Viscosity as an Experimental Tool in Studying the Mechanism of Stereoselective and Product-Selective Chemical Transformations through Frictional Impositions

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ABSTRACT
In the present Account, we examine the viscosity dependence as a function of temperature, pressure, and solvent polarity for the double inversion in the photolytic azoalkane denitrogenation, the thermal isomerization of housanes, and stereochemical memory versus Curtin–Hammett behavior in radical-cation rearrangements. The analysis of these stereoselective and product-selective viscosity studies in terms of the simple free-volume model demonstrates the utility of frictional effects for the elucidation of complex reaction mechanisms in molecular transformations.

Introduction

More than a century ago, it was realized that valuable insight into chemical mechanisms could be gained through the variation of the reaction conditions, in particular, temperature and pressure. In this context, the activation energy introduced by Arrhenius[1] and activation volume put forward by Röntgen,[2] concepts placed on a solid basis by Eyring,[3] have served generations of chemists effectively.

Solvent viscosity constitutes an informative medium variable, whose utility is of prime importance for understanding the nature of solvent–solute interactions.[4] In this context, the diversity of physical models developed to rationalize the viscosity dependence of molecular transformations is impressive.[4a] Nevertheless, viscosity has also played a definitive role in the detection of reaction intermediates and the elucidation of their chemical behavior. The classical cage-effect studies constitute an example par excellence of solvent viscosity as a powerful mechanistic tool.

Herein, we address the novel facet of harnessing viscosity for mechanistic studies, in particular, for the elucidation of the stereoselectivity[5] and product selectivity[6] in unimolecular transformations. The very fact that the viscosity effects in condensed media control selectivity in molecular rearrangements provides the opportunity to diagnose the mechanism of such complex reactions, which may otherwise be difficult to scrutinize.

Viscosity may be altered by the variation of the solvent at a constant temperature and pressure or, vice versa, in one solvent through temperature or pressure changes. Clearly, viscosity is not the only medium variable, which acts through the external (frictional) impositions on the molecular rearrangements; temperature and pressure may

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superimpose internal effects on the chemical transformations under scrutiny. Additional external influences that may derive from changing the viscosity under isothermal and isobaric conditions relate to a solvent properties such as polarity. Herein, we consider a few illustrative examples, which demonstrate to the general readership that the superimposed effects of temperature, pressure, and polarity may be readily sorted out in viscosity studies and that the latter experimental parameter offers definitive information on chemical mechanisms.

Our approach is based on the conceptually simple free-volume model of viscosity (η), in which the fractional-power viscosity dependence ($\sim \eta^{-\alpha}$) provides the effective volume available for the molecular transformation under scrutiny: it determines the frictional effects imposed by the medium on the structural changes! The α parameter depends decisively on the substituents of those transforming molecular entities which suffer major spatial displacements during the reaction. Conversely, the substituents distant from the reaction center contribute smaller amount to α value. Hence, the dependence of the α parameter on strategically placed substituents in the reacting molecule discloses valuable mechanistic details about the reaction coordinate.

In principle, the viscosity dependence may be explored in mechanistic studies on any chemical process that involves a substantial structural change and is thereby subject to external frictional effects; however, the presented viscosity approach is most advantageous for the elucidation of competitive pathways in selective organic transformations, since the distinct structural changes are subject to different frictional impositions. As examples to illustrate the mechanistically informative viscosity model, in the present Account, we consider two cases. On one hand is the stereochemical inversion upon nitrogen extrusion from cyclic azoalkanes,[5] which furnishes a fascinating case of a stereoselective process; on the other hand, radical-cation rearrangement[6] constitutes a prominent example of a product-selective transformation, which discloses a unique case of Curtin−Hammett versus stereochemical memory behavior. In the former stereoselective process, two housane diastereomers are formed, whereas in the latter product-selective case, two distinct products are generated. On the basis of our original publications,[5,6] we show that our viscosity approach is particularly appropriate for the elucidation of both stereo- and product-selective transformations. Our incentive for the present Account is to demonstrate the general utility of viscosity as a mechanistic tool and kindle interest among the physical organic chemists in employing it in their mechanistic work.

Free-Volume Model of Viscosity. The free-volume model of viscosity dates back to Doolitle,[7] who intuitively pointed out that the translational motion of a molecule in a liquid is only possible when sufficient free volume (V_f) is available, i.e., when V_f 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 of an ensemble of molecules. Hence, the free-volume de-
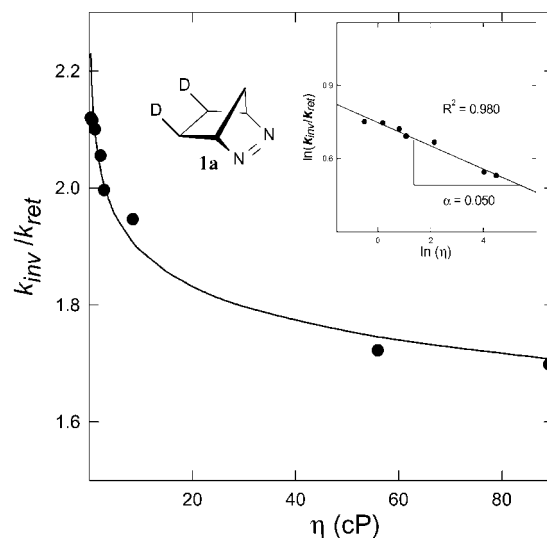

FIGURE 1. Viscositydependence of the k_{inv}/k_{ret} ratio in the DBH (1a) photolysis ($\lambda = 333$ nm) in alcohol solvents (cf. ref 5a,d); the insert displays the double-logarithmic plots (η in cP).

pendence of the viscosity may be expressed by eq 1, in which A is a proportionality factor

$$\eta = A \exp(V_0/V_f) \tag{1}$$

In contrast to translational diffusion, molecular rearrangements involve only a portion of the molecule. Thus, only a fraction αV_0 ($\alpha < 1$) of the critical volume V_0 is required to execute the internal molecular motion, for which the rate constant k of the molecular rearrangement is given by eq 2. Substitution of eq 1 into eq 2 affords eq 3, an expression that
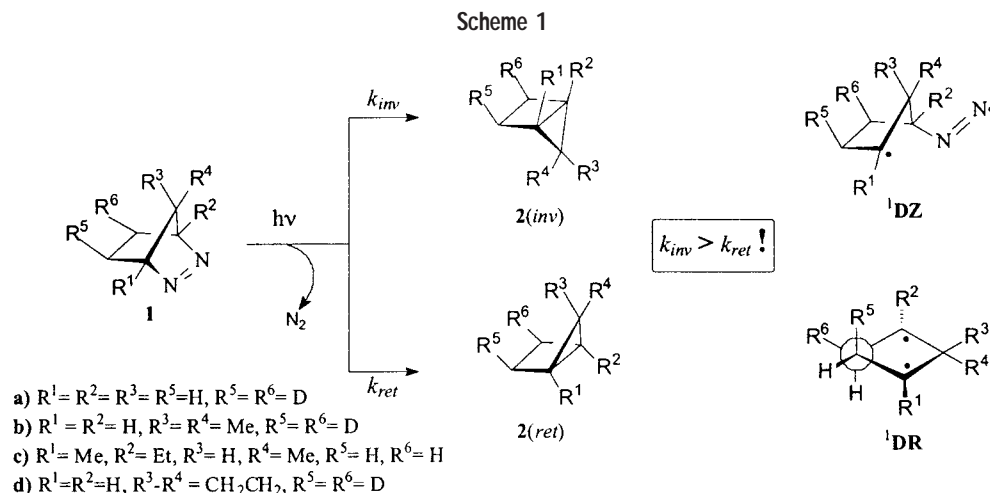
$$k = k^0 \exp(-\alpha V_0/V_f) \tag{2}$$

$$k = k^0 (A/\eta)^\alpha \tag{3}$$

was first applied to rationalize the viscosity behavior of molecular isomerizations.[8]

As already stated above, the α parameter is the mechanistically significant quantity; its structural dependence is of prime import for the elucidation of the reaction coordinate. According to eq 3, the α value may be readily assessed from the double-logarithmic plot of the experimental viscosity data. A typical example is displayed in Figure 1, discussed below.

The Stereochemical Double Inversion in the Photochemical Nitrogen Extrusion from the DBH-Type Azoalkanes

Mechanistic Background. The preferred formation of inverted housane **2**(inv) in the photochemical denitrogenation of diazabicyclo[2.2.1]heptenes (DBH), **1** (Scheme 1), constitutes an intriguing stereoselective process.[9] A long-standing mechanistic query on this nitrogen extrusion concerns stepwise versus concerted breakage of the two CN bonds in the electronically excited azoalkane (**1**): The stepwise CN-bond rupture necessarily implicates the

Scheme 1

a) $R^1 = R^2 = R^3 = R^5 = H$, $R^5 = R^6 = D$
b) $R^1 = R^2 = H$, $R^3 = R^4 = Me$, $R^5 = R^6 = D$
c) $R^1 = Me$, $R^2 = Et$, $R^3 = H$, $R^4 = Me$, $R^5 = H$, $R^6 = H$
d) $R^1 = R^2 = H$, R^3-$R^4 = CH_2CH_2$, $R^5 = R^6 = D$

singlet diazenyl diradical **¹DZ** as a pivotal intermediate, whereas the concerted process passes through the nitrogen-free singlet **¹DR** species (Scheme 1). Homolytic displacement of the nitrogen molecule in the singlet **¹DZ** diradical leads to the inverted housane **2**(inv) through a backside attack (S_H2 process). Alternatively, the nitrogen-free singlet **¹DR** diradical affords both the inverted and the retained housanes **2**(inv) and **2**(ret) in equal amounts.

A recent ab initio study on the thermolysis of the parent DBH (**1a**) has concluded that the lower-energy pathway of the deazetation is the concerted expulsion of N_2 directly to **¹DR**.[10] The observed stereoselection, namely, more **2**(inv) than **2**(ret), was attributed to dynamic effects in the nonstatistical **¹DR** diradical intermediate. Contrary to the thermal denitrogenation, computational[11] and experimental[11,12] work on the photolysis of azoalkanes favors the stepwise nitrogen elimination, with the diazenyl diradical **¹DZ** as intervening species. Indeed, even simple symmetry considerations in terms of the Dauben−Salem−Turro theory[13] predict a stepwise process for the n,π*-excited azo chromophore.[12c]

Liquid-Phase Photolysis: Solvent and Temperature Effects on the Viscosity Dependence. The stepwise mechanism with the unsymmetrical **¹DZ** diradical is corroborated by the different viscosity effects observed for the inversion (k_{inv}) versus retention (k_{ret}) channels.[5] The stereoselectivity, expressed in terms of the k_{inv}/k_{ret} ratio, decreases with increasing viscosity (Figure 1). Were synchronous nitrogen extrusion through the intermediacy of the ¹DR diradical involved for such a C_2-symmetric nitrogen-free ¹DR diradical,[14] the k_{inv} and k_{ret} terms would engage identical spatial displacements; consequently, they should depend to the same extent on the frictional impositions by the medium. In contrast, for the unsymmetrical, puckered diazenyl diradical ¹DZ, a viscosity dependence of the selectivity ratio k_{inv}/k_{ret} should be expected. As a matter of fact, we have observed[5] that the stereoselectivity (k_{inv}/k_{ret}) decreases as viscosity increases and the k_{inv}/k_{ret} ratio depends on viscosity to the fractional power, i.e., $k_{inv}/k_{ret} = const \ \eta^{-\alpha}$, which clearly speaks in favor of stepwise photodenitrogenation. Since the change of the molecular geometry in the retention process (k_{ret})

Table 1. The α Values for the Photochemical Skeletal Inversion[a]

Reactant	α
1a	0.050 ± 0.003
1d	0.105 ± 0.005
1b	0.146 ± 0.005
1e	0.20 ± 0.01
1c	0.27 ± 0.01

[a] See ref 5.

is nominal, the α value obtained from the viscosity dependence of the k_{inv}/k_{ret} ratio mainly pertains to the inversion process (k_{inv}).

It is noteworthy that, contrary to the stereoselectivity, the photodenitrogenation quantum yield for the parent DBH is independent of solvent viscosity.[5g] Thus, the extruded nitrogen does not influence the stereoselection.

Structural Dependence of the Stereoselectivity in the Viscosity-Controlled Denitrogenation. To convey how impressively the α parameter reflects structural effects on the denitrogenation coordinate through appropriate substitution of the DBH skeleton, in Table 1 are compiled the experimental α data for the photolysis of azoalkanes **1**. As expected, the lowest α value is observed for the parent

DBH (**1a**), while dimethyl substitution in the methylene bridge (azoalkane **1b**) increases the α value by a factor of 3. This is consistent with the inversion process (k_{inv}) along the S$_H$2 trajectory, which should be slowed due to the frictional retardation of the methylene-bridge inversion motion. For the spirocyclic azoalkane **1d**, the α value is ca. 1.4 times lower than for **1b**. This diminution of the α value may be accounted for by a smaller substituent size in the methylene bridge of azoalkane **1d**.

The data in Table 1 reveal another mechanistically important fact: The bridgehead substitution in the azoalkane **1c** further increases the α parameter. Its value is ca. twice as high as the one of the merely methylene-bridge-substituted azoalkane **1b** and ca. five times higher than the parent DBH **1a**. This observation manifests that besides the flap motion of the methylene bridge; also the displacement of the bridgehead substituents is significant in the skeletal inversion during nitrogen extrusion.

In contrast, the cyclopentene annelation in azoalkane **1e**, which is distant from the reaction site, does not cause a large effect, as the comparison of the α values with **1c** reveals (cf. Table 1). Thus, our comparative analysis of the viscosity dependence as a function of the azoalkane structure (Table 1) reveals that not only the flap motion of the methylene bridge, but also the bridgehead substitutents participate in the double-inversion process, as required for the S$_H$2 trajectory. This novel mechanistic feature, recognized through viscosity effects, is in accord with recent work in which the importance of bridgehead substitution has been demonstrated for the stereoselective inversion in the temperature-dependent photolysis of DBH-type azoalkanes.[11]

Temperature-Controlled Viscosity Dependence in the DBH Photolysis. The variation of temperature may impose a composite effect on chemical transformations: Besides altering the solvent viscosity and thereby modifying the external frictional effects on the molecular rearrangement in a condensed medium, the temperature change may also exert an internal influence on the chemical process, if the latter possesses a noticeable activation energy. The DBH photolysis definitively exemplifies such a case. Figure 2 displays the viscosity dependence of the stereoselectivity (k_{inv}/k_{ret} ratio) in the DBH photolysis as a function of temperature. Clearly, the temperature-controlled viscosity profile (Figure 2) is steeper than that under isothermal conditions (Figure 1);[5a] this is particularly evident from the higher α value (0.14, cf. insert in Figure 2). We have attributed the observed deviation in the solvent- and temperature-varied viscosity profiles of the k_{inv}/k_{ret} ratio (Figures 1 and 2) for the parent DBH to the difference ($\Delta E^i = E_{inv}^i - E_{ret}^i$) in the internal activation energies of the inversion (E_{inv}^i) and retention (E_{ret}^i) channels,[5a] which is superimposed on the external energy difference (ΔE^e) due to the viscosity dependence. Thus, the complete energy difference ($\Delta E = \Delta E^i + \Delta E^e$) is the sum of the internal (ΔE^i) and the external (ΔE^e) energy terms. While the former term represents the inherent difference in the activation energies, the latter corresponds
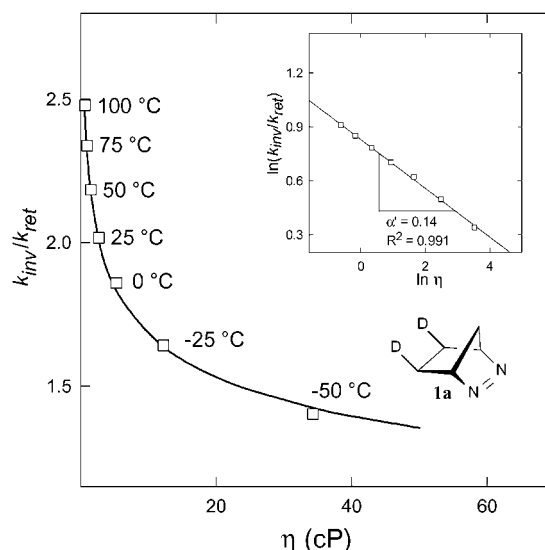

FIGURE 2. Viscositydependence of the k_{inv}/k_{ret} ratio in the DBH (**1a**) photolysis ($\lambda = 333$ nm) as a function of temperature in *n*-butanol (cf. ref 5a); the insert displays the double-logarithmic plots (η in cP).

to the energy required to overcome the frictional impediment provided by the medium for the inversion mode.

The ΔE^e term is linearly proportional to the activation energy (E_η) of the solvent fluidity (η^{-1}), i.e., $\Delta E^e = \alpha E_\eta$ (cf. ref 5a). Thus, the difference in the total energy change is $\Delta E = \Delta E^i + \alpha E_\eta$, for which the values $\Delta E = 0.62 \pm 0.03$ kcal/mol and $\alpha E_\eta = 0.23 \pm 0.01$ kcal/mol have been obtained from the Arrhenius plots of the k_{inv}/k_{ret} ratio and *n*-butanol viscosity (cf. Figure S-1 in Supporting Information); from these data the internal contribution is calculated to be $\Delta E^i = 0.39 \pm 0.03$ kcal/mol. Thus, the superimposed internal temperature effect ($\Delta E^i = 0.39$ kcal/mol) outweighs the external viscosity dependence ($\Delta E^e = 0.23 \pm$ kcal/mol), but what should be stressed is that both energy terms may be assessed through such a composite temperature/viscosity study. Moreover, although the value $\Delta E^i = 0.39$ kcal/mol is small, it accounts adequately for the difference in the viscosity behavior of the k_{inv}/k_{ret} ratio for the thermal (Figure 2) and constant-temperature (Figure 1) viscosity variations.[5a]

The featured example demonstrates how sensitive the viscosity probe is for determining experimentally small energy differences in the activation barriers for competitive processes. This constitutes an additional advantage of harnessing viscosity as a powerful mechanistic tool. It should be mentioned, however, that on substitution of the DBH molecule, the external frictional effects begin to dominate the internal contributions, and it becomes difficult to acquire the internal energy (ΔE^i) term through the viscosity assay. Indeed, for the substituted derivative **1c**, the isothermal and thermally controlled viscosity profiles coincide (cf. Figure S-2, Supporting Information),[5b] which implies that the ΔE^i term is negligible compared to ΔE^e.

Polarity Effect on the Viscosity Dependence in the DBH Photolysis. As a competing external effect, polarity may play a role, which invariably arises when various

solvents are employed. In this regard, a comparison of the viscosity effects on the stereoselection for the DBH photolysis in polar solvents (alcohols) and nonpolar media (isooctane/Nujol mixtures) has disclosed an intriguing feature: the k_{inv}/k_{ret} ratios possess similar viscosity profiles in both solvent series (i.e., the α values in the aprotic isooctane/Nujol mixtures and in various alcohols perfectly match), but the viscosity dependence in alcohols is shifted down from that in isooctane/Nujol mixtures by a constant factor of ca. 1.3 (cf. Figure S-3, Supporting Information). This observation reveals that the inversion process is obstructed more effectively (ca. 30%) in the polar (alcohols) than in the nonpolar (hydrocarbon) medium. The origin of this decrease of the k_{inv}/k_{ret} ratio may be understood in terms of solvent-polarity effects on the intermediary ^{1}**DZ** species: The dipole moment (charge separation) in the diazenyl diradical ^{1}**DZ** is stabilized more efficiently in a polar environment through solvation, which retards the inversion process.[5d]

It is tempting to attribute this polarity effect to hydrogen bonding between the electronically excited DBH (**1a**) and surrounding solvent molecules; however, if this were significant, it would be difficult to conceive that the same frictional effects (same α values) would operate in the alcohol and in the hydrocarbon media. Instead, we have suggested that the bulk polarity is responsible for the observed 1.3-fold shift of the viscosity profiles.[5d] Thus, besides viscosity (η), the solvent dielectric constant (ϵ) should be considered as an additional variable in the medium dependence of the k_{inv}/k_{ret} ratio. This has been done in terms of Onsager's reaction-field model[15] for the k_{inv}/k_{ret} values normalized to a constant viscosity.[5d]

Such an analysis of the polarity effect on the stereoselection was carried out for a wide variety of solvents and a good correlation of the k_{inv}/k_{ret} data (at same viscosity) with the Onsager polarity parameter $(\epsilon - 1)/(2\epsilon + 1)$ was found (cf. Figure S-4, Supporting Information). It is noteworthy that the observed polarity effect levels off at $\epsilon > 10$, a behavior which concords with the Onsager model.[5d] These studies have demonstrated that in the determination of the viscosity dependence, it is advantageous to utilize either nonpolar ($\epsilon < 3$) or polar ($\epsilon > 10$) media and avoid solvents of intermediate polarity ($3 < \epsilon < 10$).

Photochemical versus Thermal Skeletal Inversion: Azoalkane Photolysis and Thermal *syn*-to-*anti* Housane Isomerization. To confirm the validity of the viscosity control observed in the photolytic denitrogenation of an azoalkane, the thermal syn-to-anti isomerization of the corresponding housane was probed, since both molecular rearrangements involve a similar spatial transposition of the dimethyl-substituted methano bridge during the inversion process. For this purpose, the azoalkane **1e** and its housane product **2e** were chosen (Scheme 2), since these DBH derivatives enable studies on the photolysis (azoalkane **1e**) and isomerization (housane **2e**) at the same temperature (25 °C).[5e] Our studies have disclosed the similar viscosity profiles for the stereochemical inversion

Scheme 2
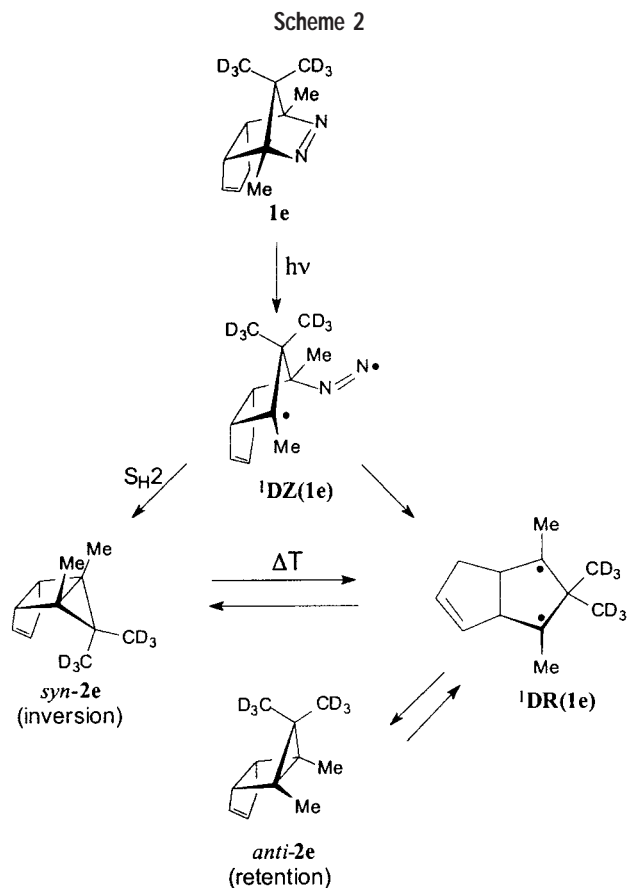
in the photolysis of **1e** and in the syn-to-anti isomerization of **2e** (cf. Figure S-5, Supporting Information).

The mechanistically significant feature common to the photolysis[5] of azoalkanes **1e** and the thermal isomerization[16] of its housane **2e** resides in the intermediacy of the nitrogen-free cyclopentanediyl ^{1}**DR** species (Scheme 2). As is evident from the composite mechanism in Scheme 2, the substituted methylene bridge in the inversion processes ^{1}**DZ** $\rightarrow$ *syn*-**2e** and *syn*-**2e** $\rightarrow$ *anti*-**2e** experiences flap motions of similar amplitudes. Indeed, the computed change of the flap angle[16] for both skeletal inversions differs by less than 1°. Thus, one may expect similar viscosity effects for these rearrangements, as is manifested by the nearly equal values of α (photolysis of the azoalkane **1e**) and α' (thermolysis of the housane syn-**2e**).[5e]

A computational study[16] on the thermal isomerization of the parent housane **2a** has concluded the statistical nature of such a process: the calculated intramolecular energy-relaxation rates significantly exceed the rate of the **2**(inv) $\rightarrow$ **2**(ret) skeletal inversion. For the structurally more elaborate housane **2e**, intramolecular energy randomization should be even faster since for **2e** more internal degrees of freedom are available to dissipate any excess energy along the reaction coordinate. Thus, no dynamic effects operate in the thermal isomerization of **2e**. From the similar viscosity dependence of the k_{inv}/k_{ret} data for the azoalkane **1e** photolysis and the k_{iso} data for the housane syn-**2e** thermolysis,[5e] we contend that the photodenitrogenation is also not subject to dynamic effects;

Scheme 3
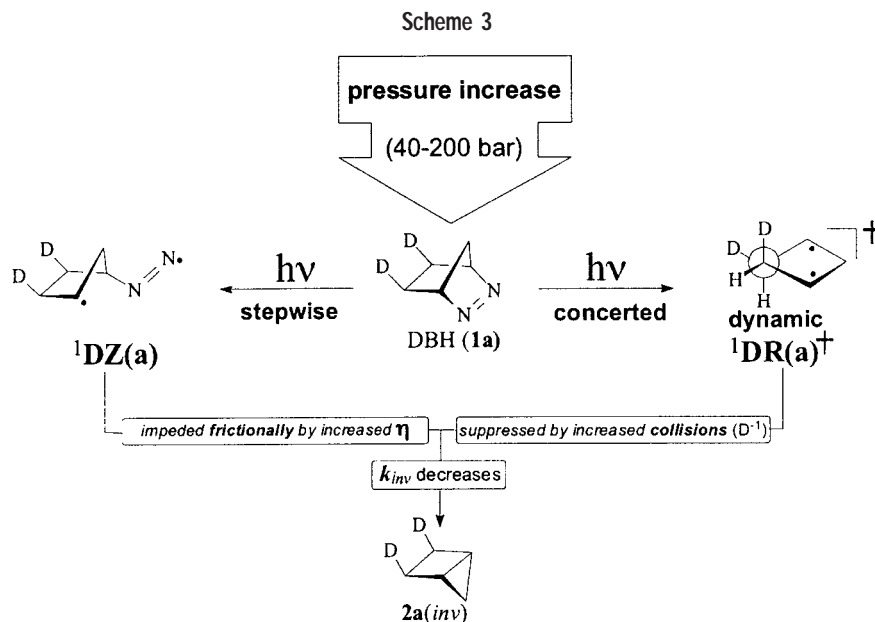
rather, frictional impediments in the liquid medium determine the stereoselectivity.

The choice of the azoalkane **1e** has been fortunate, since its photodenitrogenation quantum yield was found to decrease with increasing viscosity.[5g] The importance of this observation must be stressed, since it manifests for the first time the reversibility of the photodenitrogenation process, a mechanistic feature that confirms unequivocally the intermediacy of [1]**DZ**. Specifically, the retardation of the flap motion of the methylene bridge along the S_H2 coordinate through the frictional impediments exerted by the viscous medium makes the competitive reclosure of the [1]**DZ** diradical to its azoalkane more efficient. This leads to a reduction of the photodenitrogenation quantum yield in high-viscosity solvents. Our detailed analysis[5g] revealed that the observed viscosity behavior of the quantum yield is accounted for in terms of the fractional-power viscosity dependence of the photodenitrogenation rate constant, $k_r \sim \eta^{-\alpha}$. Furthermore, the α parameter in this quantum-yield/viscosity dependence takes the value 0.140 ± 0.007,[5g] which is similar to what we obtained for the formation of the inverted product syn-**2e** ($\alpha = 0.20 \pm 0.01$) in the photolysis of **1e** and for the thermal syn–anti isomerization of housane *syn*-**2e** ($\alpha = 0.16 \pm 0.03$).[5e,g] The similarity of these α values implies that the viscosity effect results from similar frictional impositions on the skeletal inversion process, namely, the flap motion of the methylene bridge in the photodenitrogenation of the azoalkane **1e** as well as the thermal isomerization of housane *syn*-**2e**. It is difficult to conceive which alternative experimental method would reveal such valuable mechanistic information on such diverse but related transformations.

DBH Photolysis in Supercritical Fluids: Pressure Dependence of the Diastereoselectivity. As a third experimental variable, we shall now consider pressure effects. Indeed, the stereoselection in the DBH photolysis is sensitive to pressure, as experiments in supercritical

fluids (sc-CO_2 and sc-C_2H_6) have revealed.[5c] The raise of pressure up to 200 bar leads to a ca. 2.3-fold decrease of the stereoselectivity for the DBH (**1a**) photolysis (cf. Figure S-6, Supporting Information). To rationalize the observed pressure dependence of the stereoselective inversion, two mechanistic alternatives (Scheme 3) may be considered, i.e., the concerted (at the right) and stepwise (at the left) pathways.

If the photolytic nitrogen extrusion is concerted and proceeds through the [1]**DR** diradical, the observed pressure effect is collisional in nature, as it has been suggested for the thermal deazetation.[10] For the latter, the preferred inversion is ascribed to the nonstatistical diradical intermediate [1]**DR(a)**, which ring-closes to the inverted product **2a**(inv) prior to stereochemical randomization (the dynamic model). The pressure-intensified collisions of this intermediate with solvent molecules should redistribute its internal energy and thereby deflect it from the impulse-driven inversion trajectory.

On the contrary, for the stepwise denitrogenation by way of the [1]**DZ(a)** diradical, the pressure effect on the stereochemical inversion is proposed to derive from frictional interactions with the solvent. The pressure increase from 40 to 200 bar causes a significant viscosity increase, for carbon dioxide ca. 4-fold and ethane ca. 5-fold.[5c] This viscosity increase enhances the frictional impediment sufficiently during the nitrogen loss from [1]**DZ** to the inverted housane **2**(inv) that a decrease in the k_{inv}/k_{ret} product ratio is expected.

To differentiate between these two mechanistic alternatives (Scheme 3), the pressure dependence of the k_{inv}/k_{ret} data in sc-CO_2 and sc-C_2H_6 media was examined in terms of collisional (diffusion coefficient) and frictional (viscosity) effects.[5c] This analysis has shown that the k_{inv}/k_{ret} ratio decreases with increasing inverse values of the diffusion coefficient (D^{-1}), a measure of the collision frequency,[17] which is consistent with the dynamic model.[10] However, although the k_{inv}/k_{ret} data correlate well with D^{-1}

Scheme 4
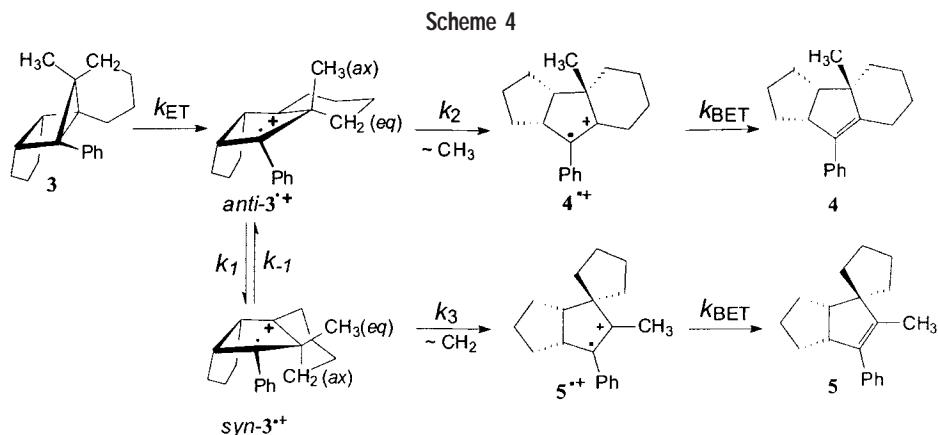
for each supercritical fluid taken alone, a marked difference of the D^{-1} profiles appears between sc-CO_2 and sc-C_2H_6: The two curves diverge as the D^{-1} value decreases, that is, as the collision frequency is lowered (cf. Figure S-7a, Supporting Information). Extrapolation of these curves to zero collision frequency (vacuum) results in two different k_{inv}/k_{ret} values for the same process under the same conditions, definitively an inconsistent physical behavior.

Contrary to the correlation of the k_{inv}/k_{ret} values with D^{-1}, the viscosity profiles of the k_{inv}/k_{ret} ratio in sc-CO_2 and sc-C_2H_6 are reasonably well superimposed (cf. Figure 7b Supporting Information), and a similar fractional-power dependence on the viscosity, $k_{inv}/k_{ret} \sim \eta^{-\alpha}$, operates for both fluids under supercritical conditions. Thus, the k_{inv}/k_{ret} ratio for the photolysis of the azoalkane **1a** in supercritical media correlates satisfactorily with the medium viscosity. As it was elaborated above for the liquid phase, this fact is consistent with the stepwise denitrogenation, in which the diazenyl diradical ^{1}**DZ(a)** functions as key intermediate.

Noteworthy is that the α values obtained through the pressure variation in supercritical media are significantly higher than those for the liquid-phase photolysis at ambient pressure, which is, however, not unusual. Stronger viscosity effects on the reaction kinetics in supercritical media than in conventional solvents have been documented.[18] Furthermore, for the photochemical isomerizations, a higher viscosity dependence has been reported for the pressure variation compared to the use of different solvents at constant pressure.[4a] Whereas such phenomena are of theoretical interest to understand solute–solvent dynamics, for our mechanistic purposes, it suffices to realize that the pressure-varied viscosity differentiates between the inversion (k_{inv}) and retention (k_{ret}) channels in the DBH photolysis.

Viscosity Dependence of the Product Selectivity in Radical-Cation Rearrangements

The rearrangement of cyclopentane-1,3-diyl radical cations[19] comprises a fascinating chapter in electron-transfer chemistry.[20] The reactivity of these short-lived intermediates is controlled by internal (electronic) and external (medium) features; the latter have received little attention
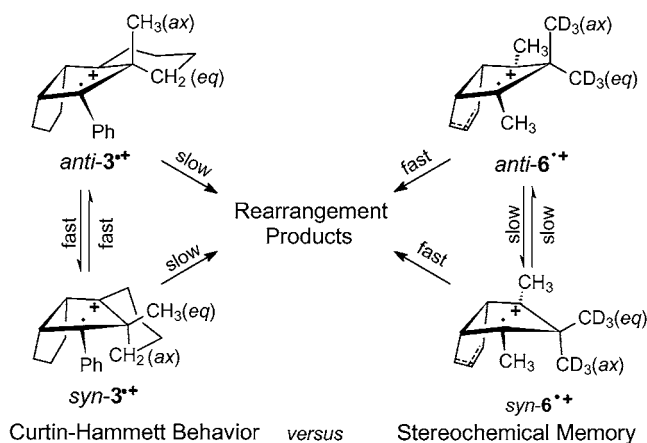
to date. Recently we reported on the solvent effects in the rearrangement of the cyclopentane-1,3-diyl radical cation derived from the cyclohexane-annelated housane **3** (Scheme 4),[6] with the incentive to demonstrate the general utility of the viscosity approach in acquiring valuable mechanistic details on chemical transformations.

It should be noted that in the radical cation (Scheme 4), structurally similar to the previously discussed diradicals (Scheme 2), the 1,2 shift of the alkyl substituents involves major bond-breaking and bond-making events. In contrast, in the double inversion of the ^{1}**DR** diradical merely bond formation (cyclization) occurs as the methylene-bridge flap changes its relative position in space, but no major structural reorganization through bond-changing events takes place. It must also be stressed that in the radical-cation rearrangement (Scheme 4) two distinct products are generated, namely, the annelated cyclopentene **4** and the spirocyclic product **5**, whereas in the diradical cyclization (Scheme 2) two diastereomeric housanes are obtained. The question of mechanistic import is whether the radical-cation rearrangement (Scheme 4) is also influenced by viscosity.

The product selectivity, expressed in terms of the [**4**]/[**5**] product ratio, has been studied in a variety of solvents.[6] In acetonitrile, a solvent of low viscosity ($\eta = 0.36$ cP), nearly equal amounts of the products **4** and **5** have been observed, whereas the cyclopentene **4** dominates more than 2-fold in 1,4-butanediol, the solvent of highest viscosity ($\eta = 89.2$ cP). As the case of the stereoselectivity in the azoalkane photolysis, the similar fractional-power viscosity dependence has been established for the product selectivity [**4**]/[**5**] in the radical-cation rearrangement, i.e., [**4**]/[**5**] $\sim \eta^{-\Delta\alpha}$, where $\Delta\alpha = 0.112 \pm 0.007$ (cf. Figure S-8, Supporting Information). Thus, an analogous viscosity effect operates in this more complex chemical transformation!

The nearly equal amounts of the rearrangement products **4** and **5** at low viscosity[6] imply that the syn/anti conformational changes (k_1, k_{-1}) in Scheme 4 proceed faster than the chemical transformation (k_2, k_3), that is, a case of Curtin–Hammett behavior.[21] To rationalize the observed viscosity dependence, the [**4**]/[**5**] product ratio must be related to the rate constants k in Scheme 4. Similar kinetics has been worked out by Seeman,[21] who

Scheme 5

anti-**3**$^{\bullet+}$ slow   Rearrangement Products   fast   anti-**6**$^{\bullet+}$

syn-**3**$^{\bullet+}$

syn-**6**$^{\bullet+}$

Curtin-Hammett Behavior   *versus*   Stereochemical Memory

showed that when the conformational changes (k_1, k_{-1}) are faster than the migration steps (k_2, k_3), the expression for the [**4**]/[**5**] product ratio acquires the simple Curtin–Hammett form shown in eq 4.[21] Application of the free-volume model to the [**4**]/[**5**] product ratio (eq 4) according to eq 3

$$[\mathbf{4}]/[\mathbf{5}] \approx k_2 k_{-1}/(k_3 k_1) \tag{4}$$

affords eq 5 for the viscosity dependence of the product selectivity,[6] where $\Delta\alpha = \alpha_3 - \alpha_2$

$$[\mathbf{4}]/[\mathbf{5}] = \text{const } \eta^{\,\Delta\alpha} \tag{5}$$

α_2 expresses the free-volume dependence for step k_2 and α_3 for step k_3. This simple relation (eq 5) for the product distribution reveals the following mechanistic recognition: The viscosity effect on the product selectivity is governed by the difference in the free-volume requirements for the group migrations k_3 and k_2 (cf. Scheme 4).

The double-logarithmic form of eq 5 predicts a linear relation between $\ln([\mathbf{4}]/[\mathbf{5}])$ and $\ln \eta$, which corroborates the experimental observation (cf. Figure S-8, Supporting Information). The positive $\Delta\alpha$ value manifests that the viscosity effect is larger for the methylene (k_3) than methyl (k_2) migration. This fact implies a larger structural change for the ring-contraction process to afford the spirocyclic cyclopentene **5** than for the methyl shift to the annelated product **4**. This Curtin–Hammett behavior (k_1, $k_{-1} \gg k_2$, k_3) constitutes an unprecedented feature of such short-lived intermediates, which more usually display stereochemical memory (Scheme 5). For example, the bicyclic radical cations anti-**6**$^{\bullet+}$ (k_2) and syn-**6**$^{\bullet+}$ preserve the initial housane configuration, with only little conformational leakage, as confirmed by the lack of a viscosity dependence for the diastereomeric cyclopentene products.[6b] Thus, this study has demonstrated that the simple free-volume viscosity approach provides valuable mechanistic insight into the major structural reorganization incurred during radical-cation rearrangements.

Conclusions

The two case studies reviewed herein demonstrate that viscosity, considered by most physical organic chemists as the "black sheep" physical property, serves as a promising tool to elucidate complex reaction mechanisms. It is thus not surprising that the free-volume viscosity model has been ignored by mechanistic organic chemists for so long. Clearly, our demonstrative examples evidence the potential value of the conceptually simple free-volume viscosity approach. We contend that this straightforward methodology constitutes a general experimental tool that may be applied to mechanistic studies on chemical transformations, which involve major spatial reorganization and, thus, are subject to external frictional effects. The provisio, however, is that the transient engages in competitive transformations.

We have demonstrated herein the applicability to the diastereoselective ring-closure of diradicals and product-selective rearrangement of radical cations, but it should also help to understand regioselective processes and asymmetric transformations. Our original work[5,6] provides detailed instructions of how to proceed, to be stressed must be the convenience of the experimental technique, the low cost of the experimental setup, and the simplicity of data processing. The incentive of this Account is not only to entertain the mechanistic chemists, but to stimulate them to employ this simple viscosity probe for the elucidation of complex reaction trajectories.

Supporting Information Available: Figures showing Arrhenius plots, viscosity dependence, isoviscosity plots, pressure dependence, and the dependence on the inverse of the self-diffusion coefficient. This material is available free of charge via the Internet at http://pubs.acs.org.

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