Electronic Substituent Effects for the Fine-Tuning of the Regioselectivity in the Diastereoselective Rearrangement of 1,3-Cyclopentanediyl Radical Cations Generated from Tricyclo[3.3.0.0^{2,4}]octanes (Housanes) by Chemical Electron Transfer

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Abstract: 1,3-Cyclopentanediyl radical cations **5**$^{\bullet+}$ were generated from tricyclo[3.3.0.0^{2,4}]octanes (housanes) **5** through chemical oxidation with tris(4-bromophenyl)aminium hexachloroantimonate (TBA$^{\bullet+}$SbCl$_6^-$) and shown to afford the regioisomeric olefinic products **6** and **7** on methyl 1,2 migration. A complete reversal in the regioselectivity of the 1,2 shift was observed, which reflects the electronic character of the X substituent at the migration terminus in the radical cation **5**$^{\bullet+}$. The regioselectivity is rationalized in terms of a simple MO interaction diagram by considering the ϵ_{SOMO} orbital energies (AM1 method) of the X-substituted radical fragments in the intermediary 1,3 radical cations **5**$^{\bullet+}$ relative to that of the cumyl radical fragment. The excellent correlation between the calculated orbital energy differences ($\Delta\epsilon$) and the experimentally observed regioisomeric ratios allows a quantitative assessment of the electronic substituent effects. The diastereoselectivity of the 1,2 shift is controlled by the steric factors in the intermediary 1,3 radical cations **5**$^{\bullet+}$.

Introduction

Electron-transfer oxidations are of current interest and numerous studies have been employed not only for mechanistic but also for synthetic purposes.[1,2] Particularly, radical cations with strained rings have attracted considerable attention.[2a,b,3−5] For example, the electron-transfer photochemistry of vinylcyclopropane derivatives has been well examined by Roth and was found to proceed in a high degree of regio- and stereoselectivity.[3] For instance, the products of the [1,3]-sigmatropic hydrogen shift of the (1*R*,5*R*)-(+)-sabinene radical cation preserved their optical activity. Dinnocenzo studied the reaction of substituted arylcyclopropane cation radicals with nucleophiles and found substantial electronic substituent effects on the rate and regiochemistry.[4] These transformations may be understood as nucleophilic displacements on one-electron σ bonds and occur stereoselectively with inversion of configuration. Ab initio calculations by Borden have dealt with the ring opening of the cyclopropane radical cation to the propene radical cation and display no chemically significant stability for the trimethylene radical cation.[2b] Bicyclic derivatives of cyclopropanes are the much more strained bicyclo[2.1.0]pentanes (housanes), whose electron-transfer chemistry has in recent years been extensively explored. Mechanistic studies have demonstrated that the intermediary 1,3-cyclopentanediyl radical cations exhibit a high propensity to rearrange by 1,2 shift to the corresponding 1,2 radical cations, which after electron back-transfer (BET) yield substituted cyclopentenes.[5] EPR spectroscopy under matrix isolation conditions[5f,g] and pulse radiolysis studies[5c] proved helpful in detecting and characterizing the transient radical cations for the elucidation of the rearrangement. The bicyclo[3.2.0]hept-6-ene-2,4-diyl radical cation, generated from the corresponding housane, is intramolecularly trapped by the juxtaposed cyclobutenyl double bond to afford quadricyclane radical cations.[5d]

The intermediary 1,3 radical cations are generated either photochemically (PET) or chemically (CET), the latter by using one-electron oxidants such as the readily available aryl aminium salts.[6] Since in the catalytic CET mode no radical ion pairs are formed as intermediates, electron back-transfer is minimized and excellent yields of rearrangement products have been obtained.[5b,e] Therefore, this oxidative rearrangement methodology may serve as a useful synthetic tool for tailor-made target molecules.[5e] Such electron-transfer oxidations, which engage the well-known and highly exothermic cyclopropane−propene

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(1) For a recent review, see: Schmittel, M.; Burghart, A. *Angew. Chem.* **1997**, *109*, 2658.

(2) (a) Shaik, S. S.; Dinnocenzo, J. P. *J. Org. Chem.* **1990**, *55*, 3434. (b) Du, P.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1988**, *110*, 3405. (c) Maslak, P.; Chapman, W. H., Jr.; Vallombroso, T. M., Jr.; Watson, B. A. *J. Am. Chem. Soc.* **1995**, *117*, 12380. (d) Bauld, N. L.; Yueh, W. *J. Am. Chem. Soc.* **1994**, *116*, 8845.

(3) (a) Weng, H.; Sethuraman, V.; Roth, H. D. *J. Am. Chem. Soc.* **1994**, *116*, 7021. (b) Weng, H.; Sheik, Q.; Roth, H. D. *J. Am. Chem. Soc.* **1995**, *117*, 10655. (c) Herbertz, T.; Roth, H. D. *J. Am. Chem. Soc.* **1996**, *118*, 10954. (d) Herbertz, T.; Roth, H. D. *J. Am. Chem. Soc.* **1997**, *119*, 9574.

(4) (a) Dinnocenzo, J. P.; Lieberman, D. R.; Simpson, T. R. *J. Am. Chem. Soc.* **1993**, *115*, 366. (b) Dinnocenzo, J. P.; Simpson, T. R.; Zuilhof, H.; Todd, W. P.; Heinrich, T. *J. Am. Chem. Soc.* **1997**, *119*, 987. (c) Dinnocenzo, J. P.; Zuilhof, H.; Lieberman, D. R.; Simpson, T. R.; McKechney, M. W. *J. Am. Chem. Soc.* **1997**, *119*, 994.

(5) (a) Adam, W.; Handmann, V.-I.; Kita, F.; Heidenfelder, T. *J. Am. Chem. Soc.* **1998**, *120*, 831. (b) Adam, W.; Corma, A.; Miranda, M. A.; Sabater-Picot, M.-J.; Sahin, C. *J. Am. Chem. Soc.* **1996**, *118*, 2380. (c) Adam, W.; Kammel, T.; Toubartz, M.; Steenken, S. *J. Am. Chem. Soc.* **1997**, *119*, 10673. (d) Adam, W.; Heidenfelder, T.; Sahin, C. *J. Am. Chem. Soc.* **1995**, *117*, 9693. (e) Adam, W.; Heidenfelder, T.; Sahin, C. *Synthesis* **1995**, 1163. (f) Adam, W.; Sahin, C.; Sendelbach, J.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1994**, *116*, 2576. (g) Adam, W.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1992**, *114*, 3007.

(6) Schmidt, W.; Steckhan, E. *Chem. Ber.* **1980**, *113*, 577.

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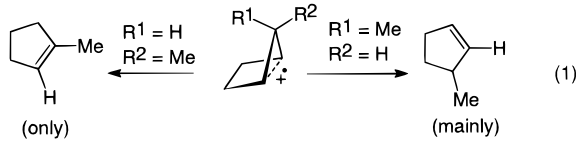
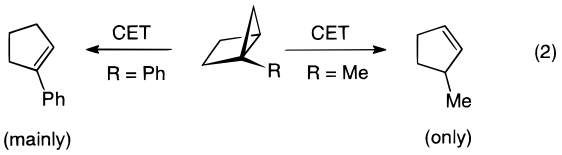
rearrangement,[7] proceed not only catalytically but also diastereo- and regioselectively. For the symmetrical, stereolabeled *anti*- and *syn*-5-methylbicyclo[2.1.0]pentanes, a remarkable *stereochemical memory effect* was disclosed (eq 1).[5g]



(1)

The anti stereoisomer furnished only 1-methylcyclopentene as the rearrangement product, while the syn one afforded predominantly 3-methylcyclopentene. These product studies, combined with the direct observation of the transient radical cations by EPR spectroscopy under matrix isolation, demanded a persistent conformation as precursor, whose stereochemical arrangement is dictated by the configuration of the starting housane. In the case of unsymmetrical derivatives of bicyclo-[2.1.0]pentane, a reversal in the regioselectivity of the 1,2 migration was observed (eq 2).[5b] Thus, 1-methylbicylopentane



(2)

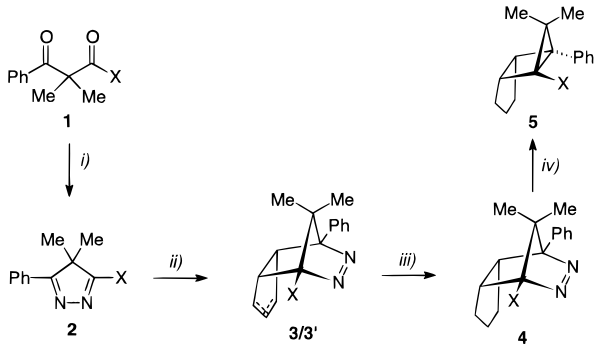
yielded exclusively 3-methylcyclopentene, while 1-phenylbicyclopentane gave 1-phenylcyclopentene as the major product. These remarkable regioselectivities were rationalized in terms of preferred positive-charge localization at the migration terminus in these Wagner−Meerwein-type rearrangements. Thus, the site that stabilizes the positive charge in the 1,3-diyl radical cation better than the unpaired electron promotes migration in that direction.

Although the chemistry of 1,3-cyclopentanediyl radical cations has been extensively studied and the mechanistic features are reasonably well understood,[5] the fundamental question of the relative stabilization of their cation and radical sites is still largely open-ended. Thus, mechanistic information is essential in rationalizing the chemical behavior of these elusive intermediates, which intervene in most thermal and photochemical electron-transfer processes. Unquestionably, the radical cations derived from housanes are ideally suited to aquire such data, since from the aforementioned (eq 2) it should be evident that the rearrangement regioselectivities offer the unique opportunity to assess what electronic factors control the relative stabilization of the cation versus radical centers. For this purpose, a wide range of bridgehead-substituted housanes would be necessary, a rather formidable synthetic chore for the parent bicyclo[2.1.0]-pentane system. Fortunately, the Hünig azoalkane route[8] (Scheme 1) provides a general and convenient method, in which the substitution pattern in the 1,3-dione **1** becomes the desired structural feature in the housane derivative **5**. The additional advantage of the tricyclic skeleton of **5**, besides the large variety of X substituents, is that the cyclopentane-annelated ring serves as stereochemical label to monitor the diastereoselectivity of the rearrangement process.

(7) (a) Boche, G.; Walborsky, H. M. In *Updates from the Chemistry of Functional Groups: Cyclopropane-derived Reactive Intermediates*; Patai, S., Rappaport, Z., Eds.; Wiley & Sons: Chichester, U.K., 1990; p 207. (b) Qin, X.-Z.; Snow, L. D.; Williams, F. *Chem. Phys. Lett.* **1985**, *117*, 383. (c) Qin, X.-Z.; Williams, F. *Chem. Phys. Lett.* **1984**, *112*, 79.

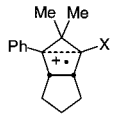
(8) Beck, K.; Hünig, S. *Chem. Ber.* **1987**, *120*, 477.

Scheme 1[a]



[a] Conditions: (*i*) $N_2H_4 \cdot H_2O$; (*ii*) CF_3COOH, cyclopentadiene; (*iii*) H_2, Pd/C, EtOAc; (*iv*) *hν* (333−364 nm), *n*-pentane.

The 1,3-cyclopentanediyl radical cations $\mathbf{5}^{\bullet+}$ were chosen for the present study, since in a preliminary study their suitability was demonstrated.[5a] The methyl-substituted (**a**−**g**) and the



$\mathbf{5}^{\bullet+}$

5	**a**	**b**	**c**	**d**	**e**	**f**	**g**
X	CH_3	CH_2Br	CH_2OAc	CH_2OH	CH_2OMe	CH_2F	CH_2CN

5	**h**	**i**	**j**	**k**	**l**	**m**
X	CHO	COMe	C_6H_4-*p*-Me	C_6H_4-*p*-Cl	C_6H_4-*p*-CO_2Me	C_6H_4-*p*-CN

Note: The radical cations $\mathbf{5}^{\bullet+}$, as drawn, are structurally not to be construed to constitute closed cyclopropane-type radical cations; they are planar, open 1,3-diyl radical cations $\mathbf{5}^{\bullet+}$, with the unpaired electron located either on the phenyl- or the X-bearing terminus and the two possible limiting structures are represented for convenience and economy by means of the dashed line.

carbonyl (**h**, **i**) derivatives were selected to probe electronic substituent effects. Such fine-tuning should disclose what electronic factors operate in the relative stabilization of the cation versus the radical center in the 1,3 radical−cation intermediate. To elucidate possible steric perturbations, the aryl (**j**−**n**) derivatives were employed, in which the para substituent should act only electronically. For comparison, the acid-catalyzed rearrangement of the housanes **5** was examined in order to establish the chemical behavior of the carbocations $\mathbf{5}(H)^+$ versus the radical cations $\mathbf{5}^{\bullet+}$. Our novel results confirm that pronounced electronic effects operate on the regioselectivity of the rearrangement for the radical cations $\mathbf{5}^{\bullet+}$, while the diastereoselectivity is governed by steric features at the diyl sites.

Results

Synthesis of the Azoalkanes and Tricyclooctanes. The preparation of the known azoalkanes **4a,j**−**m** and housanes **5a,j**−**m** has already been published.[5e,9] The hitherto unknown azoalkanes **4b**−**i** were prepared according to Hünig's isopyrazole cycloaddition method (Supporting Information) and from them the housanes **5** by photodenitrogenation (Scheme 1).

Electron-Transfer Reactions of the Tricyclooctanes. The product data are summarized in Table 1 (Scheme 2). The configurations of the diquinanes **6** and **7** were assigned by means of a prominent (∼8%) NOE effect between the 4α substituent at the C-4 position and the bridgehead hydrogen at C-1 but none

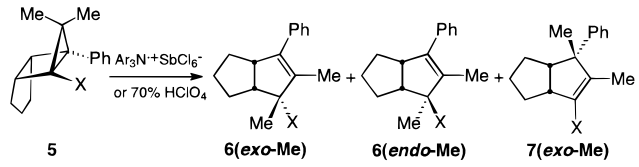
(9) Adam, W.; Kita, F.; Harrer, H. M.; Nau, W. M.; Zipf, R. *J. Org. Chem.* **1996**, *61*, 7056.

Table 1. Product Data of the Chemical Electron-Transfer and Acid-Induced Rearrangements of Housanes **5**

								product distribution[c]		
entry	substrate	X	solvent	mode[a]	time	base[b]	convn (%)	**6**(*exo*-Me)	**6**(*endo*-Me)	**7**(*exo*-Me)
1	**5a**[d]	CH_3	CH_2Cl_2	$TBA^{\bullet+}$ (0.1)	5 min	0.1	95	100	0	0
2	**5a**	CH_3	CH_3CN	$HClO_4$	24 h		100	21	0	79
3	**5c**	CH_2OAc	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	24 h	1.5	95[e]			
4	**5c**	CH_2OAc	$CDCl_3$	$HClO_4$	20 min		100	0	0	100
5	**5d**	CH_2OH	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	5 min	1.3	49	86	14	0
6	**5d**	CH_2OH	acetone-d_6	$HClO_4$	6 h		100	0	0	100[f]
7	**5e**	CH_2OMe	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	10 min	1.5	100	85	15	0
8	**5e**	CH_2OMe	acetone-d_6	$HClO_4$	10 min		100	0	0	100
9	**5f**	CH_2F	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	12 h	1.5	100	57	12	31
10	**5f**	CH_2F	$CDCl_3$	$HClO_4$	10 min		100	0	0	100[f]
11	**5g**	CH_2CN	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	19 h		100	30	8	62
12	**5h**	CHO	CD_3CN	$TBA^{\bullet+}$ (0.5)	24 h	1.5	100	0	0	100
13	**5h**	CHO	CH_2Cl_2	$HClO_4$	30 min		100	0	0	100
14	**5i**	COMe	$CDCl_3$	$TBA^{\bullet+}$ (0.5)	15 min	1.2	100	0	0	100
15	**5i**	COMe	CH_2Cl_2	$HClO_4$	30 min		100	0	0	100
16	**5j**	C_6H_4-*p*-Me	CH_2Cl_2	$TBA^{\bullet+}$ (0.1)	1 d		100	67	0	33
17	**5k**	C_6H_4-*p*-Cl	CH_2Cl_2	$TBA^{\bullet+}$ (0.1)	2 h		100	21	0	79
18	**5l**	C_6H_4-*p*-CO_2Me	CH_2Cl_2	$TBA^{\bullet+}$ (0.1)	30 min		100	0	0	100
19	**5m**	C_6H_4-*p*-CN	$CDCl_3$	$TBA^{\bullet+}$ (0.1)	3 d		100	0	0	100

[a] $TBA^{\bullet+}$ is tris(4-bromophenyl)aminium hexachloroantimonate, molar equivalents (in parentheses) are given relative to the housane; 70% $HClO_4$; at 20 °C, except entry 11 at reflux. [b] 2,6-Di-*tert*-butylpyridine, molar equivalents are given relative to the housane. [c] Determined by ^{1}H NMR spectroscopy (error ~5% of the stated values) on the crude product mixture; mass balances >90%, except entry 3 (<5%). [d] See ref 5e. [e] Undefined complex product mixture. [f] Cyclopentene *exo*-**7n** was formed.

Scheme 2



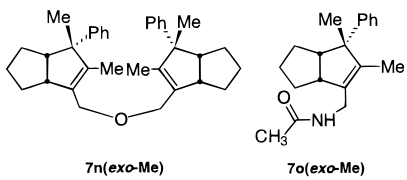
for the methylene hydrogens at C-6,7. Furthermore, the high-field displacement of the 6-H protons ($\delta = 0.8$) in the diquinanes **6j,k** and **7** derives from shielding by the proximate aryl group, which signifies that the original *syn*-methyl group in the housane has migrated. The cis arrangement of the two fused cyclopentenes was established by an appreciable (~7%) reciprocal NOE effect for the hydrogen atoms at the C-1,5 positions. Additionally, the structure of the diquinanes **6** and **7** was determined by 2D-INADEQUATE NMR experiments for **6** and **7j,k**.

The desired 1,3 radical cations $\mathbf{5}^{\bullet+}$ were generated by chemical electron transfer with tris(4-bromophenyl)aminium hexachloroantimonate ($TBA^{\bullet+}SbCl_6^-$) as one-electron oxidant.[6] The reactions were carried out in either CH_2Cl_2 or CH_3CN as solvents for all substrates. Since no solvent dependence was found in the CET reactions, only one example for each housane is given in Table 1. Treatment of the tricyclooctanes **5** with catalytic amounts of $TBA^{\bullet+}$ afforded exclusively the rearranged olefins **6** and **7** in high yields. The CET reactions of the acid-sensitive housanes **5a**−**f,h,i** were carried out in the presence of an excess of the hindered base 2,6-di-*tert*-butylpyridine to prevent undesirable acid-catalyzed rearrangements.

For the methyl-, hydroxymethyl-, and methoxymethyl-substituted housanes **5a,d,e** (entries 1, 5, and 7), only migration to the methyl-bearing site occurred. The housanes **5d,e** (entries 5 and 7) yielded the diastereomeric cyclopentenes **6d,e**(*exo, endo*-Me) through migration of both methyl groups in the starting housanes. The CET oxidation of the acetoxy-substituted housane **5c** (entry 3) afforded an undefined product mixture. The fluoromethyl- and cyanomethyl-substituted housanes **5f,g** (entries 9 and 11) led to a mixture of regioisomeric cyclopentenes **6f,g**(*exo, endo*-Me) and **7f,g**(*exo*-Me) due to 1,2-methyl shift to both the methyl- and phenyl-bearing sites. For the formyl- and acetyl-substituted tricyclo[3.3.0.0^{2,4}]octanes **5h,i** (entries 12 and 14), only the cyclopentenes **7h,i**(*exo*-Me) were observed, i.e., migration of the endo substituent exclusively to the phenyl terminus.

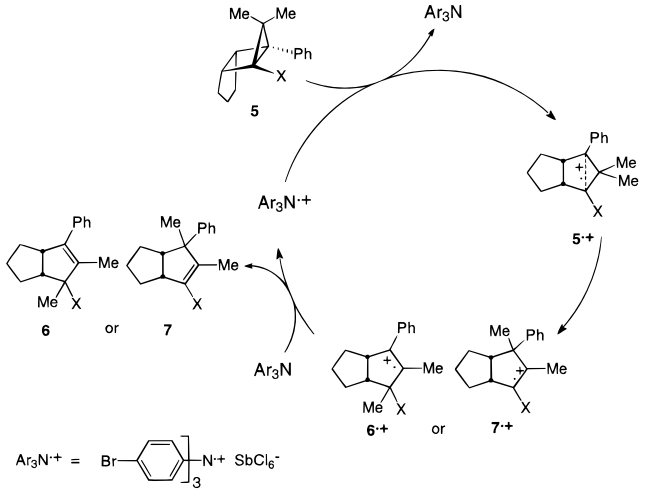
A similar trend of electronic substituent effects on the regioselectivity was observed in the CET oxidation for the aryl-substituted housanes **5j**−**m** (Table 1). The *p*-CN- and *p*-CO_2-Me-substituted derivatives **5l,m** (entries 18 and 19) afforded exclusively the diquinanes **7l,m**(*exo*-Me) by 1,2-methyl migration to the phenyl-bearing terminus. In contrast, the *p*-Me- and *p*-Cl-substituted derivatives **5j,k** (entries 16 and 17) gave both regioisomeric oxidation products **6j,k**(*exo*-Me) and **7j,k**(*exo*-Me). The **6j**(*exo*-Me) regioisomer is preferred for the methyl case **5j**, while the **7k**(*exo*-Me) one dominates for the *p*-Cl derivative **5k**. For all these aryl substrates, only the exo diastereomers were formed.

Acid-Catalyzed Rearrangement of the Housanes 5. For all acid-catalyzed reactions (Table 1), 70% $HClO_4$ was used as the proton source (Scheme 2). Only the conditions under which the highest mass balances (>90%) were achieved are given. Contrary to the CET reactions, the acid-induced rearrangement of the housanes **5a,c,e,h,i** yielded in all cases the **7**(*exo*-Me) cyclopentenes as the major (entry 2) or as the exclusive (entries 4, 8, 13, and 15) rearrangement product. The housanes **5d,f** (entries 6 and 10), instead of the expected rearrangement products **7d,f**(*exo*-Me), gave the ether **7n**(*exo*-Me), which is the



result of the acid-catalyzed condensation of the diquinanes **7d,f**(*exo*-Me). Suprisingly, the cyanomethyl-substituted housane **5g** and the aryl-substituted housanes **5j**−**m** persisted acid treatment. For the latter, presumably the steric bulk of the two bridgehead phenyl groups prevents protonation of these housanes.

Scheme 3



In CH_3CN, the housanes **5c**−**f** afforded the Ritter product **7o**(*exo*-Me) on acid treatment. By monitoring the product distribution of these acid-catalyzed reactions as a function of time, it was established that the cyclopentene **7c**(*exo*-Me) is converted significantly slower to the Ritter product than the corresponding housane **5c**. Thus, this control experiment reveals that the Ritter product **7o**(*exo*-Me) is formed directly from the housane **5c** rather than subsequently from the cyclopentene **7c**(*exo*-Me).

Discussion

Reaction Mechanism. The results presented in Table 1 show that the oxidative rearrangement of the tricyclooctanes **5** proceeds cleanly to the corresponding diquinanes **6** and **7** (Scheme 2). Since in all cases catalytic amounts of oxidant were enough to achieve complete conversion, we propose that the catalytic cycle in Scheme 3 operates. Electron transfer from the housane **5** to $Ar_3N^{\bullet+}$ initiates the cycle, the subsequent Wagner−Meerwein 1,2 rearrangement of the radical cation **5**$^{\bullet+}$ leads to the regioisomeric cyclopentene radical cations **6**$^{\bullet+}$ and/or **7**$^{\bullet+}$. Electron back-transfer from Ar_3N to **6**$^{\bullet+}$ or **7**$^{\bullet+}$ forms the diquinanes **6** and/or **7** and completes thereby the catalytic cycle. Alternatively, BET could also occur directly from the housane **5** to the radical cations **6**$^{\bullet+}$ and/or **7**$^{\bullet+}$ to yield the diquinanes **6** and/or **7** and a new housane radical cation **5**$^{\bullet+}$. Energy considerations, however, speak against this alternative pathway. From cyclovoltammetric measurements for the reference system, the reported[5b] oxidation potentials are 1.42 V (SCE) for housane **5a**, 1.58 V (SCE) for cyclopentene **6a**, and 1.06 V (SCE) for TBA$^{\bullet+}$. Thus, the BET step **6a**$^{\bullet+}$ + **5a** → **6a** + **5a**$^{\bullet+}$ is only by ∼0.16 V exothermic, while for **6a**$^{\bullet+}$ + Ar_3N → **6a** + $Ar_3N^{\bullet+}$ it is ∼0.5 V, and the latter process is favored. Note that the overall reaction proceeds although the aminium salt possesses a lower oxidation potential than the housane **5**. This is attributed to the highly exergonic rearrangement step, which follows the initial electron-transfer process.

Regioselectivity of the 1,2 Migration in the Radical Cations. The regioselectivity of the CET-mediated housane **5** rearrangement expresses the competition between the X (regioisomer **6**) and the Ph terminus (regioisomer **7**) for the migrating methyl group (Scheme 3). Indeed, reversal in the regioselectivity of the 1,2 migration was observed: For the CH_3 (**5a**), CH_2OH (**5d**), CH_2OCH_3 (**5e**), CH_2F (**5f**), and C_6H_4-*p*-Me (**5j**) derivatives, the **6** regioisomer is preferred, but for the CH_2-CN (**5g**), CHO (**5h**), $COCH_3$ (**5i**), C_6H_4-*p*-Cl (**5k**), C_6H_4-*p*-CO_2-CH_3 (**5l**), and C_6H_4-*p*-CN (**5m**) cases, the **7** regioisomer is favored.

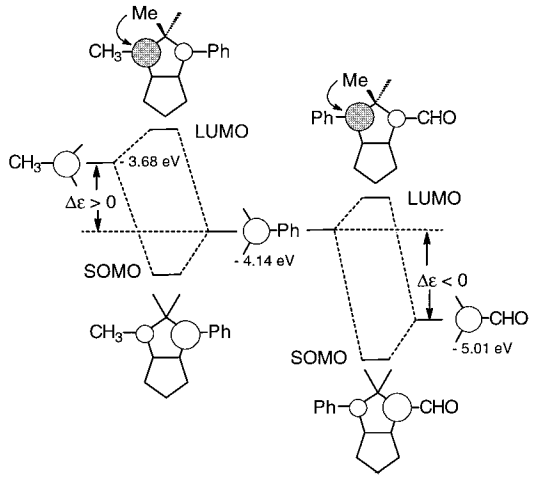


Figure 1. Schematic orbital interaction diagram of the radical fragments in the 1,3 radical cations **5a**$^{\bullet+}$ (left) and **5h**$^{\bullet+}$ (right).

How can these regioselective substituent effects be mechanistically rationalized? The rearrangement of a 1,3 radical cation is of the Wagner−Meerwein type and, thus, a cationic process.[2a,5] Accordingly, the regioselectivity in the CET-induced rearrangement of the housanes **5** is governed by the orbital interaction of the LUMO(σ^*) orbital of the 1,3-cyclopentanediyl radical cations **5**$^{\bullet+}$ with the HOMO(σ) of the migrating C−Me σ bond. Consequently, the orbital coefficients at the 1,3 termini in the LUMO(σ^*) of the radical cations are required to rationalize the experimental regioselectivities of the rearrangement. The desired SOMO(σ) and LUMO(σ^*) orbitals may be assembled in a qualitative manner through the interaction of the orbitals for the fragments R−CMe_2 and Ph−CMe_2 in the 1,3 radical cation, as shown in Figure 1 for the two extreme cases **5a**$^{\bullet+}$ (complete methyl migration to the X terminus) and **5h**$^{\bullet+}$ (complete methyl migration to the Ph terminus).

The relative ordering of the orbital fragments is given by the corresponding ϵ_{SOMO} orbital energies, which are readily accessible through AM1 calculations (Table 2).[10] The experimental E_{ox} data[11] for the CH_3, C_6H_5, and C_6H_4-*p*-CN cases confirm the relative order of the ϵ_{SOMO} values; unfortunately, no E_{ox} data is available for the remaining radicals. For convenience, we define the $\Delta\epsilon$ quantity, for which positive values ($\Delta\epsilon > 0$) apply when the ϵ_{SOMO} of the X-substituted fragment lies above the cumyl one (the phenyl substituent is taken as reference point), while negative values ($\Delta\epsilon < 0$) are observed when the ϵ_{SOMO} of the X-substituted fragment lies below the cumyl one. As a consequence, for $\Delta\epsilon > 0$, the LUMO in the radical cation **5**$^{\bullet+}$ will be in energy more similar to the X-substituted fragment and also carry the larger coefficient on this site (Figure 1). Hence, the 1,2 shift will take place preferentially to the X site to yield the **6** regioisomer, as observed for the radical cation **5a**$^{\bullet+}$ (X = CH_3). Analogously, for $\Delta\epsilon < 0$, the LUMO of the radical cation **5**$^{\bullet+}$ lies in energy closer to the cumyl fragment; now the phenyl terminus (Figure 1) bears the larger coefficient

(10) The AM1 method was used; cf.: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902 (VAMP program on a Silicon Graphics Iris Indigo workstation: Rauhut, G.; Alex, A.; Chandrasekhar, J.; Steinke, T.; Clark, T. *VAMP 5.0*; Universität Erlangen; Erlangen, FRG, 1993).

(11) (a) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132. (b) Sim, B. A.; Milne, P. H.; Griller, D.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635.

Table 2. SOMO Energies and Orbital Energy Differences of the Radical Fragments in the 1,3 Radical Cations $\mathbf{5}^{\bullet+}$ and the Regioselectivities of the Rearrangement

radical fragment[a]		ϵ_{SOMO} (eV)[b]	$\Delta\epsilon$ (eV)[c]	regioselectivity **6** : **7**[d]
CH_3	(**5a**)	- 3.68 (0.09)	0.46	100 :0
$MeOCH_2$	(**5e**)	- 3.75	0.39	100 :0
$HOCH_2$	(**5d**)	- 3.78	0.36	100 :0
FCH_2	(**5f**)	- 4.06	0.08	69 :31
p-Me-C_6H_4	(**5j**)	- 4.07	0.07	67 :33
C_6H_5	[e]	- 4.14 (0.16)	0.0	50 :50
$NCCH_2$	(**5g**)	- 4.23	- 0.09	38 :62
p-Cl-C_6H_4	(**5k**)	- 4.31	- 0.17	21 :79
p-CO_2CH_3-C_6H_4	(**5l**)	- 4.56	- 0.42	0 :100
p-CN-C_6H_4	(**5m**)	- 4.61 (0.46)	- 0.47	0 :100
O	(**5i**)	- 4.84	- 0.70	0 :100
O, H	(**5h**)	- 5.01	- 0.87	0 :100

[a] In parentheses is given the corresponding radical cation $\mathbf{5}^{\bullet+}$ to which the radical fragment belongs. [b] AM1 method;[10] in parentheses experimental E_{ox} (eV) values.[11] [c] Relative to the cumyl radical. [d] **6**(*exo/endo*-Me) represents migration to the X and **7**(*exo*-Me) to the Ph terminus. [e] Phenyl taken as reference system.

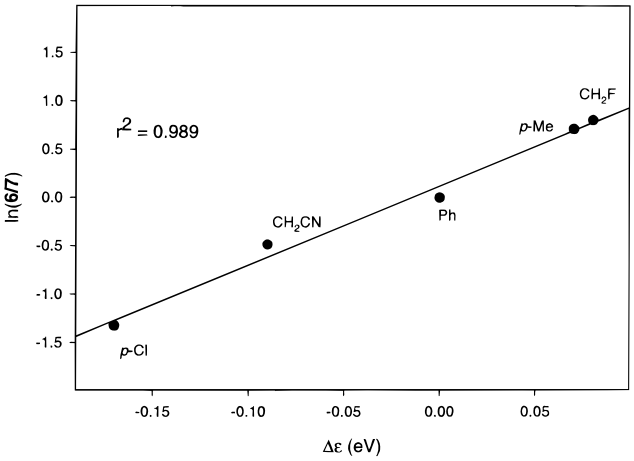
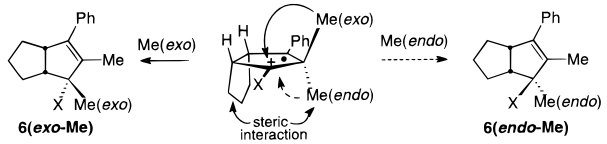


Figure 2. Orbital energy differences $\Delta\epsilon$ versus the regioisomeric ratios ln(**6**/**7**).

and the **7** regioisomer is preferred, as is the case for the radical cation $\mathbf{5h}^{\bullet+}$ (X = CHO). That these regioselectivities are governed by electronic and not steric effects of the X substituent should be evident from the aryl-substituted derivatives **5j**−**m**, because the para substituent in the aryl group is too remote to cause steric perturbations relative to the phenyl reference case.

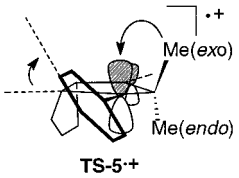
This simple MO approach also allows one to rationalize the regioselectivities for the intermediate cases, namely, CH_2F (**5f**), CH_2CN (**5g**), C_6H_4-*p*-Me (**5j**), and C_6H_4-*p*-Cl (**5k**), for which both regiosiomers **6** and **7** are formed (Table 2). The plot in Figure 2 of the semiempirical orbital energy differences ($\Delta\epsilon$) versus the logarithm of the experimentally observed regioisomeric ratios [ln(**6**/**7**)] of the radical cations $\mathbf{5f,g,j,k}^{\bullet+}$ displays an excellent linear correlation (r^2 = 0.989). This linear correlation substantiates once more that electronic and not steric properties of the substituent decide the observed regioselectivities. Thus, it is now possible to predict the regioisomeric ratio

Scheme 4



for the rearrangement of unsymmetrically substituted radical cation $\mathbf{5}^{\bullet+}$ if the two ϵ_{SOMO} orbital energies of the corresponding radical fragments are known, provided the orbital energy differences fall in the range of -0.42 eV $< \Delta\epsilon < +0.36$ eV (Table 2). For $\Delta\epsilon$ values of $\geq$0.36 eV, exclusively migration to the X site (regioisomer **6**) is observed, e.g., CH_3, CH_2OMe and CH_2OH, whereas the opposite (regioisomer **7**) is obtained for $\Delta\epsilon$ values of ≤ -0.42 eV, e.g., CHO, COMe, C_6H_4-*p*-CO_2-Me, and C_6H_4-*p*-CN.

Diastereoselectivity of the 1,2 Migration. While housanes **5h**−**m** yielded exclusively **6**(*exo*-Me), the housanes **5d**−**g** gave additionally small amounts (8−15%) of the **6**(*endo*-Me) diastereomer (Table 1). Thus, some migration of the endo substituent is observed only when the rearrangement terminus bears alkyl groups, i.e., CH_2OH (**5d**), CH_2OMe (**5e**), CH_2F (**5f**), and CH_2CN (**5g**), whereas exclusively the *exo*-methyl group migrates when this site carries aryl substituents. The formation of both the *exo*-Me and *endo*-Me diastereomers suggests a planar radical-cation geometry in the rearrangement step (Scheme 4), since for a persistent puckered conformation only one diastereomer would be expected.[5g] The preference for the *exo*-Me diastereomer is presumably due to the larger steric interaction during the transposition of the *endo*-methyl group at the 2 position with the annelated cyclopentane ring. Also, steric effects appear to be responsible for why aryl substitution at the rearrangement terminus suppresses *endo*-methyl migration completely. Inspection of molecular models reveals that severe steric interactions between the aryl group and the annelated cyclopentane ring in the radical cation obliges the phenyl ring to align conformationally in a skewed orientation with respect to the planar cyclopentane-1,3-diyl ring, as displayed in the transition-state structure **TS-5**$^{\bullet+}$. As a consequence, the *endo*-



TS-5$^{\bullet+}$

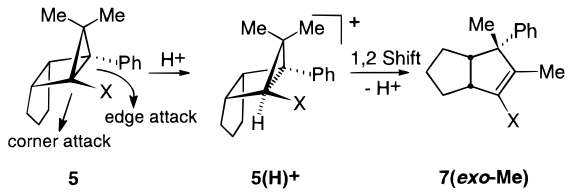
methyl group is sterically blocked by the skew aryl substituent and only the *exo*-methyl group migrates to give exclusively the *exo*-Me diastereomer of the regioisomer **7**.

Acid-Catalyzed 1,2 Migration. The acid-catalyzed rearrangement of the housanes **5** (Table 1, entries 2, 4, 6, 8, 10, 13, and 15) affords preferrably the **7**(*exo*-Me) over the **6**(*exo*-Me) cyclopentenes (Scheme 2). Such regio- and stereoselective electrophilic carbon−carbon bond cleavages of cyclopropane derivatives have been the subject of considerable investigation.[12] For example, it has been documented that corner attack on cyclopropanes by protons is generally favored over edge attack.[13] Furthermore, Wiberg reported that the acid-catalyzed addition

(12) Coxon, J. M.; Battiste, M. A. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; J. Wiley & Sons: Chichester, 1987; Chapter 6.

(13) (a) Lehn, J.-M.; Wipff, G. *J. Chem. Soc., Chem. Commun.* **1973**, 747. (b) Coxon, J. M.; Steel, P. J.; Whittington, B. I.; Battiste, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 2988. (c) Coxon, J. M.; Steel, P. J.; Whittington, B. I. *J. Org. Chem.* **1990**, *55*, 4136.

Scheme 5



to housane generates the most stable carbocation on rate-determining protonation.[14] The rearrangement products have been proposed to be formed directly from the protonated housane before the latter has become a genuine carbocation, to account for stereoselective capture by nucleophiles, migration, or proton loss. Presumably, the same mechanism also applies for the housanes **5** in that initial corner attack of the proton leads to the protonated housane **5**(H)$^+$ (Scheme 5). The carbocation **5**(H)$^+$ is expected to be preferred, since the positive charge is better stabilized at the phenyl-substituted site (cumyl type).[15] Hence, the charge-stabilizing ability of the aryl substituent at the cationic site is responsible for the regioselectivity in the 1,2 migration for this Wagner−Meerwein rearrangement. As for the diastereoselectivity, the subsequent 1,2 shift of the *endo*-methyl group to the developing C-4 carbocation occurs before a planar bona fide carbocation is attained, which thereby accounts for the stereoselective formation of the **7**(*exo*-Me) isomers (Scheme 5). However, the stereoselective generation of the **7**(*exo*-Me) cyclopentenes is also consistent with the intermediacy of a cyclopentyl cation **5**(H)$^+$, since the rationale offered for the ***exo*-**methyl diastereoselectivity of the radical cations TS-**5**$^{\bullet+}$ (Scheme 4) also applies for the 1,2 shift in a open, planar carbocation **5**(H)$^+$.

(14) Wiberg, K. B.; Kass, S. R.; Bishop, K. C., III *J. Am. Chem. Soc.* **1985**, *107*, 996.

(15) Arnett, E. M.; Hafelich, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 2889.

Conclusions

The housanes **5** have offered the unique opportunity to explore electronic and steric substituent effects on the regio- and diastereoselectivity of the CET-induced rearrangement of 1,3 radical cations. The regioselectivity of the migration may be tuned through the electronic character of the substituents on the diyl sites, which is rationalized in terms of a simple MO interaction diagram by considering the SOMO orbital energies of the corresponding radical fragments. Indeed, the excellent correlation between the calculated orbital energy differences ($\Delta\epsilon$) and the experimentally observed regioisomeric ratios allows a quantitative assessment of the electronic substituent effects. The diastereoselectivity of the 1,2 shift is controlled by the steric factors in the intermediary 1,3 radical cation.

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Supporting Information Available: Text describing experimental data (30 pages, print/PDF). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet. See any current masthead page for ordering information and Internet access instructions.

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