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Viscosity-Controlled Stereoselective Inversion in the Photochemical Denitrogenation of a Stereolabeled Diazabicyclo[2.2.1]heptene (DBH)-Type Azoalkane

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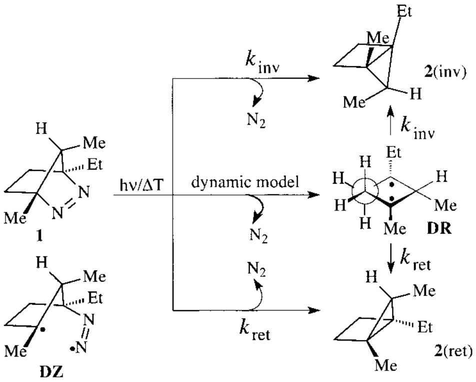
The preferred formation of the doubly inverted bicyclo[2.1.0]-pentane (housane) product is a general feature for both the thermal and photochemical denitrogenation of diazabicyclo[2.2.1]hept-2-enes (DBH), which still constitutes a mechanistically controversial phenomenon.[1] The denitrogenation of the azoalkane **1**, the DBH derivative under present scrutiny, serves as an illustration (Scheme 1).

Scheme 1



To rationalize the stereoselective inversion, two mechanisms have been proposed:[1c−e,2,3] The originally postulated S_H2 mechanism[1a] involves concerted CN-bond cleavage and CC-bond formation in the elusive diazenyl (**DZ)** diradical, in which the unpaired electron in the carbon-centered 2p orbital displaces N_2 by backside attack. Recent experimental evidence argues in favor of this concerted S_H2 process.[2] In contrast, the alternative dynamic model[3] implicates a stepwise process, with the cyclopentane-1,3-diyl diradical (**DR**)[4] as second intermediate, formed by CN-bond cleavage in the **DZ** species prior to CC-bond formation to the housane **2** product.[5] In this mechanism, the preference for the inverted housane **2**(inv) product is ascribed to the singlet-state cyclopentane-1,3-diyl (**DR**) species, whose excess internal energy is utilized to form the inverted product **2**(inv) prior to stereochemical randomization. Any collision of this intermediate with solvent molecules redistributes the excess internal energy and thereby deflects it from the inversion trajectory. Experiments on the thermal denitrogenation of the deuterium-labeled parent DBH in supercritical propane, in which the pressure was increased up to ~200 atm, provided support for the dynamic model.[3a] Since the collision frequency increases with pressure, it was expected and experimentally observed that the $\boldsymbol{k}_{\text{inv}}/\boldsymbol{k}_{\text{ret}}$ ratio should decrease.

Table 1. Ratios of Inverted versus Retained Housanes **2** in the Photolysis of Azoalkane **1** as Function of Viscosity[a]

entry	solvent	viscosity (η) (cP)	housane **2** [**2**(inv)]$_\infty$:[**2**(ret)]$_\infty$[b]	
1	*n*-hexane	0.33	81	19
2	acetonitrile	0.36	78	22
3	*n*-heptane	0.41	79	21
4	methanol	0.60	74	26
5	*n*-decane	0.92	74	26
6	ethanol	1.20	71	29
7	n-dodecane	1.51	73	27
8	*n*-propanol	2.26	68	32
9	*n*-butanol	2.95	66	34
10	*n*-octanol	8.50	59	41
11	1,2-propanediol	56.0	48	52
12	1,4-butanediol	89.2	46	54

[a] Photolysis of azoalkane **1** (λ = 333−364 nm) at 20 °C and 1 atm. [b] Determined by GC analysis; > 95% conversion; error ± 5%.

The formation of the inverted housane **2**(inv) involves a large-amplitude rotational motion of the pertinent molecular fragment (the methylene bridge) and, thus, its rate should depend on the friction with the medium and, thereby, on its viscosity; the latter increases with pressure.[6] For supercritical propane such a pressure-controlled viscosity increase has been taken into account[3a] in terms of the Troe model.[6b] To extend the viscosity effect to the liquid phase, we have presently examined the photochemical denitrogenation of the known[7] stereolabeled azoalkane **1** (Scheme 1) under constant pressure and temperature. The viscosity was varied over a *wide* range (from 0.33 to 89.2 cP) by proper choice of solvents.

The experimental data on the ratio of the stereoisomeric products **2**(inv) and **2**(ret) as a function of viscosity are given in Table 1, and confirm our expectations. Kinetic analysis of Scheme 1 leads to a simple expression (eq 1) for the yield (Φ_{inv}) of the inverted housane **2**(inv). From this expression, the $\boldsymbol{k}_{\text{inv}}/\boldsymbol{k}_{\text{ret}}$ ratio may be expressed as $\Phi_{\text{inv}}/(1-\Phi_{\text{inv}})$, as shown in eq 2.

$$\Phi_{\text{inv}} = \frac{[\mathbf{2}(\text{inv})]_\infty}{[\mathbf{2}(\text{inv})]_\infty + [\mathbf{2}(\text{ret})]_\infty} = \frac{\boldsymbol{k}_{\text{inv}}}{\boldsymbol{k}_{\text{inv}} + \boldsymbol{k}_{\text{ret}}} \tag{1}$$

$$\frac{\Phi_{\text{inv}}}{1-\Phi_{\text{inv}}} = \frac{\boldsymbol{k}_{\text{inv}}}{\boldsymbol{k}_{\text{ret}}} \tag{2}$$

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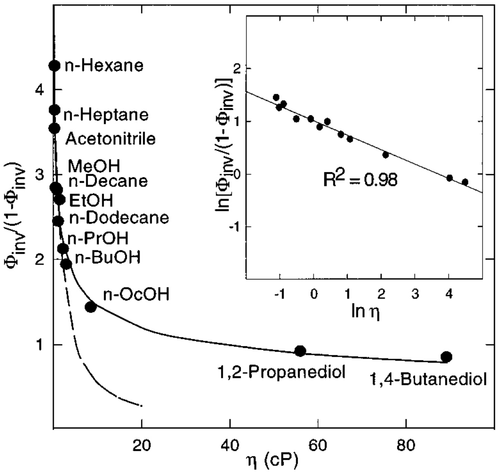

Figure 1. Dependence of the yield (Φ_{inv}) of inverted housane **2**(inv) [Scheme 1] on the solvent viscosity (η) at 20 °C and 1 atm in the photolysis of azoalkane **1**.

The $\Phi_{\mathrm{inv}}/(1 - \Phi_{\mathrm{inv}})$ values versus solvent viscosity (η) are plotted in Figure 1, which displays a definite medium effect that requires rationalization. Since only the inversion channel involves a large-amplitude rotation of the pertinent molecular fragment, frictional effects by the solvent should mainly act on the $\boldsymbol{k}_{\mathrm{inv}}$ term of the $\boldsymbol{k}_{\mathrm{inv}}/\boldsymbol{k}_{\mathrm{ret}}$ ratio. Such large-amplitude motion is similar to that observed for photochemical[8,9] and thermal[10] isomerizations, which are viscosity-controlled.

To express $\boldsymbol{k}_{\mathrm{inv}}$ as a function of η, the physical models for the viscosity dependence of the radiationless processes involving large-amplitude motions need to be considered. For this purpose, the free-volume model[11,12] seems appropriate. According to Doolitle,[11a] molecular motion in a liquid is possible when sufficient free volume (V_f) is available for such a motion,[8,9,12] that is, when the free volume V_f per molecule is larger than some "critical" value V_0. The fluidity (η^{-1}) is thereby proportional to the probability factor [$\exp(-V_0/V_f)$] for the translational motion of molecules in the liquid medium. Hence, the free-volume dependence of the viscosity may be expressed by eq 3, in which

$$\eta = A \exp(V_0/V_f) \tag{3}$$

A is a proportionality factor. The critical volume (V_0) for the molecular translational diffusion may be considered as the van der Waals volume per molecule. In contrast to the translational diffusion of a molecule, molecular rearrangements (i.e., the inversion process in Scheme 1) involve only a portion of the molecule and, thus, only a fraction αV_0 ($\alpha < 1$) of the critical free volume V_0 is required. Therefore, the rate constant $\boldsymbol{k}_{\mathrm{inv}}$ for the inversion process is given by eq 4, an expression which was first applied to rationalize the viscosity dependence for the photoisomerization of stilbenes.[12] Substitution of eq 3 into eq 4 gives eq 5 for the viscosity dependence of the inversion rate constant $\boldsymbol{k}_{\mathrm{inv}}$. Finally, the combination of eqs 2 and 5 leads to eq 6; its double-logarithmic form (eq 7) predicts a linear dependence of Φ_{inv} on the solvent viscosity (η).

$$\boldsymbol{k}_{\mathrm{inv}} = \boldsymbol{k}^0_{\mathrm{inv}} \exp(-\alpha V_0/V_f) \tag{4}$$

$$\boldsymbol{k}_{\mathrm{inv}} = \boldsymbol{k}^0_{\mathrm{inv}} (A/\eta)^{\alpha} \tag{5}$$

$$\frac{\Phi_{\mathrm{inv}}}{1 - \Phi_{\mathrm{inv}}} = \frac{\boldsymbol{k}^0_{\mathrm{inv}}}{\boldsymbol{k}_{\mathrm{ret}}} (\mathrm{A}/\eta)^{\alpha} \tag{6}$$

$$\ln \frac{\Phi_{\mathrm{inv}}}{1 - \Phi_{\mathrm{inv}}} = \mathrm{const} - \alpha \ln \eta \tag{7}$$

As evident from Figure 1, the experimental viscosity dependence of the inverted housane **2**(inv) yield is well accounted for by eq 6, as manifested by the good fit of all the data points (solid curve) and the expected linear double-logarithmic plot according to eq 7 ($R^2 = 0.98$, cf. insert in Figure 1). The slope of the double-logarithmic plot provides $\alpha = 0.27$, which matches well the values (~0.1 to 0.6) obtained for a number of viscosity-controlled photoisomerizations.[8,9,12] The fact that $\alpha < 1$ means that the motion of only a fraction of the molecule is subject to the viscosity effect, which in present case corresponds to the rotation of the pertinent molecular fragment during formation of the inverted housane **2**(inv) in Scheme 1. Thus, our experimental data for the yield (Φ_{inv}) of the inverted housane **2**(inv) obey the free-volume model over a wide viscosity range (from 0.33 to 89.2 cP).

An alternative approach to treat the viscosity dependence of molecular rearrangement (isomerization) processes is the well-known Kramers theory.[13] Application of the Kramers theory to our experimental data (Table 1) provides a poor fit over the entire viscosity range, as shown in Figure 1: The predicted curve for low viscosities ($\eta < 3$ cP, dashed line) fails to accommodate the data points at higher viscosities. This failure is similar to that reported for other viscosity-controlled reactions (isomerizations), in which the deviation from the Kramers theory is manifested by a similar leveling effect at high viscosity.[9]

The data presented herein on the photochemical denitrogenation of the DBH-type azoalkane **1** clearly show that the inversion process is strongly controlled by the viscosity of the medium. Evidently, the frictional impediment (viscosity) of molecular motion (in the present case rotations) by the medium provides an attractive and simple physical picture at the molecular level to understand the stereoselectivity in the mechanistically complex thermal and photochemical deazetation of DBH-type azoalkanes to inverted housanes. This simple concept merits further attention.

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