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Kinetics and Activation Parameters for the Thermal 1,5-Hydrogen Shifts Interconverting the Four Monodeuterio-*cis*,*cis*-1,3-cyclooctadienes

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In 1962, thermally activated 1,5-hydrogen shifts in deuterium-labeled cycloheptatrienes were demonstrated and followed kinetically by ter Borg, Kloosterziel, and Van Meurs,[1] and similar interconversions among deuterium-labeled cyclopentadienes were reported by Russian workers.[2] Winstein and his collaborators noted such reactions in 1,3-cyclooctadienes and cyclooctatrienes in 1963.[3] Thus, thermal [1,5] sigmatropic migrations of hydrogen were widely recognized even before Woodward and Hoffmann in 1965 provided a theoretical account of such isomerizations.[4]

In 1966, Glass, Boikess, and Winstein recapitulated these developments and reported a kinetic study of thermal interconversions among the four isomeric monodeuterio-*cis*,*cis*-1,3-cyclooctadienes (Scheme 1).[5]

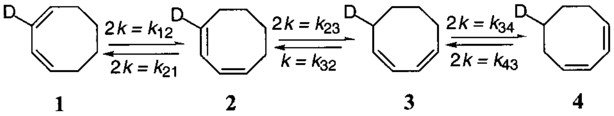
This noteworthy experimental study provided kinetic information and derived activation parameters for the isomerizations in the face of daunting technical limitations associated with the analyses of reaction mixtures using proton NMR spectroscopy at 60 MHz, especially since the resolution was unable to resolve C(1,4)−H and C(2,3)−H absorptions. The three observable NMR absorption intensity ratios, functions of the time-dependent concentrations of isomers **1**−**4**, were expressed as shown in eqs 1−3.

$$y_1 = M/A = (55 - 2x + 5x^4 + 2x^6)/(55 - x - 5x^4 - 4x^6) \quad (1)$$

$$y_2 = V/A = (55 + 3x + 2x^6)/(55 - x - 5x^4 - 4x^6) \quad (2)$$

$$y_3 = (M + A)/V = (110 - 3x - 2x^6)/(55 + 3x + 2x^6) \quad (3)$$

Scheme 1



In eqs 1−3, the letters *M*, *A*, and *V* stand for methylenic, allylic, and vinylic proton absorption intensities and $x = \exp(-kt)$. The equations themselves were derived from an undetailed kinetic treatment of the reversible first-order reactions of Scheme 1. Values for the rate constants *k* and the related activation parameters secured for isomerizations run with neat liquid samples were found to be $3.46(\pm 1.06) \times 10^{-5}$ s^{-1} at 150.2 °C, $1.42(\pm 0.37) \times 10^{-5}$ s^{-1} at 137.1 °C, and $3.64(\pm 1.14) \times 10^{-6}$ s^{-1} at 125.3 °C; $\Delta H^{\ddagger} = 29.3$ kcal/mol and $\Delta S^{\ddagger}$ −10 eu; $E_a = 30.1$ kcal/mol and $\log A = 11.1$.

The relatively large error bars on values of rate constants followed from the NMR instrumental limitations at that time, the modest temperature range covered, and relatively small dynamic changes for the variables y_1, y_2, and y_3. In kinetic runs starting with 100 mol % isomer **3**, as reaction times increased from 0 to infinity and $\exp(-kt)$ decreased from 1.00 to 0, y_1 and y_2 decreased from 1.33 to 1.00 while y_3 increased from 1.75 to 2.00. Unfortunately, the relatively large error bars on estimations of rate constants led inexorably to relatively large uncertainties in activation parameters.

The error limits in rate constants are consistent with straight-line fits having significantly different slopes and intercepts, correlations that would extrapolate to very different rate constants at substantially higher or lower temperatures. Assuming that the uncertainty in E_a stems only from uncertainties in the rate constants—that errors associated with temperature measurements or the relatively small temperature spread of the kinetic work, 24.9 °C, contributes nothing to the uncertainty in E_a—then the relationship of eq 4 applies;[6] here, $k_a = k(150.2\ °\mathrm{C})$ and $k_b = k(125.3\ °\mathrm{C})$. According to this estimate, ΔE_a is 5.9 kcal/mol. Similarly,[6] $\Delta[\log A] = \Delta E_a/2.303RT = 3.1$.

$$\Delta E/E = [(1/\ln(k_a/k_b))^2((\Delta k_a/k_a)^2 + (\Delta k_b/k_b)^2)]^{1/2} \quad (4)$$

A continuing interest in prototypical pericyclic reactions of "simple" hydrocarbons prompted a return and reconsideration of the interconversions shown in Scheme 1. More precise values for the activation parameters could be of importance in assessments of computational efforts toward understanding the role of conformational factors impinging on the rates of 1,5-hydrogen shifts. They could also contribute to a clearer understanding of just how bicyclo[4.2.0]oct-7-ene is converted thermally to *cis*,*cis*-1,3-cyclooctadiene. This reaction has attracted serious mechanistic attention for at least 25 years and still seems to be inconclusively rationalized.[7]

Kinetic Equations. The expressions of eqs 1−3 for variables y_1, y_2, and y_3 may seem to the casual reader to come out of the blue, but they may be understood readily, given the theoretical expressions for the time-dependent

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mole percents of isomers **1**−**4**. For kinetic runs starting with isomer **3** (**1**(0) = 0, **2**(0) = 0, **3**(0) = 100, **4**(0) = 0), the kinetic situation posed by the reactions of Scheme 1 leads to the integrated kinetic expressions given in eqs 5−8. The derivation of these equations is in principle a simple matter, although perhaps it has not been undertaken by all readers of the 1966 kinetic study. An explicit account has recently been provided along with parallel derivations for related kinetic schemes.[8]

$$\mathbf{1}(\mathrm{t}) = 50/3 - (40/3)\exp(-kt) - (50/3)\exp(-4kt) + (40/3)\exp(-6kt) \quad (5)$$

$$\mathbf{2}(\mathrm{t}) = 50/3 - (20/3)\exp(-kt) + (50/3)\exp(-4kt) - (80/3)\exp(-6kt) \quad (6)$$

$$\mathbf{3}(\mathrm{t}) = 100/3 + (20/3)\exp(-kt) + (100/3)\exp(-4kt) + (80/3)\exp(-6kt) \quad (7)$$

$$\mathbf{4}(\mathrm{t}) = 100/3 + (40/3)\exp(-kt) - (100/3)\exp(-4kt) - (40/3)\exp(-6kt) \quad (8)$$

Given these functions, the formulas of eqs 1−3 for variables y_1, y_2, and y_3 may be derived readily through simple algebra, noting the number of protons in each isomer contributing to overall integrated M, A, and V absorption intensities. An alternative presentation of the theoretical equations, appropriate for the same initial conditions, is provided in eqs 9−12.

$$\mathbf{1}(\mathrm{t}) = 16.67 - 13.33\exp(-kt) - 16.67\exp(-4kt) + 13.33\exp(-6kt) \quad (9)$$

$$\mathbf{2}(\mathrm{t}) = 16.67 - 6.67\exp(-kt) + 16.67\exp(-4kt) - 26.67\exp(-6kt) \quad (10)$$

$$\mathbf{3}(\mathrm{t}) = 33.33 + 6.67\exp(-kt) + 33.33\exp(-4kt) + 26.67\exp(-6kt) \quad (11)$$

$$\mathbf{4}(\mathrm{t}) = 33.33 + 13.33\exp(-kt) - 33.33\exp(-4kt) - 13.33\exp(-6kt) \quad (12)$$

Results. The kinetics of 1,5-hydrogen shifts equilibrating the monodeuterio-*cis*,*cis*-1,3-cyclooctadienes have been redetermined to gain more precise estimates of activation parameters. 5-Deuterio-*cis*,*cis*-1,3-cyclooctadiene (**3**) was prepared from 5-bromo-*cis*,*cis*-1,3-cyclooctadiene[9] through a reduction with $LiAlD_4$.[5,7g] Material used for kinetic runs was purified by preparative gas chromatography; analysis by deuterium NMR at 92.124 MHz (600 MHz for proton spectrometer) indicated that the starting material was 0.7% **1**, 1.0% **2**, 96.5% **3**, and 1.8% **4**. Some of the contributions attributable to isomers **1**, **2**, and **4** stem from deuterium in natural abundance, some to very small amounts of thermal isomerization during chromatography. In any event, these mole percent values dictate a revised set of theoretical expressions, appropriate for the starting concentrations **1**(0) = 0.7, **2**(0) = 1.0, **3**(0) = 96.5, **4**(0) = 1.8; they are easily derived[8] and are given in eqs 13−16.

Table 1. Mole Percent Relative Concentration Data for Monodeuterio-*cis*,*cis*-1,3-cyclooctadienes as Functions of Reaction Temperature and Time

T (°C)	time (s)	**1**(t) (%)	**2**(t) (%)	**3**(t) (%)	**4**(t) (%)
	0	0.7	1	96.5	1.8
170	300	1	4	86.5	8.5
170	900	1.9	8.3	70.3	19.5
170	1500	3.2	10.2	61.1	25.5
170	2100	4.4	11.9	53.3	30.4
154	2400	1.8	7	76.1	15.1
154	4800	2.2	9.9	63	24.8
154	7200	4.1	11.4	54.7	29.9
139	14400	1.9	9.3	66.3	22.6
139	28800	4.2	11.7	51.8	32.2
139	43200	6.0	13.2	44.3	36.5
125	28800	1.4	7.0	75.8	15.8
125	64800	3.2	11.0	58.8	27.0
125	126000	6.0	12.3	46.4	35.3

$$\mathbf{1}(\mathrm{t}) = 16.67 - 12.71\exp(-kt) - 15.83\exp(-4kt) + 12.57\exp(-6kt) \quad (13)$$

$$\mathbf{2}(\mathrm{t}) = 16.67 - 6.35\exp(-kt) + 15.83\exp(-4kt) - 25.15\exp(-6kt) \quad (14)$$

$$\mathbf{3}(\mathrm{t}) = 33.33 + 6.35\exp(-kt) + 31.67\exp(-4kt) + 25.15\exp(-6kt) \quad (15)$$

$$\mathbf{4}(\mathrm{t}) = 33.33 + 12.71\exp(-kt) - 31.67\exp(-4kt) - 12.57\exp(-6kt) \quad (16)$$

The kinetic runs used samples of starting material diluted with *tert*-butylbenzene; they were sealed in NMR tubes without added $(CH_3)_4Si$. The natural abundance deuterium NMR absorptions for *tert*-butylbenzene do not overlap with signals for the monodeuterio-*cis*,*cis*-1,3-cyclooctadienes **1** (at δ 5.5), **2** (δ 5.25), **3** (δ 1.8), or **4** (δ 1.1). After defined reaction times the samples were examined by ^{2}H NMR to gain mol percent data. The relative concentrations of isomers **1** to **4** as functions of temperature and time are summarized in Table 1.

Even with such relatively few kinetic runs at each temperature, one gets fair precision in estimates of rate constants, since every time-dependent concentration at a given temperature depends on the same parameter k. Thus, even three kinetic runs give 12 values of concentrations, all dependent on a single parameter and completely defined kinetic expressions. The data fit the theoretical expressions quite satisfactorily, as exemplified in Figure 1.

The best values for rate constants k for 1,5-hydrogen migrations equilibrating isomers **1**−**4** at each temperature were those giving the smallest values of estimated variance, $\sigma^2_C = \Sigma(C_i(\mathrm{obs}) - C_i(\mathrm{cal}))^2/(n-1)$: 1.33×10^{-4} s^{-1} at 170 °C, 3.68×10^{-5} s^{-1} at 154 °C, 1.05×10^{-5} s^{-1} at 139 °C, and 3.25×10^{-6} s^{-1} at 125 °C. The σ^2_C values were calculated to be 0.17, 0.20, 0.43, and 0.29, respectively; the corresponding values of $\partial\sigma^2_C/(\partial k)^2$, estimated numerically as $\Delta\sigma^2_C/(\Delta k)^2$ with $\Delta k = 0.03\,k$, lead to values for standard deviations of $\sigma_k = 3.0 \times 10^{-6}$, 3.1×10^{-7}, 2.9×10^{-7}, and 8.1×10^{-8} (all times s^{-1}).[10] Thus, the rate

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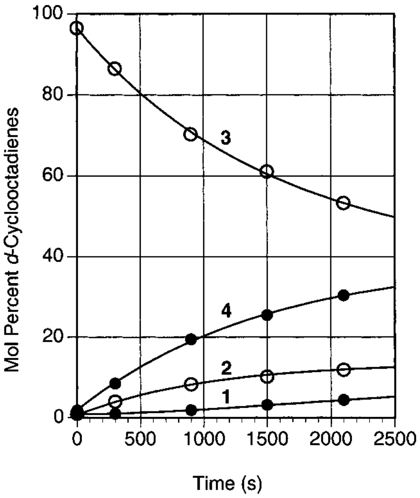

Figure 1. Time-dependent mole percent proportions of monodeuteriocyclooctadiene isomers **1**−**4** at 170 °C. The theoretical functions are eqs 9−12 with rate constant $k = (1.33 \pm 0.06) \times 10^{-4}\ s^{-1}$.

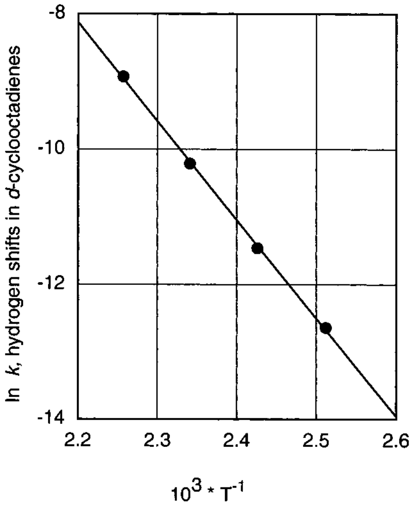

Figure 2. Arrhenius plot: $\ln(k)$ versus $(1/T) \times 10^3$; the slope and intercept are −14.58 and +23.95.

constants and uncertainties (taken to be $\pm\ 2\sigma_k$) are estimated to be $(1.33 \pm 0.06) \times 10^{-4} s^{-1}$ at 170 °C, $(3.68 \pm 0.06) \times 10^{-5} s^{-1}$ at 154 °C, $(1.05 \pm 0.06) \times 10^{-5}$ at 139 °C, and $(3.25 \pm 0.16) \times 10^{-6}$ at 125 °C. These rate constants are about as precise as one could hope for given analytical data derived from integrating NMR absorption intensities. The average C_i(obs) − C_i(cal) value for all 52 comparisons was less than 0.5 mol %.

From these rate constants one obtains a good Arrhenius plot (Figure 2) and the parameters $E_a = 29.0$ kcal/mol and $\log A = 10.4$. The estimated uncertainties in activation parameters based on the standard deviations in slope and intercept of the Arrhenius plot are $\Delta E = 0.6$ kcal/mol and $\Delta[\log A] = 0.7$. The related $\Delta H^\ddagger$ and $\Delta S^\ddagger$ terms are calculated to be 28.1 kcal/mol and −13.7 eu. Thus, relative to the earlier estimates,[5] the enthalpy of activation is slightly lower, by just 1.2 kcal/mol, but with a significantly diminished estimated uncertainty, while the entropy of activation is more negative by 3.7 eu, corresponding to a more conformationally restricted transition structure.

Thorough understandings of conformational limitations on transition structures for 1,5-hydrogen shifts in cyclic dienes must await suitable kinetic work and theoretical assessments. Roth has reported kinetic studies on 1,5-deuterium shifts equilibrating the isomeric d_5-cyclopentadienes,[11] but no kinetic work on 1,5-hydrogen shifts involving monodeuteriocyclopentadienes, 1,3-cyclohexadienes, 1,3-cycloheptadienes,[12] or 1,3-cyclononadienes has been reported. These lacunae of experimental data for a fundamental type of thermal transformation, one unequivocally characterized as a concerted process,[13] seem lamentable gaps; they could be bridged by studies such as the present effort using ^{2}H NMR spectroscopy and exact theoretical kinetic expressions.[8]

On the theoretical side there has been no paucity of calculational treatments of 1,5-hydrogen shifts in pentadiene and related systems,[14] but no systematic effort directed toward predicting transition structures and $\Delta H^\ddagger$ values for a series of *cis,cis*-1,3-cyclodienes has been forthcoming. Thus, basic experimental and theoretical work on the concerted thermal 1,5-hydrogen migrations shown by cyclic dienes remains on the agenda as clearly accessible and attractive objectives.

Experimental Section

5-Bromo-*cis,cis*-1,3-cyclooctadiene was prepared through the benzoyl peroxide promoted reaction of recrystallized *N*-bromosuccinimide with *cis,cis*-1,3-cyclooctadiene in CCl_4 at reflux.[9]

5-Deuterio-*cis,cis*-1,3-cyclooctadiene. To a flame-dried 50-mL round-bottomed flask containing $LiAlD_4$ (0.3 g, 7.1 mmol, 0.66 equiv) and 10 mL of dry ether under nitrogen was added slowly with stirring by syringe 5-bromo-*cis,cis*-1,3-cyclooctadiene (2 g, 10.7 mmol). After 24 h at room temperature, the reaction mixture was cooled in an ice bath and treated with 3 mL of H_2O. A conventional workup and distillation gave crude product of bp 72 °C (16 mm). Preparative GC using a 2.3-m 20% β,β'-ODPN column at 59 °C gave deuterium-labeled *cis,cis*-1,3-cyclooctadiene; by ^{2}H NMR it was estimated to be only 96.5% **3**; the other isomers present were estimated to be 0.7% **1**, 1.0% **2**, and 1.8% **4**. A trace of 3-deuterio-*cis,cis*-1,4-cyclooctadiene was also apparent at δ 2.25. It remained a constant impurity in kinetic mixtures.

Thermal Isomerizations. Samples of **3** diluted with *tert*-butylbenzene sealed in NMR tubes were heated for specified periods, suspended above phenetole (ethyl phenyl ether, bp 170 °C; lit.[15] bp 169−170 °C), anisole (bp 154 °C; lit.[15] bp 154 °C), *m*-xylene (bp 139 °C; lit.[15] bp 138−139 °C), or butyl acetate (bp 125 °C; lit.[15] bp 124−126 °C) maintained at reflux. Analyses of reaction mixtures were secured through ^{2}H NMR spectroscopy. The kinetic data are summarized in Table 1.

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