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Collision-induced Dissociation Study of Stereospecific Elimination Processes of Stereoisomeric Phenylcyclohexanols and Their Derivatives Upon Electron Ionization

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The electron ionization (EI)-induced elimination of water, methanol and acetic acid from the $M^{+\cdot}$ ions of stereoisomeric 2-, 3- and 4-phenylcyclohexanols and their methyl ethers and acetates, respectively, was studied by deuteration and collision-induced dissociation (CID) techniques. The highly stereospecific elimination processes in *trans*-3- and -4-phenylcyclohexanols and in the corresponding methyl ethers and acetates take place with the involvement of the benzylic hydrogen atom, suggesting *syn*-1,3- and *syn*-1,4-elimination via cyclic transition states. The elimination processes from the *cis*-alcohols and their methyl ethers occur mainly after ring opening, and result in the formation of mixtures of product ions. The elimination processes are non-stereospecific in the stereoisomeric 2-phenyl-substituted systems, and are preceded by ring cleavage in both *cis*- and *trans*-isomers, resulting in mixtures of cyclic and acyclic product ions. All *cis*-2-, -3- and -4-phenylcyclohexyl acetates undergo elimination by a McLafferty-type mechanism with the abstraction of a hydrogen atom from positions 2 and/or 6. An interesting outcome of this work is that the majority of the gas-phase isomeric hydrocarbon phenyl-C_6H_9 radical cations, formed either by EI-induced fragmentation of stereoisomeric phenylcyclohexyl derivatives or by EI of a variety of phenyl-C_6H_9 isomers, retain their structural integrities. On the other hand, the CID spectra of the even-electron phenyl-$C_6H_{10}^+$ ions produced by chemical ionization (CI)-induced fragmentation from isomeric phenylcyclohexanols and their methyl ethers and acetates are similar, indicating loss of structural information under CI in this system. © **1998 John Wiley & Sons, Ltd.**

KEYWORDS: stereochemical effects; electron ionization; chemical ionization; collision-induced dissociation; deuterium labelling; phenylcycloalkanols; ethers; acetates

INTRODUCTION

The stereochemistry of elimination processes of gas-phase ionized alcohols, ethers and esters has been of considerable interest since the early times of organic mass spectrometry.[1–6] The elimination of H_2O from 3- and 4-arylcyclohexanols **2t** and **3t** under electron ionization (EI) is a highly stereospecific process (the isomeric 2-arylcyclohexanols **1c** and **1t** were not reported).[7] Highly abundant $[M - H_2O]^{+\cdot}$ ions are formed from the *trans*-isomers **2t** and **3t** while the *cis*-analogs **2c** and **3c** afford relatively low abundance dehydration product ions (Scheme 1).

Deuterium labeling studies have shown that the H_2O elimination process involves the benzylic hydrogens with high specificity in the *trans*-alcohols.[7] This finding suggests the mechanism shown in Scheme 2 for the EI-induced dehydration of *trans*-arylcyclohexanols **2t** and **3t**.

Similar behavior has been observed for the elimination of methanol from the analogous 3- and 4-arylcyclohexyl methyl ethers **5** and **6** (the 2-aryl-substituted analogs **4** have not been reported): a highly stereo- and regiospecific efficient elimination of methanol from the *trans*-ethers involving the benzylic hydrogen atoms, in contrast to the *cis*-isomers, which afford low abundance $[M - MeOH]^{+\cdot}$ ions (although with significant abstraction of hydrogens from the benzylic position).[8] *trans*-3- and 4-aryl acetates **8** and **9** (the 2-aryl-substituted acetates **7** have not been reported) also exhibit a similar highly stereo- and regiospecific elimination of acetic acid involving the benzylic position, while the *cis*-isomers undergo a 1,2-elimination.[9]

Deuterium labeling studies provide preliminary information on the mechanistic pathways of the elimination processes, but not necessarily on the structures of the resulting fragment ions. An extensive collision-induced dissociation (CID) study has been undertaken in order to solve the ion structure problem, and consequently to obtain a better understanding of the above elimination

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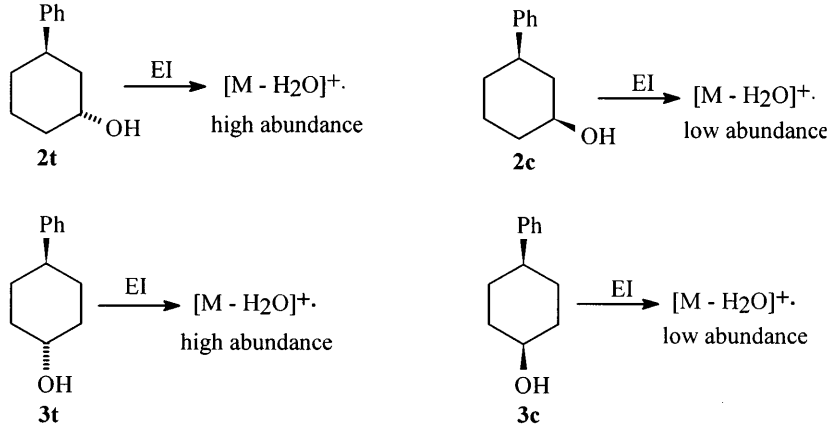


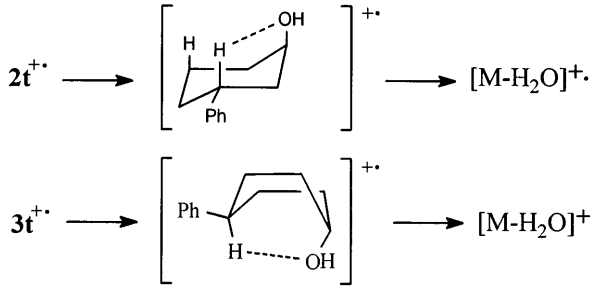
Scheme 1.

processes of stereoisomeric phenylcyclohexanols and their derivatives upon EI.

RESULTS AND DISCUSSION

The results of the present EI mass spectral measurements of the *cis–trans* pairs of 2-, 3- and 4-phenylcyclohexanols and their methyl ethers and acetates are listed in Tables 1–3. The pronounced difference in the fragmentation behavior of the *cis*- and *trans*-isomers, previously reported for the 3- and 4-phenyl series, has been reproduced in the present measurements. In contrast to the stereospecific nature of the fragmentation of the latter pairs of stereoisomers, *cis*- and *trans*-2-phenylcyclohexanols **1c** and **1t** and their derivatives **4c**, **4t**, **7c** and **7t** exhibit non-stereospecific elimination of H_2O, MeOH and AcOH, respectively, affording comparable abundances of the *m/z* 158 [M – ROH]$^{+\cdot}$ ions.

A preliminary CID study of the structures of the [M – ROH]$^{+\cdot}$ ions obtained upon EI from **1–9**, using a small number of standards, which are possible products of elimination of H_2O, MeOH and AcOH from



Scheme 2.

Table 1. Relative abundances (%) of $M^{+\cdot}$ and $[M - H_2O]^{+\cdot}$ ions in the EI mass spectra of stereoisomeric 2-, 3- and 4-phenylcyclohexanols

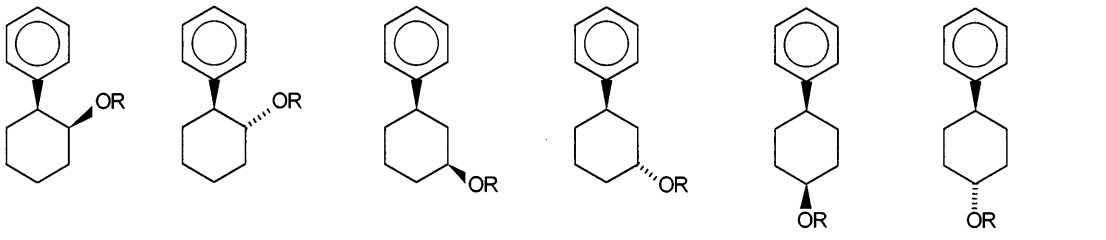
	$[M]^{+\cdot}$	$[M - H_2O]^{+\cdot}$	$[M - H_2O]^{+\cdot}/[M]^{+\cdot}$	*trans/cis*[a]
1c	100	19.4	0.2	
1t	100	20.9	0.2	1.0
2c	100	25	0.25	
2t	8	100	12.5	50
3c	100	20	0.2	
3t	3.4	100	29	145

[a] The ion abundance ratio $([M - H_2O]^{+\cdot}/[M]^{+\cdot})_{trans}/([M - H_2O]^{+\cdot}/[M]^{+\cdot})_{cis}$ is considered as the degree of stereospecificity in the fragmentation of stereoisomers.

phenylcyclohexanols and their methyl ethers and acetates, was performed in order to determine the structures of these elimination ions. This study showed that the problem is involved, and consequently the relatively large set of isomeric *m/z* 158 standard precursors **10–31** shown in Scheme 3 was prepared. The low-energy CID spectra of the *m/z* 158 radical cations, obtained upon EI from these materials, are shown in Figs 1–9.

Table 2. Relative abundances (%) of $M^{+\cdot}$ and $[M - CH_3OH]^{+\cdot}$ ions in the EI mass spectra of stereoisomeric 2-, 3- and 4-phenylcyclohexyl methyl ethers

	$[M]^{+\cdot}$	$[M - CH_3OH]^{+\cdot}$	$[M - CH_3OH]^{+\cdot}/[M]^{+\cdot}$	*trans/cis*
4c	100	40	0.5	
4t	100	40	0.3	1
5c	100	35	0.4	
5t	<0.5	100	>200	>500
6c	100	26.4	0.3	
6t	6.8	100	15	50



1c. R=H **1t**. R=H **2c**. R=H **2t**. R=H **3c**. R=H **3t**. R=H
4c. R=CH3 **4t**. R=CH3 **5c**. R=CH3 **5t**. R=CH3 **6c**. R=CH3 **6t**. R=CH3
7c. R=OCOCH3 **7t**. R=OCOCH3 **8c**. R=OCOCH3 **8t**. R=OCOCH3 **9c**. R=OCOCH3 **9t**. R=OCOCH3

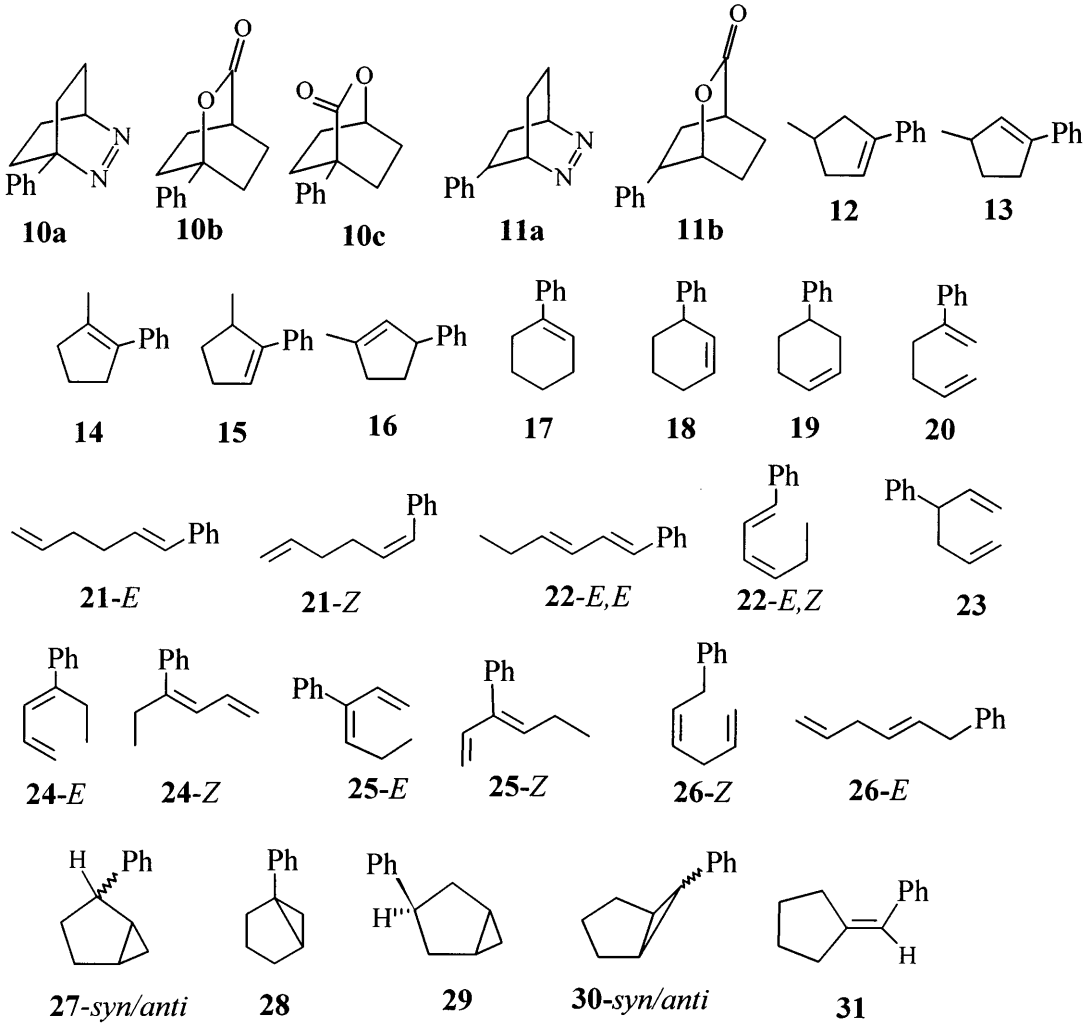
Table 3. Relative abundances (%) of $M^{+\cdot}$ and $[M - AcOH]^{+\cdot}$ ions in the EI mass spectra of stereoisomeric 2-, 3- and 4-phenylcyclohexyl acetates

	$[M]^{+\cdot}$	$[M - AcOH]^{+\cdot}$	$[M - AcOH]^{+\cdot}/[M]^{+\cdot}$	*trans/cis*
7c	<0.5	100	>200	
7t	<0.5	100	>200	>1
8c	20	100	5	
8t	<0.5	100	>200	>30
9c	<0.5	40	>80	
9t	<0.5	100	>200	>2.5

CID standards

We were not successful in our attempts to synthesize 1-phenylbicyclo[2.2.0]hexane (**32**), which is the most probable intermediate of the product of elimination of H_2O, MeOH and AcOH from *trans*-4-phenylcyclohexanol (**3t**) and its methyl ether (**6t**) and acetate (**9t**).[10] Standard materials **10a**, **10b** and **10c** were used as potential precursors of ionized **32**. As expected, the *m/z* 158 ions, obtained by decarboxylation of the two lactones **10b** and **10c** and by the loss of N_2 from **10a** under EI conditions, exhibit very similar CID spectra (correlation coefficients $r_{10b-10c} = 0.9978$, $r_{10a-10b} = 0.9878$). Comparison of the CID spectra of these *m/z* 158 ions with that obtained by EI of 2-phenyl-1,5-hexadiene (**20**) (see Figs 4 and 7) also show a high degree of similarity ($r_{10a-20} = 0.9895$, $r_{10b-20} = 0.9970$, $r_{10c-20} = 0.9973$). These results lead to the conclusion that the *m/z* 158 ions obtained from **10a**, **10b**, **10c** and **20** may have identical structures (Scheme 4). Ring opening of the aryl- and alkyl-substituted cyclohexane-1,4-diyl cation radicals has been demonstrated previously in the condensed phase.[11] On the other hand, the results of the CID measurements show that these ions do not isomerize to phenylcyclohexene structures **17**, **18** and **19** by hydrogen migrations ($r_{10a-17} = 0.5543$, $r_{10b-18} = 0.5650$, $r_{10c-19} = 0.0149$; see Figs 4 and 6), in contrast to the data reported on the chemistry of cyclohexane-1,4-diyl radical cation in solution,[12,13] or to methyl phenylcyclopentenes **12**–**16** ($r_{10a-12} = 0.0201$; $r_{10b-13} = 0.0190$, $r_{10c-14} = 0.0280$, $r_{10a-15} = 0.0305$, $r_{10b-16} = 0.0289$; see Figs 4 and 5), by a skeletal rearrangement, which might be involved in the elimination processes, by analogy to the ion chemistry of cyclohexyl derivatives.[14–16] The above information on the isomerization and structure retention behavior of the $C_{12}H_{14}^{+\cdot}$ radical cations is summarized in Scheme 4.

The isomeric ionized phenylcyclohexenes **17**, **18** and **19** may be formed by a 1,2-elimination of acetic acid from phenylcyclohexyl acetates **7**, **8** and **9**. The isomeric



Scheme 3.

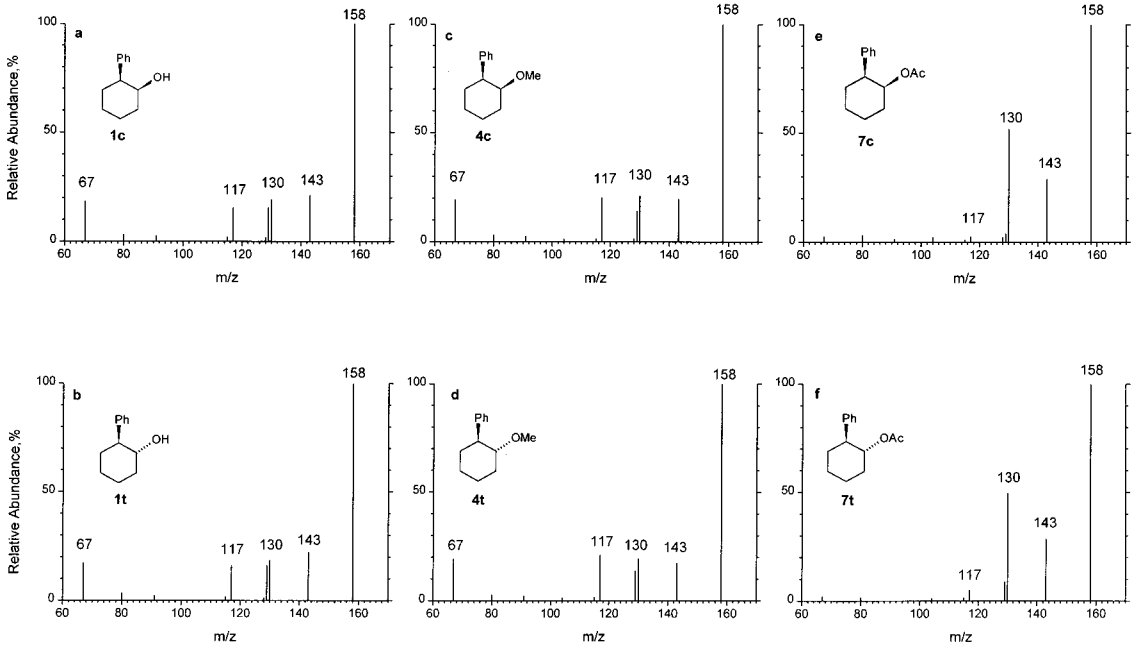


Figure 1. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $[M-ROH]^{+\cdot}$ ions, obtained upon EI from stereoisomeric 2-phenylcyclohexanols and their methyl ethers and acetates: (a) **1c**; (b) **1t**; (c) **4c**; (d) **4t**; (e) **7c**; (f) **7t**.

1- and 3-phenylcyclohexenes **17** and **18** exhibit similar CID spectra ($r_{17-18} = 0.9849$), which are entirely different from that of 4-phenylcyclohexene **19** ($r_{17-19} = 0.0250$; see Fig. 6). The most abundant *m/z* 104 ion in the CID spectrum of **19** corresponds to ionized styrene, which is obtained by a retro-Diels–Alder fragmentation from this particular isomer. These findings suggest possible isomerization of ionized **18** to the more stable ionized **17**, in contrast to the retention of structure of the molecular ion of **19** (Scheme 5). It should be noted that similar CID spectra do not exclude retention of structural features of isomeric ions, which may undergo similar fragmentations.

1,4-Elimination of H_2O and MeOH from *cis*-1,2- and 1,3-phenylcyclohexanols **1c** and **2c** and from their methyl ethers **4c** and **5c** may result (at least in part) in ionized 2-phenylbicyclo[2.2.0]hexane (**34**). We were not successful in our attempts to synthesize this standard compound. Therefore, diazine **11a** and lactone **11b** were used as precursors of $[\mathbf{34}]^{+\cdot}$. The *m/z* 158 ions, obtained by loss of N_2 from **11a** and by decarboxylation of **11b** under EI conditions, exhibit identical CID

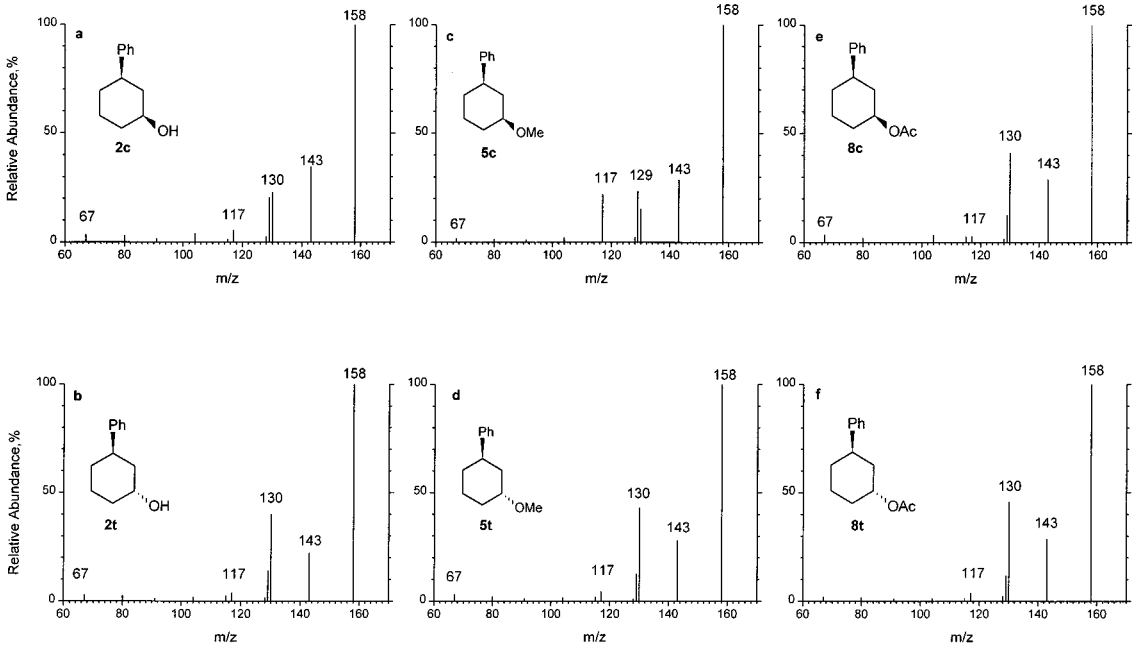


Figure 2. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $[M-ROH]^{+\cdot}$ ions, obtained upon EI from stereoisomeric 3-phenylcyclohexanols and their methyl ethers and acetates: (a) **2c**; (b) **2t**; (c) **5c**; (d) **5t**; (e) **8c**; (f) **8t**.

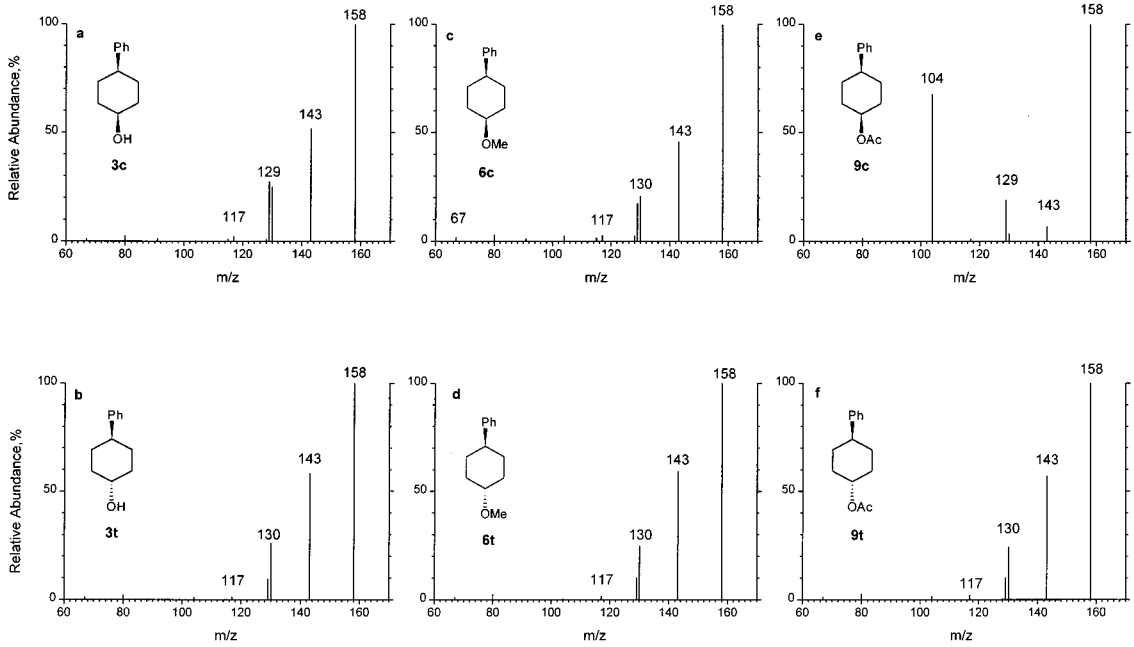


Figure 3. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 [M − ROH]$^{+\cdot}$ ions, obtained upon EI from stereoisomeric 4-phenylcyclohexanols and their methyl ethers and acetates: (a) **3c**; (b) **3t**; (c) **6c**; (d) **6t**; (e) **9c**; (f) **9t**.

spectra ($r_{\mathbf{11a-11b}} = 0.9876$). These CID spectra are similar to those of **17** and **18** ($r_{\mathbf{11a-17}} = 0.9878$, $r_{\mathbf{11a-18}} = 0.9810$), suggesting possible isomerization of [**34**]$^{+\cdot}$ or its corresponding 2-phenylcyclohexane-1,4-diyl cation radical to [**17**]$^{+\cdot}$ (see Scheme 5).

The phenylbicyclo[3.1.0]hexane CID standards **27–30** were prepared in order to examine various possible *cis*-1,3-elimination processes. The CID spectrum of the *m/z* 158 molecular ion of 1-phenylbicyclo[3.1.0] hexane (**28**) is also similar to the CID spectra of 1- and 3-phenylcyclohexenes **17** and **18** ($r_{\mathbf{17-28}} = 0.9891$, $r_{\mathbf{18-28}} = 0.9915$). This finding indicates isomerization of ionized 1-phenylbicyclo[3.1.0]hexane (**28**) to the 1-phenylcyclohexene structure **17** by opening of the cyclopropane ring followed by hydrogen transfer (Scheme 5). Isomerization of cyclopropane radical cations by ring opening has been observed and discussed long time ago.[17] It is interesting to note here that, in contrast to **28**, the different CID spectra of **29** and of the stereoisomeric *syn*- and *anti*-bicyclo[3.1.0]hexane pairs **27** and **30** indicate retention of the original structures in their radical cations.

The above results suggest isomerization of the cation radicals of **18** and of the strained bicyclic structures **28**

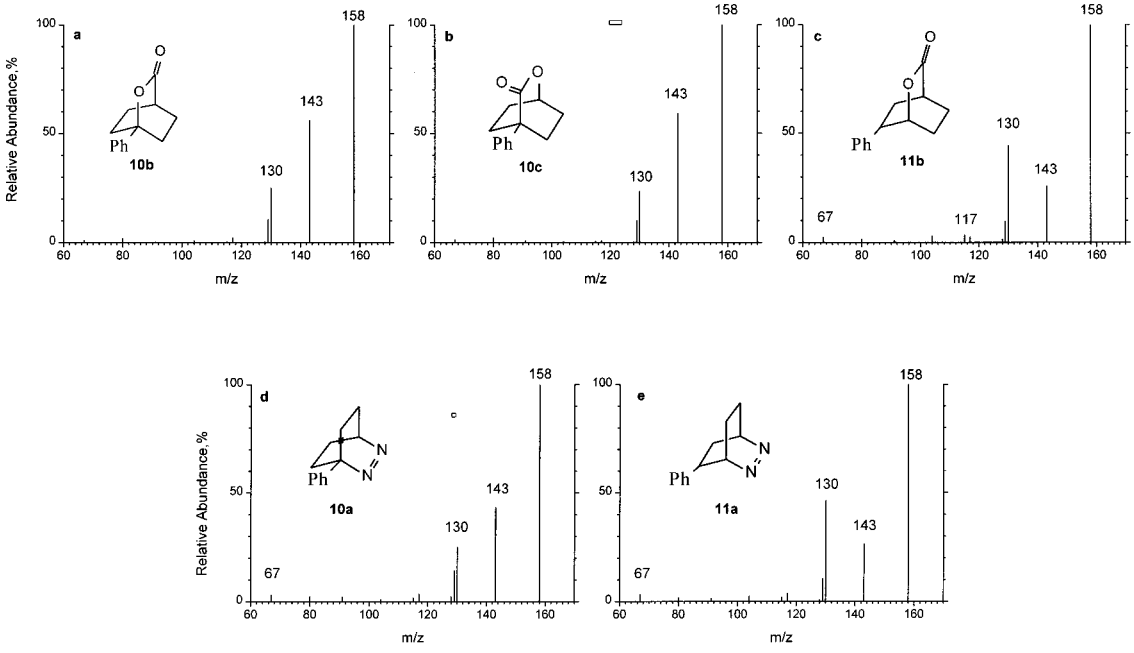


Figure 4. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 [M − CO_2]$^{+\cdot}$ and [M − N_2]$^{+\cdot}$ ions, obtained upon EI from bicyclic lactones and azines: (a) **10b**; (b) **10c**; (c) **11b**; (d) **10a**; (e) **11a**.

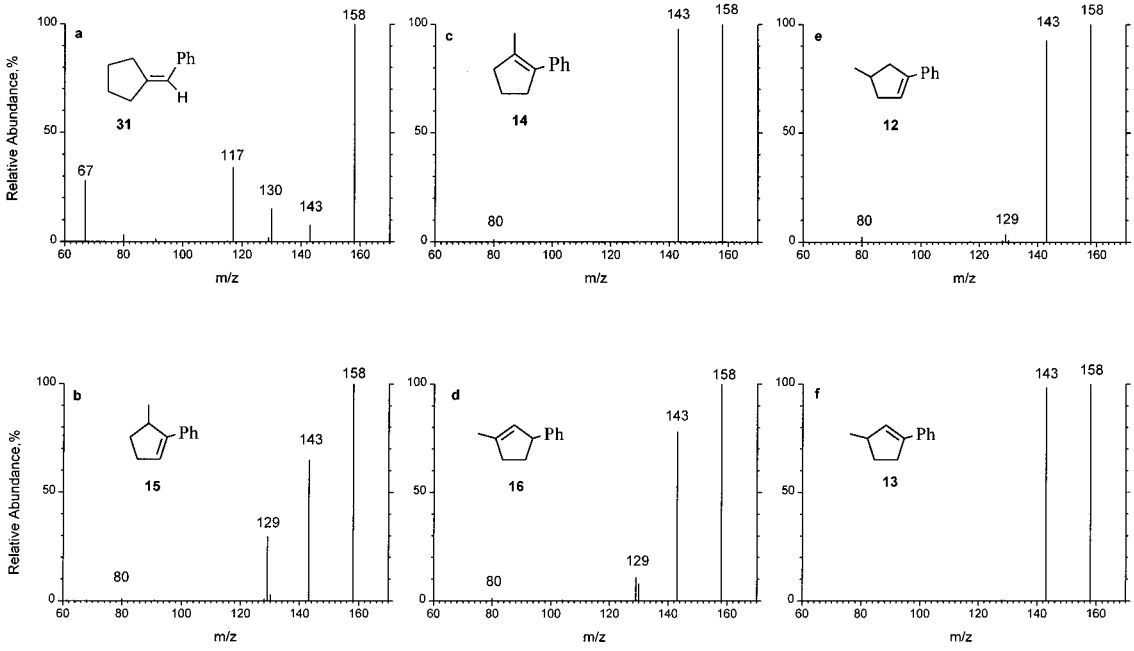


Figure 5. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $M^{+\cdot}$ ions, obtained upon EI from isomeric substituted cyclopentenes: (a) **31**; (b) **15**; (c) **14**; (d) **16**; (e) **12**; (f) **13**.

and **34** to the monocyclic isomer **17** (Scheme 5) and that of **32** to the acyclic isomer **20** (Scheme 4).

With the exception of the above species, the CID spectra of the *m/z* 158 ions obtained from the examined isomeric standards exhibit significantly different features (often in terms of relative ion abundances), which permit clear structural distinctions. The isomerization processes proposed in Schemes 4 and 5 show that struc-

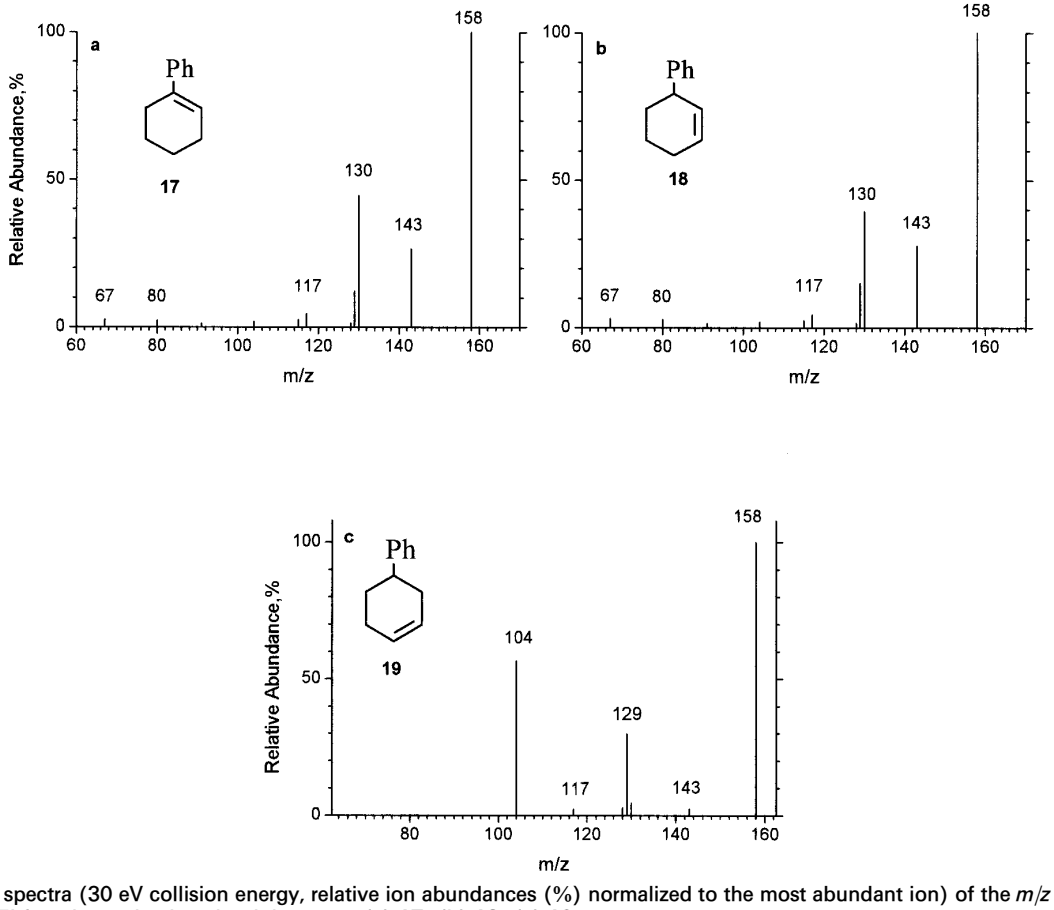


Figure 6. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $M^{+\cdot}$ ions, obtained upon EI from isomeric phenylcyclohexenes: (a) **17**; (b) **18**; (c) **19**.

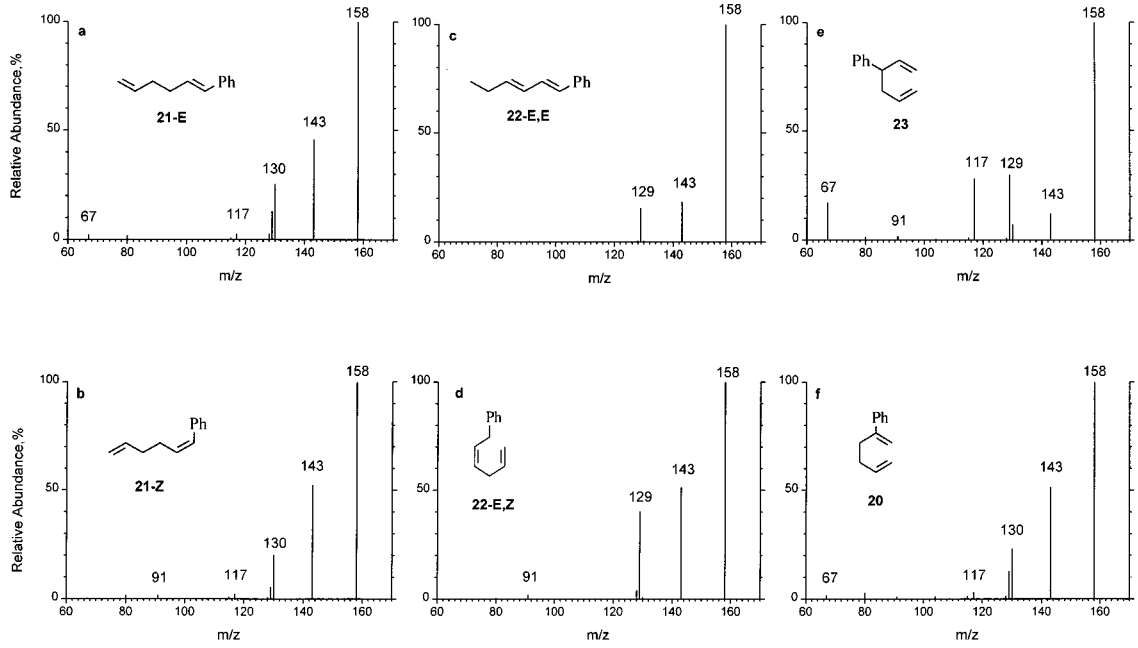


Figure 7. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $M^{+\cdot}$ ions, obtained upon EI from isomeric phenylhexadienes: (a) **21-*E***; (b) **21-*Z***; (c) **22-*EE***; (d) **22-*EZ***; (e) **23**; (f) **20**.

tural assignments of the *m/z* 158 ions, based on comparison of CID spectra, are not unlimited.

trans-4-Phenylcyclohexanol and its methyl ether and acetate

The *m/z* 158 $[M - H_2O]^{+\cdot}$ ion, obtained from *trans*-4-phenylcyclohexanol (**3t**), the $[M - MeOH]^{+\cdot}$ ion from *trans*-4-phenylcyclohexyl methyl ether (**6t**) and the $[M - AcOH]^{+\cdot}$ ion from *trans*-4-phenylcyclohexyl acetate (**9t**), show identical CID spectra ($r_{\mathbf{3t-6t}} = 0.9986$, $r_{\mathbf{3t-9t}} = 0.9987$) and, consequently, the elimination product ions obtained from the alcohol, ether and acetate appear to have the same structure. The common structure of the elimination product ions indicates similar mechanism for the three elimination processes.

The CID spectra of the above *m/z* 158 $[M - ROH]^{+\cdot}$ ion formed from **3t**, **6t** and **9t** exhibit great similarity to those obtained from **10a**, **10b** and **10c** (see Scheme 4; compare Figs 3 and 4; $r_{\mathbf{3t-10a}} = 0.9989$, $r_{\mathbf{3t-10b}} = 0.9973$, $r_{\mathbf{3t-10c}} = 0.9981$), whereas they differ considerably from those of other precursors (e.g. $r_{\mathbf{3t-17}} = 0.5653$,

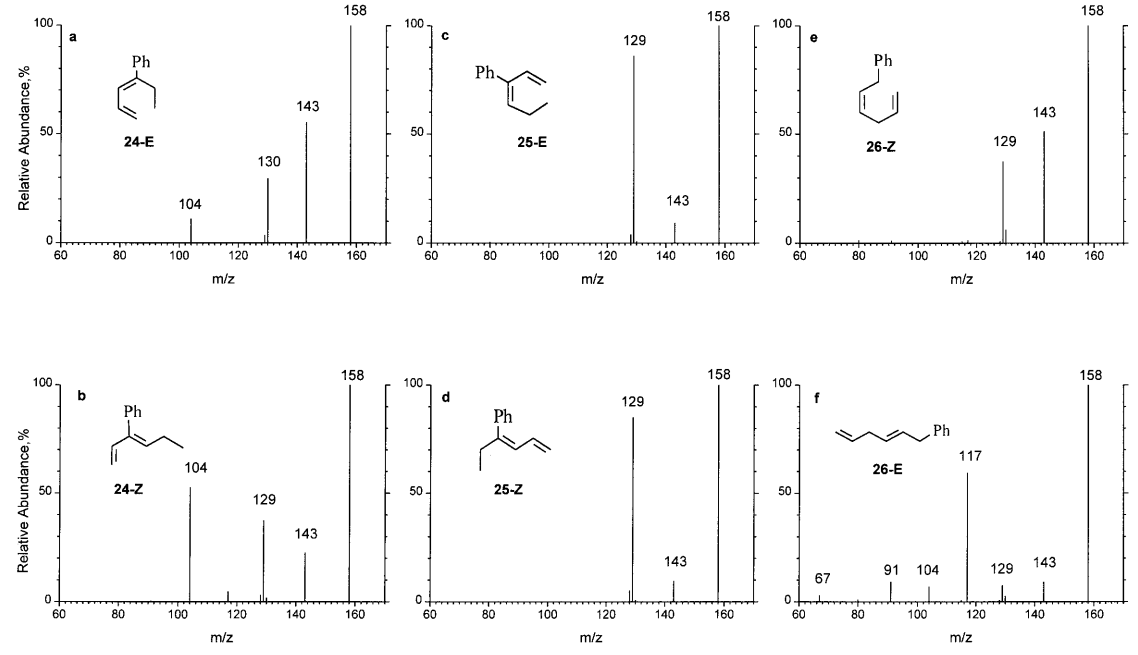


Figure 8. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $M^{+\cdot}$ ions, obtained upon EI from isomeric phenylhexadienes: (a) **24-*E***; (b) **24-*Z***; (c) **25-*E***; (d) **25-*Z***; (e) **26-*Z***; (f) **26-*E***.

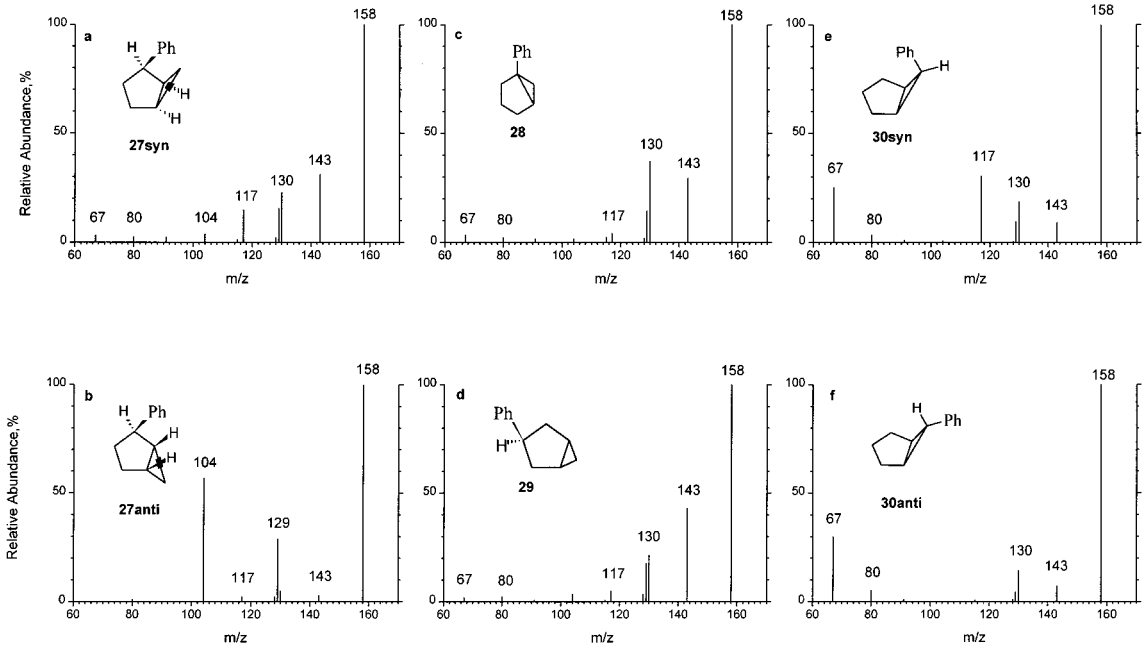
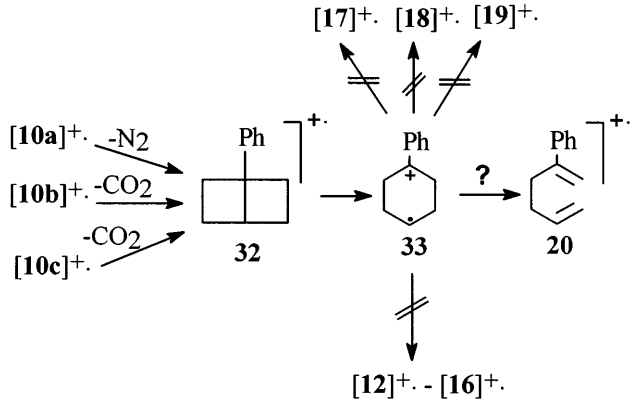
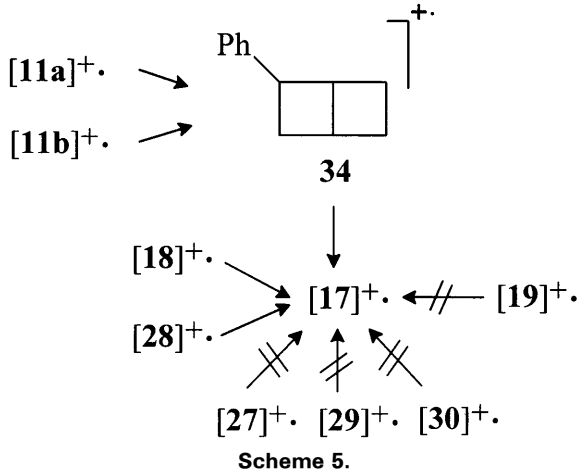


Figure 9. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 158 $M^{+\cdot}$ ions, obtained upon EI from isomeric phenylbicyclo[3.1.0]hexanes: (a) **27-*syn***; (b) **27-*anti***; (c) **28**; (d) **29**; (e) **30-*syn***; (f) **30-*anti***.

$r_{3t-18} = 0.6433$, $r_{3t-19} = 0.015$). These CID results, summarized in Scheme 6, are in good agreement with the results of the EI mass spectral measurements and of the deuterium labeling studies (see Scheme 2).[7,8]



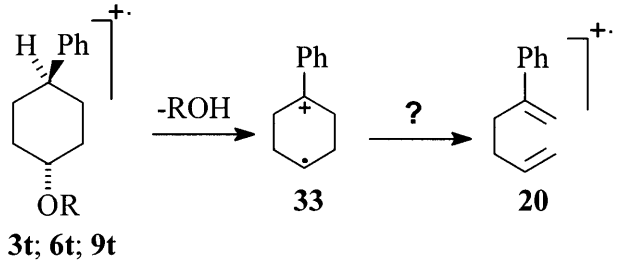
Scheme 4.



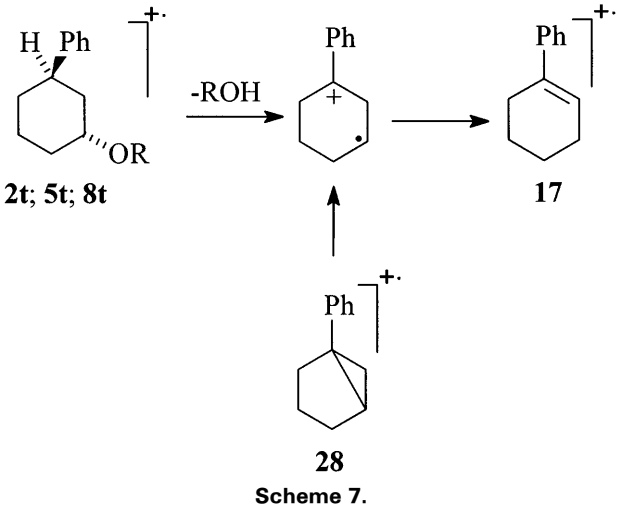
Scheme 5.

trans-3-Phenylcyclohexanol and its methyl ether and acetate

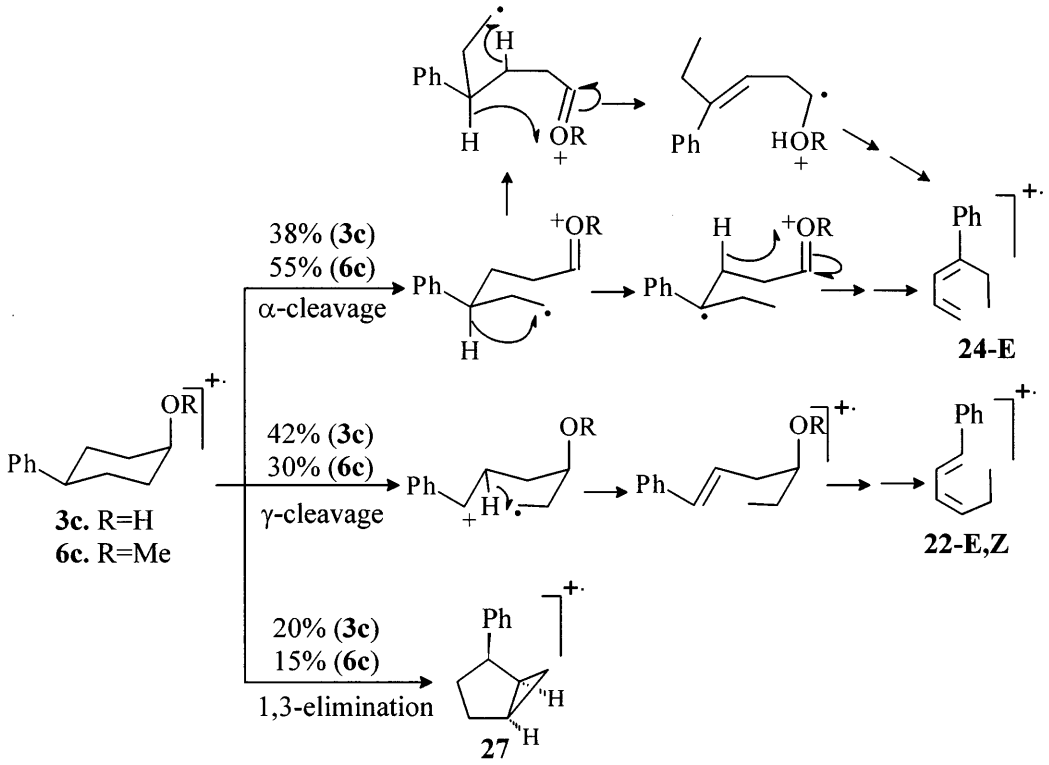
In analogy to *trans*-4-phenylcyclohexanol, the *m/z* 158 $[M - H_2O]^{+\cdot}$ ion obtained from *trans*-3-phenylcyclohexanol (**2t**), the $[M - MeOH]^{+\cdot}$ ion from *trans*-3-phenylcyclohexyl methyl ether (**5t**) and the $[M - AcOH]^{+\cdot}$ ion from *trans*-3-phenylcyclohexyl acetate



Scheme 6.



Scheme 7.



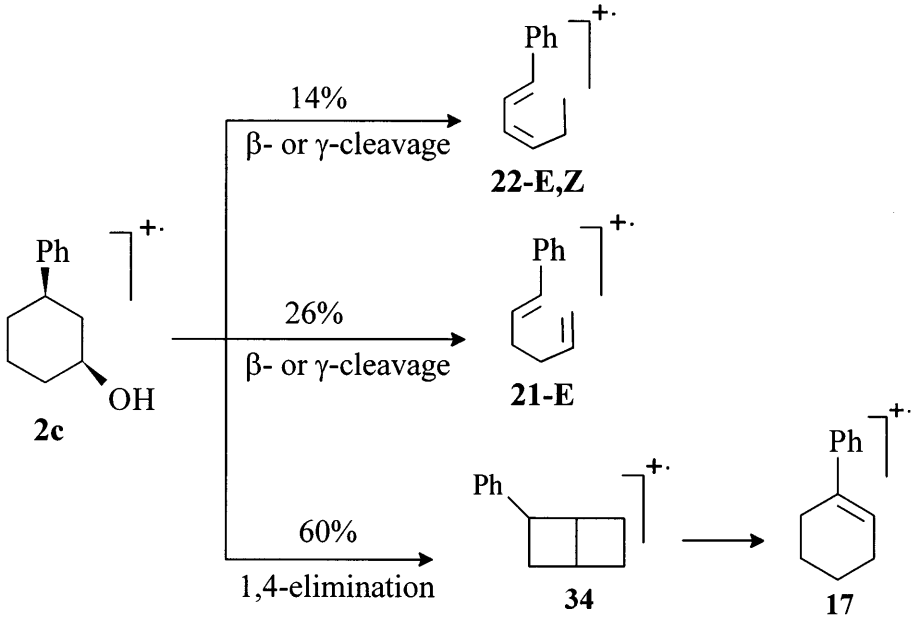
Scheme 8.

(**8t**) also show almost identical CID spectra (r_{2t-5t} = 0.9985, r_{2t-8t} = 0.9887). Consequently, the elimination product ions obtained from alcohol, ether and acetate appear to have a common structure, indicating the occurrence of a similar mechanism for the three elimination processes.

The CID spectra of the above *m/z* 158 $[M - ROH]^+$ ions formed from **2t**, **5t** and **8t** exhibit great similarity to those of **17** and **28** (compare Fig. 2 with Figs 6 and 9; r_{2t-17} = 0.9886, r_{2t-28} = 0.9976), whereas they considerably differ from those of other precursors. This conclusion, summarized in Scheme 7, is fully consistent with the results of the EI mass spectral measurements and of the deuterium labeling studies (see Scheme 2).

cis-4-Phenylcyclohexanol and its methyl ether

Previous deuterium labeling studies have shown that the elimination of H_2O from the $M^{+\cdot}$ ion of *cis*-4-phenylcyclohexanol (**3c**) and of methanol from its methyl ether (**6c**) involves the benzylic hydrogen atom from position 1 to a relatively small extent (24–30%).[7,8] This finding is consistent with the large distance between that H-atom and the oxygen in the *cis*-isomers, which does not allow a 1,4-elimination involving the bezylic position. The major origin of the hydrogen atom abstracted in the course of this elimination has not been established in that study.



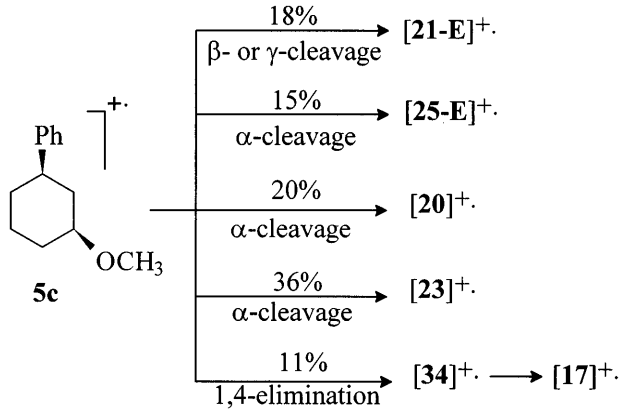
Scheme 9.

It could be expected that in the absence of the 1,4-elimination channel, a 1,3-elimination process involving one of the hydrogen atoms from positions 3 or 5 will occur. Competing elimination processes initiated by ring cleavage are also possible in the cyclohexanol system. More than one location is accessible in the elimination of the ring-open species.

The computer-aided analysis of the CID spectral data leads to the conclusion that the $[M - H_2O]^{+\cdot}$ and $[M - MeOH]^{+\cdot}$ ions, obtained from **3c** and **6c**, respectively, are indeed mixtures of three isomeric ions [**22-EZ**]$^{+\cdot}$, [**24-E**]$^{+\cdot}$ and [**27**]$^{+\cdot}$, which are formed by initial α- or γ-cleavage, and, to a smaller extent, by a 1,3-elimination from the intact $M^{+\cdot}$ ions involving one of the hydrogen atoms from the homoallylic positions 3 and 5 (see Scheme 8). The CID study indicates preferential α-cleavage for the *cis*-ether **6c** (55%), in contrast to the corresponding alcohol **3c**, where the elimination of H_2O is initiated to a similar extent by the α- and γ-cleavages (~40%). The preferential α-cleavage, preceding the elimination of methanol from the $M^{+\cdot}$ ions of *cis*-ethers, has been previously deduced from the deuterium labeling study, and it has been ascribed to the lower energy of α-cleavage of ethers as compared with the corresponding alcohols.[18,19]

cis-3-Phenylcyclohexanol and its methyl ether

The comparative analysis of the CID measurements of *cis*-3-phenylcyclohexanol (**2c**) and of its methyl ether (**5c**) with a variety of standards leads to the conclusion that the $[M - H_2O]^{+\cdot}$ and $[M - MeOH]^{+\cdot}$ ions obtained from **2c** and **5c**, respectively, are mixtures of isomeric ions, which are formed by elimination processes initiated by α-, β- or γ-cleavage, and by a 1,4-elimination from the intact $M^{+\cdot}$ ions involving one of the hydrogen atoms from position 4. The difference between the alcohol and the ether in this series is much more pronounced than in the case of **3c** and **6c**. *cis*-3-Phenylcyclohexanol (**2c**) gives rise to three $[M - H_2O]^{+\cdot}$ ions shown in Scheme 9, while five isomeric $[M - MeOH]^{+\cdot}$ ions, shown in Scheme 10, are formed from the corresponding methyl ether **5c**. The 1,4-elimination of H_2O is the predominant process taking place in **2c** (60%), in contrast to **5c**, where the 1,4-elimination of MeOH is of minor importance (only 11%). The CID study indicates preferential α-cleavage for the *cis*-ether **5c** affording three isomeric fragment ions (see Scheme 10), in contrast to the corresponding alcohol **2c**, where the elimination initiated by α-cleavage is insignificant, and no structure related to such a process has been suggested by the CID data analysis (see Scheme 10). Here again the preferential α-cleavage of the *cis*-ethers may be ascribed to the lower energy of such bond cleavage in ethers, as compared with the corresponding alcohols.[18] Mechanistic pathways for three elimination processes preceded by α-, β- and γ-C—C bond cleavages are proposed in Scheme 11.

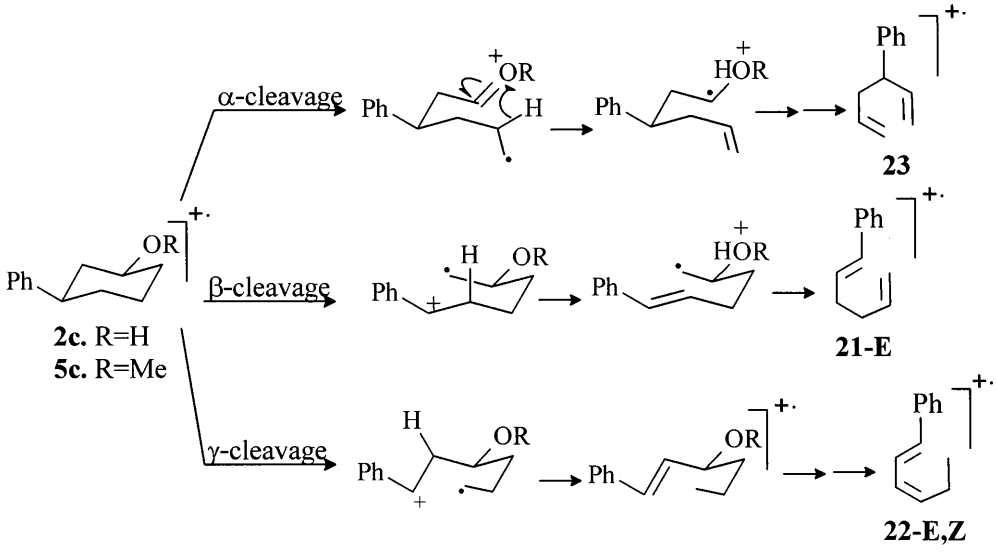


Scheme 10.

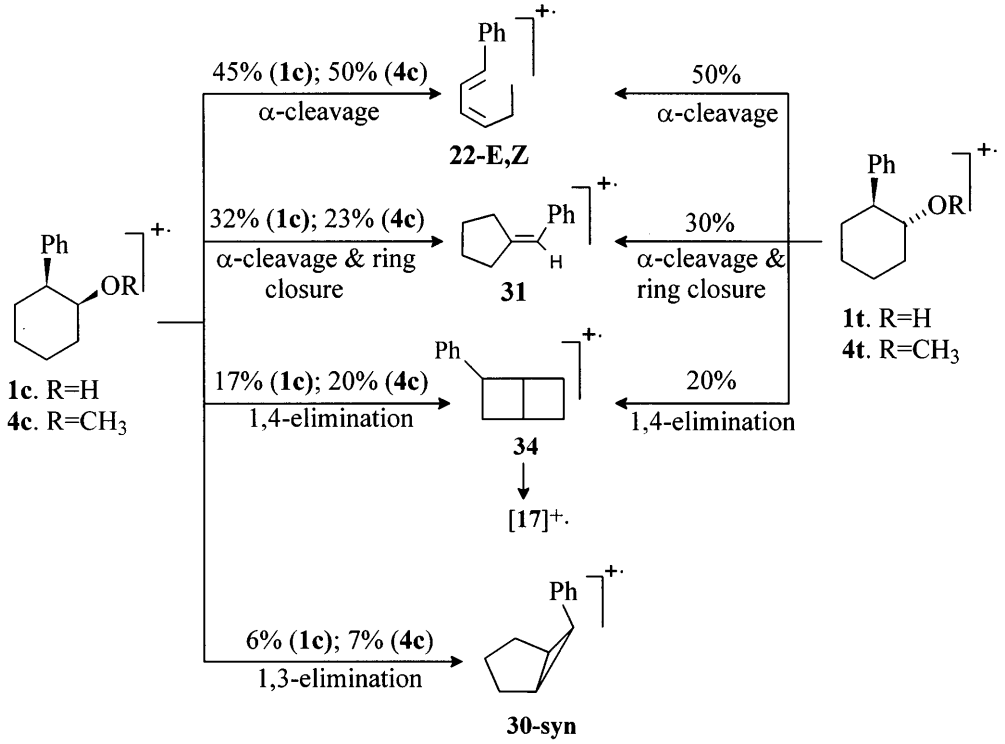
cis- and *trans*-2-phenylcyclohexanols and their methyl ethers

The results of the EI mass spectral measurements, listed in Tables 1 and 2, show similar behavior for *cis*- and *trans*-2-phenylcyclohexanols (**1c** and **1t**) and for the corresponding stereoisomeric methyl ethers (**4c** and **4t**). This behavior suggests similar mechanistic pathways for each of the two stereoisomeric pairs.

The CID spectra of the *m/z* 158 ions obtained from the stereoisomeric alcohols **1c** and **1t** are similar ($r_{1c-1t} = 0.9700$). The $[M - MeOH]^{+\cdot}$ ions obtained



Scheme 11.

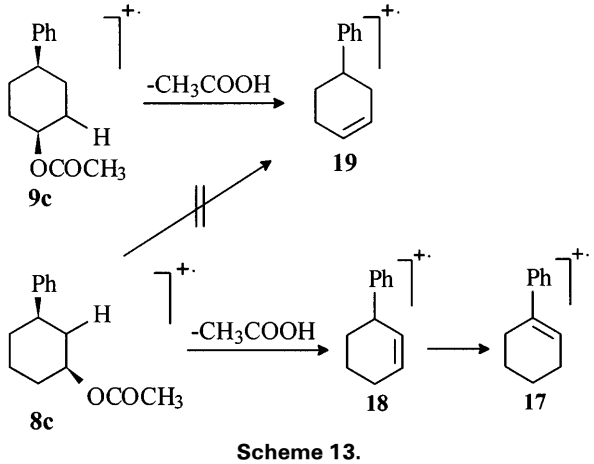


Scheme 12.

from the corresponding methyl ethers **4c** and **4t** also give rise to similar CID spectra ($r_{4c-4t} = 0.9789$). Moreover, identity has been found in the CID spectra of the $[M - H_2O]^{+\cdot}$ and $[M - MeOH]^{+\cdot}$ ions ($r_{1c-4c} = 0.9880$, $r_{1t-4t} = 0.9989$). Consequently, the elimination product ions obtained from the stereoisomeric alcohols and ethers appear to have similar structures, indicating similar mechanisms for the elimination processes of these precursors.

The comparative analysis of the CID measurements of *trans*-2-phenylcyclohexanol **1t** and of its methyl ether **4t** with a variety of standards leads to the conclusion that the *m/z* 158 $[M - H_2O]^{+\cdot}$ and $[M - MeOH]^{+\cdot}$ ions obtained from them are a mixture of three isomeric ions, **23-EZ**, **31** and **17**, which are formed by elimination processes initiated by an α-cleavage (the former two) and by a 1,4-elimination from the intact $M^{+\cdot}$ ions involving one of the hydrogen atoms from position 4 (see Scheme 12).

The analysis of the results of CID measurements of the *cis*-isomers **1c** and **4c** suggests the formation of an additional minor bicyclic fragment ion, **30-*syn*** (6–7%), by a 1,3-elimination process from the intact $M^{+\cdot}$ ions involving the homobenzylic hydrogen atom from position 3 (see Scheme 12). The axial conformation of the hydroxy and methoxy groups in the *cis*-alcohol and ether, respectively, may explain the formation of this fourth product ion from **1c** and **4c** under EI conditions.

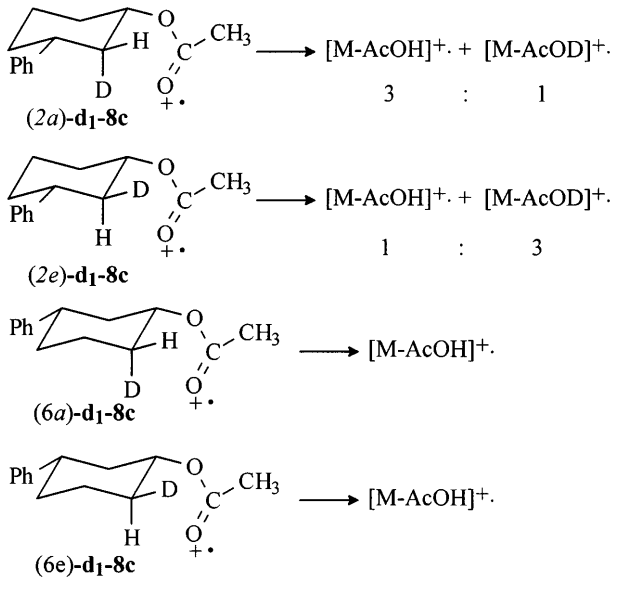


Scheme 13.

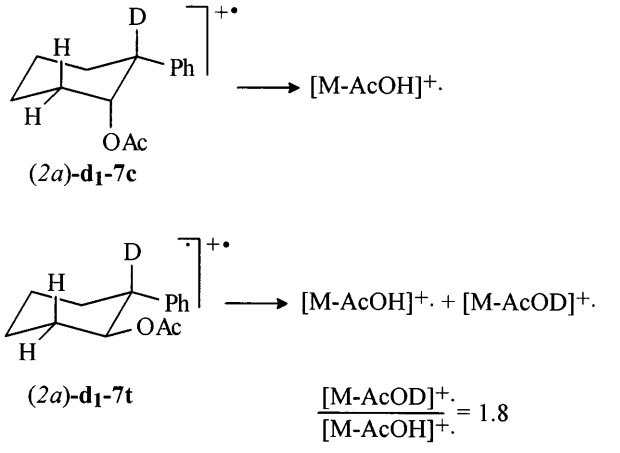
2-, 3- and 4-phenylcyclohexyl acetates

It has been shown before that the mechanisms of the EI-induced elimination of acetic acid from *trans*-3- and -4-phenylcyclohexyl acetate (**8t** and **9t**) are similar to those of the corresponding *trans*-alcohols and methyl ethers (**2t** and **5t** and **3t** and **6t**) (Schemes 6 and 7). The deuterium labeling study demonstrated major abstraction of a hydrogen atom from the benzylic position, which is accessible in the *trans*-isomers, and the analysis of the present results of CID measurements indicate identical structures of the $[M - AcOH]^{+\cdot}$, $[M - MeOH]^{+\cdot}$ and $[M - H_2O]^{+\cdot}$ ions in each of the two series.

The previously reported deuterium labeling study of *cis*-3- and -4-phenylcyclohexyl acetates **8c** and **9c** has shown major abstraction of hydrogen from the β-positions in the course of the elimination of AcOH, which is consistent with the expected McLafferty-type 1,2-elimination.[9] This pathway would lead to the formation of 4-phenylcyclohexene radical cation $[19]^{+\cdot}$ from **9c** and of a mixture of $[19]^{+\cdot}$ and $[18]^{+\cdot}$ (the latter is indistinguishable from $[17]^{+\cdot}$) from **8c**. The results of the CID measurements support the above suggestion for **9c**: the CID spectrum of its $[M - AcOH]^{+\cdot}$ ion is identical with that of $[19]^{+\cdot}$ ($r_{9c-19} = 0.9980$). On the other hand, the CID spectrum of *cis*-3-phenylcyclohexyl acetate (**8c**) indicates the formation of $[18]^{+\cdot}$, which



Scheme 14.



Scheme 15.

Table 4. Relative abundances of MH^+ and $[MH - ROH]^+$ ions in the isobutane-CI mass spectra of stereoisomeric 4-phenylcyclohexanols and their methyl ethers and acetates

	$[MH]^+$	$[MR - ROH]^+$	$[MH - ROH]^+/[MH]^+$	*trans/cis*
3c	16	100	6.2	
3t	0.2	100	500	83
6c	90	100	1.1	
6t	54	100	1.9	1.7
9c	19	100	5.3	
9t	18	100	5.5	1.0

presumably rearranges to $[\mathbf{17}]^{+\cdot}$, as the only elimination product ($r_{\mathbf{8c-17}} = 0.9990$, $r_{\mathbf{8c-18}} = 0.9985$, $r_{\mathbf{8c-19}} = 0.2558$; see Scheme 13). No formation of $[\mathbf{19}]^{+\cdot}$ from **8c** was indicated in this measurement. The latter result indicates preferential abstraction of hydrogen from the homobenzylic position 2 and no abstraction from position 6, in the course of this elimination process.

The above conclusion finds support in the EI mass spectral measurements of the stereospecifically deuterium labeled acetates (*2a*)-$\mathbf{d_1}$-**8c**, (*2e*)-$\mathbf{d_1}$-**8c**, (*6a*)-$\mathbf{d_1}$-**8c** and (*6e*)-$\mathbf{d_1}$-**8c** (Scheme 14). Only the first two isotopomers, (*2a*)-$\mathbf{d_1}$-**8c** and (*2e*)-$\mathbf{d_1}$-**8c**, deuterium labeled at C-2, exhibit partial elimination of AcOD, whereas the other two, (*6a*)-$\mathbf{d_1}$-**8c** and (*6e*)-$\mathbf{d_1}$-**8c**, with the label at position 6, undergo exclusive elimination of AcOH. The $[M - AcOH]^{+\cdot}/[M - AcOD]^{+\cdot}$ ion abundance ratios in the mass spectra of (*2a*)-$\mathbf{d_1}$-**8c** and (*2e*)-$\mathbf{d_1}$-**8c** show preferential abstraction of the equatorial hydrogen atom in the course of this elimination process. The latter result is consistent with the reported stereospecificity of the McLafferty rearrangement and of related processes in various *trans*-4-substituted *tert*-butylcyclohexanes.[20]

The analysis of the results of the CID measurements

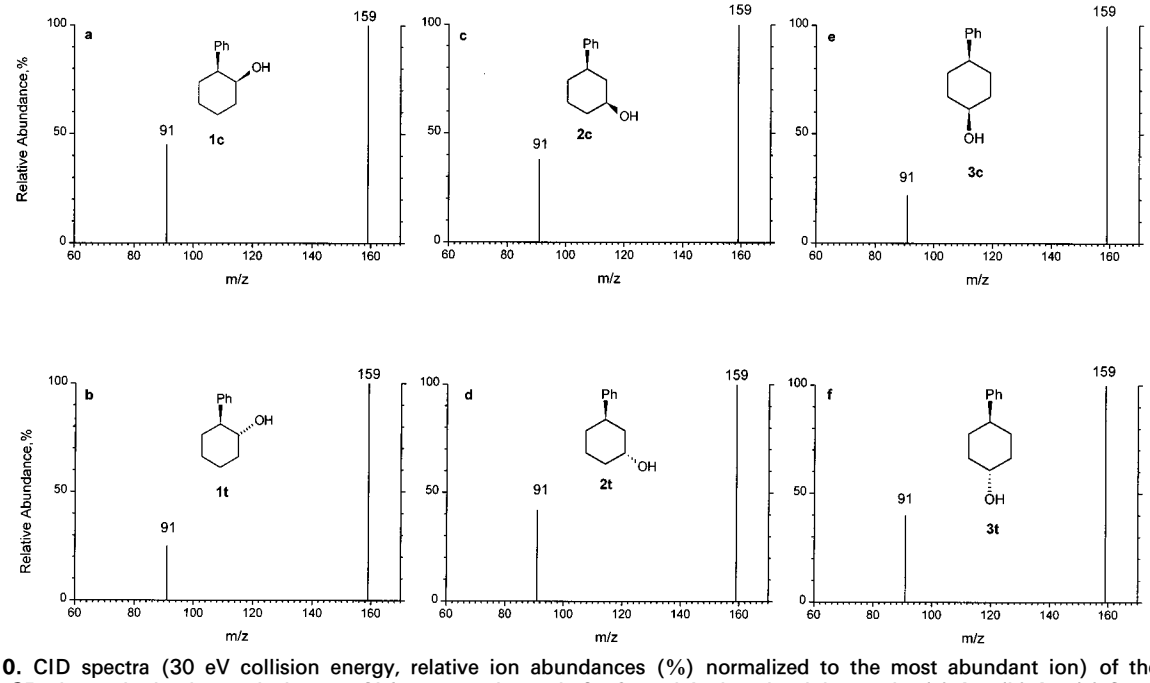


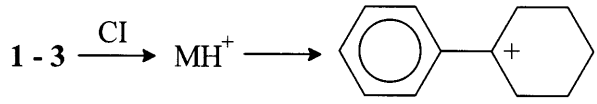
Figure 10. CID spectra (30 eV collision energy, relative ion abundances (%) normalized to the most abundant ion) of the *m/z* 159 $[MH - H_2O]^{+\cdot}$ ions, obtained upon isobutane-CI from stereoisomeric 2-, 3- and 4-phenylcyclohexanols: (a) **1c**; (b) **1t**; (c) **2c**; (d) **2t**; (e) **3c**; (f) **3t**.

of 2-phenylcyclohexyl acetates (**7c** and **7t**) show that the elimination of acetic acid in these two stereoisomers gives rise to the same product ion $[\mathbf{17}]^{+\cdot}$ (indistinguishable from $[\mathbf{18}]^{+\cdot}$, $r_{\mathbf{7c-7t}} = 0.9992$, $r_{\mathbf{7c-18}} = 0.9998$, $r_{\mathbf{7t-18}} = 0.9956$, $r_{\mathbf{7c-17}} = 0.9789$, $r_{\mathbf{7t-17}} = 0.9849$). This result might be interpreted as an indication of a common route of elimination in **7c** and **7t**. However, deuterium labeling of the benzylic position shows that the elimination of acetic acid occurs via distinctly different mechanistic pathways in the two stereoisomeric acetates (Scheme 15). The benzylic hydrogen (at position 2) is largely involved in the elimination only in the *trans*-acetate **7t**, whereas exclusive abstraction of a hydrogen from position 6 occurs in the *cis*-isomer **7c**.

Elimination upon chemical ionization

The isobutane-CI mass spectra of the stereoisomeric pairs of 4-phenylcyclohexanols **3** and their methyl ethers **6** and acetates **9** afford most abundant *m/z* 159 [phenyl-C_6H_{10}]$^+$ cations by the elimination of H_2O, MeOH and AcOH, respectively, from the MH^+ ions. The ion abundance ratios (shown in Table 4) are systematically higher in the isobutane-CI mass spectra of the *trans*-isomers. The difference between the stereoisomers is relatively large in the alcohols, but much smaller in the case of the ethers and acetates. This distinctive behavior, which indicates greater stability for the MH^+ ions of the *cis*-isomers, may be explained by the internal hydrogen bonding between the oxygen functions and the phenyl ring, which is possible only in the *cis*-configuration. This behavior is consistent with the reported higher proton affinities of *cis*-4-phenylcyclohexyl methyl and ethyl ethers, as compared with the *trans*-epimers.[21]

The CID spectra of the *m/z* 159 ions obtained from the three *cis–trans* pairs of 2-, 3- and 4-phenylcyclohexanols **1–3** (presented in Fig. 10) show a single fragment at *m/z* 91 ($C_7H_7^+$ product ion). This similar behavior of all the isomers suggests isomerization of the *m/z* 159 ion to a common structure in the course of the elimination processes. The simplicity of the CID spectra of the *m/z* 159 ions is consistent with the 1-phenylcyclohexyl structure of these ions (Scheme 16). The variation in the ion abundance ratios [*m/z* 91]$^+$/[*m/z* 159]$^+$ in the CID spectra may be due to the different internal energies of the *m/z* 159 ions when obtained upon CI by different pathways from different isomeric and stereoisomeric precursors.



Scheme 16.

It has often been stated that mass spectral stereochemical effects observed in stereoisomers are pronounced under CI conditions, which are less energetic than those upon EI.[22] The above results show that this proposed generalization, which is often true, does not hold in the case of the isomeric phenylcyclohexanol methyl ethers and their acetates. The cyclic transition states, which are involved in the mechanistic pathways of the EI-induced lower energy eliminations from the *cis*-isomers (specifically involving the benzylic hydrogens in these particular stereoisomers), result in highly stereospecific behavior upon EI. On the other hand, the elimination processes occurring under CI conditions are simple C—O bond dissociations, and they involve the external proton in both *cis*- and *trans*-isomers. The quantitative difference between the stereoisomers results in this case from the small difference (slightly above 1 kcal/mol (1 kcal = 4.184 kJ)[20]) in the thermochemical stability of the MH^+ ions.

Table 5. CID mass spectra of [MH − ROH]$^+$ ions obtained from stereoisomeric 4-phenylcyclohexanols and their methyl ethers and acetates upon isobutane-CI

	[MH − ROH]$^+$	*m/z* 91
1c	100	46.1
1t	100	22.1
2c	100	38.7
2t	100	41.4
3c	100	22.5
3t	100	40.3
6c	100	52.3
6t	100	41.6
9c	100	37.6
9t	100	40.1

CONCLUSIONS

The results of this study demonstrate the power of the CID methodology in deducing detailed structural and mechanistic information in the chemistry (and stereochemistry) of gas-phase ions. It is important to note that the majority of the gas-phase isomeric phenyl-C_6H_9 radical cations, formed either by EI-induced fragmentation of stereoisomeric phenylcyclohexyl derivatives or by EI of a variety of phenyl-C_6H_9 isomers, retain their structural integrities. This behavior indicates relatively high energy barriers for the hydrogen transfer processes and for some skeletal rearrangements, which would result in the formation of the thermodynamically most stable species in the EI mass spectra of the phenylcyclohexyl derivatives and of the isomeric standards studied in this work. On the other hand, the CID spectra of the even-electron phenyl-$C_6H_{10}^+$ ions, produced by the CI-induced fragmentation from isomeric phenylcyclohexanols and their methyl ethers and acetates, show a high degree of similarity, suggesting loss of structural information under CI in this system.

EXPERIMENTAL

Mass spectrometry

EI- and CI-GC/MS analyses and CID measurements were carried out on a Finnigan TSQ-70B triple-stage quadrupole mass spectrometer. Separations by GC were performed on a DB-5 (0.25 μm film thickness) 30 m × 0.25 mm i.d. capillary column. The column temperature was programmed from 60 to 280 °C at 15–20 °C min^{-1}. The scan rate was 0.7 scan s^{-1}. EI measurements were performed at 70 eV and 150 °C ion source temperature. CI measurements were performed at 120 eV, 150 °C ion source temperature and 0.4 Torr

(indicated) reagent gas pressure (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 data presented for each system were obtained on a single day under identical conditions, in order to ensure reliable comparisons.

The computer-aided calculation of the relative contributions of the CID spectra of various standards was performed by minimization of the sums of mean squared differences between the intensity values of the simulated and the experimental spectra. The minimization was achieved by a standard procedure using the algorithm of Powell.[23]

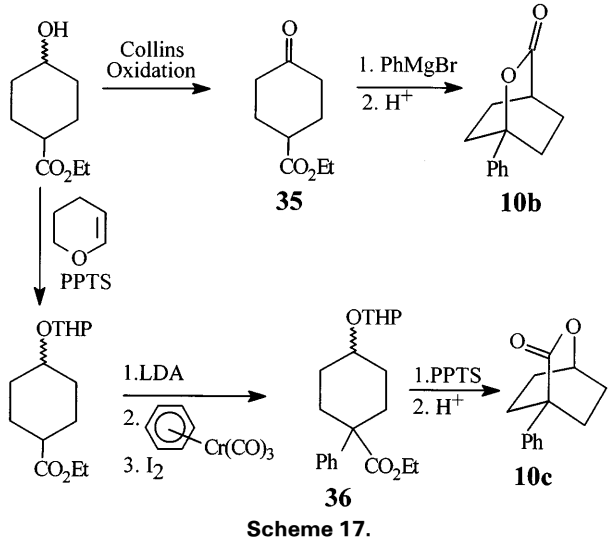
Materials

Tetrahydrofuran (THF), diethyl ether and benzene were freshly distilled under nitrogen from sodium benzophenone prior to use. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride and stored over 13X molecular sieves under argon.

Stereoisomeric **1**–**9**,[7–9] **10a**,[24] **12**,[25] **13**,[25] **14**,[26] **15**,[26] **16**,[27] **17**,[28] **18**,[29a] **19**,[29,30] **20**,[30] **21**,[30] **22**,[31] **23**,[30] **24**,[32] **27**,[33] **28**,[34] **29**,[35] **30**,[34,36] and **31**[37] were prepared by routes reported in the literature.

Lactones **10b** and **10c** were prepared following routes shown in Scheme 17.

Lactone 10b.[38] Phenylmagnesium bromide, prepared from 0.1 g (4.6 mmol) of magnesium turnings and 0.7 g (4.6 mmol) of bromobenzene in 10 ml of dry diethyl ether, was added drop-wise to a solution of 0.65 g (3.8 mmol) of ethyl 4-oxocyclohexanecarboxylate (**35**) (prepared by CrO_3 oxidation of ethyl 4-hydroxycyclohexanecarboxylate) in 20 ml of diethyl ether. The white precipitate was dissolved in THF, the solution was stirred for 3.5 h, cooled to −5 °C, quenched with ice-cold 7% sulfuric acid and stirred overnight. The reaction mixture was extracted with diethyl ether, washed with saturated NaCl solution, dried over $MgSO_4$, concentrated under vacuum, and the resulting yellow oil was chromatographed on silica gel with 1:4 diethyl ether–hexane to yield 45% of **10b**. IR (film) 1720, 1680 cm^{-1}; ^1H NMR, δ 1.8–2.25 (m, 8H), 2.76 (s, 1H), 7.39 (m, 5H).



Scheme 17.

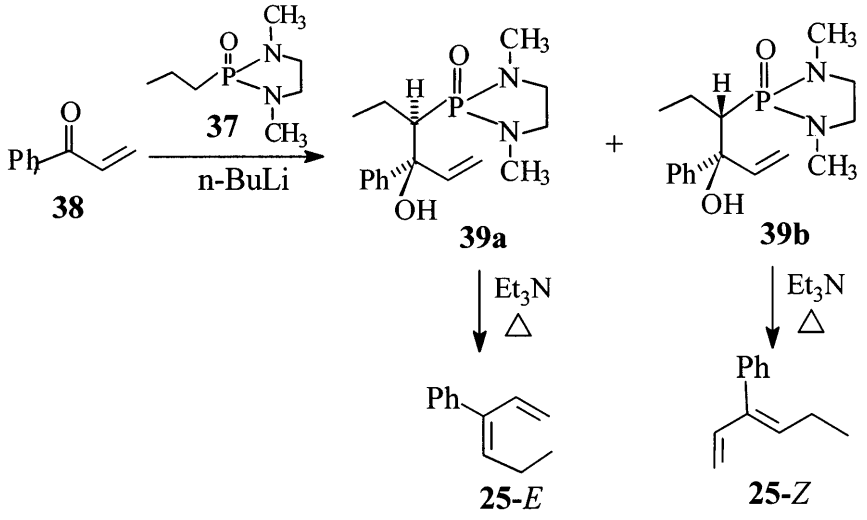
Lactone 10c. THP-ether of ethyl 4-hydroxycyclohexanecarboxylate (2.1 g, prepared with the use of pyridinium *p*-toluenesulfonate (PPTS)[39]) was added dropwise to a THF solution of lithium diisopropylamide (generated from n-butyllithium (5.25 ml of a 1.6 M solution in hexane) and diisopropylamine (1.3 ml, 9.3 mmol) in 15 ml of THF) at −78 °C under nitrogen. The mixture was warmed to 0 °C and stirred for 15 min, 20 ml of HMPA were added and a solution of 1.78 g of π-benzenechromium tricarbonyl in 25 ml of THF was added over 5 min at −78 °C. The resulting yellow solution was warmed to 0 °C, stirred for 30 min, cooled to −78 °C, a solution of 8.5 g (33 mmol) of iodine in 25 ml of THF was added and the mixture was allowed to warm to room temperature and left overnight with stirring. The THP-ether of ethyl 4-hydroxy-1-phenylcyclohexanecarboxylate (**36**) was extracted with diethyl ether, washed with 5% $NaHCO_3$, $Na_2S_2O_3$ and, saturated NaCl, dried over $MgSO_4$ and purified by column chromatography with diethyl ether–hexane (1:3). ^1H NMR, δ 1.23 (t, 3H), 1.4–2.0 (m, 14 H), 3.5 (m, 2H), 3.85 (m, 1H), 4.1 (q, 2H), 4.67 (br s, 1H), 7.3 (m, 5H).

A solution of **36** and PPTS (1 g, 8 mmol) in ethanol (4 ml) was stirred at 55 °C for 3 h. The solvent was evaporated in vacuum and the residue was chromatographed on a silica gel column to afford pure ethyl 1-phenyl-4-hydroxycyclohexanecarboxylate. This material was treated with 7% H_2SO_4, extracted with diethyl ether, washed with saturated NaCl solution, dried over $MgSO_4$, concentrated under vacuum and the resulting yellow oil was chromatographed on silica gel with 1:4 diethyl ether–hexane to yield **10c**. ^1H NMR, δ 1.8–2.25 (m, 8H), 4.76 (s, 1H), 7.8 (m, 5H).

25-*E* and 25-*Z*. (*E*)- and (*Z*)-3-phenyl-1,3-hexadienes **25-*E*** and **25-*Z*** were prepared following the route shown in Scheme 18.

Propylphosphonic dichloride (4 g, prepared by the reaction of 1-bromopropane with phosphorus trichloride and aluminum chloride) in diethyl ether was added to a solution of 2.5 g of *s*-dimethylethylenediamine in 200 ml of anhydrous diethyl ether and 50 ml of triethylamine with stirring at 0 °C under a nitrogen atmosphere and the solution was stirred for 3 h at 0 °C and overnight at room temperature. Addition of methylene chloride (50 ml) followed by filtration and evaporation yielded 3.12 g (73%) of *N*,*N*′-dimethyl-2-propyl-1,3,2-diazaphospholidene 2-oxide (**37**). ^1H NMR, δ 3.1 (m, 4H), 2.61 (d, J = 9.5 Hz, 6H), 2.2 (m, 2H), 1.1 (d, J = 15 Hz, 3H), 1.2 (d, J = 15 Hz, 2H).

n-BuLi (1.6 M in hexane, 2 ml) was added at −78 °C to a stirred solution of 0.5 g (2.8 mmol) of **37** in 20 ml of THF and 5 ml of HMPA under a nitrogen atmosphere. The solution was stirred for 30 min and 0.5 ml of 1-phenyl-2-propen-1-one (**38**) was added. After stirring for 2 h at −78 °C, the solution was allowed to warm to −20 °C, stirred for an additional 2 h, allowed to warm to room temperature, 0.5 ml of water was added and the reaction mixture was extracted with CH_2Cl_2. The resulting mixture of stereoisomers **39a** and **39b** was separated on a silica gel column (diethyl ether–hexane (1:4) as eluent). ^1H NMR of **39a**, δ 7.4 (m, 5H), 5.9–6.8 (m, 3H), 5.4 (br s, 1H), 3.0–3.3 (m, 4H), 2.68 (d) and 2.74



Scheme 18.

(d, $J = 9$ Hz) superimposed on 2.5–2.9 (m, PCH) (total 7H), 1.2 (m, 2H), 0.92 (m, 3H). ^{1}H NMR of **39b**, δ 7.3 (m, 5H), 5.9–6.8 (m, 3H), 5.1 (br s, 1H), 2.8–3.0 (m, 4H), 2.6 (d) and 2.71 (d, $J = 9$ Hz) superimposed on 2.5–2.7 (m, PCH) (total 7H), 1.0 (m, 2H), 0.9 (m, 3H).

A benzene (4 ml) solution of a mixture of **39a** and **39b** (0.35 g) and triethylamine (1 ml) was stirred and refluxed for 4.5 h, then the solvent was evaporated. The residue was extracted with pentane and the solvent was evaporated. Bulb-to-bulb distillation in the presence of anhydrous potassium carbonate gave a mixture of the two geometrical isomers **25-*E*** and **25-*Z*** as a clear liquid (yield 42%), which was separated by preparative TLC (diethyl ether–hexane (1 : 3). ^{1}H NMR of **25-*Z***, δ 1.0 (t, 3H), 2.1 (m, 2H), 5.20 (d, $J = 10$ Hz, 1H), 5.27 (d, $J = 16$ Hz, 1H), 5.65 (m, 1H), 6.55 (m, 1H), 7.25 (m, 5H). ^{1}H NMR of **25-*E***, δ 1.1 (t, 3H), 2.1 (m, 2H), 5.21 (d, $J = 11$ Hz, 1H), 5.3 (d, $J = 17$ Hz, 1H), 6.01 (m, 1H), 6.57 (m, 1H), 7.3 (m, 5H).

26-*E* and 26-*Z*. n-BuLi (20% in hexane, 3.5 ml) was added dropwise to a stirred slurry of 3-butenyltriphenylphosphonium bromide (4 g) in 10 ml of dry diethyl ether under a nitrogen atmosphere. After 2 h of stirring at room temperature, phenylacetaldehyde (1.4 ml) dissolved in 10 ml of diethyl ether was added slowly and the mixture was stirred overnight. Et_2O was added to the mixture and the precipitate formed was removed by filtration. The organic phase was washed with water, dried over $MgSO_4$ and the solvent was removed under vacuum to afford 2.1 g of a mixture of **26-*E*** and **26-*Z*** (38% yield), which was separated on a silica gel column impregnated with $AgNO_3$ with diethyl ether–hexane (1 : 20) as eluent.

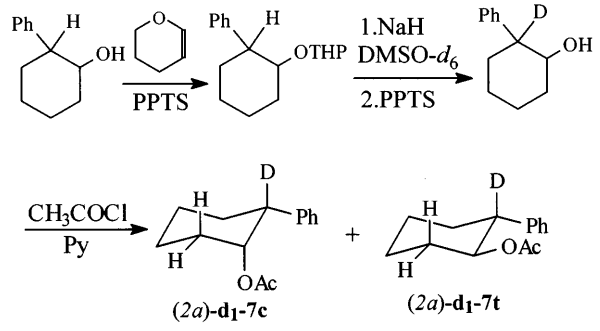
Synthesis of deuterium-labeled compounds

Acetates (*2a*)-$\mathbf{d_1}$-7c and (*2a*)-$\mathbf{d_1}$-7t (Scheme 15). 2-Phenyl-2-d_1-cyclohexanols were prepared by the exchange of the benzylic hydrogen by heating the tetrahydropyranyl ether[39] of 2-phenylcyclohexanol (mixture of *cis*- and *trans*-isomers) with dry hexadeuterodimethyl sulfoxide (DMSO-d_6) and sodium hydride (Scheme 19).

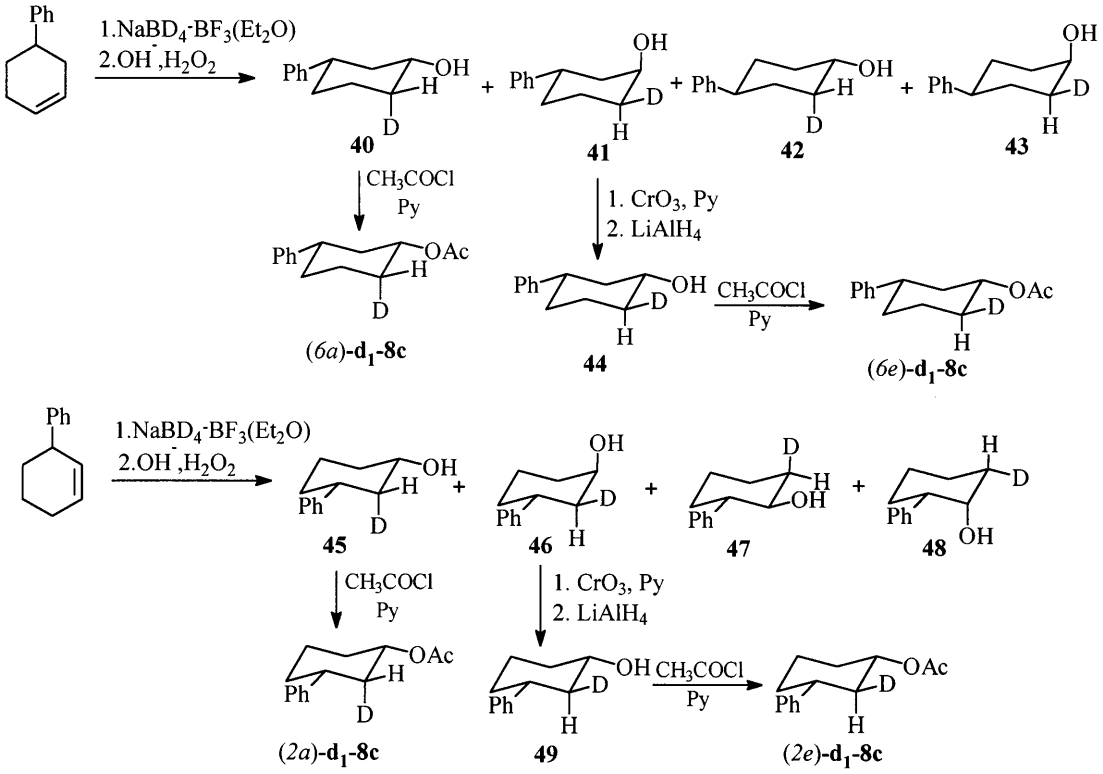
Freshly distilled tetrahydropyran (THP, 5 ml) was added to a solution of 2-phenylcyclohexanol (1.3 g) and pyridinium *p*-toluenesulfonate (PPTS, 1 g) in 5 ml of CH_2Cl_2 below 5 °C, and the reaction mixture was stirred for 6 h at room temperature. Extraction (CH_2Cl_2) afforded the THP-ether, which was used without further purification (98% pure by GC/MS, yield 99%). The THP-ether (1.9 g), NaH (0.2 g) and DMSO-d_6 (5.5 ml) were refluxed for 3 h. Extraction (CH_2Cl_2) and purification of the residue on a small silica gel column (elution with hexane to remove DMSO and then hexane–ethyl acetate (3 : 1) yielded the deuterium-labeled THP-ether (>96% deuterium content by GC/MS). The protection group was removed by stirring in ethanol solution in the presence of PPTS (1 g) at 55 °C for 3 h. Acetylation (acetyl chloride in pyridine) of the resulting 2-*d*-2-phenylcyclohexanol afforded a mixture of the two stereoisomeric acetates (*2a*)-$\mathbf{d_1}$-7c and (*2a*)-$\mathbf{d_1}$-7t.

Acetates $\mathbf{d_1}$-8c (Scheme 14). The stereospecifically labeled acetates (*6a*)-$\mathbf{d_1}$-8c, (*6e*)-$\mathbf{d_1}$-8c, (*2a*)-$\mathbf{d_1}$-8c and (*2e*)-$\mathbf{d_1}$-8c were prepared by routes shown in Scheme 20.

Boron trifluoride etherate (7 ml) was added dropwise over 10 min to a solution of $NaBD_4$ (1.3 g) and 4-phenylcyclohexene (3 g) in diglyme (35 ml) in an ice-bath under N_2. The reaction mixture was stirred for another 2 h at room temperature, cooled to 0 °C and 3 M NaOH (10 ml) was added rapidly. Subsequently, 30% H_2O_2 (10 ml) was added slowly with stirring at −10 °C, the reaction mixture was stirred for 3 h, the layers were separated, the aqueous layer was extracted with diethyl



Scheme 19.



Scheme 20.

ether and the organic layers were dried over $MgSO_4$ and evaporated. The resulting mixture of *cis*-3-phenyl-*cis*-6-*d*-cyclohexanol (**40**), *trans*-3-phenyl-*cis*-6-*d*-cyclohexanol (**41**), *trans*-4-phenyl-*cis*-2-*d*-cyclohexanol (**42**) and *cis*-4-phenyl-*cis*-2-*d*-cyclohexanol (**43**) was separated by chromatography on a silica gel column with acetone–hexane (1 : 3) as eluent. Final separation of **41** and **43** was achieved by fractional crystallization of their 3,5-dinitrobenzoates, followed by mild basic hydrolysis.

trans-3-Phenyl-*cis*-6-*d*-cyclohexanol (**41**) was oxidized to the corresponding 3-phenyl-*cis*-6-*d*-cyclohexanone by reaction with CrO_3 in pyridine–CH_2Cl_2 solution.[40] Reduction with excess of $LiAlH_4$ in THF afforded a mixture of *cis*- and *trans*-3-phenyl-*cis*-6-*d*-cyclohexanol (**41** and **44**), which was separated on a silica gel column with acetone–hexane (1 : 3) as eluent. Acetylation (acetyl chloride in pyridine) of **40** and **44** gave rise to the corresponding acetates, (*6a*)-$\mathbf{d_1}$-**8c** and (*6e*)-$\mathbf{d_1}$-**8c**.

Hydroboration of 3-phenylcyclohexene led to the formation of *cis*- and *trans*-3-phenyl-*cis*-2-*d*-cyclohexanol (**45** and **46**) and *trans*- and *cis*-2-phenyl-*cis*-6-*d*-cyclohexanol (**47** and **48**), which were separated on a silica gel column followed by fractional crystallization of dinitrobenzoates (final separation of the axial alcohols **46** and **48**) and their hydrolysis. Oxidation of alcohol **46** with CrO_3 followed by reduction and separation led to *cis*-3-phenyl-*trans*-2-*d*-cyclohexanol (**49**). Acetylation (acetyl chloride in pyridine) of **45** and **49** gave rise to the corresponding acetates, (*2a*)-$\mathbf{d_1}$-**8c** and (*2e*)-$\mathbf{d_1}$-**8c**.

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