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Variable Transition State Structure in 3,3-Sigmatropic Shifts from α-Secondary Deuterium Isotope Effects

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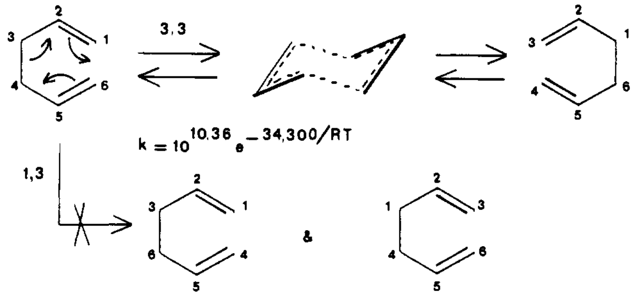
Abstract: The relative values of secondary α deuterium kinetic isotopic effects at the terminal and central carbons of 1,5-dienes undergoing the 3,3-shifts vary as a function of substitution. With radical stabilizing groups on C_3, the transition state more resembles two weakly coupled allyl radicals. With radical stabilizing substituents at C_2 and C_5, the transition state more resembles cyclohexane-1,4-diyl. A thermochemical argument renders unlikely cyclohexane-1,4-diyl as an intermediate in the 3,3 shift of 1,5-hexadiene. Comparison of the KIEs at C_4 and C_6 in the rearrangement of 3-oxa-1,5-hexadiene (allyl vinyl ether to 4-pentenal) to appropriate equilibrium isotope effects reveals that the transition state "comes early" with more bond breaking than making. The transition state structures for many 3,3 shifts are discussed in terms of the relative stabilities of the two nonconcerted alternatives arising from either complete bond breaking or complete bond making.

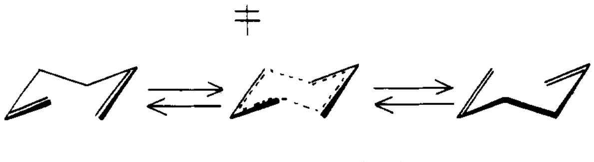
Introduction

The double allylic rearrangement of 1,5-hexadienes discovered by Hurd[1a] and by Cope[1b] is a facile thermal reaction which is accompanied by a single allylic rearrangement only when the terminal carbons cannot strongly interact.[2]

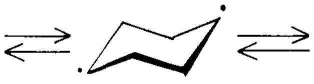


$k = 10^{10.36}e^{-34,300/RT}$

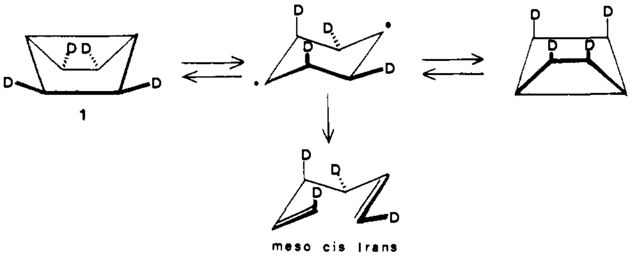
Early speculation on the mechanism of the rearrangement of 1,5-hexadiene focused on a concerted process whose transition state involved C_1–C_6 bond formation assisting C_3–C_4 bond cleavage.[1e] Doering and Roth provided evidence for a four center, "chair", transition state,[3] and, though a "twist" or "helix" arrangement could also rationalize the data,[4] an asymmetry transfer experiment by Hill rejects all but the chair arrangement of atoms in the lowest energy pathway for the reaction.[5] Doering subsequently determined the activation parameters for the reaction in 1,5-hexadiene itself (log k = 10.36 − 34 300/2.3RT) and raised the specter of a nonconcerted two-step pathway via cyclohexane-1,4-diyl whose estimated heat of formation is near that for the transition state of the Cope rearrangement.[6] The stereochemical observations could then be rationalized in terms of favored formation and decomposition of a chair-like diyl. The chair diyl also appears to be involved in the thermolysis of bicyclo[2.2.0]hexane, **1**, which undergoes cleavage to 1,5-hexadiene with high stereospecificity and bridgehead double inversion,[7] although Goldstein indicates that both bridgehead double inversion and cleavage could be separate concerted processes.



or



intermediate



In support of the diyl hypothesis of the 3,3 shift is Dewar's observation that 2-phenyl and 2,5-diphenyl-1,5-hexadiene rearrange 69 and 4900 times faster, respectively, than the parent indicating some radical character at C_2 and C_5 in the transition state.[8] Wehrli and Schmidt made similar observations with 2,5-dicyano-1,5-hexadiene, and since activation free energies for the dicyano materials were (somewhat) lower than for the diphenyl materials, the suggestion was made that the diyl is more favorable in the dicyano case.[9] Wehrli and Schmidt also recognized that the Cope rearrangement transition state structure could be dependent on substitution, a point that is the major focus of this paper.

In addition to the experimental work with the phenylhexadienes, Dewar found that the MINDO/3 calculated energy surface for the rearrangement of the parent diene puts the diyl (with significant distortions of the C_2- and C_5-bond angles) in a potential energy well 5–15 kcal/mol deep relative to an unsymmetrical transition state linking it to 1,5-hexadiene.[10] Moreover, the transition state is "displaced to a remarkable

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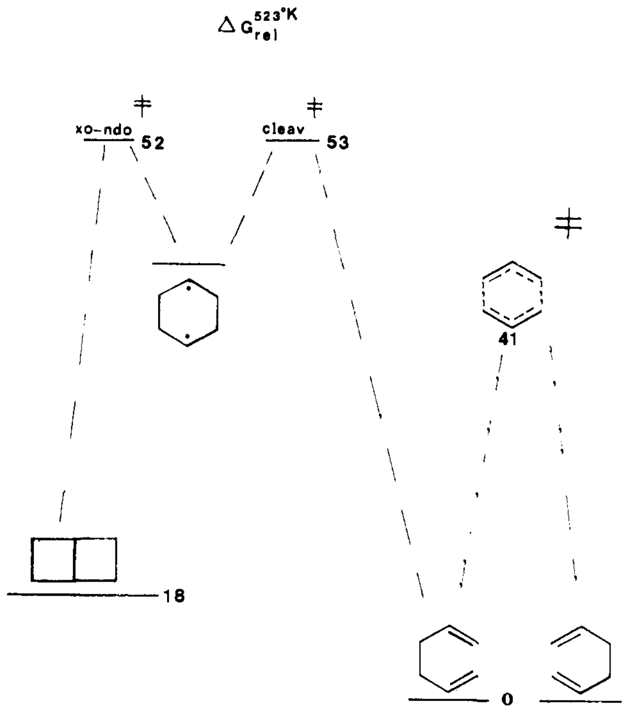
Scheme I



extent toward . . . 1,5-hexadiene", i.e., the C_1-C_6 bond distance is 1.90 Å and the C_3-C_4 bond distance is 1.56 Å. McIver has calculated a similar energy surface using the MINDO/2 approximation, with the exception that the diyl resides in only a 2 kcal/mol potential well.[11] Furthermore, McIver's rules for transition state structures rule out the symmetrical, delocalized species as a transition state.[12]

It is important to recall Goldstein's data on the rearrangements of **1**[7b] and recognize that, if the chair diyl is involved in the cleavage and bridgehead double inversion of **1**, as even the MINDO calculations indicate,[10,11] then from thermochemical estimates of the relative stabilities of **1** and 1,5-hexadiene the chair diyl is energetically inaccessible in the low energy, chair-like 3,3 shift.[13] The energy surface is shown in Scheme I.

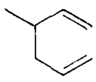
The thermochemistry therefore indicates that chair cyclohexane-1,4-diyl, regardless of its stability, is insulated from the low energy 3,3-shift energy surface by a kinetic barrier 12 kcal/mol above the actual transition state, which, by elimination, is that for the single stage concerted route.

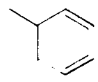
It is conceivable that the symmetrical delocalized species is not a transition state in the 3,3 shift but an intermediate. This represents a unique situation in thermal reactions which has not yet been addressed.

If the diyl is not involved in the 3,3 shift then to what must be attributed the rate enhancements by cyano and phenyl substitution at C_2 and C_5? This question has a companion question: why are there substantial rate accelerations with cyano and phenyl substitution at C_3 and C_4?[14] The latter question clearly cannot be answered by the diyl species, but both questions yield an answer upon examination of secondary deuterium isotope effects on bond breaking and bond making in the 3,3 shift of C_3 and C_4 substituted as well as C_2 and C_5 substituted 1,5-hexadienes. That is, the transition state structure changes in response to substituents presenting a moving target which can be felled only by rate studies with innocuous substitution.

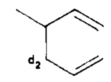
Results

Synthesis and Pyrolysis of 3-Methyl-1,5-hexadienes. 3-Methyl-1,5-hexadiene, **2**, and 1,1,6,6-tetradeuterio-3-methyl-1,5-hexadiene, **2**-d_4, were prepared by pyrolysis of the bisamine oxide resulting from conversion of 3-methyladipic acid to its bisdimethylamide followed by LAH or LAD reduction and oxidation. **2**-d_4 had 86.6% tetra- and 13.2% trideuteration at the 1 and 6 positions (assuming only d_4 and d_3 species to be present). 4,4-Dideuterio- and 6,6-dideuterio-3-methyl-1,5-hexadiene, **2**-$4d_2$ and **2**-$6d_2$, were prepared from

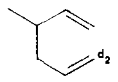

2



2-d_4



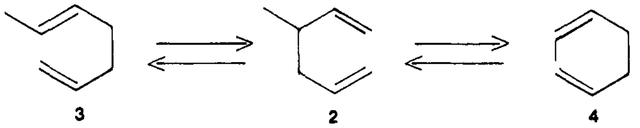
2-$4d_2$



2-$6d_2$

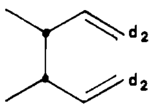
methyl 3-methyl-4-pentenoate which was obtained via an Ireland-Cope rearrangement of the enol silyl ether of 2-butenyl acetate.[15a] A Wittig reaction was used to introduce C_6 with or without deuteriums by using either undeuterated 3-methyl-4-pentenal or 2,2-dideuterio-3-methyl-4-pentenal obtained from LAH reduction of the ester followed by chromium trioxide-pyridine oxidation. **2**-$6d_2$ had 80.2% di- and 19.8% monodeuteration at the 6 position, while NMR analysis of **2**-$4d_2$ revealed 99% di- and 1% monodeuteration at the 4 position (assuming only d_2 and d_1 species present).

Thermolysis of **2** in the gas phase at 248 °C gave *trans*-1,5-heptadiene, **3**, and *cis*-1,5-heptadiene, **4**, in agreement with

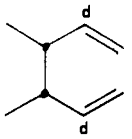


Frey and Solly.[15b] The rate and equilibrium constants, obtained by a Simplex[16] fit to the equations of Frey and Solly (see Appendix B), are shown in Table I along with the isotope effects.

Synthesis and Pyrolysis of *meso*-3,4-Dimethyl-1,5-hexadienes. *meso*-3,4-Dimethyladipic acid was prepared by the method of Casadevall et al.[17] from *cis*-1,2,5,6-tetrahydrophthalic anhydride. The diacid was converted to *meso*-3,4-dimethyl- (**5**), *meso*-1,1,6,6-tetradeuterio-3,4-dimethyl- (**5**-d_4), and *meso*-2,5-dideuterio-3,4-dimethyl-1,5-hexadiene (**5**-d_2) by the amine oxide pyrolysis route. **5**-d_4 showed 91.6%



5-d_4

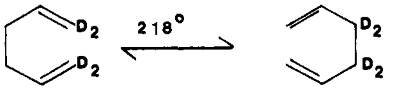


5-d_2

tetra- and 8.4% trideuteration at the 1 and 6 positions, while **5**-d_2 showed 89.0% di- and 11.0% monodeuteration at the 2 and 5 positions.

Pyrolysis of **5** at 218 °C in the gas phase gave *cis,trans*-2,6-octadiene in agreement with Doering and Roth.[3] The rate constants, obtained by the method of least-squares, and the isotope effects are shown in Table II.

1,1,6,6-Tetradeuterio-1,5-hexadiene was prepared by the method of Humski et al.[18] and showed 93.8% tetra- and 6.2% trideuteration at the 1 and 6 positions. Pyrolysis in the gas phase at 218 °C for 14 days gave an equilibrium mixture of 1,1,6,6- and 3,3,4,4-tetradeuterio-1,5-hexadiene, K_{eq} = 1.21 ± 0.03 as determined by HR-220 NMR integrations.



$K = 1.21 \pm 0.03$

Synthesis and Pyrolysis of 3-Methyl-2-phenyl-1,5-hexadienes. 3-Methyl-2-phenyl-1,5-hexadiene, **6**, 4,4-dideuterio-

Table I. Rate[a] and Equilibrium Constants and Isotope Effects[b] for the Thermal Isomerization of **2**, **2**-d_4, **2**-$4d_2$, and **2**-$6d_2$

$$3 \underset{k_2}{\overset{k_1}{\leftrightarrows}} 2 \underset{k_4}{\overset{k_3}{\rightleftarrows}} 4$$

diene	temp, °C	k_1	k_2	k_3	k_4	$K(3/2)$[c]	$K(4/2)$[c]
2[e]	248.6	18.33 ± 0.22[d]	4.119 ± 0.073	4.331 ± 0.067	2.129 ± 0.043	4.418 ± 0.057	2.021 ± 0.026
2-d_4[e]		20.61 ± 0.20	3.858 ± 0.056	4.983 ± 0.057	2.001 ± 0.032	5.310 ± 0.060	2.475 ± 0.029
$k(H/D_4)$		0.885 ± 0.014	1.07 ± 0.025	0.865 ± 0.017	1.07 ± 0.027	0.827 ± 0.010	0.811 ± 0.014
2[e]	248.3	17.90 ± 0.23	4.104 ± 0.073	4.433 ± 0.064	2.128 ± 0.044	4.395 ± 0.054	2.098 ± 0.030
2-$6d_2$[f]		18.75 ± 0.21	3.789 ± 0.063	4.659 ± 0.059	1.984 ± 0.042	4.881 ± 0.060	2.316 ± 0.039
$k(H/D_2)$		0.951 ± 0.017	1.092 ± 0.027	0.946 ± 0.020	1.081 ± 0.032	0.889 ± 0.019	0.896 ± 0.025
2-$4d_2$[f]		17.37 ± 0.23	4.298 ± 0.080	4.302 ± 0.064	2.262 ± 0.046	4.096 ± 0.054	1.931 ± 0.028
$k(H/D_2)$		1.030 ± 0.019	0.955 ± 0.027	1.030 ± 0.021	0.941 ± 0.031	1.073 ± 0.019	1.086 ± 0.022

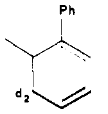
[a] All rate constants × 10^5 s. [b] Corrected to 100% deuteration. [c] Obtained from equilibrium runs. [d] Errors are standard deviations (see text). [e] See Appendix Table A-1 for raw data. [f] See Appendix A-2 for raw data.

Table II. Rates Constants and Isotope Effects for Thermal Isomerization of *meso*-3,4-Dimethyl-1,5-hexadienes

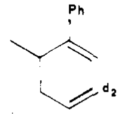
1,5-diene	temp, °C	$k \times 10^5$ s	
5[c]	218.1	5.327 ± 0.025[a]	$k(H/D_4)^b = 0.881 \pm 0.009$
5-d_4[c]		6.023 ± 0.020	
5[d]	228.2	11.52 ± 0.03	$k(H/D_2) = 1.015 \pm 0.004$
5-d_2[d]		11.36 ± 0.03	

[a] Errors are standard deviations. [b] Corrected to 100% deuteration. [c] See Appendix Table A-3 for raw data. [d] See Appendix Table A-4 for raw data.

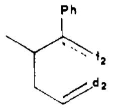
and 6,6-dideuterio-3-methyl-2-phenyl-1,5-hexadiene, **6**-$4d_2$ and **6**-$6d_2$, were prepared from methyl 3-methyl-4-phenyl-4-pentenoate. Thus, the silyl ether of benzaldehyde cyanohydrin was treated with LAD and reacted with methyl crotonate to give the Michael adduct. Decyanotrimethylsilylation with silver nitrate and sodium fluoride in Me_2SO gave methyl 3-phenacylbutyrate which was subjected to a Wittig condensation with methylenetriphenylphosphorane to give methyl 3-methyl-4-phenyl-4-pentenoate. The spectral properties of **6** were in agreement with those published by Marvell.[19] NMR analysis of **6**-$6d_2$ revealed 86.0% di- and 14.0% monodeuteration at the 6 position, while **6**-$4d_2$ showed 87.0% di- and 13.0% monodeuteration at the 4 position.



6-$4d_2$



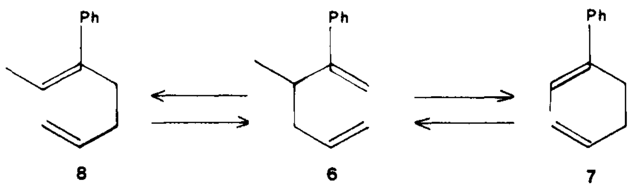
6-$6d_2$



6-d_4

1,1,6,6-Tetradeuterio-3-methyl-2-phenyl-1,5-hexadiene, **6**-d_4, was prepared from 2-phenyl-3-methyladipic acid by using the amine oxide pyrolysis route. NMR analysis revealed 93.0% tetra- and 7.0% trideuteration at the 1 and 6 positions.

Pyrolysis of **6** in sealed ampules in the gas phase at 245 °C gave a mixture of starting material, (*E*)-5-phenyl-1,5-heptadiene, **7** (major product), and (*Z*)-5-phenyl-1,5-hexadiene, **8** (minor product).

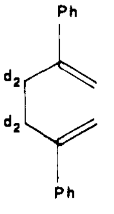


8 **6** **7**

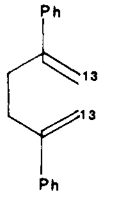
The NMR spectrum of **7** had a methyl signal at δ 1.77 and the C_6-vinyl proton appeared at δ 5.61–5.82, while the corresponding signals for **8** appeared at δ 1.07 and 5.46. The assigned stereochemistry is in agreement with predictions based upon the chemical shifts in α-methyl-β-benzylstyrenes.[20]

The rate and equilibrium constants, obtained by the method used for **2** along with the isotope effects, are presented in Table III.

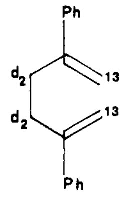
Synthesis and Pyrolysis of 2,5-Diphenyl-1,5-hexadienes. 3,3,4,4-Tetradeuterio-2,5-diphenyl-1,5-hexadiene, **9**-d_4, was prepared by the method of Dewar and Wade by Wittig olefination of 1,1,2,2-tetradeuteriodibenzoylethane.[8] [6,6-$^{13}C_2$]- and 3,3,4,4-tetradeuterio[6,6-$^{13}C_2$]-2,5-diphenyl-1,5-hexadiene, **9**-$^{13}C_2$ and **9**-$^{13}C_2$-d_4, were prepared in a similar fashion.



9-d_4



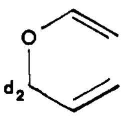
9-$^{13}C_2$



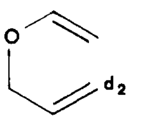
9-$^{13}C_2$-d_4

The approach to equilibrium of these compounds at 55.5 °C was followed by NMR and rate constants were obtained by a least-squares fit to $\ln (A - A_e)/(A_0 - A_e) = kt$ and by a simplex fit to the concentration curves. Since slightly different values were obtained by each method, the results were averaged. The averaged rate constants and isotope effects are presented in Table IV.

Synthesis and Pyrolysis of Allyl Vinyl Ethers. Allyl vinyl ether, **10**, was prepared by mercuric acetate catalyzed transetherification of allyl alcohol by using *n*-octyl vinyl ether.[21] 1,1-Dideuterioallyl alcohol was prepared by the method of Schuetz and Millard,[22] while 3,3-dideuterioallyl alcohol was synthesized by the method of McMichael.[23] 4,4-Dideuterioallyl vinyl ether, **10**-$4d_2$, showed 87.7% di- and 12.3% monodeuteration at the 4 position, while 6,6-dideuterio and allyl vinyl ether, **10**-$6d_2$, showed 95.5% di- and 2.5% monodeuteration at the 6 position.



10–$4d_2$



10 — $6d_2$

Pyrolysis of **10** in the gas phase at 160 °C gave 4-pentenal as the only product in agreement with Schuler and Murphy.[24] The rate constants, obtained by the method of least squares, and isotope effects are presented in Table V.

Table III. Rate[a] and Equilibrium[b] Constants and Isotope[c] Effects for the Thermal Isomerization of **6**, **6**-d_4, **6**-$6d_2$, and **6**-$4d_2$ at 174.6 ± 0.1 °C[f]

$$\mathbf{8} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathbf{6} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} \mathbf{7}$$

diene	k_1	k_2[e]	k_3	k_4	$K(\mathbf{8}/\mathbf{6})$[e]	$K(\mathbf{7}/\mathbf{6})$
6	7.609 ± 0.043[d]	1.567 ± 0.022	69.03 ± 0.10	11.90 ± 0.156	4.856 ± 0.074	5.801 ± 0.077
6-d_4	8.937 ± 0.052	1.360 ± 0.019	88.99 ± 0.15	10.97 ± 0.14	6.571 ± 0.101	8.112 ± 0.107
$k(H/D_4)$	0.847 ± 0.007	1.155 ± 0.023	0.772 ± 0.002	1.09 ± 0.020	1.353 ± 0.016	0.715 ± 0.013
6-$6d_2$	8.424 ± 0.061	1.703 ± 0.022	75.75 ± 0.16	11.99 ± 0.16	4.947 ± 0.082	6.318 ± 0.085
$k(H/D_2)$	0.897 ± 0.008	0.914 ± 0.019	0.905 ± 0.003	0.992 ± 0.019	1.02 ± 0.022	0.918 ± 0.017
6-$4d_2$	7.400 ± 0.058	1.726 ± 0.026	66.62 ± 0.25	13.16 ± 0.18	4.287 ± 0.017	5.062 ± 0.071
$k(H/D_2)$	1.030 ± 0.010	0.903 ± 0.019	1.039 ± 0.004	0.898 ± 0.017	1.133 ± 0.026	1.146 ± 0.024

[a] All rate constants × 10^6 s. [b] Obtained from rate constants. [c] Corrected to 100% deuteration. [d] Errors are standard deviations. [e] The error analysis for these values is probably underestimated. [f] See Appendix Table A-5 for raw data.

Table IV. Rate[a] and Equilibrium Constants and Isotope Effects[b] for Thermal Isomerization of **9**-d_4, **9**-$^{13}C_2$, and **9**-^{13}C-d_4 at 55.5 ± 0.01 °C

$$\mathbf{9}\text{-}3,3,4,4\text{-}d_4 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathbf{9}\text{-}1,1,6,6\text{-}d_4$$

diene	k_1[c]	k_2	K
9-d_4[d]	1.276 ± 0.014	2.176 ± 0.026	0.586 ± 0.010
9-$^{13}C_2$[e]	1.363 ± 0.025	1.363 ± 0.025	1.000 ± 0.022
9-$^{13}C_2$-d_4[f]	1.272 ± 0.016	2.142 ± 0.027	0.594 ± 0.011
k^{11}/k^{D_4}	1.07 ± 0.024	0.636 ± 0.014	0.586 ± 0.010
k^{12}/k^{13}	1.003 ± 0.017	1.017 ± 0.018	0.987 ± 0.028

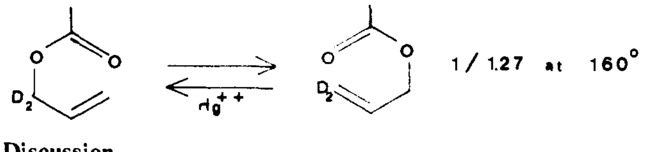
[a] All rate constants are × 10^6 s and were obtained by averaging the least-squares and Simplex results. [b] Corrected to 100% labeling. [c] Errors are standard deviations. [d] See Appendix Table A-6 for raw data. [e] See Appendix Table A-7 for raw data. [f] See Appendix Table A-8 for raw data.

Table V. Rate Constants[a] and Isotope Effects[b] for Thermal Rearrangement of **10**, **10**-$4d_2$, and **10**-$6d_2$ at 160.3 ± 0.1 °C[d]

diene	$k \times 10^5$ s	$k(H/D_2)$
10	1.988 ± 0.007[c]	
10-$4d_2$	1.822 ± 0.006	1.092 ± 0.005
10-$6d_2$	2.032 ± 0.006	0.976 ± 0.005

[a] From least-squares line. [b] Corrected to 100% deuteration. [c] Errors are standard deviations. [d] See Appendix Table A-9 for raw data.

Synthesis and Equilibration of Dideuterioallyl Acetates. 1,1-Dideuterio- and 3,3-dideuterioallyl acetate were prepared by the method of Schuetz and Millard.[22] and NMR analysis revealed greater than 98% dideuteration for the 1,1 isomer and 87% dideuteration for the 3,3 isomer. Separate pyrolysis of each isomer for 17 days at 160 °C in the presence of mercuric acetate gave an average equilibrium isotope effect of 1.27 ± 0.03.



Discussion

Origins of Isotope Effects. Discussions on the origins of isotope effects center on vibrational frequency differences between initial and final states of isotopically labeled molecules where the final state may be a stable entity or a transition state.[25] The Bigeleisen equation for isotope effects may be written in general form as:

$$K_1/K_2 = \text{MMI*EXC*ZPE}$$

where MMI is the contribution due to the ratio of ratios of translational and rotational partion functions between the two isotopic species in the initial and final states, EXC is the effect due to vibrational levels above the zeroth being populated, and ZPE is the contribution due to zero point energy differences between initial and final states. For rate effects, the reaction coordinate motion, ν_{1L}/ν_{2L}, may be factored from the MMI term leaving a term VP‡ which is the ratio of ratios of all vibrational frequencies between two isotopic molecules in initial and transition states.

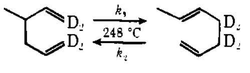
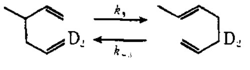
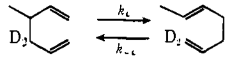
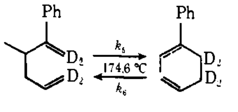
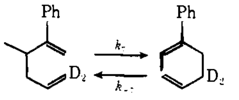
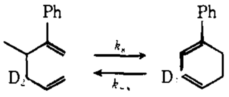
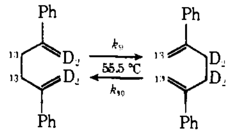
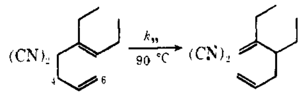
$$k_1/k_2 = \nu_{1L}/\nu_{2L}\text{VP}^\ddagger\text{*EXC}^\ddagger\text{*ZPE}^\ddagger$$

For most reactions, even those at 200–300 °C, the ZPE‡ term is the major contribution to α-secondary deuterium kinetic isotope effects unless the deuteriums become involved in a reaction coordinate motion[25,26] like twisting of CD_2 vs. CH_2.[27] For the 3,3 shift, molecular models suggest that a little twisting of the methylene groups is necessary, and so changes in the force field perpendicular to the reaction coordinate dominate the KIE. These force field changes result primarily from changes in the number of ligands attached to the reacting carbon and the electronegativity of groups attached to that carbon.[25] Substituents or atoms β to the reacting carbon are usually assumed to have relatively little effect except where hyperconjugation is important.[25] Judging by the values of the KIEs listed in Table VI, this is the case (see next section).

Bond Making and Bond Breaking KIEs. In sigmatropic shifts where one σ bond is broken and a new σ bond is made, the secondary kinetic deuterium isotope effects on each bond change should be independent and would be expected to relate to the extent of bond breaking and bond making, respectively, as demanded by the rate-determining transition state. In a degenerate sigmatropic rearrangement of order $[i,j]$, it is reasonable to assume that the transition state or composite of unsymmetrical transition states either has or has on the average equivalent partial bonds between the ith component and jth component.[28] These partial bonds need not be half-bonds but may have any bond order between 0 and 1. For instance, the low energy transition state in the Cope rearrangement may in the extreme resemble either two allyl radicals or cyclohexane-1,4-diyl, both, of course, in the chair rearrangement of carbons.

In such degenerate rearrangements, the KIE resulting from deuterium substitution on the bond breaking sites, BBKIE, and that resulting from deuterium substitution on the bond making sites, BMKIE, are related by an equilibrium isotope effect, EIE, which may be determined simply by equilibrating the two substrates. For the 3,3 shift a determination of the EIE is straightforward requiring only a determination of the equilibrium constant between 1,1,6,6- and 3,3,4,4-tetradeuterio-1,5-hexadiene. However, measurement of the forward and reverse rate constants for the parent 1,5-hexadiene in order to

Table VI. Summary of KIEs for Various 3,3 Shifts

		BMKIE	BBKIE	$\frac{\text{BMKIE} - 1.0}{\text{BBKIE} - 1.0}$
	$k_1^{D_4}/k_1^H$ $k_2^H/k_2^{D_4}$	1.129 ± 0.018	1.07 ± 0.025	1.85 ± 1.0
	$k_3^{D_2}/k_3^H$ $k_{-3}^H/k_{-3}^{D_2}$	1.052 ± 0.019	1.09 ± 0.027[b]	1.71 ± 1.1
	$k_4^H/k_4^{D_2}$ $k_{-4}^{D_2}/k_{-4}^H$	1.047 ± 0.003	1.03 ± 0.019	
	$k_5^{D_4}/k_5^H$ $k_6^H/k_6^{D_4}$	1.295 ± 0.003	1.09 ± 0.02	3.3 ± 0.9
	$k_7^{D_2}/k_7^H$ $k_{-7}^H/k_{-7}^{D_2}$	1.105 ± 0.004	0.992 ± 0.019[b]	2.7 ± 0.4[c]
	$k_8^H/k_8^{D_2}$ $k_{-8}^{D_2}/k_{-8}^H$	1.11 ± 0.02	1.039 ± 0.004	
	$k_9^{D_4}/k_9^H$ $k_{10}^H/k_{10}^{D_4}$	1.57 ± 0.035	1.07 ± 0.024	8.1 ± 2.0
	$k_{11}^{4\text{-}D_2}/k_{11}^H$ $k_{11}^H/k_{11}^{6\text{-}D_2}$	1.06 ± 0.02	1.19 ± 0.02	0.31 ± 0.1

[a] Determined from k_3 and k_4. [b] See discussions for source of errors in these two cases. [c] Determined from k_7 and k_8.

determine the KIEs requires addition of an innocuous label that would also allow rate constants to be measured with high accuracy. Since this is difficult to achieve, the 3-methyl-1,5-hexadiene and 3-methyl-2-phenyl-1,5-hexadiene interconversions with their respective 3,3-shift isomers were chosen for study. In these reactions, the equilibrium constants do not dramatically favor products so that the transition state or average of transition states should be nearly symmetrical. Thus, a determination of the BBKIE and the BMKIE is possible with a single deuterated substrate in each case, i.e., **2**-d_4 and **6**-d_4. In effect, the response of one bond to cleavage and recombination is being studied with a single deuterated substrate. Concern that the transition state might not be symmetrical prompted examination of the BMKIE and BBKIE in one direction with different dideuterated isomers of starting material and these reveal the same trend (Table VI). This trend is that the isotope effect on bond making in the nearly unperturbed parent case, **2**, is 1.8 ± 1.0 times that of the bond breaking effect when both are expressed as a percent increase or decrease relative to the protio material (i.e., (BMKIE − 1.0)/(BBKIE − 1.0); see Table VI). With 2-phenyl substitution, this BMKIE − 1.0 is 3.3 ± 1.0 times that of the BBKIE. In the 2,5-diphenyl case, the BMKIE − 1.0 is 8.1 ± 2.0 times the BBKIE. By comparison, the BMKIE − 1.0 in an irreversible 3,3 shift of a 3,3-dicyano-1,5-hexadiene is only 0.31 ± 0.1 times that of the BBKIE − 1.0.[18] Thus, the relative KIEs in the 3,3 shift vary over a large range as a function of substitution.

Before discussing the origin of the variation in relative KIEs, it should be noted that there is but a small KIE with deuteria at C_2 and C_5 in the 3,3 shift of *meso*-3,4-dimethyl-1,5-hexadiene. This is not unexpected in view of no bonding change at C_2 and C_5 in the reaction.[25,26] It also indicates that significant movement of the hydrogens at C_2 and C_5, as calculated by the MINDO-3 method,[10] cannot be a large contributor to the reaction coordinate motion or a large normal KIE should have been observed.

Secondary Deuterium KIEs in 3,3 Shifts: Experimental Errors. The rate constants found in the present study for isomerization of **2**, **5**, **9**, and **10** are in good agreement with those calculated from their activation parameters. The values for **6** disagree with those reported by Marvell who found only one rearrangement product.

In the present study, **6** was found to isomerize to both the *E* and *Z* isomers of 5-phenyl-1,5-heptadiene under conditions similar to those employed by Marvell.

The magnitudes of the errors in the determination of the rate constants are reflected by the standard deviations. For the isomerizations of **5** and **10**, the kinetic scheme is that for a simple first-order reaction and the error analysis is straightforward. In the case of **9**, the reaction is reversible first order, and the rate constants vary within 4% depending on the method of calculation. Therefore, the rate results were averaged.

The thermolyses of **2** and **6** follow a parallel reversible first-order kinetic scheme and the errors had to be approximated (see Appendix B). The largest rate constant, k_1, for isomerization of **2** is about nine times that of the smallest, k_4 (see Table I) and for **6** the largest (k_3) is 46 times the value of the smallest, k_2 (see Table II). Although the error analyses are favorable for all of the rate constants, the errors in the smaller rate constants are probably underestimated since large variations in the values of the smaller rate constants affect the calculated concentrations only to a small extent. Therefore, more confidence should be placed in the rate constants for isomerization to the major product from each starting material listed in Table VI.

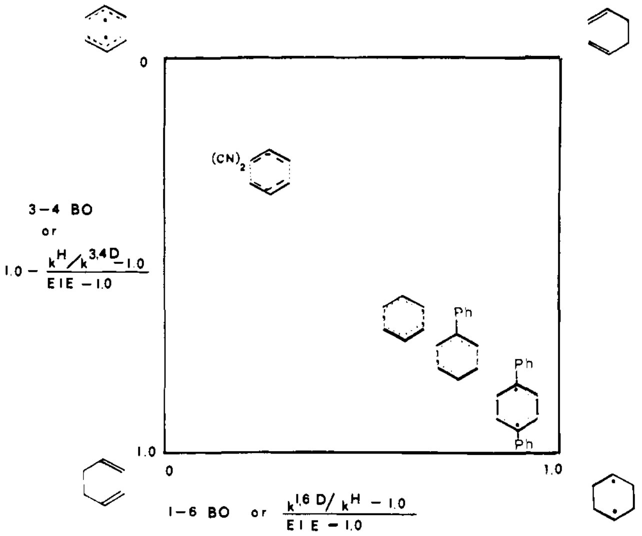
In examining the data of Table VI, an obvious inconsistency is the near equivalence of the BBKIE from **3**-d_2(k_{-3}) and that from **3**-d_4(k_{-2}); it might have been expected that the magnitude of the former would be the square root of the latter or 1.03. The reverse situation applies to the lack of a BBKIE with **7**-$d_2(k_{-7})$, where the value of the square root of the KIE on k_6 (1.044) might have been expected. In both of these cases, the rate constant being evaluated is that which converts product back to starting material, and its value is determined almost solely by the forward rate constant and the equilibrium constant since its magnitude affects the calculated concentrations only to a small extent. Given a small error in the equilibrium constant, the reverse rate constant suffers a large error. In the case of **3**-d_2, it is important to note that the equilibrium isotope effect from **2**-$6d_2$ is 1/1.125, and from **2**-$4d_2$ it is 1.073, and both values straddle the square root of the equilibrium IE from **2**-d_4 which is 1/1.10. Thus, the EIE in the dideuterio cases may be distorting the KIE from k_{-3} and k_{-4}. Therefore, focus should be placed primarily on the BMKIE on k_3 and the BBKIE on k_4 which are determined directly and primarily from the fit to the experimental data. And these KIEs are within experimental error of the square root of the BBKIE and BMKIE of **2**-d_4 as measured from k_1 and k_2. The same situation obtains with the EIE from **6**-$6d_2$ where the value observed is practically unity while the EIE from **6**-d_4 is 1/1.353. Clearly the EIE in this dideuterio case is in error and so the KIE on the reverse rate constant k_{-7} must be in error.

Variable Transition State Structure in Degenerate 3,3 Shifts. The large variation in the relative magnitudes of the BMKIE and the BBKIE in the 3,3 shift occurs in the direction expected on the basis of substituents altering the structure of the transition state.[29] If bond breaking between C_3 and C_4 is carried to its logical extreme with no bond making between C_1 and C_6, two allyl radicals result, which should recombine to give rearranged product; however, if only bond making between C_1 and C_6 occurs with no bond breaking between C_3 and C_4, cyclohexane-1,4-diyl results which should undergo cleavage to give rearranged product.[9] Radical stabilizing substituents on C_3 and C_4 should stabilize the former alternative more than the latter, and the transition state should more resemble the former. Radical stabilizing substituents on C_2 and C_5 should stabilize the diyl relative to two allyl radicals; thus, the transition state should more resemble the diyl. Indeed the relative KIEs are interpretable on this basis, the formal statement of which is due to Thornton who called this the "perpendicular" effect.[29]

To depict the range of transition state structures available to the 3,3 shift, a More O'Ferrall-Jencks diagram[30] is useful (Scheme II). The two structural coordinates lead to the two nonconcerted extremes—two allyl radicals or cyclohexane-1,4-diyl—but, rather than plotting bond distances or bond orders, the ratios of the α-secondary kinetic to the thermodynamic isotope effects at the reacting sites are used as structural coordinates. The reason for this is that neither bond distances nor bond orders in transition states have been measured, but to the extent that the KIEs result only from bonding changes at the reacting center and represent some fractional change in bonding relative to the complete change that the equilibrium IE represents, these structural coordinates are experimentally accessible and meaningful—certainly qualitatively if not quantitatively. However, since no established relationship between KIEs and bond order changes (although a linear variation is often used; see, however, ref 18),[25b,26] we prefer to use experimental rather than assumed quantities to locate transition state structures on the diagram. Thus, when a KIE-bond order relationship is found, a transformation of these results should be straightforward.

The data of Table VI allow placement of the all-carbon systems so far studied on the diagram provided that a single symmetrical transition state is involved. If the symmetrical delocalized species is an intermediate, then the average transition state is being located. That a bona fide cyclohexane-1,4-diyl is involved in the 3,3 shift is ruled out in the parent case on energetic grounds, but, in the 3,3 shift of 2,5-diphenyl-1,5-hexadiene rough estimates of the energetics suggest that the diyl may just barely be accessible, although the small but substantial BBKIE for this compound would then require rationalization on grounds other than bonding changes.

Scheme II



Comparison with Other Degenerate 3,3 Shifts. The diagram makes graphic the notion that stabilizing either of the two nonconcerted alternatives—that from either pure bond breaking or pure bond making—will draw the transition state in the direction of the stabilization.[29] In the case of the parent 1,5-hexadiene, the activation free energy for each of the nonconcerted alternatives at 523 K is available,[7b,13,31] and it is clear that the activation free energy for formation of two allyl radicals is 4 kcal/mol less stable than the transition state for formation of the diyl; therefore, the transition state for the relatively unperturbed all-carbon 3,3 shift resembles more the diyl than two allyl radicals. Radical stabilizing substituents at C_2 and C_5 further enhance the energy difference and alter the transition state accordingly.[32]

On the other hand, the diyl alternatives are destabilized by requisite "boat-like" transition states and by steric interference with strong terminal carbon interaction as with 4-vinylcyclohexene[33a] and semibullvalene[33b,c] (as well as other degenerate 3,3 shifts of the divinylcyclopropane type). In these cases, the transition state should more resemble the two-allyl-radical alternative. Indeed, boat-like 3,3 shifts have a smaller entropy demand than chair-like 3,3 shifts,[7b,34] and in the degenerate 3,3 shifts of 4-vinylcyclohexene, biradical formation competes favorably with the concerted reaction.[33a]

In a nearly degenerate 3,3 shift, Padwa has provided good evidence for the intermediacy of a cyclohexane-1,4-diyl in the pyrolysis of 3-methyl-3-allyl-1,2-diphenylcyclopropenes.[35] The observation of 5-methyl-1,2-diphenyltricyclo[2.2.0.0^{2,6}]hexane as a product was explained by formation of a chair diyl that may undergo cleavage to the 3,3 shift product or ring flip to the boat diyl. The boat diyl then undergoes radical recombination to form the tricyclohexane. The nonconcerted alternatives for this case are the aforementioned chair-diyl and allyl-cyclopropenyl radicals. The allyl radical alternative is destabilized since cyclopropenyl radical stabilization is small[36] and there is increase in strain brought about by an additional trigonal center in the cyclopropane ring (13 kcal/mol).[37] On the other hand, the diyl gains benzyl radical stabilization and relieves the strain of one trigonal center but has a slight increase in strain due to forming a five-membered ring (~5 kcal/mol). The net overall effect favors the diyl alternative by roughly 35 kcal/mol and, therefore, it is not surprising that the diyl with its very favorable stabilization is involved in the pyrolysis.

Finally, just why the strained potential [2.2.2]propellane-like and therefore two-allyl-radical-like degenerate 3,3 shift of 1,4-dimethylenecyclohexane has such a low preexponential term[38] is unclear, although even a little terminal methylene interaction may extract a large entropy price from the system. Here as in the simple boat-like 3,3 shift, it would be useful to determine the secondary KIEs on bond making and breaking.

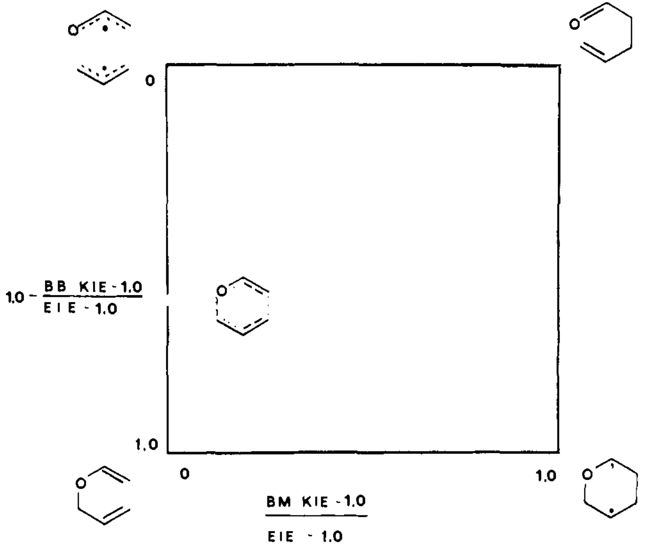
The Unsymmetrical 3,3 Shifts. In 1,5-diene systems having C_3 and C_4 as part of a strained ring like *cis*-1,2-divinylcyclopropane[39] and 5-*endo*-vinylbicyclo[2.2.2]octene,[40] the two-allyl-radical alternative is much more stable than the 1,4-diyl and so the transition states involve more bond breaking than bond making. In addition, these reactions are highly exothermic, and therefore the transition states should also come early.[29,41]

An important 3,3 shift is that of the conjugate base of *endo*-5-vinylbicyclo[2.2.2]octen-5-ol which rearranges roughly 10^{17} times faster than the parent alcohol.[40] Evans not only discovered the reaction but demonstrated that radicals adjacent to oxy anion are stabilized by ca. 20 kcal/mol.[42b] Therefore, in this case, the transition state for the 3,3 shift must resemble the two allyl radical alternative even more than the parent.

3,3 Shift of Allyl Vinyl Ether. The aliphatic Claisen rearrangement of allyl vinyl ether represents a 3,3 shift where the transition state is no longer symmetrical due to the presence of the heteroatom in the ring. The 3,3 shift of **10** has $\Delta H^{\ddagger}$ = 30.6 kcal/mol and $\Delta S^{\ddagger} = -7.7$ eu,[24] while for 1,5-hexadiene $\Delta H^{\ddagger}$ = 33.5 kcal/mol and $\Delta S^{\ddagger} = -13.8$ eu.[6] The difference in activation parameters suggests that the Claisen transition state is looser than that for the Cope rearrangement and that little energy benefit is derived from the developing carbonyl in the Claisen transition state despite an overall 17 kcal/mol exothermicity. Thus, the transition state should be "early".[29,41] This has been used to rationalize[43] the fact that the boat-chair transition state free energy difference for the Claisen rearrangement is only 3.0 kcal/mol[43] vs. 5.7 kcal/mol for the Cope rearrangement.[3] To correlate the thermochemical and stereochemical differences between the aliphatic Claisen and Cope rearrangements, the kinetic secondary deuterium isotope effects for the former were measured.

The normal KIE at the 4 position of allyl vinyl ether is roughly four times the inverse KIE at the 6 position (Table V). Thus, the transition state would seem to resemble that for 3,3-dicyano-1,5-hexadiene;[18] however, the equilibrium isotope effects at the 4 and 6 positions are quite different. The equilibrium isotope effect at the 6 position was determined from a plot of appropriate EIEs as a function of temperature[44] and found to be 1.16 at 160.0 °C. The EIE at the 4 position was found by pyrolysis of allyl-d_2 acetate in the presence of mercuric acetate [$K(D/H) = 1.27 \pm 0.03$]. Therefore, the bond making IE fraction is less than one-sixth, while the bond breaking IE fraction is roughly one-third. Thus, in the pyrolysis of **10**, the transition state is in the lower left quadrant of the More O'Ferrall-Jencks diagram and more resembles reactant in agreement with predictions from the Hammond postulate (Scheme III). The isotope effects do suggest, however, that the transition state resembles two allyl radicals much more than the diyl; that is, bond making has proceeded to less of an extent than bond breaking. Why this is so can be seen by a thermochemical analysis of the effect of oxygen on the nonconcerted alternatives. From group additivities and ground state energy differences, the oxygen lowers the relative free energy of formation of two allyl radicals by 9 kcal/mol, while the diyl is lowered by less than 3.5 kcal/mol.[31b] Thus, the transition state is drawn toward the two allyl radical alternative—relative to the all-carbon 3,3 shift.[32]

Scheme III



Finally, in the aromatic Claisen rearrangement McMichael has shown that at 185 °C the BBKIE at C_α is 1.18 ± 0.02, while the BMKIE at C_γ is 1/1.065.[45] At 185 °C the corresponding EIEs are 1.225 and 1/1.135[44] indicating that in the transition state 80% of the O–C_α bond is broken and 50% of the C_γ–C_{ortho} bond is made. Thus, the transition state comes late, as predicted by Hammond, and it involves more bond cleavage than bond making in accord with expectations that the diyl alternative is destabilized relative to the bond cleavage due to loss of benzene resonance energy.

Experimental Section

Syntheses. General. Nuclear magnetic resonance spectra were recorded on Varian EM-360, T-60, and HR-220 spectrometers with carbon tetrachloride or deuteriochloroform as solvent, and the chemical shifts are reported in δ values in parts per million downfield from internal tetramethylsilane. Infrared spectra were obtained with Perkin-Elmer Model 137 and 437 spectrometers. High resolution mass spectra were recorded on an AEI Model MS-9. Vapor phase chromatography (VPC) was performed on Varian Aerograph A90P-3 and Series 1220-2 instruments by using the indicated columns. Boiling and melting points are uncorrected. Reactions sensitive to air or moisture were carried out under a nitrogen atmosphere. Deuterium incorporations were determined by multiple NMR integrations at 220 MHz and were calculated by assuming only d_n and d_{n-1} materials were present.

3-Methyl-1,5-hexadiene (2). To 4.8 g (30 mmol) of 3-methyladipic acid was added dropwise 16.5 g (130 mmol) of oxalyl chloride. The solution was stirred at 25 °C for 23 h and then excess oxalyl chloride was removed in vacuo. The liquid residue was dissolved in dry ether and added dropwise to a solution of 6.8 g (150 mmol) of dimethylamine in 150 mL of dry ether at 0 °C. Following stirring at 0 °C overnight, the mixture was filtered, and the solvent was evaporated affording 6.0 g of a light yellow liquid. A 3.0-g portion of the liquid was dissolved in dry THF and added dropwise to 1.1 g (30 mmol) of lithium aluminum hydride in 40 mL of THF. Following heating at reflux for 20 h, the reaction mixture was quenched with saturated sodium sulfate solution; the solvent was evaporated affording 2.4 g of a light yellow liquid. The liquid was dissolved in 5 mL of methanol, and 6.4 g (56 mmol) of 30% hydrogen peroxide was added in four portions over a 4-h interval, and the mixture was stirred until a negative amine test was obtained. The excess peroxide was decomposed by stirring with a catalytic amount of 10% palladium on carbon; then the mixture was filtered and the solvent was evaporated leaving a viscous liquid. The liquid was heated to 170 °C at 1 Torr, and the pyrolysate was collected in a dry ice-acetone cooled receiver. The pyrolysate was washed with cold 5% hydrochloric acid, then with saturated sodium bicarbonate and sodium chloride solutions and then was cooled to −78 °C and transferred to a weighed receiver affording 0.60 g of a clear colorless liquid. The IR spectrum is in agreement with that published.[15] NMR (220 MHz, CCl_4) δ 0.99 (d, J = 7 Hz, 3 H), 1.95-2.40 (m, 3 H), 4.80-4.96 (m, 4 H), and 5.41-6.15 (m, 2 H).

1,1,6,6-Tetradeuterio-3-methyl-1,5-hexadiene (2-d_4) was prepared in a manner similar to that used for **2** except that lithium aluminum deuteride was the reducing agent. NMR analysis showed 86.8% tetra- and 13.2% trideuteration at the 1 and 6 positions: NMR (220 MHz, CCl_4) δ 0.98 (d, J = 7 Hz, 3 H), 1.86–2.30 (m, 3 H), and 5.61 (broad s, 2 H).

Methyl 2,2-Dideuterio-3-methyl-4-pentenoate. To a solution of sodium methoxide in 45 g of methanol-d_1, prepared by using a 4-mm cube of sodium metal, was added 3.6 g (28 mmol) of methyl 3-methyl-4-pentenoate;[46] the solution was stirred under reflux for 22 h. The yellow solution was poured into water and was extracted with pentane. The extracts were washed with water, saturated sodium bicarbonate, and sodium chloride solutions and were dried over magnesium sulfate. The product was isolated by distillation as described above giving 3.2 g (88%) of a colorless liquid, bp 137–138 °C. NMR analysis showed 98% di- and 2% monodeuteration at the 2 position. NMR (60 MHz, CCl_4) δ 1.07 (d, J = 7 Hz, 3 H), 2.45–2.87 (m, 1 H), 3.62 (s, 3 H), 4.80–5.18 (m, 2 H), and 5.49–6.11 (m, 1 H).

3-Methyl-4-pentenal. To a stirred suspension of 0.83 g (22 mmol) of lithium aluminum hydride in 50 mL of dry ether was added dropwise a solution of 2.80 g (21.8 mmol) of methyl 3-methyl-4-pentenoate in 5 mL of ether. Following stirring at 25 °C for 30 min, the reaction mixture was hydrolyzed with sodium sulfate solution. Distillation through a 15 × 1 cm packed column left 2.3 g of a colorless liquid. The liquid was added in one portion to a stirred mixture of 13.1 g (131 mmol) of chromium trioxide and 20.7 g (262 mmol) of dry pyridine in 330 mL of dry methylene chloride. Following stirring for 15 min, the mixture was filtered through neutral alumina over Florisil, and the filtrate was washed with 5% sodium hydroxide, 5% hydrochloric acid, saturated sodium bicarbonate, and sodium chloride solutions and was dried over magnesium sulfate. Distillation through a 30 × 1 cm packed column followed by simple distillation under nitrogen afforded 1.34 g (63%) of a colorless liquid, bp 117–118 °C. NMR (60 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 2.23–3.04 (m, 3 H), 4.77–5.21 (m, 2 H), 5.45–6.10 (m, 1 H), and 9.71 (t, J = 3 Hz, 1 H). IR (10% in CCl_4) 3080, 2810, 2715, 1720, 1640, 995, and 917 cm^{-1}. m/e^+ 98.0726 (calcd for C_6H_{10} 98.0732).

2,2-Dideuterio-3-methyl-4-pentenal. Reduction then oxidation of 3.1 g (23.8 mmol) of methyl 2,2-dideuterio-3-methyl-4-pentenoate by the above procedure gave 1.48 g of a colorless liquid, bp 117–118 °C. However, NMR analysis showed that partial deuterium exchange had occurred. The liquid was dissolved in 36 mL of pyridine-D_2O (1:1 v/v) and stirred under nitrogen for 3 days. After pouring into water and extracting with pentane, the extracts were washed with water and dried over magnesium sulfate. Isolation as described above gave 1.21 g of a colorless liquid, bp 117–118 °C, which under NMR analysis showed greater than 99% deuteration at the 2 position. NMR (60 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 2.51–2.90 (m, 1 H), 4.74–5.20 (m, 2 H), 5.45–6.10 (m, 1 H), and 9.70 (s, 1 H).

6,6-Dideuterio-3-methyl-1,5-hexadiene (2-$6d_2$). To a stirred suspension of 4.90 g (13.7 mmol) of triphenylphosphonium-*methyl*-d_3 bromide in 50 mL of dry ether was added 7.6 mL of a 1.8 M solution of *tert*-butyllithium in pentane, and the solution was stirred at 25 °C for 4 h. To the red solution was added in one portion a solution of 1.34 g of 3-methyl-4-pentenal in 10 mL of ether, and the thick mixture was stirred at 25 °C for 10 min. To the mixture was added 25 mL of D_2O, and the layers were separated. The aqueous layer was extracted with ether, and the extracts were dried over magnesium sulfate. The solution was concentrated to a volume of 20 mL by distillation through a packed column, and 30 mL of pentane was added. After repeating the distillation–dilution procedure twice, the triphenylphosphine oxide was filtered, and the filtrate was distilled until the vapor temperature reached 40 °C. Evaporative distillation gave 1.4 g of a colorless liquid that was purified by preparative VPC (5 ft × 0.25 in. 30% SE-30 on Chromosorb W). A total of 0.68 g (51%) of a colorless liquid was collected. NMR analysis revealed 80.2% di- and 19.8% monodeuteration at the 6 position. NMR (220 MHz, CCl_4) δ 0.97 (d, J = 7 Hz, 3 H), 1.88–2.26 (m, 3 H), 4.80–4.95 (m, 2 H), and 5.56–5.74 (m, 2 H).

4,4-Dideuterio-3-methyl-1,5-hexadiene (2-$4d_2$) was prepared in 34% yield by the procedure for preparation of **2-$6d_2$** by using methyl triphenylphosphonium bromide and 4,4-dideuterio-3-methyl-4-pentenal. NMR analysis revealed greater than 99% dideuteration at the 4 position. NMR (220 MHz, CCl_4) δ 0.97 (d, J = 7 Hz, 3 H), 2.06–2.23 (pentuplet, 1 H), 4.81–5.44 (m, 4 H), and 5.56–5.74 (m, 2 H).

***meso*-2,5-Dideuterio-3,4-dimethyl-1,5-hexadiene (5-d_2).** Dimethyl *meso*-3,4-dimethyladipate (4.1 g) was heated for 18 h in 49 g of deuteriomethanol containing 10 mmol of freshly prepared sodium methoxide. Workup gave 3.3 g of a yellow liquid that was saponified overnight in 50% aqueous methanol containing 176 mmol of potassium hydroxide affording 1.60 g of 2,2,5,5-tetradeuterio-*meso*-3,4-dimethyladipic acid, mp 128–130 °C (from ethyl acetate–hexane). Conversion of this diacid to **5-d_2** was accomplished by the amine oxide pyrolysis route above affording 0.42 g of a colorless liquid. Analysis by NMR showed 89.0% di- and 11.0% monodeuteration at the 2 and 5 positions. NMR (220 MHz, CCl_4) δ 0.95 (d, J = 7 Hz, 6 H), 2.00 (sextet, 2 H), and 4.92 (t, 4 H).

1,1,6,6-Tetradeuterio-1,5-hexadiene was prepared from adipic acid by the amine oxide pyrolysis route described above. NMR analysis revealed 93.8% tetra- and 6.2% trideuteration at the 1 and 6 positions.

***meso*-3,4-Dimethyl-1,5-hexadiene (5)** was prepared from *meso*-3,4-dimethyladipic acid[17] by the procedure used for synthesis of **2**. The IR spectrum was in agreement with that published.[3] NMR (60 MHz, CCl_4) δ 1.00 (d, J = 7 Hz, 6 H), 1.89–2.30 (m, 2 H), 4.85 (overlapping d of d, 2 H), 5.05 (d, 2 H), and 5.40–6.00 (m, 2 H).

***meso*-1,1,6,6-Tetradeuterio-3,4-dimethyl-1,5-hexadiene (5-d_4)** was prepared in the same manner as **2-d_4**. NMR analysis showed 91.6% tetra- and 8.4% trideuteration at the 1 and 6 positions. NMR (220 MHz, CCl_4) δ 0.93 (d, J = 7 Hz, 6 H), 1.89–2.30 (pentuplet, 2 H), and 5.57 (broad singlet, 2 H).

Methyl 3-Benzoylbutyrate. To a solution of lithium diisopropylamide in 75 mL of dry THF, prepared from 9.09 g (90 mmol) of diisopropylamine and 43 mL of a 2.1 M solution of *n*-butyllithium in hexane, was added dropwise at −78 °C, a solution of 16.8 g (90.0 mmol) of *O*-(trimethylsilyl)benzaldehyde cyanohydrin[47] in 25 mL of THF. The red solution was stirred at −78 °C for 15 min and then a solution of 9.00 g (90 mmol) of methyl crotonate in 25 mL of THF was added dropwise. The clear yellow solution was stirred at −78 °C for 1 h, then was poured into water, and then was extracted with ether. The extracts were washed with water, saturated sodium chloride solution, dried over magnesium sulfate, and evaporated leaving 25.4 g of a yellow liquid. The liquid was dissolved in Me_2SO and added to a mixture of 41.6 g of silver nitrate (245 mmol) and 10.3 g of sodium fluoride (245 mmol) in 165 mL of 80% aqueous Me_2SO. Following stirring at 25 °C for 2 h, the mixture was poured into water and extracted with ether. The extracts were filtered, washed with water, saturated sodium chloride solution, dried over magnesium sulfate, and evaporated leaving 15.6 g (92%) of a faint yellow liquid. NMR (60 MHz, CCl_4) δ 1.20 (d, J = 7 Hz, 3 H), 2.10–3.17 (overlapping ddd, 2 H), 3.63 (s, 3 H), 3.55–4.15 (m, 1 H), 7.52 (m, 3 H), and 8.05 (m, 2 H). IR 3065, 3030, 1735, 1675, 1595, 1581, 1460, and 702 cm^{-1} m/e^+ 206.0935 (calcd for $C_{12}H_{14}O_3$ 206.0944).

Methyl 3-Methyl-4-phenyl-4-pentenoate. To a suspension of 8.93 g (25.0 mmol) of methyltriphenylphosphonium bromide in 25 mL of dry THF was added 11.9 mL of a 2.1 M solution of *n*-butyllithium in hexane, and the resulting red solution was stirred at room temperature for 45 min. To the solution was added dropwise a solution of 5.16 g (25 mmol) of methyl 3-benzoylbutyrate in 30 mL of dry Me_2SO, and the clear red solution was stirred at room temperature for 20 h. The solution was poured into water and was extracted with pentane. The extracts were washed with 50% aqueous Me_2SO, water, saturated sodium chloride solution, dried over magnesium sulfate, and evaporated leaving 3.0 g of a liquid which was column chromatographed on silica gel. Elution with benzene afforded 2.51 g (45%) of a clear colorless liquid. NMR (60 MHz, CCl_4) δ 1.50 (d, J = 7 Hz, 3 H), 2.10–2.70 (dq, 2 H), 2.95–3.55 (m, 1 H), 3.65 (s, 3 H), 5.05 (s, 1 H), 5.20 (s, 1 H), and 7.35 (s, 5 H). IR 3090, 3060, 3030, 1737, 1630, 1600, 1576, 1495, 1455, 900, 769, and 701 cm^{-1}. m/e^+ 204.1155 (calcd for $C_{13}H_{16}O_2$ 204.1151).

3-Methyl-4-phenyl-4-pentenal was prepared in 83% yield from methyl 3-methyl-4-phenyl-4-pentenoate by the procedure used for the preparation of 3-methyl-4-pentenal. NMR (60 MHz, CCl_4) δ 1.14 (d, J = 7 Hz, 3 H), 2.12–2.60 (m, 2 H), 3.00–3.52 (m, 1 H), 5.01 (s, 1 H), 5.18 (s, 1 H), 7.24 (s, 5 H), and 9.66 (t, J = 4 Hz, 1 H). IR 3090, 3065, 3035, 2725, 1728, 1628, 1600, 1576, 1490, 1455, 901, 780, and 705 cm^{-1}. m/e^+ 174.1044 (calcd for $C_{12}H_{14}O$: 174.1045).

3-Methyl-2-phenyl-1,5-hexadiene (6) was prepared from 3-methyl-4-phenyl-4-pentenal in 55% yield by the procedure described for the synthesis of **2-$6d_2$**. NMR (220 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 1.89–2.05 (m, 1 H), 2.16–2.31 (m, 1 H), 2.62–2.76 (m, 1 H), 4.89 (s, 1 H), 4.95 (s, 1 H), 5.10 (s, 1 H), 5.57–5.77 (m, 1 H), and

7.12-7.26 (m, 5 H). IR 3085, 3075, 3030, 1643, 1629, 1602, 1578, 1495, 1455, 900, 779, and 700 cm^{-1}. m/e^+ 172.1253 (calcd for $C_{13}H_{16}$ 172.1253).

6,6-Dideuterio-3-methyl-2-phenyl-1,5-hexadiene (6-*6d*$_2$) was prepared from 3-methyl-2-phenyl-4-pentenal in 39% yield by using triphenylphosphonium-*methyl-d*$_3$ bromide and a D_2O quench following the procedure for preparation of **2**-*6d*$_2$. NMR analysis showed 86.0% di- and 14.0% monodeuteration at the 6 position. NMR (220 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 1.90-2.04 (m, 1 H), 2.18-2.30 (m, 1 H), 2.62-2.77 (sextet, 1 H), 4.96 (s, 1 H), 5.11 (s, 1 H), 5.70 (broad s, 1 H), and 7.12-7.26 (m, 5 H).

2,2-Dideuterio-3-methyl-4-phenyl-4-pentenal. A solution of 2.49 g (14.3 mmol) of unlabeled aldehyde, 20 mL of D_2O, and 30 mL of dry pyridine was stirred at room temperature for 7 days, poured into a large excess of water, and extracted with pentane. The extracts were washed with water, 5% hydrochloric acid, saturated sodium bicarbonate, and sodium chloride solutions, and then dried over magnesium sulfate. Evaporation of the solvent gave 2.00 g of a liquid. NMR analysis indicated 95% deuteration at the 2 position. NMR (60 MHz, CCl_4) δ 1.14 (d, J = 7 Hz, 3 H), 3.20 (q, J = 7 Hz, 1 H), 4.97 (s, 1 H), 5.20 (s, 1 H), 7.23 (s, 5 H), and 9.62 (s, 1 H).

4,4-Dideuterio-3-methyl-2-phenyl-1,5-hexadiene (6-*4d*$_2$) was obtained in 47% yield by the procedure for the preparation of **2**-*4d*$_2$. NMR analysis revealed 87.0% di- and 13.0% monodeuteration at the 4 position. NMR (220 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 2.71 (q, J = 7 Hz, 1 H), 4.91 (s, 1 H), 4.97 (s, 1 H), 5.12 (s, 1 H), 5.68 (m, 1 H), and 7.10-7.26 (m, 5 H).

4-Methyl-3-phenylcyclohexene. 4-Carbethoxy-3-phenylcyclohexene[48] (25.1 g, 109 mmol) was reduced with lithium aluminum hydride in ether followed by aqueous workup affording 20.5 g of a liquid, bp 106-110 °C (0.2 Torr). NMR (60 MHz, CCl_4) δ 1.30-2.40 (m, 6 H), 3.10 (d, J = 7 Hz), and 3.30-3.80 (m) (3 H total), 5.60-6.20 (m, 2 H), and 7.20 (s, 5 H). IR 3600-3100, 3085, 3060, 3025, 1645, 1605, 1492, 1452, 760, 700, and 680 cm^{-1}.

The liquid was treated with 23.7 g (207 mmol) of mesyl chloride in pyridine at 0 °C for 21 h affording, after the usual workup, 28.0 g of a yellow liquid. NMR (60 MHz, CCl_4) δ 1.20-2.60 (m, 5 H), 2.85 (s, 3 H), 3.30 (m, 1 H), 3.75 and 4.00 (pair of doublets, J = 8 and 5 Hz, ratio of 1.8/1.0, 2 H total), 5.50-6.20 (m, 2 H), and 7.29 (s, 5 H). IR 3090, 3070, 3030, 1650, 1602, 1493, 1455, 1350, 1177, 960, 765, 735, 702, and 685 cm^{-1}.

The crude mesylate (27.0 g) was reduced by using a mixture of 3.8 g (101 mmol) of lithium aluminum hydride and 1.2 g of lithium hydride vide supra giving 16.0 g (91%) of a colorless liquid, bp 93-95 °C (3 Torr). NMR (60 MHz, CCl_4) δ 0.65 and 0.90 (pair of doublets in the ratio of 2:1, J = 7 Hz, and 7 Hz, 3 H total), 1.20-2.40 (m, 5 H), 2.80 and 3.40 (pair of doublets, 1 H), 5.50-6.10 (m, 2 H), and 7.20 (s, 5 H). IR 3085, 3065, 3025, 1650, 1602, 1490, 1455, 760, 740, 725, 700, and 680 cm^{-1}. m/e^+ 172.1254 (calcd for $C_{13}H_{16}$ 172.1253).

3-Methyl-2-phenyladipic Acid. To a stirred mixture of 3.07 g (17.8 mmol) of 4-methyl-3-phenylcyclohexene and 0.66 g (7.8 mmol) of sodium bicarbonate in 25 mL of acetone was added, over a 3-h period at 0 °C, 12.4 g (78.3 mmol) of potassium permanganate. Following stirring at 0 °C for 2.5 h and at room temperature for 15 h, the acetone was evaporated, and the residue was suspended in 200 mL of water. The suspension was clarified by the alternate addition of saturated sodium bisulfite and 10% sulfuric acid solutions and then was extracted with methylene chloride. The acidic components were isolated in the usual fashion affording 2.88 g of a liquid acid. Attempts to obtain an analytical sample were unsuccessful. NMR (60 MHz, $CDCl_3$) δ 0.70 and 1.25 (pair of doublets, J = 7 and 7 Hz, 3 H total), 1.40-2.70 (m, 5 H), 3.10-3.60 (m, 1 H), 7.20-7.75 (m, 4 H), 7.85-8.30 (m, 1 H), and 10.80 (s, br, 2 H). IR (10% in $CHCl_3$) 3600-2300, 1710, 1600, 1500, and 1455 cm^{-1}.

1,1,6,6-Tetradeuterio-3-methyl-2-phenyl-1,5-hexadiene (6-*d*$_4$) was obtained by the amine oxide pyrolysis route described above. NMR analysis indicated 93.0% tetra- and 7.0% trideuteration at the 1 and 6 positions. NMR (220 MHz, CCl_4) δ 1.09 (d, J = 7 Hz, 3 H), 1.89-2.02 (m, 1 H), 2.18-2.29 (m, 1 H), 2.63-2.76 (m, 1 H), 5.68 (s, br, 1 H), and 7.12-7.26 (m, 5 H).

3,3,4,4-Tetradeuterio-2,5-diphenyl-1,5-hexadiene (9-*d*$_4$) was prepared by the method of Dewar and Wade.[8] NMR analysis revealed 97.2% tetra- and 2.8% trideuteration at the 3 and 4 positions. NMR (60 MHz, CCl_4) δ 4.98 (s, 1 H), 5.10 (s, 1 H), and 7.22 (s, 5 H).

[1,6-^{13}C]-2,5-Diphenyl-1,5-hexadiene (9-^{13}*C*$_2$) was obtained in 14% yield by the method of Dewar and Wade[8] from dibenzoylethane[49] and [*methyl*-$^{13}C_2$]triphenylphosphonium iodide ([^{13}C]methyl iodide, at least 90 atom % ^{13}C, was purchased from MSD Isotopes Inc.). Analysis of the vinyl proton region of the NMR spectrum revealed 92.9% ^{13}C and assuming a statistical distribution of the label gives the composition as 86.4% di-, 13.1% mono-, and 0.5% unlabeled material. NMR (60 MHz, CCl_4) δ 2.63 (s, 4 H), 5.00 (d, J = 156 Hz, 2 H), 5.12 (d, J = 155 Hz, 2 H), and 7.22 (s, 10 H).

3,3,4,4-Tetradeuterio-[1,6-$^{13}C_2$]-2,5-diphenyl-1,5-hexadiene (9-^{13}*C*$_2$-*d*$_4$) was obtained in 12% yield by the method used for synthesis of **9**-$^{13}C_2$. NMR analysis showed 97.2% tetra- and 2.8% trideuteration at the 3 and 4 positions, while there was 83.5 % di-, 15.7% mono-, and 0.7% unlabeled carbon-13 material present (91.4% overall).

4,4-Dideuterioallyl vinyl ether (10-*4d*$_2$) was prepared from 3,3-deuterioallyl alcohol[33] in 41% yield by the procedure of Watanabe and Conlon.[21] NMR analysis revealed 87.7% di- and 12.3% monodeuteration at the 3 position. NMR (60 MHz, CCl_4) δ 3.9-4.3 (m, 4 H), 5.7-6.0 (m, 1 H) and 6.2-6.6 (m, 1 H).

6,6-Dideuterioallyl vinyl ether (10-*6d*$_2$) was obtained in 32% yield from 1,1-dideuterioallyl alcohol[32] by the procedure of Watanabe and Conlon.[21] NMR analysis showed 97.5% di- and 2.5% monodeuteration at the 1 position. NMR (60 MHz, CCl_4) δ 3.9-4.3 (m, 2 H), 5.0-5.5 (m, 2 H), 5.7-6.1 (m, 1 H), and 6.2-6.6 (m, 1 H).

1,1-Dideuterioallyl acetate was prepared by the method of Schuetz and Millard[22] from 1,1-dideuterioallyl alcohol. NMR analysis showed at least 97% deuteration at the 1 position.

3,3-Dideuterioallyl acetate was prepared in a manner similar to that used for synthesis of the 1,1-dideuterio isomer. NMR analysis revealed 87% dideuteration at the 3 position.

Experimental Isotope Effects. General. The pyrolysis apparatus for study of reactions in the gas phase has been described previously.[27] For a typical pyrolysis, 7 μL of pure sample was flushed into an evacuated 2-L conditioned bulb with sufficient dinitrogen to bring the pressure to 100 Torr, timing being started when the valve to the bulb was opened. After heating for the stated time intervals, the pyrolysate was collected by vacuating the contents of the bulb through a liquid nitrogen-cooled spiral trap. The pyrolysate was then vacuum transferred into a receiver. The pyrolysate was diluted with 10 μL of pentane or toluene and analyzed by VPC by using syringe injections with the indicated columns. Integrations were performed with a Vidar-Autolab Model 6210 digital integrator (FID detector). Liquid samples for pyrolysis were purified by preparative VPC and were greater than 99.9% pure.

3-Methyl-1,5-hexadienes 2, 2-*d*$_4$, 2-*4d*$_2$, and 2-*6d*$_2$. The pyrolysis of **2** in the gas phase gave *trans*-1,5-heptadiene, **3**, and *cis*-1,5-heptadiene, **4**, as the only products in agreement with Frey and Solly.[15] The VPC analyses (200-ft DBTCP capillary column at 60 °C) for isomerization of **2** and **2**-*d*$_4$ at 248.6 ± 0.1 °C and of **2**, **2**-*4d*$_2$, and **2**-*4d*$_2$ at 248.3 ± 0.1 °C are shown in Appendix A. The rate constants (Table I) were obtained by a simplex[16] fit to the rate expressions of Frey and Solly[15] that minimized the sums of the squares of the residuals of the experimental and calculated concentrations. The errors are the standard deviations approximated as described in Appendix B. The kinetic and thermodynamic isotope effects are listed in Table I and were corrected to 100% deuteration by using the relationship $X_nK + X_{n-1}K^{[(n-1)/n]} = K_{obsd}$, where X's are mole fractions, n is the number of deuterium atoms in the species of interest, and K's are isotope effects.

***meso*-3,4-Dimethyl-1,5-hexadienes 5, 5-*d*$_4$, and 5-*d*$_2$.** Gas phase thermolysis of **5** gave (E,Z)-2,6-octadiene as the only product.[3] The isomerizations of **5** and **5**-*d*$_4$ at 218.1 ± 0.1 °C were followed by VPC (200-ft DBTCP capillary column at 60 °C) and the results are shown in Appendix A along with the results for rearrangement of **5** and **5**-*d*$_2$ at 228.2 ± 0.1 °C (50-ft XF-1150 capillary column at 45 °C). The rate constants, obtained by the method of least squares, and the isotope effects are presented in Table II where the errors are the standard deviations in the slopes of plots of $\ln C/C_0 = -kt$.[50]

3,3,4,4-Tetradeuterio-1,5-hexadiene. A 47-μL sample of the diene-d_4 was heated at 218.1 ± 0.1 °C and 100 Torr of nitrogen for 14 days (44 half-lives)[18] in the static reaction vessel. The ratio of methylene to terminal vinyl protons was determined by multiple NMR integrations at 220 MHz as 1.23 ± 0.023. Correction for a higher methylene:vinyl ratio in unlabeled 1,5-hexadiene (1.02 ± 0.02) and incomplete deuteration gave the equilibrium constant as 1.21 ± 0.03.

3-Methyl-2-phenyl-1,5-hexadienes 6, 6-*d*$_4$, 6-*6d*$_2$, and 6-*4d*$_2$. Pyrolysis of **6** at 245 °C in a sealed ampule for 4 h gave a liquid com-

Table A-1. Analysis Data for the Thermal Isomerization of **2** and **2**-d_4 at 248.6 ± 0.1 °C

		pyrolysate composition		
time, s	reactant	fraction of reactant[a]	fraction of **3**	fraction of **4**
1800	MHD ≡ **2**	0.6750 (0.6754)[b]	0.2598 (0.2616)	0.0654 (0.0630)
	MHD-d_4	0.6455 (0.6414)	0.2853 (0.2878)	0.0691 (0.0708)
3600	MHD-	0.4736 (0.4735)	0.4201 (0.4226)	0.1064 (0.1039)
	d_4[c]	0.4272 (0.4289)	0.4571 (0.4565)	0.1156 (0.1146)
4500	MHD	0.4047 (0.4032)	0.4782 (0.4780)	0.1171 (0.1188)
	d_4	0.3534 (0.3578)	0.5164 (0.5123)	0.1301 (0.1300)
5400	MHD	0.3491 (0.3478)	0.5190 (0.5212)	0.1319 (0.1310)
	d_4	0.3089 (0.3030)	0.5501 (0.5548)	0.1410 (0.1423)
6300	MHD	0.3013 (0.3041)	0.5584 (0.5548)	0.1403 (0.1411)
	d_4	0.2596 (0.2608)	0.5870 (0.5870)	0.1534 (0.1522)
7200	MHD	0.2675 (0.2696)	0.5833 (0.5809)	0.1492 (0.1495)
	d_4	0.2271 (0.2283)	0.6117 (0.6114)	0.1612 (0.1604)
8100	MHD	0.2440 (0.2424)	0.5992 (0.6011)	0.1568 (0.1565)
	d_4	0.2018 (0.2032)	0.6315 (0.6297)	0.1668 (0.1671)
9000	MHD	0.2180 (0.2209)	0.6180 (0.6167)	0.1640 (0.1624)
	d_4	0.1823 (0.1839)	0.6430 (0.6434)	0.1747 (0.1727)
9900	MHD	0.2044 (0.2039)	0.6291 (0.6286)	0.1665 (0.1675)
	d_4	0.1670 (0.1690)	0.6559 (0.6536)	0.1768 (0.1774)
10800	MHD	0.1940 (0.1905)	0.6343 (0.6376)	0.1717 (0.1720)
	d_4	0.1597 (0.1575)	0.6595 (0.6610)	0.1808 (0.1815)
12600	MHD	0.1690 (0.1715)	0.6525 (0.6493)	0.1792 (0.1786)
	d_4	0.1436 (0.1418)	0.6693 (0.6700)	0.1870 (0.1882)
14400	MHD	0.1611 (0.1595)	0.6546 (0.6553)	0.1843 (0.1852)
equilibrium	MHD	0.1344 (0.1336)	0.5938 (0.5946)	0.2716 (0.2718)
	d_4	0.1138 (0.1132)	0.6043 (0.6048)	0.2816 (0.2820)

[a] Mean values. The average reproducibilities of the analyses were 0.60% for starting materials, 0.30% for **3**, and 1.0% for **4**—all as % of the mole fractions. [b] Values in parentheses are calculated values; see Table I. [c] MHD-d_4 is abbreviated as d_4 throughout this table.

prised of three components which were separated by VPC by using a 5 ft × 0.25 in. 30% XF-1150 on Chromosorb WAW column at 125 °C. Peak 1: NMR (220 MHz, CCl_4) δ 1.07 (d, J = 7 Hz, 3 H), 1.99 (overlapping triplets, J = 8 and 8 Hz, 2 H), 2.36 (t, J = 8 Hz, 2 H), 4.72–4.94 (m, 2 H), 5.46 (q, J = 7 Hz, 1 H), 5.59–5.77 (m, 1 H), and 7.00–7.27 (m, 5 H); m/e^+ 172.1249 (calcd for $C_{13}H_{16}$ 172.1253). Peak 2 had an NMR spectrum and retention time identical with the starting material. Peak 3: NMR (220 MHz, CCl_4) δ 1.77 (d, J = 7 Hz, 3 H), 2.03 (overlapping triplets, J = 8 and 8 Hz, 2 H), 2.53 (t, J = 8 Hz, 2 H), 4.82–4.98 (m, 2 H) 5.61–5.82 (m, 2 H), and 7.02–7.22 (m, 5 H); m/e^+ 172.1251. Based upon the chemical shifts for α-methyl-β-benzylstyrenes,[20] the first material is (*Z*)-5-phenyl-1,5-heptadiene, while the last eluted material is (*E*)-5-phenyl-1,5-heptadiene. The approach to equilibrium at 176.4 ± 0.1 °C was followed starting from **6** by using 4% solutions of diene in cyclohexane containing 4% tridecane as internal standard and 0.013% diphenylamine as inhibitor. The ratio of total diene to internal standard remained constant within experimental error (1%) over all time intervals. Degassed solutions were sealed in Pyrex ampules (that had been previously washed with concentrated ammonium hydroxide and dried) and heated in a thermostated salt bath (KNO_3-$NaNO_2$). After heating, the ampules were opened and analyzed by VPC (5-ft × 0.125 in. 15% XF-1150 on Chromosorb WAWDMCS) and the results are shown in Appendix A. The rate constants were determined as described for **2** and along with the isotope effects are shown in Table III.

2,5-Diphenyl-1,5-hexadienes 9-*d*$_4$, 9-$^{13}C_2$, and 9-$^{13}C_2$-*d*$_4$. The reversible first-order kinetics of these compounds were followed by NMR in benzene-d_6 solution at 55.5 ± 0.01 °C. NMR tubes that had been washed with concentrated ammonium hydroxide and dried were charged with 50 mg of substrate, a trace of diphenylamine, and 0.75 mL of benzene-d_6. After degassing and sealing under vacuum, the tubes were immersed in a thermostated mineral oil bath for the indicated time intervals. The NMR spectra were recorded at 220 MHz and the same samples used throughout the studies. For **9**-d_4 the ratio of vinylic to methylene protons was followed, while for **9**-$^{13}C_2$-d_4 the ratio of vinylic to carbon-12 bonded methylene plus twice the high field carbon-13 bonded methylene protons was used. This was done due to an impurity, present in all three samples, that overlapped with the low field carbon-13 methylene signal. For **9**-$^{13}C_2$ the ratio of the inner vinylic signals minus the outer ones to the vinylic total was followed. Unfortunately, the tube containing **9**-$^{13}C_2$-d_4 developed a leak and was contaminated with mineral oil before equilibrium was established, so the equilibrium constant was assumed to be the same as with **9**-$^{13}C_2$. The analytical results are presented in Appendix A. Rate constants for the forward and reverse reactions were obtained by a least-squares analysis of:

$$\ln\frac{A - A_e}{A_0 - A_e} = -kt = -(k_1 + k_2)t$$

For **9**-d_4 $y = \exp(-3.489 \times 10^{-6}t + 0.0103)$, $k_1 = (1.287 \pm 0.013) \times 10^{-6}$ and $k_2 = (2.202 \pm 0.022) \times 10^{-6}$/s; **9**-$^{13}C_2$, $y = \exp(-2.677 \times 10^{-6}t - 0.02347)$, $k_1 = (1.335 \pm 0.024) \times 10^{-6}$, and $k_2 = (1.342 \pm 0.024) \times 10^{-6}$/s; **9**-$^{13}C_2$-$d_4$, $y = \exp(-3.464 \times 10^{-6}t + 0.02809)$, $k_1 = (1.278 \pm 0.014) \times 10^{-6}$, and $k_2 = (2.186 \pm 0.024) \times 10^{-6}$/s.

Rate constants were also obtained by Simplex variation of k_1, k_2, and A_0 until the residuals in a plot of A_t vs. t were minimized where A(calculated) was given by:

$$A = \left(A_0 - \frac{k_2k_0}{k_2 + k_1}\right)\exp(-(k_1 + k_2)t) + \frac{k_2k_0}{k_2 + k_1}$$

Simplex places no particular emphasis on either A_0 or A_e as does the least-squares analysis. For **9**-d_4 $k_1 = (1.265 \pm 0.015) \times 10^{-6}$ and $k_2 = (2.150 \pm 0.031) \times 10^{-6}$/s; **9**-$^{13}C_2$, $k_1 = (1.369 \pm 0.026) \times 10^{-6}$ and $k_2 = (1.404 \pm 0.027) \times 10^{-6}$/s; **9**-$^{13}C_2$-$d_4$, $k_1 = (1.256 \pm 0.018) \times 10^{-6}$ and $k_2 = (2.097 \pm 0.030) \times 10^{-6}$/s.

Examination of the analytical data (Appendix A) reveals that Simplex gave less satisfactory results at longer reaction times, while the least-squares method had difficulties at shorter reaction times. Therefore, the individual values for k_1 and k_2 from each method were averaged. Furthermore, since **9**-d_4 and **9**-$^{13}C_2$-d_4 had comparable rates within experimental error and since a small but normal EIE would be expected for **9**-$^{13}C_2$, the results for k_1 and k_2 for **9**-$^{13}C_2$ were combined to give a grand average. The rate constants and isotope effects calculated in this fashion are presented in Table IV.

Allyl Vinyl Ether 10, 10-*4d*$_2$, and 10-*6d*$_2$. Thermolysis of **10** in the gas phase at 160.3 ± 0.1 °C gave 4-pentenal as the only product in agreement with Schuler and Murphy.[24] The VPC analyses (6 ft × 0.125 in. 10% Apiezon L on Chromosorb Z at 50 °C) are presented in Appendix A and the rate constants and isotope effects are listed in Table V.

Equilibration of 1,1-Dideuterioallyl Acetate. One hundred milligrams of mercuric acetate and 0.10 mL of 1,1-dideuterioallyl acetate were sealed in an ampule at 0.1 Torr and heated at 160 ± 5 °C for 11 days. The volatile components were collected by vacuum transfer and analyzed by VPC and NMR. VPC analysis revealed a mixture comprised of roughly equal amounts of allyl acetate and acetic acid, while the NMR spectrum of an unpurified sample revealed a methylene to terminal vinyl proton ratio of 1.32 ± 0.02. The liquid was combined with 80 mg of mercuric acetate and heating at 160 ± 5 °C continued for 6 days. Recovery of the liquids by vacuum transfer and collection of the allyl acetate by preparative VPC gave approximately 25 μL of a liquid. NMR analysis revealed a methylene/terminal vinyl proton ratio of 1.31 ± 0.03.

Similarly, mercuric acetate catalyzed pyrolysis of 3,3-dideuterioallyl acetate at 160 ± 5 °C for 17 days revealed a methylene/terminal vinyl proton ratio of 1.28 ± 0.013. Correcting for a methylene/vinyl proton ratio of 1.02 ± 0.01 in unlabeled allyl acetate and for incomplete deuteration gave an averaged equilibrium isotope effect of 1.27 ± 0.03.

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Appendix A: Analysis Data for the Thermolysis of 1,5-Hexadienes

Table A-1 has been included here as representative of a typical KIE determination; the remainder of Appendix A (Tables A-2 through A-9) can be obtained as supplementary material (see paragraph concerning supplementary material at the end of this paper).

Appendix B: Treatment of Data for Parallel Reversible First-Order Reactions

Starting from II (**2** or **6**), the reaction scheme is that for simultaneous reversible first-order reactions. Frey and Solly have

$$\mathrm{I} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \mathrm{II} \underset{k_4}{\overset{k_3}{\rightleftarrows}} \mathrm{III}$$

derived equations that express the concentration as a function of time involving all four rate constants:

$$[\mathrm{I}] = \frac{k_1k_4}{\lambda_2\lambda_3} + \frac{k_1(k_4 - \lambda_2)}{\lambda_2(\lambda_2 - \lambda_3)} \times \exp(-\lambda_2 t) - \frac{k_1(k_4 - \lambda_3)}{\lambda_3(\lambda_2 - \lambda_3)} \exp(-\lambda_3 t)$$

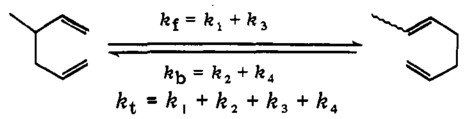
$$[\mathrm{II}] = \frac{k_2k_4}{\lambda_2\lambda_3} + \frac{(k_4 - \lambda_2)(k_2 - \lambda_2)}{\lambda_2(\lambda_2 - \lambda_3)} \times \exp(-\lambda_2 t) - \frac{(k_2 - \lambda_3)(k_4 - \lambda_3)}{\lambda_3(\lambda_2 - \lambda_3)} \exp(-\lambda_3 t)$$

$$[\mathrm{III}] = \frac{k_2k_3}{\lambda_2\lambda_3} + \frac{k_3(k_2 - \lambda_2)}{\lambda_2(\lambda_2 - \lambda_3)} \times \exp(-\lambda_2 t) - \frac{k_3(k_2 - \lambda_3)}{\lambda_3(\lambda_2 - \lambda_3)} \exp(-\lambda_3 t)$$

where $\lambda_2 = \frac{1}{2}(P + Q)$, $\lambda_3 = \frac{1}{2}(P - Q)$, and $P = k_1 + k_2 + k_3 + k_4$ and $Q = (P^2 - 4(k_2k_3 + k_1k_4 + k_2k_4))^{1/2}$.

The problem of obtaining the best fit to the data was simplified by using a Simplex computer program, written by Mr. Dennis Nollen of this department, in conjunction with the Frey and Solly equations to systematically vary the four rate constants, minimizing the sums of the squares of the experimental-calculated concentration differences. Various different starting sets of rate constants were used to ensure that the final Simplexed values gave the best fit to the concentration data.

The complexity of the Frey and Solly equations precludes the usual method of determining the errors associated with each of the rate constants. Therefore, the standard deviations in the rate constants were approximated as follows: The three-component scheme was assumed to be similar to a two component reversible first-order scheme so that the standard deviations in the sum of the four rate constants were found by analysis of the residuals for the starting material using the expression:



$$k_f = k_1 + k_3 \qquad k_b = k_2 + k_4$$
$$k_t = k_1 + k_2 + k_3 + k_4$$

$$Y_c - Y_x = \ln\left(\left(\frac{A_cK_c - B_c}{A_xK_x - B_x}\right)\frac{K_x}{K_c}\right)$$

K is the equilibrium constant and the subscripts c and x refer to calculated and experimental values. The standard deviation is then given by:

$$\underset{\text{in } k}{\mathrm{SD}} = \left(\frac{\Sigma(Y_c - Y_x)^2}{n - 2}\,\frac{n}{n\Sigma t^2 - (\Sigma t)^2}\right)^{1/2}$$

where t is time and n the number of data points. Using the analytical error in the determination of the equilibrium concentrations and the relationship $k_f = k/(1 + 1/K)$ gave the estimated error in $k_1 + k_3$. The error in k_1 or k_3 was determined from the average error in the average ratio of the two products and the error in k_f

$$k_1 = k_f(1 + 1/R) \qquad k_3 = k_f(1 + R);\ R = [\mathrm{I}]/[\mathrm{III}_{\mathrm{av}}]$$

The standard deviations in k_2 and k_4 were approximated by using the errors in k_1 or k_3 and the errors in the equilibrium constants.

$$k_2 = K_{12}/k_1 \qquad k_4 = K_{32}/k_3$$

Supplementary Material Available: Tables A-2 through A-9 are available (11 pages). Ordering information is given on any current masthead page.

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Deuterium Isotope Exchange between Molecular Hydrogen and Cyclohexylamine[1a,c]

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Abstract: Deuterium isotope exchange between molecular hydrogen and cyclohexylamine (CHA) has been studied by using the LiCHA, NaCHA, KCHA, and CsCHA salts as catalysts in a stirred reactor over the temperature range −15 to +15 °C. The reaction in solution is very fast (comparable to the amide/ammonia and methylamide/methylamine systems), and even at −15 °C (CHA fp −17.8 °C) rate constants independent of mass transfer could be obtained only for the Li and Na salts in the present apparatus. For these, the kinetic isotope effect (k.i.e., 1.7–2.0) and activation parameter (E_a, 11–17 kJ·mol^{-1}) data have been compared with literature values for base-catalyzed exchange with other protic solvents. Reasons for the observed relative catalyst reactivity LiCHA ≪ NaCHA < KCHA < CsCHA are considered. It has been found that, under some experimental conditions, mass transfer effects can lead to an incorrect k.i.e. value when this is derived from data for a single kinetic run $D_2 \rightarrow HD \rightarrow H_2$. The solubility of H_2 in CHA has been measured over the temperature range −15 to +15 °C.

Introduction

Isotope exchange between molecular hydrogen and simple liquid amines under base catalysis has been the subject of considerable study since Wilmarth and co-workers first reported, in the early 1950's, deuterium exchange in the ammonia-D_2 system with potassium amide as catalyst.[2] Since then, much effort has been applied to determining the mechanism of this reaction in liquid ammonia,[3-7] by using various isotopes and alkali metal amide catalysts. The reaction was shown to be first order in dissolved hydrogen, but the question of the relative roles of the free amide ions and ion pairs present in this solvent (dielectric constant $\epsilon = 22.4$ at −33.4 °C) was more difficult to resolve. From the dependence of the rate constant on free amide ion concentration, which was derived from electrical conductivity data for the catalyst solutions, Delmas et al.[7] finally concluded that only the free $^-NH_2$ ion is active in liquid ammonia.

Some work has been done with alkylamines like methylamine,[8-10] dimethylamine,[8,9] ethylamine,[8] and isopropylamine,[9] and aniline,[11] with the anion of each solvent as catalyst. Here the dielectric constants are lower than for ammonia, and the relative importance of free alkylamide ions and their corresponding ion pairs as catalysts is less certain; Rochard and Ravoire[9] state that ion pairs "appear to be the main catalytic species", although electrical conductivity data for these solutions were lacking. We have recently reported conductivity data for potassium methylamide in methylamine.[12] However, it is practically impossible to apply such data, valid only for *ion pairing* in such a low dielectric constant solvent ($\epsilon = 10.8$ at

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