Divergent Pathways in the Rearrangement of Tricyclo[3.3.0.0^{2,4}]octanes (Housanes) on Chemical Electron Transfer (CET) *versus* Acid Catalysis: A Comparison of Radical Cations and Carbocations

Waldemar Adam,* Vera-Iris Handmann, Fumio Kita, and Thomas Heidenfelder

Institut für Organische Chemie, Universität Würzburg Am Hubland, D-97074 Würzburg, Germany

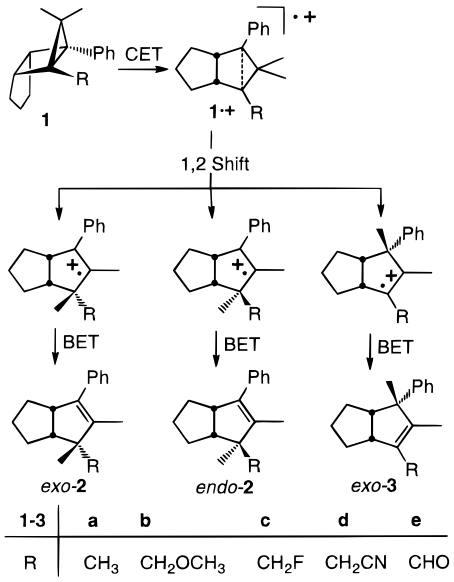
Received September 15, 1997

The importance of radical cations in electron-transfer oxidations is reflected in the vast number of recent studies on these short-lived intermediates.[1] We had found that 1,3-diyl radical cations, generated from bicyclo[2.1.0]pentane derivatives, exhibit a high propensity to rearrange by 1,2 shift to the corresponding 1,2 radical cations, which after electron back-transfer yield cyclopentenes.[2] For instance, the tricyclo[3.3.0.0^{2,4}]octane (housane) **1a** affords only the cyclopentene *exo*-**2a** upon electron-transfer oxidation, and thus, the 1,2 migration in the intermediary radical cation **1a**$^{\bullet+}$ occurs exclusively to the methyl and none to the phenyl terminus (Scheme 1). The unusual regioselectivity of this 1,2 migration demands a comprehensive mechanistic study of substituent effects on the rearrangement terminus through suitable "electronic tuning" of the R substituent. The dearth of information on this problem, as well as the need to compare the regioselectivities in the rearrangement of such radical cations **1**$^{\bullet+}$ with the corresponding carbocations, generated from the same precursor, prompted us to examine the electron-transfer oxidation and protonation of the housanes **1**. Our results clearly demonstrate the distinct nature of the radical cation and the carbocation rearrangements, although both entail Wagner−Meerwein 1,2 shifts. The regioselectivity of the electron-transfer oxidation is rationalized in terms of a qualitative MO interaction diagram, whereas that of the protonation follows the relative stability of the initially formed carbocations.

For our comparative study, we prepared the unsymmetrically bridgehead-substituted housane derivatives **1** according to the Hünig route.[3] The desired 1,3 radical cations **1**$^{\bullet+}$ were generated under chemical electron-transfer conditions (CET) with tris(4-bromophenyl)aminium hexachloroantimonate (TBA$^{\bullet+}$SbCl$_6^-$) as one-electron oxidant.[4] For the acid-sensitive housanes, the CET reactions were carried out in the presence of an excess of base to rule out the possible involvement of acid-catalyzed rearrangement. For the acid-catalyzed reactions, 70% $HClO_4$ was used as proton source. The product distributions in Table 1 clearly reveal the different nature of the radical cation and the carbocation rearrangements.

In the acid-induced rearrangement of the housanes **1** (Table 1, entries 2, 4, 6, 9, and 11), the formation of the *exo*-**3** cyclopentenes is preferred over *exo*-**2** (Scheme 2), a 1,2 methyl shift which is not only regioselective but also stereoselective. The exclusive exo diastereoselectivity is presumably due to the steric hindrance between the annellated cyclopentane ring and the *endo*-methyl group in the carbocation **1(H)**$^+$, which favors the migration of the *exo*-methyl substituent. Since the positive charge is better stabilized at the phenyl-substituted site (cumyl-type),[5] the carbocation **1(H)**$^+$ is preferentially formed and the subsequent 1,2 shift of the *exo*-methyl group leads to the observed *exo*-**3** regioisomer after proton loss (Scheme 2).

Scheme 1



Contrary to the acid-catalyzed rearrangement, treatment of the housanes **1** with TBA$^{\bullet+}$SbCl$_6^-$ led to significantly different product distributions (Table 1, entries 1, 3, 5, 7, 8, and 10). For example, in the chemical electron-transfer (CET) process (Scheme 1), housane **1a** exclusively rearranges to *exo*-**2a** (entry 1), whereas protonation yields *exo*-**3a** as the main product (entry 2). The same dichotomy in the regioselectivity is displayed by the related methoxymethyl-substituted housane **1b** (entries 3 and 4), i.e., the **2b** regioisomer is preferred in the electron-transfer and **3b** in the acid catalysis, while for the fluoromethyl derivative **1c** (entries 5 and 6) already appreciable amounts (31%) of *exo*-**3c** (the exclusive product of the acid-catalyzed rearrangement) are observed. Indeed, for the cyanomethyl-substituted housane **1d** (entries 7 and 8), the major oxidation product is *exo*-**3d** [unfortunate for our comparison, no rearrangement was promoted on $HClO_4$ treatment (entry 9)].[6] For the formyl-substituted derivative **1e** (entries 10 and 11), both the electron-transfer oxidation and protonation afford exclusively the *exo*-**3e** regioisomer. Thus, the regioselectivity of the electron-transfer-catalyzed rearrangement depends on the electronic nature of the R substituent in the housane **1** (Table 1), with exclusively the regioisomer **2** for the methyl (**1a**) and exclusively regioisomer **3** for the formyl (**1e**) derivative (Scheme 1). Mechanistically significant, these regioselectivities are in competition between R and Ph at the rearrangement termini, for R = Me (**1a**) away from Ph and with R = CHO (**1e**) toward Ph.

Like that of carbocations, the rearrangement of 1,3 radical cations is of the Wagner−Meerwein type,[1e,2] and consequently,

(1) (a) Dinnocenzo, J. P.; Simpson, T. R.; Zuilhof, H.; Todd, W. P.; Heinrich, T. *J. Am. Chem. Soc.* **1997**, *119*, 987. (b) Dinnocenzo, J. P.; Zuilhof, H.; Lieberman, D. R.; Simpson, T. R.; McKechney, M. W. *J. Am. Chem. Soc.* **1997**, *119*, 994. (c) Maslak, P.; Chapman, W. H., Jr.; Vallombroso, T. M., Jr.; Watson, B. A. *J. Am. Chem. Soc.* **1995**, *117*, 12380. (d) Weng, H.; Sheik, Q.; Roth, H. D. *J. Am. Chem. Soc.* **1995**, *117*, 10655. (e) Shaik, S. S.; Dinnocenzo, J. P. *J. Org. Chem.* **1990**, *55*, 3434. (f) Du, P.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1988**, *110*, 3405.

(2) (a) Adam, W.; Corma, A.; Miranda, M. A.; Sabater-Picot, M.-J.; Sahin, C. *J. Am. Chem. Soc.* **1996**, *118*, 2380. (b) Adam, W.; Heidenfelder, T.; Sahin, C. *Synthesis* **1995**, 1163. (c) Adam, W.; Sahin, C.; Sendelbach, J.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1994**, *116*, 2576. (d) Adam, W.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1992**, *114*, 3007.

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

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

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

(6) (a) Interestingly, the cyclopentenes *endo*-**2b**−**d** were detected as side products in the CET reaction of the housanes **1b**−**d**. The formation of both the exo and endo diastereomers suggests a planar radical cation geometry for the rearrangement, since for a puckered conformation only one diastereomer would be expected.[2d] The preference for the exo diastereomer is due to the larger steric interaction of the *endo*-methyl group at the 2 position with the annellated cyclopentane ring, analogous to the explanation offered for the exo diastereoselectivity observed for the carbocation. (b) Presumably, the different reaction times required in the CET mode derive from the different oxidation potentials of the housanes **1**.

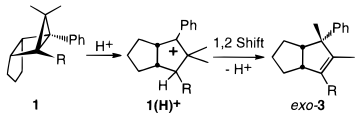
S0002-7863(97)03234-4 CCC: $15.00
Published on Web 01/16/1998

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

								product distribution[a]		
entry	substrate	R	solvent	mode[b]	time	base[c]	convn[a] (%)	*exo*-**2**	*endo*-**2**	*exo*-**3**
1	**1a**[d]	CH_3	CH_2Cl_2	$TBA^{\bullet+}$ (0.1)	5 min	0.1	95	100	0	0
2	**1a**	CH_3	CH_3CN	$HClO_4$	24 h		100	21	0	79
3	**1b**	CH_2OMe	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	10 min	1.5	100	85	15	0
4	**1b**	CH_2OMe	$CDCl_3$	$HClO_4$	10 min		100	0	0	100
5	**1c**	CH_2F	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	12 h	1.5	100	57	12	31
6	**1c**	CH_2F	$CDCl_3$	$HClO_4$	10 min		100	0	0	100[e]
7	**1d**	CH_2CN	CD_3CN	$TBA^{\bullet+}$ (0.3)	3 weeks		100	32	13	55
8	**1d**	CH_2CN	CH_2Cl_2	$TBA^{\bullet+}$ (0.3)	19 h		100	30	8	62
9	**1d**	CH_2CN	CD_3CN	$HClO_4$	4 weeks		0	0	0	0
10	**1e**	CHO	CD_3CN	$TBA^{\bullet+}$ (0.5)	24 h	1.5	100	0	0	100
11	**1e**	CHO	CH_2Cl_2	$HClO_4$	30 min		100	0	0	100

[a] Determined by ^{1}H NMR spectroscopy (error ca. 5% of the stated values) on the crude product mixture; mass balances >90%. [b] $TBA^{\bullet+}$ = tris(4-bromophenyl)aminium hexachloroantimonate, molar equivalents (in parenthesis) are given relative to the housane; 70% $HClO_4$; at 20 °C, except entry 8 at reflux. [c] 2,6-Di-*tert*-butylpyridine, molar equivalents are given relative to the housane. [d] See ref 4b. [e] Product does not persist under the reaction conditions.

Scheme 2



the preferred site of positive charge localization in the 1,3 diyl species $\mathbf{1}^{\bullet+}$ determines the regioselectivity. In a Wagner−Meerwein 1,2 methyl shift, the interaction of the LUMO at the cation site and the HOMO of the C−Me bond dominates; consequently, also for the 1,3 radical cation $\mathbf{1}^{\bullet+}$, we need to know the orbital coefficients of the LUMO to assess the theoretically expected regioselectivities.

A simple qualitative approach is to assemble the desired radical cation MOs through the interaction of MOs of the two radical fragments R−CMe_2 and Ph−CMe_2, as outlined in Figure 1 for the two extreme cases $\mathbf{1a}^{\bullet+}$ (R = Me) and $\mathbf{1e}^{\bullet+}$ (R = CHO). For this purpose, we have chosen the SOMOs of the methyl- and formyl-substituted fragments, whose orbital energies (ϵ_{SOMO}) were calculated by the AM1 method[7] (Table 2), and compared them with the phenyl (cumyl radical) one. The latter is taken as reference point since all radical cations $\mathbf{1}^{\bullet+}$ possess this fragment and the regioselectivity of the rearrangement expresses the competition between the R (regioisomer **2**) and the Ph terminus (regioisomer **3**) for the migrating methyl group.

For the Me derivative $\mathbf{1a}^{\bullet+}$, the ϵ_{SOMO} of the Me-substituted fragment lies above that of the Ph one, and thus, the LUMO in the radical cation $\mathbf{1a}^{\bullet+}$ will be in energy more similar to the Me fragment and also carry the larger coefficient at this site. Hence, the 1,2 methyl shift will occur preferentially to the Me terminus to give the **2a** regioisomer, as observed (Table 1, entry 1). In contrast, for the derivative $\mathbf{1e}^{\bullet+}$, the ϵ_{SOMO} of the formyl-substituted fragment lies below that of the Ph one, such that the LUMO of the radical cation $\mathbf{1e}^{\bullet+}$ lies in energy closer to the Ph fragment. That terminus now bears the larger coefficient, and Me migration affords the **3e** regioisomer (Table 1, entry 10).

The regioselectivities of the CET-catalyzed rearrangements for the other derivatives **1b**−**d** are also readily rationalized in terms of the qualitative orbital interaction diagram in Figure 1. The methoxymethyl case **1b** behaves like **1a** with exclusive formation of the **2b** regioisomer (Table 1, entry 3), while mixtures of the regioisomers **2** and **3** are produced for the fluoro- and cyano-substituted substrates **1c,d** (Table 1, entries 5 and 7). In fact,

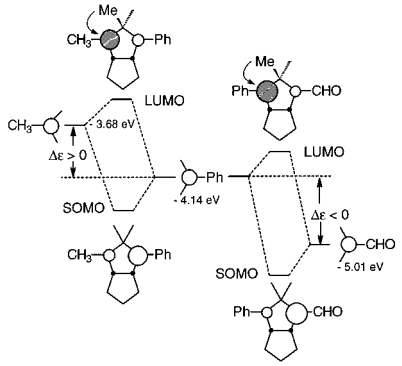


Figure 1. Schematic orbital interaction diagrams of the radical fragments in the 1,3 radical cations $1a^{\bullet+}$ (left) and $1e^{\bullet+}$ (right).

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

radical fragment	ε_{SOMO} (eV)[a)]	$\Delta\varepsilon$ (eV)[b)]
CH_3	- 3.68 (0.09)	0.46
$MeOCH_2$	- 3.75	0.39
FCH_2	- 4.06	0.08
Ph	- 4.14 (0.16)	0.0
$NCCH_2$	- 4.23	- 0.09
O, H	- 5.01	- 0.87

[a] AM1 method (ref 7); experimental E_{ox} (eV) values (ref 8) are given in parenthesis. [b] Relative to the cumyl radical as reference.

when the $\Delta\epsilon$ values (Table 2) are ca. 0.1 eV or less, poor regioselectivities are to be expected, presumably because the ϵ_{SOMO} values of the fragments are quite similar and the orbital coefficients in the radical cation LUMO not sufficiently different to express an absolute preference in the methyl migration.

From this first detailed comparison of the rearrangement of 1,3 radical cations and carbocations derived from the same housane precursor, we have learned that electronic substituent effects on the diyl sites profoundly influence the regioselectivities of the 1,2 shift. Although the rearrangements are of the Wagner−Meerwein type, these data unequivocaly illustrate the distinct electronic character of the cationic intermediates involved in the electron-transfer oxidation *vs* acid catalysis of the housanes **1**.

Acknowledgment. We express our gratitude to the Fonds der Chemischen Industrie and the Volkswagen-Stiftung for generous financial support of this work. We thank Birgit Beck for technical assistance.

JA9732340

(7) 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). The experimental E_{ox} data (ref 8) confirm the relative order of the ϵ_{SOMO} values; unfortunately, no E_{ox} data is available for the remaining radicals.

(8) (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.