

be obtained with fluoropyridine substrates in acidic solution. Evidently, a slow reaction of the product may follow the initial hydrolysis.

¹⁸O-Label Studies. Buffer containing ¹⁸O-labeled water was prepared by dissolving 2.7 mg of sodium acetate (0.033 mmol) and 5.2 μL of acetic acid (0.087 mmol) in 400 μL of labeled water (99% ¹⁸O, Stohler Isotopes), giving a solution 0.08 M in acetate. A stock solution of substrate was prepared by dissolving 0.7 mg of 1 in 120 μL of labeled water. Hydrolysis samples were prepared by combining 30 μL of each stock solution in tubes, giving a final acetate concentration of 0.04 M. The tubes were sealed with rubber septa and heated at 50 °C for 50 min, approximately 10 half-lives for hydrolysis. A reference sample was prepared by dissolving 0.6 μL of 2 in 60 μL of the same 0.04 M buffer and also heated for 50 min.

Buffer containing labeled acetate was prepared by dissolving 84.3 mg of acetic acid (1.32 mmol, 90% ¹⁸O, Stohler) in distilled water, adding 3.30 mL of 0.100 M KOH, and diluting to 5.0 mL with distilled water, resulting in a solution 0.066 M in labeled acetate. Hydrolysis samples were prepared by dilution of 1.0 mL

of the 0.066 M stock solution to 1.65 mL to give a 0.040 M solution into 0.066 mL of which was dissolved 2.8 mg of 1, and the resulting solution was divided into three portions. Each portion was heated for 1 h (approximately 11 half-lives) in tubes sealed with rubber septa.

Upon completion of the hydrolyses, the reaction tubes were refrigerated until GC-MS analysis with a Hewlett-Packard 5985 system. ¹⁸O incorporation was determined from the relative peak intensities of the M and M + 2 parent ions in the mass spectra, as well as from total ionization at M and M + 2 masses. Results from spectral peak intensities and total ionization were in agreement.

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Kinetics and Stereochemistry of the Thermal Interconversion of 4,5-Dimethyl-2,6-octadienes

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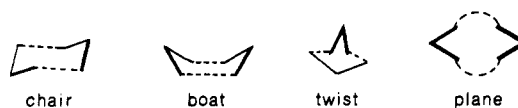
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Gas-phase pyrolysis of *threo*-4,5-dimethyl-*cis,cis*-1,1,1,8,8,8-hexadeuterio-2,6-octadiene over the temperature range 220.0–260.0 °C resulted in formation of the *threo,trans,trans* isomer with $\log k = 11.36 - 36000/2.303RT$. NMR analysis with Simplex minimization of the residuals from a Gear numerical integration provided a nearly identical rate constant for the degenerate interconversion of the deuterium isomers of the *threo,trans,trans* diastereomer at 240 °C. All six 4,5-dimethyl-2,6-octadienes are interconverted at temperatures above 290 °C. Mass spectral analysis of the reaction products from a 1:1 mixture of protio and D₆ diene provided evidence for cleavage-recombination as the pathway for conversion to *erythro,trans,trans*, *erythro,cis,cis*, and *threo,trans,cis* isomers. Competing with the cleavage-recombination is the boatlike shift to the *erythro,trans,cis* isomer. NMR analysis of the (–)-α-phenylethylamine bis salt of the *threo*-2,3-dimethylsuccinic acid derived from a 33.5-h 240 °C pyrolysis of optically pure hexadeuterio starting material provided evidence for little incursion of antarafacial-antarafacial 3,3-shifts via a twist transition state competing with the chair transition state. An analysis of the energy surface for all the interconversions reveals that at 300 °C, the boat transition state is ~6 kcal/mol higher in energy than the sterically most favorable chair transition state, and the cleavage reaction transition state is only 0.6 kcal/mol higher in energy than the boat transition state.

Doering and Roth's classic work on the stereochemistry of the thermally induced all-carbon 3,3-sigmatropic shift (Cope rearrangement) suggested that the low-energy pathway has a chair transition-state geometry and the boat geometry is ~6 kcal/mol higher in energy.¹ Both of these processes involve suprafacial use of each allylic moiety.² Unfortunately, the chair and boat products from the *meso*- and *threo*-3,4-dimethyl-1,5-hexadienes studied could also result from two other orbital symmetry "allowed" pathways involving antarafacial uses of the two three-carbon units, processes which Goldstein described as twist and plane, respectively³ (Scheme I). To distinguish between all suprafacial and antarafacial possibilities, stereochemical labels at the double bond termini are necessary. In such an

Scheme I



experiment, Hill found that, indeed, the chair was the low-energy path, but the stereochemical labels would not allow a distinction between boat or twist for the higher energy path.⁴

The 3,3-shift in bicyclo[3.2.0]hepta-2,6-diene systems first reported by Mukai,⁵ which formally involves the twist pathway, has been interpreted by Baldwin⁶ to be a conrotatory cyclobutene ring opening to a *cis,trans,cis*-triene followed by conrotatory closure to the twist product. The basis for this hypothesis rests on the fact that bicyclo[3.3.0]octa-2,6-dienes do not undergo the 3,3-shift—a reaction which must formally be a twist process. Given the central position of the Cope rearrangement in organic

(1) Doering, W. v. E.; Roth, W. R. *Tetrahedron* 1962, 18, 67. For reviews, see: Rhodes, S. J.; Raulins, N. R. *Org. React. (N. Y.)* 1970, 22. Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic: New York, 1981.

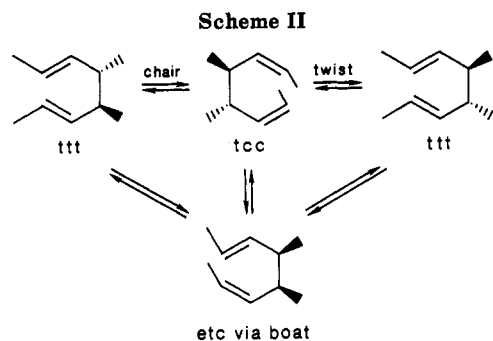
(2) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* 1969, 8, 781.

(3) (a) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* 1972, 94, 7149. (b) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* 1972, 94, 7147. There is an error in the interconversions in the top scheme of Figure 2 of ref 3b: specifically, ZSSZ and ZRRZ should be interchanged and then ZSSZ interconverts with ESRZ not ERSZ by a boat; ZRRZ interconverts with ERSZ not ESRZ by a boat.

(4) Hill, R. K.; Gilman, N. W. *Chem. Commun.* 1967, 619.

(5) Miyashi, T.; Nitta, M.; Mukai, T. *J. Am. Chem. Soc.* 1971, 93, 3441 and references therein.

(6) Baldwin, J. E.; Kaplan, M. S. *J. Am. Chem. Soc.* 1971, 93, 3969; 1972, 94, 668; *J. Chem. Soc., Chem. Commun.* 1970, 1560.



chemistry, a complete characterization of the energy surface of a relatively simple 1,5-hexadiene system appeared necessary. To this end, the racemic and optically active 1,3,4,6-tetramethyl-1,5-hexadienes (4,5-dimethyl-2,6-octadienes) were prepared with deuteriated terminal vinyl methyls.

Results and Discussion

A. Synthesis and Isolation of the 4,5-Dimethyl-2,6-octadienes. *meso*- and *threo*-2,3-dimethylsuccinic acids were prepared by the method of Bone and Sprankling.⁷ Separation of the diastereomers and recrystallization provided purified diacids used for the synthesis of the dimethyl octadienes. Esterification of each diacid followed by Red-Al reduction and Wittig olefination at -78°C gave the *erythro*- and *threo*-4,5-dimethyl-2,6-octadienes as a mixture of *cis,cis*-, *cis,trans*-, and *trans,trans*-double bond isomers in the ratio 69:28:3 for *erythro,cis,cis/erythro,cis,trans/erythro,trans,trans* (*ecc/ect/ett*) and in the ratio 76:19:5 for *threo,cis,cis/threo,cis,trans/threo,trans,trans* (*tcc/tct/ttt*), respectively. The assignment of double bond geometries is based on the well-known preference for formation of *cis* 1,2-disubstituted double bonds in the Wittig reaction of aldehydes without any added base.⁸ The relative stabilities of the isomers under conditions of thermal interconversion confirm these assignments (*vide infra*). Importantly, all six isomers were separated to within 5% of base line on a UCON 50HB2000 capillary GC column.

B. Pyrolysis of Racemic tcc at 220, 240, and 260 $^{\circ}\text{C}$. The interconversion of racemic tcc and ttt by either a chair or possibly a twist pathway was observed when tcc was pyrolyzed in the gas phase at 220, 240, and 260 $^{\circ}\text{C}$ (Scheme II).

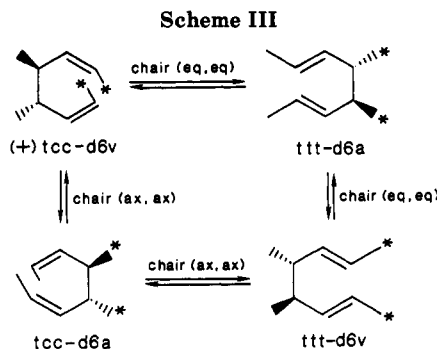
Values for the reversible first-order rate constants were obtained by two methods. The first used a linear least-squares calculation of the standard integrated rate expression. The second method used a Gear algorithm for numerical integration of differential equations⁹ and a Simplex optimization written for IBM-PC and VAX computers.¹⁰ The equilibrium constants used in the calculation were extrapolated from the measured equilibrium values of tcc and ttt at 320 and 305 $^{\circ}\text{C}$ by using the van't Hoff equation. The results of the calculations are given in Table I.

The rate constants determined at the three temperatures were used to calculate $\log k(\text{tcc-ttt}) = 11.36(0.22) - 36000(500)/2.3RT$ and $\log k(\text{ttt-tcc}) = 10.73(0.5) - 37400(1000)/2.3RT$.

Table I. Rate Constants^a for the Interconversion of tcc and ttt

temp, $^{\circ}\text{C}$	$k_1(\text{tcc-ttt})$		$k_1(\text{ttt-tcc})$		K_{eq}
	1st sq	Gear	1st sq	Gear	
220	1.703 (0.031)	1.799	0.147 (0.026)	0.156	11.57
240	7.076 (0.34)	7.151	0.643 (0.031)	0.6495	11.01
260	27.26 (0.58)	29.03	2.572 (0.055)	2.738	10.60

^a k values are $\times 10^5$. Figures in parentheses are the standard deviations.



It was found that ttc (present in small amounts in tcc) rearranges to ett under the reaction conditions (the mole fractions of the two were constant over 3 half-lives of tcc). The stereochemistry of this interconversion is also consistent with either a chair or twist transition state. Pyrolysis of tcc at 240 $^{\circ}\text{C}$ for 15 h resulted in the formation of a new isomer. By comparison of retention times to those of the products from the Wittig reaction which gave the dienes, this material was identified as etc, which could arise from either tcc or ttt by either a boat or a plane transition state. Under these conditions less than 0.35% of etc was formed; however, at 260 $^{\circ}\text{C}$ 0.35% was formed in 2 h, and after 17 h the amount of etc had increased to 4.48% of the total mixture. Concurrent with the formation of etc (260 $^{\circ}\text{C}$, 17 h) was a 17.5% increase in the amount of ttc and ett.

Comparison of the Arrhenius parameters in the rearrangement of tcc to ttt with those obtained by Frey and Solly¹¹ for the interconversion of *cis*- and *trans*-2,6-heptadiene with 3-methyl-1,5-hexadiene at 220–290 $^{\circ}\text{C}$ reveals that the activation energies and entropic demands in the transition state are similar. Doering and Roth and Frey and Solly attributed the preference for the formation of a *trans* isomer over a *cis* isomer as the difference between an axial and equatorial methyl group in the transition state. However, products ttc and ett are unexpected from any of the 3,3-shift transition states described above. In order to characterize these processes higher reaction temperatures were necessary, but examination of the low-temperature degenerate rearrangement of ttt logically precedes that discussion which begins in section E.

C. Degenerate Rearrangement of *threo,trans*-4,5-Dimethyl-2,6-octadiene at 240 $^{\circ}\text{C}$. As a probe of the degenerate rearrangement of ttt and of the twist transition state, the isotopically labeled, optically active form of tcc, (+)-4(*S*),5(*S*)-dimethyl-1,1,1,8,8,8-hexadeuterio-2(*Z*),6(*Z*)-octadiene, (+)tcc-d6v, was synthesized from (*R,R*)-2,3-dimethylsuccinic acid (note that the optical centers are not disturbed in tcc-d6v relative to (*R,R*)-2,3-

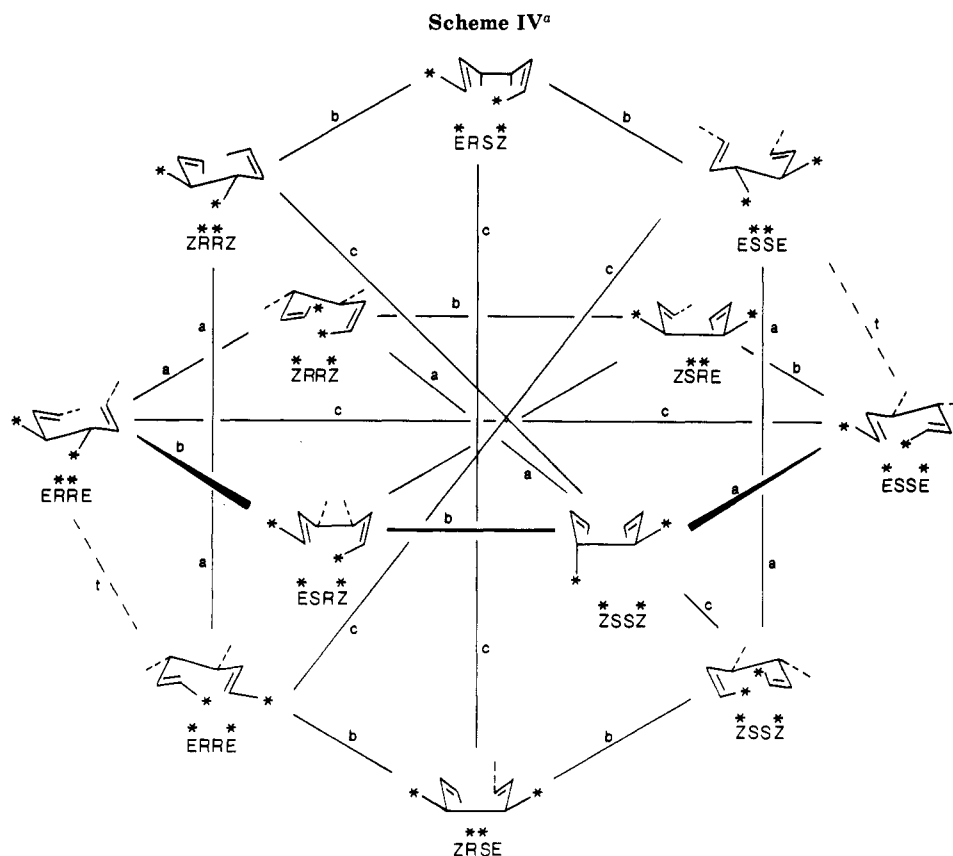
(7) Bone, W. A.; Sprankling, C. H. G. *Trans. J. Chem. Soc.* 1899, 75, 839.

(8) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin/Cummings: Menlo Park, CA, 1972.

(9) Gear, C. W. *Numerical Initial Value Problems in Ordinary Differential Equations*; Prentice-Hall: Englewood Cliffs, NJ, 1971.

(10) Gilbert, K. E.; Gajewski, J. J. *Comput. Chem.* 1985, 9, 191.

(11) Frey, H. M.; Solly, R. K. *J. Chem. Soc., Trans. Faraday Soc.* 1968, 64, 1858.



^a Paths: a, axial chair; b, boat; c, equatorial chair; t, twist (only two are shown). * = CD₃. See text for discussion of the stereo designations.

dimethylsuccinic acid but the group priorities change in so subtle a manner that in Scheme IV and subsequent sections it is still abbreviated as *ZRRZ*). Pyrolysis of (+)tcc-d6v for short reaction times at 240 °C, should result in the formation of three new species ignoring optical activity. Scheme III shows the expected result from chair transition states; note that chair transition states with two vicinal axial methyls (ax,ax) are possible as well as the chair transition state with all equatorial methyls. A twist transition state will give the enantiomers of the dienes in Scheme III.

The chair or twist rearrangement of ttt-d6a to ttt-d6v can be observed by combined NMR and GC analyses. The NMR chemical shift of the methine protons at C4 and C5 differ by approximately 0.4 ppm in tcc and ttt. In addition, the difference between a *cis*- or *trans*-propenyl group can be seen in the methyl chemical shift. Therefore, comparison of the ratio of the methine protons at C4 and C5 to the integration of the methyl resonance for the *trans*-propenyl group allows determination of the ratio of ttt-d6a to ttt-d6v. This ratio equals 2/6 for pure ttt-d6a and 2/3 for a 1:1 mixture of ttt-d6 and ttt-d6v. At any pyrolysis time, the mol fraction of ttt-d6v can be calculated from the NMR integration. Since the mole fractions of ttt and tcc in the pyrolysate (irrespective of label position) can be determined by GC analysis, the relative concentrations of all species can be determined.

Pyrolysis of tcc-d6v for 3, 5, and 8 h at 240 °C resulted in the formation of two new isomers, ttt-d6a and ttt-d6v. Little tcc-d6a was detected. The results of these pyrolyses appear in Table II.

The one way rate constant for the ttt degenerate rearrangement was calculated to be $k(\text{ttt-ttt}) = 3.8(1.0) \times 10^{-5}/\text{s}$ at 240 °C by assuming the rate equations required by Scheme III, using the data in Tables I and II, employing

Table II. NMR Analysis of 240 °C (+)tcc-d6v Pyrolysis

pyro. time, h	relative area			
	methine H	trans-CH ₃	ttt-d6a	ttt-d6v
3.0	1.3	3.1	0.795	0.205
5.0	1.68	3.5	0.694	0.307
8.0	1.75	3.5	0.667	0.333

Concentrations of tcc-d6v, ttt-d6a, and ttt-d6v

pyro. time, h	relative area			
	tcc-d6v ^a	total ttt-d6 ^a	ttt-d6a ^b	ttt-d6v ^b
3.0	47.50	52.50	41.74	10.76
5.0	30.07	69.93	48.53	21.40
8.0	17.38	82.62	55.11	27.51

^a From GC analysis (1.0% error in measurement). ^b From NMR analysis (10.0% error in measurement).

the Gear numerical integration algorithm and Simplex optimization, fixing the previously determined rate constants for the interconversion of tcc and ttt, and fixing the appropriate equilibrium constants to unity (assuming no β equilibrium isotope effects). The free energy of activation at 240 °C is 41.5 kcal/mol and is almost identical with that for the tcc to ttt conversion and with that for the 3,3-shift in 1,5-hexadiene itself.¹²

D. 240 °C Pyrolysis of (+)-4(*S*),5(*S*)-Dimethyl-1,1,1,8,8,8-hexadeuterio-2(*Z*),6(*Z*)-octadiene. To determine the extent of involvement of the twist transition state, it is necessary to examine Scheme IV, which categorizes the stereochemical possibilities for interconversion of the 4,5-dimethyl-2,6-octadienes. Shown in the horizontal hexagonal array are the interconversions of tcc, ttt, and etc expected via classical chair and boat transition states

(12) Doering, W. v. E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* 1971, 27, 5299.

for one optical series. The vertical hexagonal array represents chair and boat interconversions in the opposite series of enantiomers. It is not possible to interconvert the stereoisomers of the horizontal with those of the vertical arrays by chair or boat transition states; however, twist and plane transition states will allow these interconversions. Other mechanistic pathways can be responsible for this interconversion and will be discussed subsequently.

In an effort to determine the energetics of the twist transition state 25–45- μ L samples of (+)tcc-d6v (*ZRRZ* of Scheme IV, named RR there because it is derived from (R,R)-2,3-dimethylsuccinic acid) were pyrolyzed at 240 °C in the gas phase for 33.5 h. The ratio of products was similar to those reported in Table II of the supplementary material; of particular note is the presence of a 10.5:1 ratio of the ttt and tcc isomers with 1.5% of etc, 1% of ttc, and 2% of ett also present. Ozonolysis of the reaction mixture gave the 2,3-dimethyl succinic acids, DMSA, which were treated with 2 equiv of *l*-(-)- α -phenylethylamine (Aldrich). At 360 MHz in CDCl₃ the ¹H NMR of the bis amine salt of racemic DMSA consists of two three-hydrogen doublets at δ 0.897 and 0.963 and two one-hydrogen multiplets at δ 1.857 and 1.975. The upfield resonance in each case results from the *R,R* enantiomer. In the NMR of the bis amine–DMSA salt from the pyrolysis the ratio of the two one-hydrogen singlets was 1:1 as expected for racemic material. However, the *S,S* enantiomer with protio methyls was in excess relative to the *R,R* enantiomer with protio methyls by a factor of 8.5 (1.0). If only the chair transition state were involved, the *S,S* enantiomer with protio methyls and the RR enantiomer with deuterio methyls would result from the ttt diene (see Scheme IV, which depicts the stereochemistry—see also ref 13). The opposite result would be obtained from the bis amine–DMSA salt resulting from the tcc diene formed by a chair transition state or the bis amine–DMSA salt resulting from the ttt diene by the twist transition state (see Scheme IV). The observations are consistent with little incursion of the twist transition state under conditions where the chair transition state had been involved for more than 5 half-lives of ttt interconversions. Ideally, however, the diene should be subjected to conditions where the higher energy boat transition state were traversed to a substantial extent. Unfortunately, other reactions occurred which interfered with the NMR analysis. These are described in part E below.

E. Pyrolysis of ecc and tcc at 290, 305, and 320 °C. The gas-phase pyrolysis of a mixture of tcc or ecc and an internal standard (*n*-nonane) at 290, 305, and 320 °C resulted in the formation of all six diastereomeric dimethyloctadienes. In addition, five minor GC peaks having longer retention times were detected. The relative mole percentage of these five unknowns increased with time. However, the maximum amount formed did not exceed 5% of the total mixture at the longest pyrolysis times. An increase in the relative amount of nonane was observed at all temperatures with the most significant increases occurring during long pyrolysis times at 305 and 320 °C. This is indication of a loss of analyzable material due to either polymerization or the formation of low boiling (gaseous) compounds. The relative percentage increase of internal standard remained below 8% at 320 °C. For short reaction times at 305 or 320 °C or over all time

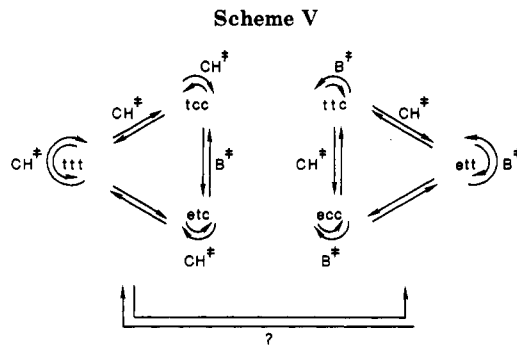


Table III. Deuterium Analysis of Dimethyl Esters of Dimethylsuccinic Acid from Oxidation of the Pyrolysate of (+)-tcc-6vd at 305 °C

	<i>m/e</i>	mDMS rel area	tDMS rel area
1-h Pyrolysis			
<i>d</i> ₀	143	4.4	38.5
<i>d</i> ₃	146	4.7	4.9
<i>d</i> ₆	149	5.0	42.5
3-h Pyrolysis			
<i>d</i> ₀	143	8.0	31.6
<i>d</i> ₃	146	9.3	11.1
<i>d</i> ₆	149	8.8	31.2
6-h Pyrolysis			
<i>d</i> ₀	143	11.2	21.3
<i>d</i> ₃	146	15.7	18.4
<i>d</i> ₆	149	11.6	21.9

intervals at 290 °C, the increase was not relevant.

Scheme V depicts the expected interconversion of the six isomers by chair and boat 3,3-shifts and reveals that the two triads of isomers cannot be interconverted by any "allowed" 3,3-shift transition state.

F. Pyrolysis of (+)-4(*S*),5(*S*)-Dimethyl-1,1,1,8,8,8-hexadeuterio-2(*Z*),6(*Z*)-octadiene: GCMS Analysis. In an effort to determine the energetics of the twist transition state and to provide information on the pathway for interconversion of all six dienes, 25–45- μ L samples of (+)tcc-d6v (*ZRRZ* of Scheme IV, named RR there because it is derived from (R,R)-2,3-dimethylsuccinic acid) were pyrolyzed at 305 °C in the gas phase for 1, 3, and 6 h. Ozonolysis of the 1-h reaction mixture and treatment with 2 equiv of (-)- α -phenylethylamine as described above revealed that the *S,S* enantiomer with protio methyls was in excess relative to the *R,R* enantiomer with protio methyls by a factor of roughly 10; but after the 6-h reaction time the ratio was 1.3. Observation of (R,R)-DMSA with deuterio methyls could indicate incursion of a twist or plane 3,3-shift, but subsequent GCMS experiments revealed an alternative explanation for these observations.

Aliquots of DMSA from the pyrolyses described above were esterified and analyzed by chemical ionization mass spectroscopy CIMS using methane/argon mixed reagent gas. The GCMS of an independently prepared dimethyl *meso*- and *threo*-2,3-dimethylsuccinate mixture (mDMS, tDMS) was obtained and used as a reference for the pyrolysate analyses. In summary, the CIMS spectra were typical of carboxylic esters,¹⁴ and not only were *d*₀ and *d*₆ diesters present but substantial quantities of *d*₃ diesters were found in quantities increasing with pyrolysis time (Table III).

There are two obvious hypotheses for observation of *d*₃ diesters from oxidative degradation of the diene reaction mixture: (1) incursion of a 1,3-shift, possibly by a spiro-

(13) The tcc-*vd* isomer from (R,R)-DMSA would give the ttt-*ad* isomer via chair which gives deuterio-(R,R)-DMSA; a chair 3,3-shift from this ttt-*ad* isomer gives ttt-*vd*, whose degradation product is protio-(S,S)-DMSA; a twist 3,3-shift from the ttt-*ad* isomer gives ttt-*vd*, whose degradation product is protio-(R,R)-DMSA.

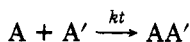
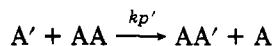
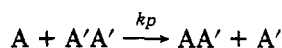
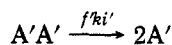
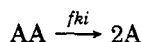
(14) Harrison, H. G. *Chemical Ionization Mass Spectra*; CRC: Boca Raton, FL, 1983.

conjugated bisallyl species¹⁵ or (2) cleavage to two allylic radicals followed by recombination. Formal 1,3-shifts in thermal reactions of 1,5-dienes are not unknown; Koch observed the formation of 1,4-diphenyl-1,5-hexadiene and 1,6-diphenyl-1,5-hexadiene in the irreversible reaction of *meso*-3,4-diphenyl-1,5-hexadiene at 150 °C.¹⁶

G. Crossover Experiment: Pyrolysis of (+)tcc-d6v and tcc. To determine if the formation of *threo*-2,3-dimethylsuccinic-*d*₃ acid upon oxidation of the *d*₆ diene mixture from pyrolysis occurs by an intramolecular mechanism (path 1 above) or an intermolecular process (path 2), a mixture of (+)tcc-d6v and tcc (1:1) was pyrolyzed in the gas phase for 6 h at 305 °C. The material recovered from 10- and 40-μL pyrolyses of this mixture was diluted with methylene chloride and analyzed by GCMS in the CI mode. Despite the fact that (+)tcc-d6v and tcc were separable on capillary GC, the mixture of these dienes from the pyrolysate were inseparable, suggesting the presence of other deuterium isotopomers; further the CIMS revealed the presence of substantial quantities of *d*₃ olefins (Table IV). The areas of the GCMS envelopes for these three ions are reported as a percentage value in Table IV (the GCMS the order of elution of isotopically substituted dienes to be *d*₆, *d*₃, and *d*₀).

The data in Table IV show that the formation of the *d*₃ diene is the result of an intermolecular process that is independent of concentration. It should be noted that the amount of the *d*₃ diene formed in the 5- and 20-μL pyrolyses is roughly equal to the total amount of ecc, ett, and ttc formed after 6 h at 305 °C. If these latter isomers are formed by random combination of the dimethylallyl radicals then half their amount should be *d*₃, but an equivalent amount of *d*₃ material should appear in the other isomers, tcc, ttt, and etc.

The recombination of a dimethylallyl-*d*₀ with a dimethylallyl-*d*₃ radical is not the only conceivable process for the formation of dimethyloctadiene-*d*₃. An alternate proposal involves the S_AR addition of an allyl radical to a diene followed by β-scission to give an allyl radical and *d*₃-substituted diene in a chain process. Both intermolecular processes can be described by the pathways of the reaction scheme below where A is an allyl-*d*₀ moiety, A' is an allyl-*d*₃ moiety, and *f* is the fraction of allyl radicals that recombine to the *d*₀ diene, and *f*' is the fraction of allyl radicals that recombine to the *d*₆ diene.



$$\text{rate} = \frac{d(AA')}{dt} =$$

$$kp[A][A'A'] + kp'[A'][AA] + kt[A][A']$$

If $fki = f'ki'$, $[AA] = [A'A']$, and $kp = kp'$ so that $A = A'$ then the rate law is

$$\text{rate} = 2fki[AA] + kp(2fki/kt)^{1/2}[AA]^{3/2}$$

where the first term results exclusively from cleavage-re-

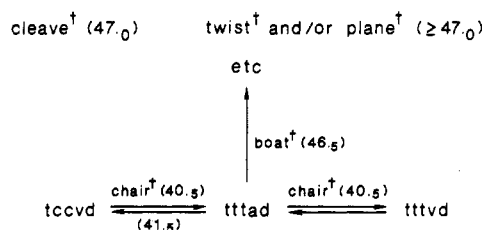
Table IV. CH₄ CIMS and GC Analysis of (+)tcc-d6v + tcc Pyrolysis for 6 h at 305 °C

	<i>m/e</i>	diene <i>d</i> content	rel area
5 μL <i>d</i> ₀ + 5 μL <i>d</i> ₆	137	<i>d</i> ₀	37.0
	140	<i>d</i> ₃	32.7
	143	<i>d</i> ₆	30.4
20 μL <i>d</i> ₀ + 20 μL <i>d</i> ₆	137	<i>d</i> ₀	35.1
	140	<i>d</i> ₃	34.0
	143	<i>d</i> ₆	30.9

GC Analysis of Reaction Mixture

etc, 21.3%; ttt, 39.5%; tcc, 4.1%; ett, 20.4%; ecc, 2.1%; ttc, 12.8%

Scheme VI



combination. The lack of compound concentration rate dependence rules out the addition-β-elimination chain process which has the ³/₂ order term in the rate law.

The kinetic data shows the formation of etc, the product of a presumed boat TS of tcc or ttt, occurs at a rate similar to the tcc,ttt,etc triad and ecc,ett,ttc triad interconversion. Assuming that the ecc,ett,ttc triad is formed by the cleavage-recombination pathway, then the meso esters formed from the other triad by oxidation of ecc and ett would have *d*₃ incorporation, whereas the meso ester from etc would only be *d*₀ or *d*₆. At 3 and 6 h (Tables III and IV) the areas of the *d*₀ and *d*₆ base peaks approximates the known concentration of etc in the kinetic analysis. Thus, not much of the boat transition-state product is formed by cleavage-recombination despite its energetic accessibility. The analyses are consistent in that the total base peak areas at 3 and 6 h for *m/e* 146 are identical with the sum of the concentrations of the ecc, ett, ttc group in the kinetic analysis.

A kinetic analysis of the scheme for interconversion of all protio diastereomers at 290–320 °C [using the Simplex-Gear program with data sets starting from both tcc and ecc and with the constraints of equilibrium constants and *k*(tcc,ttt) fixed by the Arrhenius parameters reported above so that only 14 of the 30 rate constants were to be determined] gave rate constants which reasonably reproduced the experimental data at each temperature. However, good Arrhenius behavior was not obtained, indicating that the correct set of rate constants was not found at each temperature. Evidently, the system is underdetermined and requires data starting with the other diastereomers. This was not pursued because the results were deemed to be unrelated to the propositions defined in the introductory section of this paper.

H. Summary. The major pathways for reaction for ttt (besides its conversions back to tcc and itself via a chair and not a twist transition state) are formation of the boat product, etc, and the cleavage-recombination product, ett, in nearly equal quantities at short reaction times with the tct isomer formed to a much smaller extent (20% of etc and ett). It would appear that the boat pathway is only slightly more favorable than cleavage-recombination in this tetramethyl-substituted 1,5-diene system in contrast to the parent system studied by Goldstein, where the activation free energy for the boat process is ca. 7–8 kcal/mol

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lower in energy than the cleavage activation free energy.¹⁷ Scheme VI summarizes the energy surface for the interconversions of the tetramethyl-1,5-hexadienes at 300 °C.

Experimental Section

General. NMR spectra were recorded on a Varian T-60, EM-390, HR-220, or Nicolet NT-360 spectrometer. Tetramethylsilane (TMS) was used as an internal standard, except when the Nicolet instrument was used. Spectra (360 MHz) were obtained by using the deuteron resonance of the solvent CDCl₃. Chemical shifts are reported in parts per million (ppm) downfield of TMS. Infrared spectra were obtained with a Perkin-Elmer Model 298 spectrometer. Mass spectra were obtained with a Hewlett-Packard Model 5985 B GCMS, equipped with a 30 m DB-5 capillary column, in the chemical ionization mode by using an argon/methane mixed reagent gas. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are reported uncorrected. Preparative gas chromatography was performed with a Varian Aerograph Model 90-P, with helium as the carrier gas. Analytical gas chromatography utilized a Varian Model 3700 GC, adapted to accept capillary columns, and a Hewlett-Packard Model 3390-A integrator.

(*R,R*)-(-)-Dimethyl *trans*-2,3-Dimethylsuccinate ((-)-tDMS). (*R,R*)-(+)-*trans*-2,3-Dimethylsuccinic acid (5.2 g, 0.036 mol), mp 124–125 °C, [α]_D²⁵ (H₂O) +8.26° (0.03), reported [α]_D²¹ +8.42° (H₂O),¹⁸ dissolved in 80 mL dry THF and slowly added to 300 mL of an ethereal solution of diazomethane (prepared from 17.3 g of *n*-methylnitrosourea) cooled to 0 °C. The reaction mixture was stirred at room temperature until the faint yellow color was discharged. The bulk of the ether and THF was removed by rotary evaporation. The remaining solvent was removed under vacuum, leaving 5.25 g of a pale yellow liquid. The yield after vacuum transfer was 5.2 g (colorless liquid), 0.059 mol, 83%: [α]_D²⁵ (cyclohexane) -11.74° (0.5°) (reported [α]_D²¹ -9.42°, [α]_D²² -9.32°¹⁸).

Ethyltriphenylphosphonium Bromide. Bromoethane (28 g, 0.26 mol), triphenylphosphine (53 g, 0.20 mol), and 190 mL of toluene were placed in a thick-walled glass vessel and sealed with a crown cap. The stirred mixture was heated in an oil bath at 110 °C for 36 h. After cooling, the crystals were isolated by suction filtration, washed with benzene, and dried at 10 Torr. Recrystallization from water gave 50.6 g (0.136 mol, 68% yield) of white crystals, mp 195–198 °C.

***threo*-4,5-Dimethyl-2,6-octadienes (tcc, ttc, ttt).** The procedure follows that of Berson et al.²⁰ A typical reaction is described. tDMS (8.1 g, 46.6 mmol), dried over K₂CO₃, and 200 mL of dry THF were added to a flame-dried, nitrogen-purged 1000-mL round-bottom flask fitted with a low-temperature thermometer, addition funnel, N₂ inlet with septum, and magnetic stir bar. The mixture was cooled to -70 °C in a dry ice/acetone bath. Red-Al (18.8 mL, 47 mmol, 3.4 M in toluene) and 25 mL dry THF were combined inside the addition funnel and cooled to -70 °C in a funnel wrapped loosely with aluminum foil so as to hold powdered dry ice. The Red-Al solution was slowly added over 1 h while the internal temperature of the flask was maintained below -65 °C. The reaction solution was stirred under nitrogen at -70 °C for 12 h.

Ethylenetriphenylphosphorane (94 mmol) was prepared in THF by treating a suspension of 34.9 g of ethyltriphenylphosphonium bromide (dried at 2 Torr, 50 °C) with 37.6 mL (94 mmol) of *n*-butyllithium in hexane (Aldrich) at 0 °C. This bright red ylide solution was stirred at room temperature until all of the solid dissolved. This solution was cooled to -70 °C and forced through a glass tube (precooled to -78 °C) under a positive pressure of nitrogen into the dialdehyde solution. The reaction solution was slowly warmed to room temperature and stirred for 5 h. Water

(10 mL) was added, and the light brown suspension was stirred for 30 min, cooled to 0 °C, and acidified by the slow addition of 100 mL of a 20% H₂SO₄ solution. The colorless solution was stirred for 30 min, diluted with 300 mL of H₂O, and extracted four times with 100 mL of pentane. The combined pentane extracts were washed twice with 50 mL of a 10% (wt/vol) sodium bicarbonate solution, three times with 50 mL of H₂O, and twice with 30 mL of a saturated NaCl solution. After drying over MgSO₄, the solvents were removed by distillation through a 7-cm Vigreux column packed with glass helices. tcc, ttc, and ttt were isolated from the reaction solvents by preparative GC using a 20 ft × 1/4 in. copper column packed with 25% Carbowax 20M on 60/80 mesh Chromosorb P (130 °C, He flow 60 mL/min, t_R 21–22 min). GC peaks for these three isomers overlapped, but purified tcc could be obtained by peak splitting. The ratio of the crude tcc/ttc/ttt mixture was determined by capillary GC to be 76:19:5, respectively (70 m × 0.25 mm ID capillary column coated with UCON 50 HB 2000, FID detector): typical yield, 52%; IR (neat) [three diene mixture] 720, 960 cm⁻¹; IR (neat) [tcc] 720, 960 cm⁻¹ moderate; NMR (360 MHz, CDCl₃) [tcc] δ 0.925 (d, 6, *J* = 6.5 Hz), 1.614 (d, 6, *J* = 6.84), 2.435 (p, 2, *J* = 6.12 Hz), 5.213 (d of t, 2), δ 5.42 (m, 2), [ttc] δ 0.894–0.947 (m, 6), 1.607–1.660 (m, 6), 2.05 (m, 1), 2.42 (m, 1), 5.18–5.50 (m, 4), [ttt] δ 0.903 (d, 6, *J* = 6.48 Hz), 1.656 (d, 6, *J* = 5.04 Hz), 2.04 (p, 2, *J* = 5.04 Hz), 5.342 (m, 4).

***erythro*-4,5-Dimethyl-2,6-octadienes (ecc, etc, ett).** Following the procedure used for the synthesis of the three dienes, mDMS was transformed into ecc, etc, and ett. Isolation and analysis (using the columns previously described) indicated that ecc, etc, and ett were formed in a 69:31:2 ratio: typical yield 50%; NMR (360 MHz, CDCl₃) [ecc] δ 0.883 (d, 6, *J* = 6.19 Hz), 1.610 (d, 6, *J* = 6.48), 2.272 (p, 2, *J* = 5.8 Hz), 5.20 (t, 2, *J* = 10.0 Hz), 5.424 (m, 2), [ett] δ 0.900 (d, 6, *J* = 6.12), 1.65 (d, 6, *J* = 5.4 Hz), 1.917 (p, 2, *J* = 4.68 Hz), 5.24–5.40 (m, 4).

2,2,2-Trideuterioethanol.²¹ Diethylene glycol dimethyl ether (diglyme, Fisher) was dried over KOH and distilled from sodium at 10 Torr. Dry diglyme (500 mL) was added to a nitrogen-purged 1-L three-necked round-bottom flask equipped with a reflux condenser, addition funnel, and magnetic stir bar. This was followed by the cautious addition of 20 g (0.53 mol) of LAH. A solution of 25 g (0.39 mol) of acetic-*d*₄ acid (99.5% D, Aldrich) in 250 mL of dry diglyme was added slowly to the LAH slurry, which had been precooled to 0 °C. The mixture was stirred at room temperature for 10 h and then heated at 90 °C for 20 h. After cooling to 0 °C, the excess LAH was quenched by the addition of 125 mL of diethylene glycol monoethyl ether (dried over MgSO₄ and distilled at 5 Torr). Distillation at reduced pressure into a dry ice/acetone cooled receiver gave 150 mL of diglyme/alcohol mixture. Redistillation at atmospheric pressure through a 7-cm Vigreux column isolated 26.4 g of wet 2,2,2-trideuterioethanol, bp 78 °C.

2,2,2-Trideuterioethanol.²² The 2,2,2-trideuterioethanol from above (26.4 g) was placed in a 100-mL round-bottom flask and was cooled to -5 °C in an ice/salt bath. PBr₃ (56.9 g, 0.22 mol) was slowly added, and when the addition was complete the mixture was stirred for an additional 2 h at 0 °C. The ethyl-*d*₃ bromide was removed by distillation, the liquid being collected in a receiver cooled to 0 °C. The product was washed with a 10% sodium bicarbonate solution to neutralize the HBr and then dried over MgSO₄. 2,2,2-Tribromoethane (20 g, 0.18 mol) was obtained in 46% yield from acetic-*d*₄ acid: NMR (60 MHz CCl₄) δ 3.38 (br s), 2.6 (s) (H₂O).

(2,2,2-Trideuterioethyl)triphenylphosphonium Bromide. 2,2,2-Trideuterioethanol (20 g, 0.18 mol), 47 g (0.018 mol) of triphenylphosphine, and 120 mL of toluene were sealed in an autoclave. The mixture was stirred while being heated at 120 °C for 36 h. After cooling to room temperature, white, hairlike crystals were isolated by suction filtration and were washed with benzene. After drying at 10 Torr, 56.8 g (0.15 mol, 84% yield) of phosphonium salt was obtained: mp 194–195 °C.

(+)-4(*R*),5(*R*)-Dimethyl-1,1,1,8,8,8-hexadeuterio-2(*Z*),6-*(Z)*-octadiene (*ZRRZ* or (+)tcc-d₆v). The procedure used to synthesize the three dienes was followed by using 18 mmol of

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(-)-tDMS, $[\alpha]^{25} -11.74^\circ$. The dialdehyde was treated with 36 mmol of ethylidide- d_3 , prepared by deprotonating (2,2,2-trideuterioethyl)triphenylphosphonium bromide with 1 equiv of a 2.5 M *n*-butyllithium solution. After workup, 0.62 g of (+)tcc-d6v, $[\alpha]^{25} +46.1^\circ$ (cyclohexane), and 0.21 g of a mixture of ttc-d6v and ttt-d6v were isolated by preparative GC: total yield, 32%; NMR (360 MHz, $CDCl_3$) [(+)tcc-d6v] δ 0.921 (d, 6, $J = 6.12$ Hz), 2.424 (p, 2, $J = 6.48$ Hz), 5.213 (t, 2, $J = 9.72$ Hz), 5.402 (d, 2, $J = 10.8$ Hz).

2,3-Dimethylsuccinic Acid, Bis[(-)- α -methylbenzylamine] Salt. The salts of *meso*- and *threo*- and optically active (+)-*threo*-DMSA were prepared by dissolving a small quantity of the diacid in a minimum amount of absolute methanol. A slight excess of (-)- α -phenylethylamine (PEA) (Aldrich, $[\alpha]^{20} -39^\circ$, neat) was added, and the methanol was removed under vacuum. The white solid was washed with a small amount of benzene and dried at 10 Torr. The NMR (220 MHz) spectrum of the racemic *threo*-DMSA bis(PEA) salt was obtained by using different solvents to achieve the greatest NMR chemical shift difference between the methyl resonances of (+)- and (-)-2,3-dimethylsuccinic acid. A 14-Hz chemical shift difference from using CCl_4 was the largest of the six solvent systems examined (CCl_4 , $CDCl_3$, $CCl_4/CDCl_3$ (1:2), acetone- d_6 , CD_3CN , and $CDCl_3$ /benzene- d_6 (2:3) were tested). However the low solubility of the salt resulted in an NMR spectrum with a very low signal-to-noise ratio. Spectrum clarity was maximized while some resolution was sacrificed by using $CDCl_3$ as the solvent. Clean base line separation of the methyl resonances in the (+)- and (-)-isomers was only achieved when a 360-MHz instrument was used: NMR (360 MHz, $CDCl_3$) [(+)tDMSA bis(PEA) salt] δ 0.897 (d, 6, $J = 6.12$ Hz), 1.504 (d, 6, $J = 6.84$), 1.857 (br s, 2), 4.18 (q, 2, $J = 6.84$ Hz), 7.2–7.41 (m, 10), [tDMSA + (+)tDMSA bis(PEA) salt] δ 0.894 (d, $J = 5.4$ Hz), 0.963 (d, $J = 5.4$ Hz) [total 1H in δ 0.894 and 0.963 = 6], 1.503 (d, 6, $J = 6.84$ Hz), 1.811 (br s), 1.975 (br s) [total 1H in δ 1.811 and 1.975 = 2], 4.162 (q, 2, $J = 6.84$ Hz), 7.21–7.41 (m, 10), [mDMSA bis(PEA) salt] δ 0.946 (d, 3, $J = 6.84$ Hz), 0.951 (d, 3, $J = 6.84$ Hz), 1.528 (d, 6, $J = 6.48$ Hz), 2.384 (q, 2, $J = 6.84$ Hz), 4.259 (q, 2, $J = 6.84$ Hz), 7.26–7.40 (m, 10).

Pyrolyses. All pyrolyses were conducted in a well-conditioned 2-L Pyrex glass bulb fitted with a Teflon vacuum stopcock and immersed in a molten sodium nitrite/potassium nitrate (7:10) salt bath. The conditioning of the bulb, the construction of the constant temperature bath, and the construction of the vacuum system for sample input and retrieval have been previously described.²²

The bath temperature was maintained by two devices. A 500-W Vycor immersion resistance heater attached to a variable transformer was used for crude adjustments. A Bayley precision temperature controller Model 124 and a 250-W knife blade immersion resistance heater was used to maintain the temperature of the bath to within 0.1 °C. Temperature was monitored by an Omega platinum resistance thermometer and an Omega trendicator Model 410A digital thermometer.

All pyrolyses used samples (tcc, ecc, (+)tcc-d6v) that were obtained from a single synthesis and were therefore uniform throughout the course of this work. All kinetic runs used sample sizes of 1.5 μ L or less. The pyrolysate was diluted with pentane and analyzed by capillary VPC soon after it was recovered. Experiments had shown that the starting material and pyrolysate were stable at room temperature.

Pyrolysate Oxidation: Formation of *meso*- and *threo*-DMSA. The diene mixture recovered after pyrolysis (25–45 μ L) was dissolved in 2–3 mL of dry ethyl acetate and treated with ozone at -78 °C until the blue color persisted for 10 min. The solvent was concentrated to ca. 15 mL under vacuum, and then 0.6 mL of acetic acid and 1.2 mL of 30% hydrogen peroxide were added via glass pipet. This mixture was heated at reflux for 1 h, and then the peroxide solution was reduced under vacuum to

a very small volume. The colorless residue was twice taken up with 1 mL of water and concentrated in vacuo. For the pyrolysis of (+)tcc-d6v at 240 °C the residue was dissolved in 1 mL of dry methanol and 0.04 mL (*S*)- α -phenylethylamine was added. After removal of all volatiles under vacuum, the residue was dissolved in $CDCl_3$, and the 1H NMR spectrum was recorded at 360 MHz.

GCMS Analysis of the Dimethyl 2,3-Dimethylsuccinates from the Pyrolysate of (+)tcc-d6v at 305 °C. After recrystallization from benzene, the diacids were esterified with diazomethane. The GC peaks of the diester diastereomers were separated by 25 s (30 m \times 0.25 mm i.d. DB-5 column, 80–150 °C ramped 10 deg/min), with the *meso* diester being eluted first. Both *meso* and *threo* diesters had CIMS spectra typical of carboxylic esters.¹⁴ For comparison, a mixture of tcc, ttt, and ttc (with 5% erythro impurity) was oxidized and esterified. The GC retention times and the CIMS were identical with those obtained with the independently prepared sample.

The diesters from the oxidative degradation of the 3-h, 305 °C, *ZRRZ* pyrolysis mixture showed two broad GC peaks with retention times corresponding to the *meso* and *threo* diesters. The larger *threo* diester peak was saddle shaped (retention times of the two apexes were 6.58 and 6.68 min), indicating the presence of at least two unique species. Examination of various ions revealed the presence of d_0 , d_3 , and d_6 diesters with little of the d_1 , d_2 , d_4 , and d_5 isotopomers being present. Selective ion monitoring of the $M - 31$, $M + 1$, $M + 29$, and $M + 43$ peaks for the d_0 , d_3 , and d_6 diesters was used to analyze the pyrolysates. The results appear in Tables XI and XII of the supplementary material. Table III lists the relative areas of the $M - 31$ base peaks for the d_0 , d_3 , and d_6 diesters from the 1-, 3-, and 6-h pyrolyses.

Crossover Experiment: Pyrolysis of (+)tcc-d6v and tcc. The material recovered from 10- and 40- μ L pyrolyses of a 1:1 mixture of tcc and (+)tcc-d6v at 305 °C for 6 h was diluted with methylene chloride and analyzed by GCMS in the CI mode. The CIMS of (+)tcc-d6v (FW = 144) had m/e 72 (100, base peak), 143 (17.5), and 142 (6.7) with other ions at m/e 86 (14.3), 100 (15.5), and 145 (1.9). The peaks at m/e 143 and 142 correspond to $[M - H]^+$ and $[M - D]^+$, respectively, resulting from abstraction of allylic H or D. The m/e 100 peak is the result of loss of $HC=CHCD_3$. The spectral pattern and the observation of an $M - 1$ peak is typical for olefins.¹⁴ The possibility of hydrogen-deuterium exchange was ruled out by the absence of peaks in the m/e 130–141 range. As expected for tcc (FW = 138) the CIMS had m/e 69 (100, base peak), 137 (18.4), and 97 (18.5). No m/e 136 was observed. The $M - 1$ peaks [m/e 137 (d_0), 140 (d_3), 143 (d_6)] were monitored in the analysis of the three pyrolyses. The areas of the GCMS envelopes for these three ions are reported as a percentage value in Table IV.

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Registry No. (-)-tDMS, 58342-54-4; tcc, 110269-18-6; ttc, 110269-19-7; ttt, 110269-20-0; mDMS, 29800-12-2; ecc, 110269-21-1; etc, 110269-22-2; ett, 110269-23-3; (+)tcc-d6V, 110205-72-6; 2,2,2-trideuterioethanol, 1759-87-1; 2,2,2-trideuteriobromoethane, 7439-86-3; (2,2,2-trideuterioethyl)triphenylphosphonium bromide, 1560-55-0; 2,3-dimethylsuccinic acid bis[(-)- α -methylbenzylamine] salt, 110205-73-7.

Supplementary Material Available: Data for the gc analyses of all pyrolyses, GCMS runs, and the 1H NMR of the DMSA-PEA salts (11 pages). Ordering information is given on any current masthead page.