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Stereochemical Memory in the Regioselective and Diastereoselective Rearrangement of Tricyclo[3.3.0.0^{2,4}]octanes (Housanes) by Electron Transfer (1,3-Cyclopentanediyl Radical Cations) and Acid (Cyclopentyl Carbenium Ions) and Silver-Ion Catalysis

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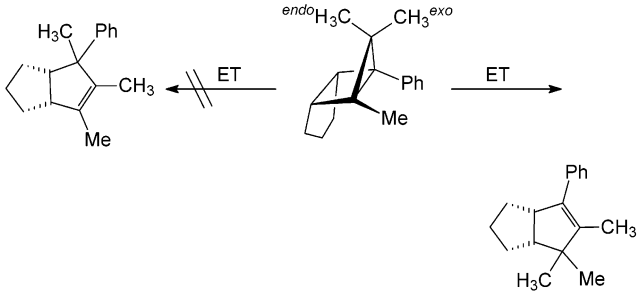
Abstract: The electron-transfer-catalyzed rearrangement of the housanes **5** affords regioselectively only the two cyclopentenes **6** (CH_3 migration) and **7** (R migration) by 1,2-migration of the two groups at the methano bridge to the methyl terminus. The 1,2-shift of the CH_3 group prevails, and the rearrangement ratio is essentially insensitive to the migratory aptitude of the R substituent. This *stereochemical memory* effect derives from the conformational impositions on the stereoelectronic requirements during the 1,2-migration in the 1,3-radical-cation intermediates. Similar regioselectivities and diastereoselectivities are observed for the TFA-catalyzed and silver(I)-ion-promoted rearrangements, whereas the rearrangement catalyzed by $HClO_4$ affords a complete reversal in the product selectivity and both the regioselectivity and the diastereoselectivity are much reduced. Migration to the phenyl terminus is favored to afford the **6′** and **7′** cyclopentenes, of which the former (CH_3 migration) dominates. For the minor regioisomer, only the cyclopentene **6** is formed by an exclusive 1,2-shift of the CH_3 group. This dichotomy in product selectivities is rationalized in terms of two distinct mechanisms for the various activation modes: a common one for the electron-transfer-induced, TFA-catalyzed, and silver(I)-ion-promoted rearrangements and a different one for $HClO_4$.

Introduction

The chemistry of 1,3-cyclopentanediyl radical cations (housane radical cations) has been extensively studied during the past decade, and the regiochemical features are quite well understood.[1] For example, the housane affords on treatment with catalytic amounts of trisarylaminium hexachloroantimonate exclusively the cyclopentene with methyl migration to the methyl-substituted terminus, whereas the regioisomer with methyl migration to the phenyl-bearing site is not observed (Scheme 1).[1] This remarkably high regioselectivity has been rationalized in terms of preferred localization of the positive charge at the methyl-carrying migration terminus in this Wagner−Meerwein-type rearrangement.[1,2]

In contrast, less thoroughly investigated has been the diastereoselectivity of such radical-cation rearrangements. For the particular housane in Scheme 1, with exclusive methyl migration to the methyl-substituted terminus, the two possible cyclopentenes that result from a CH_3^{exo} or CH_3^{endo} 1,2-shift are identical and information on the diastereoselectivity is inaccessible. This problem may be solved by introducing a distinct migrant R at the methano bridge, for example a benzyl group, since now the R substituent serves as a stereochemical label to assess the diastereoselectivity in terms of the product distribution.

Scheme 1. Regioselective Rearrangement of the Housane Radical Cations



In previous work,[2] a planar radical-cation intermediate was proposed to account for the minor amounts of exo-substituent migration. However, from the fact that for Wagner−Meerwein rearrangements the stereoelectronic requisite of coplanarity of the migrant relative to the migration terminus should be fulfilled,[3,4] the necessity arises to consider two interconverting nonplanar radical-cation conformers as rearrangement precursors

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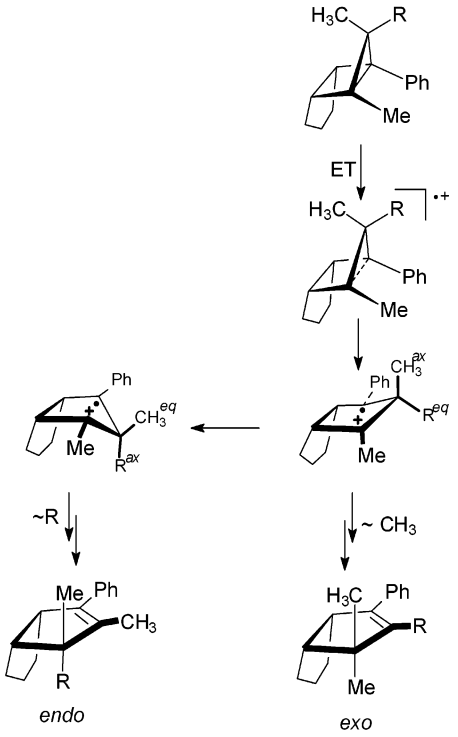
(1) Adam, W.; Heidenfelder, T. *J. Am. Chem. Soc*. **1998**, *120*, 11858−11863.
(2) Adam, W.; Librera, C. P. *J. Org. Chem*. **2002**, *67*, 576−581.

Scheme 2. Stereoelectronic Requirement for the Wagner−Meerwein-Type Rearrangement of Housane Radical Cations



(Scheme 2). Hence, for the initial conformer with the pseudoaxial CH_3 group, migration of this group should be preferred, whereas in the interconverted conformer the R group occupies the pseudoaxial position and should be prone to migrate. Since for carbocation rearrangements it is known that a benzyl group possesses a much higher migratory aptitude (more than 1600 times) than a methyl group,[5] the replacement of the methyl for a benzyl substituent at the migration origin would introduce a significant electronic bias in favor of the benzyl shift and thereby possibly preclude any conformational effects on the two interconverting radical cations. Thus, while it is certainly of mechanistic interest to determine the migratory aptitude, for example for the benzyl versus the methyl group, in such radical-cation rearrangements, to separate the electronic and conformational factors, the same migrant should be used at the migration origin. Fortunately, in the present case of Scheme 1, this may be readily achieved by replacing the CH_3^{exo} and CH_3^{endo} groups at the methano bridge of the housane by CD_3 groups, since then diastereochemically distinct rearrangement products would result.

We anticipate two limiting cases for the rearrangement of the radical cations derived from the deuterium-labeled housanes in Scheme 2: Should the 1,2-shift of the CH_3^{ax} (actually CD_3^{ax}) migrant take place faster than the conformational change, the exo product will be formed preferentially, which would signify stereochemical memory;[6] alternatively, should the conformational change be faster, then the R^{eq} group (actually CD_3^{eq}) will be placed into the favorable pseudoaxial alignment and also migrate such that a significant amount of endo product is expected. In the case where the R group is benzyl, in view of its much greater propensity to migrate,[5] the endo rearrangement should dominate. In other words, the question arises whether the known migratory aptitudes for cation rearrangements[5] are also reflected in housane-type radical cations, or does the stereochemical memory effect,[6] observed in the rearrangement of the radical cations derived from simple bicyclo[2.1.0]-pentanes,[7] operate as well in the more elaborate cases of Scheme 2? Such interplay of conformational and electronic effects in the rearrangement of housane-type radical cations have so far not been scrutinized but should provide valuable mechanistic information on the chemical behavior of these transient species. In fact, this fundamental mechanistic query has also not been posed for the genuine Wagner−Meerwein rearrangement of the carbocations generated by protonation (acid catalysis) and argentation (silver(I)-ion catalysis) of housane-type substrates.[1,8]

Herein, we report on the rearrangement of the radical cations (generated by electron transfer with triarylaminium hexachloroantimonate) and carbocations (formed by protonation with trifluoroacetic and perchloric acid) and argentation (silver(I) tetrafluoroborate) of tailor-made housanes, which were prepared by way of the Hünig isopyrazole route under high-pressure conditions.[9] This elaborate comparative study provides a mechanistic assessment of the interplay of conformational, electronic, and steric effects on the product selectivity in the rearrangement of radical cations and the corresponding carbocation intermediates as required by stereoelectronic control.

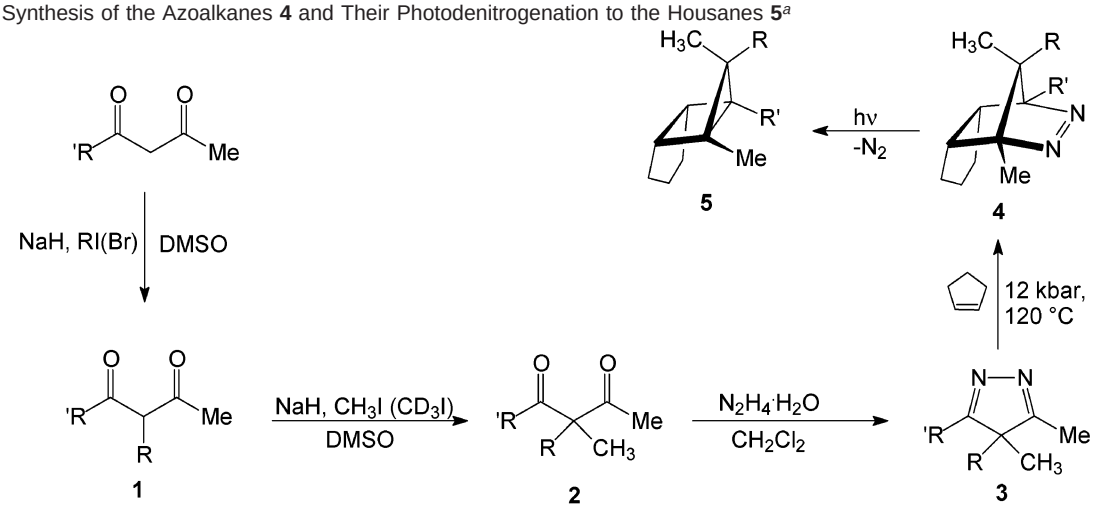
Results

Synthesis of the Azoalkanes 4 and Their Photolyses to the Housanes 5. The required triyclo[3.3.0.$0^{2,4}$]octanes (housanes **5**) were prepared according to previously reported synthetic strategies (Scheme 3).[3,4,8−10] For maximum yields of the geminally substituted β-diketones, the larger substituent (R) was incorporated first.[3] Condensation of the geminally dialkylated β-diketones **2** with hydrazine hydrate afforded the corresponding isopyrazoles **3**, which in turn were subjected to high-pressure (12 kbar) cycloaddition at 120 °C with cyclopentene as dienophile, to afford the azoalkanes **4**. The pressure-induced endo-Diels−Alder reaction of the cyclopentene proceeds stereoselectively with the isopyrazoles **3b**−**e** syn to the bridgehead methyl group to afford the cycloadducts **4b**−**e** as the only products. The traditional synthetic route for the preparation of the azoalkanes **4**, namely cycloaddition with cyclopentadiene at ambient pressure and temperature and subsequent catalytic hydrogenation, failed at the cycloaddition stage for these sterically encumbered isopyrazoles. As for the stereochemical structure of the azoalkanes **4**, the endo configuration was assigned to the annelated cyclopentane ring, confirmed by means of NOE effects and by comparison of chemical shifts of known[4] related cyclopentenes (for details, see the Supporting Information).

The corresponding housanes **5** were obtained quantitatively by photodenitrogenation of the azoalkanes **4**, which exhibit an absorption maximum at ca. 360 nm. Thus, the photolyses were carried out by irradiation at the 364 nm line of the argon-ion laser in d_8-toluene at 20 °C.

(3) Paquette, L. A.; Leichter, L. M. *J. Am. Chem. Soc*. **1980**, *102*, 4397−4403.
(4) Adam, W.; Heidenfelder, T.; Sahin, C. *Synthesis* **1995**, 1163−1170.
(5) Rüchardt, C.; Wistuba, E. *Tetrahedron Lett*. **1981**, *22*, 3389−3392.
(6) Berson, J. A. *Angew. Chem., Int. Ed. Engl*. **1968**, *7*, 779−791.
(7) Adam, W.; Heidenfelder, T. *Chem. Soc. Rev*. **1999**, *28*, 359−365.
(8) Paquette, L. A.; Leichter, L. M. *J. Am. Chem. Soc*. **1972**, *94*, 3653−3655.
(9) Beck, K.; Hünig, S.; Klärner, F.-G.; Kraft, P.; Artschwager-Perl, U. *Chem. Ber*. **1987**, *120*, 2041−2051.
(10) Beck, K.; Hünig, S. *Chem. Ber*. **1987**, *120*, 477−483.

Scheme 3. Synthesis of the Azoalkanes **4** and Their Photodenitrogenation to the Housanes **5**[a]



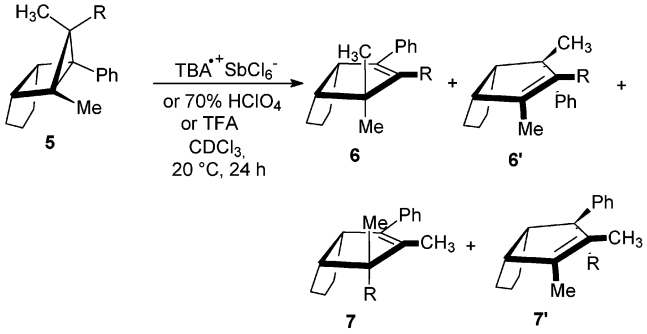
1 - 5	R	R'
a	CH_3	Ph
b	CH_3CH_2	Ph
c	$HC{\equiv}C{-}CH_2$	Ph
d	$H_2C{=}CH{-}CH_2$	Ph
e	$PhCH_2$	Ph
f	CH_3	Me

[a] In the housanes **5a** and **5f**, both methylene-bridge substituents are CD_3 groups, to distinguish them from the bridgehead Me groups.

Electron-Transfer-Induced, Acid-Catalyzed, and Silver-(I)-Ion-Promoted Rearrangement of the Housanes 5. The desired 1,3-radical cations were generated by chemical electron transfer with $TBA^{\bullet+}SbCl_6^-$ (tris(4-bromophenyl)aminium hexachloroantimonate) as one-electron oxidant in $CDCl_3$ at room temperature (ca. 20 °C). To suppress possible acid-catalyzed rearrangement,[1,2] the electron-transfer reactions were carried out in the presence of a slight excess (1.25 equiv) of the sterically hindered base 2,6-di-*tert*-butylpyridine as buffer. As previously established,[1] the electron transfer is not affected by the pyridine base. Complete conversion of the housanes **5** occurred within 1 day (Table 1, $TBA^{\bullet+}SbCl_6^-$), to afford regioselectively only the two cyclopentenes **6** and **7** (exclusive 1,2-shift of the CH_3 or R groups to the methyl-bearing terminus). Thus, methyl migration results in cyclopentene **6** and R migration in cyclopentene **7**, whereas the appearance of the regioisomeric cyclopentenes **6′** (migration of the methyl group) and **7′** (migration of the R group) by rearrangement to the phenyl-bearing carbon atom was not observed. The stereochemical course of the methyl shift in the dimethyl housane **5a** was determined by the use of the deuterated derivative **5a**-d_6. The migration of the *endo*- and *exo*-CD_3 groups leads either to **6a**-d_6 or **7a**-d_6, which may be readily distinguished in the ^1H NMR spectrum of the product mixture (Scheme 4). The data in Table 1 show that for all the derivatives **5a**−**e**, the electron-transfer-induced rearrangement proceeds predominantly by methyl migration with retention of configuration; that is, methyl migration affords only the exo diastereomer **6** and R migration only the endo diastereomer **7**.

For the acid-catalyzed rearrangement, trifluoroacetic acid (TFA) or 70% $HClO_4$ was used as the proton source. For TFA, similar to the electron-transfer case, only the two cyclopentenes **6** (methyl migration) and **7** (R migration) were observed. Again, as in the electron-transfer-induced rearrangement, methyl migration dominates, but the differences in the product selectivities are more pronounced (Table 1, TFA). For example, the dimethyl-substituted housane **5a** yields the two isomers **6** and

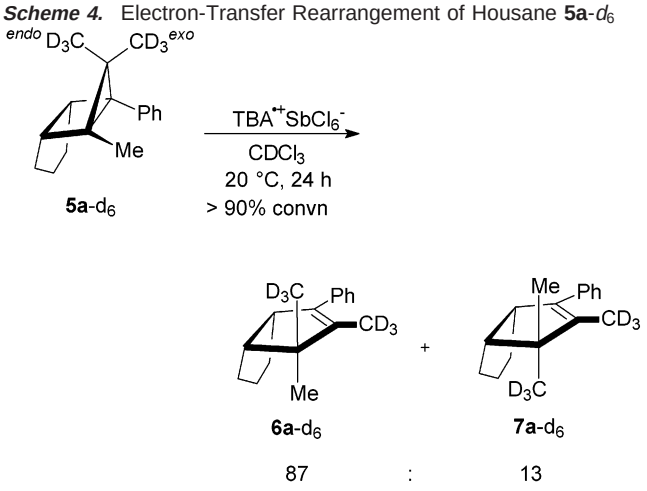
Table 1. Product Distribution for the Electron-Transfer-Induced ($TBA^{\bullet+}SbCl_6^-$) and Acid-Catalyzed (TFA or $HClO_4$) Rearrangement of the Housanes **5a**−**e**



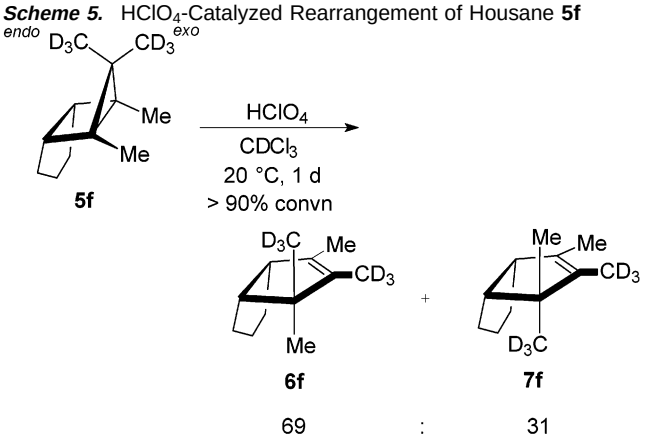
			product distribn (%)[a]									
			$TBA^{\bullet+}SbCl_6^-$				TFA				$HClO_4$			
			CH_3		R		CH_3		R		CH_3		R	
entry	housane	R	**6**	**6′**	**7**	**7′**	**6**	**6′**	**7**	**7′**	**6**	**6′**	**7**	**7′**
1	**5a**	CH_3[b]	87	13			88	12			34	46		20
2	**5b**	CH_3CH_2	82	18			75	25			31	49		20
3	**5c**	$HC{\equiv}CCH_2$	87	13			93	7			35	48		17
4	**5d**	$H_2C{=}CHCH_2$	79	21			66	34			33	46		21
5	**5e**	$PhCH_2$	77	23			65	35			28	47		25

[a] Determined directly on the crude product mixture by ^1H NMR spectroscopy (400 MHz, $CDCl_3$). The error is ca. 3% of the stated value; conversion and mass balances were >90%. [b] For the stereochemical assignment of the rearrangement product, the CD_3 group was employed for both substituents at the methylene bridge, to distinguish them from the bridgehead Me group.

Scheme 4. Electron-Transfer Rearrangement of Housane **5a**-d_6



Scheme 5. $HClO_4$-Catalyzed Rearrangement of Housane **5f**



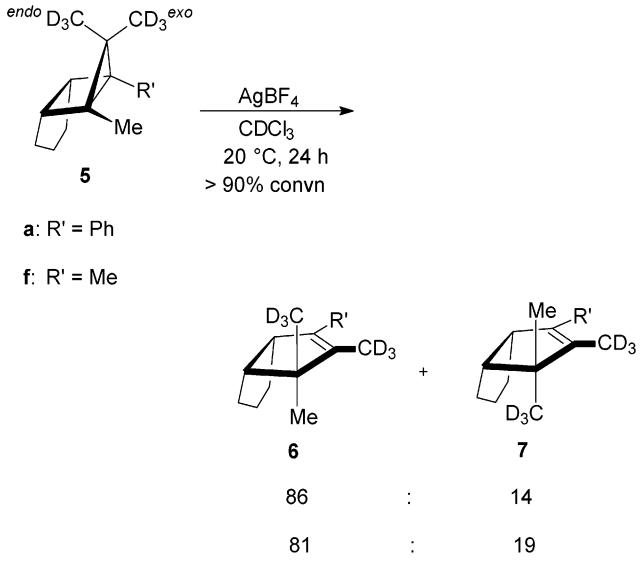
7 in a 88:12 ratio (Table 1, entry 1, TFA), while for the benzyl derivative **5e** the ratio is 65:35 (Table 1, entry 5, TFA).

In contrast to the above results for the electron-transfer-induced and TFA-catalyzed rearrangements, the use of $HClO_4$ (a heterogeneous reaction) led to a significantly lower regioselectivity in the product distribution (Table 1, $HClO_4$). For all derivatives **5a**−**e** (Table 1, $HClO_4$), the regioisomeric cyclopentene **6′** is the major product (methyl migration to the phenyl terminus), along with appreciable amounts of **6** (methyl migration to the methyl terminus) and **7′** (R migration to the phenyl terminus). The cyclopentene **7** (R migration to the methyl terminus) was not observed.

Replacement of the bridgehead Ph group by a Me group results in the symmetric housane **5f**, for which no regiochemical differentiation is possible such that only $HClO_4$ was employed as acid catalyst (Scheme 5). On $HClO_4$ treatment of **5f**, a mixture of diastereomers was obtained by a 1,2-shift of both migrating groups, of which transposition of the *endo*-CD_3 group to afford **6f** is favored over that of the *exo*-CD_3 group to produce the diastereomer **7f**.

For the deuterium-labeled derivatives **5a** and **5f**, also the silver(I)-ion-promoted rearrangement was investigated (Scheme 6). Treatment of the housane **5a** with catalytic amounts of silver tetrafluoroborate ($AgBF_4$) in $CDCl_3$ led regioselectively only to the two diastereomeric cyclopentenes **6a** (*endo*-CD_3 group migration) and **7a** (*exo*-CD_3 group migration); the **6′a** and **7′a** regioisomers (migration to the Ph terminus) were not observed. Similarly, for the symmetrical derivative **5f** (no regioisomers possible) both diastereomers **6f** and **7f** were obtained with

Scheme 6. Silver(I)-Ion-Promoted Rearrangement of Housanes **5a** and **5f**

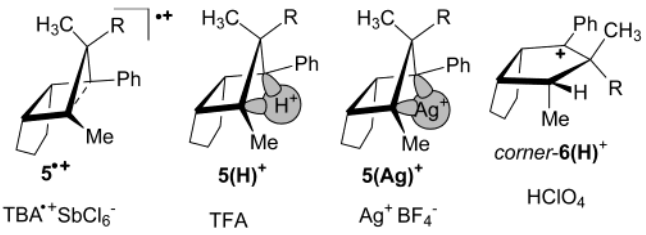


$AgBF_4$, for which also migration of the *endo*-CD_3 group dominates (Scheme 6).

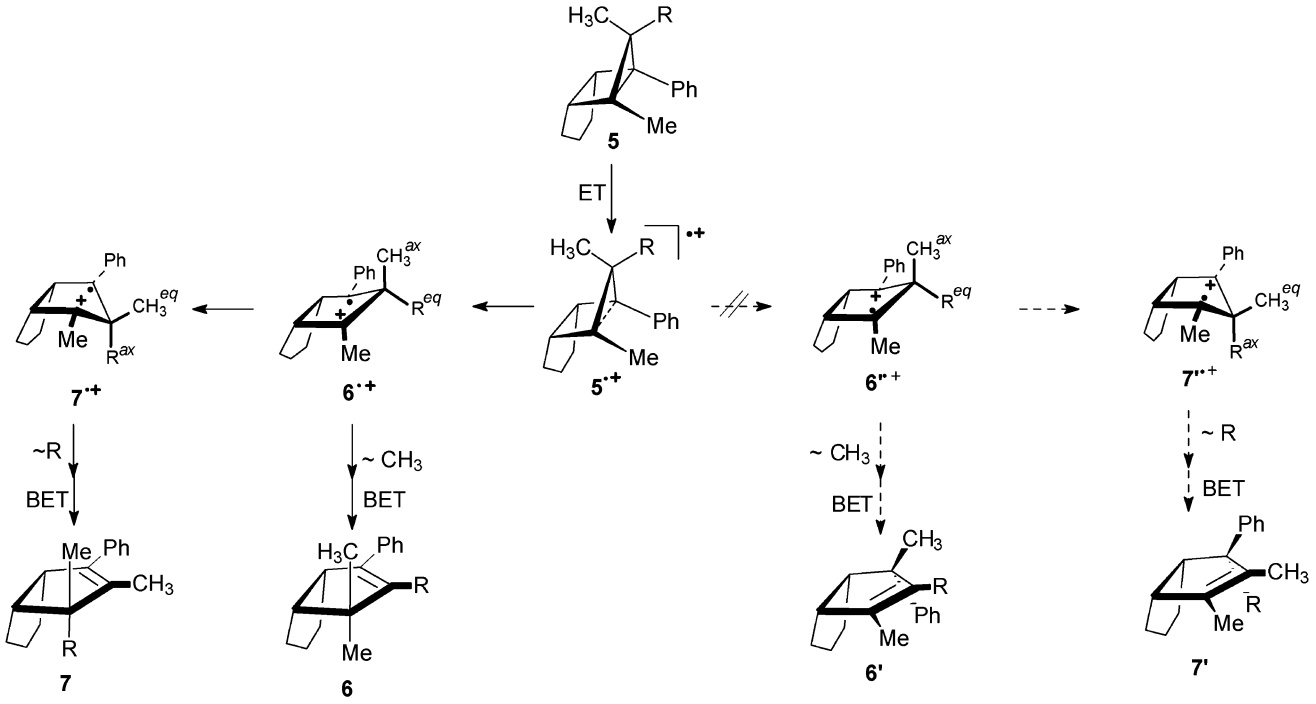
The structural assignment of the rearrangement products is based on ^1H NMR spectra, on NOE effects with HH and CH correlations, and on spectral comparison with known cyclopentene derivatives of this type.[4] The details are given in the Supporting Information.

Discussion

Before entering into the mechanistic rationalization of the product data in Table 1 and Schemes 4−6, it is instructive to focus on the salient similarities and differences in the electron-transfer-induced, acid-catalyzed, and silver-ion-promoted rearrangement of the housane **5** to the regioisomeric and diastereomeric cyclopentenes **6**/**6′** and **7**/**7′**.[11] What stands out, and which could hardly have been anticipated, is the fact $TBA^{\bullet+}SbCl_6^-$, TFA, and $Ag^+BF_4^-$ all give within the experimental error the same product ratios, as exemplified for the model substrate **5a** (Table 1, Schemes 4−6). Thus, only the diastereomers **6** and **7** are produced, with predominant migration of the *endo*-CD_3 group exclusively to the Me-bearing terminal. In contrast, $HClO_4$ (Table 1) generates from substrate **5a** both regioisomers, but now migration to the Ph-carrying site is favored to afford the **6′** and **7′** diastereomers, of which the former (*endo*-CD_3 migration) dominates; for the minor regioisomer only the **6** diastereomer is produced by an exclusive 1,2-shift of the *endo*-CD_3 substituent. This dichotomy in the rearrangement results of the various activation modes implies different mechanisms: namely, a common one for the electron-transfer, TFA-catalyzed, and Ag^+-induced processes and a distinct one for the $HClO_4$-catalyzed case. We propose the related bridged structures $\mathbf{5}^{\bullet+}$, $\mathbf{5(H)}^+$, and $\mathbf{5(Ag)}^+$ versus the



Scheme 7. Regioselectivity in the Diastereoselective Electron-Transfer Rearrangement



open *corner*-**6′(H)**$^+$ species as dominant key intermediates. The puckered **5(H)**$^+$ and **5(Ag)**$^+$ species result from *edgewise* entry of the electrophile and are structurally similar to the bridged 1,3-radical cation **5**$^{\bullet+}$ obtained from one-electron oxidation, whereas the open structure *corner*-**6(H)**$^+$ arises from the *cornerwise* protonation by the perchloric acid.

Another mechanistically important feature about the product data in Table 1 is the fact that the ratio of rearrangement products is relatively insensitive to the migratory aptitude of the R substituent in the housanes **5**. In fact, for all cases, the *endo*-CH_3 group migrates in pronounced preference even relative to a benzyl group (Table 1, entry 5), which usually dominates by more than a factor of 1600 in Wagner−Meerwein-type rearrangements.[5]

The rearrangement of the 1,3-radical cations is of the Wagner−Meerwein type,[12] and the following electronic and stereoelectronic conditions must be fulfilled: The electronically preferred site of positive-charge localization determines the regioselectivity,[1,2] whereas the migrating group requires conformationally a coplanar alignment with the 2p orbital at the migration terminus.[3,4] The mechanism in Scheme 2 needs to be expended to account for the observed migrant selectivities of the radical cations **5**$^{\bullet+}$ as proposed in Scheme 7. Initially, the puckered radical cation **5**$^{\bullet+}$ is generated on electron transfer,[4,13] which transforms to the regioisomeric opened conformers **6**$^{\bullet+}$ and **6′**$^{\bullet+}$. As in the **5a** case,[1] for all derivatives, the positive charge is mainly localized at the Me terminus and the 1,2-shift occurs exclusively to the methyl-substituted bridgehead site to afford regioselectively the diastereomeric cyclopentenes **6** and **7** by migration of the CH_3 or the R group. The cyclopentene **6** is formed predominantly (Table 1, TBA$^{\bullet+}$$SbCl_6^-$), because in the **6**$^{\bullet+}$ conformer the stereoelectronic requirement of coplanarity of the migrating pseudoaxial CH_3 group is optimally fulfilled.[3,4] For the R group to migrate, the **6**$^{\bullet+}$ conformer must invert to the **7**$^{\bullet+}$ conformer and acquire the essential pseudoaxial alignment, but steric interactions between the R^{ax} group and the annelated cyclopentyl ring disfavor this conformer. From the experimental fact that for all R substituents the ratio of rearrangement products **6** (CH_3) and **7** (R) is nearly constant (Table 1, TBA$^{\bullet+}$$SbCl_6^-$) and does not reflect the expected migratory aptitude sequence CH_3 < C_2H_5 < allyl, benzyl,[14] it may be concluded that the population of the two radical-cation conformers **6**$^{\bullet+}$ and **7**$^{\bullet+}$ determines whether the CH_3 or the R group migrates in preference. Evidently, CH_3 migration in the conformer **6**$^{\bullet+}$ is faster than the conformational change to the radical cation **7**$^{\bullet+}$. This stereochemical memory effect[6,7] accounts for the observed migrant selectivity in the electron-transfer-induced rearrangement of the housanes **5**.

The TFA-catalyzed rearrangement leads to a regioselectivity similar to that in the case of electron transfer (Table 1). Edgewise attack affords the center-protonated housane **5(H)**$^+$ (Scheme 8), which may open up to the two pairs of carbocations *edge*-**6(H)**$^+$/*edge*-**7(H)**$^+$ and *edge*-**6′(H)**$^+$/*edge*-**7′(H)**$^+$. It may be presumed that the two cations *edge*-**6(H)**$^+$ and *edge*-**6′(H)**$^+$ interconvert rapidly,[3] the *edge*-**6′(H)**$^+$ regioisomer of which should be preferred for the usual reasons of phenyl stabilization; however, the product data (Table 1) show unequivocally that migration to the Me terminus through the *edge*-**6(H)**$^+$ and *edge*-**7(H)**$^+$ cations occurs exclusively.

We suspect that kinetic control operates in that the activation barrier from **5(H)**$^+$ to *edge*-**6′(H)**$^+$ is greater than to *edge*-**6(H)**$^+$. The steric repulsions of the phenyl group with the

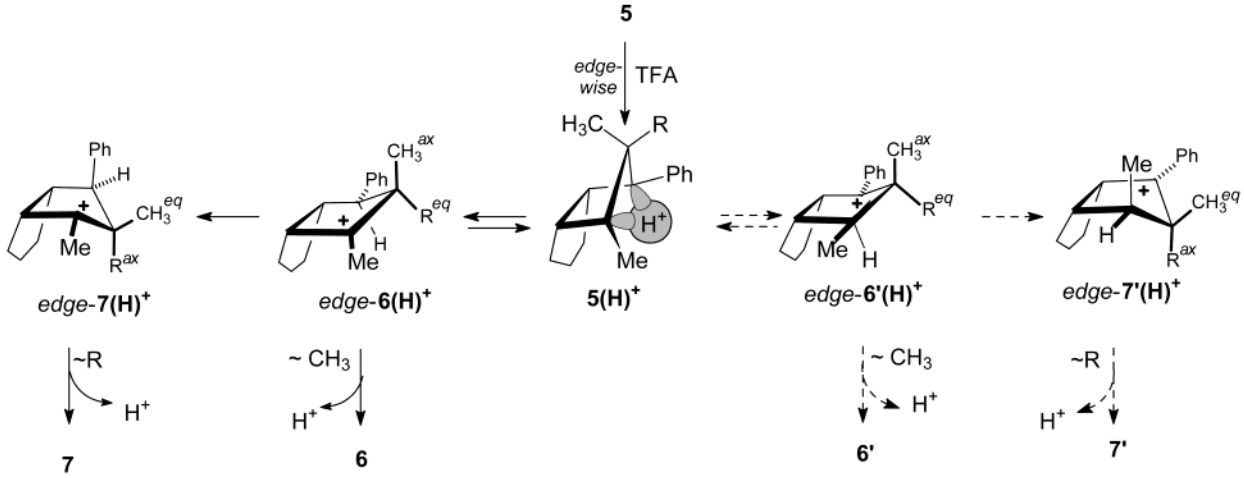
(11) It should be noted that the isomeric cyclopentenes **6**/**7** and **6′**/**7′** are only diastereomeric pairs when R is CD_3; for all other R derivatives they are different substances. However, for ease of comparison, the **6**/**7** and **6′**/**7′** pairs are considered as diastereomers.

(12) (a) Shaik, S. S.; Dinnocenzo, J. P. *J. Org. Chem.* **1990**, *55*, 3434−3436. (b) Schmittel, M.; Burghart, A. *Angew. Chem.* **1997**, *109*, 2659−2699; *Angew. Chem. Int. Ed.* **1997**, *36*, 2550−2589.

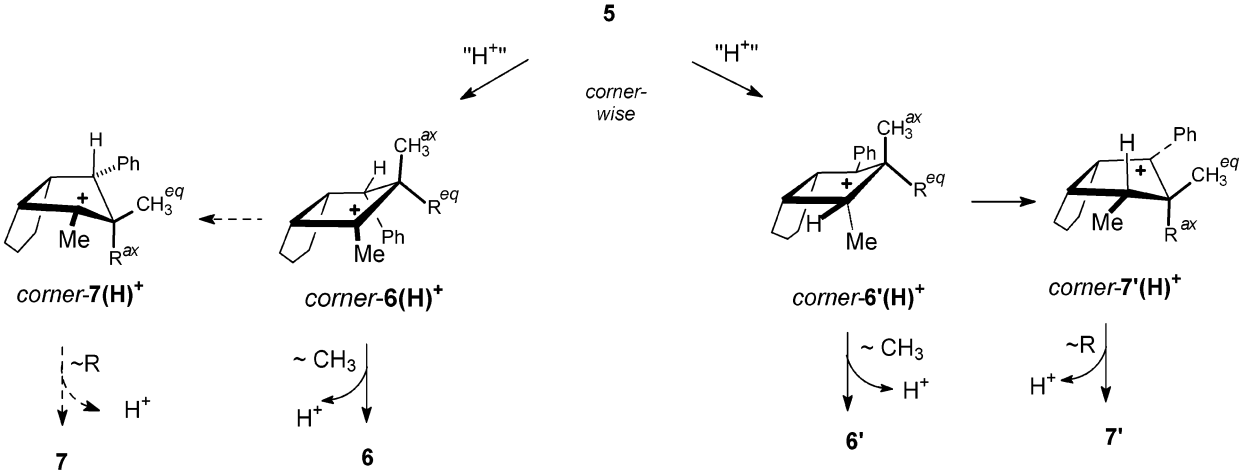
(13) Adam, W.; Sahin, C.; Sendelbach, J.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1994**, *116*, 2576−2584.

(14) Rüchardt, C.; Wistuba, E. *Tetrahedron Lett.* **1981**, *22*, 4069−4072.

Scheme 8. Regioselectivity of the TFA-Catalyzed Diastereoselective Rearrangement



Scheme 9. Regioselectivity of the $HClO_4$-Catalyzed Diastereoselective Rearrangement



annelated cyclopentane ring and the disubstituted methylene bridge (migration origin) should be sufficiently severe to twist the benzene ring out of conjugation,[15] and the twisted phenyl substituent in the *edge*-**6′(H)**$^+$/*edge*-**7′(H)**$^+$ cation pair should sterically obstruct transposition of the migrant to the phenyl-bearing terminus.

With regard to the diastereoselectivity (Table 1), the TFA-catalyzed rearrangement reflects only nominally the well-known migratory-aptitude sequence methyl < ethyl < allyl, benzyl in carbocation rearrangements.[14] Similar to the electron-transfer case, migration of the *endo*-CH_3 group is favored; again, stereochemical memory is manifested through conformational control. Once the **5(H)**$^+$ cation opens up to the cation conformer *edge*-**6(H)**$^+$, its pseudoaxial *endo*-CH_3 group slides over to the Me-bearing migration terminus to afford cyclopentene **6** before the ring flip to the *edge*-**7(H)**$^+$ carbocation conformer occurs to transpose the R group to the cyclopentene **7** (Scheme 8). The conformational change of **6(H)**$^+$ to **7(H)**$^+$ is encumbered by the prominent steric interaction between the R^{ax} group and the annelated cyclopentane ring.

The regioselectivity and diastereoselectivity of the silver(I)-ion-promoted[8,16] rearrangement (Scheme 6) of the **5a** housane are identical, within the experimental error, to the TFA-catalyzed case. Consequently, the mechanism in Scheme 8 applies, except that the rearrangement process commences with the puckered **5a(Ag)**$^+$ species. Instead of the previously suggested initial π coordination of the Ag^+ ion with the phenyl ring to explain the high regioselectivity of migration to the methyl terminus,[8] *edgewise* argentation initiates the rearrangement process through the **5a(Ag)**$^+$ intermediate. Indeed, the very similar selectivities for the silver(I)-ion-induced reaction of the substrates **5f** (Scheme 6) and **5a** (Table 1) suggest that coordination with the bridgehead phenyl substituent is not necessary. In marked contrast, the rearrangement catalyzed by $HClO_4$ affords a complete reversal in the product distribution compared to the above-described rearrangements (Table 1). A different mechanism must operate, and we propose that direct *cornerwise* protonation of the housane by the strong acid $HClO_4$ generates the most stable carbocation,[1,2,17,18] which determines the regioselectivity (Scheme 9).[2]

Of the two possible corner attacks of a proton on the housanes **5**, the carbocation regioisomer *corner*-**6′(H)**$^+$ is favored over *corner*-**6(H)**$^+$ due to phenyl stabilization. A 1,2-shift of the CH_3^{ax} group in the *corner*-**6′(H)**$^+$ cation results in the cyclopentene **6′** diastereomer as the major rearrangement product after proton

(15) Semiempirical calculations on the corresponding 1,3-cyclopentanediyl triplet diradicals confirm that the benzene ring is substantially twisted out of conjugation; see: Adam, W.; Harrer, H. M.; Heidenfelder, T.; Kammel, T.; Kita, F.; Nau, W. M.; Sahin, C. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2085−2089.
(16) Wiberg, K. B.; Bishop, K. C., III. *Tetrahedron Lett.* **1973**, *29*, 2727−2730.
(17) Arnett, E. M.; Hafelich, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 2889−2895.
(18) Wiberg, K. B.; Kass, S. R.; Bishop, K. C., III. *J. Am. Chem. Soc.* **1985**, *107*, 996−1002.

loss. Inversion to the cation conformer *corner*-**7′(H)**$^+$ and migration of the R^{ax} group affords the cylopentene **7′** diastereomer as the minor product. The inversion of the *corner*-**6′(H)**$^+$ to the *corner*-**7′(H)**$^+$ conformer should be facilitated, since the interactions between the pseudoaxial Me group at the protonated bridgehead position with the annelated cyclopentane ring and the R^{eq} group would be relieved; however, during this ring flip steric repulsions between the R group and the annelated cyclopentane ring build up. Consequently, the *endo*-CH_3^{ax} group migrates faster than the conformational inversion and the greater migratory aptitude of the R substituent is not expressed.

Also, protonation at the phenyl-substituted bridgehead takes place in appreciable amounts to generate the *corner*-**6(H)**$^+$ conformer. Subsequent CH_3 migration affords exclusively the cyclopentene **6** in a constant amount for all derivatives (Table 1), which implies that the *corner*-**7(H)**$^+$conformer is not populated (Scheme 9). This appears surprising at first sight, because cornerwise protonation of the housane **5** at the phenyl-substituted bridgehead position obligates the phenyl group to be placed at the pseudoaxial position of the *corner*-**6(H)**$^+$ cation. One would expect that the congested phenyl group should foment ring inversion to the *corner*-**7(H)**$^+$conformer to avoid the steric repulsions between the annelated cyclopentene ring and the R^{ax} substituent. However, inspection of molecular models reveals that the pseudoaxial phenyl group is sterically obstructed to slide past the R substituent in the conformational change of *corner*-**6(H)**$^+$ to the *corner*-**7(H)**$^+$ and, consequently, the CH_3 group migrates exclusively. Additionally, it should be realized that the less stabilized *corner*-**6(H)**$^+$ cation (methyl conjugation) is more eager to undergo the methyl shift than the more stabilized *corner*-**6′(H)**$^+$ cation (phenyl conjugation).[3]

This mechanistic speculation is supported by the finding that on treatment of the deuterium-labeled symmetrical derivative **5f** with $HClO_4$ both diastereomeric rearrangement products **6f** and **7f** are formed (Scheme 5), by migration of the *endo*-CD_3 as well as *exo*-CD_3 group to the cationic Me terminus. Relevant in this case is the fact that the *corner*-**6f(H)**$^+$ conformer inverts to the *corner*-**7f(H)**$^+$ species, which means that the pseudoaxial Me group is sterically little hindered to pass by the CD_3 substituent at the methylene bridge and both diastereomer **6f** and **7f** are accessible (Scheme 5).

Conclusion

The structurally more complex housane derivatives **5** have offered the unique opportunity to explore conformational and steric effects on the diastereoselectivity in the electron-transfer ($TBA^{\bullet+}SbCl_6^-$) as well as in the acid-catalyzed (TFA, $HClO_4$) and metal-ion-promoted ($Ag^+BF_4^-$) rearrangements in a comparative manner. The present study reveals that the diastereoselectivity of the 1,2-migration is decisively determined by conformational and steric factors and emphasizes the complexity of the structure/reactivity interplay in the housane-derived intermediates. For all activation modes, the stereochemical memory effect operates in these rearrangements, which is imposed by the conformational requirements that are dictated by the stereoelectronics of the 1,2-migration. As a consequence, the ratio of the rearrangement products is essentially insensitive to the migratory aptitude of the R substituent in the housanes **5**. Unprecedented is the fact that, for the carbocations generated by protonation of the housanes **5**, the kinetically controlled methyl shift is faster than the competing conformational changes, which accounts for the observed stereochemical memory effect. The regioselectivity of the 1,2-migration is, however, determined by the electronic stabilization of the substituent at the rearrangement terminus in the intermediate that results from a particular activation mode.

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Supporting Information Available: Text giving the experimental section. This material is available free of charge via the Internet at http://pubs.acs.org.

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