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Intramolecular electrophilic aromatic substitution in gas-phase-protonated difunctional compounds containing one or two arylmethyl groups

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A variety of dibenzyl esters and ethers undergo a rearrangement process upon isobutane chemical ionization and collision-induced dissociation of their MH^+ ions, whereby a new bond is formed between the two benzyl groups, giving rise to abundant $[C_{14}H_{13}]^+$ (*m/z* 181) ions. This rearrangement has been explained as an intramolecular electrophilic substitution in the gas phase occurring in an ion–neutral complex formed by the cleavage of one of the benzyl–oxygen bonds. A similar highly efficient intramolecular electrophilic substitution takes place in di-α- and β-naphthylmethyl adipates affording *m/z* 281 $[C_{22}H_{17}]^+$ ions, but not in the sterically hindered di-9-anthracylmethyl adipate. An analogous efficient rearrangement occurs in benzyl α- and β-naphthylmethylcyclohexane-1,4-dicarboxylates and in benzyl α- and β-phenylethylcyclohexane-1,4-dimethanol ethers. The analogous rearrangement is much less efficient in benzylallyl, benzylpropargyl and benzyl-9-anthracylmethyl derivatives, even less in benzylisopropyl and benzylacetyl analogs, and it is absent in benzyltetrahydropyranyl derivatives. The distinctive behavior of the protonated difunctional benzyl derivatives is interpreted in terms of the energy requirements of the O—R bond heterolysis of the protonated functionalities, the ability of the neutral R′ groups (non-dissociated from the oxygen atom) to play the role of the nucleophile in the intramolecular electrophilic substitution processes and the electrophilicity of the R^+ ions.

KEYWORDS: aromatic electrophilic substitution; rearrangements; intramolecular interactions; benzyl derivatives; difunctional compounds; ion–neutral complexes; chemical ionization; collision-induced dissociation; stereochemical effects

INTRODUCTION

A great part of the fragmentation processes occurring in organic ions in the gas phase involves intramolecular formation of new bonds between originally non-bonded atoms. Such rearrangements have been of interest since the early days of organic mass spectrometry, and a large amount of work has been invested in the exploration of their mechanistic pathways.[1–4] Rearrangement processes may create pitfalls in structural assignments of unknown materials by mass spectrometry. On the other hand, they are the basis of many stereochemical effects in mass spectrometry, which may facilitate configurational assignments of stereoisomers by this technique.[5–9] In certain cases meaningful correlations have been found between rearrangement processes of gas-phase ions under chemical ionization (CI) conditions and acid-catalyzed molecular rearrangements in solution.[10–12]

We have recently reported a highly efficient rearrangement process occurring in a large number of gas-phase protonated benzyl diesters and diethers under isobutane-CI and collision-induced dissociation (CID) conditions.[13,14] This rearrangement involves an intramolecular C—C bond formation between the two benzyl groups giving rise to abundant $[C_{14}H_{13}]^+$ (*m/z* 181) ions. A CID study of the $[C_{14}H_{13}]^+$ ions has shown that they are an almost equimolar mixture of isomeric α-*o*-tolylbenzyl, α-*p*-tolylbenzyl and *p*-benzylbenzyl cations in all cases. In contrast to the dibenzyl diesters, diethers and ether esters, this rearrangement reaction is insignificant in protonated sulfur analogues, and absent in the nitrogen-containing derivatives (benzyldiamines, -diamides and -aminoamides).[15] The proposed mechanistic pathway for this rearrangement process is shown in Scheme 1. The initial step in this mechanism is the cleavage of the benzylic C—O bond of the protonated ether or ester function to form an ion–neutral complex[16–20] **A**, followed by the electrophilic attack of the benzyl cation at the *ortho* and *para* positions of the neutral benzyl group (non-dissociated from the oxygen function) within the ion–neutral complex, resulting in the two σ-complexes $\mathbf{B_1}$ and $\mathbf{B_2}$. Intramolecular proton transfers from the *ipso* positions to the oxygen atom and the heterolytic fission of the second benzyl–oxygen bond afford the α-*o*-tolylbenzyl, α-*p*-tolylbenzyl and *p*-benzylbenzyl cations **a, b** and **c**. The proposed mechanism resembles that of

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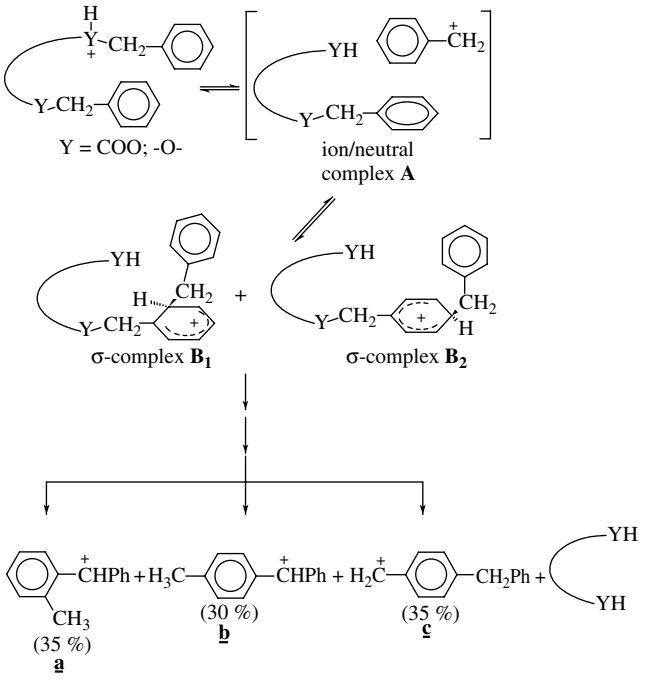
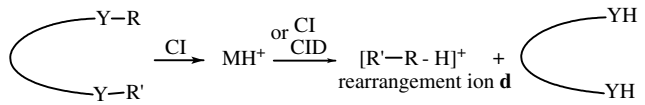
the aromatic electrophilic substitution in the condensed phase.



Scheme 1

In view of the above results, it was of interest to explore whether the bond-forming intramolecular interactions, analogous to those occurring in benzyl diesters and diethers, also take place if one or both benzyls are replaced by other aryl groups or by non-aromatic moieties (Scheme 2). In this paper, we present a study of the mass spectrometric behavior of a series of difunctional oxygen derivatives bearing benzyl, α- and β-naphthylmethyl, 9-anthracylmethyl, α- and β-phenylethyl, allyl, propargyl, isopropyl, acetyl and tetrahydropyranyl groups.



Y = -COO-; -O-
R, R'=Benzyl, Naphthylmethyl, 9-Anthracylmethyl, Allyl, Propargyl, Acetyl, 2-Propyl, Tetrahydropyranyl

Scheme 2

EXPERIMENTAL

Mass spectrometry

Gas chromatographic and direct exposure probe chemical ionization mass spectrometric analyses (GC/CI-MS and DEP/CI-MS) and CID measurements were carried out on a Finnigan TSQ-70B triple-stage quadrupole mass spectrometer. The stereoisomeric pairs **1–6** were introduced as mixtures and separated on a DB-5 capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness, temperature programmed from 60 to 280 °C at 15 °C min^{-1}). The scan rate was 1 scan s^{-1}. The *cis*-isomers were first and followed by the *trans*-counterparts in the GC/MS analyses of the six stereoisomeric pairs **1–6**. CI measurements were performed at an ion source temperature of 150 °C and 0.4 Torr (indicated) reagent gas pressure (isobutane, acetonitrile) (1 Torr = 133.3 Pa). CID measurements were performed with argon as the target gas (0.3 mTorr, indicated) at 30 eV collision energy (indicated). All the data presented in each table were obtained on the same day under identical conditions, in order to ensure reliable comparisons.

Materials

Diesters **1–3, 6, 8, 9, 12** and **13** were synthesized by esterification of *cis*- and *trans*-1,4-cyclohexane dicarboxylic and adipic acids by the corresponding alcohols (or by a mixture of the alcohols in the cases of **1–3, 6, 8** and **9**) in the presence of a catalytic amount of *p*-toluenesulfonic acid monohydrate.[21] 1- and 2-naphthalenemethanols were prepared from 1- and 2-naphthoic acids by reduction with lithium aluminum hydride.[22]

Cis- and *trans*-1-benzyloxymethyl-4-tetrahydropyranoxymethylcyclohexanes (**4**) were synthesized by partial etherification of cyclohexane-1,4-dimethanol (*cis* and *trans* mixture) to afford *cis*- and *trans*-1-benzyloxy-4-hydroxymethylcyclohexanes (by reaction with sodium hydride and benzyl bromide)[14] and subsequent tetrahydropyranylation of the monoethers following a previously described procedure.[23]

1-Benzyloxymethyl-4-α-phenylethylcyclohexane (**5**) (mixture of *cis*- and *trans*-isomers) was obtained from *cis*- and *trans*-1-benzyloxy-4-hydroxymethylcyclohexanes by reaction with sodium hydride and α-phenylethyl bromide (in THF) following a previously described procedure.[14]

To prepare 1-acetoxycarbonyl-4-benzyloxymethylcyclohexane (**7**) (mixture of *cis*- and *trans*-isomers), 1-benzyloxymethyl-4-cyclohexanecarboxylic acid (*cis* and *trans* mixture) was synthesized by partial etherification of a mixture of *cis*- and *trans*-cyclohexane-1,4-dimethanols (by benzyl chloride and 50% aqueous sodium hydroxide solution)[24] to yield the corresponding benzyl monoether, and subsequent oxidation of the hydroxymethyl group with pyridinium dichromate.[25] Triethylamine (0.34 ml, 2.42 mmol) was added dropwise to a cold (ice–water bath) mixture of *cis*- and *trans*-1-benzyloxymethyl-4-cyclohexanecarboxylic acids (0.3 g, 1.21 mmol) and acetyl chloride (0.14 g, 1.82 mmol) in dry diethyl ether (8 ml). The reaction mixture was stirred at room temperature overnight, filtered and washed with 5 ml portions of diethyl ether. Concentration of the filtrate under reduced pressure yielded 80% of the mixed anhydride **7**.

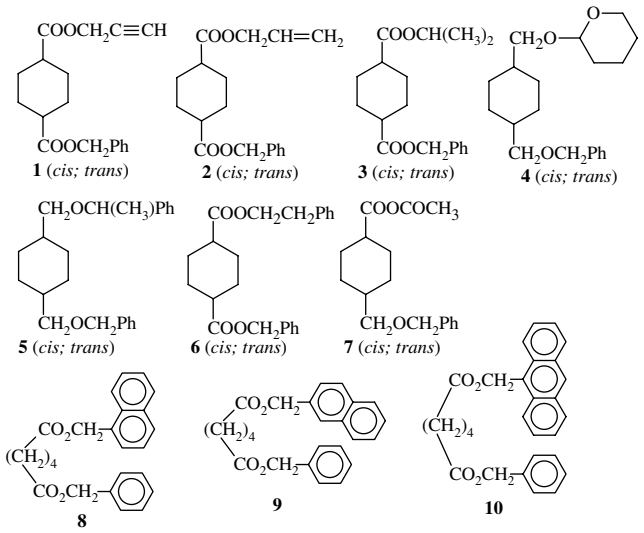
Benzyl-9-anthracylmethyl adipate (**10**) was synthesized from adipic acid dichloride by reaction with a 1:1 mixture of benzyl and 9-anthracylmethyl alcohols and 4-dimethylaminopyridine. To a stirred solution of adipic acid dichloride (0.05 g, 0.27 mmol) in dichloromethane (1 ml) at 0 °C under an N_2 atmosphere was added a solution of DMAP (0.08 g, 0.68 mmol) in CH_2Cl_2 (1 ml), followed by addition of a mixture of benzyl (0.04 g, 0.324 mmol) and 9-anthracylmethyl (0.07 g, 0.324 mmol) alcohols in the same solvent (2 ml). After stirring for 24 h at room temperature, water (4 ml) was added and the dichloromethane layer was washed with 10% hydrochloric acid and 5% $NaHCO_3$. The

organic phase was dried over $MgSO_4$ and evaporated under vacuum. The diester **10** was obtained in 83% yield after purification on a silica gel column (hexane–ethyl acetate (3:1)). Adipic acid dichloride was obtained by reaction of adipic acid with thionyl chloride, following a reported procedure.[26] 9-Anthracylmethyl alcohol was prepared by formylation of anthracene with dimethylformamide in the presence of phosphorus oxychloride (Vilsmeier reaction)[27] and subsequent reduction of the resulting 9-anthraldehyde with sodium borohydride.[28]

Di-9-anthracylmethyl adipate (**11**) was prepared from adipic acid dichloride and 9-anthracylmethyl alcohol in the same manner as **10**.

RESULTS AND DISCUSSION

Mixed derivatives of dicarboxylic acids, diols and acid alcohols **1–10** were prepared for this study. The isobutane-CI mass spectral data for these compounds are given in Table 1 and the CID spectra of their MH^+ ions are given in Table 2.



Phenylethyl and naphthylmethyl derivatives

The results of the CI and CID measurements reveal that the MH^+ ions of *trans*-**5**, **6**, **8** and **9** containing α- or β-phenylethyl and α- or β-naphthylmethyl groups, respectively, undergo an efficient rearrangement leading to the formation of benzyl–R covalent bonds (ions $\mathbf{d_5}$, $\mathbf{d_6}$, $\mathbf{d_8}$ and $\mathbf{d_9}$ in Scheme 3), in analogy with the generation of the $[C_{14}H_{13}]^+$ (m/z 181) ion in the fragmentation of the protonated dibenzyl derivatives.[13–15] Plausible structures of the abundant ions $\mathbf{d_5}$, $\mathbf{d_6}$, $\mathbf{d_8}$ and $\mathbf{d_9}$ are proposed in Scheme 3.

The results of the CID measurements of the m/z 195 ions $\mathbf{d_5}$ and $\mathbf{d_6}$, summarized in Table 3, show significant difference in the formation of the m/z 167 production, which is present (at relatively low abundance) in the spectrum of ion $\mathbf{d_6}$, but absent in that of $\mathbf{d_5}$. The presence of this [parent $- C_2H_4$]$^+$ ion is consistent with the ethyldiphenylmethyl structure proposed for ion $\mathbf{d_6}$ in Scheme 3. The preferential cleavage of the O–benzyl bond on the way to the formation of the ion–neutral complex $\mathbf{C_6}$, as compared with the O–β-phenethyl bond, is proposed to be the origin of the formation of the m/z 195 ion $\mathbf{d_6}$ from the MH^+ ion of **6**.

The rearrangement leading to the formation of ion $\mathbf{d_5}$ from **5** is highly stereospecific, affording an abundant ion (relative abundance (RA) 66%) in the isobutane-CI mass spectrum of *trans*-**5**, but a very low one (RA 1%) in the *cis*-isomer. The low abundance of ion $\mathbf{d_5}$ in the mass spectrum of *cis*-**5** presumably results from the high efficiency of the competing elimination of styrene, which affords the most abundant m/z 235 fragment ion. The high efficiency of this competing dissociation may result from stabilization of the [MH $-$ styrene]$^+$ ion by the internal hydrogen bond between the two oxygen functions, which is possible only in the *cis*-isomer. A detailed study of a similar stereospecific behavior has been reported recently for tetrahydropyranyl (THP) ethers of *cis*- and *trans*-1-alkoxymethyl-4-cyclohexylmethanols and for THP esters of *cis*- and *trans*-1,3-cyclohexanedicarboxylic acids.[23]

Propargyl, allyl and 9-anthracylmethyl derivatives

The data in Tables 1 and 2 show that the benzyl group of the MH^+ ions of **1**, **2** and **10** interacts also with the propargyl, allyl and 9-anthracylmethyl moieties to give rise to new C—C bonds. However, in these cases the abundances of the rearrangement ions **d** are much lower than those of the protonated molecules of *trans*-**5**, **6**, **8** and **9**. The extents of the rearrangement for the stereoisomeric benzylisopropyl diesters **3** and the benzyloxy anhydrides **7** are even smaller, and the rearrangement ions **d** are entirely absent in the CI and CID mass spectra of *cis*- and *trans*-1-benzyloxymethyl-4-tetrahydropyranoxymethylcyclohexanes **4**.

The observed lower efficiencies of the intramolecular benzyl–propargyl and benzyl–allyl interactions occurring in the CI and CID fragmentation of diesters **1** and **2**, respectively, relative to those of the corresponding benzyl–benzyl interactions,[13–15,29] can be rationalized on the basis of the following arguments. The hydride ion affinities of the propargyl and allyl cations are considerably higher than that of the benzyl cation (by 33 and 18 kcal mol^{-1}, respectively[30] (1 kcal = 4.184 kJ)). The hydride ion affinity scale is considered as a reliable convenient basis for the comparison of the relative stabilities of carbocations.[31] Consequently, the heterolysis of the O—R bonds of the protonated propargyloxy- and allyloxycarbonyl groups, resulting in the formation of propargyl and allyl cations, respectively, is expected to be more endothermic than that of the O–benzyl bond. The preferential heterolysis of the O–benzyl bonds in the MH^+ ions of **1** and **2** presumably leads to the ion–neutral complexes $\mathbf{C_1}$ and $\mathbf{C_2}$, respectively, as shown in Schemes 4 and 5. The propensity of ethylene and acetylene for electrophilic substitution is known to be much lower than that of benzene.[32] Therefore, the electrophilic substitution of the propargyl and allyl groups by the benzyl cation in the ion–neutral complexes $\mathbf{C_1}$ and $\mathbf{C_2}$, respectively, via the corresponding intermediates $\mathbf{D_1}$ and $\mathbf{D_2}$ is expected to be slow, resulting in relatively low abundance ions $\mathbf{d_1}$ and $\mathbf{d_2}$.

Isopropyl and tetrahydropyranyl derivatives

The reluctance of *cis*- and *trans*-1-benzyloxycarbonyl-4-isopropoxycarbonylcyclohexanes **3** to undergo a similar rearrangement (very low abundance m/z 133 ion, see Tables 1

Table 1. Isobutane-CI mass spectral data[a] (relative abundance, %) of compounds **1–10**

		Ion						
Compound	R	MH^+	Ion d[b]	$[C_7H_8]^+$ m/z 91	$[MH - BnOH]^+$	$[MH - ROH]^+$	$[MH - BnOR]^+$	Other fragments
cis-**1**	Propargyl	100	8	8	5	6	11	m/z 127 (3%); m/z 147 (7%); m/z 211 $[MH - 90]^+$ (1%); m/z 263 (7%)
trans-**1**	Propargyl	100	7	16	0.1	2	4	m/z 127 (5%); m/z 147 (3%); m/z 211 $[MH - 90]^+$ (2%); m/z 263 (15%); m/z 273 (3%)
cis-**2**	Allyl	100	3	4	6	3	3	m/z 213 $[MH - 90]^+$(1%)
trans-**2**	Allyl	100	7	7	0.2	<0.1	2	m/z 213 $[MH - 90]^+$(2%)
cis-**3**	Isopropyl	100	1	2	5	6	1	m/z 131 (0.5%); m/z 263 $[MH - propene]^+$ (7%); m/z 291 (19%)
trans-**3**	Isopropyl	100	1	13	<0.1	1	1	m/z 131 (0.6%); m/z 263 $[MH - propene]^+$ (97%); m/z 291 (2%)
cis-**4**	Tetrahydropyranyl	<0.1	<0.1	0.1	0.1	1	<0.1	m/z 143 (7%); m/z 235 $[MH - DHP]^+$ (100%)[b]; m/z 233 $[MH - 86]^+$ (5%)
trans-**4**	Tetrahydropyranyl	100	<0.1	1	0.1	4	<0.1	m/z 143 (19%); m/z 199 (2%); m/z 217 (4%); m/z 227 $[MH - C_7H_8]^-$(2%); m/z 233 $[MH - 86]^+$(3%); m/z 235 $[MH - DHP]^+$ (7%)[c]
cis-**5**	α-Phenylethyl	<0.1	1	<0.1	<0.1	0.4	<0.1	m/z 105 $[C_8H_9]^-$ (3%); m/z 233 $[MH - 106]^+$ (6%); m/z 235 $[MH - styrene]^+$ (100%)
trans-**5**	α-Phenylethyl	<0.1	66	4	<0.1	1	8	m/z 105 $[C_8H_9]^-$ (22%); m/z 125 (32%); m/z 143 (48%); m/z 233 $[MH - 106]^+$ (21%); m/z 235 $[MH - styrene]^+$ (100%); m/z 247 $[MH - C_7H_8]^+$ (2%)
cis-**6**	β-Phenylethyl	100	50	3	1	0.7	0.2	m/z 105 $[C_8H_9]^+$ (1%); m/z 349 $[MH - H_2O]^+$(29%)
trans-**6**	β-Phenylethyl	75	100	0.3	<0.1	0.1	0.1	m/z 105 $[C_8H_9]^+$ (7%)
7 (*cis; trans*)[d]	Acetyl	2	1	100	2	81	11	m/z 125 (16%); m/z 199 $[MH - C_7H_8]^+$ (4%); m/z 203 $[MH - AcOH - CO]^+$ (37%); m/z 249 $[MH - CH_2CO]^+$ (13%)
8	α-Naphthylmethyl	100	33	—[e]	<0.1	<0.1	—[e]	—
9	β-Naphthylmethyl	100	68	—[e]	<0.1	<0.1	<0.1	m/z 141 $[C_{11}H_9]^+$ (75%); m/z 157 (4%); m/z 183 (6%)
10	9-Anthracylmethyl	<0.1	4	<0.1	<0.1	<0.1	<0.1	m/z 191 $[C_{15}H_{11}]^+$ (100%); m/z 207 (11%); m/z 237 $[MH - 190]^+$(21%); m/z 329 (19%)

[a] Mass ranges of the CI measurements: m/z 90–400 for 1–7; m/z 160–450 for **8**; m/z 110–450 for **9**; m/z 90–500 for **10**.

[b] The ions **d** of **1**, **2**, *trans*-**5**, **6**, and **8–11** have been characterized by CID (20 eV, 40–60 eV collision energies). in order to ensure that they result from the rearrangement illustrated in Scheme 2.

[c] DHP = dihydropyran.

[d] The data are given for a mixture of the *cis*- and *trans*-epimers.

[e] The m/z values are below the range of the CI measurements.

Table 2. CID[a] mass spectral data[b,c] of MH^+ ions obtained from **1–3** *trans*-**4** and **6–9** on isobutane-CI

		Ion					
Compound	R	Ion d	$[C_7H_7]$ m/z 91	$[MH - BnOH]^+$	$[MH - ROH]^+$	$[MH - BnOR]^+$	Other fragments
cis-**1**	Propargyl	22	29	2	4	12	m/z 109 (3%): m/z 127 (7%): m/z 147 (22%)
trans-**1**	Propargyl	25	33	1	<0.1	6	m/z 109 (4%): m/z 127 (18%): m/z 147 (9%)
cis-**2**	Allyl	14	63	8	5	8	m/z 109 (1%): m/z 127 (1%)
trans-**2**	Allyl	30	45	<0.1	2	2	m/z 41 (2%): m/z 109 (1%): m/z 127 (3%): m/z 171 (4%): m/z 199 (7%): m/z 217 (4%)
cis-**3**	Isopropyl	0.4	56	8	14	1	m/z 263 $[MH - propene]^+$ (21%)
trans-**3**	Isopropyl	0.5	39	<0.1	2	1	m/z 263 $[MH - propene]^+$ (57%)
trans-**4**	Tetrahydropyranyl	<0.1	14	6	<0.1	<0.1	m/z 85 $[C_5H_7O]^+$ (41%): m/z 109 (8%): m/z 125 (5%): m/z 213 (15%): m/z 235 $[MH - DHP]^+$ (8%)
cis-**6**	β-Phenylethyl	46	18	3	2	0.6	m/z 105 $[C_8H_9]^+$ (1%): m/z 349 $[MH - H_2O]^+$ (30%)
trans-**6**	β-Phenylethyl	52	3	<0.1	<0.1	<0.1	m/z 105 $[C_8H_9]^+$ (45%)
7 (*cis: trans*)[d]	Acetyl	0.4	62	0.6	3	2	m/z 139 (2%): m/z 199 $[MH - C_7H_8]^+$ (2%): m/z 249 $[MH - CH_2CO]^+$ (28%)
8	α-Naphthylmethyl	29	<0.1	<0.1	<0.1	<0.1	m/z 141 $[C_{11}H_9]^+$ (67%): m/z 359 $[MH - H_2O]^+$ (4%)
9	β-Naphthylmethyl	41	0.2	<0.1	0.4	0.4	m/z 141 $[C_{11}H_9]^+$ (56%): m/z 157 (2%)

[a] 30 eV collision energy.

[b] The CID spectra of the MH^+ ions of *cis*-**4**, *cis*-**5**, *trans*-**5** and **10** were not measured because of the low abundances of the MH^+ ions in the isobutane-CI mass spectra.

[c] The ion abundances are listed as percentages of the total product ion current (%Σ).

[d] The data are given for a mixture of the *cis*- and *trans*-epimers.

and 2) is obvious. Similarly to the propargyl and allyl derivatives **1** and **2**, the rupture of the O–benzyl bond in diesters **3**, resulting in the formation of the benzyl cation, is favored over that leading to the isopropyl cation[31] (the hydride ion affinity of the isopropyl cation ($D(s\text{-}C_3H_7^+ - H^-)$) is higher than that of the benzyl carbocation ($D(PhCH_2^+ - H^-)$) by 14 kcal mol^{-1} (Ref. 30)). The m/z 43 isopropyl ion is indeed absent in the CID spectra of the MH^+ ions of *cis*-**3** and *trans*-**3** (it is below the mass range of isobutane-CI measurements). The m/z 91 cation is relatively abundant in the CI mass spectra of *cis*-**3** and *trans*-**3**, and even more in the CID spectra of their MH^+ ions (see Tables 1 and 2). However, there are no π-electrons in the isopropoxy moiety to be attracted by the benzyl cation in the ion–neutral complex $\mathbf{C_3}$.

The high abundance of the m/z 85 tetrahydropyranyl (THP) ion and the very low abundance of the benzyl ion in the CI and CID spectra of the stereoisomeric benzyl tetrahydropyranyl ethers **4** suggest preferential cleavage of the THP–O bond, possibly leading to the ion/neutral complex $\mathbf{C_4}$. The absence of the m/z 175 rearrangement ion in the CI and CID spectra of the diethers **4** suggests non-occurrence of an electrophilic attack of the THP^+ ion at the phenyl ring of the benzyloxy group. Such attack would result in the formation of intermediate $\mathbf{D_4}$ (see Scheme 6), that would be destabilized as compared with the ion–neutral

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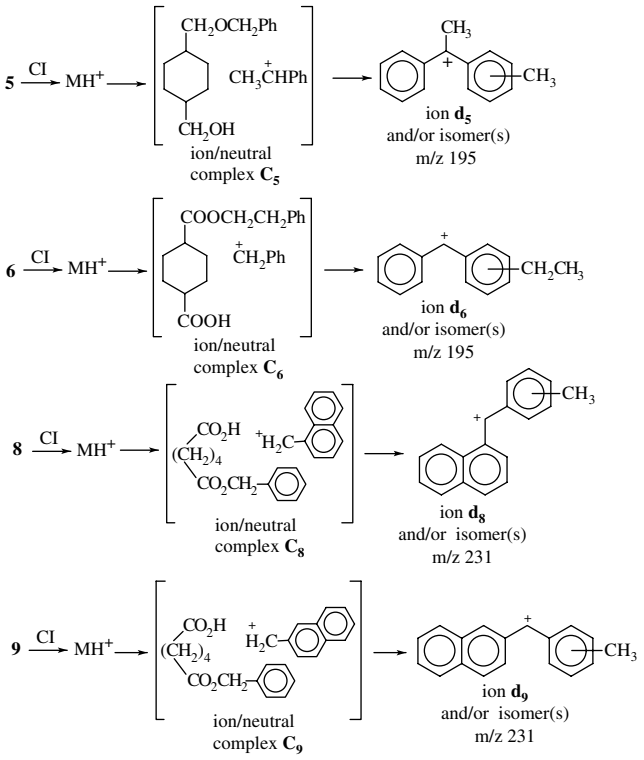


Scheme 3

complex $\mathbf{C_4}$ (benzenium ion in $\mathbf{D_4}$ instead of the phenyl group in $\mathbf{C_4}$, and tetrahydropyranyl moiety in $\mathbf{D_4}$ instead of the THP cation in $\mathbf{C_4}$). Steric hindrance may also have an effect in the reluctance of the ion–neutral complex $\mathbf{C_4}$ to form intermediate $\mathbf{D_4}$.

Acetyl derivative

The very high abundance of the $[C_7H_7]^+$ ion in the CI mass spectrum of the benzyloxy anhydride **7** (*cis*- and *trans*-isomer mixture) and in the CID spectrum of the MH^+ ion (Tables 1 and 2), and the absence of the acetyl cation in the CID spectrum (it could not be measured upon CI), indicate preferential cleavage of the O–benzyl bond. This behavior explains the very low efficiency of the rearrangement leading to the low-abundance m/z 133 ion $\mathbf{d_7}$ (Scheme 7). The highly abundant $[MH - CH_3COOH]^+$ ion in the CI mass spectrum of **7** shows the elimination of acetic acid is the most efficient fragmentation involving the acetyl group.

Table 3. CID[a] mass spectral data[b] of ions $\mathbf{d_5}$ and $\mathbf{d_6}$ (m/z 195), obtained from **5** and **6** on isobutane-CI

	Compound			
Ion	*cis*-**5**	*trans*-**5**	*cis*-**6**	*trans*-**6**
m/z 180	<0.1	<0.1	3	3
m/z 167	<0.1	<0.1	3	3
m/z 117	38	16	21	22
m/z 103	<0.1	<0.1	2	2
m/z 91	62	84	71	70

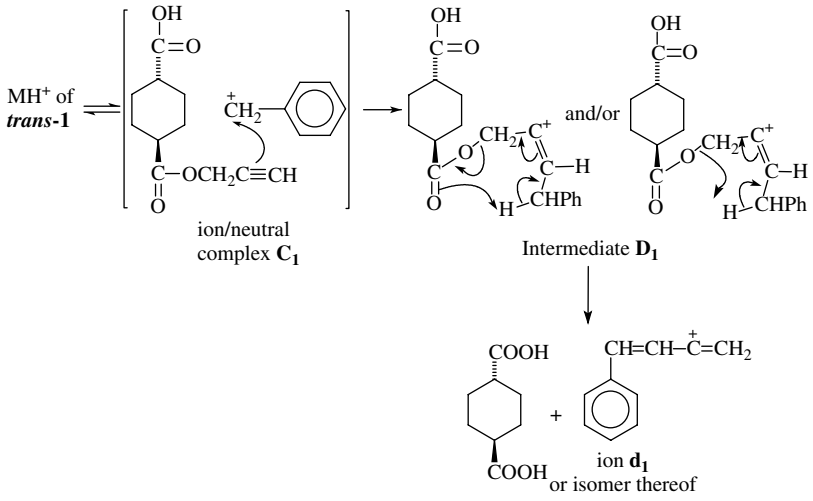
[a] 40 eV collision energy.

[b] The ion abundances are listed as percentages of the total product ion current (%Σ).

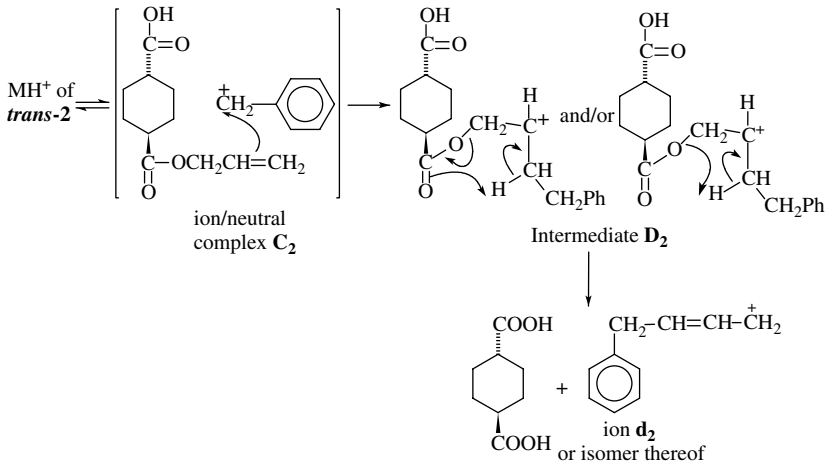
9-Anthracylmethyl derivatives — steric hindrance

The m/z 191 9-anthracylmethyl cation is highly abundant in the isobutane-CI mass spectrum of benzyl-9-anthracylmethyl adipate (**10**), while the $[C_7H_7]^+$ ion is absent. In this respect the behavior of **10** resembles that of the α-and β-naphthylmethyl analogues **8** and **9**. However, unlike **8** and **9**, **10** undergoes inefficient rearrangement giving rise to a low-abundance (4%) m/z 281 ion $\mathbf{d_{10}}$ (see Table 1). This different behavior of the naphthylmethyl and 9-anthracylmethyl derivatives is attributed to a steric factor. Unlike the α- and β-naphthylmethyl ions, the methylene group of the 9-anthracylmethyl cation is hindered from both sides by the 1-H and 8-H atoms of the anthracene ring, resulting in a higher energy barrier for the electrophilic attack at the phenyl ring of the benzyloxy group (Scheme 8).

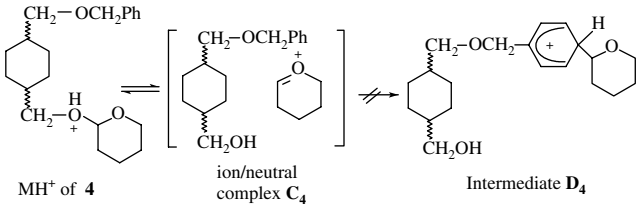
The isobutane-CI and CID data listed in Tables 1 and 2 show that the abundance of the rearrangement ion $\mathbf{d_9}$ obtained from the protonated molecule of benzyl-β-naphthylmethyl adipate (**9**) is significantly higher than that of the isomeric benzyl-α-naphthylmethyl dicarboxylate (**8**). This behavior is in agreement with the steric hindrance at the methylene carbon of the α-naphthylmethyl cation by the



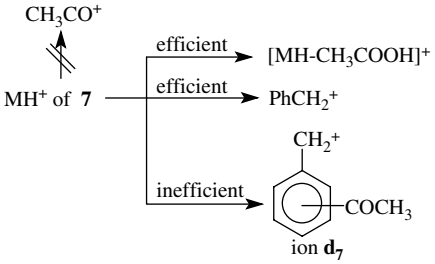
Scheme 4



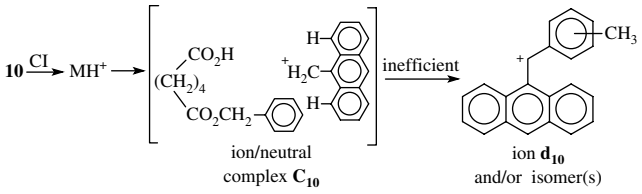
Scheme 5



Scheme 6



Scheme 7



Scheme 8

8-H atom of the naphthalene ring of the carbocation, which is absent in the corresponding β-isomer.

The effect of steric hindrance at the 9-anthracylmethyl position is demonstrated in the behavior of di-9-anthracylmethyl adipate (**11**) under isobutane-CI conditions (the CID spectrum could not be measured because of the absence of the MH^+ ion). The m/z 191 anthracylmethyl cation is the most abundant ion in the mass spectrum, and the m/z 381 rearrangement ion $\mathbf{d_{11}}$ is absent (see Table 4 and Scheme 9). In contrast, the m/z 281 rearrangement ions $\mathbf{d_{12}}$ and $\mathbf{d_{13}}$ are the most abundant products in the isobutane-CI and CID spectra of α- and β-naphthylmethyl adipates **12** and **13** (Figs 1 and 2). The different CID spectra (50 eV collision energy) of ions $\mathbf{d_{12}}$ and $\mathbf{d_{13}}$ (m/z 266 and 265 in both, but an m/z 252 [parent $- C_2H_4$]$^+$ ion only in that of $\mathbf{d_{12}}$) indicate different structures for these two ions.

Table 4. Isobutane-CI[a] and CID[b] (of MH^+ ions) mass spectral data for dianthracylmethyl and dinaphthylmethyl adipates (**11–13**)

	Isobutane-CI (relative abundance, %)		CID (%Σ)[c]
Compound	MH^+	Ion **d**	Ion **d**
11[d]	<0.1	<0.1	[i]
12[e,f]	5	100	65
13[g,h]	13	100	85

[a] Ranges of the CI measurements: m/z 220–600 (**11**); m/z 170–500 (**12** and **13**).
[b] 30 eV collision energy.
[c] The CID data are listed as percentages of the total product ion current (%Σ).
[d] Relative abundances of additional fragments in the isobutane-CI mass spectrum: m/z 233 (37%); m/z 247 (86%); m/z 336 (100%); m/z 351 (11%); m/z 369 (13%); m/z 382 (26%); m/z 383 (20%).
[e] Relative abundance of an additional fragment in the isobutane-CI mass spectrum: m/z 183 (6%).
[f] Additional fragments in the CID spectrum: m/z 141 $[C_{11}H_9]^+$ (12%); m/z 157 (11%); m/z 285 (5%); m/z 286 (7%).
[g] Relative abundance of additional fragment in the isobutane-CI mass spectrum: m/z 183 (3%).
[h] Additional fragments in the CID spectrum: m/z 141 $[C_{11}H_9]^+$ (6%); m/z 157 (7%); m/z 285 (1%); m/z 286 (1%).
[i] The CID spectrum was not measured because of the low abundance of the MH^+ ion in the isobutane CI mass spectrum.

CONCLUSION

We have shown that the previously reported rearrangement of a variety of gas-phase protonated dibenzyl derivatives, resulting in abundant $[C_{14}H_{13}]^+$ (m/z 181) cations, takes place also when one or both benzyls are replaced by other

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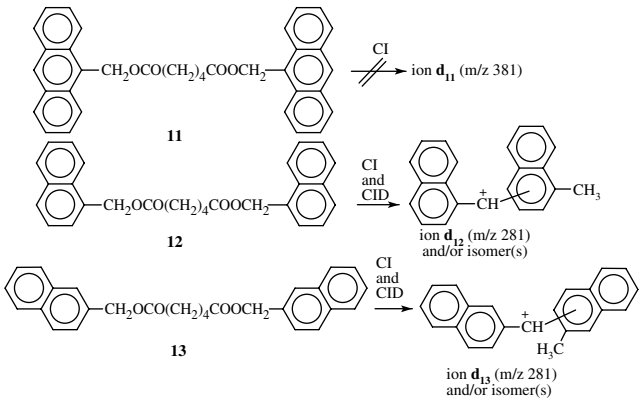

Scheme 9

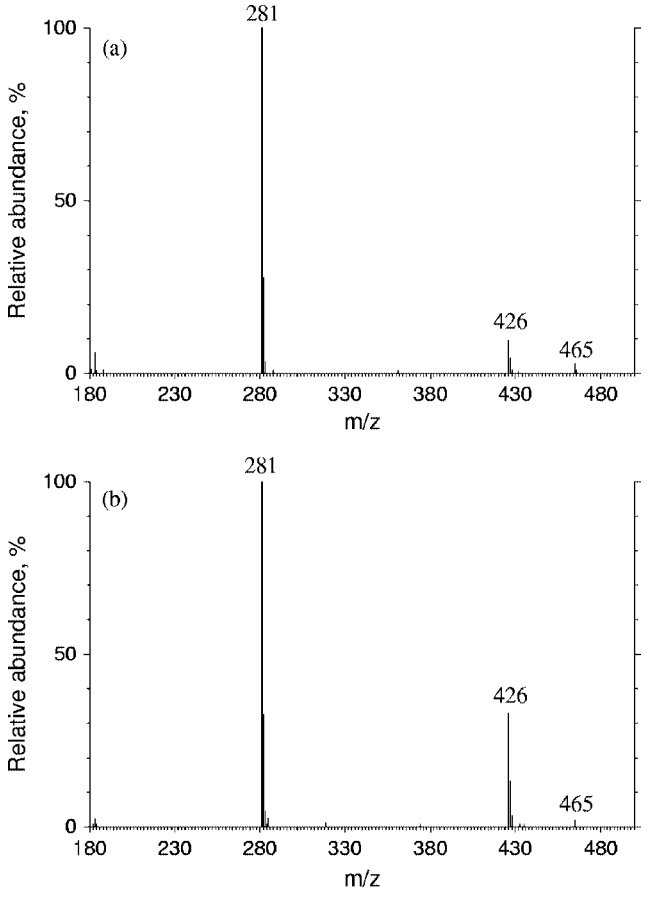

Figure 1. Isobutane-CI mass spectra of (a) **12** and (b) **13**.

arylmethyl moieties, such as α- and β-phenylethyl or α- and β-naphthylmethyl groups. Similar intramolecular bond-forming interactions are less favorable for compounds bearing allyl, propargyl, 9-anthracylmethyl, isopropyl and acetyl groups, and in the case of *cis*- and *trans*-1-benzyloxymethyl-4-tetrahydropyranoxymethylcyclohexanes this rearrangement is completely suppressed. This distinctive behavior of the protonated difunctional benzyl derivatives has been interpreted in terms of the energy requirements of the O—R bond heterolysis of the protonated functionalities, the ability of the neutral R groups (non-dissociated from the oxygen atom in the initial step) to play the role of the nucleophile in the intramolecular electrophilic substitution processes, and the

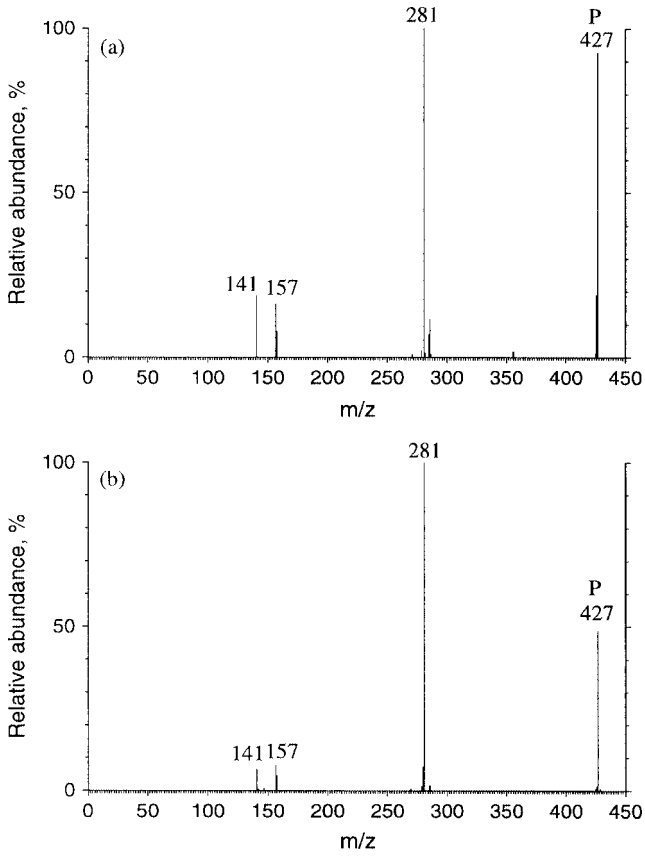

Figure 2. CID mass spectra (30 eV collision energy) of the MH^+ ions obtained on isobutane-CI from (a) **12** and (b) **13**.

electrophilicity of the R^+ ions. The low efficiency of this rearrangement in 9-anthracylmethyl derivatives, in contrast to α- and β-naphthylmethyl analogs, indicates high sensitivity of this unique process to steric hindrance.

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