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Unidirectional Triple and Double Hydrogen Rearrangement Reactions in the Radical Cations of γ-Arylalkanols

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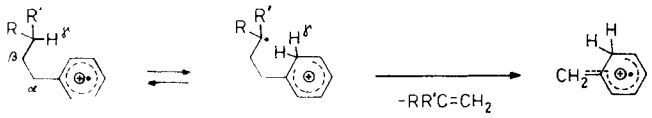
A novel fragmentation reaction accompanied by the unidirectional migration of three hydrogen atoms has been found in the radical cations of γ-arylpropanols with electron-donating substituents in the *para* position. This triple hydrogen (3H) rearrangement reaction is the dominant fragmentation channel of the long-lived molecular ions of *trans*-2-(4′-dimethylaminobenzyl)-1-indanol, 2, but it occurs also in simpler γ-arylpropanol ions. Deuterium labelling of 2 reveals that the three hydrogen atoms originate with extraordinarily high specificity from the C(1), C(2) and O positions of the alcohol moiety. *Cis*- and 3′-substituted isomers do not undergo this reaction. Along with the 3H rearrangement reaction a unidirectional double hydrogen (2H) rearrangement reaction takes place independently and with less specificity in the *trans*-2-(4′-X-benzyl)-1-indanol ions $1^{+\cdot}$ and $2^{+\cdot}$. No hydrogen exchange occurs during the 3H and 2H rearrangement reactions. Mechanistic alternatives of these unusual fragmentation reactions are discussed; the experimental evidence strongly favours pathways via several intermediate ion–neutral complexes.

INTRODUCTION

Fragmentation reactions involving an intramolecular transfer of a hydrogen atom in a six-membered cyclic transition state are very common in organic mass spectrometry.[2] In the case of higher alkyl benzenes, for example, the reversible rearrangement of a γ-hydrogen atom to the ionized aromatic nucleus followed by cleavage of the C(α)—C(β) bond has been investigated in a number of laboratories (Scheme 1).[3–6] We have studied this *single hydrogen* (1H) rearrangement reaction in detail for 1,ω-diphenylalkanes ($\omega = 3$[5a] and $4 \leqslant \omega \leqslant 22$[5b]) and for 2-benzylindans;[5c] it has been found to govern also, in a stereospecific way, the fragmentation of 2-benzyl-1-indanols.[7]



Scheme 1

Hydrogen rearrangement reactions involving other than six-membered cyclic transition states and/or the migration of more than one hydrogen atom from one part of the ion to another ('unidirectional' H rearrangements) are less common.[8] Among the examples known, long-range hydrogen rearrangements have been reported for long-chain benzoic acids and related compounds[2,9–11] as well as for difunctionalized steroids.[12] Unidirectional double hydrogen (2H) rearrangement reactions are characteristic features in the mass spectra of many aliphatic and aromatic esters,[9–11] and higher alkyl vinyl ethers,[2,13a] whereas unidirectional triple hydrogen (3H) rearrangement reactions are extremely rare.[2,9,13,14]

We have found that both triple and double hydrogen rearrangement reactions take place in the radical cations of γ-arylalkanols, e.g. *trans*-2-(4-methoxybenzyl)-1-indanol, **1** (Scheme 2). They are prominent fragmentation channels in the metastable molecular ions, in particular. These novel intramolecular redox reactions are of special interest since they appear to represent further examples for mass spectrometric fragmentations occurring via unimolecularly formed ion–neutral complexes.[12,15–17]

1 X = OCH_3
2 X = $N(CH_3)_2$

Scheme 2

In this paper we report on the origin of the migrating hydrogen atoms and on some other details of these unusual rearrangement reactions. Some suggestions concerning the mechanisms are discussed on the basis of deuterium labelling experiments.

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RESULTS AND DISCUSSION

The occurrence of the 3H and 2H rearrangement reactions

The 3H and 2H rearrangement reactions have been found by studying a series of stereoisomeric 2-benzyl-1-indanols.[7,18] The mass-analysed ion kinetic energy (MIKE) spectra of the molecular ions of two particular derivatives, viz. *trans*-2-(4′-methoxybenzyl)-1-indanol, **1** (Fig. 1(a), and *trans*-2-(4′-dimethylaminobenzyl)-1-indanol, **2** (Fig. 1(b)), showed a surprising variety of hydrogen rearrangement reactions. Ions $\mathbf{1}^{+\cdot}$ and $\mathbf{2}^{+\cdot}$ undergo 3H rearrangement reactions to give ions $[C_6H_7OCH_3]^{+\cdot}$ (*m/z* 110) and $[C_6H_7N(CH_3)_2]^{+\cdot}$ (*m/z* 123), respectively, as well as 2H rearrangement reactions to give ions $[C_7H_8OCH_3]^{+\cdot}$ (*m/z* 123) and $[C_7H_8N(CH_3)_2]^{+\cdot}$ (*m/z* 136), respectively. Considering the OCH_3 and $N(CH_3)_2$ substituents as labelling entities it follows from the mass shifts that in both types of fragmentations the hydrogen atoms are transferred from the indanol parts of the molecular ion to the substituted benzyl groups followed by the cleavage of the C(α)—C(1′) and the C(α)—C(2) bonds, respectively (Scheme 2). Deuterium labelling of the indanol moiety corroborates this interpretation (see next section).

There are two prerequisites for the occurrence of the multiple hydrogen rearrangement reactions in ionized 2-benzyl-1-indanols: (i) the presence of an electron-donating substituent at the *para* (4′) position of the benzyl group and (ii) the *trans* orientation of the hydroxy and the benzyl group. This is illustrated by the MIKE spectra of Fig. 2. Unsubsituted *trans*-2-benzyl-1-indanol, **3** (Fig. 2(a)), exhibits three single hydrogen rearrangement reactions. One of these, viz. the elimination of C_6H_6, giving rise to ions *m/z* 146, deserves special notice because the migrating hydrogen atom is transferred to the *ipso* (1′) position of the benzyl group. This step occurs also in the case of the para-substituted analogues (*vide infra*). With an OCH_3 substituent in *meta* (3′) position (**4**, Fig. 2(b)), again no 2H or 3H rearrangement occurs, the major fragmentation being a *single* γ-hydrogen rearrangement giving rise to ions *m/z* 122 as found generally for *meta*-alkylanisoles.[5c,19,20] The MIKE spectrum of *cis*-2-(4′-methoxybenzyl)-1-indanol, **5** (Fig. 2(c)), shows loss of water as the only hydrogen rearrangement reaction, as do all of the *cis*-2-benzyl-1-indanols studied so far.[7,18] Accordingly, *cis*-2-(4′-dimethylaminobenzyl)-1-indanol, **6** (Fig. 2(d)), in contrast to its *trans* isomer **2**, exhibits exclusively loss of water and, in addition, formation of the particularly stable *para*-dimethylaminobenzyl ion (*m/z* 134).

Obviously, the molecular ions of 2-benzyl-1-indanols fragment by stereospecific reaction channels,[7] in con-

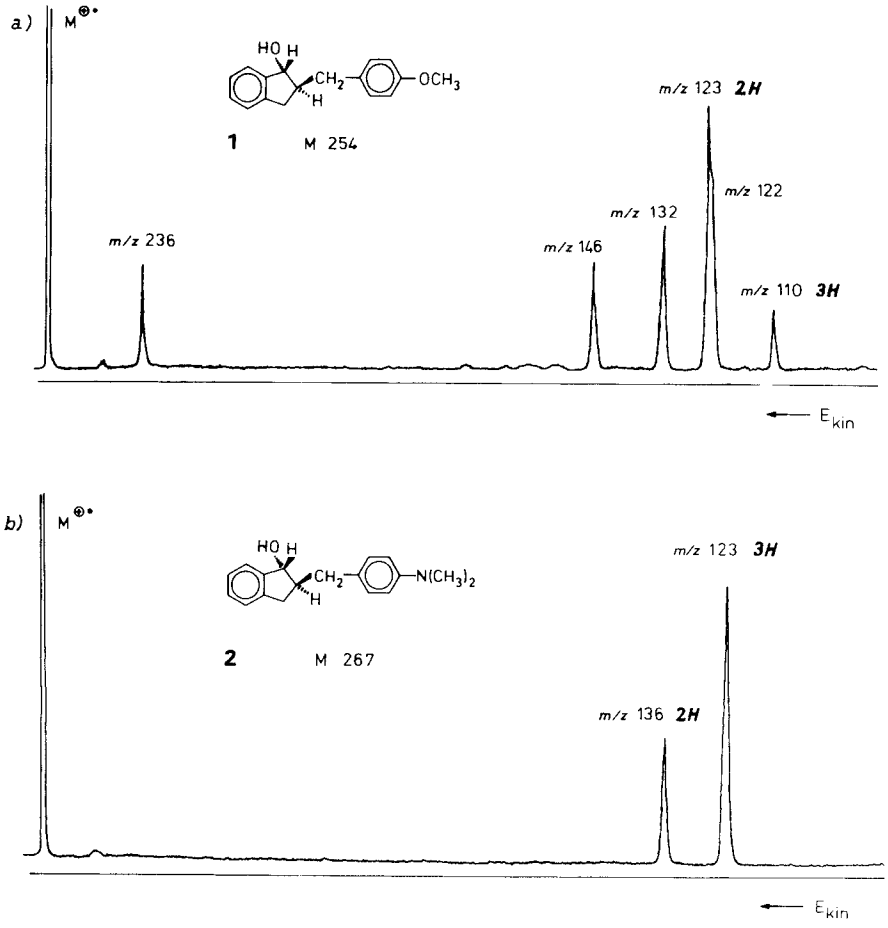


Figure 1. MIKE spectra of *para*-substituted *trans*-2-benzyl-1-indanols **1** (a) and **2** (b). 3H and 2H indicate the signals due to multiple hydrogen rearrangement reactions.

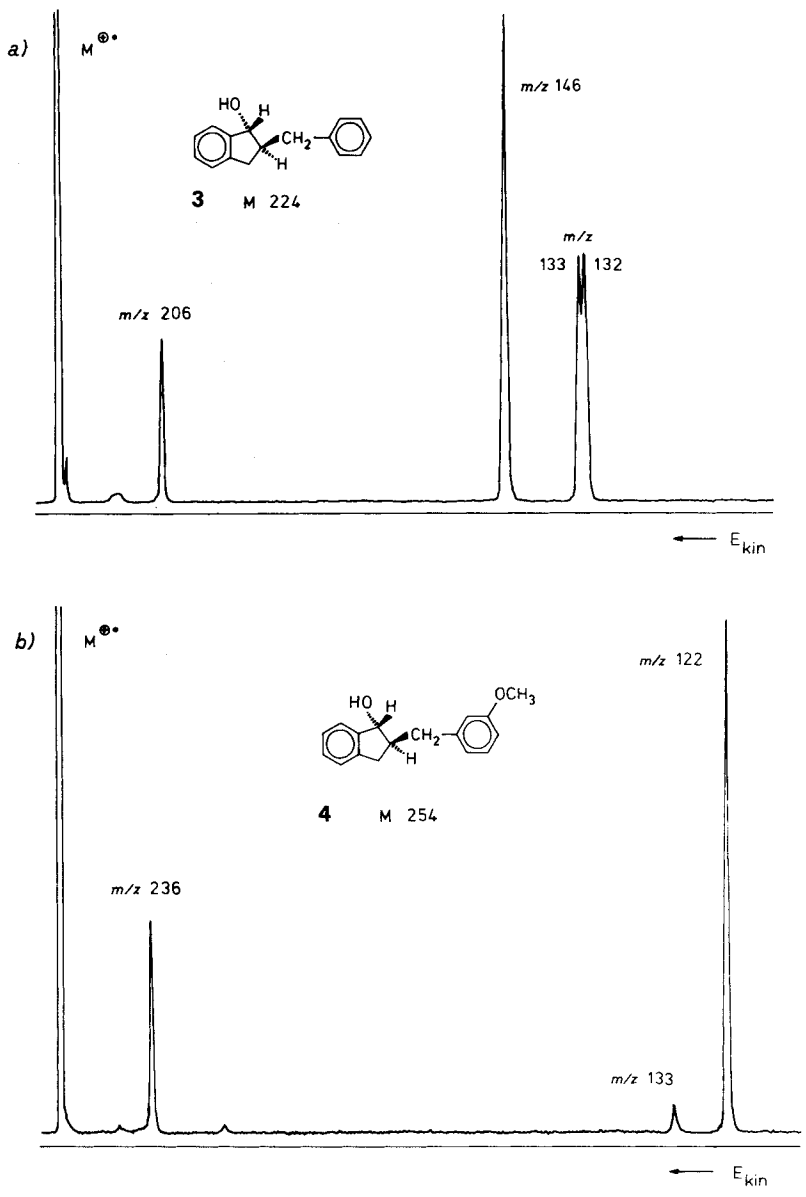


Figure 2. MIKE spectra of *trans*-2-benzyl-1-indanols **3** (a) and **4** (b) and of *cis*-2-benzyl-1-indanols **5** (c) and **6** (d).

trast to unsubstituted 1-indanol ions studied by Gross *et al.*[21] Moreover, the relative rates of the 2H and 3H rearrangement reactions increase with the proton affinity of the *ipso* position ($PA^{1'}$) of the benzyl group. This follows from a comparison of the fragmentation behaviour of metastable ions $\mathbf{3}^{+\cdot}$, $\mathbf{1}^{+\cdot}$ and $\mathbf{2}^{+\cdot}$. The increase of the local proton affinities due to the introduction of the *para* substituents can be estimated to be $PA^{1'}(\mathbf{1}) - PA^{1'}(\mathbf{3}) = +57$ kJ mol^{-1} and $PA^{1'}(\mathbf{2}) - PA^{1'}(\mathbf{3}) = +167$ kJ mol^{-1}, by analogy to simple arenes.[22] Thus, a crucial step in the source of the 3H and 2H rearrangement reactions could be the migration of a hydrogen atom to the *ipso* position of the ionized benzyl group of the molecular ions. Correspondingly, with a relatively high proton affinity at the *ortho* instead of the *ipso* position (cf. **4**, Fig 2(b)), only the common 1H rearrangement is observed.

The occurrence of the 3H and 2H rearrangement reactions is not limited to indanols. In fact, the alcohol function does not necessarily have to be benzylic. This follows from the MIKE spectra of three increasingly simpler γ-arylalkanols given in Fig. 3. The MIKE spectrum of 1-phenyl-3-(4′-dimethylaminophenyl)-1-propanol (**7**, Fig. 3(a)) shows the 3H rearrangement products $[C_6H_7N(CH_3)_2]^{+\cdot}$ (*m/z* 123) in considerable relative abundance. This example demonstrates also that in suitably substituted acyclic γ-arylpropanol ions the 3H rearrangement reaction competes with the loss of water, i.e. in these cases the activation energies of the two fragmentation channels must be similar. Therefore, steric restrictions govern the course of fragmentation in the cyclic analogues of $\mathbf{7}^{+\cdot}$, e.g. in the stereoisomeric molecular ions $\mathbf{1}^{+\cdot}$ and $\mathbf{5}^{+\cdot}$, increasing the relative abundance of the 3H rearrangement ions as compared to the $[M - H_2O]^{+\cdot}$ ions in the case of the *trans* isomer.

A similar effect is observed for the metastable molecular ions of 4-(4′-dimethylaminophenyl)-2-butanol (**8**, Fig. 3(b)), although the 3H rearrangement ions (*m/z* 123) are less abundant as compared to **7**. This is attributed to the lack of benzylic activation at the carbinol H donor function. However, even in the case of a primary alcohol function and a less basic *ipso* position, viz. 3-(4′-

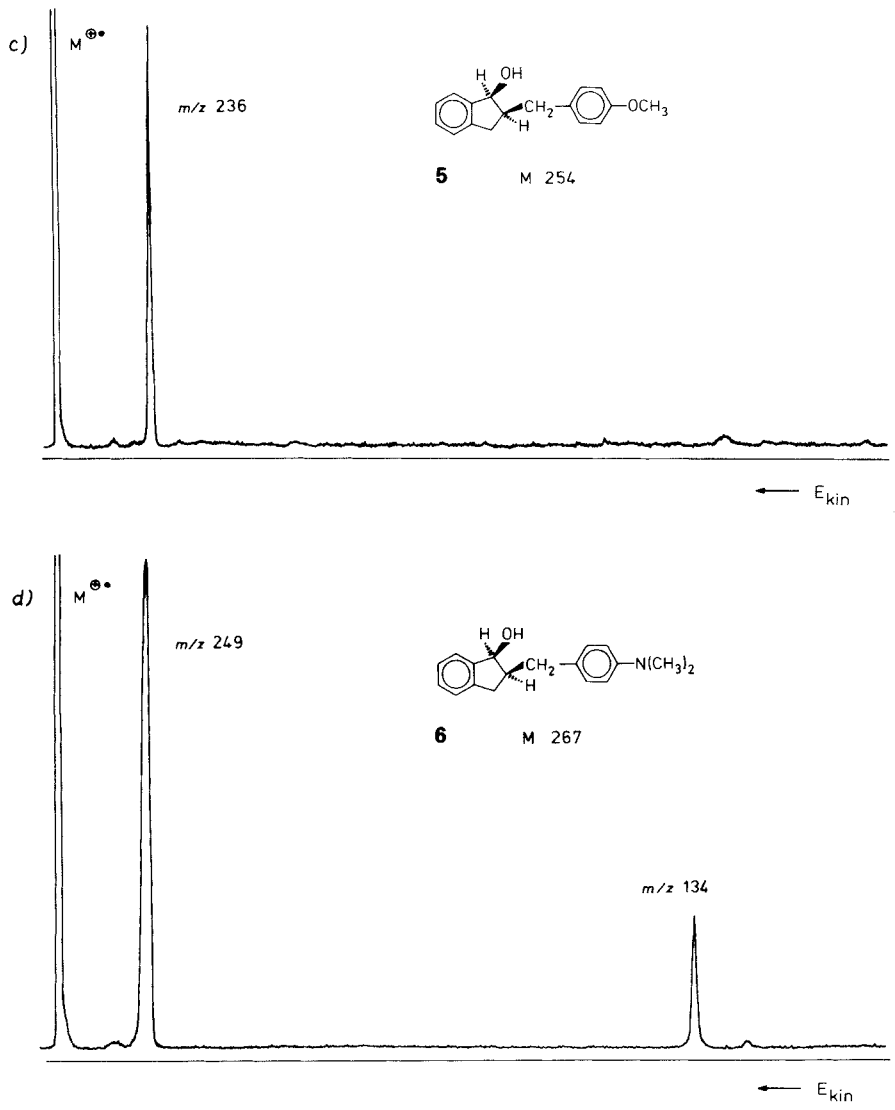


Figure 2. continued

methoxyphenyl)-1-propanol (**9**, Fig. 3(c)), the 3H rearrangement reaction yielding ions $[C_6H_7OCH_3]^{+\bullet}$ (*m/z* 110) is still observed in a minor relative abundance.

With the acyclic molecular ions $\mathbf{7}^{+\bullet}$, $\mathbf{8}^{+\bullet}$, and $\mathbf{9}^{+\bullet}$, the 2H rearrangement reaction is scarcely detectable. Obviously, the structural prerequisites for the 3H rearrangement reaction are less restricting than that for the 2H rearrangement reaction. As will be shown below, the latter reaction is in fact more complex than the former one, suggesting completely different mechanisms.

The 3H and the 2H rearrangement ions are of minor or even negligible abundance in the 'normal' 70 eV mass spectra of the γ-arylalkanols **1**, **2**, **7**, **8** and **9**. However, they represent significant features in the spectra of **1** and **2**. As the most prominent case, the abundance of the 3H rearrangement product *m/z* 123 from **2** amounts to 25% relative to that of the base peak, *m/z* 134 (Fig. 4). Due to a very low frequency factor of the 3H rearrangement reaction this value changes markedly with the mean residence time of the ions in the ion source.

It is evident from the MIKE spectra discussed so far that the carbinol C—H bond is one of the hydrogen donor functions. To determine the origin of the other hydrogen atoms transferred, six specifically deuterium-labelled analogues of **2** have been synthesized and investigated by MIKE spectrometry.

The origin of the rearranged hydrogen atoms

2 has been chosen as the model compound because 3H and 2H rearrangement reactions are the only fragmentation channels of metastable $\mathbf{2}^{+\bullet}$ ions. Six specifically deuterated isotopomers (**2a**–**2f**) have been studied (Scheme 3). The mass shifts observed in the MIKE spectra of ions $\mathbf{2a}^{+\bullet}$–$\mathbf{2f}^{+\bullet}$ are collected in Table 1, together with the relative abundances of the 3H and 2H rearrangement ions. The ratio of the relative abundances, k_{3H}/k_{2H}, and the isotope effects $i = (k_{3H}/k_{2H})_{\mathbf{2x}^{+\bullet}}/(k_{3H}/k_{2H})_{\mathbf{2}^{+\bullet}}$ (x = **a**–**f**) are given in Table 2.

The mass shifts obtained for the 3H rearrangement reaction are strikingly clear. Both for ions $\mathbf{2a}^{+\bullet}$ and $\mathbf{2b}^{+\bullet}$ a complete shift of the ions *m/z* 123 to *m/z* 124 is observed, whereas ions $\mathbf{2d}^{+\bullet}$ give complete retention at the original mass. In the case of ions $\mathbf{2c}^{+\bullet}$, again, more than 95% of the ions *m/z* 123 are shifted to *m/z* 124.

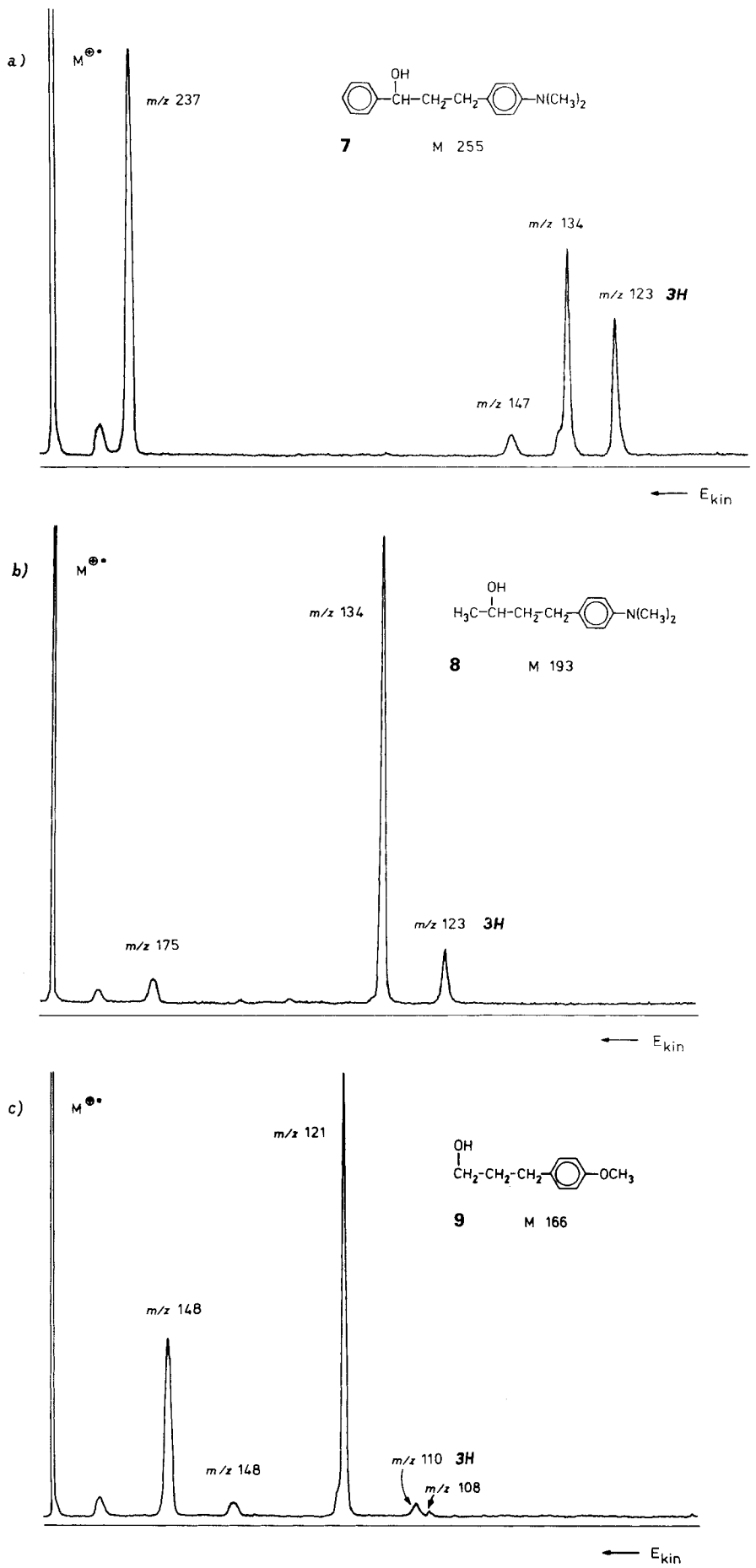


Figure 3. MIKE spectra of open-chain γ-arylpropanols **7**–**9**.

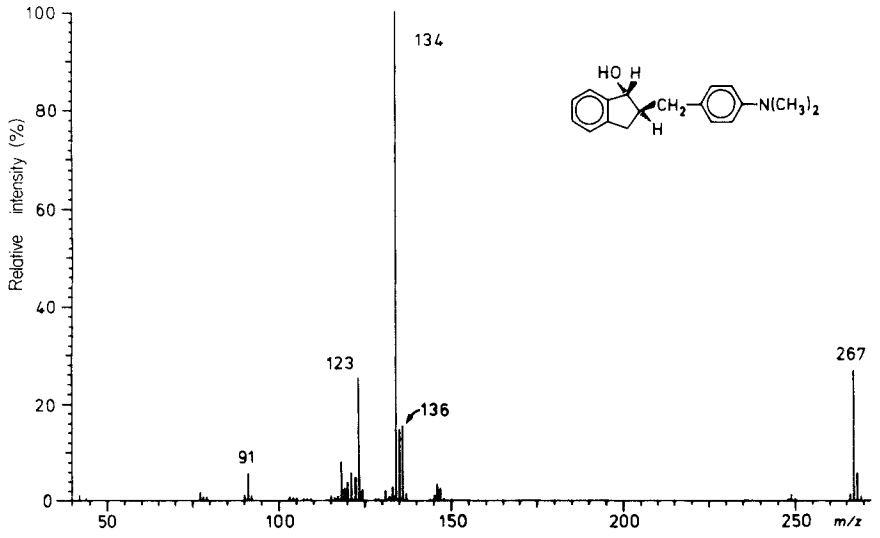
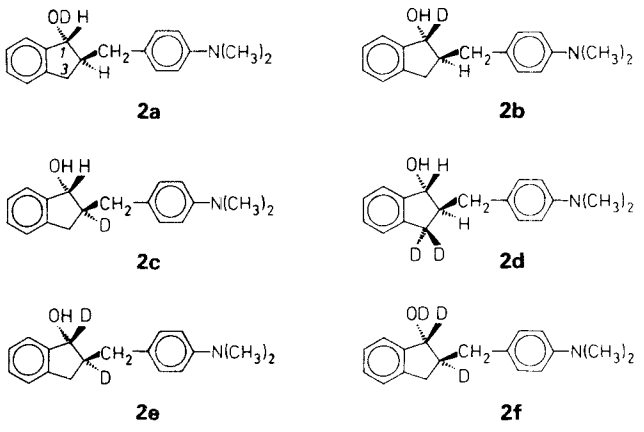


Figure 4. 70 eV mass spectrum of **2**.



2a **2b** **2c** **2d** **2e** **2f**

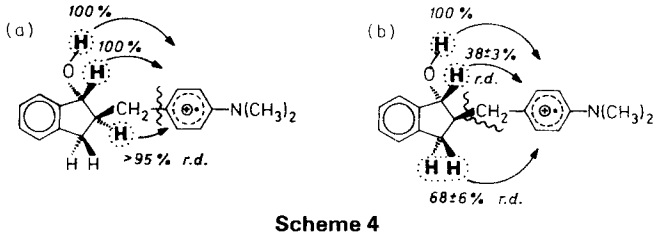
Scheme 3

Thus, the three atoms H(OH), H(1) and H(2) are transferred to the benzyl moiety of ions $2^{+\cdot}$ in the course of the 3H rearrangement reaction. H(3) atoms are not involved. It is interesting to note that no exchange of hydrogen atoms occurs prior to or during this fragmentation in contrast to the single-hydrogen rearrangement reactions of ionized alkyl arenes.[3–6] The mass shifts found for ions $\mathbf{2e}^{+\cdot}$ and $\mathbf{2f}^{+\cdot}$ are in line with the results of the single labelled analogues. Scheme 4(a) illustrates the three hydrogen donor sites of the 3H rearrangement reaction.

Table 2. Competition ratios and isotope effects of the 3H and 2H rearrangement reactions of metastable ions $2^{+\cdot}$–$2f^{+\cdot}$

Ion	k_{3H}/k_{2H}	$\frac{(k_{3H}/k_{2H})_{2x^{+\cdot}}}{(k_{3H}/k_{2H})_{2^{+\cdot}}}$
$2^{+\cdot}$	2.54 ± 0.05	—
$2a^{+\cdot}$	2.62 ± 0.07	1.03
$2b^{+\cdot}$	3.89 ± 0.05	1.53
$2c^{+\cdot}$	1.37 ± 0.10	0.54
$2d^{+\cdot}$	3.22 ± 0.10	1.27
$2e^{+\cdot}$	1.91 ± 0.06	0.75
$2f^{+\cdot}$	2.16 ± 0.10	0.85

The 2H rearrangement reaction is more complex. Again, H(OH) is transferred completely and without hydrogen exchange; but H(2) is not at all involved in this process. Also contrasting to the 3H rearrangement



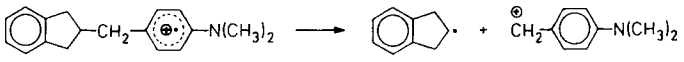
Scheme 4

Table 1. MIKE spectra of deuterium-labelled ions $2^{+\cdot}$–$2f^{+\cdot}$ [a]

		3H rearrangement reaction				2H rearrangement reaction		
		m/z				m/z		
Ion	Label	123	124	125	126	136	137	138
$2^{+\cdot}$	D_0	71.8	—	—	—	28.6	—	—
$2a^{+\cdot}$	*O*-D	—	72.4	—	—	—	27.6	—
$2b^{+\cdot}$	1-D	—	79.5	—	—	12.7	7.8	—
$2c^{+\cdot}$	2-D	1.6	56.2	—	—	42.2	—	—
$2d^{+\cdot}$	3,3-D_2	76.3	—	—	—	7.6	16.1	—
$2e^{+\cdot}$	1,2-D_2	3.3	—	62.4	—	20.2	14.1	—
$2f^{+\cdot}$	*O*,1,2-D_3	—	2.1	1.4	65.0	—	20.2	11.4

[a] See Scheme 3; values are given in %Σ.

reaction, only a fraction of the other migrating H atoms originates from the carbinol (C(1)) position (cf. $\mathbf{2b}^{+\cdot}$); the other fraction being transferred from the ring methene (C(3)) position (cf. $\mathbf{2d}^{+\cdot}$). Similar results are found for the other analogues ($\mathbf{2e}^{+\cdot}$ and $\mathbf{2f}^{+\cdot}$) labelled at the carbinol position; hence, besides 100% of the H(OH) atoms, 38 ± 3% of the H(1) atoms and 68 ± 6% of the H(3) atoms are transferred to the dimethylaminobenzyl group during the 2H rearrangement reaction. Since these two values are complementary within the limits of experimental error a hydrogen exchange between the C(1) and C(3) positions and the *ortho* positions of the benzyl group can be excluded. As pointed out above, the local proton affinity of the *ortho* positions in **2** should be much lower than that of the *ipso* position, thus suppressing a hydrogen exchange. In accord with this, no H(γ)/H(*ortho*) exchange occurs in the molecular ions of the corresponding hydrocarbon, viz. 2-(4′-dimethylaminobenzyl)-indan, **10**.[18] Here, benzylic cleavage is the only fragmentation reaction observed for metastable $\mathbf{10}^{+\cdot}$ ions (Scheme 5).



$10^{+\cdot}$ *m/z* 134

Scheme 5

The rate-determining steps of the 3H and 2H rearrangement reactions

The primary isotope effects on the rates of fragmentation of the metastable ions $\mathbf{2}^{+\cdot}$ (Table 1) lead to marked changes of the relative abundances of the 3H and 2H rearrangement ions. Owing to the high specificity of the various hydrogen transfer steps the competition ratio k_{3H}/k_{2H} can be used to confine the rate-determining steps of the two reactions. As shown in Table 2, the labelling affects k_{3H}/k_{2H} in all cases except $\mathbf{2a}^{+\cdot}$, hence, the migration of H(OH) is not the rate-determining step in either of both reactions. H(OH) are the only migrating atoms which participate completely in both rearrangement reactions. Accordingly, the other (two) H atoms are transferred to the benzyl moiety independently, i.e. by different mechanisms.

In contrast, ions $\mathbf{2b}^{+\cdot}$ and $\mathbf{2d}^{+\cdot}$ exhibit a considerable increase of k_{3H}/k_{2H}, whereas for ions $\mathbf{2c}^{+\cdot}$ k_{3H}/k_{2H} decreases to 54% of the original value. In the latter case, the primary isotope effect must be necessarily due to a discrimination of k_{3H} since the D(2) atom does not migrate during the 2H rearrangement reaction.[23] Thus, the transfer of H(2) is the rate-determining step of the 3H rearrangement reaction, H(1) being transferred in a non-rate-determining step (Scheme 4(a)). On the other hand, k_{3H}/k_{2H} increases for both ions $\mathbf{2b}^{+\cdot}$ and $\mathbf{2d}^{+\cdot}$. Since the migration of H(1) is not rate-determining during the 3H rearrangement reaction it must be so during the competing 2H rearrangement process. The same holds for H(3) atoms, in line with the fact that C(1) and C(3) are competing hydrogen donor sites in the 2H rearrangement reaction. Thus, the competing migrations of H(1) and H(3) are rate-determining in the 2H rearrangement reaction (Scheme 4(b)).

Although secondary isotope effects cannot be ruled out competely (cf. k_{3H}/k_{2H} for ions $\mathbf{2b}^{+\cdot}$ and $\mathbf{2d}^{+\cdot}$) the above interpretation holds also for the multiply labelled analogues $\mathbf{2e}^{+\cdot}$ and $\mathbf{2f}^{+\cdot}$. The k_{3H}/k_{2H} ratios found for these analogues match within ±10% those obtained by combining the values of the singly labelled compounds, e.g.

$$(k_{3H}/k_{2H})_{\mathbf{2f}^{+\cdot}} = (k_{3H}/k_{2H})_{\mathbf{2}^{+\cdot}} \cdot i_{\mathbf{2a}^{+\cdot}} \cdot i_{\mathbf{2b}^{+\cdot}} \cdot i_{\mathbf{2c}^{+\cdot}}$$

In conclusion, the rate-determining steps of the 3H and the 2H rearrangement reactions involve different hydrogen atoms. Thus, in accord with the argument of the previous section, the mechanisms of these fragmentation reactions must be independent.

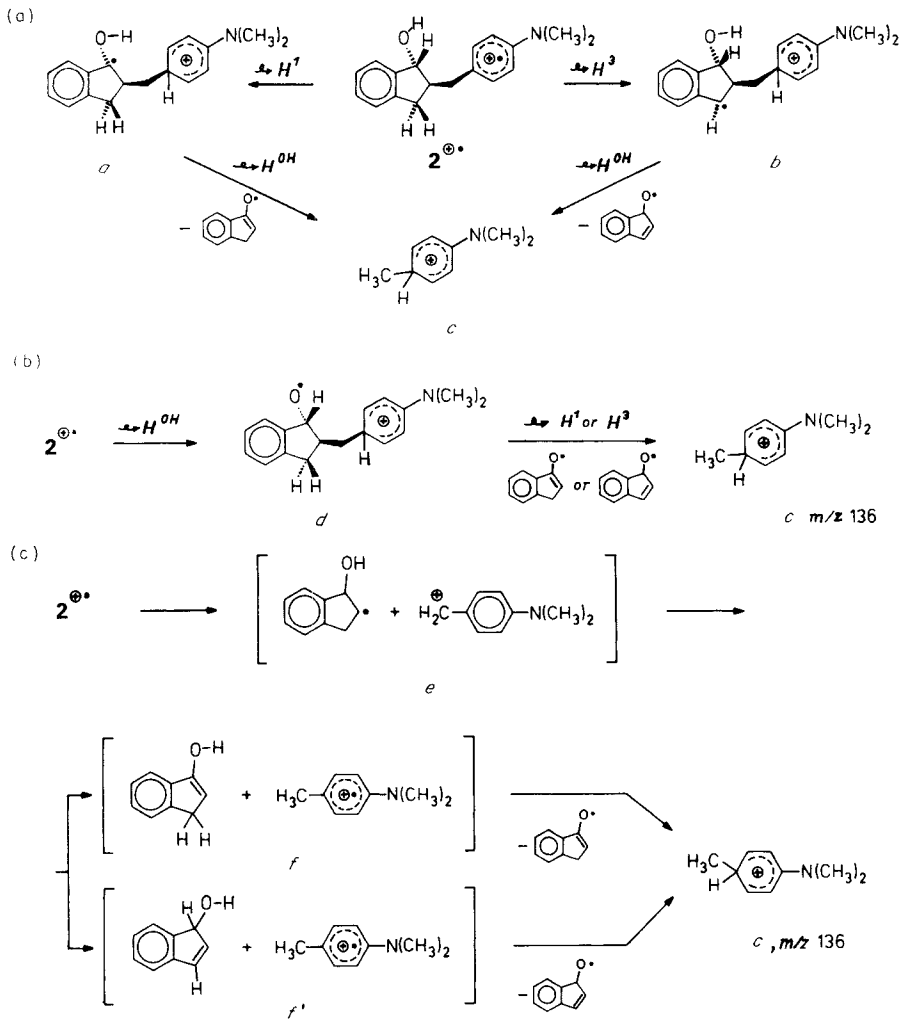
MECHANISTIC SUGGESTIONS—THE NECESSITY OF ION–NEUTRAL COMPLEXES

Although the origin of the various migrating hydrogen atoms is defined, it is difficult to formulate conclusive mechanisms for the rearrangement reactions described. However, because of the unusual course of the fragmentation of the γ-arylalkanol ions, tentative mechanistic suggestions are presented and discussed in the following section. The most reasonable mechanisms for both the 2H and the 3H rearrangement reaction include the formation of ion–neutral complexes as intermediates prior to final fragmentation.

The 2H rearrangement reaction

As depicted in a classical way (Scheme 6), this reaction should start with the migration of H(1) or *cis*-H(3) to the *ortho* position of the benzyl group. Owing to the high proton affinity of the *ipso* position and in line with the results of labelling, ions *a* and *b* should be formed as intermediates in the rate-determining step, H(OH) being transferred subsequently to the α position to give, finally, ion *c* as the most stable ionic product (Scheme 6(a)). However, the fact that the migration of H(1) and H(3) is rate-determining renders this mechanism less convincing. H(1) should migrate particularly easily owing to the activation by the hydroxy group; however, migration of H(3) is found to be roughly twice as fast as that of H(1). In a similar manner, H(OH) could be transferred to the *ipso* position first, giving rise to the formation of intermediate *d*, from which then fragment ion *c* is formed by competing 1,2-elimination steps (Scheme 6(b)). In addition to the above argument, this mechanism seems unlikely because of the steric restrictions due to the *trans* stereochemistry of $\mathbf{2}^{+\cdot}$. Note that in the *cis* isomer, $\mathbf{6}^{+\cdot}$, H(OH) does not migrate (Fig. 2(d)). Instead, the particularly stable *para*-dimethylaminobenzyl ion *m/z* 134 is formed from $\mathbf{6}^{+\cdot}$ and, as mentioned above, as the only fragment ion from $\mathbf{10}^{+\cdot}$.

Therefore, the cleavage of the C(2)—C(α) bond has to be envisaged as the first step in the 2H rearrangement reaction (Scheme 6(c)), corresponding to the fragmentation of $\mathbf{10}^{+\cdot}$. An ion–radical complex *e* is formed, which

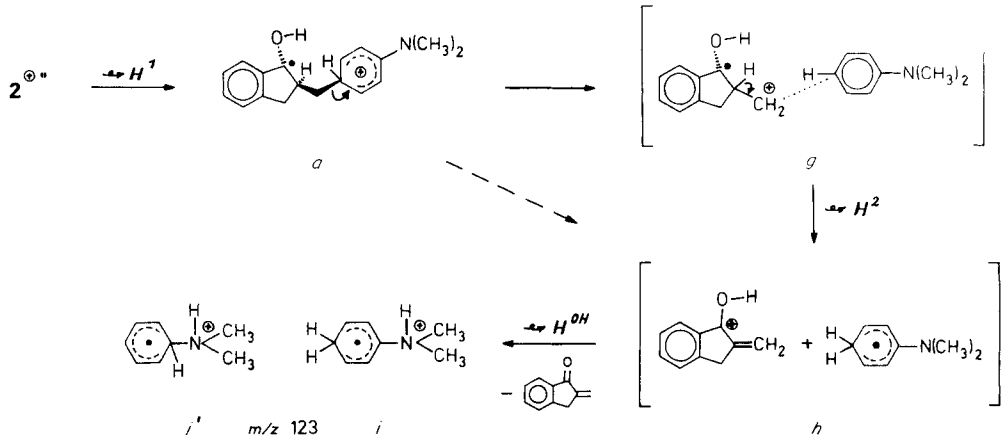


Scheme 6

is strongly stabilized by ion–dipole interactions. Within this complex, H(1) or one of the H(3) atoms is then transferred in a near-statistical (1:2) ratio. In line with the experimental results, this is the rate-determining step of the reaction. The new ion–neutral complexes *f* and *f'* may gain additional stabilization by internal hydrogen bonding. In the last step, complexes *f* and *f'* are cleaved by transfer of H(OH) to the *para*-dimethylaminotoluene moiety, forming ion *c* as the final charged product.

The 3H rearrangement reaction

Again, the most reasonable yet unconventional mechanism for this reaction requires the formation of ion–neutral complexes (Scheme 7). Obviously, the first step of the 3H rearrangement reaction is not a C—C bond cleavage. The fission of the particularly strong C(α)—C(*ipso*) bond has to be induced by one of the three individual hydrogen transfer steps. Here, the energetically favourable rearrangement of H(1) to the *ipso*



Scheme 7

Scheme 8

position of the *para*-dimethylaminobenzyl group is envisaged to occur first, giving rise to intermediate ion *a*. Protonation of the *ipso* position is considered to weaken or even cleave the C(α)—C(*ipso*) bond in *a*, as known for protonated arenes.[24,25] Another ion–molecule complex *g* may be formed in this way, which is then converted to complex *h* by transfer of H(2) in the rate-determining step. Alternatively, *h* is formed directly from *a*. In both cases, migration of H(2) may reasonably be identified as the most energy-demanding step.

Similar to the 2H rearrangement reaction, hydrogen bonding involving the hydroxy group may afford additional stabilization of the ion–neutral complexes. Accordingly, H(OH) should be the last atom transferred to the dimethylaniline moiety. Probably, a relatively free rotation of the two components of the complexes is required to achieve interaction of the originally remote hydroxy and the dimethylamino groups.

Structures *i* or *i'* are proposed for the final ionic product, $[C_8H_{13}N]^{+\cdot}$ (*m/z* 123). They should be more stable than all acyclic isomers. As expected, loss of a hydrogen atom is the most important fragmentation channel of the $[C_8H_{13}N]^{+\cdot}$ ions upon collisional induced dissociation (CID).[26] However, more detailed structural investigation is needed to understand the chemistry of this peculiar distonic[27] radical cation. It is interesting to note that species of type *i'* represent the primary covalent addition product formed during the homolytic aromatic substitution of benzene and alkylbenzenes (Scheme 8).[28]

EXPERIMENTAL

The MIKE spectrometric measurements were performed with a ZAB-2F double-focusing instrument (Vacuum Generators, Manchester, UK) at 5.6 kV accelerating voltage, 70 eV electron energy, and 100 μA trap current. The mass spectrum of **2** (Fig. 4) was measured with a 311 A doublé-focusing instrument (Finnigan MAT, Bremen, FRG) at 3.0 kV accelerating voltage. The samples were introduced by the solids probe inlet with slight heating of the quartz crucible. The temperature of the ion source was 180 ± 10 °C. The relative ion abundances in the MIKE spectra of ions $\mathbf{2a}^{+\cdot}$–$\mathbf{2f}^{+\cdot}$ were found to be very sensitive to source and focusing conditions. Therefore, several series of measurements were performed, each of which included at least twelve scans for an individual isotopomer, and the parameters were held strictly constant throughout each series.

Melting points were determined with an Electrothermal apparatus and are uncorrected. ^{1}H nuclear magnetic resonance (^{1}H NMR) spectra were measured with a Bruker WP 80 (80 MHz) instrument with $CDCl_3$/TMS as the solvent. The ^{1}H-NMR spectra of the stereoisomeric indanols were recorded after H/D exchange with D_2O in order to resolve the stereospecific carbinol doublet resonances at ~4.95 (*trans*) and ~5.05 p.p.m. (*cis*). Combustion analysis of the new indanols **1**, **2** and **4–6** gave satisfactory results.

The 2-benzyl-1-indanols **1–6** were obtained from the corresponding 2-benzyl-1-indanones described in the literature[29–32] by reduction with $LiAlH_4$ in dry diethyl ether. The usual workup—but without acidification of the reaction mixture because of the facile epimerization of the carbinol center—gave the *cis*- and *trans* isomer in a ~1:1 ratio, as monitored by thin-layer chromatography (silica gel; petroleum ether/ethyl acetate (PE/EE) 3:1) and ^{1}H-NMR spectrometry. The *trans* isomers **1–4** were separated with ⩾97% stereochemical purity (^{1}H-NMR) by fractional crystallization from PE/EE (~10:1) in yields of 35–45%. The *cis* isomers **5** and **6** could be obtained from the mother liquors by recrystallization from petroleum ether/diethyl ether (PE/DE) 5:1 (yields 10–20%) with ⩾90% stereochemical purity (^{1}H-NMR). Alternatively, the 2-benzyl-1-indanones (2 mmol) were reduced in 10 ml tetrahydrofuran under nitrogen by dropwise addition of 4.5 cm^3 of a molar solution of lithium tri-*sec*-butylborohydride (L-Selectride, Aldrich).[33] After stirring for 5 h at −75 °C the mixture was warmed up to room temperature, and 30% H_2O_2 was added dropwise, causing a highly exothermic reaction. Excess H_2O_2 was reduced with aqueous Fe_2SO_4 and the product extracted with ether and purified by recrystallization with PE/DE (yields of **5**, 65%; **6**, 52%).

The following physical properties were found for the various 2-benzyl-1-indanols. *Trans*-2-(4'-methoxybenzyl)-1-indanol (**1**), m.p. 117–118 °C (PE/EE); ^{1}H-NMR, δ (p.p.m.) 2.3–3.2 (*m*, 5H), 3.79 (*s*, 3H), 4.94 (*d*, ^3J = 6.1 Hz, 1H), 6.9 (*AA'*, 2H), 7.1–7.5 (*BB'*, *m*, 6H). *Trans*-2-(4'-dimethylaminobenzyl)-1-indanol (**2**), m.p. 101 °C (PE/EE); ^{1}H-NMR δ (p.p.m.) 2.3–3.3 (*m*, 5H), 2.92 (*s*, 6H), 4.94 (*d*, ^3J = 6.0 Hz, 1H), 6.75 (*AA'*, 2H), 7.1–7.5 (*BB'*, *m*, 6H). *Trans*-2-benzyl-1-indanol (**3**),[31] m.p. 104 °C (PE/EE); ^{1}H-NMR δ (p.p.m.) 2.35–3.25 (*m*, 5H), 4.95 (*d*, ^3J = 5.9 Hz, 1H), 7.1–7.5 (*m*, 9H). *Trans*-2-(3'-methoxybenzyl)-1-indanol (**4**), m.p. 59–60 °C (PE/EE), cf. *cis/trans* mixture, m.p. 44–47 °C;[34] ^{1}H-NMR δ (p.p.m.) 2.3–3.3 (*m*, 5H), 3.78 (*s*, 3H), 4.88 (*d*, ^3J = 6.0 Hz, 1H), 6.7–7.0 (*m*, 3H), 7.2–7.5 (*m*, 5H). *Cis*-2-(4'-methoxybenzyl)-1-indanol (**5**), m.p. 88–89 °C (PE/DE); ^{1}H-NMR δ (p.p.m.) 2.6–3.2 (*m*, 5H), 3.81 (*s*, 3H), 5.02 (*d*, ^3J = 4.7 Hz, 1H), 6.9 (*AA'*, 2H), 7.2–7.5 (*BB'*, *m*, 6H). *Cis*-2-(4'-dimethylaminobenzyl)1-1-indanol (**6**), m.p. 90 °C (PE/DE); ^{1}H-NMR δ (p.p.m.) 2.6–3.1 (*m*, 5H), 2.93 (*s*, 6H), 5.03 (*d*, ^3J = 4.4 Hz, 1H), 6.78 (*AA'*, 2H), 7.2–7.5 (*BB'*, *m*, 6H).

The known acyclic alcohols **7**[35] and **8**[36] were obtained by reduction of the corresponding ketones[35,36] with $LiAlH_4$ in diethyl ether using the standard procedure (yields ⩾80%). ^{1}H-NMR of **8** ($CDCl_3$) δ (p.p.m.) 1.21 (*d*, ^3J = 6.2 Hz, 3H), 1.38 (*br s*, 1H), 1.6–2.0 (*m*, 2H), 2.5–2.75 (*m*, 2H), 2.91 (*s*, 6H), 3.81 (*hx*, ^3J = 6 Hz, 1H), 6.68, 7.03 (*AA'BB'*, 4H). **9** was a commercial product (Aldrich, ⩾99%) measured without further purification.

Trans-[*O*-D]-2-(4′-dimethylaminobenzyl)-1-indanol (**2a**) was prepared by stirring a solution of 15 mg **2** in 0.5 cm^3 dry tetrahydrofuran and 0.4 ml D_2O for 5 min at room temperature, evaporation of the solvents *in vacuo* and repeating this procedure twice. The ion source of the mass spectrometer was flushed with $\sim 5 \times 10^{-3}$ cm^3 D_2O directly before the measurement. The initial isotope purity of **2a** upon measurement was $\geqslant 80\%$ d. *Trans*-[1-D]-(4′-dimethylaminobenzyl)-1-indanol (**2b**) was obtained from 2-(4′-dimethylaminobenzyl)-1-indanone[30] by reduction with $LiAlD_4$ (Merck, $\geqslant 99\%$ d) corresponding to the procedure used for **2**. Isotope purity of **2b** was $\geqslant 99\%$ d (mass spectrometry, 70 eV). *Trans*-[2-D]-(4′-dimethylaminobenzyl-1-indanol (**2c**) was obtained by reduction of [2-D]-2- (4′-dimethylaminobenzyl)-1-indanone with $LiAlH_4$. This ketone was prepared by stirring 1.0 g (3.8 mmol) of the d_0-analogue dissolved in 3 cm^3 dry THF and 1.5 cm^3 of a 10% solution of NaOD in D_2O in a closed bulb at 60 °C for 24 h. The liquids were evaporated to dryness, and the procedure was repeated thrice without using THF in the last run. The isotope purity of **2c** was $\geqslant 95\%$ d (MS, 70 eV).

Synthesis of *trans*-[3,3-D_2]-2-(4′-dimethylaminobenzyl)-1-indanol (**2d**): [1,1,3-D_3]-indene (90% d) was prepared by repeated H/D exchange[37] and converted to [1,1,3-D_3]-3-chloroindan by addition of gaseous HCl.[38] Isotope purity of the indan was 90% d, as measured by ^{1}H-NMR ($CDCl_3$), δ (p.p.m.) 2.35, 2.60 (*AB*, J = 14 Hz, ~2 H), 7.2–7.5 (*m*, 4 H), and, subsequently, to [3,3-D_2]-1-indanone (85% d, ^{1}H-NMR, $CDCl_3$), δ (p.p.m.) 2.67 (br *s*, 2 H), 3.1 (*m*, ~0.2 H), 7.25–7.8 (*m*, 4 H). In analogy to known procedures,[30] this ketone was condensed with 4-dimethylaminobenzaldehyde to give [3,3-D_2]-2-(4′-dimethylaminobenzylidene)-1-indanone, which was hydrogenated with Pd/C in 1,4-dioxane to [3,3-D_2]-2-(4′-dimethylaminobenzyl)-1-indanone, without significant loss of label. **2d** was obtained by reduction of this ketone with $LiAlH_4$ in diethyl ether with an isotope purity of $\geqslant 85\%$ d (MS, 70 eV).

Trans-[1,2-D_2]-2-(4′-dimethylaminobenzyl)-1-indanol (**2e**): this compound was obtained from **2c** by reduction with $LiAlH_4$; isotope purity $\geqslant 95\%$ (mass spectrometry, 70 eV). *Trans*-[*O*,1,2-D_3]-2-(4′-dimethylaminobenzyl)-1-indanol (**2f**): this isotopomer was prepared from **2e** by treatment with D_2O/THF and measured as described for **2a**. The initial isotope purity upon MIKE measurement was $\geqslant 80\%$.

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