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Effect of Deuterium on the Kinetics of 1,5-Hydrogen Shifts: 5-Dideuteriomethylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene

William von E. Doering* and Edmund J. Keliher

Contribution from the Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts 02138-2902

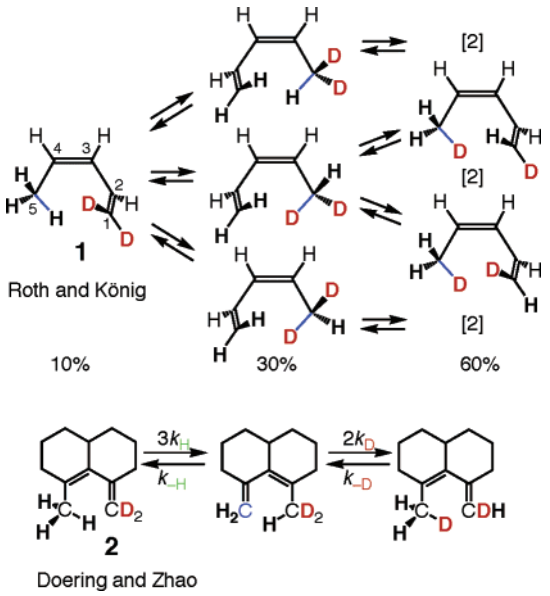
Received August 18, 2006; E-mail: doering@chemistry.harvard.edu

Abstract: To obtain a more reliable temperature dependence of the kinetic deuterium isotope effect in a 1,5-hydrogen shift, the title compound has been designed to repress compromising side reactions, arguably arising from second-order ene−ene unions. The values of k_H/k_D, 4.58−5.15, in the range 185.8−153.8 °C, on extrapolation by the derived Arrhenius equation, lead to 8−14 at 25 °C. Another goal is the evaluation of the effect on rates of the free rotation available to the phenyl groups in 2,4-diphenyl-1,3(*Z*)-pentadiene compared to the constraint to coplanarity of the phenyl groups in the title compound. The effect is insignificant. Incidental to the presence of the sterically effective methyl groups in the title compound, participation of the hydrogen atoms of an aromatic methyl group as part of the 1,3(*Z*)-pentadienyl system has been uncovered in 6,8-dimethyl-1-methylene-1,2,3,4-tetrahydronaphthalene. The rate of the rearrangement is too slow to compromise the kinetics of the hydrogen shifts in the title compound. A reassessment of the conventional procedure for estimating uncertainties in Arrhenius parameters based on a small number of rate constants has led to the proposal of an alternative procedure based on the statistically more significant uncertainties associated with the individual rate constants.

Introduction

The pioneering work of Roth and König on the kinetic deuterium isotope effect (KDIE) in the thermal 1,5-hydrogen shift in 1,3(*Z*)-penta-1,3-diene at 185−201 °C revealed a large value of 5.7 and a dramatic increase to 12.2 on extrapolation to 25 °C.[1] Taken with the definitive establishment of the stereochemistry of the rearrangement,[2] their work prompted theoretical interest in the possible role for tunneling in the mechanism of the thermal 1,5-hydrogen shift.[3] As already cautioned,[4] the Arrhenius parameters providing the basis for the temperature dependence of the KDIE were of insufficient precision to justify their acceptance as experimentally assured points for comparison with theoretical results (Scheme 1). In the hope of obtaining more reliable results, Doering and Zhao studied an example frozen in the reaction-competent cis conformation of the diene without achieving a satisfactory improvement (**2**, Scheme 1).[5] Disturbing complications were unsatisfactory levels of recovery over time and a persistent failure to reach the statistically expected ratios among the three products at long times of reaction.

Scheme 1



The present work was undertaken to obtain a more accurate value for the temperature dependence of the KDIE in a 1,5-hydrogen shift and to compare 2,4-diphenyl-1,3(*Z*)-pentadienes (**3**) with previously published work on 1-*p*-tolyl-5-phenyl-1,3-(*Z*)-pentadiene.[4]

(1) Roth, W. R.; König, J. *Liebigs Ann. Chem.* **1966**, *699*, 24−32.
(2) Roth, W. R.; König, J.; Stein, K. *Chem. Ber.* **1970**, *103*, 426−439.
(3) (a) Liu, Y.-p.; Lynch, G. C.; Truong, T. N.; Lu, D.-h.; Truhlar, D. G.; Garnett, B. C. *J. Am. Chem. Soc.* **1993**, *115*, 2408−2415. (b) Chantranupong, L.; Wildman, T. A. *J. Am. Chem. Soc.* **1990**, *112*, 4151−4154. (c) Dewar, M. J. S.; Healy, E. F.; Ruiz, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 2666−2667. (d) Jensen, F.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 3139−3140.
(4) Doering, W. v. E.; Keliher, E. J.; Zhao, X. *J. Am. Chem. Soc.* **2004**, *126*, 14206−14216.
(5) Doering, W. v. E.; Zhao, X. *J. Am. Chem. Soc.* **2006**, *128*, 9080−9085.

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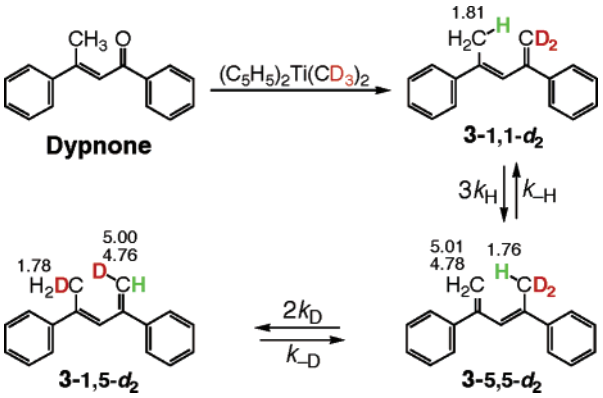


Figure 1. Preparation from dypnone of **3**-1,1-d_2 and its thermal rearrangement to **3**-5,5-d_2 and **3**-1,5-d_2 are shown. The shifts in the ^{1}H NMR spectrum of the hydrogen atoms used in the analysis of the kinetics are shown in ppm (δ).

Results

Preparation of 1,1-dideuterio-2,4-diphenyl-1,3(*Z*)-pentadiene (**3**-1,1-d_2) from (*E*)-dypnone[6] involved methylenation (conversion of the carbonyl group to methylene) following the method of Petasis and Bzowej employing dimethyltitanocene (Figure 1).[7,006]

Early in the study of the kinetics of **3**-1,1-d_2, a steady decline in recovery with time of reaction made the achievement of reliable results problematic. As an illustration, recovery of deuterium isotopomers at 118 °C after 815 h was only 50%, while the 1,5-hydrogen shift had itself proceeded barely 50% toward equilibrium (Table S1).

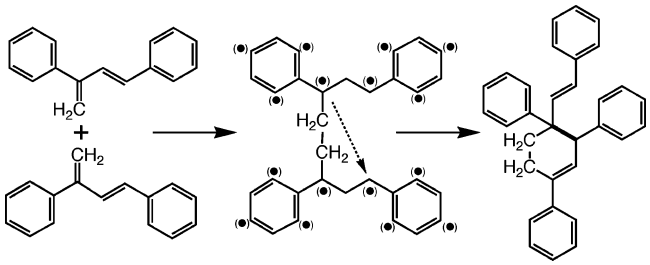
A likely culprit was thought to be the competitive formation of dimeric side products initiated by an ene−ene union to a 1,4-diradical (Scheme 2). This type of dimerization had been estimated to have an activation energy of 24.0 kcal mol^{-1} in the paradigm, butadiene (experimental: 26 kcal mol^{-1}).[8] Enhancement of stabilization in the allylic radical moieties by two phenyl groups could amount to 6.6−4.3 kcal mol^{-1} by one phenyl group and 2.3 kcal mol^{-1} by the second.[9] Mulzer had indeed reported an activation enthalpy of 12.4 kcal mol^{-1} for the dimerization of 1,3-diphenylbuta-1,3-diene in fine agreement with a predicted value of 11.4 kcal mol^{-1} (24.6 − 2 × 6.6 kcal mol^{-1}).[10] However, a traditional plot of the reciprocal of concentration against time to confirm second-order kinetics was not linear. Nor did a doubling of the concentration of starting material improve recovery by more than 20%. Even if the effect of byproducts on the kinetics might have been handled credibly by introducing an extra irreversible second-order step, the effect on the accuracy of analysis by NMR would have remained difficult to estimate. It is noted that the relative ratios of hydrogen shift to loss of material is smallest at the lowest temperature, 118.0 °C, and largest at the highest temperature, 169.5 °C. That behavior is consistent with the prediction of a lower energy of activation for loss of monomer through ene−ene union.

Table 1. Specific First-Order Rate Constants for 1,5-Hydrogen Shifts

T, °C	$3k_H$[a,e]	$3k_H$[b,e]	$3k_H$[c,e]	$3k_D$[d,e]
201.5			97.3	15.4[f]
185.0		63.0 ± 0.6[g]	27.0	4.14
169.5	95.7 ± 2.5[g]		6.91	
154.0	29.3 ± 0.76[g]	5.24 ± 0.06[g]	2.08	
118.0	1.46 ± 0.05[g]			

[a] In 1,1-dideuterio-2,4-diphenylpenta-1,3(*Z*)-diene. [b] In 1-phenyl-5-*p*-tolylpenta-1,3(*Z*)-diene. [c] In 2-methyl-10-methylenebicyclo[4.4.0]dec-1-ene. [d] In penta-1,3(*Z*)-diene. [e] All values of *k* in units of 10^{-6} s^{-1}. [f] Calculated from Arrhenius equation (experimental: 13.4 at 200.0 °C).[4] [g] 95% confidence level.

Scheme 2

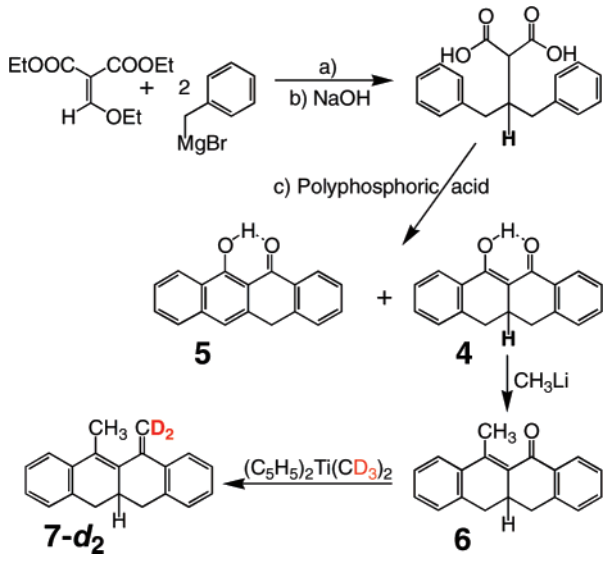


The kinetics of deuterium exchange was followed at four temperatures, analysis being by 600-MHz ^{1}H NMR spectroscopy. Two sets of signals relating concentration to time were employed: the first, those of the methyl groups; the second, the CH_3 at 1.81, the $=CH_2$ group at 5.01 and 4.78, and the $=CHD$ group at 5.00 and 4.76 ppm (δ) (Figure 1). By both methods, baseline separation was nearly, but not completely, achieved. There was no obvious basis for choosing between the two methods of analysis.

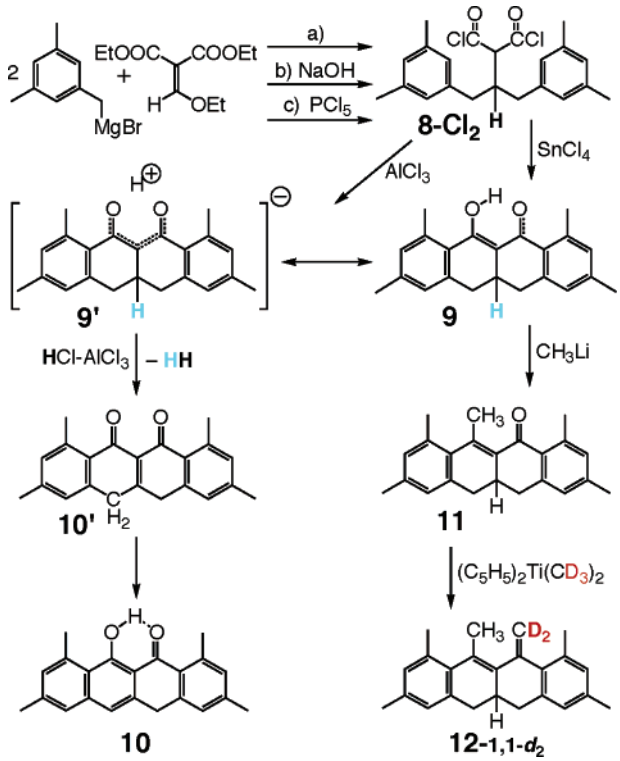
Rate constants for the conversion of **3**-1,1-d_2 to **3**-5,5-d_2 have been obtained by extrapolation to zero time of the tangents to the plot of data relating concentration and time given in Table S1 in the Supporting Information. These are summarized in Table 1 along with the corresponding rate constants for 1-phenyl-5-*p*-tolyl-1,3(*Z*)-penta-1,3-diene.[4] The ratios of those from the 2,4-diphenyl isomer **3** to the 1-phenyl-5-*p*-tolyl are 4.4, while the Arrhenius parameters are $E_a = 30.6 \pm 3.4$ kcal/mol^{-1}, log $A = 11.05 \pm 0.14$, and $E_a = 30.1 \pm 0.9$ kcal/mol^{-1}, log $A = 10.14 \pm 0.9$, respectively. These values may be compared with those of $E_a = 36.1 \pm 2.2$ and log $A = 11.34 \pm 1.0$ reported for the paradigm by Roth and König.[1] The corresponding values of enthalpies of activation, 29.7 and 29.3 kcal/mol^{-1}, respectively, compare very well with the B3LYP calculational results of Hayase, Hrovat, and Borden: 28.8 and 28.8 kcal/mol^{-1}, respectively.[11,12] These authors discuss exhaustively the steric and electronic factors that may account for the ∼7-kcal/mol^{-1} differences to the paradigm. Electronic stabilization was in any event not expected to contribute more than that seen in the comparison of allyl radical with cinnamyl or the 1,3-diphenylallyl radical. These are of the same magnitude as the loss of electronic stabilization by steric forcing out of coplanarity of phenyl groups and conventional steric repulsions in the cis and trans starting materials. Whether the "aromatic" transition region is especially resistant to electronic stabilization by substituents is not clear.

(6) Muzart, J. *Synthesis* **1982**, 60−61.
(7) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392−6394.
(8) Doering, W. v. E.; Belfield, K. D.; He, J. *J. Am. Chem. Soc.* **1993**, *115*, 5414−5421.
(9) Doering, W. v. E.; Benkhoff, J.; Shao, L. *J. Am. Chem. Soc.* **1999**, *121*, 962−968.
(10) Mulzer, J.; Kühl, U.; Huttner, G.; Evertz, K. *Chem. Ber.* **1988**, *121*, 2231−2238.
(11) Hayase, S.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **2004**, *126*, 10028−10034.
(12) In footnote 11 of ref 11, attention is directed to the success of the calculations in the absence of inclusion of a tunneling component.

Scheme 3



Scheme 4



1,5-Hydrogen Shift in Naphthacenes. Forcing the phenyl groups in **3** into coplanarity with the sterically vulnerable methylene group was deemed a reasonable way to fix the pentadiene in the cisoid conformation, to slow dimerization relative to hydrogen transfer, and to limit loss of electronic stabilization by non-coplanarity. The consequent tetracyclic structure **7** was prepared from the known 5,6-dioxo-5,5a,6,11,-11a,12-hexahydronaphthacene (**4**) (Scheme 3).[13]Of the various conditions mentioned in that reference for the conversion of (dibenzylmethyl)malonic acid to **4**, polyphosphoric acid/phosphorus pentoxide afforded variable yields accompanied by a deep red product of dehydrogenation, proposed to be 6-hydroxy-12*H*-naphthacen-5-one (**5**). Gupte and co-workers had noted the appearance of a red, non-enolizable α,*β*-unsaturated diketone in the cyclization of di-α-naphthylmethylmalonic acid following a procedure of Clar and co-workers.[14]

Although the change from acyclic **3**-1,1-d_2 to cyclic **7** did improve recovery somewhat, the ratio of 1,5-hydrogen shift to recovery remained too unfavorable to hold promise of affording reliable kinetics.

In a final effort to suppress the competitive formation of frustrating byproducts, a further increase in steric shielding was introduced by the addition of ortho methyl groups as in compound **12** of Scheme 4. For convenience in synthesis, 3,5-dimethylbenzyl magnesium bromide was employed instead of 3-methylbenzyl magnesium bromide in order to avoid the formation of several unwanted constitutional isomers. The structure of **12** was confirmed by X-ray diffraction analysis. Although it could be assumed that the two superfluous methyl groups remaining in the para positions would not constitute a perturbation of disturbing magnitude, the presence of the ortho methyl groups opened the possibility of a competing 1,5-hydrogen shift.

In this preparation, a red impurity is formed in variable amount when the diacid chloride and aluminum trichloride as catalyst are used but can be avoided by the use of stannic chloride as the Lewis acidic catalyst. Its structure has been shown by X-ray diffraction analysis to be that of **10**. Further support is thereby given to the structure proposed for **5**, the analogue without the four methyl groups (Scheme 3). Parenthetically this oxidation, if by hydride abstraction, would be favored by a direct coupling with the enolized *β*-diketone depicted in an extreme electronic form in **9′** of Scheme 4.

Specific rate constants have been calculated by numerical integration by use of the program KINETIK of Dr. R. Fink, which employs a Runge−Kutta procedure of fourth order, allows up to seven components to be handled by ad libitum kinetic schemes, and provides errors at the 95% confidence interval for individual rate constants by incorporation of the method of Marquardt.[15,16]

The rearrangement of the tetramethylnaphthacene analogue **12**-1,1-d_2 of the unsubstituted **7** is clean. Recovery remains undiminished over the entire length of the kinetic study. In the previous work on the KDIE of the 1,5-hydrogen shift[4] and now with **12**-1,1-d_2, the equilibrium ratios among the three isomers at long times of reaction deviate slightly from those predicted *in neglect of secondary deuterium isotope effects*, 0.100:0.300:0.600 (Scheme 1). The experimental ratios at each of the three temperatures are 0.098, 0.308, and 0.594 (see Table SI-3 in the Supporting Information). These deviations are consistent with the difference in bond strengths between the relatively weaker sp^2 and stronger sp^3 carbon deuterium bonds.[17] This factor increases the equilibrium concentration of the methylene-dideuteriomethyl isotopomer, **12**-5,5-d_2, relative to the other two (Figure 2).

(13) Gupte, S. D.; Nabar, D. P.; Sunthankar, S. V. *J. Sci. Ind. Res.* **1960**, *19*B, 411−412.
(14) Clar, E.; Kemp, W.; Stewart, D. G. *Tetrahedron* **1958**, *3*, 325−333.
(15) Roth, W. R.; Fink, R., unpublished.
(16) Marquardt, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431−441.
(17) Sunko, D. E.; Humski, K.; Molojcic, R.; Borcic, S. *J. Am. Chem. Soc.* **1970**, *92*, 6534−6538. Barborak, J. C.; Chari, S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 5275−5277. Günther, H.; Pawliczek, J. B.; Ulmen, J.; Grimme, W. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 517−518. Gajewski, J, J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 6693−6704.

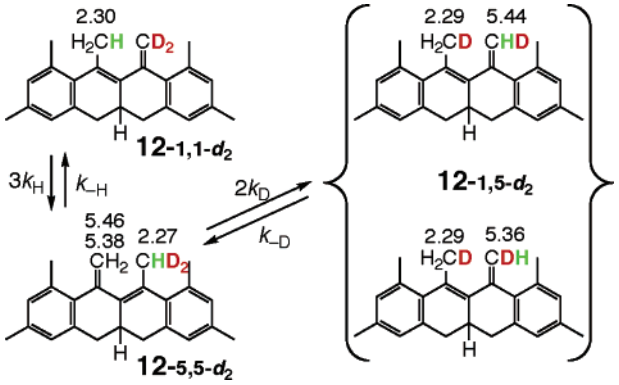


Figure 2. Kinetic scheme for the interconversions starting from **12-1,1-*d*$_2$** are shown along with the ^{1}H NMR signals employed in the analyses of concentrations versus time.

The thermodynamic (equilibrium) isotope effect is likely also to compromise the values of KDIE evaluated from $^2/_3(3k_H/2k_D)$ and k_{-H}/k_{-D} to the extent that it has begun to take effect in the transition region. In the former, $3k_H$ will be slightly accelerated and $2k_D$ slightly decelerated, while, in k_{-H}/k_{-D}, k_{-H} will be decelerated, and k_{-D}, accelerated in comparison to the nonobservable rates in the all-protium and all-deuterium analogues. This effect may contribute to the higher values of KDIE in column six of Table 2 vis-à-vis the lower values in column seven but cannot provide the entire explanation. The thermodynamic isotope effect is reduced in the ratios $^1/_3(3k_H)/k_{-D}$ and $2(k_{-H})/2k_D$ (columns eight and nine of Table 2, respectively).

Questioning the validity of the assumption that the ortho methyl groups in **12** would not engage in a 1,5-hydrogen shift, we prepared a truncated version (**13**) of **12** and examined it enough to demonstrate that at higher temperatures the hydrogen shift did occur, but at a rate too slow to be a disturbing factor at the temperatures of the study of **12** (see Figure 3). At 258.4 ± 0.2 °C, **13-1,1-*d*$_2$** rearranged cleanly in tubes of lead-potash glass to **13-1,5-*d*$_2$** and **13-5,5-*d*$_2$**, presumably reversibly, but demonstrably without contaminating rearrangement to 1,6,8-trimethyl-3,4-dihydronaphthalene. A rough rate constant, 3.1×10^{-6} s^{-1} at 258 °C, was estimated by extrapolation to zero time of a first-order plot of the data in Table S4 for the disappearance of **13-1,1-*d*$_2$**. As was to be expected, the two hypothetical nonbenzenoid intermediates could not be detected.

The specific rate constant for **13-1,1-*d*$_2$** (3.1×10^{-6} s^{-1} at 258 °C) may be compared to the values for **2** and **12-1,1-*d*$_2$** extrapolated to the same temperature: 4.1×10^{-3} s^{-1} and 2.5×10^{-2} s^{-1}, respectively. The resulting factors, 1300 and 8000 ($\Delta\Delta G^{\ddagger}_{258°C} = 9500$ cal/mol), respectively, are compatible with expectation (vide infra).[18]

Discussion

To begin, three comparisons may be of interest. The first is that between the equilibrated pair, transoid and cisoid penta-1,3(*Z*)-diene **1**, in which the transoid is favored by ~3.5 kcal mol^{-1}, and the rigidly cisoid 2-methyl-10-methylenebicyclo-[4.4.0]dec-1-ene **2**. The latter reacts faster at both 201.5 and 185.0 °C by a factor of ~6 (ΔE_a ~3−4 kcal mol^{-1}). This point has been discussed recently at length.[5]

The second compares the obligatorily cisoid **2** and the equilibrated transoid and cisoid pair, 2,4-diphenylpenta-1,3(*Z*)-diene **3**, in which the cisoid conformation is favored. [11] After calculation by means of the reported Arrhenius equation, the specific rate constants estimated for **2** at 169.5 °C (6.91×10^{-6} s^{-1}) and 154.0 °C (2.08×10^{-6} s^{-1}) are found to be slower than those of **3** at the same temperatures by factors of 13.9 and 14.1, respectively. The radical-stabilizing effect of the two phenyl groups can be expressed at the 1- and 3-positions of an allyl radical but not at the 2- and 4- positions of a pentadienyl radical (nodal positions) as depicted in Figure 4. In this comparison the transoid/cisoid complication is avoided. The conjugative stabilization of the phenyl groups in the starting material has been more than overcome in the transition region consistent with a compromised conformation behaving substantially like a relatively insensitive "aromatic" system (Figure 4). Note that the effect of radical-stabilizing substituents in the two 5-positions of the Cope rearrangement are much larger because they operate on a simple secondary radical, not on an already well stabilized allyl or pentadienyl radical.

The third is a comparison of **3** and **12-1,1-*d*$_2$**, in which the phenyl groups are rigidly confined to coplanarity with the rearranging pentadienyl system. The surprising closeness of the specific rate constants—at 169.5 °C, 95.7 and 81.4×10^{-6} s^{-1}, and at 154.0 °C, 29.3 and 23.4×10^{-6} s^{-1}, respectively—suggest almost identical interaction of the two phenyl groups in the starting materials and transition regions.

If the rearrangement of the hydrogen atom in the aromatic methyl group of **13-1,1-*d*$_2$** at a temperature as low as 258 °C seemed surprising, Grimme and his co-workers have established in several examples that benzo-annelation in a transition state leads to an increase in free energy of activation in the range 10−12 kcal mol^{-1}, a value much less than that expected if the entire resonance energy of benzene was to have been lost in the transition region.[18] Among other examples quoted in that reference, fusion of a benzene ring with one of the double bonds in the 1,7-hydrogen shift has been extensively examined by the late Hans Schmid and his co-workers.[19] Their rate constant may be compared, if imperfectly, with that of the acyclic 1,7-hydrogen shift studied by Baldwin and Reddy.[20] The result is a ratio of 210 000 at 225 °C ($\Delta\Delta G^{\ddagger} = 12.1$ kcal mol^{-1}) between the acyclic and benzo-fused trienes. Also of note is a ratio of ~270 000 ($\Delta\Delta G^{\ddagger} = 11.5$ kcal mol^{-1}) for the hydrogen shifts in cyclopentadiene and indene calculated from the data of Roth.[21]

In our initial attempts to extrapolate in the accepted manner the KDIE of the naphthacene **12-1,1-*d*$_2$** from the higher temperatures to the much lower temperature of 25 °C, plotting the natural logarithms of the three values of the ratio, $(3k_H/2k_D)$ $(^2/_3)$ (as they were first calculated) against the reciprocal of temperature revealed an almost perfect straight line! The fortuity of this linearity prompted us to rethink the uncertainties associated with the conventional evaluation by least-squares of an Arrhenius equation based on a small number of specific rate constants! (Uncertainty in the slope and intercept is, of course, indeterminate by this approach when only two data are available.) Individual rate constants fall randomly within an error

(18) Grimme, W.; Grommes, T.; Roth, W. R.; Breuckmann, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 872−874. Grommes, T. Ph.D. Dissertation, "Pericyclic Reactions with Participation of a Double Bond of Benzene," University of Cologne, 1991.

(19) Heimgartner, H.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1970**, *52*, 173−176.

(20) Baldwin, J. E.; Reddy, V. P. *J. Am. Chem. Soc.* **1988**, *110*, 8223−8228.

(21) Roth, W. *Tetrahedron Lett.* **1964**, 1009−1013.

Table 2. Specific Rate Constants[a] of the Thermal Rearrangements of 5-Dideuteriomethylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene (**12-$_{1,1}$-d_2**) (Figure 2)

T, °C	$3k_H$	k_{-H}	$2k_D$	k_{-D}	$^2/_3(3k_H/2k_D)$	k_{-H}/k_{-D}	$^1/_3(3k_H)/k_{-D}$	$2(k_{-H})/2k_D$
185.8 ± 0.3	27.62	8.649	4.019	2.091	4.582	4.136	4.403	4.304
	±0.20	±0.152	±0.0425	±0.0311	±0.059	±0.095	±0.073	±0.088
	±0.72%	±1.76%	±1.06%	±1.49%	±1.28%	±2.31%	±1.65%	±2.05%
169.2 ± 0.3	8.144	2.602	1.116	0.589	4.865	4.418	4.609	4.663
	±0.0763	±0.0561	±0.0157	±0.0122	±0.082	±0.132	±0.105	±0.120
	±0.94%	±2.16%	±1.41%	±2.07%	±1.69%	±2.99%	±2.27%	±2.58%
153.8 ± 0.3	2.342	0.721	0.303	0.162	5.153	4.451	4.819	4.759
	±0.0343	±0.0245	±0.0063	±0.051	±0.131	±0.206	±0.167	±0.190
	±1.46%	±3.39%	±2.09%	±3.15%	±2.55%	±4.63%	±3.47%	±3.98%
Arrhenius and Eyring Parameters[b]								
E_a	30.01 ± 0.20		30.25 ± 0.62		31.37 ± 0.15		31.05 ± 0.17	
log A	10.74 ± 0.10		10.35 ± 0.31		10.55 ± 0.07		10.11 ± 0.09	
$\Delta H^{\ddagger}$	29.13 ± 0.21		29.37 ± 0.63		30.49 ± 0.19		30.17 ± 0.18	
$\Delta S^{\ddagger}$	−12.17		−13.95		−13.04		−15.05	

[a] All specific rate constant in units of 10^{-5} s^{-1}; uncertainties at the 95% confidence level. [b] E_a and $\Delta H^{\ddagger}$ in kcal mol^{-1}; standard error in the conventional manner − linear regression on the three specific rate constants.

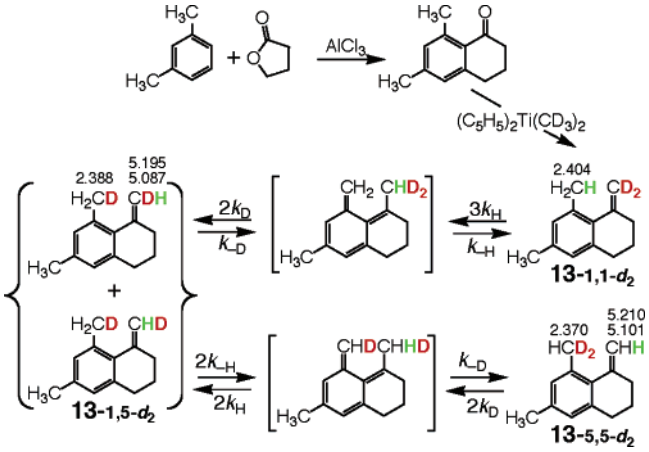


Figure 3. Preparation and kinetic profile of 6,8-dimethyl-1-dideuteriomethylene-1,2,3,4-tetrahydronaphthalene are depicted. The ^{1}H NMR used in quantitative analysis are give in ppm (δ) above the relevant groups.

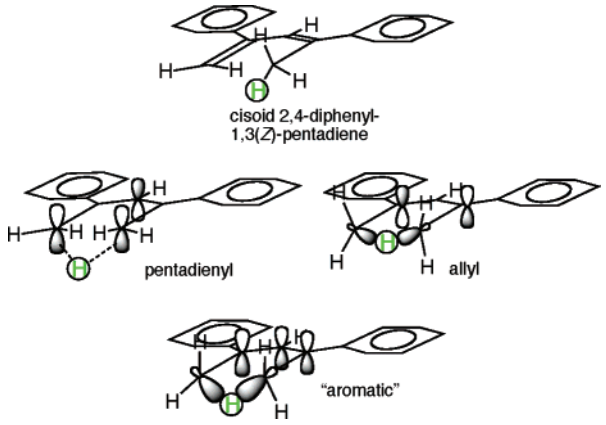


Figure 4. A compromise between two extreme representations of the transition region for the 1,5-hydrogen shift in 2,4-diphenyl-1,3(*Z*)-pentadiene is depicted.

bar that is assumed to include their unknowable *true* value. The error bar in the slope of such a plot of a small number of observed rate constants against the reciprocal of temperature reflects the randomness of the points comprising that particular sample. The error bar does not reflect the uncertainty in temperature but only the happenstance within that collection of points.

In an alternative approach to the estimation of error in the translation to the Arrhenius parameters, the rate constants at the two extreme temperatures—the original van't Hoff method—are employed, each with its associated error bar. The error bar ($\pm\Delta$) associated with each specific rate constant is based on a dozen or more observations of concentration versus time (t) and has some statistical significance by the usual method of least-squares. Recall that the error bar in k contains the responses of the rates to random fluctuations in temperature during their determination. In addition to the Arrhenius parameters derived from the specific rate constants (k_{T1}, k_{T2}), customarily as far apart in temperature as is experimentally convenient, two additional two-point Arrhenius equations are then created: the one from the higher value of the error bar of the first datum and the lower value of the error bar of the second datum (or last, if more than two), ($k_{T1} + \Delta$) and ($k_{T2} - \Delta$); the other, the reverse, from the lower value of the error bar of the first datum and the higher value of the error bar of the second datum, ($k_{T1} - \Delta$) and ($k_{T2} + \Delta$). From the differences between the original Arrhenius parameters and the additional pair of Arrhenius parameters, error bars for the energy of activation and the A factor are obtained. By this method, for example, for $3k_H$ ($k_1 = 27.62 \pm 0.20 \times 10^{-5}$ s^{-1} at 185.8 °C and $k_2 = 2.341 \pm 0.035 \times 10^{-5}$ s^{-1} at 153.8 °C [Table 2]), $E_a = 30028 \pm 265$ (0.9%) and log $A = 10.755 \pm 0.109/-0.145$ (1.2%) are obtained. This method produces generous values for the uncertainties and can perhaps be refined to give statistically more valid uncertainties. Implicit in this approach is the assumption that the unknowable *true* value of a specific rate constant falls within its error bar with a probability related to the specification of the error bar (95% confidence limit in the example above: 19 out of 20 measurements).[22]

Extrapolation of the KDIEs from the range of temperature 185.8−153.8 °C to 25.0 °C is accomplished by calculation of the two sets of three specific rate constants, each from the two sets of the three Arrhenius equations, for $3k_H$ and $2k_D$, respectively.[23] The extrapolated value of k_H/k_D [$^2/_3(3k_H/2k_D)$] from **12-$_{1,1}$-d_2** is 10.6 (+3.3/−2.4); that is, the *true* value should

(22) In respect to experimental design, when, for example, four determinations of k were contemplated, uncertainties in E_a would be lower if two measurements were made each at the highest and lowest temperature rather than four measurements equally spaced in 1/T.

lie between 8.2 and 13.9 at the 95% confidence interval. The spread is large despite the satisfactory level of uncertainties in the rate constants and their ratio because of amplification by the large extent of the extrapolation.

Conclusion

A discussion of the conventional basis for estimating uncertainties in Arrhenius parameters determined from a small number of rate constant/temperature data has been opened by proposing an alternative procedure based on the more significant uncertainties usually achieved in specific rate constants.

The experimental determination of the dependence of the KDIE on temperature initiated by Roth and König, and furthered by Doering and Zhao, has now been brought to a more satisfactory level of reliability. The value of k_H/k_D for the system **12-**$_{1,1}$**-*d*$_2$** (Figure 2) is 4.6 ± 0.1 at the highest temperature (185.8 °C) and considerably higher, 10.6 (+3.3, −2.4), on extrapolation to the lower temperature of 25 °C. Whether this increase in KDIE at 25 °C constitutes compelling support for the case that tunneling is a *significant* contributor to the rate of the hydrogen shift even at this low temperature, which is not realistically accessible to kinetic observation, we leave to theoreticians to conclude.[12] A more precise explication of the criteria to the satisfaction of which an experimentalist could and should aspire would be welcome.

The extrapolation to 25 °C is, of course, linear. Were tunneling to be an increasingly important component of the rate constants as temperature decreased, the line would become a curve and k_H/k_D would be larger than the value linearly extrapolated from the higher range of temperature.[24] With the extrapolated rate constants having $t_{1/2}$ ~4000 years, only were tunneling to increase dramatically over this range of temperature would its effect become observable as a statistically valid curvature departure from the Arrhenius, over-the-barrier linear plot and nonvirtual to the practicing mechanistic organic chemist of realistic lifespan.

Experimental Section

General Procedures. All ^{1}H NMR spectra were measured on a Varian Unity/Inova 600 instrument at 600 MHz in $CDCl_3$, unless otherwise noted; ^{1}H NMR (400 MHz) spectra were measured on a Varian Mercury 400 instrument; ^{13}C NMR(125.7 MHz) spectra were measured in $CDCl_3$ on a Varian Unity 500 instrument. Chemical shifts are reported in ppm relative to tetramethylsilane (δ) with respect to residual C_6D_5H (7.15 ppm for ^{1}H and 128.0 ppm for ^{13}C). Spin−lattice relaxation times (T_1) were determined by the inversion−recovery method in benzene-d_6. Preparative GC on a Varian Aerograph A90-P3 instrument employed a 3-m column of 20% Carbowax 20M on Anachrom AS with He as a carrier gas. Analytical gas chromatography was conducted on a Hewlett-Packard (HP) 5890A gas chromatograph equipped with a J&W Scientific, Inc. DB-225 (0.53 mm i.d. × 30-m, 1 μm film thickness) megabore column and an HP 3393A integrator.

2,4-Diphenyl-1,3(*Z*)-pentadiene (3). (*E*)-Dypnone (200 mg) was prepared by the procedure of Wayne and Adkins.[25] Dimethyltitanocene was prepared following a procedure of Petasis and Bzowej:[7] to a stirred solution of 1.0 g of dichlorotitanocene in 45 mL of diethyl ether freshly distilled from lithium aluminum hydride, 5 mL of a 1.6 M solution of methyllithium in diethyl ether were added at 0 °C. After 3 h of standing, 5 mL of water were added, and the reaction mixture was worked up in the usual way to yield 0.8 g (96%) of dimethyltitanocene as an orange solid.

To a solution of 0.62 g of dimethyltitanocene in 5 mL of toluene, 200 mg of dypnone were added. The reaction mixture was heated for 18 h at 65 °C. Purification by column chromatography (1 cm × 15 cm, alumina; 14:1 petroleum ether/ethyl acetate) afforded 150 mg of 2,4-diphenyl-1,3(*Z*)-pentadiene **3** as a colorless oil: ^{1}H NMR (cyclohexane-d_{12}) 7.40 (d, J = 7.61 Hz, 2H), 7.37 (d, J = 7.32 Hz, 2H), 7.21 (q, J = 7.61 Hz, 4H), 7.15 (t, J = 7.32 Hz, 2H), 6.50 (s, 1H), 5.57 (d, J = 1.47 Hz, 1H), 5.15 (s, 1H), 2.07 (d, J = 1.17 Hz, 3H); ^{13}C NMR 145.7, 143.4, 140.9, 137.9, 129.0, 128.31, 128.28, 127.6, 127.4, 126.6, 125.6, 115.4, 17.6.

1,1-Dideuterio-2,4-diphenyl-1,3(*Z*)-pentadiene (3-$_{1,1}$**-*d*$_2$).** The same procedure as that above was followed but for the substitution of di-(trideuteriomethyl)titanocene for dimethyltitanocene. Dichlorotitanocene (1.22 g)[7] was converted in the usual way with trideuteriomethyllithium (28 mL of a 1.6 M ethereal solution; Aldrich Co.) to 1.28 g of di-(trideuteriomethyl)titanocene, which was then allowed to react with dypnone (300 mg).

Kinetics of Thermal Rearrangement of 1,1-Dideuterio-2,4-diphenyl-1,3(*Z*)-pentadiene (3-$_{1,1}$**-*d*$_2$).** Kinetics were effected as already described.[4] Samples were prepared by placement in NMR tubes with benzene-d_6 as solvent and sealing under a vacuum after three freeze−dry cycles. Heating was in the vapors of boiling liquids: acetophenone, average temperature: 201.6 ± 0.2 °C; diethyl oxalate, 184.4 ± 0.3 °C; *tert*-butylbenzene, 167.7 ± 0.2 °C. To confirm that the borosilicate glass of the NMR tubes used as reaction vessels was not interfering with accuracy by acid catalysis of undesired constitutional changes, two experiments were conducted in soft-glass tubes using *p*-xylene-d_{10} as solvent at 201.6 °C for 112 h (403 200 s) and 205 h (738 000 s). Analysis of compounds **3-**$_{1,1}$**-*d*$_2$**, **3-**$_{1,5}$**-*d*$_2$**, and **3-**$_{5,5}$**-*d*$_2$**, (Figure 1) revealed concentrations that did not differ from the comparable runs in conventional NMR tubes within experimental uncertainties: i.e., ±5% (Table SI-2).

For quantitative analysis, acquisition times were 4.00 s, the relaxation time delay was 40 s, and the number of accumulations was 16. Even at 600 MHz, baseline separation of the isotopomers in Figure 1 was not always achievable. In order to achieve better separation, the data were processed by using resolution enhancement by 1.0 Hz and Gauss apodization by 0.4 s. The first of two sets of signals relating concentration to time was based on the methyl groups CH_3, 1.81; CH_2D, 1.78; and CHD_2, 1.76 ppm (δ); the second, on the methyl group CH_3, 1.81; the $=CH_2$ group, 5.01, 4.78; and the $=CHD$ group, 5.00, 4.76 ppm (δ). The raw data are given in Table S1.

Dibenzylmethylmalonic Acid. Following the procedure of Kim and co-workers,[26] to a solution of benzylmagnesium chloride (from 4.2 g of benzyl chloride) in ether was added diethyl ethoxymethylenemalonate (3.69 g). Conventional workup afforded 6.3 g of crude product, which was purified by evaporative distillation at 1 mmHg and 185° to afford 5.0 g (76%) of diethyl dibenzylmethylmalonate of 96% of purity by NMR: ^{1}H NMR 7.28 (t, J = 7.32 Hz, 4H), 7.19 (m, 6H), 4.18 (q, J = 5.86 Hz, 4H), 3.39 (d, J = 4.39 Hz, 1H), 2.79 (dd, J = 5.62, 12.45 Hz, 2H), 2.67 (m, 3H), 1.28 (t, J = 7.32 Hz, 6H).

This ester was hydrolyzed in 2.5 mL of 25% NaOH and 30 mL of methanol to give 3.95 g (94% of theoretical yield) of dibenzylmethylmalonic acid as a colorless solid: ^{1}H NMR 11.15 (br s, 2H), 7.29 (t, J = 7.61 Hz, 4H), 7.20 (m, 6H), 3.66 (d, J = 3.54 Hz, 1H), 2.91−2.85 (m, 2H), 2.80−2.73 (m, 3H); ^{13}C NMR (100.6 MHz) 174.6, 139.4, 129.2, 128.5, 126.5, 52.3, 43.3, 37.2.

6-Hydroxy-11a,12-dihydro-11*H*-naphthacen-5-one (4). Cyclization of the diacid above (2.7 g) was effected by treatment with polyphos-

(23) Alternatively, the equivalent calculation of the three Arrhenius equations from the high and low temperature values of k_H/k_D in Table 2, column 6, including the extremes of + and −, and − and + of the estimated uncertainties.

(24) Kohen, A., Limbach, H.-H., Eds. *Isotope Effects in Chemistry and Biology*; CRC Press: 2006.

(25) Wayne, W.; Adkins, H. *Org. Syn. Col. Vol. III* **1955**, 367−369.

(26) Kim, Y. M.; Kwon, T. W.; Chung, S. K.; Smith, M. B. *Synth. Commun.* **1999**, *29*, 343−350.

phoric acid (60 mL) at 75 °C for 15 min. Quenching with ice, diluting further with water, and extraction with ether gave an ethereal extract, which, when washed with aqueous $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated, afforded 1.3 g of **4**: ^{1}H NMR 16.55 (s, 1H), 8.03 (d, J = 7.62 Hz, 2H), 7.46 (t, J = 7.42 Hz, 2H), 7.38 (t, J = 7.42 Hz, 2H), 3.05 (m, 6H), 7.26 (t, J = 7.42 Hz, 2H), 3.05 (m, 3H), 2.80 (t, J = 14.14 Hz, 2H); ^{13}C NMR (100.6 MHz) 180.2, 140.2, 132.3, 131,3, 127.8, 127.1, 125.9, 107.0, 35.6, 30.1.

From the $NaHCO_3$ washes, 1.4 g. of unreacted dicarboxylic acid was recovered (^{1}H NMR).

6-Methyl-11a,12-dihydro-11*H*-naphthacen-5-one (6). To a solution of 200 mg of **4** in 10 mL of anhydrous THF, 2.5 mL of a 1.6 M solution of methyllithium in diethyl ether were added with stirring at 0 °C under argon. Worked up in the usual manner, 230 mg (76%) of **6** were obtained as a viscous oil: ^{1}H NMR 8.01 (d, J = 7.62 Hz, 1H), 7.62 (d, J = 7.91 Hz, 1H), 7.46 (t, J = 7.32 Hz, 1H), 7.36 (t, J = 7.32 Hz, 1H), 7.31 (m, 2H), 7.23 (t, J = 7.31 Hz, 2H), 3.02 (m, 1H), 2.96 (m, 1H), 2.89 (m, 2H), 2.77 (d, J = 1.76 Hz, 3H), 2.76 (t, J = 13.18 Hz, 1H); ^{13}C NMR 189.5, 145.8, 141.0, 136.7, 136.5, 135.8, 132.5, 132.1, 129.0, 127.7, 127.4, 127.1, 127.0, 126.9, 125.8, 36.0, 35.1, 34.4, 17.3.

12-Methyl-11-methylene-5,5a,6,11-tetrahydro-naphthacene (7). Dimethyltitanocene (0.8 g) was dissolved in 20 mL of toluene and added to 0.3 g of **6**. After 6 h of being heated at 65 °C, the reaction mixture was diluted with 20 mL of petroleum ether, filtered, concentrated, and subjected to column chromatography (2 cm × 15 cm, alumina, 15:1 petroleum ether/ethyl acetate) to yield 140 mg (45%) of **7**: ^{1}H NMR 7.58 (d, J = 7.62 Hz, 1H), 7.51 (d, J = 7.62 Hz, 1H), 7.34−7.30 (m, 3H), 7.27−7.23 (m, 3H), 5.73 (d, J = 1.17 Hz, 1H), 5.45 (d, J = 1.17 Hz, 1H), 2.97 (dd, J = 4.25, 13.91 Hz, 2H), 2.92 (dd, J = 3.22, 12.89 Hz, H), 2.88−2.75 (m, 3H), 2.45 (d, J = 1.46 Hz, 3H); ^{13}C NMR (100.6 MHz) 144.1, 139.4, 137.1, 137.0, 136.7, 135.9, 127.4, 127.3, 127.1, 127.0, 126.6, 126.5, 126.4, 124.3, 123.9, 115.4, 35.8, 35.7, 35.1, 16.2.

Bis-(3′,5′-dimethylbenzyl)methylmalonic Acid. Following a procedure adapted from Baldwin and O'Neill,[27] a Grignard reagent was prepared from 1.41 g of Mg shavings (0.06 mol) in 50 mL of ether and 10.0 g (0.05 mol) of α-bromomesitylene in 40 mL of ether. To this solution, diethyl ethoxymethylenemalonate (10 g in 30 mL of ether) was added over a period of 30 min. After being boiled under reflux for 18 h, the cooled reaction mixture was quenched with 10 mL of saturated aqueous NH_4Cl and separated into an ether and aqueous layer, which was diluted with 70 mL of saturated aqueous NH_4Cl, extracted three times with 40-mL portions of ether, dried over $MgSO_4$, and concentrated. Purification of the 10.4-g residue by column chromatography (silica gel, 5:1 hexane/ethyl acetate) afforded 4.46 g of diethyl bis(3′,5′-dimethylbenzyl)methylmalonate.

This diethyl ester was hydrolyzed by treatment with 2.5 mL of 25% aqueous NaOH and 30 mL of methanol at reflux for 4 h. Addition of 50 mL of water, extraction with ether (3 × 20 mL each), acidification with dilute HCl to pH 2, and extraction with ether (3 × 30 mL each) gave an ethereal solution, which was dried over $MgSO_4$ and concentrated to yield 3.71 g of the malonic acid: ^{1}H NMR 6.83 (s, 2H), 6.80 (s, 4H), 3.54 (d, J = 6.78 Hz, 1H), 2.72 (m, 5H), 2.28 (s, 12H); ^{13}C NMR 174.8, 139.3, 137.9, 128.0, 127.1, 52.4, 43.0, 37.1, 21.3.

6-Hydroxy-2,4,7,9-tetramethyl-11a,12-dihydro-11*H*-naphthacen-5-one (9). A 100-mL, three-necked, round-bottomed flask containing 1.30 g of the malonic acid above was fitted with a Tygon tube charged with 1.89 g of PCl_5. After evacuation and three cycles with argon, benzene (40 mL) and the PCl_5 were added. After 18 h of stirring, stannic chloride (1.3 mL) was added. Stirring was continued for 14 h. Diluted with 150 mL of water, the mixture was extracted five times with 30 mL each of CH_2Cl_2. The combined extracts were dried ($MgSO_4$), filtered, and concentrated to 1.54 g of a dark residue, which was dissolved in 1.1 mL of THF and cooled at −78 °C for 4 h to give 360 mg of orange plates. A second crop (180 mg) was obtained for a total of 540 mg of **9** (46% of theoretical yield): ^{1}H NMR (500 MHz) 17.61 (s, 1H), 6.95 (s, 2H), 6.89 (s, 2H), 2.89 (dd, J = 14.42, 4.95 Hz, 2H), 2.79 (m, 1H), 2.69 (s, 6H), 2.67 (t, J = 13.45 Hz, 2H), 2.33 (s, 6H); ^{13}C NMR 182.8, 141.7, 141.4, 139.7, 131.8, 127.3, 126.4, 109.5, 36.9, 30.1, 22.7, 21.4.

6-Hydroxy-2,4,7,9-tetramethyl-12*H*-naphthacen-5-one (10). Phosphorus pentachloride (0.59 g) was added to bis(3′,5′-dimethylbenzyl)-methylmalonic acid (300 mg) suspended in 50 mL of benzene. To this solution, having been stirred for 3 h at room temperature, freshly sublimed aluminum trichloride (0.37 g) was added. The mixture was heated at 35 °C for 17 h (reflux condenser), cooled, and extracted with ether (3 × 15 mL each). This extract was dried over Mg_2SO_4, filtered, and concentrated to 221 mg of a dark brown solid, which was crystallized from 0.5 mL of THF at room temperature to give 76 mg of deep red needles. Recrystallization afforded a sample suitable for X-ray crystallographic analysis: ^{1}H NMR 15.55 (s, 1H), 7.27 (s, 1H), 7.07 (s, 1H), 7.04 (s, 1H), 7.02 (s, 1H), 7.01 (s, 1H), 4.33 (s, 2H), 2.98 (s, 3H), 2.83 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H); ^{13}C NMR 192.1, 166.6, 143.1, 142.1, 139.5, 139.0, 138.6, 134.4, 132.0, 129.9, 128.5, 127.5, 126.8, 124.4, 121.2, 115.5, 111.8, 33.6, 24.9, 24.2, 21.6, 21.5.

2,4,6,7,9-Pentamethyl-11a,11-dihydro-12*H*-naphthacen-5-one (11). To a cooled (0 °C) solution of compound **9** (0.87 g) in 20 mL of THF in a flame-dried, 50-mL round-bottomed flask, 5.0 mL of a 1.6 M ethereal solution of methyl lithium were added. Stirring under argon of the dark green solution was continued for 14 h. Analysis by TLC (5:1 hexane/ethyl acetate) revealed three spots, R_f = 0.43, 0.32, and 0.22 (starting material: R_f = 0.51). Diluted with 10 mL of water and 30 mL of ether, the mixture was washed with 70 mL of 10% aqueous HCl and 100 mL of brine. The separated ethereal solution was dried over $MgSO_4$ and concentrated to a residue (0.57 g). Dissolved in 15 mL of benzene, the residue was transferred to a 25-mL flask fitted with a Dean−Stark trap, treated with a few crystals of *p*-toluenesulfonic acid, and boiled under reflux for 2 h. Cooled to 25 °C and diluted with diethyl ether, the reaction mixture was washed successively with aqueous $NaHCO_3$ (2 × 70 mL) and brine (2 × 70 mL), dried over $MgSO_4$, and concentrated. The residue was chromatographed (3 cm × 22 cm silica gel column:10:1 hexane/ethyl acetate) to afford 0.45 g of **11** as an orange solid: ^{1}H NMR (500 MHz) 6.94 (s, 1H), 6.93 (s, 1H), 6.88 (s, 1H), 6.87 (s, 1H), 2.89 (dd, J = 14.89, 4.15 Hz, 1H), 2.72 (m, 5H), 2.59 (s, 3H), 2.54 (m, 2H), 2.45 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H); ^{13}C NMR 191.3. 146.3, 141.5, 141.4, 139.4, 138.9, 137.7, 135.9, 135.7, 135.2, 132.6, 131.7, 131.3, 125.7, 125.2, 37.6, 34.7, 34.4, 23.0, 22.0, 21.7, 21.4, 21.0.

5-Methylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene (12-d_0). A solution of dimethyltitanocene (1.22 g, 6.0 mmol) in toluene (10 mL) was added to ketone **11** (600 mg, 2.0 mmol) under argon and stirred at 60 °C for 60 h following the procedure of Petasis and Bzowej.[7] A solution of the cooled reaction mixture and 20 mL of pentane were filtered and evaporated to a concentrate, from which column chromatography (1″ × 15″ alumina, 14:1 petroleum ether/ethyl acetate) afforded 100 mg of 5-methylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene **12-d_0**, which was purified by recrystallization from pentane (90 mg): ^{1}H NMR (benzene-d_6) 6.84 (s, 1H), 6.79 (s, 1H), 6.74 (s, 1H), 6.72 (s, 1H), 5.45 (d, J = 2.13 Hz, 1H), 5.37 (d, J = 2.05 Hz, 1H), 2.94 (dd, J = 14.35, 7.15 Hz, 1H), 2.74 (m, 1H), 2.50 (t, J = 14.86 Hz, 1H), 2.42 (s, 3H), 2.40 (dd, J = 14.42, 2.78 Hz, 1H), 2.35 (s, 3H), 2.30 (d, J = 2.05 Hz, 3H), 2.24 (dd, J = 14.28, 4.10 Hz, 1H), 2.17 (s, 3H), 2.15 (s, 3H); ^{13}C NMR 142.5, 141.6, 138.5, 137.8, 136.7, 136.1, 135.5, 135.3, 134.3, 132.7, 130.9, 129.5, 126.2, 125.3, 116.5, 37.1, 35.1, 34.9, 22.9, 21.0, 20.8, 20.3, 20.2.

5-Dideuteriomethylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene (12-$_{1,1}$-d_2). A solution of di(trideuteriomethyl)-titanocene (1.61 g) in toluene (10 mL) is added to the ketone **11** (300 mg, 0.9 mmol) under argon and stirred at 60 °C for 60 h following the procedure above for **12-d_0**. The yield of recrystallized **12-$_{1,1}$-d_2** was 80 mg. Its ^{1}H NMR spectrum was identical to that of **12-d_0** except for the

(27) Baldwin, S. W.; O'Neill, T. H. *Synth. Commun.* **1976**, *6*, 109−112.

absence of the signals at 5.45 and 5.37 ppm and two slightly different coupling constants at 2.40 and 2.94 ppm: ^{1}H NMR (benzene-d_6) 6.84 (s, 1H), 6.79 (s, 1H), 6.74 (s, 1H), 6.72 (s, 1H), 2.94 (dd, J = 14.35, 7.25 Hz, 1H), 2.74 (m, 1H), 2.50 (t, J = 14.86 Hz, 1H), 2.42 (s, 3H), 2.40 (dd, J = 14.46, 2.74 Hz, 1H), 2.35 (s, 3H), 2.30 (d, J = 2.05 Hz, 3H), 2.24 (dd, J = 14.31, 4.10 Hz, 1H), 2.17 (s, 3H), 2.15 (s, 3H).

Kinetics of the Thermal Rearrangement of 5-Dideuteriomethylene-2,4,6,7,9-pentamethyl-11,11a-dihydro-12*H*-naphthacene (12-$_{1,1}$-d_2). Individual samples in ampoules of lead-potash glass of **12-$_{1,1}$-d_2** (6 mg in 0.7 mL of benzene-d_6) were prepared from a stock solution consisting of 75.9 mg of **12-$_{1,1}$-d_2** in 0.4 mL of benzene-d_6. The ampoules were degassed three times by freeze−thaw cycles prior to being sealed under a vacuum. Heating was provided by the vapors of freshly distilled compounds boiling under reflux: anisole, bp 153.8 ± 0.3 °C; *tert*-butylbenzene, bp 169.2 ± 0.5 °C; and diethyl oxalate, bp 185.8 ± 0.3 °C. For analysis, the ampoules were opened and their contents were transferred to Pyrex NMR tubes, which were examined by ^{1}H NMR spectroscopy (600 MHz with the aid of a resolution-enhancing Gaussian function set to 0.4 and line-broadening to −1.0). Two sets of signals were used to determine relative concentrations: method A: 2.30, 2.27, and 2.29 ppm; method B: 2.30, 5.46, 5.38, 5.44, and 5.36 ppm (see Figure 2). Following analysis, the samples were transferred to soft-glass (lead-potash) ampoules, sealed under a vacuum, and returned to the heating bath. The unrefined data are given in Table S3 of the Supporting Information.

6,8-Dimethyl-3,4-dihydro-2*H*-naphthalen-1-one. This compound was prepared as a mixture with the 5,8-dimethyl isomer following the procedure of Jung and Koreeda for *p*-xylene, but employing *m*-xylene instead.[28] The pure compound (not obtained by Jung and Koreeda) was obtained by preparative gas chromatography (2.7 m × 6 mm column of 20% Carbowax 20M on Anakrom AS (50−60 mesh) at 180 °C) (0.43 g from 4.0 g of γ-butyrolactone and 40 mL of *m*-xylene): ^{1}H NMR 2.06 (quin, J = 6.74 Hz, 2H), 2.32 (s, 3H), 2.62 (m, 5H), 2.91 (t, J = 6.15 Hz, 2H), 6.90 (s, 1H), 6.91 (s, 1H); ^{13}C NMR 21.4, 23.0, 23.2, 31.0, 41.0, 127.3, 128.8, 131.4, 141.6, 142.8, 145.8, 199.9.

6,8-Dimethyl-1-methylene-1,2,3,4-tetrahydronaphthalene 13. A solution of 1.25 g of dimethyltitanocene in 6 mL of toluene was added to 250 mg of 6,8-dimethyl-3,4-dihydro-2*H*-naphthalen-1-one in 2 mL of toluene. The reaction mixture was stirred for 60 h at 60 °C under argon, cooled, diluted with 5 mL of pentane, and filtered though a pad of alumina. The resulting pentane/toluene solution was concentrated to 100 mg of an oil, which was separated into three fractions by GC (1.7 m × 6 mm column of 5% OV-225 on 50−60 mesh Anakrom ABS at 97 °C): 6.3−10.3 min, compound **13**; 10.3−15 min, a mixture; and 15−20 min, 1,2-dihydro-4,5,7-trimethylnaphthalene. (A solution obtained by extraction of the alumina pad with ether was concentrated to give 121 mg of starting ketone, determined by ^{1}H NMR.) 6,8-Dimethyl-1-methylene-1,2,3,4-tetrahydronaphthalene **13** : ^{1}H NMR 1.86 (quin, J = 6.44 Hz, 2H), 2.27 (s, 3H), 2.43 (s, 3H), 2.47 (t, J = 6.74 Hz, 2H), 2.72 (t, J = 6.74 Hz, 2H), 5.07 (s, 1H), 5.23 (d, J = 1.46 Hz, 1H), 6.80 (s, 1H), 6.90 (s, 1H); ^{13}C NMR 20.9, 21.0, 23.9, 30.2, 34.1, 113.3, 126.6, 129.9, 133.7, 134.8, 136.0, 139.1, 143.5. When this sample was allowed to stand for 48 h at room temperature, the spectrum had changed to that of 1,2-dihydro-4,5,7-trimethylnaphthalene:[29] ^{1}H NMR 2.09 (m, 2H), 2.22, (d, J = 1.46 Hz, 3H), 2.30 (s, 3H), 2.47 (s, 3H), 2.64 (t, J = 7.45 Hz, 2H), 5.96 (t, J = 4.50 Hz, 1H), 6.87 (s, 1H), 6.89 (s, 1H).

6,8-Dimethyl-1-dideuteriomethylene-1,2,3,4-tetrahydronaphthalene (13-$_{1,1}$-d_2). This dideuterium isotopomer was prepared as described above for **13**: ^{1}H NMR 1.68 (tt, J = 6.66, 6.74, 6.48 Hz, 2H), 2.14 (s, 3H), 2.34 (t, J = 6.70 Hz, 2H), 2.40 (s, 3H), 2.57 (t, J = 6.55 Hz, 2H), 6.68 (s, 1H), 6.81 (s, 1H).

Heating 6,8-Dimethyl-1-dideuteriomethylene-1,2,3,4-tetrahydronaphthalene 13-$_{1,1}$-d_2. A solution of 2.3 mg of the hydrocarbon in 40 mL of benzene-d_6 was split into two portions, each of which was placed in a soft glass (lead-potash) tube, subjected to three freeze−evacuate−thaw cycles, and sealed under a vacuum. Immediately prior to insertion into a bath of the vapors of diphenyl ether boiling under reflux (258.4 ± 0.2 °C) to be heated for 24 and 90 h, respectively, the tubes were warmed for 1.5 min at 185 °C (vapors above boiling diethyl oxalate). The contents of a cooled tube were transferred to an NMR tube, diluted with 0.66 mL of benzene-d_6, and analyzed by methods A (the signals of the three methyl group) and B (CH_3 and methylenes CHD and CH_2) (see Figure 4). The contents of the 90-h tube were transferred to a soft-glass tube, concentrated by a slow stream of natural gas, and prepared for heating an additional 90 h as described above. The resulting data are given in Table S4.

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Supporting Information Available: Four tables of kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) Jung, K.-Y.; Koreeda, M. *J. Org. Chem.* **1989**, *54*, 5667−5675.
(29) Heimgartner, H.; Zsindely, J.; Hansen, H. J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 2924−2945.