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2-Benzylindane radical cations in the gas phase (Part I): Substituent effects on a stereoselective McLafferty reaction and related hydrogen transfer processes

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In memoriam Nico M. M. Nibbering, a friend in science and beyond.

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ABSTRACT

In the present and the accompanying article, the unimolecular fragmentation of the radical cations of 2-benzylindane and eleven derivatives bearing *meta*- or *para*-substituents at the benzylic moiety has been studied with a special focus on the hydrogen exchange that precedes the McLafferty reaction. Standard EI mass spectra, low-energy (11 eV) mass spectra and mass-analyzed ion kinetic energy (MIKE) spectra were recorded to probe the excitation-energy and ion-lifetime dependence of the fragmentation and the hydrogen exchange. Density-functional theory calculations were used to rationalize the substituent effects on the competition between the benzylic cleavage and the McLafferty reaction and to clarify the role of the distonic arenium ion-type intermediate formed by the γ-hydrogen-transfer step of the McLafferty reaction. The *ipso*-protonolysis of the benzyl residue giving rise to the loss of substituted benzenes specifically from most of the *para*-isomers was also found to reflect the hydrogen exchange.

1. Introduction

Hydrogen transfer reactions and hydrogen exchange ("H scrambling") preceding mass spectrometric fragmentation reactions constitute important elementary processes that are both relevant for the understanding of the fundamentals of gas-phase ion chemistry and the analytical interpretation of mass spectra. Since the early discoveries by Meyerson and his coworkers in the late 1950s on scrambling processes occurring in the radical cations of lower alkylbenzenes [1–3] and later studies by Lightner et al. [4], numerous reports have been published on this subject. The chemical and physical factors that govern hydrogen transfer and hydrogen scrambling and their mechanistic implications have been investigated and reviewed [5–10]. Hydrogen exchange can occur in various ways: It can be fast or slow with respect to the given lifetime of the ions, leading to "complete" or "incomplete" scrambling, its extent is lifetime-dependent and mostly increases with increasing ion lifetime ("progressive scrambling"), and it may even take place by different mechanisms for distinct populations of the same fragmenting ions ("composite scrambling") [8].

Hydrogen exchange occurring in the molecular ions, $M^{\bullet+}$, of the higher alkylbenzenes and their derivatives was found to be regioselective [1,4,11–19]. The H atoms of the γ-position of the aliphatic chain are involved with high preference and those at the *ortho*-positions of the aromatic nucleus participate exclusively. This special feature of the radical cations does not apply to protonated alkylbenzenes, $[M+H]^+$, both in the regimes of unimolecular fragmentation [20–22] and bimolecular ion-molecule reactions [23], where only the ring hydrogens, but all of them, are involved in a very fast proton exchange in most cases [8,10,20–23]. In contrast, the hydrogen scrambling preceding the EI-induced fragmentation of 2-benzylindane (**1**, Scheme 1) was found to be particularly clear-cut [24]. The radical cations $\mathbf{1}^{\bullet+}$ undergo a highly regioselective hydrogen exchange that involves the four H atoms at the two *cis*-positions of the five-membered ring (1-H^{cis} and 3-H^{cis}) and the two *ortho*-positions of the benzyl group (2′-H and 6′-H) prior to fragmentation by McLafferty reaction, giving the 5-methylenecyclohexa-1,3-diene ion, $C_7H_8^{\bullet+}$ (*m*/*z* 92). Such a "4-H exchange" (or "4-H scrambling") process has been known for a long time to occur in the radical cations of 1,3-diphenylpropane [11,12] and also, in a modified manner, in those of dihydrocinnamates [25–27]. Ionized 1,3-diphenylpropane represents a special case because it undergoes two relatively slow and mutually merged 4-H exchange processes that involve the H^{γ} and H^{ortho} atoms, on

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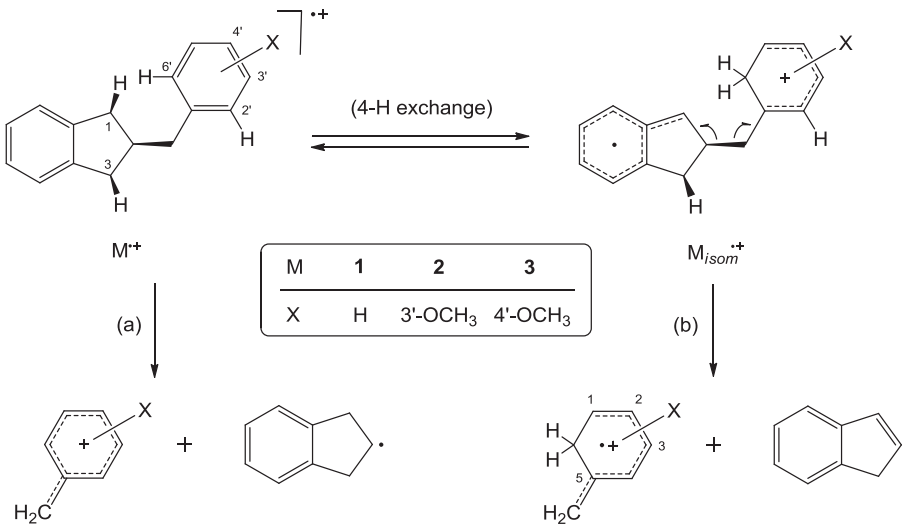
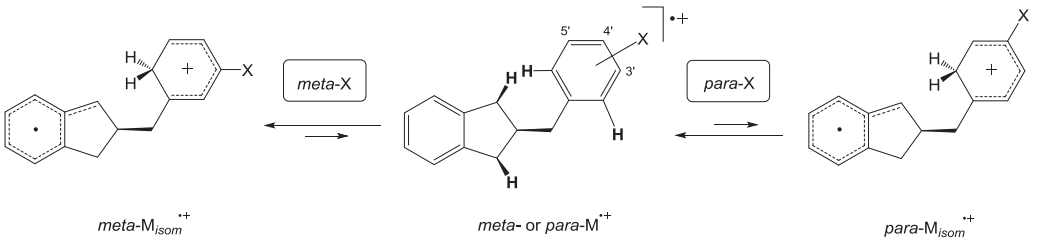


Scheme 1. Major fragmentation reactions of the radical cations of 2-benzylindanes **1**–**3** and preceding intramolecular hydrogen exchange [24]: (a) benzylic cleavage, (b) McLafferty reaction.

the one hand, and the H^{α} and $H^{ortho'}$ atoms, on the other. The hydrogen exchange in ionized 1,3-diphenylpropane, as well as in 2-benzylindane, **1**$^{\bullet+}$, was found to increase with the ions' lifetime and to be complete for metastable ions that decompose after 30–50 μs in the 2nd field-free region of a sector-field mass spectrometer. Model calculations suggested that, in the simpler case of ions **1**$^{\bullet+}$, where only one 4-H exchange operates, more than seven exchange cycles, **1**$^{\bullet+}$ → **1**$_{isom}$$^{\bullet+}$ → **1**$^{\bullet+}$, are necessary to reach the "statistical distribution" ("complete scrambling") [8,10,24], with **1**$_{isom}$$^{\bullet+}$ representing the distonic ion intermediate formed by transfer of a H^{γ} atom [28].

A *meta*-methoxy substituent at the benzylic residue of ionized 2-(3-methoxybenzyl)indane, **2**$^{\bullet+}$, strongly accelerates the γ-H transfer and the 4-H exchange, whereas a *para*-methoxy group in the isomeric 2-(4-methoxybenzyl)indane, **3**$^{\bullet+}$, markedly decreases these processes in all regimes of the molecular ions' lifetime [24]. The strongly varying extent of the 4-H exchange is attributed to the differences of the unimolecular equilibria between the original molecular ions, M$^{\bullet+}$, and the corresponding distonic intermediates, M$_{isom}$$^{\bullet+}$, the latter representing more or less stabilized σ-complexes containing a remote benzylic radical (Scheme 2) [11,12,24,29]. The relative stability of the isomeric molecular ions **2**$^{\bullet+}$ and **3**$^{\bullet+}$ is mainly determined by the ionization energies of the substituted aromatic moieties and should be similar for both isomers. In contrast, the stabilities of the distonic ions **2**$_{isom}$$^{\bullet+}$ and **3**$_{isom}$$^{\bullet+}$ depend mainly on the site-specific ("local") proton affinity (PA) of the benzylic residues at their *ortho* positions and, thus, on the electronic nature and the position of the substituent X. Notably, a hydrogen ring walk within the "protonated" benzylic residues of the intermediates M$_{isom}$$^{\bullet+}$, which is an ubiquitous feature of arenium ions [8,10,21], does not occur [12,24]. As a consequence, the distonic ion **2**$_{isom}$$^{\bullet+}$ bearing the *meta*-methoxy substituent is significantly more stable than the *para*-isomer **3**$_{isom}$$^{\bullet+}$. In this and the accompanying paper [30], we report on an extension of this model system, including a much larger set of ionized *meta*- and *para*-substituted 2-benzylindanes, **4**$^{\bullet+}$–**12**$^{\bullet+}$ (Scheme 2), and their deuterium-labelled isotopologs. In the present article, we discuss the fragmentation of ions **1**$^{\bullet+}$–**12**$^{\bullet+}$ as a function of the substituents X and the ions' lifetime, using density functional theory calculations to substantiate, in particular, the competition of the McLafferty reaction and the benzylic cleavage (Scheme 1). In the accompanying paper, we report in detail on the effect of the substituents on the relative rate of the reversible hydrogen transfer and, thus, on the extent of H/D scrambling that precedes the McLafferty reaction of ions **1**$^{\bullet+}$–**12**$^{\bullet+}$. It will be shown that the extent of H/D exchange in the corresponding isotopologs also depends markedly on electronic nature and the position of the substituents X in all lifetime regimes. In addition, it will be shown that the electronic nature of the substituents also affects the



Scheme 2. Effects of *meta*- and *para*-substituents X on the equilibrium between the conventional molecular ions, M$^{\bullet+}$, and the corresponding distonic ions, M$_{isom}$$^{\bullet+}$, of 2-benzylindanes studied in the previous (**1**–**3**) [24] and in the present (**4**–**12**) work.

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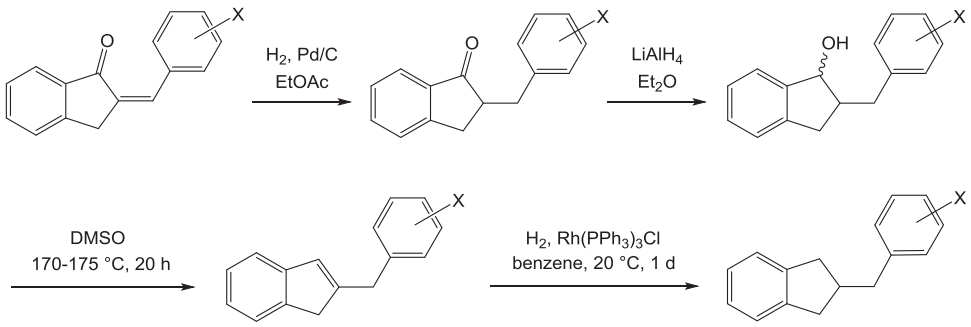

Scheme 3. Synthesis of the unlabelled 2-benzylindane derivatives **4**–**12**.

stereoselectivity of the hydrogen scrambling process. Finally, *ipso*-protonolysis of ions $\mathbf{1}^{\bullet+}$ and most of its *para*-substituted derivatives will be also addressed in view of the preceding hydrogen scrambling [30].

2. Experimental and Computations

2.1. Synthesis of compounds

The synthesis of the unlabelled 2-benzylindanes **4**–**12** was based on the same procedures used for that of the congeners **1**–**3** [24,31]. In brief, 1-indanone was condensed with the appropriate benzaldehydes to give the corresponding 2-benzylidene-1-indanones (Scheme 3). Catalytic hydrogenation to the dihydrochalcones followed by reduction using lithium aluminum hydride furnished the respective substituted 2-benzyl-1-indanols as mixtures of the *cis*- and *trans*-isomers. Conversion of these alcohols to the corresponding 2-benzylindenes was achieved by dehydration in formic acid under reflux [32] or, more reliably, by heating in dimethylsulfoxide at 170 °C [33]. Undesired cyclodehydration of electron-rich benzylindanols can be largely excluded by applying the latter method [34,35]. Hydrogenation of the 2-benzylindenes was performed by use of hydrogen gas in the presence of Wilkinson's catalyst in benzene, a method that proved to be superior to the use of palladium-on-charcoal as a catalyst in dipolar or protic solvents in view of regio- and stereoselective deuteration [24,30,31]. All compounds were purified by recrystallization (solids) or by kugelrohr distillation (oils) and characterized by EI mass spectrometry (70 eV) and ^{1}H NMR spectroscopy (300 MHz, $CDCl_3$).

2.2. Mass spectrometry

The standard 70 eV mass spectra were recorded with a 311 A double-focusing mass spectrometer (Finnigan MAT, Bremen, Germany) at 3.0 kV accelerating voltage. Other than standard mass spectra (70 eV and 11 eV) as well as the mass-analyzed ion kinetic energy (MIKE) spectra were measured with a ZAB-2F double-focusing instruments (Vacuum Generators, Manchester, UK) at 6.0 kV accelerating voltage and 100 μA trap current. The samples were introduced through the solids probe inlet with slight heating of the quartz crucible, in part after absorption on silica gel or, if volatility permitted, via the septum inlet heated to 230 °C. The temperature of the ion source was kept at 200–220 °C. For the measurements carried out at 11 eV, the electron energy was adjusted by correcting the nominal value according to the ionization energy of benzene (9.24 eV [36]), using the semi-log plot technique. The mass spectrometric data presented here are average values obtained from five to eight consecutive runs and most of the measurements were repeated on other days. Particular attention was paid, where necessary, to the significant decrease of the partial pressure of the samples upon evaporation into the ion source.

2.3. Computational methods

Molecular orbital calculations were performed with the Gaussian 03 suite of programs [37]. The geometry of the stationary points was optimized at the unrestricted B3LYP level of the density functional theory (DFT) using the 6-31+G basis set. The transition state geometries that connect the stationary points were optimized at the same level. The calculated structures represent local minima on the reaction energy surface and those of the transition states exhibit only one imaginary frequency as expected for a saddle point. The correctness of the transition states was checked by visualizing the structure using the Gauss View 4.1 [38] program and by activating the vibration exhibiting the imaginary frequency.

Following the optimization of the geometry, single point calculation of the electronic energy E_0 for all species was performed using BHLYP with the 6-311+G(2d,p) basis set. The combination with zero point energy (ZPE) correction and thermochemical corrections to the enthalpy H°_{298} at 298 K, respectively, which were obtained from the harmonic vibrational analysis, afforded standard enthalpy differences shown in the tables and discussed in the text.

For large systems, B3LYP/6-311+G(2d,p)//B3LYP/6-31+G(d) has been recommended as a reasonable compromise between expected accuracy and computational economy [39], and this should carry over to UBHLYP/6-311+G(2d,p)/UBHLYP/6-31+G used here. A special problem for the computational study of the 2-benzylindanes is the presence of a rather large number of conformations of the molecular ions $M^{\bullet+}$ and their isomers $M_{isom}^{\bullet+}$, which differ in energy only by ~10 kJ mol^{-1}; this renders it difficult to localize the global minima on the energy surface of these species in every case. Therefore, the calculations were concentrated to those conformers of $M^{\bullet+}$ and $M_{isom}^{\bullet+}$ that are relevant for the hydrogen transfer between them.

3. Results and discussion

A tremendous amount of knowledge has been gained about the local PA values of aromatics in the recent decades both by experimental [29,36,40–44] and computational studies [45–48]. As a good approximation, the local proton affinities at the benzylic *ortho*-position C-6′, in particular, of the *meta*-isomers **2**, **4**, **6**, **8**, and **10**, that are oriented *para* to the substituent X at C-3′ in each case, should be similar to the experimentally known ("global") proton affinities of the corresponding *meta*-substituted toluenes [36,40]. However, the local proton affinities at the very same benzylic *ortho*-positions of the *para*-isomers **3**, **5**, **7**, **9**, and **11** should be considerably lower and can only be estimated by using increments obtained by computation.[1] Therefore, we performed extensive syn-

[1] *Note*: The local proton affinities of the relevant *ortho*-positions of *meta*-xylene (C-6) and *para*-xylene (C-2), which can be used as simpler models

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thesis and mass spectrometric work on a large set of variously deuterium-labelled isotopologs of the 2-benzylindanes **4**–**12** [30], as an extension of the previous studies on **1**–**3** [24], and combined this with theoretical computations on the unimolecular hydrogen transfer and fragmentation reactions of the parent molecular ions, $\mathbf{1}^{\bullet+}$, and of selected pairs of *meta*- and *para*-substituted analoga, $\mathbf{2}^{\bullet+}/\mathbf{3}^{\bullet+}$, $\mathbf{6}^{\bullet+}/\mathbf{7}^{\bullet+}$ and $\mathbf{10}^{\bullet+}/\mathbf{11}^{\bullet+}$, employing density functional calculations [37–39]. The fragmentation was determined in three different lifetime regimes of the fragmenting molecular ions to gain further information on the effect of the substituents. On this basis, a rather comprehensive picture of the physical and chemical factors that govern the fragmentation of the molecular ions of 2-benzylindanes and the preceding unimolecular hydrogen exchange will be presented in the present and the accompanying paper [30].

3.1. Fragmentation routes and substituent effects on the competing McLafferty reaction and benzyl cleavage

The standard EI mass spectra of the 2-benzylindanes investigated in this work and of those studied previously [24] show molecular ion peaks of medium relative intensities and essentially two sets of fragment ions peaks that reflect the charge-retaining indanyl and benzyl moieties of the original structures (Table 1). The great majority of the molecular ions decompose by cleavage of the exocyclic benzylic C^2-C^α bond, with or without hydrogen rearrangement (Scheme 1). Similar to the fragmentation of 1,3-diphenylpropane under EI conditions [11,12], the McLafferty reaction generating $C_7H_7X^{\bullet+}$ ions (m/z 92 for X = H) by loss of indene and the simple benzyl cleavage generating benzyl ions $C_7H_6X^+$ (m/z 91 for X = H) and the 2-indanyl radical dominate in most cases. These two fragmentation routes will be discussed in detail below. The complementary fragmentation channels, that is, the McLafferty reaction leading to ionized indene, $C_9H_8^{\bullet+}$ (m/z 116) and neutral C_7H_8, as well as the simple cleavage giving 2- (or possibly 1-) indanyl cation(s), $C_9H_9^+$ (m/z 117) and a benzyl radical, occur with lower relative abundance in most cases, with the exception of the *para*-fluoro-substituted ion $\mathbf{7}^{\bullet+}$. These channels have least significance in the mass spectra of the electron-rich derivatives [X = OCH_3, OH and $N(CH_3)_2$] in accordance with a previous report on methoxy-substituted 1,3-diphenylalkanes [11]. Along with ions $C_9H_8^{\bullet+}$ and $C_9H_9^+$, the formation of the indenyl cation, $C_9H_7^+$ (m/z 115), is observed exclusively in the high-energy (70 eV) mass spectra of all 2-benzylindanes and is attributed to the secondary fragmentation process $C_9H_9^+ \rightarrow C_9H_7^+ + H_2$. A fragmentation channel of minor general importance but representing a structure-specific feature is the elimination of benzene or the corresponding arene by γ-H transfer to the *ipso*-position of the benzylic residue, giving rise to ions $C_{10}H_{10}^{\bullet+}$ (m/z 130). Electron-donating substituents in the *para*-position [X = 4′-OCH_3, 4′-CH_3, 4′-F, 4′-OH, but not 4′-$N(CH_3)_2$] enhance this pathway significantly, whereas *meta*-substituents rather suppress it. According to the general understanding outlined above, this fragmentation is attributed to the increased local proton affinity of the *ipso*-position of the benzylic residues [29,44,48] and will be addressed briefly in the last sections of this and the accompanying paper.

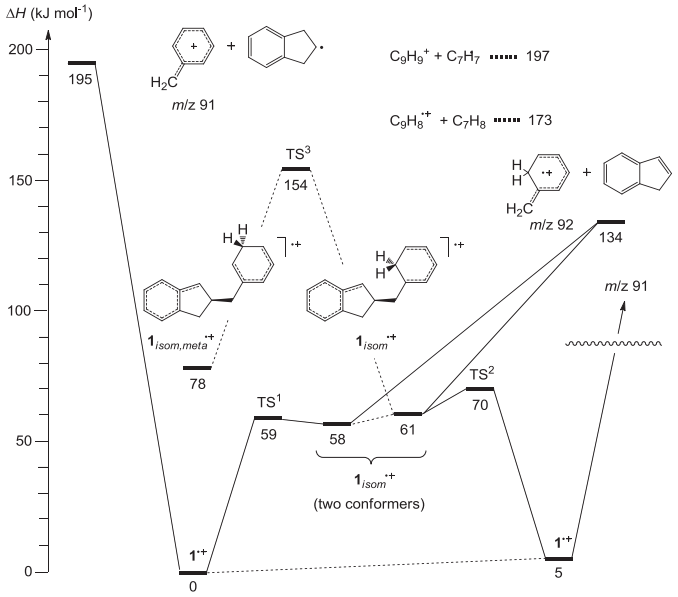

Fig. 1. Enthalpy profile calculated for isomerization and fragmentation of the molecular radical cations of 2-benzylindane, $\mathbf{1}^{\bullet+}$. The McLafferty reaction and the benzylic cleavage leading to ions $C_7H_8^{\bullet+}$ and $C_7H_7^+$, respectively, are displayed explicitly; the complementary fragmentation paths leading to $C_9H_8^{\bullet+}$ and $C_9H_9^+$ are only specified by the dashed energy levels. TS^1 and TS^2 indicate the transition states for the forward and backward H transfer, respectively, and TS^3 indicates the transition state for the (hypothetical) 1,2-H shift in the distonic ion intermediate, $\mathbf{1}_{isom}^{\bullet+}$, generating the "*meta*-tautomer" $\mathbf{1}_{isom,meta}^{\bullet+}$.

The enthalpy profiles for the intramolecular isomerization and the major fragmentation routes of the molecular ions of the parent 2-benzylindane radical cation, $\mathbf{1}^{\bullet+}$, and of a selected set of isomers, $\mathbf{2}^{+\bullet}/\mathbf{3}^{+\bullet}$, $\mathbf{6}^{+\bullet}/\mathbf{7}^{\bullet+}$ and $\mathbf{10}^{+\bullet}/\mathbf{11}^{+\bullet}$, were determined by density-functional calculations (B3LYP/6–31 + g//B3LYP/6–311 + g(3d,2p)). The profile for ions $\mathbf{1}^{\bullet+}$ is shown in Fig. 1. According to the calculations, fragmentation by the McLafferty reaction generating ions $C_7H_8^{\bullet+}$ (m/z 92) requires 134 kJ mol^{-1}, whereas the benzylic cleavage is much more energy-demanding (195 kJ mol^{-1}). This is in agreement with the dominance of m/z 92 peak in the 70 eV mass spectrum of **1** [24] and the general knowledge on the energetics of the fragmentation of the molecular ions of alkylbenzenes and 1,3-diphenylpropanes [6,11,36,49]. It is also in line with the fact that metastable ions $\mathbf{1}^{\bullet+}$ undergo predominantly fragmentation by the McLafferty reaction, besides the formation of $C_9H_9^+$ and $C_9H_8^{\bullet+}$, but no benzylic cleavage (Table 2). The complementary McLafferty-reaction channel, leading to ionized indene, $C_8H_8^{\bullet+}$, and (putatively) neutral isotoluene, is more energy-demanding (173 kJ mol^{-1}) but, notably, the complementary cleavage to the indanyl ion, $C_9H_9^+$, and the benzyl radical is about as endothermic (197 kJ mol^{-1}) as the formation of benzyl cation and the indanyl radical mentioned above. The finding that metastable ions $\mathbf{1}^{\bullet+}$ do not form $C_7H_7^+$ (m/z 91) but do form abundant ions $C_9H_9^+$ (m/z 117) suggests that the latter ions do not have the 2-indanyl but rather the undoubtedly more stable 1-indanyl structure. Moreover, the occurrence of ions $C_9H_8^{\bullet+}$ (m/z 116) in the metastable ion spectra points to the possibility that the C_7H_8 neutral eliminated upon the formation of these fragment ions is not the isotoluene tautomer [36,50–52] but the considerably more stable toluene.[2]

for the 2-benzylindanes studied here, are known to differ by $\Delta PA = PA^{C-6}$(*m*-Xyl) – PA^{C-2}(*p*-Xyl) = 18 kJ mol^{-1}, which in this special case corresponds to the global *PA* values [41,48]. However, the corresponding difference of the *meta*- and *para*-methylanisoles was calculated to be $\Delta PA = PA^{C-4}$(3-Me-Ani) – PA^{C-3}(4-Me-Ani) ≈ 70 kJ mol^{-1} [44] and that of the *meta*- and *para*-fluorotoluenes was calculated to be $\Delta PA = PA^{C-6}$(3-F-Tol) – PA^{C-2}(4-F-Tol) = 36.8 kJ mol^{-1} [45]. For the *meta*- and *para*-cresoles, $\Delta PA = PA^{C-4}$(3-Cre) – PA^{C-3}(4-Cre) = 66.2 (±8) kJ mol^{-1} [44] was determined by computational approach. While the global protons affinities of the *meta*- and *para*-*N*,*N*-dimethyltoluidines are known by experiment [36,40,42], local *PA* values are not for either of the isomers, to the best of our knowledge.

[2] *Note*: According to calculations, the dissociation of molecular ion $\mathbf{1}^{\bullet+}$ into the indene radical cation and neutral toluene needs a reaction enthalpy of only 29.1 kJ mol^{-1} and is the thermodynamically most favorable process. However, this reaction requires the transfer of a hydrogen from the indanyl fragment to the benzyl fragment during the benzylic cleavage either "on the fly" of the departing benzyl

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Table 1
EI mass spectra (70 eV) of 2-benzylindane (**1**) and derivatives **2** – **12**[a].

Ion/comp'd	**1**[b]		**2** (3′-OMe)[b]		**3**(4′-OMe)[b]		**4** (3′-Me)		**5** (4′-Me)	
	m/z	rel. int. (%)	*m/z*	rel. int. (%)			*m/z*	rel. int. (%)		
$M^{\bullet+}$	208	32.7	238	10.3		26.6	222	29.7		36.4
$C_{10}H_{10}^{\bullet+}$[c]	130	1.5	130	<0.2		10.8	130	1.6		5.9
$C_9H_9^+$[a]	117	52.4	117	3.3		7.0	117	18.7		44.1
$C_9H_8^{\bullet+}$[a]	116	35.0	116	5.7		6.8	116	11.0		20.3
$C_9H_7^+$	115	48.6	115	13.1		12.1	115	22.0		28.3
$C_7H_7X^{\bullet+}$[a]	92	100.0	122	100.0		39.7	106	100.0		100.0
$C_7H_6X^+$	91	53.4	121	8.5		100.0	105	11.0		26.3
$C_7H_7^+$[d]	91		91	15.4		9.8	91	36.3		24.6

Ion/comp'd	**6**[e] (3′-F)		**7**[e] (4′-F)		**8** (3′-OH)		**9** (4′-OH)		**10**[f] (3′-NMe_2)		**11** (4′-NMe_2)		**12** [3′,5′-$(OMe)_2$]	
	m/z	rel. int. (%)		*m/z*	rel. int. (%)			*m/z*	rel. int. (%)			*m/z*	rel. int. (%)	
$M^{\bullet+}$	226	30.3	46.0	224	28.2		60.2	251	24.0		19.3	268	5.3	
$C_{10}H_{10}^{\bullet+}$[c]	130	1.3	8.5	130	0.4		31.7	130	3.0		1.2	130	0.1	
$C_9H_9^+$[a]	117	41.8	100.0	117	10.8		46.6	117	3.1		1.3	117	1.9	
$C_9H_8^{\bullet+}$[a]	116	43.4	80.6	116	9.4		26.3	116	3.7		1.7	116	3.6	
$C_9H_7^+$	115	47.8	68.5	115	13.4		5.9	115	8.2		3.7	115	6.7	
$C_7H_7X^{\bullet+}$[a]	110	100.0	51.3	108	100.0		67.8	135	100.0		17.1	152	100.0	
$C_7H_6X^+$	109	30.6	66.1	107	11.0		100.0	134	8.2		100.0	151	2.9	
$C_7H_7^+$[d]	91	20.4	20.8	91	6.7		3.1	91	12.7		4.0	91	7.2	

[a] Intensities of adjacent peaks are not corrected for isotope contributions.
[b] Data taken from Ref. [24].
[c] Ions $[M - C_6H_5X]^{\bullet+}$ formed by H transfer to *ipso*-position (C-1′).
[d] Ions $C_7H_7^+$ originating from the indanyl moiety.
[e] Additional characteristic fragment ions: $C_6H_5F^{\bullet+}$ (*m/z* 96) for **6** (3.1%) and **7** (4.8%).
[f] Besides the peak at *m/z* 135, a peak at *m/z* 136 (26.1%) was observed.

Table 2
Relative abundances of the fragment ions $C_7H_7^+$ and $C_7H_8^{\bullet+}$ and their substituted derivatives formed from 2-benzylindanes **1**–**12** in three energy regimes.[a,b,c]

Ions	m/z	70 eV	11 eV	m*	70 eV	11 eV	m*
$M^{\bullet+}$(X = H)	208		**1**$^{\bullet+}$				
$C_7H_7^+$	91	29.3	1.2	(<0.3)			
$C_7H_8^{\bullet+}$	92	70.7	98.8	100.0			
$M^{\bullet+}$(X = OMe)	238		**2**$^{\bullet+}$(*X meta*)			**3**$^{\bullet+}$(*X para*)	
$C_8H_9O^+$	121	7.9	0.3	0.0	80.7	51.1	33.9
$C_8H_{10}O^{\bullet+}$	122	92.1	99.7	100.0	19.3	48.9	66.1
$M^{\bullet+}$(X = Me)	222		**4**$^{\bullet+}$(*X meta*)			**5**$^{\bullet+}$(*X* = para)	
$C_8H_9^+$	105	9.9	0.3	0.0	28	1.5	0.0
$C_8H_{10}^{\bullet+}$	106	90.1	99.7	100.0	72	98.5	100
$M^{\bullet+}$(X = F)	226		**6**$^{\bullet+}$(*X meta*)			**7**$^{\bullet+}$(*X para*)	
$C_7H_6F^+$	109	23	0.6	0.0	59.3	4.2	2.6
$C_7H_7F^{\bullet+}$	110	77	99.4	100.0	40.7	95.8	97.4
$M^{\bullet+}$(X = OH)	224		**8**$^{\bullet+}$(*X meta*)			**9**$^{\bullet+}$(*X para*)	
$C_7H_7O^+$	107	15.4	0.1	0.0	71.9	28.7	8.3
$C_7H_8O^{\bullet+}$	108	84.6	99.9	100.0	28.1	71.3	91.7
$M^{\bullet+}$(X = NMe_2)	251		**10**$^{\bullet+}$(*X meta*)			**11**$^{\bullet+}$(*X para*)	
	133	4.5			2.0		0.0
$C_9H_{12}N^+$	134	17.4	1.1	0.0	84.8	90.5	100.0
$C_9H_{13}N^{\bullet+}$	135	75.1	94.5	100.0	12.4	7.5	
	136	2.9	4.4		0.8	2.0	
$M^{\bullet+}$[X = 3′,5′-$(OMe)_2$]	268		**12**$^{\bullet+}$				
$C_9H_{11}O_2^+$	151	4.3	(≤0.2)	0.0			
$C_9H_{12}O_2^{\bullet+}$	152	95.7	100.0	100.0			

[a] Given as%Σ; corrected for natural contributions of $^{13}C_1$- and $^{13}C_2$-containing isotopologs.
[b] Data for compounds **1**–**3** taken from reference [24]. They slightly deviate from the corresponding data given in Table 1 due to different instrument parameters.
[c] m*: Metastable ion data originate from mass-analyzed ion kinetic energy (MIKE) spectra obtained at 70 eV.

The intramolecular 1,5-hydrogen transfer from C-1^{cis} or C-3^{cis} to one of the *ortho*-positions of the benzyl residue can start from two distinct conformers of ions **1**$^{\bullet+}$ (Fig. 2). They differ only by 5 kJ mol^{-1} and the 1,5-H transfer leads to two likewise distinct conformers of the distonic ion **1**$_{isom}^{\bullet+}$, which themselves differ by 3 kJ mol^{-1} with the same relative tendency. Interestingly, the energies of the two respective transition states for the forward and backward H transfer differ more strongly, namely by 11 kJ mol^{-1}. In view of the relative low energy barrier of the hydrogen exchange in ions **1**$^{\bullet+}$ as compared to the calculated reaction enthalpy of the McLafferty reaction ($\Delta_r H$ = 64 kJ mol^{-1}), the extent of the H/D exchange observed experimentally for the deuterated isotopologs of ions **1**$^{\bullet+}$

fragment or in an ion-neutral complex of both fragments. It was not possible to detect any of these fragmentation routes by the computational methods used.

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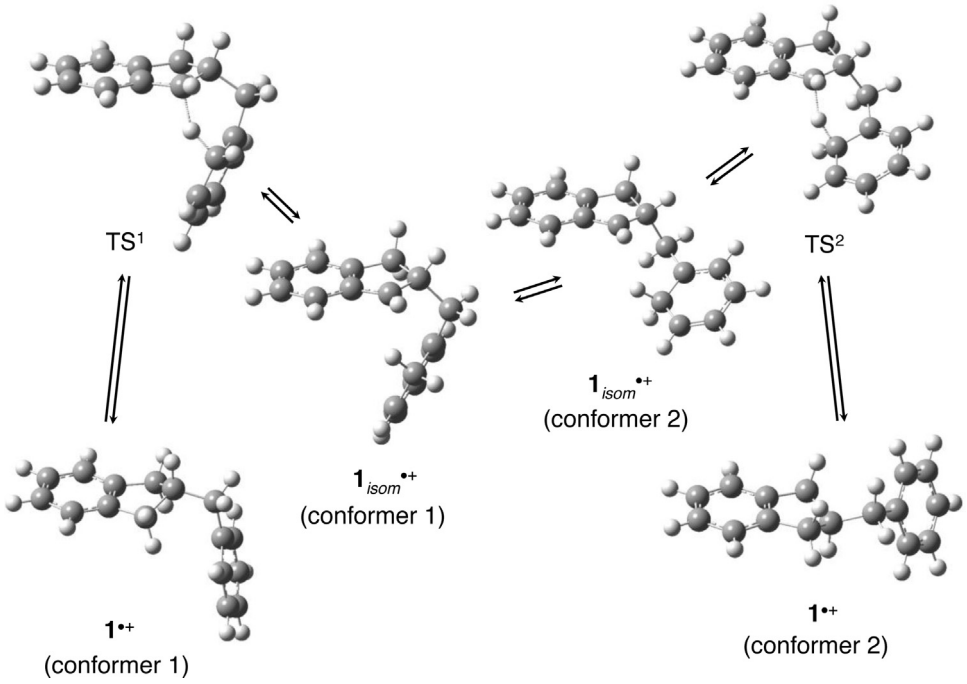

Fig. 2. Calculated structures of the molecular ions of 2-benzylidane, $\mathbf{1}^{\bullet+}$, the distonic ions, $\mathbf{1}_{isom}^{\bullet+}$, and the transition states of the respective forward and backward H transfer, TS^1 and TS^2 (cf. Fig. 1). The full sequence $\mathbf{1}^{\bullet+}$ (conformer 1) → $\mathbf{1}^{\bullet+}$ (conformer 2) constitutes one hydrogen exchange cycle (see text). Note that conformer 1, being more stable than conformer 2 in the case of ions $\mathbf{1}^{\bullet+}$, is the less stable form in some of the substituted molecular ions.

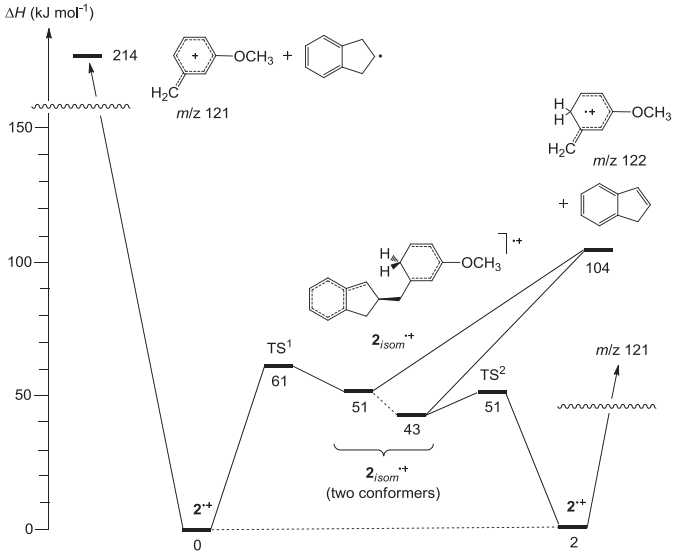

Fig. 3. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(3-methoxybenzyl)indane, $\mathbf{2}^{\bullet+}$, by McLafferty reaction and benzylic cleavage.

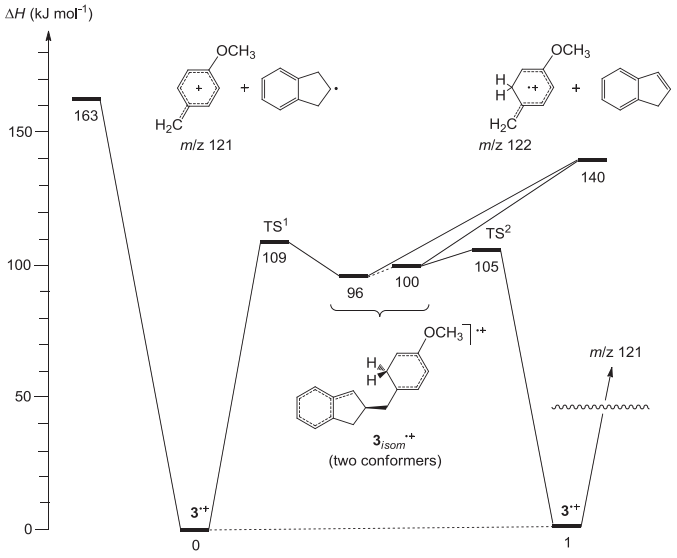

Fig. 4. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(4-methoxybenzyl)indane, $\mathbf{3}^{\bullet+}$, by McLafferty reaction and benzylic cleavage.

[24,30] and its completeness in the metastable ions' energy regime is in accordance with the enthalpy profile of ions $\mathbf{1}^{\bullet+}$. We also calculated the energy requirements for the hypothetical 1,2-H shift in the distonic ion intermediate $\mathbf{1}_{isom}^{\bullet+}$. Notably, such a process has never been observed in either the molecular radical cations of simple alkylbenzenes [4,6] or 1,3-diphenylpropane [12] and it does also not occur in any of the 2-benzylindane ions $\mathbf{1}^{\bullet+}$ – $\mathbf{12}^{\bullet+}$ studied in the present work [30] and previously [24]. As also shown in Fig. 1, the barrier for a 1,2-H shift in the "*ortho*-protonated" ion $\mathbf{1}_{isom}^{\bullet+}$ leading to the "*meta*-tautomer", $\mathbf{1}_{isom,meta}^{\bullet+}$ was calculated to be exceedingly high, 93 – 96 kJ mol^{-1} above the level of the conformers of distonic ion intermediate $\mathbf{1}_{isom}^{\bullet+}$. This barrier is clearly much higher than that toward the 1,2-proton shift in simple ring-protonated arenes (arenium ions, 32 – 40 kJ mol^{-1}) [8,10,21,53,54] and probably reflects the radical character of the molecular ions of 2-benzylindane, **1**, and its derivatives **2**–**12**.

Different from the hydrogen exchange occurring in the radical cations of open-chain alkylbenzenes and α,ω-diphenylalkanes, a complete 4-H exchange cycle in 2-benzylindane ions comprises two sets of different conformations both for the molecular ions $\mathbf{1}^{\bullet+}$ and their distonic ions, $\mathbf{1}_{isom}^{\bullet+}$. Therefore, the transitions states for the forward and the backward hydrogen transfer steps, TS^1 and TS^2, are also different (Figs. 1 and 2). In the case of the parent hydrocarbon, the enthalpies of these transitions states were

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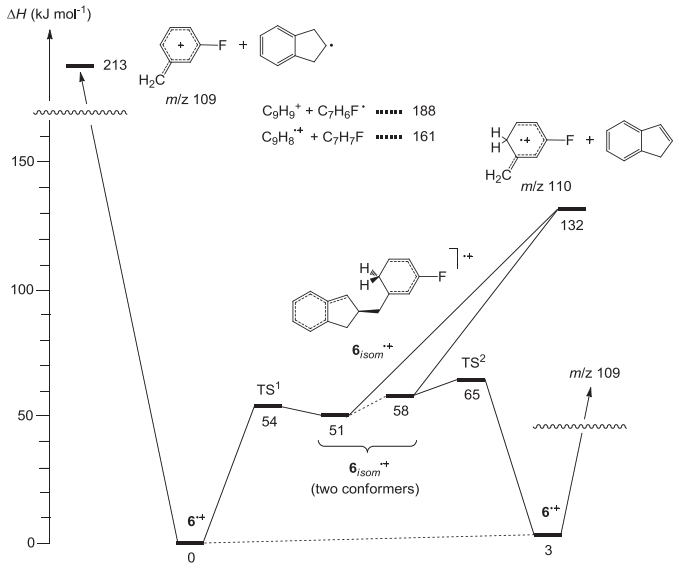

Fig. 5. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(3-fluorobenzyl)indane, **6**•+, by McLafferty reaction and benzylic cleavage.

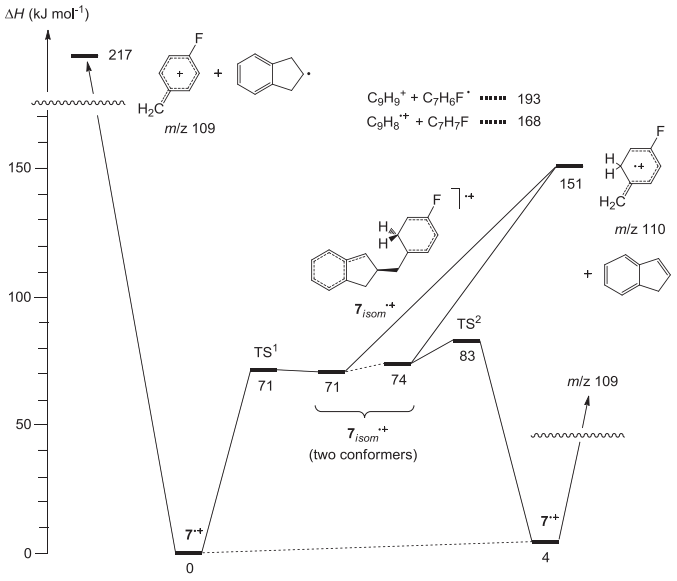

Fig. 6. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(4-fluorobenzyl)indane, **7**•+, by McLafferty reaction and benzylic cleavage.

calculated to lie both well below the final step for the McLafferty reaction. Therefore, the finding that the 2-benzylindane ions **1**•+ undergo a complete 4-H exchange prior to the fragmentation to $C_7H_8^{\bullet+}$ is in accordance with the enthalpy profile obtained by computation [24]. The structures of the starting and final conformations of the molecular ions **1**•+, the distonic ions $\mathbf{1}_{isom}^{\bullet+}$ and the transition states TS^1 and TS^2 are visualized in Fig. 2. Similar calculations have been performed for the pairs of methoxy-, fluoro- and dimethylamino-substituted molecular ions **2**•+/**3**•+, **6**•+/**7**•+ and **10**•+/**11**•+, respectively. The relative stabilities of the conformers within a given pair of isomers were found to depend on the substituent. In the following discussion, the most stable conformer is defined as the starting conformer from which the forward H transfer takes place, notwithstanding its individual geometry.

The energy profiles calculated for the methoxy-substituted derivatives **2**•+ and **3**•+ are depicted in Figs. 3 and 4, respectively. As compared to the parent ions **1**•+, the benzylic cleavage is more energy-demanding for the *meta*-isomer **2**•+ ($\Delta E = +19$ kJ mol^{-1}) and markedly less energy-demanding for the *para*-isomer **3**•+ ($\Delta E = -32$ kJ mol^{-1}). The reverse is found for the McLafferty reaction, which requires considerably less energy in the case of **2**•+ ($\Delta E = -30$ kJ mol^{-1}) but slightly more for **3**•+ ($\Delta E = +6$ kJ mol^{-1}). In agreement with the relevant local proton affinity differences of *meta*- and *para*-methylanisole discussed above, the stabilities of the distonic ions $\mathbf{2}_{isom}^{\bullet+}$ and $\mathbf{3}_{isom}^{\bullet+}$ differ strongly ($\Delta E = 51 \pm 2$ kJ mol^{-1}) in favor of the former isomer. As argued previously, the stability of the σ-complexes formed by the hydrogen transfer step is a key factor of the McLafferty reaction of the *meta*-methoxy-substituted alkylbenzenes under EI conditions [11,55,56]. Accordingly, the transitions states TS^1 and TS^2 lie much lower in energy for the *meta*-isomer as compared to the *para*-isomer. Thus, based on the calculations, it appears that the McLafferty reaction of the *meta*-methoxy-substituted ions **2**•+ samples significantly less excited ions. In addition, the energy barriers toward the hydrogen transfer in the distonic ions $\mathbf{2}_{isom}^{\bullet+}$ lie significantly deeper ($\Delta E \geq 43$ kJ mol^{-1}) with respect to the energy required for the C—C bond cleavage, as compared to the case of the distonic ions $\mathbf{3}_{isom}^{\bullet+}$ ($\Delta E \geq 31$ kJ mol^{-1}). In total, the calculated enthalpy profiles for the methoxy-substituted ions **2**•+ and **3**•+ are in good agreement with the observed fragmentation and the marked differences between the two isomers. They also rationalize the previously reported finding [24] that the 4-H exchange in the *para*-isomer **3**•+ is much slower than in the *meta*-isomer **2**•+ (see accompanying paper [30]).

The presence of a methyl group in the *meta*- or *para*-position of the benzyl residues of the molecular ions **4**•+ and **5**•+, respectively, has only a moderate effect on the competition of the fragmentation channels. A significant relative acceleration of the McLafferty reaction leading to ion $C_7H_7CH_3^{\bullet+}$ (*m*/*z* 106) is found for the *meta*-isomer, **4**•+. The direct benzylic cleavage of **4**•+, giving rise to ion $C_7H_6CH_3^+$ (*m*/*z* 105), is decreased to some extent. The relative increase of the ions $C_{10}H_{10}^{\bullet+}$ (*m*/*z* 130) formed by loss of toluene from **5**•+ through *ipso*-protonation is remarkable (see below). Calculations were not performed because of the minor substituent effect of the methyl substitutents on the fragmentation of ions **4**•+ and **5**•+.

The mass spectra of the two isomeric fluorobenzylindanes **6** and **7** also reflect the positional effect of the fluoro substituents. The McLafferty reaction leading to ions $C_7H_7F^{\bullet+}$ (*m*/*z* 110) dominates the fragmentation of the *meta*-substituted molecular ions **6**•+ to about the same extent as in the case of the parent ions **1**•+. In contrast, the *para*-fluoro substituent in the molecular ions **7**•+ gives rise to a decrease of both the McLafferty reaction and the simple benzylic cleavage to ions $C_7H_6F^+$ (*m*/*z* 109) in favor of the formation of fragment ions that originate from the indanyl moiety. Formation of the indanyl cation $C_9H_9^+$ (*m*/*z* 117) gives rise to the base peak in this case. The arene elimination giving ions $C_{10}H_{10}^{\bullet+}$ (*m*/*z* 130) by *ipso*-protonation is triggered by the *para*-fluoro substituent of **7**•+ (see below). Thus, both the characteristic inductive (electron-withdrawing) and mesomeric (electron-releasing) substituent effects of the fluoro substituent are reflected by the fragmentation of both isomers **6**•+ and **7**•+.

The energy profiles calculated for the 2-(fluorobenzyl)indanes **6**•+ and **7**•+ are shown in Figs. 5 and 6, respectively. In line with observation, the energy demand for the benzylic cleavage is increased in both cases by the presence of the fluoro substitutents as compared to the parent ions **1**•+. In contrast, the McLafferty reaction of the *meta*-isomer **6**•+ is scarcely affected in comparison to ions **1**•+ ($\Delta E = -2$ kJ mol^{-1}), whereas it requires considerable more energy in the *para*-isomer **7**•+ ($\Delta E = +17$ kJ mol^{-1}). This parallels the trend found for the methoxy analogs **2**•+ and **3**•+ discussed above. The energies of the transition states TS^1 and TS^2 and the distonic ions $\mathbf{6}_{isom}^{\bullet+}$ and $\mathbf{7}_{isom}^{\bullet+}$ are markedly lower than the ener-

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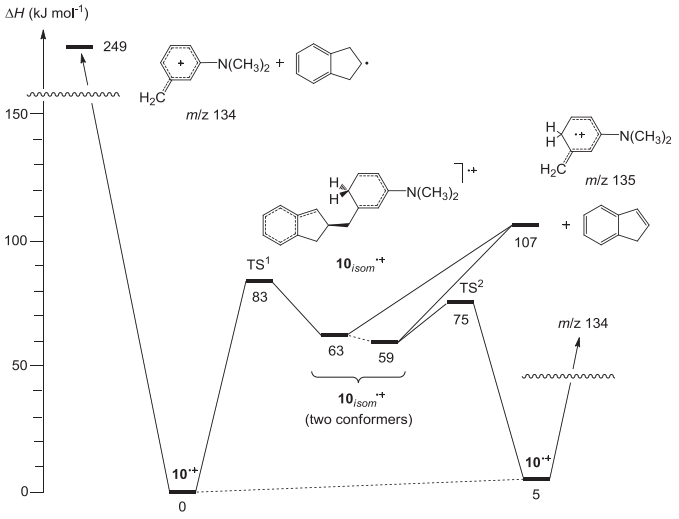

Fig. 7. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(3-*N*,*N*-dimethylaminobenzyl)indane, **10**•+, by McLafferty reaction and benzylic cleavage.

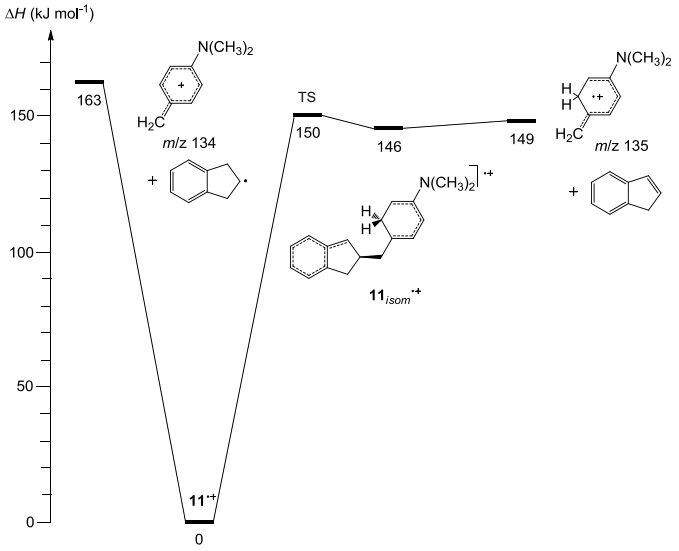

Fig. 8. Enthalpy profile calculated for the isomerization and fragmentation of the molecular radical cations of 2-(4-*N*,*N*-dimethylaminobenzyl)indane, **11**•+, by McLafferty reaction and benzylic cleavage.

gies required for C—C bond cleavage of the intermediates but the differences are very similar ($\Delta_r H = 67 - 80$ kJ mol^{-1}) in both cases. The marked stabilization of ions $\mathbf{6}_{isom}^{\bullet+}$ as compared to ions $\mathbf{7}_{isom}^{\bullet+}$ ($\Delta E = 16 - 20$ kJ mol^{-1}) is in agreement with the local proton affinity difference of *meta*- and *para*-fluorotoluene mentioned above. While the calculations are only in moderate agreement with the observed differences in the 70 eV mass spectra of **6** and **7**, they clearly show that the γ-H transfer generating the distonic ions and the overall McLafferty reaction is the energetically preferred reaction channel for the *meta*-isomer.

The fragmentation behavior of the two isomeric 2-(hydroxybenzyl)indanes **8** and **9** is similar to that of the methoxy analogs **2** and **3**. The McLafferty reaction strongly dominates the mass spectrum of the *meta*-isomer **8**, giving rise to ions $C_7H_7OH^{\bullet+}$ (*m*/*z* 108), whereas the simple benzylic cleavage leading to ions $C_7H_6OH^{\bullet+}$ (*m*/*z* 107) generates the base peak in the spectrum of the *para*-isomer **9**. Again, the *para*-hydroxy group in the molecular ions **8**•+ exerts a particular strong accelerating effect on the *ipso*-protonation channel, giving rise to ions $C_{10}H_{10}^{\bullet+}$ (*m*/*z* 130) whereas, once again, this process is practically absent in the case of the *meta*-isomer (see below). Because of the similarity of the fragmentation of the respective hydroxy- and methoxy-substituted 2-benzylindanes ions, calculations were not performed for the phenolic derivatives.

The fragmentation of the *N*,*N*-dimethylamino-substituted 2-benzylindanes **10** and **11**, as well as that of the doubly *meta*-methoxy-substituted congener **12**, also fit into the overall picture. However, the electronic effects are even more pronounced in all of these cases. The McLafferty reaction, giving rise to ions $C_7H_7N(CH_3)_2^{\bullet+}$ (*m*/*z* 135) and $C_7H_6(OCH_3)_2^{\bullet+}$ (*m*/*z* 152), respectively, governs the fragmentation of the molecular ions **10**•+ and **12**•+, whereas the benzylic cleavage, leading to the particularly stable *para*-dimethylaminobenzyl cations, $CH_2C_6H_4N(CH_3)_2^+$ (*m*/*z* 134), strongly dominates the fragmentation of ions **11**•+. Nevertheless, the particularly high electron-releasing character of the dimethylamino group does not completely suppress the McLafferty reaction in the latter case.

The energy profiles for the fragmentation of the dimethylamino derivatives **10**•+ and **11**•+ (Fig. 7 and 8, respectively) are in line with the experimental findings. The enthalpy requirements for the benzylic cleavage reactions differ strongly ($\Delta\Delta_r H = 86$ kJ mol^{-1}) in favor of the facile formation of the highly stabilized *para*-dimethylaminobenzyl cations (*m*/*z* 134) from the *para*-isomer, **11**•+. In contrast, the McLafferty reaction, giving dimethylamino-substituted 5-methylenecyclohexa-1,3-diene ions (*m*/*z* 135), is particularly thermodynamically favorable in the case of the *meta*-isomer **10**•+. This channel requires significantly less energy as compared to that of the corresponding channel in parent ions **1**•+ ($\Delta\Delta_r H = -27$ kJ mol^{-1}). In contrast, the McLafferty reaction of the isomeric *para*-substituted ions **11**•+ is calculated to be slightly more endothermic as compared to ions **1**•+ ($\Delta\Delta_r H = +15$ kJ mol^{-1}). Obviously, the strongly stabilizing effect of the dimethylamino group is much more efficient if this substituent is placed at the C-3 position of ionized 5-methylenecyclohexa-1,3-diene than at C-2. Thus, ions 3-$(CH_3)_2NC_6H_5CH_2^{\bullet+}$ (*m*/*z* 135) from **10**•+ were calculated to be by 42 kJ mol^{-1} more stable than the isomeric ions 2-$(CH_3)_2NC_6H_5CH_2^{\bullet+}$ from **11**•+. This difference exceeds that determined for the isomeric methoxy-substituted analogs, 3-$CH_3OC_6H_5CH_2^{\bullet+}$ (*m*/*z* 122, from **2**•+) and 2-$CH_3OC_6H_5CH_2^{\bullet+}$ (from **3**•+) discussed above (36 kJ mol^{-1}). Most interestingly, however, is the finding that the transition states TS^1 and TS^2 calculated for the γ-H transfer in the *meta*-isomer **10**•+ lie surprisingly high at 75–83 kJ mol^{-1} and only 24–32 kJ mol^{-1} below the threshold – much higher than those calculated for corresponding *meta*-methoxy analog **3**•+ (43–53 kJ below the threshold, cf. Fig. 3). This difference also nicely explains the diverging experimental observations made on the 4-H exchange in ions **10**•+ and **3**•+ [30].

Finally, the energy profile calculated for the *para*-dimethylamino-substituted ions **11**•+ is worth being commented (Fig. 8). It rationalizes the observation that the simple benzylic cleavage leading to ions 4-$(CH_3)_2NC_6H_4CH_2^+$ (*m*/*z* 134) is the only fragmentation channel of the metastable ions **11**•+. The transition state for the McLafferty reaction lies only 13 kJ mol^{-1} below the enthalpy required for the direct benzylic cleavage and at about the same level as the exit for the C—C bond cleavage of the distonic ions $\mathbf{11}_{isom}^{\bullet+}$. Moreover, this enthalpy profile is also in line with the finding that the *para*-dimethylaminobenzyl ions formed by fragmentation of the appropriate deuterium-labelled isotopologs do not give any indication for a preceding intramolecular hydrogen exchange [30].

3.2. Arene elimination via ipso-protonolysis

As mentioned above on several occasions, loss of benzene from the molecular ions of the parent hydrocarbon, **1**•+, and of the

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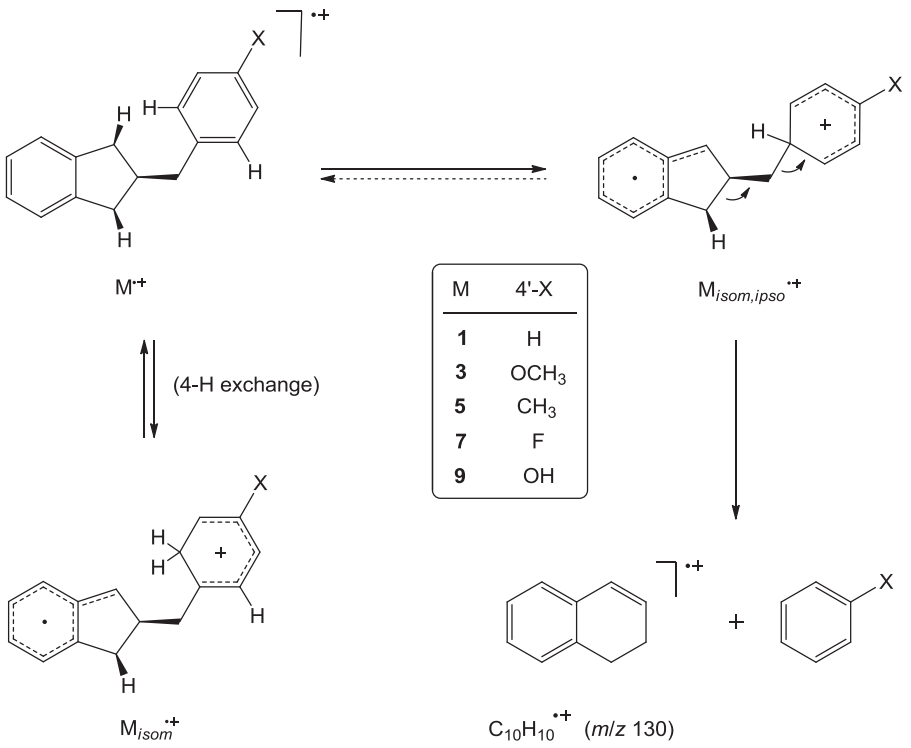

Scheme 4. Elimination of C_6H_5X by *ipso*-protonolysis of ions **1**$^{\bullet+}$ and the *para*-substituted derivatives **3**$^{\bullet+}$, **5**$^{\bullet+}$, **7**$^{\bullet+}$ and **9**$^{\bullet+}$, after incomplete 4-H exchange. The structure suggested for ions $C_{10}H_{10}^{\bullet+}$ (*m*/*z* 130) and the insinuated 1,2-C shift are hypothetical.

corresponding arenes from the molecular ions of several *para*-substituted 2-benzylindanes, **3**$^{\bullet+}$ (X = OCH_3), **5**$^{\bullet+}$ (X = CH_3), **7**$^{\bullet+}$ (X = F) and **9**$^{\bullet+}$ (X = OH) occurs as an additional fragmentation path in most cases. However, this *ipso*-protonolysis, a common fragmentation channel of protonated arenes [8,21,29], gives rise to a negligibly small peak in the mass spectrum of the *para*-dimethylamino-substituted congener **11** and only very minor peaks in the mass spectra of all *meta*-substituted 2-benzylindanes (Table 1). These trends are even more pronounced in the MIKE spectra: The $[M - C_6H_5X]^{\bullet+}$ ions ($C_{10}H_{10}^{\bullet+}$, *m*/*z* 130) are formed in varying relative abundances, but it is telling to note that they represent the dominant peak in the MIKE spectrum of the *para*-fluoro-substituted ions, **7**$^{\bullet+}$, whereas they are absent in the spectrum of the *para*-dimethylamino congener, **11**$^{\bullet+}$. Again, this points to the role of the charge distribution and the character of this hydrogen rearrangement route as a proton transfer rather than a hydrogen atom transfer path. Except for the case of ions **11**$^{\bullet+}$, it is obvious that the local proton affinity at the *ipso*-position of the benzyl residues in ions **3**$^{\bullet+}$, **5**$^{\bullet+}$, **7**$^{\bullet+}$ and **9**$^{\bullet+}$ plays an important role in this process, representing the *para*-position relative to the respective electron-releasing substituent. As mentioned above, the local proton affinities for many aromatic compounds are known by computational work and can be estimated employing the additivity rule [41,44–48]. Also, *ipso*-protonation has been discussed as a fragmentation route that can compete with the McLafferty reaction of suitably substituted alkylbenzenes, if steric and/or electronic conditions are unfavorable for the latter reaction [57]. A mechanism for the loss of arenes from the molecular ions is suggested in Scheme 4.

The *ipso*-protonolysis channel provides further, but less general, insight into the same hydrogen exchange processes that occur prior to the McLafferty reaction of the molecular ions of the 2-benzylindanes, as will be shown in the accompanying paper [30]. In a more general view, this may be expecially relevant for understanding the fragmentation of *para*-hydroxy- (and *para*-alkoxy)-substituted alkylbenzene derivatives under EI conditions [58].

4. Conclusion

The experimentally observed substituent effects on the fragmentation of the radical cations of various substituted 2-benzylindanes, as probed for three different energy and ion-lifetime regimes, have been rationalized by means of theoretical calculations of the corresponding enthalpy profiles. The energy requirements for the McLafferty reaction and the benzylic cleavage depend strongly on the position and the electronic nature of the substituent in each case, and the dominance of the McLafferty reaction for the *meta*-substituted isomers agrees with the energetically favorable formation of the distonic ion intermediates formed by the γ-hydrogen transfer step. As will be shown in the accompanying paper [30], the extent of progression of the 4-H exchange process in the various molecular ions also agrees qualitatively with the depth of the "isomerization valley" relative to the fragmentation threshold.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.ijms.2016.05.021.

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