benzyloxymethyl)cyclohexane **1** appears at m/z 181 (Fig. 1) and corresponds to the $C_{14}H_{13}^+$ ion. CID mass spectra of the protonated diethers **1** also exhibit an abundant m/z 181 ion (Fig. 2). Since the parent benzyl diethers **1** do not contain an uninterrupted sequence of fourteen carbon atoms, it is clear that a rearrangement is involved in the genesis of the m/z 181 $C_{14}H_{13}^+$ ion.

Mass spectral measurements were performed for a variety of benzyl derivatives of open-chain, alicyclic and aromatic diols (**2–21**) in order to verify the generality of the observed rearrangement in protonated molecules of benzyl diethers. The CI and CID mass spectra of all the examined benzyl diethers exhibited the m/z 181 $C_{14}H_{13}^+$ fragment ions (the mass spectral data of **1–21** are given in Tables 1–6). The m/z 181 ion was the most abundant fragment in the great majority of the studied aliphatic diethers. These results showed that the rearrangement reaction resulting in the $C_{14}H_{13}^+$ ion formation is the characteristic fragmentation pathway of protonated benzyl diethers upon chemical ionization and collision-induced dissociation conditions. The competing and generally much less efficient decomposition modes of the examined benzyl diethers under CI and CID conditions are the eliminations of benzyl alcohol ($[MH - 108]^+$ ion), dibenzyl ether ($[MH - 198]^+$ ion), diphenylmethane ($[MH - 168]^+$ ion), C_7H_8 and $C_{14}H_{12}$ molecules ($[MH - 92]^+$ and $[MH - 180]^+$ ions). A simple C–O bond cleavage yielding the m/z 91 $C_7H_7^+$ ions is an additional possible fragmentation pathway of protonated benzyl diethers. The isobutane-CI and CID mass spectra of several alicyclic benzyl diethers showed also the $[MH - PhCH_2OH - H_2O]^+$ ions (see Tables 3 and 4). This fragmentation process apparently involves migration of the benzyl group within the $[MH - PhCH_2OH]^+$ fragment ions. Low abundance $[MH - C_6H_6]^+$ fragment ions were also detected in the mass spectra of most of the aromatic benzyl diethers (see Tables 5 and 6).

Structural assignment of the rearrangement ions

The first step in the structural assignment of the $C_{14}H_{13}^+$ ions

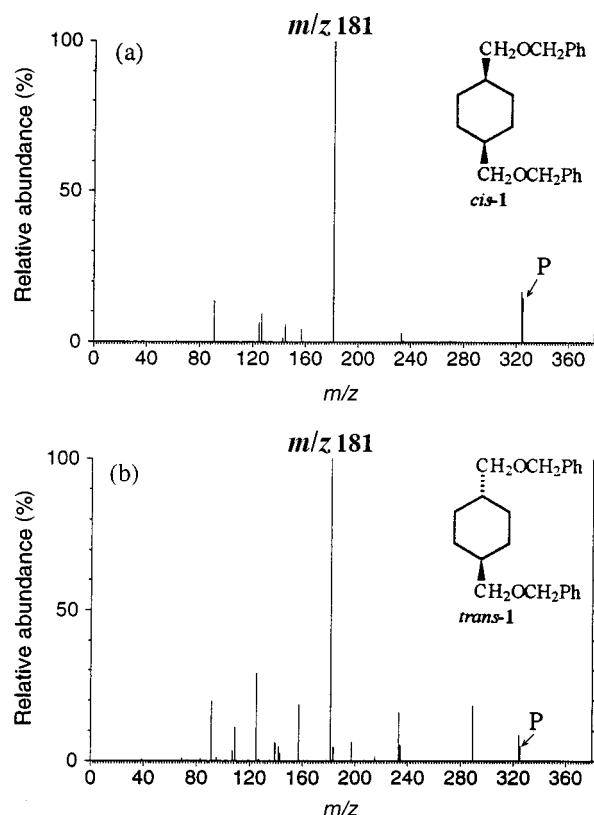
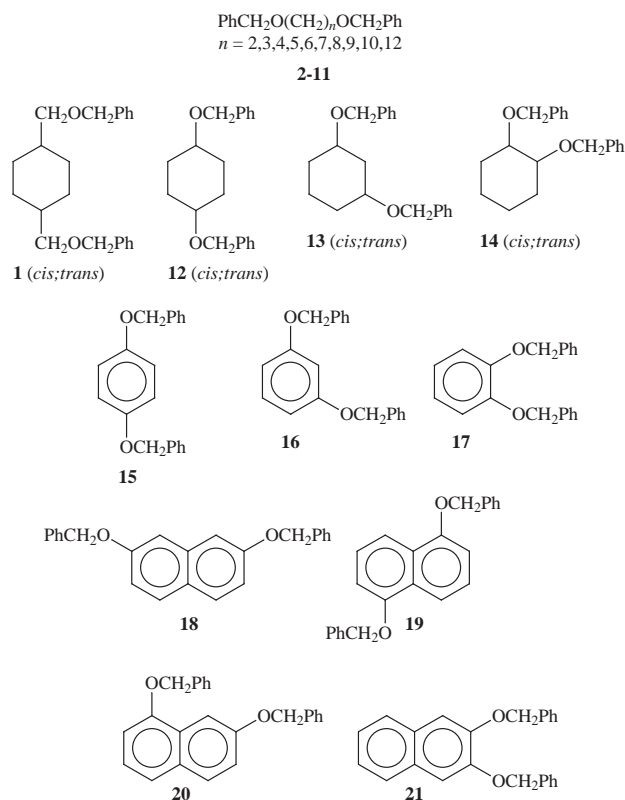


Fig. 2 CID mass spectra (30 eV collision energy) of the m/z 325 MH^+ ions, obtained upon isobutane-CI from (a) *cis*- and (b) *trans*-1,4-bis(benzyloxymethyl)cyclohexanes (*cis*-1 and *trans*-1).



was to assure their structural identity when produced from a variety of precursors. This goal was achieved by comparing the CID spectra of these m/z 181 ions. The observed close similarity of the CID spectra indicated that the $C_{14}H_{13}^+$ ions produced from various protonated benzyl diethers **1–21** have indeed a common structure. Typical CID spectra of **1**, **5** and **15** (alicyclic, linear and aromatic diethers) are shown in Fig. 3 and 4a.

Table 1 Isobutane-CI mass spectral data (relative abundance, %) of linear benzyl diethers **2–11**

$(\text{CH}_2)_n(\text{OCH}_2\text{Ph})_2$	MH^+	m/z 181	$[\text{MH} - \text{BnOH}]^+$	$[\text{MH} - 180]^+$	$[\text{MH} - 168]^+$	$[\text{MH} - \text{BnOBn}]^+$	$[\text{MH} - \text{C}_7\text{H}_8]^+$	m/z 91
$n = 2$ (2)	<0.5	100	<0.1	^a	^a	^a	18	16
$n = 3$ (3)	100	92	1	^a	^a	^a	39	25
$n = 4$ (4)	100	37	23	^b	2	^a	1	22
$n = 5$ (5)	100	81	11	4	2	^a	11	21
$n = 6$ (6)	53	100	2	5	4	6	22	17
$n = 7$ (7)	27	100	<0.1	7	4	3	22	16
$n = 8$ (8)	14	100	<0.1	11	6	2	20	12
$n = 9$ (9)	17	100	<0.1	13	7	2	30	13
$n = 10$ (10)	19	100	<0.1	13	8	4	22	14
$n = 12$ (11)	9	100	<0.1	12	9	4	19	15

^a The m/z values are below the range of the CI measurements ($>m/z$ 90). ^b The m/z value (91) of this fragment coincides with that of the C_7H_7^+ fragment ion (last column in this Table).

Table 2 CID^a mass spectral data^{b,c} of MH^+ ions obtained from linear benzyl diethers upon i-Bu-CI

$(\text{CH}_2)_n(\text{OCH}_2\text{Ph})_2$	m/z 181	$[\text{MH} - \text{BnOH}]^+$	$[\text{MH} - 180]^+$	$[\text{MH} - 168]^+$	$[\text{MH} - \text{BnOBn}]^+$	$[\text{MH} - \text{C}_7\text{H}_8]^+$	m/z 91
$n = 3$ (3)	67	<0.1	2	2	<0.1	3	25
$n = 4$ (4)	46	21	^d	1	1	<0.1	30
$n = 5$ (5)	68	4	2	1	3	<0.1	21
$n = 6$ (6)	81	<0.1	3	1	3	1	11
$n = 7$ (7)	83	<0.1	6	1	1	2	6
$n = 8$ (8)	83	<0.1	8	3	1	1	3
$n = 9$ (9)	83	<0.1	8	2	1	3	3
$n = 10$ (10)	85	<0.1	6	3	1	2	2
$n = 12$ (11)	82	<0.1	8	3	1	3	2

^a 30 eV collision energy. ^b The ion abundances are listed as percentages of the total product ion current (% Σ). ^c The CID spectrum of **2** was not measured because of the low abundance of the MH^+ ion in the isobutane-CI mass spectrum. ^d The m/z value (91) of this fragment coincides with that of the C_7H_7^+ fragment ion (last column in this Table).

Table 3 Isobutane-CI mass spectral data (relative abundance, %) of alicyclic benzyl diethers **1, 12–14**

Compound	MH^+	m/z 181	$[\text{MH} - \text{BnOH}]^+$	$[\text{MH} - 180]^+$	$[\text{MH} - 168]^+$	$[\text{MH} - \text{BnOBn}]^+$	$[\text{MH} - \text{C}_7\text{H}_8]^+$	$[\text{MH} - \text{BnOH}] - \text{H}_2\text{O}^+$
<i>cis</i> - 1	22	100	<0.1	<0.1	6	13	29	3
<i>trans</i> - 1	11	100	<0.1	<0.1	18	11	38	5
<i>cis</i> - 12	100	7	3	<0.1	2	^a	2	15
<i>trans</i> - 12	<0.1	3.4	100	<0.1	1	^a	31	46
<i>cis</i> - 13	100	5	2	<0.1	<0.1	^a	2	4
<i>trans</i> - 13	8	21	18	<0.1	4	^a	100	37
<i>cis</i> - 14	20	100	3	2	4	^a	24	<0.1
<i>trans</i> - 14	1	100	6	<0.1	2	^a	23	4

^a The m/z values of these fragments are below the range of the CI measurements ($>m/z$ 100).

Table 4 CID^a mass spectral data^{b,c} of MH^+ ions obtained from alicyclic benzyl diethers upon i-Bu-CI

Compound	m/z 181	$[\text{MH} - \text{BnOH}]^+$	$[\text{MH} - 180]^+$	$[\text{MH} - 168]^+$	$[\text{MH} - \text{BnOBn}]^+$	$[\text{MH} - \text{C}_7\text{H}_8]^+$	$[\text{MH} - \text{BnOH}] - \text{H}_2\text{O}^+$	m/z 91
<i>cis</i> - 1	75	<0.1	4	3	5	3	<0.1	10
<i>trans</i> - 1	65	<0.1	<0.1	12	1	10	<0.1	12
<i>cis</i> - 12	38	10	<0.1	9	2	3	23	15
<i>cis</i> - 13	51	3	1	3	1	2	9	30
<i>trans</i> - 13	40	5	<0.1	9	7	28	4	6
<i>cis</i> - 14	60	4	6	2	19	5	<0.1	3
<i>trans</i> - 14	74	<0.1	4	<0.1	19	<0.1	<0.1	3

^a 30 eV collision energy. ^b CID spectrum of the *trans*-**12** was not measured because of absence of MH^+ ions in the isobutane-CI mass spectrum. ^c The ion abundances are listed as percentages of the total product ion current (% Σ).

We have previously reported that protonated benzyl esters of dicarboxylic acids also undergo a rearrangement process resulting in the m/z 181 $\text{C}_{14}\text{H}_{13}^+$ ion.¹⁶ In the former study the structure of the m/z 181 ion has been determined by comparison of its CID spectrum with those of isomeric ions obtained upon isobutane-CI from ten model compounds **22–31** (by C–X cleavages, X = Br, OH). This study has shown unequivocally that the structures of the $\text{C}_{14}\text{H}_{13}^+$ ions formed from **22–25** are different

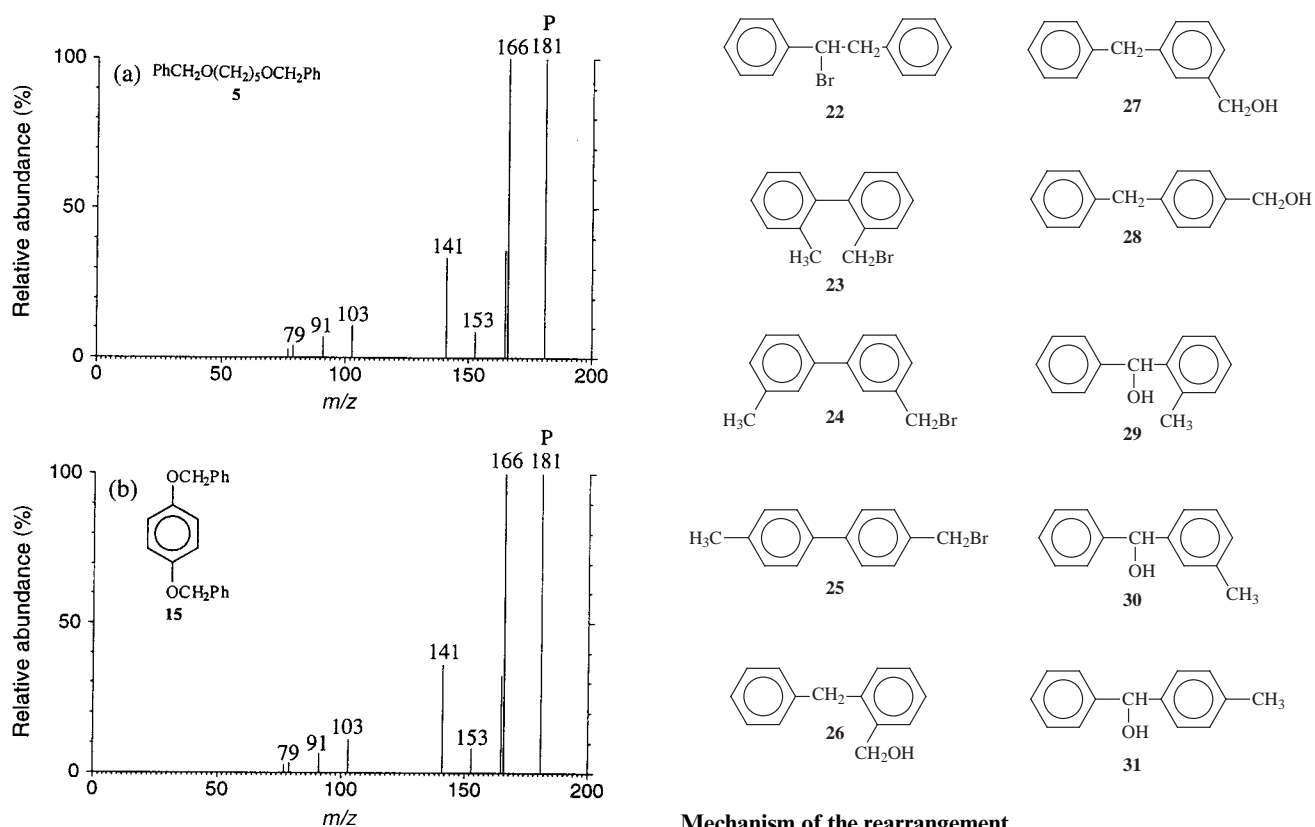
from that of the rearrangement ion obtained from the benzyl diesters. A computer-aided analysis has been performed in the course of the above study¹⁶ in order to determine an optimum combination of CID data of the models **26–31** that would fit the CID spectrum of the rearrangement product. It was found that the CID spectrum of the $\text{C}_{14}\text{H}_{13}^+$ ion obtained from the benzyl diesters is superimposable on that of the calculated CID spectrum of a mixture of three isomeric ions: *o*-tolylbenzyl

Table 5 Isobutane-CI mass spectral data^a (relative abundances, %) of benzyl derivatives of aromatic diols **15–21**

Compound	MH ⁺	<i>m/z</i> 181	[MH – 168] ⁺	[MH – C ₇ H ₈] ⁺	[MH – C ₆ H ₆] ⁺
15	100	3	1	0.4	2
16	100	1	0.1	<0.1	0.3
17	100	5	1	0.5	0.6
18	100	0.5	0.5	0.7	<0.1
19	100	<0.1	0.6	0.8	0.5
20	100	1	1	<0.1	<0.1
21	100	7	1	0.7	0.5

^a The CI mass spectra were measured from *m/z* 100.**Table 6** CID^a mass spectral data^b of MH⁺ ions obtained from benzyl derivatives of aromatic diols **15–21** upon Bu^t-CI

Compound	MH ⁺	<i>m/z</i> 181	[MH – 168] ⁺	[MH – C ₇ H ₈] ⁺	[MH – C ₆ H ₆] ⁺	<i>m/z</i> 91
15	3400	47	30	15	49	100
16	9000	49	<0.1	<0.1	11	100
17	4400	100	38	7	13	77
18	2100	36	<0.1	6	3	100
19	2100	27	100	41	<0.1	42
20	5000	86	11	32	9	100
21	2200	100	20	17	14	59

^a 30 eV collision energy. ^b The relative abundances (%) are normalized to the most abundant fragment ion.**Fig. 3** CID spectra (50 eV collision energy, the relative ion abundances normalized to the most abundant product ion) of the *m/z* 181 ions obtained upon isobutane-CI from benzyl diethers: (a) **5** and (b) **15**.

obtained from **26** (35%), *α*-*p*-tolylbenzyl from **31** (30%) and *p*-benzylbenzyl from **25** (35%).¹⁶

The CID spectra of the *m/z* 181 ions from diether **1** were compared with those of *cis*- and *trans*-dibenzyl cyclohexane-1,4-dicarboxylates **32** in order to check the structural identity of these ions originating from benzyl diethers and diesters. The close similarity of the CID spectra (see Fig. 4) leads to the conclusion that the structures of the rearrangement ions of the benzyl diethers are identical with those of the benzyl diesters, *i.e.* the C₁₄H₁₃⁺ ions originating from benzyl diethers are a mixture of the three isomeric cations **a** (35%), **b** (30%) and **c** (35%), as outlined in Scheme 1.

Mechanism of the rearrangement

In order to make sure that the C₁₄H₁₃⁺ ion formation upon CI conditions is a purely unimolecular process, isobutane-CI mass spectra of epimeric benzyl *p*-xylyl diethers of *cis*- and *trans*-cyclohexane-1,4-dimethanol **33** have been measured. The exclusive formation of *m/z* 195 C₁₅H₁₅⁺ ions and the absence of the *m/z* 181 fragment ions in the spectra (see Fig. 5 and Scheme 2) indicated an exclusively unimolecular nature of the benzyl-benzyl interaction in the CI-induced fragmentation of the benzyl diethers. Examination of the CID spectra of MD⁺ ions of **1**, **5**, **13** and **15** obtained under CD₃CN-CI conditions revealed that the external proton (or deuteron) is not transferred to the C₁₄H₁₃⁺ ions in the course of the rearrangement.

The structures of the three constituents of the C₁₄H₁₃⁺ ions clearly indicate that the mechanism does not involve bond

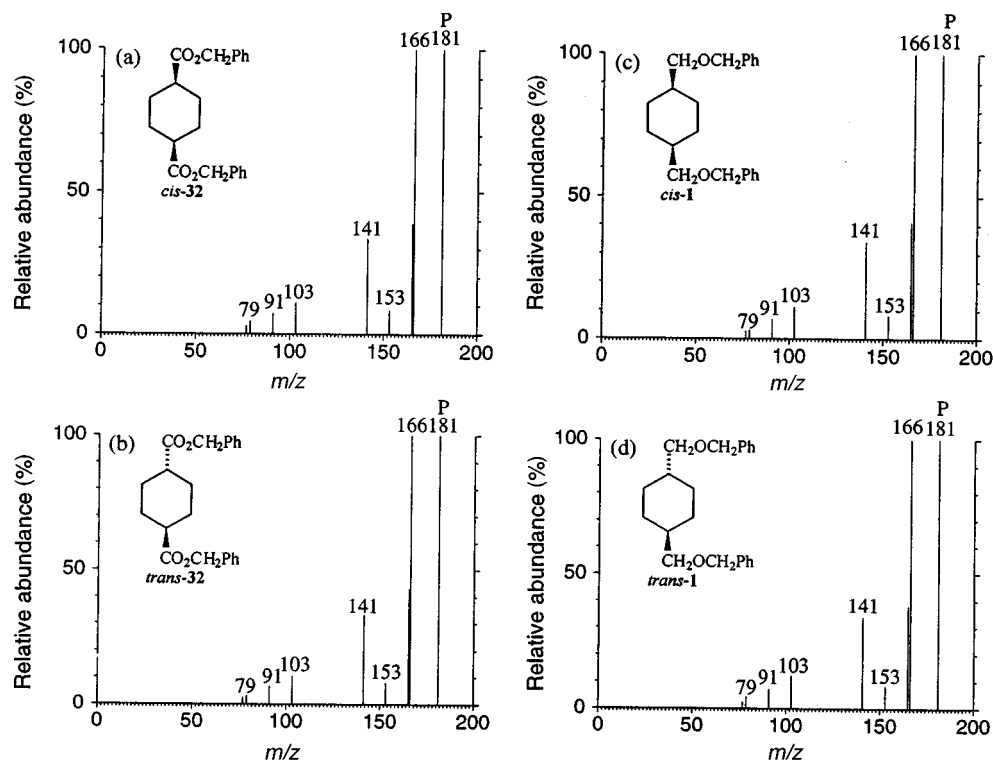
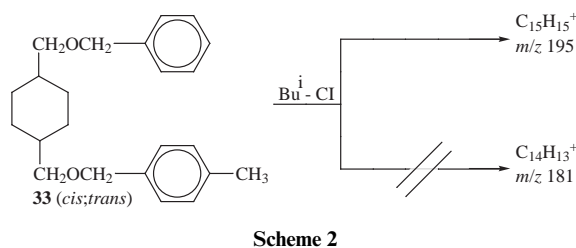
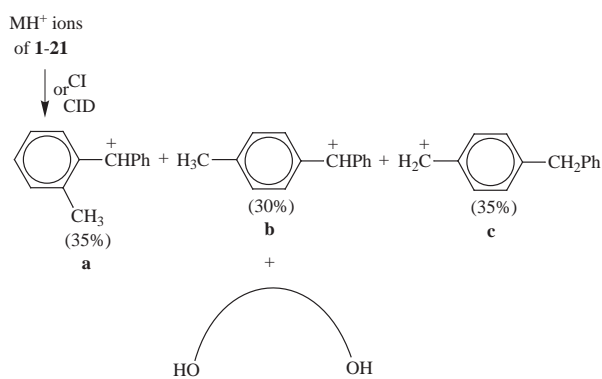


Fig. 4 CID spectra (50 eV collision energy, the relative ion abundances normalized to the most abundant product ion) of the m/z 181 ions obtained upon isobutane-Cl from benzyl diesters **32** and diethers **1**: (a) *cis*-**32**; (b) *trans*-**32**; (c) *cis*-**1**; (d) *trans*-**1**.



formation between the benzylic methylene groups or between the two phenyl rings. The presence of the m/z 181 fragments in the mass spectra of benzyl diethers with geometry like *trans*-**13**, **15** or **20** also excludes a mechanistic pathway involving an anchimerically assisted transfer of the benzyl cation, as shown in Scheme 3.

A plausible mechanistic pathway of the rearrangement of protonated benzyl diethers consistent with the above experimental results is proposed in Scheme 4. The rearrangement process starts with the heterolysis of the C–O bond at the protonated ether function, followed by the formation of the ion–neutral complex **A** and/or complexation of the resulting benzyl cation with the π -electron system of the other ether function giving rise to the π -complex **B**. The intermediacy

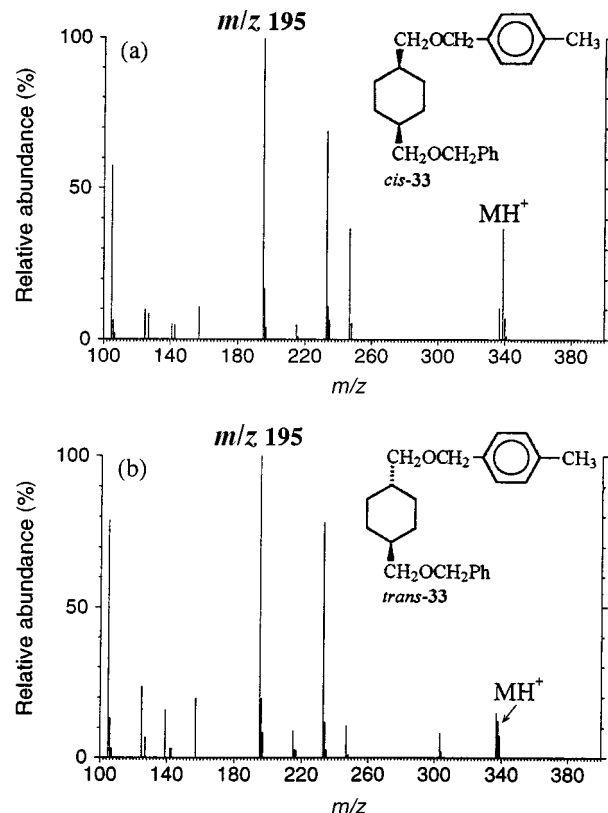


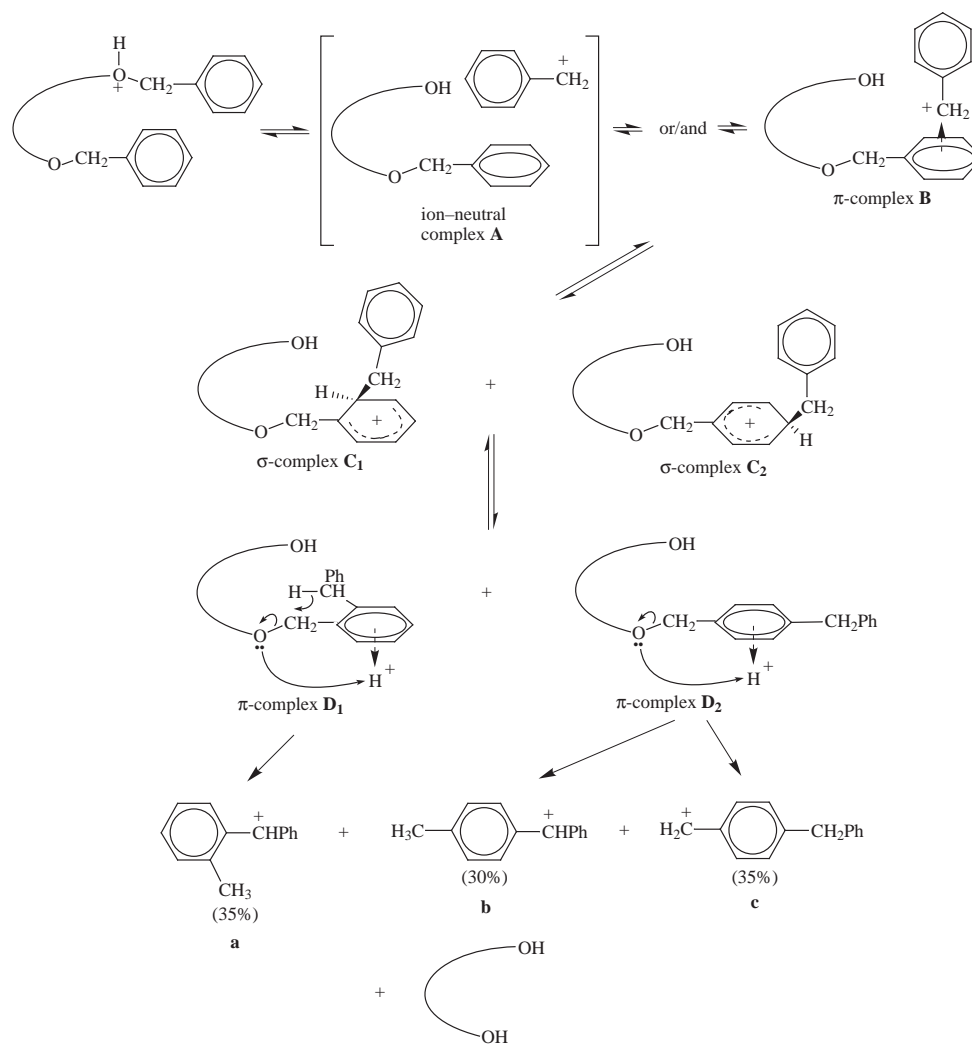
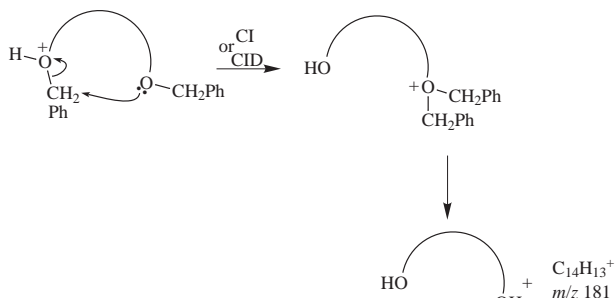
Fig. 5 Isobutane-Cl mass spectra of (a) *cis* and (b) *trans*-1-benzyl-oxyethyl-4-*p*-xylyloxymethylcyclohexanes (*cis*-**33** and *trans*-**33**).

of the ion–neutral complex **A** finds support in the production of the rearrangement $\text{C}_{14}\text{H}_{13}^+$ ions from diethers with distant benzyloxy groups (*trans*-**1**, *trans*-**13**, **15**, **20**). The formation of the π -complex **B** is supported by the previously reported work.¹⁶ The next step is the generation of two σ -complexes with *ortho* and *para* oriented benzyl substituents (σ -complexes C_1 and C_2). These σ -complexes undergo a proton transfer from the

benzenium moieties to the ether oxygen atoms, probably with the intermediacy of π -complexes **D**₁ and **D**₂. It is reasonable to assume that the formation of the proton π -complexes assists in the proton migration to the oxygen atoms, at least in the case of the σ -complex **C**₂, in which the hydrogen atom is remote from the ether moiety. The formation of the *o*-tolylbenzyl cation **a** apparently involves a benzyl hydrogen migration within the π -complex **D**₁, as shown in Scheme 4. The generation of ion **b** requires an additional rearrangement step, involving probably an intermediacy of another proton π -complex.

Homologous 1, ω -bis(benzyloxy)alkanes

Examination of the mass spectral data of the linear benzyl diethers **2–11** (Tables 1 and 2) reveals that the rearrangement resulting in the $C_{14}H_{13}^+$ ion formation is the major fragmentation mode of these compounds upon chemical ionization

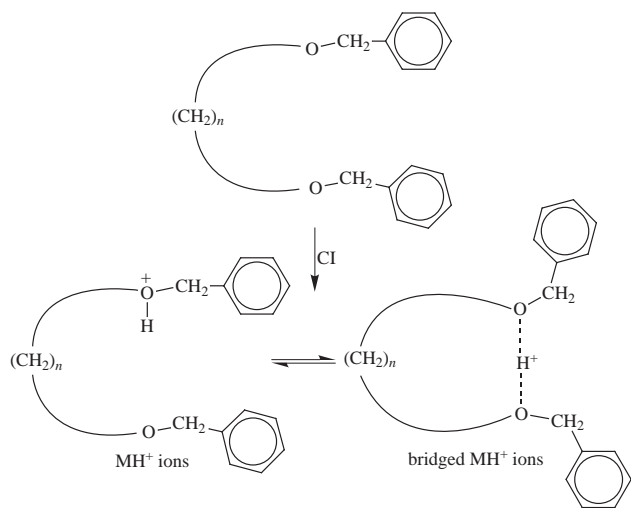


and CID conditions. The results indicate variation in the efficiency of formation of the m/z 181 ion from the examined 1, ω -bis(benzyloxy)alkanes, showing a clear chain length effect in the rearrangement process of the diethers. The data show that the rearrangement process is most favorable for compounds with two or more-than-five methylene groups in their aliphatic chains. On the other hand, the least efficient $C_{14}H_{13}^+$ ion formation takes place in the homologues in which the ether functions are separated by 3, 4 or 5 methylenes. This behavior of the protonated linear benzyl diethers leads to the assumption that the efficiency of the observed rearrangement process is correlated with the intramolecular ion-dipole interactions between the two oxygen functions of these protonated molecules. It is reasonable to expect that the facility of the $C_{14}H_{13}^+$ ion formation will decrease with increasing the capability of the benzyloxy groups to capture the external proton between the two oxygen atoms, as shown in Scheme 5. The intramolecular proton solvation would not only suppress the decomposition of the MH^+ ions but would also cause an increase of the distance between the interacting benzyloxy moieties. Thus, the rearrangement process should be more pronounced in MH^+ ions with strained proton bridging than in the highly stabilized bridged protonated molecules.

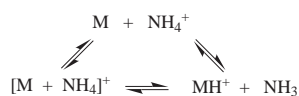
NH_3 -CI measurements of the diethers **2–11** were performed in order to verify the expected correlation between the skeletal rearrangement efficiency of the linear benzyl diethers and the strength of the intramolecular proton bridging. Since the proton affinities (PA) of the *n*-alkyl benzyl ethers (833 ± 15 kJ mol⁻¹)^{34–37} are less than that of ammonia (854 kJ mol⁻¹)³⁷ it may be assumed that the equilibrium shown in Scheme 6 would shift

Table 7 Relative abundance (%) of MH^+ and $[M + NH_4]^+$ ions in the NH_3 -CI mass spectra of linear benzyl diethers **2–11**

PhCH ₂ O(CH ₂) _n OCH ₂ Ph	MH^+		$[M + NH_4]^+$	
	<i>m/z</i>	RA%	<i>m/z</i>	RA%
<i>n</i> = 2 (2)	243	2	260	100
<i>n</i> = 3 (3)	257	100	274	37
<i>n</i> = 4 (4)	271	100	288	5
<i>n</i> = 5 (5)	285	100	302	24
<i>n</i> = 6 (6)	299	100	316	98
<i>n</i> = 7 (7)	313	46	330	100
<i>n</i> = 8 (8)	327	23	344	100
<i>n</i> = 9 (9)	341	23	358	100
<i>n</i> = 10 (10)	355	9	372	100
<i>n</i> = 12 (11)	383	21	400	100



Scheme 5



Scheme 6

towards the MH^+ ions only for benzyl diethers with relatively strong intramolecular proton bridging (PA values of the bridged difunctional molecules are considerably larger than those for monofunctional compounds³⁸). Consequently, the NH_3 -CI spectra of benzyl diethers with the geometry permitting stabilization by intramolecular proton solvation should display abundant MH^+ ions. On the other hand, diethers in which such stabilization is weak are expected to give major $[M + NH_4]^+$ adduct ions in their NH_3 -CI mass spectra. The relative abundances of the MH^+ and the attachment ions, obtained from the benzyl diethers **2–11** under NH_3 -CI conditions, are listed in Table 7. The results show that abundant MH^+ ions are formed when the two functions are separated by 3–5 methylene units. The preference of these compounds to undergo protonation under NH_3 -CI conditions can be attributed to a favorable combination of ring strain³⁹ and hydrogen bonding geometry⁴⁰ in the cyclic structure of their MH^+ ions (which makes the proton transfer exothermic). Kinetic effects may also operate in the preferable 6-, 7-, and 8-ring formation in the MH^+ ions of 1,ω-bis(benzyloxy)alkanes. The NH_3 -CI data show that the dominant species in the ammonia-CI spectra of the benzyl diethers **2** (*n* = 2) and **7–11** (*n* ≥ 7) are the attachment ions $[M + NH_4]^+$. The preferential formation of the adduct ions in these spectra (see Fig. 6) can be rationalized either by an unfavorable (far from linear, $\theta(O-H^+ \cdots O) = 120^\circ$) geometry of the hydrogen bonds and substantial ring strain³⁹ (**2**) or by significant entropy changes in the course of the bridging

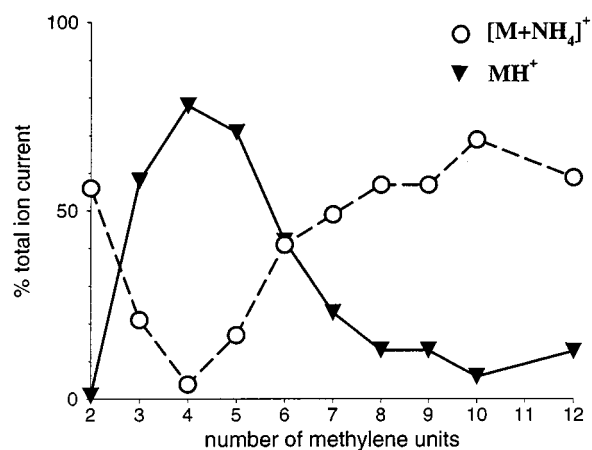
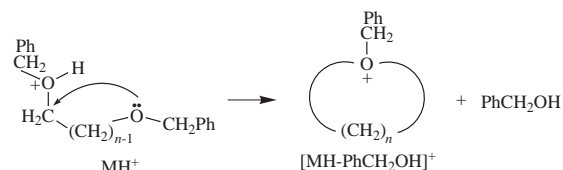


Fig. 6 Abundances (% total ion current) of the MH^+ and $[M + NH_4]^+$ ions in the NH_3 -CI mass spectra of the linear benzyl diethers **2–11** vs. the number of methylenes *n*.

process (**7–11**). The similar abundances of the MH^+ and $[M + NH_4]^+$ ions in the NH_3 -CI mass spectra of 1,6-bis(benzyloxy)hexane **6** demonstrate the intermediate strength of the intramolecular hydrogen bonding.

It is interesting to note that the observed correlation between the chain length of the protonated linear benzyl diethers and the stability of their hydrogen bridged structures is qualitatively similar to that reported for 1,ω-diamino-⁴¹ and dihydroxy-alkanes.⁴²

In summary, the mass spectral data of diethers **2–11** indicate a correlation between the facility of the $C_{14}H_{13}^+$ ion formation from protonated straight chain benzyl diethers and the energy of the intramolecular proton chelation between the two oxygen functions. The high abundance of the $C_{14}H_{13}^+$ fragment ions in isobutane-CI and CID mass spectra of diethers **2**, **6–11** is connected with the weak intramolecular hydrogen bonding between the ether functions in the MH^+ ions of these compounds. On the other hand, the suppressed rearrangement of the protonated bis(benzyloxy)-propane **3**, -butane **4** and -pentane **5** is caused by the stability of their proton bridged structures. The observed relatively low abundance of the $C_{14}H_{13}^+$ ion in the isobutane-CI and CID mass spectra of diethers **4** and **5** is partly due to the enhanced elimination of benzyl alcohol from these MH^+ ions (the $C_{14}H_{13}^+$ ion formation and the alcohol elimination are competing dissociation channels). The significant level of the $[MH - PhCH_2OH]^+$ ion formation from diethers **4** and **5** may be rationalized by the anchimeric assistance mechanism of this elimination process (Scheme 7), as previously suggested for alcohol elimination from MH^+ ions of other linear diethers.^{5c,13}



Scheme 7

The results given above demonstrate that not only NH_3 -CI mass spectra of difunctional compounds⁴³ but also that their isobutane-CI spectra can be strongly affected by the strength of the intramolecular hydrogen bridging between the two functions. In fact, one can readily find a good correlation between isobutane-CI mass spectral data ($RA\%(MH^+)/RA\%(m/z181)$ ratio) of the homologous 1,ω-bis(benzyloxy)alkanes and the relative stability of the bridged structures of those protonated molecules (Fig. 7).

Table 8 Partial NH₃-CI mass spectral data (relative abundance, %) of stereoisomeric pairs of alicyclic benzyl diethers **1**, **12–14**

Compound	MH ⁺	[M + NH ₄] ⁺
<i>cis</i> - 1	7	100
<i>trans</i> - 1	1	100
<i>cis</i> - 12	62	100
<i>trans</i> - 12	1	100
<i>cis</i> - 13	69	100
<i>trans</i> - 13	1	100
<i>cis</i> - 14	9	100
<i>trans</i> - 14	0.5	100

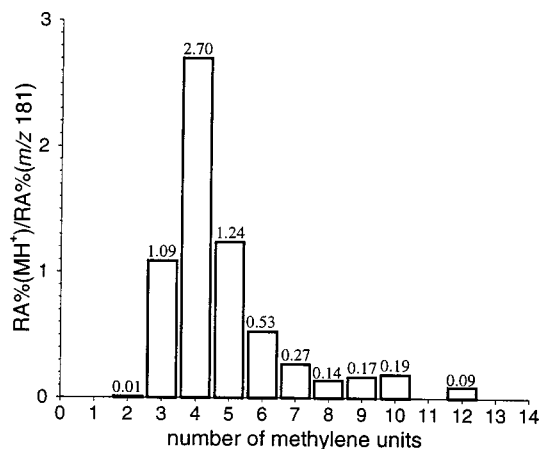


Fig. 7 The relationship of the ion abundance ratios RA%(MH⁺)/RA%(*m/z* 181) in the isobutane-CI mass spectra of the linear benzyl diethers **2–11** vs. the number of methylenes *n*.

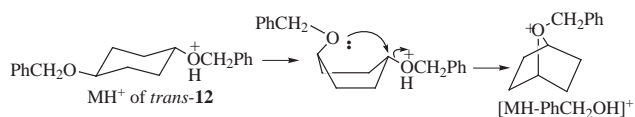
Alicyclic benzyl diethers

The isobutane chemical ionization mass spectral data of stereoisomeric pairs of benzyl diethers (**1**, **12–14**) are summarized in Table 3. The results of the low-energy collision-induced dissociation measurements of the MH⁺ ions of the saturated alicyclic benzyl diethers are listed in Table 4.

Examination of the isobutane-CI data of the stereoisomeric pairs of the diethers **1**, **13**, **14** and **15** reveals an interesting behavior: the extent of the rearrangement process (given by the ion abundance ratio [C₁₄H₁₃⁺]/[MH⁺]) of the *trans*-isomers with the remote ether functions is greater than that of the *cis*-diethers, in which the distance between the two interacting benzyloxy groups is smaller. The abundances of the *m/z* 181 ions are relatively high in the CID spectra of all the diethers, but the difference between stereoisomers is not large.

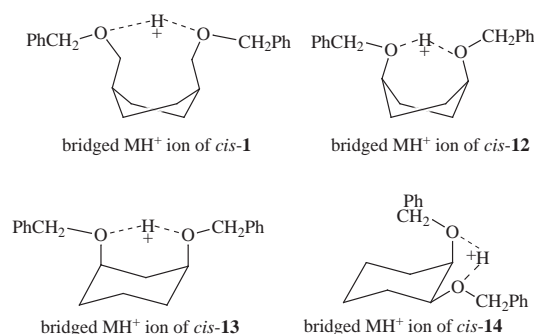
The observed stereocontrol of the rearrangement process in the alicyclic benzyl diethers indicates retention of the original configuration of the examined stereoisomers upon CI conditions, in analogy with the behavior of many other stereoisomeric systems.^{44,45} The suppressed rearrangement of the *cis*-stereoisomers is apparently a result of their capability to bring the two benzyloxy groups within a distance enabling internal hydrogen bond formation between the ether oxygens. This proton bridging causes both higher stability (kinetic and thermodynamic) of the protonated molecules and also steric suppression of the interaction between the two benzyl moieties. In the case of the *cis*- and *trans*-1,2-bis(benzyloxy)cyclohexanes **14** the internal H-bonding is possible in both stereoisomers.^{56,44} The NH₃-CI mass spectral data (Table 8) show that the bridged structure of the *cis*-isomer is more stable, which explains the observed steric effect in the rearrangement of this epimeric pair. It is important to note that the relative abundances of the *m/z* 181 C₁₄H₁₃⁺ ions in isobutane-CI mass spectra of the *trans*-alicyclic benzyl diethers are strongly affected by competing dissociation modes. Indeed, the occurrence of fragmentation by alternative channels may not only decrease the size of

the observed steric effect (see isobutane-CI data for **13**), but also can nullify it (see isobutane-CI data for epimeric 1,4-bis(benzyloxy)cyclohexanes **12**). In the case of the diether **12**, the MH⁺ ion of the *cis*-isomer gives rise to an even more abundant *m/z* 181 fragment ion than the *trans*-epimer (Table 3). The low abundance of the C₁₄H₁₃⁺ ions in the isobutane-CI mass spectrum of *trans*-**12** (the CID spectrum could not be measured because of the negligible abundance of the MH⁺ ions) can be attributed to the extreme efficiency of the [MH – PhCH₂OH]⁺ ion formation from these MH⁺ ions. Based on previous results from our laboratory¹⁰ it is reasonable to assume that the observed predominance of benzyl alcohol elimination in the isobutane-CI mass spectrum of *trans*-**12** arises from the involvement of anchimeric assistance in the mechanism of this process (Scheme 8).



Scheme 8

It is noteworthy that the isobutane-CI and NH₃-CI mass spectral data listed in Tables 3 and 8 show an inverse correlation between the extent of the C₁₄H₁₃⁺ ion formation from the examined *cis*-diethers and the strength of the intramolecular proton bonding in their bridged structures. Indeed, the substantial stabilization of the protonated *cis*-1,4- and 1,3-bis(benzyloxy)cyclohexanes by intramolecular hydrogen bonding (see Table 8) is consistent with the reduced abundances of the *m/z* 181 fragment ion in the isobutane-CI mass spectra. On the other hand, the weaker proton bridging in the MH⁺ ions of *cis*-**1** and *cis*-**14** (Table 6) results in appreciable acceleration of the rearrangement in these alicyclic benzyl diethers (see Table 3).



Aromatic benzyl diethers

The isobutane-CI and CID mass spectral data of the benzyl derivatives of isomeric dihydroxybenzenes (**15–17**) and -naphthalenes (**18–21**) are presented in Tables 5 and 6. The results indicate that in contrast to the aliphatic benzyl diethers, the formation of the *m/z* 181 C₁₄H₁₃⁺ ions from the protonated benzyl ethers of aromatic diols is strongly suppressed. The extremely low abundances of all fragment ions in the isobutane-CI spectra of the examined aromatic benzyl diethers and the very high abundances of the precursor MH⁺ ions in the CID spectra (20–90 times higher than any product ion, see Table 6 and Fig. 8) suggest highly stabilized structures for the MH⁺ ions, independent of the distance between the two benzyloxy groups. The observed magnitude of the MH⁺ ions stabilization in isomers with remote benzyloxy groups excludes the possibility of the stabilization by internal hydrogen bonding.

The above effect of stabilization of the MH⁺ ions of the aromatic diethers may be explained by the transfer of a benzyl cation originating in one of the two benzyloxy groups (presumably the protonated one) to the aromatic skeleton, which may effectively compete with the second benzyloxy group because

of the presence of the two ether substituents activating the aromatic system toward electrophilic substitution. The mechanistic pathway of the resulting rearrangement of protonated *p*-bis(benzyloxy)benzene to the isomeric protonated 2- and 3-benzyl-4-benzyloxyphenol (one stage rearrangement) and possibly to 2,3- and 2,5-dibenzylhydroquinones (two-stage isomerization) is proposed in Scheme 9.

It is highly probable that the very low abundances of the $C_{14}H_{13}^+$ ions in the mass spectra of the aromatic benzyl diethers **15–21** are partly due to the formation of skeleton ring protonated molecules, which cannot undergo the rearrangement process upon the experimental conditions (Scheme 10). The

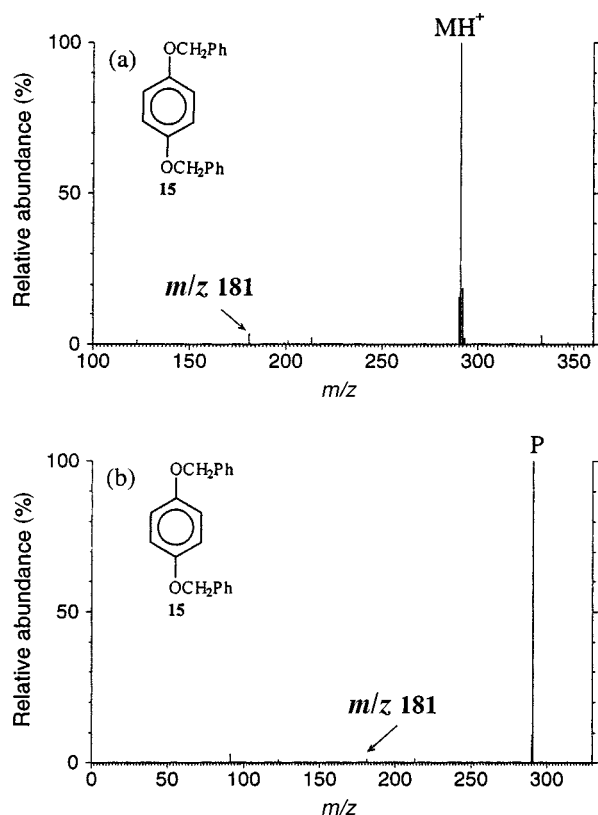


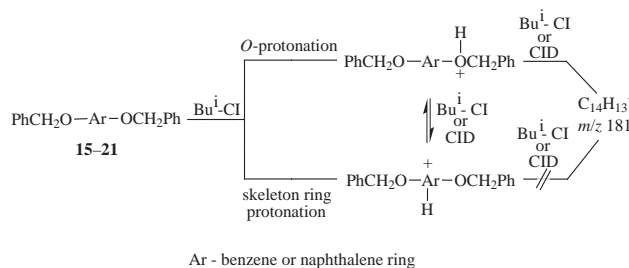
Fig. 8 (a) Isobutane-CI mass spectrum of *p*-bis(benzyloxy)benzene **15**; (b) CID mass spectrum (30 eV collision energy) of the MH^+ ion of **15**.

protonation at the aromatic ring may occur either in the course of the chemical ionization process⁴⁶ or by intramolecular proton migration in the O-protonated aromatic diethers.⁴⁷ It should be noted that both calculation and experiment suggest a thermochemical preference for protonation at the aromatic center in aromatic ethers.^{47,48}

The analysis of the relative abundances of the $C_{14}H_{13}^+$ ions in the isobutane-CI and CID spectra of the diethers **15–21** (Tables 5 and 6) reveals that the protonated aromatic benzyl diethers with neighboring benzyloxy groups (**17**, **21** and also **20**) give rise to more abundant rearrangement ions than other isomers. This behavior is consistent with the short distance between the two benzyloxy moieties 1,2-bis(benzyloxy)benzene (**17**) and 2,3- and 1,7-bis(benzyloxy)naphthalene (**21**, **20**), which increase the probability of the benzyloxy group substitution relative to the benzylation of the aromatic center. It is noteworthy that the observed correlation between the rearrangement ion abundances and the interfunctional separation in the molecules of the aromatic benzyl diethers is opposite of that observed for aliphatic analogues.

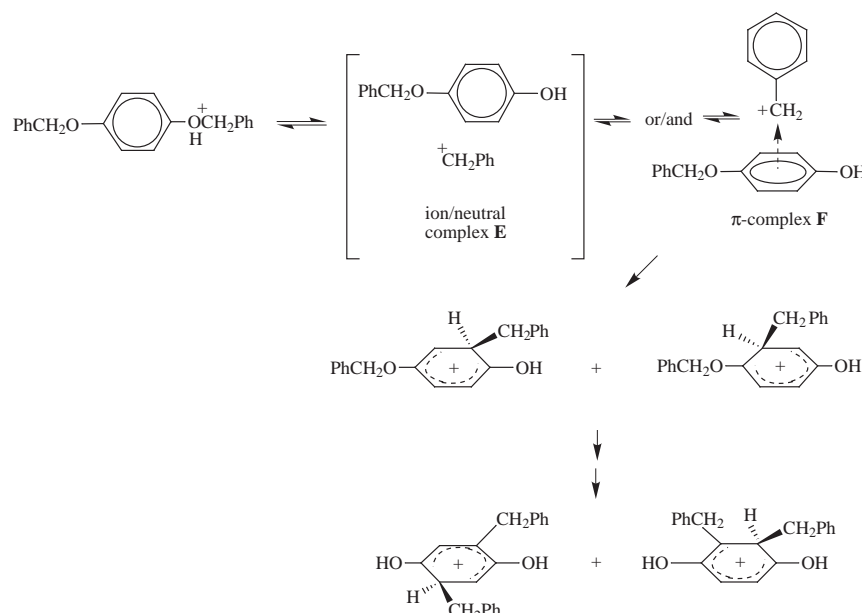
Conclusions

We have shown in this work that gas-phase protonated benzyl diethers undergo a characteristic unimolecular rearrangement process, giving rise to $C_{14}H_{13}^+$ ions by a bonding interaction of the two benzyloxy groups. A CID study has shown that this novel general rearrangement involves bond formation between the *ortho* and *para* positions of the phenyl ring of one benzyloxy group and the methylene group of the other. A mechanistic pathway has been proposed, starting with the cleavage of the C–O bond of the O-protonated benzyloxy group, followed by the formation of an ion–neutral complex and/or a π -complex



Ar - benzene or naphthalene ring

Scheme 10



Scheme 9

of the resulting benzyl cation with the other benzyl group. The π -complex is subsequently transformed into two σ -complexes through a C–C bond formation between the complexed benzyl cation and the *ortho* and *para* positions of the benzyloxy group. The latter step is analogous to the aromatic electrophilic substitution chemistry in the condensed phase.

The stereochemical course of this rearrangement process shows suppression of its occurrence when the distance between the two interacting benzyloxy functions is relatively small. This unique behavior suggests a decreased bonding interaction between the two benzylys when internal hydrogen bonding stabilizes the protonated molecule. A similar conclusion has been arrived at from the behavior of variable chain length 1, ω -bis(benzyloxy)alkanes.

In contrast to the aliphatic benzyl diethers the mass spectra of the protonated benzyl derivatives of aromatic diols show extremely low abundances of the rearrangement ions. The phenomenon is attributed to competing intramolecular benzylation of the aromatic skeleton of these compounds. The correlation between the spatial separation of the functional groups in the aromatic benzyl diethers and the abundances of the $C_{14}H_{13}^+$ ions is opposite of that observed for the aliphatic analogues.

The results of this work provide an additional aspect to the gas-phase chemistry of $C_7H_7^+$ ions, which has attracted so much attention in the past four decades.^{49,50} They may be also relevant to the chemistry of these ions in the condensed phase.⁵¹ The present study can be seen as an example of the Friedel–Crafts alkylation reaction in the gas phase.

Experimental

Mass spectrometry

The gas chromatographic-chemical ionization mass spectrometric analysis (CI-GC-MS) and CID measurements were carried out on a Finnigan TSQ-70B triple-stage quadrupole mass spectrometer. The stereoisomeric pairs **1**, **12**, **13**, **32** and **33** were introduced as mixtures (except for **14**) and separated on the capillary columns DB-210 (0.25 μ m film thickness, 30 m \times 0.25 mm id, at 200 °C, isothermal) in the case of **12** and DB-5 (0.25 μ m film thickness, 30 m \times 0.25 mm id capillary column, the temperature was programmed from 60 to 280 °C at 20 °C min⁻¹) in all other cases. The scan rate was 1 scan s⁻¹. The elution sequence for the stereoisomers in the GC-MS analyses was as follows: *cis*-**1** followed by *trans*-**1**, *trans*-**12** by *cis*-**12**, *trans*-**13** by *cis*-**13**, *cis*-**32** by *trans*-**32** and *cis*-**33** by *trans*-**33**. CI measurements were performed at 150 °C ion source temperature and 0.4 Torr (indicated) reagent gas pressure (isobutane, ammonia, d₃-acetonitrile). CID measurements were performed with argon as the target gas (0.3 mTorr, indicated) at 30 and 50 eV collision energies (indicated). All the data presented in each table and those of Fig. 3 and 4 were obtained on the same day under identical conditions, in order to ensure the reliable comparisons.

Materials

1,4-Bis(benzyloxymethyl)cyclohexane, *trans*-**1** and *cis*-**1** mixture. Cyclohexane-1,4-dimethanol (*cis* and *trans* mixture 100 mg, 0.69 mmol) dissolved in 2 ml of dry tetrahydrofuran, was added to a suspension of sodium hydride (120 mg, 5 mmol, 60% in oil, washed with hexane) in tetrahydrofuran (THF, 5 ml). The reaction mixture was heated at 60 °C for 0.5 h and benzyl bromide (0.25 ml, 2 mmol) was added, followed by further stirring at 60 °C for 12 h. The cooled reaction mixture was hydrolyzed by drop-wise addition of water. The product was extracted with diethyl ether and was obtained in 90% yield. Compounds **2–14** were prepared from the corresponding diols in the same manner.

para-, *meta*- and *ortho*-Bis(benzyloxy)benzene **15–17** and **2,7**;

1,5-; 1,7- and 2,3-bis(benzyloxy)naphthalenes **18–21** were synthesized by literature procedures from the corresponding diols with potassium carbonate and benzyl chloride.⁵²

Stereoisomeric benzyl diesters **32** were prepared by esterification (in toluene solution) of a mixture of the *cis* and *trans*-cyclohexane-1,4-dicarboxylic acid with benzyl alcohol in the presence of a catalytic amount of toluene-*p*-sulfonic acid.

1-Benzyloxymethyl-4-*p*-xylyloxymethylcyclohexane **33** (mixture of *cis*- and *trans*-isomers) was prepared from *cis*- and *trans*-1-benzyloxymethyl-4-hydroxymethylcyclohexane by the procedure described above for **1**, using *p*-xylyl bromide instead of benzyl bromide. The benzyl monoether of *cis*- and *trans*-cyclohexane-1,4-dimethanol was synthesized by the reported procedure⁵³ from the corresponding diol, benzyl chloride and 50% aqueous sodium hydroxide solution.

Acknowledgements

This work was supported by the Fund for Promotion of Research at the Technion.

References

- 1 G. L. Glish and R. G. Cooks, *J. Am. Chem. Soc.*, 1978, **100**, 6720.
- 2 C. Westemiotis and F. W. McLafferty, *Org. Mass Spectrom.*, 1981, **16**, 381.
- 3 R. Wolfschutz, H. Schwarz, W. Blum and W. J. Richter, *Org. Mass Spectrom.*, 1979, **14**, 462.
- 4 A. Maquestiau, Y. Van. Haverbeke, R. Flamming and P. Meyrant, *Org. Mass Spectrom.*, 1980, **15**, 80.
- 5 (a) C. C. Van de Sande, F. Van Gaever, P. Sandra and J. Monstrey, *Z. Naturforsch., Teil B*, 1977, **32**, 573; (b) C. C. Van de Sande, F. Van Gaever, R. Hanselaer and M. Vandewalle, *Z. Naturforsch., Teil B*, 1977, **32**, 810; (c) C. C. Van de Sande, F. Van Gaever, L. Dhaenens and R. Myngheer, *Org. Mass Spectrom.*, 1979, **14**, 191; (d) L. Dhaenens, C. C. Van de Sande and M. Schelfault, *Org. Mass Spectrom.*, 1982, **17**, 265; (e) L. Dhaenens, C. C. Van de Sande, M. Schelfault and M. Vandewalle, *Org. Mass Spectrom.*, 1987, **22**, 330.
- 6 I. Barba, F. Alonso, R. Chinchilla and C. Gomez, *Org. Mass Spectrom.*, 1989, **24**, 1029.
- 7 M. Claeys and D. Van Haver, *Org. Mass Spectrom.*, 1977, **12**, 531.
- 8 R. J. Schmitt, C. H. De Puy and R. H. Shapiro, *Abstracts of 25th Annual Conference on Mass Spectrometry and Allied Topics*, p. 125, Washington DC, 1977.
- 9 C. Denekamp and A. Mandelbaum, *J. Mass Spectrom.*, 1995, **30**, 1421.
- 10 R. Shvily, T. Muller, Y. Apeloig and A. Mandelbaum, *J. Chem. Soc., Perkin Trans. 2*, 1997, 1221.
- 11 N. Morlender-Vais and A. Mandelbaum, *Int. J. Mass Spectrom. Ion Processes*, 1997, **167/168**, 13.
- 12 O. Averin and A. Mandelbaum, unpublished results.
- 13 I. Navon and A. Mandelbaum, unpublished results.
- 14 (a) A. Idina, A. Etinger and A. Mandelbaum, *J. Am. Chem. Soc.*, 1993, **115**, 7397; (b) A. Weisz, J. Shabanowitz, A. Mandelbaum and D. Hunt, *Org. Mass Spectrom.*, 1984, **19**, 238; (c) F. J. Winkler and F. W. McLafferty, *Tetrahedron*, 1974, **30**, 2971; (d) E. S. Eichmann and J. S. Brodbelt, *Org. Mass Spectrom.*, 1993, **28**, 665.
- 15 J. March, *Advanced Organic Chemistry*, J. Wiley and Sons, 4th Edn., New York, pp. 308–312, 1992.
- 16 M. Edelson-Averbukh and A. Mandelbaum, *J. Mass Spectrom.*, 1997, **32**, 515.
- 17 E. E. Kingston, J. S. Shannon, V. Diakiw and M. J. Lacey, *Org. Mass Spectrom.*, 1981, **16**, 428.
- 18 D. Cameron and R. G. Cooks, *J. Am. Chem. Soc.*, 1979, **101**, 3162.
- 19 K. Biemann, *Abstracts of 13th Annual Conference on Mass Spectrometry*, p. 427, ASTM Committee E-14, St. Louis, MO, 1965.
- 20 T. Axenrod and G. W. A. Milne, *J. Chem. Soc., Chem. Commun.*, 1968, 67.
- 21 A. V. Danks and R. Hodges, *Aust. J. Chem.*, 1972, **25**, 2721.
- 22 T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, J. Wiley and Sons, 2nd Edn., New York, 1991.
- 23 D. J. McAdoo, *Mass Spectrom. Rev.*, 1988, **7**, 363 and references cited therein; D. J. McAdoo, *Acc. Chem. Res.*, 1993, **26**, 295.
- 24 P. Longevialle, *Mass Spectrom. Rev.*, 1992, **11**, 157 and references cited therein.

- 25 T. H. Morton, *Org. Mass Spectrom.*, 1992, **27**, 353 and references cited therein. T. H. Morton, *Tetrahedron*, 1982, **38**, 3195.
- 26 H.-F. Grutzmacher, *Int. J. Mass Spectrom. Ion Processes*, 1992, **118/119**, 825.
- 27 D. Bowen, *Org. Mass Spectrom.*, 1993, **28**, 1577 and references cited therein; R. D. Bowen, *Acc. Chem. Res.*, 1991, **24**, 364.
- 28 D. Kuck, *Mass Spectrom. Rev.*, 1990, **9**, 583 and references cited therein.
- 29 H. E. Audier, C. Monteiro, P. Mourgues and D. Berthomieu, *Org. Mass Spectrom.*, 1990, **25**, 245.
- 30 H. H. Bueker and H.-F. Grutzmacher, *Int. J. Mass Spectrom. Ion Processes*, 1991, **109**, 95.
- 31 D. Kuck and C. Matthias, *J. Am. Chem. Soc.*, 1992, **114**, 1901.
- 32 S. Fornarini, *Mass Spectrom. Rev.*, 1996, **15**, 365 and references cited therein.
- 33 R. W. Holman, T. Eary, E. Whittle and M. L. Gross, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2187.
- 34 The proton affinities of *n*-alkyl benzyl ethers were estimated using the macroincrementation method³⁵ and were determined as $833 \pm 15 \text{ kJ mol}^{-1}$, based on PA value of benzyl methyl ether ($817.1 \text{ kJ mol}^{-1}$)³⁶ and the following values found in the literature:³⁷ PA (Me_2O) = $803.8 \text{ kJ mol}^{-1}$; PA (Et_2O) = $837.6 \text{ kJ mol}^{-1}$; PA (*n*- Pr_2O) = $846.4 \text{ kJ mol}^{-1}$; PA (*n*- Bu_2O) = $852.3 \text{ kJ mol}^{-1}$.
- 35 J. F. Liebman, in *Molecular Structure and Energetics*, ed. J. F. Liebman and A. Greenberg, Vol. 2, p. 262. VCH, Deerfield Beach, FL, 1986.
- 36 NIST Chemistry Webbook, NIST Standard Reference Database No. 69. August 1997 (<http://webbook.nist.gov/chemistry/>).
- 37 S. G. Lias, J. E. Bartmess, J. F. Liebman, J. L. Holmes, R. D. Levin and W. G. Mallard, *J. Phys. Chem. Ref. Data*, 1988, **17**, Suppl. 1.
- 38 (a) C. Guenat, R. Houriet, D. Stahl and F. J. Winkler, *Helv. Chim. Acta*, 1985, **68**, 1647; (b) P. A. Kollman and L. C. Allen, *Chem. Rev.*, 1972, **72**, 283; (c) M. Meot-Ner (Mautner), *Acc. Chem. Res.*, 1984, **17**, 186; (d) R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, 1973, **95**, 3504.
- 39 M. Meot-Ner (Mautner), *J. Am. Chem. Soc.*, 1983, **105**, 4906.
- 40 R. Houriet, H. Rufenacht, P.-A. Carrupt, P. Vogel and M. Tichy, *J. Am. Chem. Soc.*, 1983, **105**, 3417.
- 41 D. H. Aue, H. M. Webb and M. T. Bowers, *J. Am. Chem. Soc.*, 1973, **95**, 2699.
- 42 Q.-F. Chen and J. A. Stone, *J. Phys. Chem.*, 1995, **99**, 1442.
- 43 J. B. Westmore and M. M. Alauddin, *Mass Spectrom. Rev.*, 1986, **5**, 381.
- 44 F. J. Winkler and J. S. Splitter, in *Application of Mass Spectrometry to Stereochemical Problems*, edited by J. Splitter and F. Turecek, Chapt. 16 and references cited therein, VCH, New York, 1994.
- 45 F. Turecek, *Collect. Chem. Commun.*, 1987, **52**, 1928.
- 46 (a) R. Mason, D. Milton and F. Harris, *J. Chem. Soc., Chem. Commun.*, 1987, 1453; (b) A. Weisz, M. Cojocaru and A. Mandelbaum, *J. Chem. Soc., Chem. Commun.*, 1989, 331; (c) H. Wincel, R. H. Fokkens and N. M. M. Nibbering, *J. Am. Soc. Mass Spectrom.*, 1990, **1**, 225; (d) J. Hrusak, D. Schroder, T. Weiske and H. Schwarz, *J. Am. Chem. Soc.*, 1993, **115**, 2015.
- 47 H. Audier, D. Berthomieu, D. Leblanc and T. H. Morton, *Int. J. Mass Spectrom. Ion Processes*, 1998, **175**, 133.
- 48 (a) Semi-empirical calculations^{48b} indicate that ring protonated *p*-dimethoxybenzene is considerably more stable (by 59 kJ mol^{-1} or 80 kJ mol^{-1} by AM1 and PM3 methods respectively) than the O-protonated form; (b) AM1 and PM3 Methods, SPARTAN 2.1. Wavefunction, Inc., Irvine, CA, 1991–1992.
- 49 D. Kuck, *Mass Spectrom. Rev.*, 1990, **9**, 187 and references cited therein.
- 50 C. Lifshitz, *Acc. Chem. Res.*, 1994, **27**, 138 and references cited therein.
- 51 M. Meot-Ner (Mautner), E. P. Hunter and F. H. Field, *J. Am. Chem. Soc.*, 1977, **99**, 5576.
- 52 A. D. Batcho and W. Leimgruber, *Org. Synth.*, 1990, Coll. Vol. **VII**, 34.
- 53 G. Coudert, M. Mpassi, G. Guillaument and C. Selve, *Synth. Commun.*, 1986, **16**, 19.