J|A|C|S
ARTICLES
Published on Web 09/14/2002

Viscosity-Controlled, Product-Selective Rearrangement of the Cyclopentane-1,3-diyl Radical Cation Derived from an Annelated Housane by Electron Transfer: A Case of Curtin−Hammett Behavior

Waldemar Adam,*,† Christian Librera,† and Alexei V. Trofimov†,‡

Contribution from the Institute of Organic Chemistry, University of Würzburg, Am Hubland, D-97074 Würzburg, Germany, and Institute of Biochemical Physics, Russian Academy of Sciences, 117977 Moscow, Russia

Received February 28, 2002

Abstract: The fractional-power viscosity dependence of the product ratio [**2**]/[**3**] $\sim \eta^{\alpha_3-\alpha_2}$ manifests the different free-volume requirements for the methylene ($k_3 \sim \eta^{\alpha_3}$) versus methyl ($k_2 \sim \eta^{\alpha_2}$) migrations. The syn/anti-conformational changes (k_1, k_{-1}) in the radical cation **1**$^{\bullet+}$ proceed faster than the structural transformations (k_2, k_3), which constitutes the first Curtin−Hammett case in radical-cation rearrangements.

Introduction

The rearrangement of cyclopentane-1,3-diyl radical cations[1] comprises a fascinating chapter in electron-transfer chemistry.[2] The chemical reactivity of these short-lived intermediates is controlled by numerous internal (electronic) and external (medium) features; the latter have received to date little attention. Herein we report on the solvent effects in the rearrangement of the cyclopentane-1,3-diyl radical cation derived from the cyclohexane-annelated housane **1** (Scheme 1) and elucidate the mechanism of this complex transformation by means of the viscosity dependence on the product selectivity.

The viscosity probe has been applied in our recent studies on the unique stereoselective double-inversion process observed in the thermal isomerization of housanes (Scheme 2).[3a] The incentive of the present work was to demonstrate the *general* utility of this simple and convenient experimental tool in acquiring valuable mechanistic details on chemical transformations substantially more complex than we have studied before.[3] In particular, most recently we have reported[4] on the electron-transfer-induced rearrangement of the structurally related housane **1** by the one-electron oxidant tris(*p*-bromophenyl)aminium hexachloroantimonate (TBA$^{\bullet+}$SbCl$_6^-$), which affords the cyclopentenes **2** and **3** by way of the intermediary cyclopentane-1,3-diyl radical cations *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ (Scheme 1). In this Wagner−Meerwein-type rearrangement,[1,5] the 1,3 radical cation *anti*-**1**$^{\bullet+}$ transforms first to the 1,2 radical cation **2**$^{\bullet+}$ by shift of the axial methyl substituent, whereas migration of the axial methylene group generates the spirocyclic **3**$^{\bullet+}$ species from the *syn*-**1**$^{\bullet+}$ conformer; recapture of an electron leads respectively to the cyclopentene products **2** and **3**.[6] Due to the better radical-stabilizing ability of the phenyl group, the positive charge is localized at the alkyl-substituted site; consequently, both the methyl (k_2) and methylene (k_3) migrations (Scheme 1) take place to this cationic center.

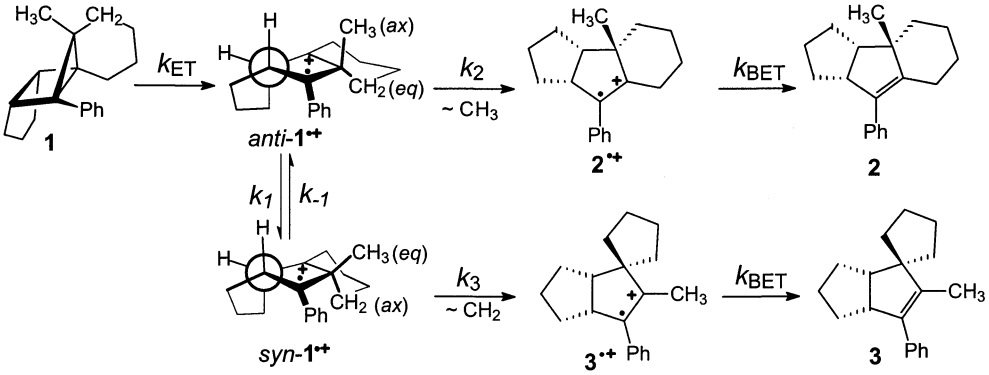
It should be noted that in the double inversion of the diradical-type diyl (Scheme 2), merely bond formation (cyclization) occurs during the observed geometrical changes (the methylene-bridge flap changes its relative position in space), but no major structural reorganization through bond-changing events takes place. The frictional effects imposed by the medium viscosity obstruct the flap motion during the ring closure such that, in more viscous solvents, the inversion process is delayed and more retained housane product is observed.[3] In contrast, in the structurally similar radical-cation-type diyls (Scheme 1), except for the positive charge, the 1,2 shift of the alkyl substituents involves major bond-breaking and bond-making events to effect the structural transformations. It must also be stressed that in the diradical cyclization (Scheme 2) two diastereomeric housanes are obtained, whereas in the radical-cation rearrangement (Scheme 1) two distinct products are generated, namely the annelated cyclopentene **2** and the spirocyclic **3**. Consequently, the question of mechanistic import was whether the radical-cation rearrangement (Scheme 1) is also influenced by viscosity.

* Corresponding author. Fax: +49 (931) 8884756. E-mail: adam@chemie.uni-wuerzburg.de. Web site: http:// www-organik.chemie.uni-wuerzburg.de.
† University of Würzburg.
‡ Russian Academy of Sciences.

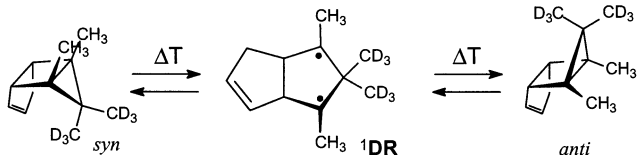
(1) Adam, W.; Heidenfelder, T. *Chem. Soc. Rev.* **1999**, *28*, 359−366.
(2) Roth, H. D. *Top. Curr. Chem.* **1992**, *163*, 131−245.
(3) (a) Adam, W.; Diedering, M.; Trofimov, A. V. *J. Am. Chem. Soc.* **2002**, *124*, 5427−5430. (b) Adam, W.; Grüne, M.; Diedering, M.; Trofimov, A. V. *J. Am. Chem. Soc.* **2001**, *123*, 7109−7112. (c) Adam, W.; Martí, V.; Sahin, C.; Trofimov, A. V. *Chem. Phys. Lett.* **2001**, *340*, 26−32. (d) Adam, W.; Diedering, M.; Trofimov, A. V. *Phys. Chem. Chem. Phys.* **2002**, *4*, 1036−1039.
(4) Adam, W.; Librera, C. P. *J. Org. Chem.* **2002**, *67*, 576−581.
(5) (a) Shaik, S. S.; Dinnocenzo, J. P. *J. Org. Chem.* **1990**, *55*, 3434−3436. (b) Blancafort, L.; Adam, W.; González, D.; Olivucci, M.; Vreven, T.; Robb, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 10583−10590. (c) Paquette, L. A.; Leichter, L. M. *J. Am. Chem. Soc.* **1980**, *102*, 4397−4403.
(6) The anti and syn descriptors refer to the migrant; i.e., in *anti*-**1**$^{\bullet+}$ the methyl group occupies the pseudoaxial position and assumes an anti relationship to the annelated cyclopentane ring, whereas in *syn*-**1**$^{\bullet+}$ it is the methylene fragment that is in the pseudoaxial position and assumes a syn relationship.

10.1021/ja026057y CCC: $22.00

Scheme 1



Scheme 2



If that should be the case, does this viscosity dependence reside mainly in the conformational equilibrium between the *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ 1,3-radical-cation intermediates or in the transposition of their alkyl migrants to the respective 1,2 radical cations **2**$^{\bullet+}$ and **3**$^{\bullet+}$ (Scheme 1)?

The necessity of considering the two equilibrating conformers *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ (Scheme 1) stems from the stereoelectronic requirement of a coplanar alignment of the migrant relative to the migration terminus.[5] This requisite is best fulfilled for pseudoaxial substituents, which migrate in preference. Hence, the methyl group occupies the pseudoaxial position in the *anti*-**1**$^{\bullet+}$ radical cation (precursor to the rearrangement product **2**) and the methylene fragment in the *syn*-**1**$^{\bullet+}$ conformer (precursor to the rearrangement product **3**). Presently, we demonstrate that the viscosity dependence, observed in the transformation of the *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ radical cations (Scheme 1), is conditioned by the different conformational requirements for the methyl migration (k_2) and the ring contraction (k_3).

Experimental Section

General Aspects. The solvents were purified according to standard procedures. The viscosities and dielectric constants were available from the literature.[8] The known housane **1** was prepared according to the reported procedure.[4]

General Procedure for the Electron-Transfer-Induced Rearrangements of the Housane 1 on the NMR Scale. For all electron-transfer reactions carried out on the NMR scale, the housane **1** (50 μmol) was dissolved in 0.7 mL of the appropriate deuterated solvent, which was passed through a short basic alumina (0.20 g) column immediately before use. For the electron-transfer reactions, 2,6-di-*tert*-butylpyridine (150 mol %) or solid K_2CO_3 (ca. 10 mg) was added to prevent acid-catalyzed rearrangement, and the solution was treated with tris(*p*-bromophenyl)aminium hexachloroantimonate (ca. 5 mol %) until the deep blue color persisted (complete consumption of the housane **1**). As before,[4] the quantitative analysis of the product distribution utilized characteristic and well-resolved ^{1}H NMR resonances (400 MHz, $CDCl_3$), namely δ 1.16 (s, 3H), 2.33 (td, J = 8.9, 5.0 Hz, 1H), 2.50 (ps d, J = 13.2 Hz, 1H), and 3.62 (td d, J = 8.9 Hz, 1H) for product **2** and δ 1.65 (d, 2.8 Hz, 3H), 2.52 (ps q, J = 7.7 Hz, 1H), 3.7 (m_c, 1H) for product **3**.

(7) Adam, W.; Sahin, C.; Sendelbach, J.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1994**, *116*, 2576−2584.
(8) Riddick, J. A.; Bunger, W. B. *Organic Solvents*; Wiley-Interscience: New York, 1970.

Table 1. Solvent Dependence of the Product Distribution in the Electron-Transfer-Induced Rearrangement of the Housane **1**[a]

solvent[b]	η (cP)	ϵ	product ratio [**2**]/[**3**][c]
CD_3CN	0.36	37.5	1.17
$CDCl_3$	0.58	4.8	1.22
MeOD	0.60	32.7	1.27
i-PrOH	2.39	32.0	1.56
$CH_3CH(OH)CH_2OH$	56.0	32.0	1.94
$HO(CH_2)_4OH$	89.2	31.5	2.33

[a] The structure is given in Scheme 1. [b] [TBA$^{\bullet+}$$SbCl_6^-$] = 3.5 mM, 20 °C, 24 h. [c] Determined by ^{1}H NMR spectroscopy; mass balance >90%; error ±4% of the stated values.

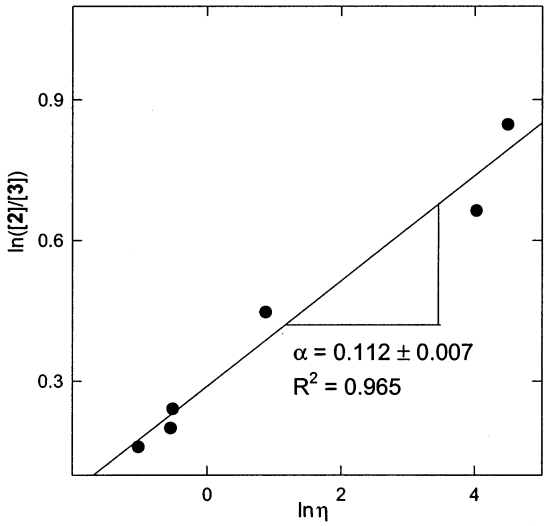
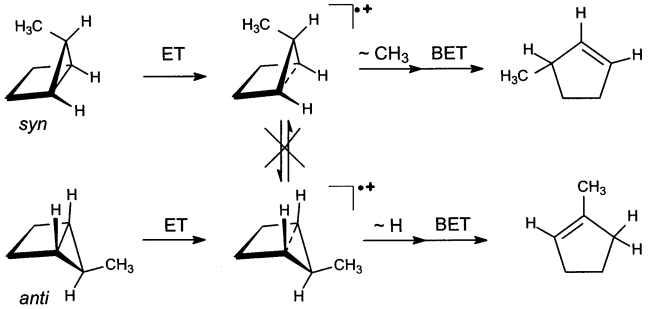


Figure 1. Double-logarithmic plot for the viscosity dependence of the [**2**]/[**3**] ratio (experimental data of Table 1) in the electron-transfer-induced rearrangement of housane **1** (for structures, cf. Scheme 1).

Results and Discussion

The product selectivity, expressed in terms of the [**2**]/[**3**] ratio, is given in Table 1 as a function of a variety of solvents. As seen from Table 1, nearly equal amounts of the products **2** and **3** are observed at low viscosity, while the cyclopentene **2** dominates more than 2-fold at higher η. The viscosity data on the [**2**]/[**3**] ratio are displayed in Figure 1 in the form of a double-logarithmic plot.[3] It is evident from Figure 1 that the plot of ln([**2**]/[**3**]) versus ln η is linear with a slope of α = 0.112 ± 0.007.

Scheme 3



The nearly equal amounts of the rearrangement products **2** and **3** at *low* viscosity (cf. Table 1) imply that the syn/anti conformational changes (k_1, k_{-1}) in Scheme 1 proceed faster than the chemical transformation (k_2, k_3), that is, a case of Curtin−Hammett behavior.[9] This behavior is in contrast with that reported for the structurally simpler housanes in Scheme 3,[1,7] for which rearrangement is faster than the syn/anti conformational changes, that is, a case of stereochemical memory.

To rationalize mechanistically the observed viscosity dependence (Figure 1), a relation between the [**2**]/[**3**] product ratio and the rate constants of the elementary reaction steps (cf. Scheme 1) is required. The kinetics similar to that in Scheme 1 has been analyzed by Seeman,[9] who showed that when the conformational change (k_1, k_{-1}) is faster than the migration steps (k_2, k_3), the expression for [**2**]/[**3**] acquires the simple Curtin−Hammett form shown in eq 1.[9]

$$[\mathbf{2}]/[\mathbf{3}] \approx k_2 k_{-1}/(k_3 k_1) \tag{1}$$

To establish an explicit relationship between the [**2**]/[**3**] ratio and the solvent viscosity (η), the rate constants k_i ($i = 1, -1, 2, 3$) in eq 1 need to be expressed as a function of η. This may be readily done with a help of the simple *free-volume* model,[3] which had proved to be useful in rationalizing the viscosity behavior of a number of liquid-phase rearrangements.[3,10] In this model, the translational motion of a molecule in a liquid medium is possible when the free volume V_f per molecule is larger than some "critical" value V_0. The fluidity (η^{-1}) is proportional to the probability factor [$\exp(-V_0/V_f)$] for the translational motion. Hence, the free-volume dependence of the viscosity may be expressed by eq 2, in which A is a proportionality factor.

$$\eta = A \exp(V_0/V_f) \tag{2}$$

In contrast to the translational diffusion of molecules, intramolecular rearrangements involve only a portion of the molecule, and thus, merely a fraction $\alpha_i V_0$ ($\alpha_i < 1$, $i = 1, -1, 2, 3$) of the critical free volume V_0 is required. Therefore, the rate constants k_i for each transformation in Scheme 1 are given by eq 3, in which k_i^0 is the preexponential factor.

$$k_i = k_i^{\,0} \exp(-\alpha_i V_0/V_f) \tag{3}$$

From eqs 2 and 3 follows eq 4 for the viscosity dependence of each rate constant k_i.

$$k_i = k_i^{\,0}(A/\eta)^{\alpha_i} \tag{4}$$

Substitution of eq 4 into eq 1 affords eq 5, which shows the complete viscosity dependence for the [**2**]/[**3**] ratio.

$$[\mathbf{2}]/[\mathbf{3}] = \frac{k_2^{\,0}(A/\eta)^{\alpha_2}}{k_3^{\,0}(A/\eta)^{\alpha_3}} \frac{k_{-1}^{\,0}(A/\eta)^{\alpha_{-1}}}{k_1^{\,0}(A/\eta)^{\alpha_1}} \tag{5}$$

Since the k_1 and k_{-1} steps involve the same conformational changes, for which a similar free-volume requirement (i.e., $\alpha_1 \approx \alpha_{-1}$) applies, the viscosity dependence of [**2**]/[**3**] (cf. eq 5) reduces to the convenient expression in eq 6

$$[\mathbf{2}]/[\mathbf{3}] = \frac{k_2^{\,0} k_{-1}^{\,0}}{k_3^{\,0} k_1^{\,0}} \frac{\eta^{\alpha_3}}{\eta^{\alpha_3}} = \text{const} \times \eta^{\alpha_3 - \alpha_2} = \text{const} \times \eta^{\alpha} \tag{6}$$

in which η^{α_1} and $\eta^{\alpha_{-1}}$ cancel out in view of similar α_1 and α_{-1} values. The double-logarithmic form predicts a linear relation between ln([**2**]/[**3**]) and ln η, which corroborates the experimental observation in Figure 1. Thus, according to eq 6, the slope (α) of the linear plot in Figure 1 manifests the different free-volume requirements for the methylene (k_3) and the methyl (k_2) migrations. The positive slope means that the influence of the viscosity is larger for the methylene (k_3) than for methyl (k_2) migration. This fact implies larger structural change for the ring-contraction process to afford the spirocyclic cyclopentene **3** than for the methyl shift to the annelated product **2**. Thus, the observed viscosity dependence of the product selectivity (Figure 1) is consistent with Curtin−Hammett behavior (k_1, $k_{-1} \gg k_2$, k_3) for the conformationally interconverting *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ radical cations (Scheme 1), an unprecedented feature of such short-lived intermediates (Scheme 3).

A point of concern is whether the observed solvent dependence (Figure 1) is solely accounted for in terms of viscosity or if other solvent properties, e.g., polarity, play a role. In this context, we have recently assessed the polarity dependence for the stereoselective formation of inverted housane in the photodenitrogenation of diazabicyclo[2.2.1]hept-2-ene in a large variety of nonpolar, polar, aprotic, and protic solvents.[3d] Such a detailed study was, unfortunately, not possible in the present case because of the poor solubility of the housane **1** and/or TBA$^{\bullet+}$SbCl$_6^-$ in most of the solvents used in our previous work;[3d] nevertheless, it should be noticed that the dielectric constant (ϵ) has been varied over a wide range (Table 1). It is, thus, a fortuitous circumstance that Curtin−Hammett behavior applies in the present case of the conformationally interconverting *anti*-**1**$^{\bullet+}$ and *syn*-**1**$^{\bullet+}$ radical cations, which suggests that polarity effects are negligible and viscosity dominates the product selectivity. Indeed, the rate constants for conformational changes k_1 and k_{-1} in eq 1 are expectedly independent of polarity, since the distribution of the positive charge stays constant. In contrast, the structural transformations, i.e., k_2 and k_3, depend on polarity, but presumably to the *same* extent (charge preservation). Hence, the quotient $k_2 k_{-1}/(k_3 k_1)$ and the [**2**]/[**3**] ratio do not sense polarity effects in the present case.

As already mentioned, contrary to the structurally more complex radical cation **1**$^{\bullet+}$, the simpler cases in Scheme 3

(9) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83−134.
(10) (a) Tredwell, C. J.; Osborne, A. D. *J. Chem. Soc., Faraday Trans. 2* **1980**, *76*, 1627−1637. (b) Velsko, S. P.; Fleming G. R. *J. Chem. Phys.* **1982**, *76*, 3553−3562. (c) Velsko, S. P.; Waldeck, D. H.; Fleming G. R. *J. Chem. Phys.* **1983**, *78*, 249−258. (d) Keery, K. M.; Fleming, G. R. *Chem. Phys. Lett.* **1982**, *93*, 322−326.

Scheme 4

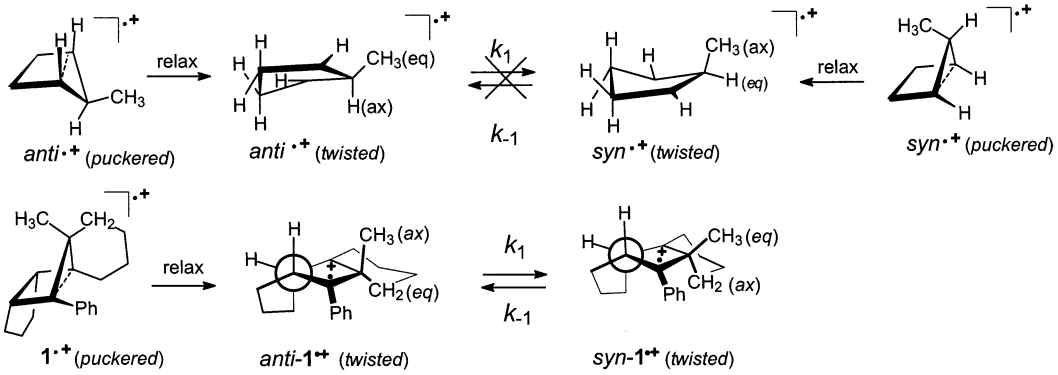


exhibit a stereochemical memory effect for the group migration, which implicates nonequilibrating structures that preserve the initial housane configuration (Scheme 4).[1] EPR spectral data[7] indicate a puckered geometry for the simple anti- and syn-stereolabeled 2-methylcyclopentane-1,3-diyl radical cations (actually, the proper stereochemical descriptors should be exo and endo, but to facilitate comparison with the structurally more complex radical cations **1**$^{\bullet+}$, the anti and syn designations[6] of the latter have been retained). Furthermore, high-level computations[5b] disclose breakage of the one-electron bond in the puckered structure to generate the ring-opened twisted radical-cation conformers (Scheme 4). A higher energy barrier was calculated for the syn/anti-conformational change of the twisted radical cation than for the rearrangement, which is consistent with the observed stereochemical memory effect.[1] Conversely, the observed lack of stereochemical memory for the structurally more complex radical cation **1**$^{\bullet+}$ (Table 1) requires fast syn/anti equilibration prior to rearrangement (Curtin−Hammett behavior).

Viscosity effect on the rearrangement process resides in the difference of the frictional impediments imposed by the solvent on the ring contraction, i.e., methylene-group migration (major structural change) and methyl-group migration (minor structural change).

What structural feature of the radical cation distinguishes the present case **1**$^{\bullet+}$ from the previous one (Scheme 4)?[1,7] No EPR spectral or computational data are available on the structurally more complex **1**$^{\bullet+}$ radical cation, and thus, we may only speculate about its geometry on the basis of what is known and has been said already above for the parent DBH-derived simpler radical cations. In analogy (Scheme 4), we propose that the initially generated puckered species relaxes to the ring-opened twisted *anti*-**1**$^{\bullet+}$ structure, which is in conformational equilibration with its *syn*-**1**$^{\bullet+}$ conformer. We suspect that the cyclohexane annelation in the radical cation **1**$^{\bullet+}$ promotes conformational reorganization to compete effectively with the 1,2 shift of the alkyl migrant, such that k_1/k_{-1} is now faster than methyl migration (k_2) and ring contraction (k_3). Evidently, for the structurally more elaborate radical cation **1**$^{\bullet+}$ studied herein, the barrier for the conformational inversion is significantly lower than for the alkyl-group migration. Presumably, the essential coplanar alignment of the migrant with the migration terminus is more difficult to acquire for the cyclohexane-annelated radical cation **1**$^{\bullet+}$ than for the parent cyclopentane-1,3-diyl radical cation,[5b] such that facile conformational equilibration erases the stereochemical memory effect observed for the latter.[1,7] It should be emphasized that this novel mechanistic feature in radical-cation rearrangements is conditioned by the structural complexity of the radical cation **1**$^{\bullet+}$, whereas viscosity manifests the difference in the frictional impediments imposed by the medium on the proportion of methyl versus methylene migration.

In conclusion, the observed Curtin−Hammett behavior of the radical cations studied herein could have hardly been anticipated[1,7] and constitutes a fortunate happenstance, because the tricyclic radical cation **1**$^{\bullet+}$ figures as the first case for which conformational equilibration precedes product formation through rearrangement (no stereochemical memory). Mechanistically significant, the present study demonstrates that valuable insight into the intricacies of radical-cation rearrangements may be acquired by examining solvent viscosity effects. Clearly, under appropriate circumstances (structural elaboration through cyclohexane annelation), conformational equilibration (Curtin−Hammett principle) may be fomented, which erases stereochemical memory effects in the rearrangement of housane-derived 1,3 radical cations.

Acknowledgment. The generous financial support from the Deutsche Forschungsgemeinschaft, the Volkswagen Stiftung, and the Fonds der Chemischen Industrie is gratefully appreciated. A.V.T. thanks also the Russian Academy of Sciences for a research grant ("Fundamentals of Chemical Bonding and Structure").

JA026057Y