Activation Parameters for 1,5-Hydrogen Transfer and Intramolecular Cycloaddition in a Thermally Generated Cyclopentane-1,3-diyl

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Abstract: The biradical 2-methyl-2-(3-phenylpropyl)cyclopentane-1,3-diyl is generated reversibly by gas-phase pyrolysis of a stereoisomeric mixture of the corresponding bicyclo[2.1.0]pentane derivatives. Three reactions of the biradical (besides ring closure) are detected. One is ring opening to 3-methyl-3-(3-phenylpropyl)-1,4-pentadiene. A second is intramolecular transfer of a benzylic hydrogen to the cyclopentane-1,3-diyl. An activation enthalpy of 8 kcal/mol is estimated for this 1,5-hydrogen transfer. The third reaction is intramolecular cycloaddition of the 1,3-diyl to the phenyl ring. An activation enthalpy of 7 kcal/mol is estimated for this cycloaddition reaction. Two reactions of the new biradical generated by 1,5-hydrogen transfer are detected. One is ring closure to give stereoisomeric *cis*-1-methyl-4-phenylbicyclo[3.3.0]octanes; the other is transfer of a second hydrogen in a reaction analogous to the disproportionation of alkyl radicals. The ring closure and second hydrogen transfer exhibit no temperature dependence in the ratio of their rate constants and are thus judged to be activationless processes. These reactions of thermally generated, presumably singlet biradicals are compared with the reactions of related monoradicals. The cyclopentane-1,3-diyl derivative is judged to have very little in the way of dipolar character and thus to be near one end of a hypothetical spectrum of intermediates encompassing singlet biradicals and zwitterions.

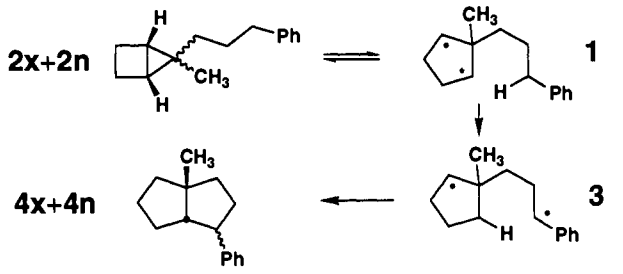
The class of reactive intermediates known as "singlet biradicals" (or diradicals) can encompass species exhibiting a wide range of properties, with varying degrees of radical and zwitterionic or dipolar character.[1] At one end of this spectrum of intermediates could be purely covalent biradicals with little or no dipolar character. At the other end might be zwitterions with little or no radical character. In between could be intermediates with some of the characteristics of each. Some examples of these middle-ground intermediates have received recent attention because of their apparent relationship to the activity of the enyne–allene antitumor antibiotic neocarzinostatin.[2]

If the structural features that determine the position of a biradical in the spectrum are to be understood, then the parameters of the problem must be clearly defined. In particular, the chemical behavior characteristic of singlet biradicals at each end of the spectrum needs to be elucidated. This paper reports the behavior of a biradical that is expected to be at or near the covalent (i.e. nonpolar) end of the spectrum.

The biradical selected for investigation was a derivative of cyclopentane-1,3-diyl.[3] Such biradicals can be reversibly generated from the corresponding bicyclo[2.1.0]pentane, by heating to about 150 °C.[4] Reversible generation is not a prerequisite for study of biradicals such as the didehydrobenzenes or didehydrotoluenes, which are protected from self-annihilation by the strain in their ring-closed isomers.[5] However, it is necessary if one hopes to study reactions of unstabilized singlet biradicals for which ring closure is feasible.

The particular derivative of cyclopentane-1,3-diyl chosen for study was compound **1**, shown in Scheme I.[6] By analogy with

Scheme I



literature precedent,[4] **1** would be formed during thermal interconversion of *exo*- and *endo*-bicyclo[2.1.0]pentanes **2x** and **2n**.

The 3-phenylpropyl substituent was selected to provide the opportunity for an exothermic 1,5-hydrogen shift, giving biradical **3**, which would close to stereoisomeric bicyclo[3.3.0]octanes **4x** and **4n** (Scheme I). The methyl substituent in **1** was introduced to inhibit cyclopentene formation by 1,2-shift from C2.

In addition to the hydrogen shift and subsequent ring-closure processes shown in Scheme I, some additional interesting and unanticipated reactions occurred. These will be described below.

Synthesis of Reactants and Identification of Products. A mixture of **2x** and **2n** was prepared as shown in Scheme II. Since rapid interconversion of **2x** and **2n** was anticipated during their pyrolysis,[4] no attempt was made to separate them.

Pyrolysis of **2** (the designation **2** will be used to indicate the mixture **2x** + **2n**) was conducted in the gas phase in sealed lead-glass tubes in a salt bath at 268–328 °C. Lead glass was used because Pyrex was found to cause acid-catalyzed reactions, even when the reaction was run in the presence of bases such as 2,6-lutidine or when the glass was pretreated with ammonium hydroxide and/or dimethyldichlorosilane. The reaction in the lead-glass tubes resulted in the formation of several products. A typical gas chromatography (GC) trace is shown in Figure 1.

Being hydrocarbons lacking functional groups, the bicyclooctanes, **4x** and **4n**, were difficult to identify purely by spectroscopic means. Hence, independent syntheses of bicyclooctanes **4** and

(1) Salem, L.; Rowland, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 92.
(2) Myers, A. G.; Dragovich, P. S.; Kuo, E. Y. *J. Am. Chem. Soc.* **1992**, *114*, 9369.
(3) (a) Buchwalter, S. L.; Closs, G. L. *J. Am. Chem. Soc.* **1975**, *97*, 3857. (b) Buchwalter, S. L.; Closs, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 4688.
(4) Baldwin, J. E.; Ollerenshaw, J. *J. Org. Chem.* **1981**, *46*, 2116.
(5) (a) Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660. (b) Breslow, R.; Napierski, J.; Clarke, T. C. *J. Am. Chem. Soc.* **1975**, *97*, 6275. (c) Dewar, M. J. S.; Li. W.-K. *J. Am. Chem. Soc.* **1974**, *96*, 5569.
(6) For the preliminary communication on this work, see: Peterson, T. H.; Carpenter, B. K. *J. Am. Chem. Soc.* **1992**, *114*, 1496.

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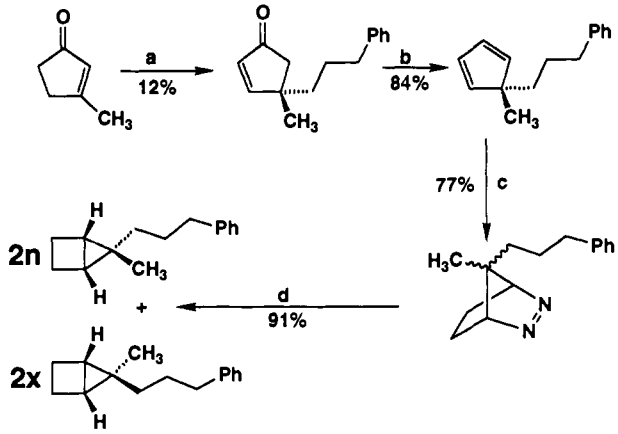
Scheme II. Synthesis of Reactants **2x** and **2n**[a]



[a] Reagents were as follows: (a) (i) $Ph(CH_2)_3MgBr/(Bu_3P)CuI$; (ii) NH_4Cl/H_2O; (iii) LDA; (iv) PhSeBr; (v) 30% H_2O_2. (b) (i) $NaBH_4$; (ii) $CH_3P(OPh)_3^+ I^-$. (c) (i) 4-Phenyl-1,2,4-triazoline-3,5-dione; (ii) H_2/Pd; (iii) KOH/CH_3OH, $(CH_3)_2CHOH$; (iv) H_3O^+; (v) $CuCl_2$; (vi) NH_4OH. (d) *hν*.

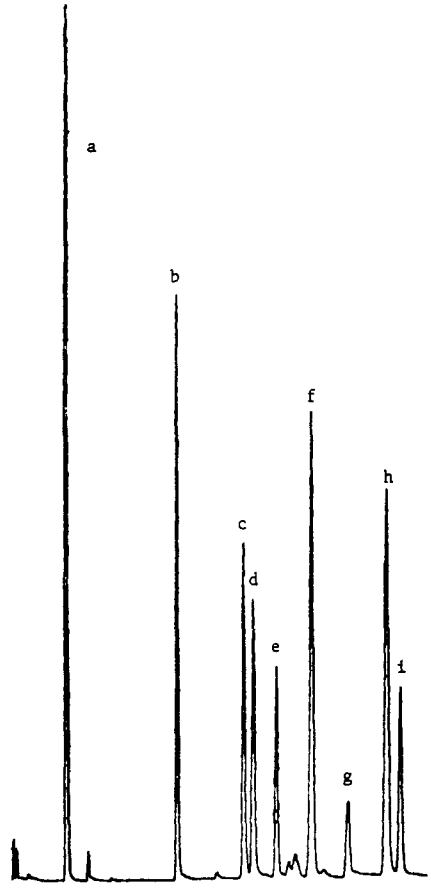
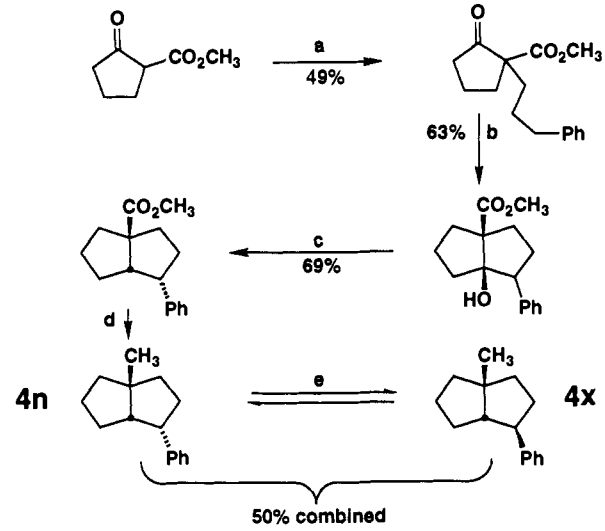


Figure 1. Gas chromatography trace of pyrolysis sample. Peak identification is as follows: (a) cyclododecane internal standard; (b) product **5**; (c) product **7**; (d) product **4x**; (e) product **4n**; (f) reactant **2n** or **2x**; (g) unknown product; (h) reactant **2x** or **2n**; (i) product **6**.

the expected diene **5** were undertaken. These syntheses are summarized in Schemes III and IV. Comparison of the GC–mass spectra of the products from pyrolysis of **2** with those of the genuine samples of **4x**, **4n**, and **5** revealed that all three compounds were formed in the pyrolysis reaction.[7]

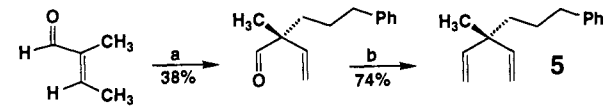
In addition to these compounds, several other products were detected. One was identified as alkene **6** by independent synthesis (Scheme V). A second was identified as the internal cycloadduct **7** by its ^1H NMR spectrum (notably showing the presence of alkene hydrogens and the absence of phenyl hydrogens), its mass

Scheme III. Independent Synthesis of **4x** and **4n**[a]



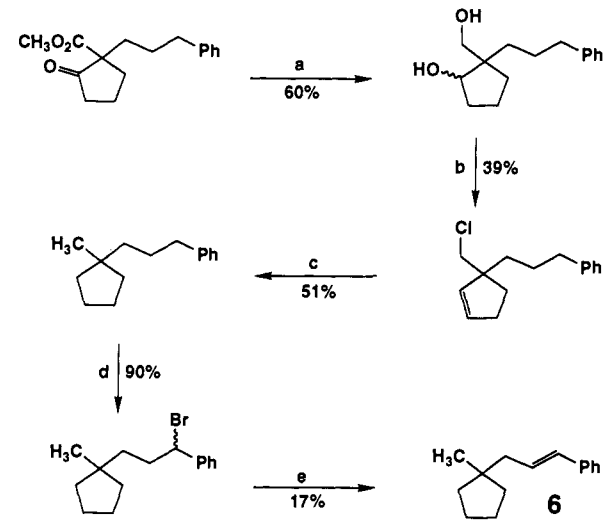
[a] Reagents were as follows: (a) (i) LiOH/DMSO; (ii) $Ph(CH_2)_3I$. (b) (i) NBS/$(PhCOO)_2$; (ii) NaI/acetone; (iii) SmI_2/THF. (c) (i) $POCl_3$/pyridine; (ii) H_2/Pd. (d) (i) $LiAlH_4$; (ii) H_3O^+; (iii) *n*-BuLi; (iv) TsCl; (v) $LiAlH_4$. (e) *n*-BuLi/*t*-BuOK.

Scheme IV. Independent Synthesis of **5**[a]



[a] Reagents were as follows: (a) (i) $C_6H_{11}NH_2/C_6H_6$; (ii) LDA; (iii) $Ph(CH_2)_3Br$; (iv) $(COOH)_2/H_2O$. (b) $Ph_3P{=}CH_2$.

Scheme V. Independent Synthesis of **6**[a]

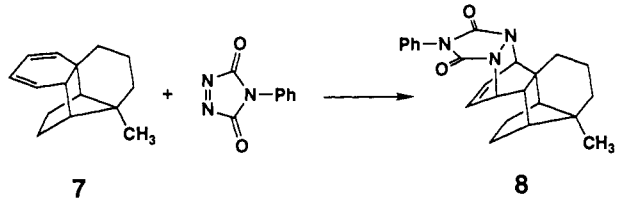


[a] Reagents were as follows: (a) (i) $LiAlH_4$; (ii) H_3O^+. (b) $POCl_3$/pyridine, DMAP. (c) (i) H_2/Pd, AcOH; (ii) Bu_3SnH/AIBN. (d) NBS/$(PhCOO)_2$. (e) *t*-BuOK/DMSO.

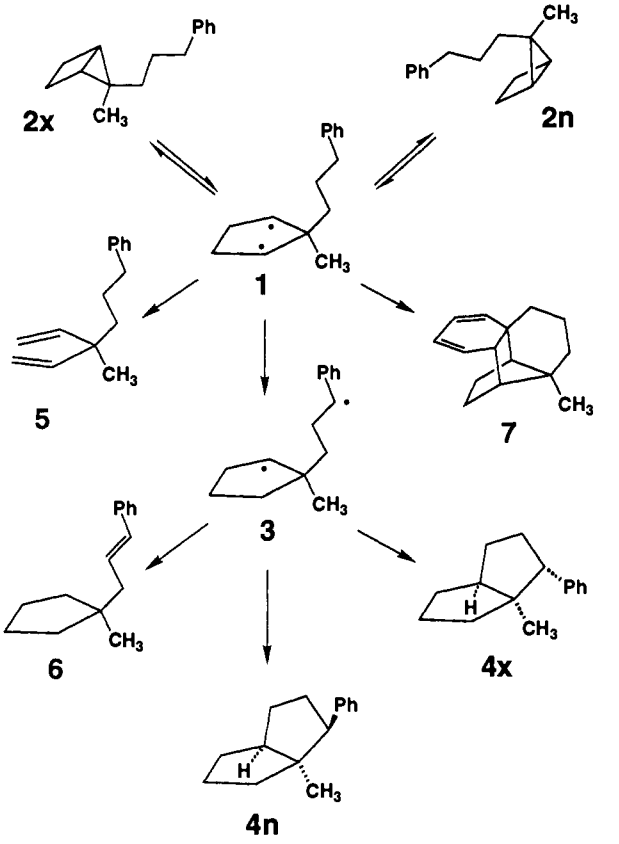
spectrum (showing it to be an isomer of the starting materials), and its ability to undergo a Diels–Alder reaction with *N*-phenyltriazolinedione, to give an adduct whose high-resolution mass spectrum and ^1H NMR spectra were consistent with structure **8** (Scheme VI). Of the remaining products, six were detected in trace quantities (totaling approximately 3% of the product) and were not investigated, but one (peak g in Figure 1) was formed

(7) The distinction between **4x** and **4n** was made on the basis of an expected *exo* stereochemistry for the hydrogenation step in the independent synthesis of **4**. It is possible that this assumption is incorrect because MMX calculations (ref 12) surprisingly suggest that **4n** is about 2 kcal/mol lower in heat of formation than **4x**. Thus, if the stereochemistry of hydrogenation reflected this difference, our assignment would be incorrect.

Scheme VI



Scheme VII. Proposed Mechanism for the Formation of the Observed Products in the Thermal Rearrangement of Bicyclo[2.1.0]pentanes **2x** and **2n**



in significant amount (approximately 5% of the product). This compound remains unidentified, despite our best efforts. The cyclopentene derivatives that would have been formed by hydrogen migration in **1** were independently synthesized, but shown not to be present.

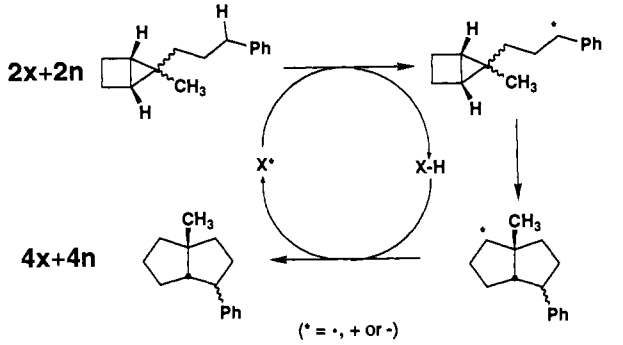
Mechanisms of Product Formation. The mechanism that we currently favor for formation of the identified products is shown in Scheme VII.

Alternative mechanisms are possible, in principle, for the formation of all of the products. The conversion of **2** to **4x** and **4n** could take place by concerted $_\sigma2 + _\sigma2$ reactions (of unknown stereochemistry) involving the C1–C4 bond and the diastereotopic benzylic hydrogens. The formation of **5** could be a concerted $_\sigma2_s + _\sigma2_a$ reaction involving the C1–C4 and C2–C3 bonds of the bicyclo[2.1.0]pentane ring.[8] The formation of alkene **6** could, in principle, be a concerted $_\sigma2_s + _\sigma2_s + _\sigma2_s$ reaction involving

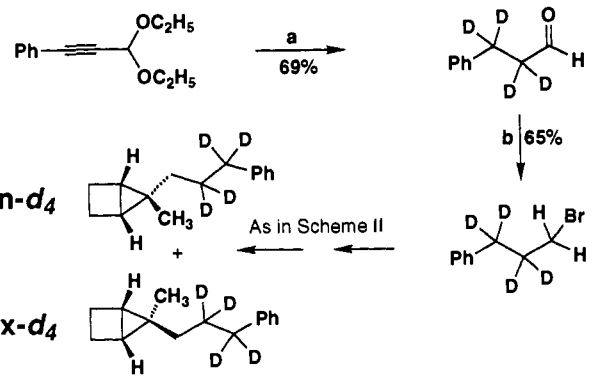
(8) The ring opening of bicyclo[2.1.0]pentanes is known to follow a stereochemical path consistent with that expected for a $_\sigma2_s + _\sigma2_s$ reaction: Berson, J. A.; Bauer, W.; Campbell, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 7515.

(9) We are unaware of any precedent for this $_\sigma2_s + _\sigma2_s + _\sigma2_s$ reaction, but the analogous $_\sigma2_s + _\sigma2_s + _\pi2_s$ process, in which two hydrogens are transferred concertedly from an alkane to an alkene, is known: (a) Hagenbuch, J.-P.; Stampfli, P.; Vogel, P. *J. Am. Chem. Soc.* **1981**, *103*, 3934. (b) Mackenzie, K.; Proctor, G.; Woodnut, D. J. *Tetrahedron* **1987**, *43*, 5981. (c) Paquette, L. A.; Kesselmayer, M. A.; Rogers, R. D. *J. Am. Chem. Soc.* **1990**, *112*, 284. (d) Frontera, A.; Suñer, G. A.; Deyà, P. M. *J. Org. Chem.* **1992**, *57*, 6731.

Scheme VIII



Scheme IX. Synthesis of **2n**-d_4 and **2x**-d_4[a]



[a] Reagents were as follows: (a) (i) D_2/Pd, EtOAc; (ii) H_3O^+. (b) (i) $LiAlH_4$; (ii) H_3O^+; (iii) NBS/Ph_3P.

simultaneous transfer of two hydrogens from the phenylpropyl side chain and cleavage of the C1–C4 bond.[9] Finally the cycloaddition leading to **7** could be a concerted (nominally forbidden) $_\sigma2_s + _\pi2_s$ reaction.

Since these alternative mechanisms do not share common intermediates, all four reactions would have to be occurring at comparable rates by coincidence in order to explain all of the products, a requirement that we feel makes the competition implausible. The lack of precedent for most of these concerted reactions adds to their implausibility, in our view.

A more plausible alternative mechanism for the reactions leading to the bicyclooctanes would be a surface-catalyzed process in which a surface site (called X* in Scheme VIII) abstracts a benzylic hydrogen to create a reactive intermediate (radical, cation, or anion) that then attacks the C1–C4 bond of the bicyclopentane, creating a bicyclo[3.3.0]octyl intermediate (radical, cation, or anion) that can take the hydrogen back from the surface. This mechanism is testable, because it would not be expected to be purely intramolecular and is thus susceptible to scrutiny by a double-labeling crossover study.

The crossover study was conducted as follows. The bicyclopentanes **2**-d_4 were synthesized, as shown in Scheme IX, and mixed with equal portions of their unlabeled analogs, **2**. Thermal rearrangement of the mixture led to the usual products. The bicyclo[3.3.0]octanes were analyzed by GC–mass spectrometry and found to contain d_0 and d_4 products, with ≤7% of the d_1 and d_3 compounds that would have been expected to be produced in the surface-catalyzed reaction.

In summary, the near-complete intramolecularity of the bicyclooctane formation and the implausibility of a competition among four unprecedented concerted reactions lead us to favor the mechanism shown in Scheme VII for the formation of the identified products.

Kinetics of the Rearrangements. Kinetic experiments were conducted in the gas phase in sealed lead-glass tubes. Capillary GC was used to analyze the reaction mixture as a function of

Table I. Rate Constants × 10^7 (s^{-1}) and Isotope Effects for Formation of the Bicyclooctanes, **4x + 4n**, and Their Tetradeuterio Analogs

	product		
T (°C)	**4x + 4n**	(**4x + 4n**)-d_4	isotope effect
268	4.42 ± 0.52	1.52 ± 0.25	2.90 ± 0.58
278	9.2 ± 1.2	3.35 ± 0.24	2.75 ± 0.41
288	18.1 ± 2.8	7.1 ± 1.1	2.54 ± 0.55
298	36.5 ± 4.1	12.1 ± 3.3	3.03 ± 0.90
315	109 ± 22	44.1 ± 9.0	2.47 ± 0.71
328	238 ± 53	105 ± 16	2.25 ± 0.61

Table II. Rate Constants × 10^7 (s^{-1}) and Isotope Effects for Formation of the Pentadiene, **5**, and Its Tetradeuterio Analog

	product		
T (°C)	**5**	**5**-d_4	isotope effect
268	3.93 ± 0.49	2.98 ± 0.55	1.32 ± 0.29
278	8.3 ± 1.2	8.11 ± 0.71	1.02 ± 0.17
288	19.4 ± 2.3	17.0 ± 2.7	1.14 ± 0.23
298	45.1 ± 6.8	52 ± 18	0.88 ± 0.33
315	198 ± 40	183 ± 40	1.08 ± 0.32
328	461 ± 115	480 ± 86	0.96 ± 0.29

Table III. Rate Constants × 10^7 (s^{-1}) and Isotope Effects for Formation of the Alkene, **6**, and Its Tetradeuterio Analog

	product		
T (°C)	**6**	**6**-d_4	isotope effect
268	2.64 ± 0.32	0.64 ± 0.11	4.12 ± 0.89
278	4.99 ± 0.66	1.45 ± 0.22	3.45 ± 0.69
288	11.9 ± 2.7	3.54 ± 0.54	3.36 ± 0.91
298	25.4 ± 2.7	6.4 ± 1.8	4.00 ± 1.23
315	72 ± 15	20.9 ± 4.3	3.44 ± 1.02
328	154 ± 35	47 ± 10	3.30 ± 1.06

time. Response factors for the flame-ionization detector of the GC were determined from the independently synthesized samples of products **4**, **5**, and **6**. An independent synthesis of **7** was not attempted, so a response factor had to be assumed for this compound. An error in the assumed magnitude of the response factor would create a systematic error in the computed activation entropy for formation of **7**, but the effect would probably be small. For example, a 50% error in the response factor would create an error of <1.5 cal/(mol K) in $\Delta S^{\ddagger}$. An error in the response factor would have no effect on the estimated activation enthalpy for formation of **7**.

Rate constants for disappearance of **2** and appearance of each of the products were determined by weighted, nonlinear least-squares fit to the appropriate integrated rate equations for irreversible first-order reactions. Reactions were carried to at least 5 half-lives in order to check for any non-first-order behavior. Errors were propagated from the individual GC injections to the final rate constants. The uncertainties in these rate constants are reported as standard errors in the mean and have been adjusted for the sample size by multiplying by the Student *t* parameter for a 95% confidence interval.[10] The results are summarized in Tables I–IV.

Activation parameters were determined by weighted, nonlinear least-squares fit of the rate constants to the Eyring equation. Errors were propagated from the rate constants to the activation parameters. The uncertainties in these activation parameters are reported as standard errors in the mean and have been adjusted for the sample size by multiplying by the Student *t* parameter for a 95% confidence interval. It is perhaps worth remarking that these experimental errors appear significantly larger than the standard deviations from unweighted linear regressions that are frequently reported, but we believe they are more meaningful

(10) Miller, J. C.; Miller, J. N. *Statistics for Analytical Chemistry*, 2nd ed.; Ellis Horwood Ltd.: Chichester, 1988.

Table IV. Rate Constants × 10^7 (s^{-1}) and Isotope Effects for Formation of the Intramolecular Cycloadduct, **7**, and Its Tetradeuterio Analog

	product		
T (°C)	**7**	**7**-d_4	isotope effect
268	2.66 ± 0.34	2.59 ± 0.41	1.03 ± 0.21
278	4.96 ± 0.69	5.36 ± 0.33	0.93 ± 0.14
288	10.7 ± 2.3	10.5 ± 1.6	1.02 ± 0.27
298	20.7 ± 2.0	20.1 ± 5.6	1.03 ± 0.30
315	62 ± 13	60 ± 13	1.03 ± 0.30
328	120 ± 28	135 ± 30	0.89 ± 0.29

Table V. Overall Activation Parameters for Formation of the Specified Products from **2** or **2**-d_4

product	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (cal/(mol K))
bicyclooctanes **4x + 4n**	41.9 ± 2.3	−11.4 ± 4.1
bicyclooctanes (**4x + 4n**)-d_4	44.1 ± 2.1	−9.5 ± 3.7
pentadiene **5**	50.9 ± 2.5	5.1 ± 4.5
pentadiene **5**-d_4	52.9 ± 2.2	8.5 ± 3.9
alkene **6**	43.9 ± 2.3	−8.7 ± 4.1
alkene **6**-d_4	45.0 ± 2.6	−9.3 ± 4.6
cycloadduct **7**	40.9 ± 2.3	−14.3 ± 4.2
cycloadduct **7**-d_4	41.2 ± 2.4	−13.7 ± 4.4

Table VI. Calculated Heats of Formation for Species Involved in the Conversion of **2** to **3**

compd	Benson	MMX	AM1	PM3
2x	39.2	34.7	50.9	43.3
2n	39.2	34.1	51.2	43.1
1	75.9	72.4	S: 44.3[b]	S: 44.1[b]
			T: 36.9[c]	T: 36.1[d]
TS[a]			S: 63.8[b]	S: 60.8[b]
			T: 53.4[e]	T: 49.1[f]
3	59.6	61.0	S: 42.5[b]	S: 44.1[b]
			T: 26.5[g]	T: 29.5[h]

[a] Transition state for conversion of **1** to **3** by 1,5-H transfer. [b] Computed with 2 × 2 CI. [c] UHF wavefunction $\langle S^2 \rangle = 2.0227$. [d] UHF wavefunction $\langle S^2 \rangle = 2.0290$. [e] UHF wavefunction $\langle S^2 \rangle = 2.2317$. [f] UHF wavefunction $\langle S^2 \rangle = 2.2301$. [g] UHF wavefunction $\langle S^2 \rangle = 2.4780$. [h] UHF wavefunction $\langle S^2 \rangle = 2.4622$.

estimates of the real uncertainties in the activation parameters. For example, the rate constants for appearance of **4x + 4n** in Table I would seem to give activation parameters $\Delta H^{\ddagger} = 41.88 \pm 0.15$ kcal/mol and $\Delta S^{\ddagger} = -11.52 \pm 0.26$ cal/(mol K) if treated by an unweighted linear regression, without error propagation, and with the uncertainties being equated with the standard deviations. The uncertainties that come from a more rigorous analysis, including full error propagation, weighted nonlinear least-squares fit, and correction for sample size, are more than an order of magnitude larger. The results are summarized in Table V.

Comparisons with Theory. The formation of **1** and its conversion to **3** were analyzed by Benson group-additivity calculations,[11] molecular mechanics (MMX),[12] and the AM1[13] and PM3[14] semiempirical molecular orbital procedures. The molecules were too big to be studied by *ab initio* methods, at least with basis sets that would be large enough to give meaningful results.

The results of the calculations are summarized in Table VI. The data in Table VI allow calculation of the following heats of reaction for conversion of **1** to **3**: Benson, −16.3 kcal/mol; MMX,

(11) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley-Interscience: New York, 1976.

(12) Molecular mechanics calculations with the MMX force field were conducted using the program PCMODEL from Serena Software, Bloomington, IN, on a Silcon Graphics Personal Iris computer.

(13) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. AM1 and PM3 calculations both employed the program package "MOPAC 6.0" on an IBM RS/6000 computer.

(14) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209.

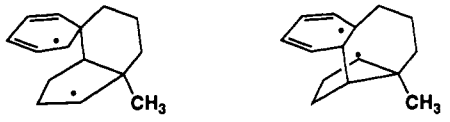
-11.3 kcal/mol; AM1, -1.8 kcal/mol for the singlet and -10.5 kcal/mol for the triplet; PM3, +0.05 kcal/mol for the singlet and -7.3 kcal/mol for the triplet. The two semiempirical molecular orbital models also allow calculation of activation enthalpies for the 1,5-H transfer that converts **1** to **3**. They are as follows: AM1, 19.5 kcal/mol for the singlet and 16.4 kcal/mol for the triplet; PM3, 16.7 kcal/mol for the singlet and 12.9 kcal/mol for the triplet.

In order to compare biradical and monoradical behavior, PM3 calculations were conducted on the hydrogen transfer converting **9** to **10**. The reaction and activation enthalpies were computed to be respectively -7.1 and 12.4 kcal/mol. These are quite similar to the PM3 reaction and activation enthalpies for benzylic H abstraction from phenylethane by isopropyl radical, calculated to be respectively -6.7 and 11.3 kcal/mol.

9 **10**

To our knowledge, experimental activation parameters are not available for any of these hydrogen-transfer reactions. Hence, in order to assess the reliability of the semiempirical calculations, PM3 calculations were compared with *ab initio* results[15] and with the experimental activation enthalpy[16] for allylic hydrogen abstraction from propene by methyl radical. The PM3 calculations gave an enthalpy of reaction of -16.9 kcal/mol and an activation enthalpy of 5.4 kcal/mol. For the same reaction, the corresponding potential energy changes (corrected for zero-point energy differences at the UHF/6-31G(d) level) were computed to be -19.3 and 14.0 kcal/mol at the PMP4(SDTQ)/6-31G(d)//UHF/6-31G(d) level and -18.4 and 10.0 kcal/mol at the PMP2/6-311G(d,p)//UHF/6-31G(d) level of *ab initio* theory. The experimental enthalpy of reaction is -17.6 kcal/mol, and the activation enthalpy is 8.2 kcal/mol.[16]

MMX calculations were performed on biradicals **11** and **12**, which could be intermediates in the conversion of **1** to **7**. Their heats of formation were computed to be 67.4 and 68.3 kcal/mol, respectively. The product, **7**, was calculated by MMX to have a heat of formation of 22.3 kcal/mol.



11 **12**

Discussion

In the analysis that follows, we assume that the first-formed biradical generated by thermolysis of **2** is the lowest singlet state of **1** and that no significant leakage to the triplet manifold takes place during the subsequent reactions. There is no unassailable evidence to show that this assumption is valid. On the other hand, we find the following two pieces of evidence to be generally supportive. First, it is known that reactions involving direct thermal formation of a triplet biradical from a singlet precursor are characterized by unusually low Arrhenius *A* factors or activation entropies.[17] No such phenomenon was detected in the reactions of **2**. Second, triplet-state cyclopentane-1,3-diyl, generated by sensitized photolysis of 2,3-diazabicyclo[2.2.1]hept-2-ene, has a lifetime of about 100 ns,[18] indicating quite slow intersystem crossing (presumably in both directions, since the singlet and triplet state are nearly equal in energy). 2,2-Dialkyl substitution of the biradical does increase the rate constant for triplet → singlet intersystem crossing,[19] but that apparently is caused by lowering the energy of the singlet state with respect to the triplet state. Such a change would *decrease* the rate constant for singlet → triplet intersystem crossing.

In its lowest-energy C_2-symmetry geometry, cyclopentane-1,3-diyl belongs to the class of biradicals identified as "homosymmetric" by Salem and Rowland.[1] In singlet-state homosymmetric biradicals, the covalent ground state, which can be approximated in the Salem–Rowland notation as $(\psi_+^2 - \psi_-^2)/2^{1/2}$ when the overlap between the atomic orbitals containing the nominally unpaired electrons is small, can, by symmetry, have no contribution from the ionic configuration $^1\psi_+\psi_-$. A geometry-optimized CASSCF(2,2)/6-31G(d) calculation[15] on singlet cyclopentane-1,3-diyl, correlating just the two "unpaired" electrons, confirms this picture, giving the ground state as $0.7114\psi_+^2 - 0.7028\psi_-^2 + 0.0000\psi_+\psi_-$, where ψ_+ is the molecular orbital with the A-symmetry combination of carbon 2p orbitals on C1 and C3, and ψ_- is the corresponding B-symmetry molecular orbital.[20]

In the absence of a significant ionic component to its ground-state description, one could expect cyclopentane-1,3-diyl to be among the most "radical-like" of singlet biradicals and, hence, perhaps most likely to exhibit chemistry akin to that of doublet-state monoradicals. The present experimental observations appear to confirm that expectation.

Formation of Bicyclo[3.3.0]octanes 4x and 4n. The lowest singlet state of cyclopentane-1,3-diyl has been estimated from photoacoustic calorimetry experiments[21] to have a heat of formation of 71.5 ± 2.3 kcal/mol. This is in excellent agreement with Benson group-additivity calculations,[11] which give a value of 71.3 kcal/mol if one uses a ring strain equal to that for cyclopentene (5.9 kcal/mol) and a "Doering correction" [22] of 5.4 kcal/mol for the two secondary radical centers. The experimental value places singlet cyclopentane-1,3-diyl 34.2 kcal/mol above bicyclo[2.1.0]pentane.[23] Given an activation enthalpy of 36.9 kcal/mol[4] for the epimerization of bicyclo[2.1.0]pentane-*cis*-2,3-d_2, one computes a barrier to ring closure of just 2.7 kcal/mol for singlet cyclopentane-1,3-diyl. The experimental uncertainties on this value mean that it can be taken to be consistent with high-level ab initio calculations, which place the barrier to closure at about 1 kcal/mol.[24]

The rate constant for epimerization of 5,5-dimethylbicyclo[2.1.0]pentane-*cis*-2,3-d_2 is (9.83 ± 0.35) × 10^{-6} s^{-1} at 160.0 °C,[25] translating to an activation free energy of 35.60 ± 0.03 kcal/mol at this temperature. The published rate constants[4] for epimerization of bicyclo[2.1.0]pentane-*cis*-2,3-d_2 correspond to an activation free energy of 35.4 kcal/mol at 160.0 °C, indicating that 5,5-dialkyl substitution has very little effect on the energetics

(15) *Ab initio* molecular orbital calculations were carried out using the Gaussian 92 program (*Gaussian 92*, Revision C; Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1992) on an IBM RS/6000 computer.

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of the reaction. Hence, we set the enthalpy difference between **1** and **2** at 34.2 kcal/mol, the same as the enthalpy difference between the parent cyclopentane-1,3-diyl and bicyclo[2.1.0]-pentane. Given an activation enthalpy for the overall conversion of **2** to **4** of 41.9 ± 2.3 kcal/mol, and assuming that the hydrogen transfer is the rate-determining step, this makes the enthalpic barrier to intramolecular 1,5-hydrogen abstraction in **1** about 8 kcal/mol. The large, negative overall activation entropy for conversion of **2** to **4** is consistent with the need to "freeze out" internal rotations of the phenylpropyl side chain in the transition state for hydrogen transfer.

As has been noted previously,[26] the semiempirical AM1 molecular orbital model is spectacularly unsuccessful in reproducing the enthalpy difference between bicyclo[2.1.0]pentane and cyclopentane-1,3-diyl (singlet or triplet). The present calculations confirm the problem and show that it exists for the PM3 parametrization as well. Perhaps even more surprising, the two methods also do very poorly in describing the relative enthalpies of **1** and **3**. By Benson group additivity, **3** should be 16.3 kcal/mol lower in heat of formation than **1**. Molecular mechanics (MMX) makes the value 11.3 kcal/mol. Applicability of either molecular mechanics or group additivity is contigent on the singlet–triplet energy difference in **1** and **3** being small,[27] but that is known to be true for **1**,[21] and seems reasonable for **3**, given the distance between the unpaired electrons. In contrast to these values, AM1 makes the hydrogen-transfer enthalpy only −1.8 kcal/mol for the singlet state, while PM3 makes it essentially thermoneutral at +0.05 kcal/mol. Perhaps in part because of these apparent errors in overall enthalpy of reaction, the two methods give activation enthalpies that differ from our experimental estimate of 8 kcal/mol by significantly more than the probable experimental error. AM1 makes the activation enthalpy for conversion of **1** to **3** 19.5 kcal/mol, while PM3 puts it at 16.7 kcal/mol.

The AM1 and PM3 calculations on the hydrogen transfer converting **1** to **3** in the triplet manifold give results that are somewhat more in line with the Benson and MMX results. The PM3 results also match quite closely the values calculated for the 1,5-hydrogen transfer in monoradical **9** and for the α-hydrogen abstraction from ethylbenzene by isopropyl radical. Even in these cases, however, the enthalpy of reaction seems too positive (by comparison with the value of −16.3 kcal/mol from Benson groups).

Interestingly, in the abstraction of the allylic hydrogen from propene by methyl radical, the PM3 method results in calculated reaction and activation enthalpies that are fairly close to the experimental values and to values from reasonably high-level ab initio calculations. Given that the ab initio calculations only get close to the experimental values with quite large basis sets (presumably at least in part because of basis-set superposition error),[28] it is quite surprising that the semiempirical method performs as well as it does. In any event, the success in reproducing experimental values for methyl radical plus propene suggests that the problems in matching the experimental activation enthalpy for conversion of **1** to **3** arise largely from an incorrect assessment of the reaction enthalpy.

If abstraction of the benzylic hydrogen, converting **1** to **3**, is the rate-determining step on the overall conversion of **2** to **4**, one would expect to see a primary kinetic isotope effect when the corresponding reaction was run with **2**-d_4. As revealed in Table I, this expectation was verified experimentally. The observed isotope effects are reasonably close to those calculated with the AM1 or PM3 models (AM1 gives an isotope effect of 2.46 at 268 °C, falling to 2.25 at 328 °C. The values from PM3 are 2.55 at 268 °C and 2.33 at 328 °C). This agreement with the experimental results might indicate that the semiempirical procedures give reasonable geometries for the transition states, even though their energies are seriously in error.

Table VII. Ratio of Bicyclo[3.3.0]octanes **4x** + **4n** to Alkene **6** as a Function of Temperature and Isotopic Composition

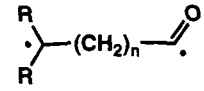
T °C	[**4x** + **4n**]/[**6**]	[**4x** + **4n**]-d_4/[**6**]-d_4	isotope effect on product ratio
268	1.461 ± 0.033	2.007 ± 0.323	1.373 ± 0.223
278	1.451 ± 0.067	1.847 ± 0.266	1.273 ± 0.193
288	1.456 ± 0.039	2.026 ± 0.131	1.392 ± 0.097
298	1.463 ± 0.018	2.024 ± 0.047	1.384 ± 0.036
315	1.448 ± 0.022	2.016 ± 0.042	1.392 ± 0.036
328	1.462 ± 0.008	2.010 ± 0.060	1.375 ± 0.042

Formation of Pentadiene 5. Assuming that the differences in activation parameters for formation of **5** and **5**-d_4 from **2** and **2**-d_4 are due to experimental error rather than some unprecedented remote isotope effect, our best estimates for the pentadiene formation will come from averaging the two sets. The results are $\Delta H^{\ddagger}$ = 51.9 ± 1.7 kcal/mol, $\Delta S^{\ddagger}$ = 6.8 ± 3.0 cal/(mol K). These figures match well the values for conversion of parent bicyclo-[2.1.0]pentane to 1,4-pentadiene:[29] $\Delta H^{\ddagger}$ = 51.2 ± 0.6 kcal/mol, $\Delta S^{\ddagger}$ = 3.9 ± 1.1 cal/(mol K), indicating, as one might expect, that 5,5-dialkyl substitution has little effect on the cleavage of the C1–C4 and C2–C3 bonds.

Formation of Alkene 6. The formation of alkene **6** is the intramolecular analog of the radical disproportionation that terminates many chain processes, including polymerization reactions.[30] This disproportionation of alkyl radicals to alkene plus alkane appears to be essentially activationless in most cases.[31] In the present example, however, the hydrogen abstraction is intramolecular and must occur via a five-membered ring. As the result of a computational study employing the AM1 method, Huang and Dannenberg[32] have suggested that intramolecular hydrogen atom transfers experience a transition-state destabilization of 6.3–6.6 kcal/mol when forced to occur via a five-membered ring. One might have expected that this transition-state destabilization would have led to a barrier to formation of **6**, which, in the absence of a barrier for closure of **3** to **4x** or **4n**, would have made the ratio of products (**4x** + **4n**):**6** temperature dependent. The experimental results are summarized in Table VII.

The lack of temperature dependence of the product ratios in Table VII appears to imply that there is no barrier to the second hydrogen abstraction. An alternative explanation would be that there are nonzero barriers of coincidentally equal magnitude for closure of **3** to **4x** + **4n** and for the hydrogen abstraction converting **3** to **6**. This latter explanation seems unsatisfactory, since one would then have to say that the barriers for formation of the stereoisomeric bicyclooctanes are also coincidentally equal, because their ratio is also temperature independent. Given the substantially greater steric interactions expected for formation of the *endo* isomer, **4n**, this seems like an improbable coincidence.

Some information about the activation parameters for the ring closure and disproportionation reactions in singlet biradicals can be gleaned from studies on photochemically generated triplet biradicals of the type represented by **13**.[33] The sum of rate



13 (R = H, CH_3)

constants for ring closure and disproportionation in biradicals of this type was found to be about 10^7 s^{-1} and essentially independent of structure in a series of alkyl/acyl biradicals.[30b] The lack of structural dependence was taken to indicate that intersystem

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crossing was probably the rate-determining step. The activation free energies for the ring closure and disproportionation of the singlet would thus have to be lower than that corresponding to a rate constant of 10^7 s^{-1}, i.e. about 8 kcal/mol at 25 °C. Some of this activation free energy would come from the large negative entropy associated with intersystem crossing. For example, a $\Delta S^{\ddagger}$ of −16 cal/(mol K) (contributing 4.7 kcal/mol to $\Delta G^{\ddagger}$ at 25 °C) has been reported for one case.[34] If a similar entropy of activation were applicable in the intersystem crossing of the alkyl/acyl biradicals, one could place an upper limit of 3–4 kcal/mol on the activation enthalpies for ring closure and disproportionation of the singlet-state species.

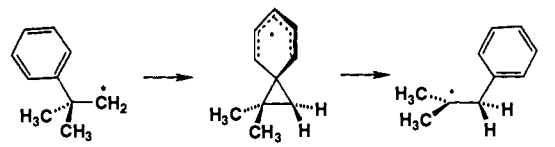
The fact that our experiments revealed no ring strain in the transition state for the hydrogen transfer does not invalidate the calculations of Huang and Dannenberg, since they investigated near-thermoneutral hydrogen transfers rather than the highly exothermic disproportionation observed here. It could well be that the disproportionation reaction has a much "earlier" transition state (with consequent lower ring strain) than the hydrogen transfer from an alkane to an alkyl radical.

If, indeed, there is no barrier to the second hydrogen transfer, then the isotope effect detected for this process cannot easily be explained by the usual zero-point-energy explanation. The fact that the isotope effect for the first hydrogen transfer was apparently temperature dependent, whereas that for the second appears temperature independent, suggests that they do have different origins. It is possible that the formation of **4** and **6** from **3** is under dynamic control,[35] in which case the isotope effect could derive from a difference in efficiency of coupling of the reaction coordinate for formation of **3** to the coordinates for its reactions in the d_0 and d_4 cases.[36] The dynamics of these processes might be particularly unusual in view of the orbital correlation barrier that is believed to separate recombination and disproportionation pathways for radical pairs or biradicals.[37]

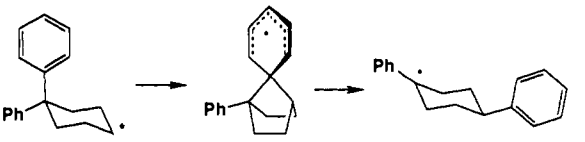
Formation of Intramolecular Cycloadduct 7. The activation entropy computed for conversion of **2** to **7** might have a systematic error due to an incorrect GC response factor, but such an error is likely to be small (<1.5 cal/(mol K), *vide supra*). The computed activation enthalpy would be unaffected by the magnitude of the response factor. The estimated heat of formation for **1** and the experimental activation enthalpy for formation of **7** imply a barrier of about 7 kcal/mol to the cycloaddition reaction.

The MMX calculations on the intramolecular cycloaddition would make either of the biradicals **11** or **12** permissible intermediates in the reaction. On the other hand, the intramolecular trapping of stabilized 1,3-diyls by alkenes exhibits the expected stereochemistry for a concerted cycloaddition.[38]

If the formation of **7** from **1** does involve stepwise C–C bond formation, then it becomes meaningful to compare the estimated barrier to the reaction with those for addition of monoradicals to arenes. Unfortunately, very little seems to be known about the activation parameters for such processes. The closest analogies to the present reaction appear to be the neophyl rearrangement of **14** to **15**, for which independent estimates have put the Arrhenius activation energy at 10.3 ± 2.2 kcal/mol[39] and 13.6 ± 1.0 kcal/mol,[40] and the "transannular neophyl rearrangement" of **16** to **17**, for which a rough estimate of E_a = 15 kcal/mol has been made.[41] In both of these rearrangements, approach to the transition state probably involves significantly greater increase in strain than would be the case for conversion of **3** to **11** or **12**, and so somewhat higher activation energies are probably to be expected.



14 **15**



16 **17**

Conclusion

The chemistry of biradical **1**, described in this manuscript, appears to support the expectation that singlet cyclopentane-1,3-diyls should behave very much like doublet-state monoradicals. The types of reactions observed—hydrogen-atom transfer, disproportionation, and addition to an arene—all have close analogies in the chemistry of monoradicals. The activation parameters for these reactions are probably similar to their counterparts in monoradical chemistry, also, although the small amount of published data on the monoradical reactions and the experimental uncertainties in the numbers deduced from the present work do not permit a very clear comparison.

In contrast to the apparent success of the qualitative theoretical arguments that predicted the radical-like behavior for cyclopentane-1,3-diyls,[1] the semiempirical molecular-orbital models used to provide more quantitative descriptions were disappointing. The models used for the calculations provided quite unsatisfactory descriptions of the reaction energetics, although the good agreement with the observed isotope effects suggests that they might have done a better job on molecular geometries.

Now that the behavior of a singlet biradical near one end of the anticipated spectrum of such intermediates has been characterized, one can start to ask how the chemistry changes as systematic perturbations of the molecular symmetry are made through addition of substituents. Would a cyano substituent added to C1 of a cyclopentane-1,3-diyl be enough to introduce significant zwitterionic character, for example? If so, how would that show up in the chemistry of the intermediate? Would C3 cease to behave like a monoradical because of the substituent at C1? Studies aimed at answering questions of this kind should enable us to obtain a clearer understanding of the structural features that determine the degree of ionic character in a biradical and the chemical behavior that varying degrees of ionic character engender.

Experimental Section

General. ^1H NMR spectra were recorded on a Varian XL-200 spectrometer. ^{13}C NMR spectra were recorded on a Varian XL-400 spectrometer. GC/MS data were obtained on a Hewlett-Packard Model 5890 gas chromatograph equipped with a 0.25 mm × 30 m DB-5 capillary column and a Hewlett-Packard 5970 Series mass selective detector. IR spectra were obtained neat on a Mattson Galaxy Series FT-IR. High-

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resolution mass spectra were provided by the University of Illinois Mass Spectrometry Laboratory, Urbana, IL 61801.

All glassware was dried at 140 °C and cooled in a desiccator or under a dry N_2 atmosphere.

Copper(II) chloride, sodium iodide, and oxalic acid were obtained from Fisher Scientific. All other reagents were obtained from Aldrich Chemical Co. and were used as received except methyltriphenylphosphonium bromide, which was dried at 0.01 Torr and 100 °C. Solvents were obtained from Fisher Scientific and were purified as follows. Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl. Benzene was distilled from sodium benzophenone ketyl or calcium hydride. Diisopropylamine was distilled from lithium aluminum hydride and was stored over potassium hydroxide. Pyridine was distilled from sodium. DMSO was distilled under reduced pressure from calcium hydride. Methylene chloride and DMPU were distilled from calcium hydride at atmospheric pressure. Pentane and hexanes were distilled from lithium aluminum hydride under N_2. Cyclohexylamine was distilled under N_2.

Column chromatography was gravity fed and performed in fritted filter funnels of the size specified in the specific procedures. Silica gel 60 (230–400 mesh) was obtained from EM Science.

3-Methyl-3-(3-phenylpropyl)cyclopentanone.[42] A three-necked 500-mL round-bottomed flask was fitted with a 125-mL pressure-equalizing addition funnel, a glass stopper, and a rubber septum and was charged with diethyl ether (250 mL) and magnesium turnings (4.1 g, 0.169 mol). The stirred mixture was blanketed with dry N_2, and 1-bromo-3-phenylpropane (30 g, 0.151 mol) was placed in the addition funnel. Approximately 1 mL of the bromide was added to the reaction flask. Once Grignard formation had been initiated, the remaining bromide was added over a period of 20 min with an ice bath applied occasionally to maintain control of the reaction. The Grignard reagent was stirred for 20 min upon completion of the addition and was subsequently cooled to 0 °C in an ice bath. Solid tetrakis[iodo(tri-*n*-butylphosphine)copper(I)][43] (7 g, 0.018 mol) was added against a strong N_2 counterflow. The dark brown solution was stirred for 5 min, and a solution of 3-methyl-2-cyclopenten-1-one (12.3 g, 0.128 mol) in ether (50 mL) was added over a 10-min period. After stirring for 30 min, the reaction was quenched by the addition of 50 mL of saturated aqueous NH_4Cl solution, stirred for 3 h, and transferred to a separatory funnel containing H_2O (50 mL). The ethereal layer was removed and was washed successively with H_2O (50 mL) and saturated aqueous NaCl solution (50 mL). After drying over $MgSO_4$, the ether was removed under reduced pressure, and the crude product was dissolved in a solution of 93% EtOH (400 mL) and glacial acetic acid (40 mL). Girard's reagent T (40 g) was added, and the solution was heated at reflux for 30 min. After cooling to room temperature, the mixture was poured into a separatory funnel containing saturated aqueous NaCl (350 mL) and was extracted with three 100-mL portions of ether. The organic extracts were discarded, and the aqueous phase was acidified with 60 mL of concentrated HCl and was heated to 60 °C for 5 min. After cooling to room temperature, the solution was extracted with three 150-mL portions of ether and the combined ethereal extracts were washed successively with H_2O (3 × 50 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL). The extract was dried over $MgSO_4$, and the ether was removed under reduced pressure to give 3-methyl-3-(3-phenylpropyl)cyclopentanone (6.81 g, 31.5 mmol) in 25% yield. Yields varied between 3% and 57%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.02 (s, 3 H), 1.35–1.85 (m, 6 H), 2.03 (br s, 2 H), 2.25 (m, 2 H), 2.60 (t, J = 7.6 Hz, 2 H), 7.10–7.38 (m, 5 H).

4-Methyl-4-(3-phenylpropyl)-2-cyclopenten-1-one. A three-necked 500-mL round-bottomed flask equipped with a 125-mL pressure-equalizing addition funnel, a rubber septum, and a thermometer/thermometer adapter was charged with THF (250 mL). A few milligrams of 1,10-phenanthroline was added, and the solution was blanketed with Ar. Diisopropylamine (3.5 g, 4.8 mL, 35 mmol, 1.1 equiv) was added via syringe. The solution was cooled to 0 °C, and BuLi (approximately 1 mL) was added dropwise via syringe until the red color of the LDA/1,10-phenanthroline charge-transfer complex persisted. Additional BuLi (21.9 mL of a 1.6 M solution in hexanes, 35 mmol, 1.1 equiv) was then introduced through the septum via syringe. After stirring for 5 min at 0 °C, the solution was cooled to −95 °C in a CH_3OH–liquid N_2 slush bath. A solution of 3-methyl-3-(3-phenylpropyl)cyclopentanone (6.81 g, 31.5 mmol) in THF (40 mL) was added dropwise from the addition funnel over a period of 10 min and at a rate that maintained the reaction flask temperature at or below −89 °C. The dark solution was stirred an additional 20 min at −95 °C, and a solution of benzeneselenenyl bromide (8.26 g, 35 mmol, 1.1 equiv) in THF (40 mL) was transferred via cannula to the addition funnel. The THF solution was added dropwise to the reaction flask at a rate that again maintained the reaction temperature at or below −89 °C. Upon completion of the addition, the reaction mixture was allowed to warm to 0 °C over a period of 1 h. A solution of 30% H_2O_2 (15 g, 132 mmol) in H_2O (18 mL) and acetic acid (4.4 mL) was then added, and the mixture was allowed to warm to room temperature over a period of 2 h (**CAUTION**: Rapid warming of the reaction mixture can cause excessive foaming!). The reaction mixture was transferred to a separatory funnel containing an equivalent volume of saturated aqueous NaCl. The mixture was extracted with three 150-mL portions of ether, and the combined extracts were washed successively with H_2O (10 × 50 mL), 10% aqueous HCl (2 × 50 mL), saturated aqueous $NaHCO_3$ (100 mL), and saturated aqueous NaCl (100 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (60 × 200 mm silica gel column) utilizing 10% ethyl acetate in hexanes as the eluent. Pure 4-methyl-4-(3-phenylpropyl)-2-cyclopenten-1-one (2.36 g, 11.0 mmol) was obtained in 35% yield. Typical yields ranged between 21% and 40%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.18 (s, 3 H), 1.40–1.72 (m, 4 H), 2.08 (d, J = 20.8 Hz, 1 H), 2.18 (d, J = 20.8 Hz, 1 H), 2.59 (t, 3 H), 6.01 (d, J = 5.8 Hz, 1 H), 7.10–7.36 (m, 5 H), 7.39 (d, J = 5.8 Hz, 1 H).

4-Methyl-4-(3-phenylpropyl)-2-cyclopenten-1-ol. A 100-mL round-bottomed flask equipped with a magnetic stirrer was charged with MeOH (60 mL), $CeCl_3 \cdot 7H_2O$ (8.2 g, 22 mmol), and 4-methyl-4-(3-phenylpropyl)-2-cyclopenten-1-one (2.36 g, 11.0 mmol). The stirred solution was cooled to 0 °C, and $NaBH_4$ (0.85 g, 22 mmol) was added in portions over a 5-min period. The suspension was stirred for 5 min upon completion of the addition, and excess reducing agent was destroyed by the addition of 10 mL of saturated aqueous NaCl. The reaction mixture was transferred to a separatory funnel containing an equal volume of saturated aqueous NaCl and was extracted with three 75-mL portions of ether. The combined extracts were washed successively with H_2O (2 × 50 mL) and saturated aqueous NaCl (50 mL) and were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude oil was purified by chromatography on a 40 mm × 40 mm silica gel column utilizing 20% ethyl acetate in hexanes as the eluent. Pure 4-methyl-4-(3-phenylpropyl)-2-cyclopenten-1-ol (1.39 g, 6.43 mmol) was obtained as a mixture of diastereomers (R_f = 0.33, 0.27) in 58% yield. Yields for this reaction varied between 57% and 95%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.86, 1.04 (s, 1 H), 1.006, 1.130 (s, 3 H), 1.15–1.78 (m, 4 H), 1.90–2.17 (m, 2 H), 2.58 (m, 2 H), 4.79 (m, 1 H), 5.65 (m, 2 H), 7.08–7.30 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.06, 27.18, 27.27, 28.53, 36.50, 36.53, 41.40, 41.99, 47.07, 47.18, 48.03, 48.24, 77.22, 77.58, 125.68, 128.27, 128.33, 128.37, 131.04, 131.24, 142.49, 142.52, 144.08, 144.18.

5-Methyl-5-(3-phenylpropyl)-1,3-cyclopentadiene. A 100-mL round-bottomed flask was charged with a diastereomeric mixture of 4-methyl-4-(3-phenylpropyl)-2-cyclopenten-1-ol (2.92 g, 13.52 mmol) and DMPU (70 mL). A N_2 inlet was introduced through a rubber septum, and methyltriphenoxyphosphonium iodide (13.0 g, 28.7 mmol, 2 equiv) was added to the stirred solution against a strong N_2 counterflow. The mixture was heated in a 70 °C oil bath for 8.5 h. After cooling to room temperature, the mixture was transferred to a separatory funnel and was partitioned between H_2O (100 mL) and pentane (50 mL). The pentane layer was removed, and the aqueous layer was extracted with additional pentane (2 × 50 mL). The organic extracts were combined and washed successively with H_2O (5 × 50 mL) and saturated aqueous $NaHCO_3$ (1 × 50 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure, and the crude product was chromatographed (R_f = 0.67) on a 40 mm × 50 mm silica gel column with 5% ethyl acetate in hexanes as the eluent. The desired 5-methyl-5-(3-phenylpropyl)-1,3-cyclopentadiene (2.25 g, 11.4 mmol) was obtained in 84% yield. The dehydration yield varied between 84% and 91% for the four procedures conducted. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.15 (s, 3 H), 1.40–1.68 (m, 4 H), 2.57 (t, J = 7.5 Hz, 2 H), 6.22 (s, 4 H), 7.12–7.48 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.50, 27.57, 35.93, 36.64, 56.32, 125.62, 128.23, 128.37, 128.43, 142.57, 145.52.

10-Methyl-4-phenyl-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}]-dec-8-ene-3,5-dione. Into a 250-mL round-bottomed flask were placed 5-methyl-5-(3-phenylpropyl)-1,3-cyclopentadiene (2.70 g, 13.6 mmol) and CH_2Cl_2 (100 mL). The solution was stirred, and 4-phenyl-1,2,4-triazoline-3,5-dione[44] (2.00 g, 11.4 mmol) was added in portions. The

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solution was stirred for 15 min upon completion of the addition, and the solvent was removed under reduced pressure. The crude solid was suspended in 100 mL of MeOH, and the mixture was heated on a steam bath to effect dissolution. Cooling to room temperature resulted in precipitation of fine white crystals (2.09 g, 5.60 mmol) identified by ^{1}H NMR as a single isomer of the two possible Diels–Alder adducts. Concentration of the supernatant on a rotary evaporator and purification by column chromatography (25% EtOAc in hexanes) provided an additional 1.66 g (4.45 mmol) of pure 10-methyl-4-phenyl-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione as a mixture of *syn* and *anti* isomers. Total yield for the purified Diels–Alder adduct ranged between 73% and 98%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (s, 3 H), 1.34–1.66 (m, 4 H), 2.56 (t, J = 7.8 Hz, 2 H), 4.59 (t, J = 1.8 Hz, 2 H), 6.33 (t, J = 1.8 Hz, 2 H), 7.10–7.48 (m, 10 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 18.34, 27.25, 32.92, 36.03, 62.73, 71.06, 125.54, 126.01, 128.23, 128.36, 128.41, 129.10, 130.39, 131.35, 141.47, 158.88. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.01 (s, 3 H), 1.60–1.90 (m, 4 H), 2.65 (t, J = 7.5 Hz, 2 H), 4.63 (t, J = 1.8 Hz, 2 H), 6.38 (t, J = 1.8 Hz, 2 H), 7.10–7.50 (m, 10 H).

10-Methyl-4-phenyl-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}]-decane-3,5-dione. *A solution of* 10-*methyl*-4-*phenyl*-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione was prepared by dissolving a mixture of isomers (0.61 g, 1.63 mmol) in MeOH (25 mL). The solution was placed in a high-pressure bottle, and 5% Pd/C (approximately 10 mg) was added. The mixture was shaken in a Parr hydrogenator under an atmosphere of H_2 (55 psi) for 20 h. The catalyst was removed by filtration through a 1-cm Celite pad, and the solution was concentrated on a rotary evaporator to give a pale yellow solid suspended in a viscous oil. The reduced urazoles (R_f = 0.15, 0.20) were purified by column chromatography through a 40 mm × 50 mm silica gel pad utilizing 30% EtOAc as the eluent to provide an isomeric mixture of 10-methyl-4-phenyl-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}decane-3,5-diones. Typical purified yields varied between 68% and 90%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.24 (s, 3 H), 1.36–1.52 (m, 2 H), 1.58–1.78 (m, 2 H), 1.80–1.95 (m, 4 H), 2.64 (t, J = 7.5 Hz, 2 H), 4.09 (br s, 2 H), 7.10–7.55 (m, 10 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 16.01, 26.85, 26.92, 32.09, 36.04, 54.30, 65.47, 125.46, 126.12, 128.13, 128.27, 128.47, 129.11, 131.76, 141.31, 155.26. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.13 (s, 3 H), 1.30–2.05 (m, 8 H), 2.64 (t, J = 7.5 Hz, 2 H), 4.14 (br s, 2 H), 7.10–7.55 (m, 5 H).

7-Methyl-7-(3-phenylpropyl)-2,3-diazabicyclo[2.2.1]hept-2-ene. A 300-mL round-bottomed flask was equipped with a reflux condenser and was charged with an isomeric mixture of 10-methyl-4-phenyl-10-(3-phenylpropyl)-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-diones (2.09 g, 5.57 mmol) and 1:1 MeOH–*i*-PrOH (150 mL). Potassium hydroxide (30 g, 0.53 mol) was added, and the stirred solution was heated for 20 h at reflux under an atmosphere of N_2. During the reflux period, a white solid accumulated on the walls of the reaction flask. After cooling to room temperature, the solution was adjusted to pH 2 by the addition of 3 M aqueous HCl (190 mL). The solution was then heated at 70 °C for 5 min to effect complete decarboxylation. After cooling to 0 °C in an ice bath, the solution was adjusted to pH 7 by the addition of 6 M aqueous ammonia, and a 1 M $CuCl_2$ solution (15 mL) was added, resulting in the precipitation of the red-brown copper azo complex. The precipitate was collected on a Büchner funnel and was washed with saturated aqueous NaCl (20 mL). The complex was transferred to a 1000-mL separatory funnel containing 6 M aqueous ammonia (300 mL). The Büchner funnel was rinsed with several mL of aqueous ammonia, and these rinsings were added to the separatory funnel. The deep blue solution was subsequently extracted with five 100-mL portions of diethyl ether. The combined ethereal extracts were washed successively with H_2O (2 × 100 mL), cold 5% aqueous HCl (2 × 100 mL), H_2O (1 × 100 mL), saturated aqueous $NaHCO_3$ (100 mL), and saturated aqueous NaCl (200 mL). After drying over $MgSO_4$, the solvent was removed on a rotary evaporator to give the crude azo compound as a yellow oil (1.14 g). Purification was achieved by column chromatography (40 mm × 40 mm silica gel pad) with 20% EtOAc in hexanes as the eluent. The *exo* and *endo* isomers of 7-methyl-7-(3-phenylpropyl)-2,3-diazabicyclo[2.2.1]hept-2-ene (R_f = 0.18, 0.22) were obtained as a mixture (1.14 g, 5 mmol) in 90% yield. Purified yields for the hydrolysis/oxidation ranged between 76% and 92%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.70 (s, 3 H), 0.74–0.90 (dd, 2 H), 1.20–1.33 (m, 2 H), 1.50–1.70 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 4.65 (br s, 2 H), 7.10–7.35 (m, 5 H). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.74–0.90 (dd, 2 H), 0.93 (s, 3 H), 1.00–1.80 (m, 6 H), 2.47 (t, 2 H), 4.72 (br s, 2 H), 7.10–7.35 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): for mixture δ 15.70, 16.30, 19.56, 19.62, 27.19, 28.65, 31.85, 32.47, 36.58, 36.63, 55.09, 55.32, 83.08, 83.38, 126.04, 126.23, 128.56, 128.65, 142.03, 142.34.

5-Methyl-5-(3-phenylpropyl)bicyclo[2.1.0]pentane (2). A solution of 7-methyl-7-(3-phenylpropyl)-2,3-diazabicyclo[2.2.1]hept-2-en e was prepared by dissolving a mixture of the isomers (0.65 g, 2.85 mmol) in pentane (45 mL) in a 20 mm × 200 mm Pyrex test tube. A rubber septum was placed over the tube, and an 18-gauge hypodermic needle was inserted through the septum. The tube was irradiated for 20 h in a Rayonet photochemical reactor equipped with 3500-Å black phosphor lamps. The pentane was removed on a rotary evaporator, and the crude hydrocarbon was subjected to column chromatography (40 mm × 45 mm silica gel pad) employing freshly distilled neat hexanes as the eluent. The desired 5-methyl-5-(3-phenylpropyl)bicyclo[2.1.0]pentane (0.55 g, 2.75 mmol) was isolated as a mixture of isomers (R_f = 0.50, 0.67) in 96% yield. The material was found to be analytically pure by gas chromatography. Alternatively, the deazetization could be effected thermally by sealing the neat azo compound *in vacuo* in a base-washed Pyrex tube and heating the tube at 180 °C for 20 h. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.86, 1.14 (s, s, 3 H), 0.90–1.60 (m, 8 H), 1.60–1.88 (m, 2 H), 1.90–2.10 (m, 2 H), 2.56, 2.71 (t, t, 2 H), 7.10–7.35 (m, 5 H). LRMS: *m/e* 200, 185, 157, 130, 104 (base peak), 91, 67, 41. HRMS: *m/e* found 200.1566, calculated for $C_{15}H_{20}$ 200.1565.

3-Phenylpropanal-2,2,3,3-d_4. A solution was prepared by dissolving 3-phenylpropynal diethyl acetal (23.22 g, 0.114 mol) and 10% Pd/C (0.25 g) in EtOAc (100 mL). The mixture was transferred to a high-pressure bottle and was connected to a Parr hydrogenator. The reactor was pressurized with argon (60 psi) and was vented. The process was repeated two more times. After the third purging, the hydrogenator was pressurized with D2 (60 psi), and the mixture was shaken for 11 h. The catalyst was removed by filtration through a 1-cm Celite pad, and the EtOAc was removed on a rotary evaporator. The reduced product was dissolved in a 1.25% H_2SO_4 solution in 6:1 THF–H_2O (700 mL) and was stirred at room temperature for 9 h. The reaction mixture was transferred to a separatory funnel containing saturated aqueous NaCl (200 mL). The mixture was extracted with three 150-mL portions of diethyl ether. The combined ethereal extracts were washed successively with H2O (5 × 100 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL). The extract was dried over $MgSO_4$, and the solvent was removed on a rotary evaporator to give the crude aldehyde as a yellow oil. The material was distilled at 110 °C under aspirator pressure to give pure 3-phenylpropanal-2,2,3,3-d_4 (10.90 g, 79 mmol) in 69% yield. Deuterium incorporation was greater than 99% at each position as indicated by ^{1}H NMR. ^{1}H NMR (200 MHz, CDCl3): δ 1.21 (t, J = 6.9 Hz, 6 H), 3.42–3.74 (m, 4 H), 4.48 (s, 1 H), 7.10–7.35 (m, 5 H).

3-Phenyl-1-propanol-2,2,3,3-d_4. A 500-mL round-bottomed flask was charged with 3-phenylpropanal-2,2,3,3-d_4 (10.90 g, 79 mmol) and anhydrous diethyl ether (150 mL). The stirred solution was cooled to 0 °C in an ice bath under a N_2 atmosphere, and LiAlH4 (3.79 g, 100 mmol) was added in portions. The suspension was allowed to warm to room temperature over a 90-min period. The reaction mixture was quenched by the careful addition of 15% aqueous NaOH (3.75 mL) followed by H_2O (18 mL). After stirring for 2 h, the white granular aluminum salts were removed by suction filtration. The filtrate was dried over MgSO4 and was concentrated under reduced pressure to give 3-phenyl-1-propanol-2,2,3,3-d_4 (11.0 g, 78.5 mmol) in 99% yield. No purification of the crude product was required. ^{1}H NMR (200 MHz, CDCl3): δ 1.70 (br s, 1 H), 3.66 (s, 2 H), 7.16–7.35 (m, 5 H).

1-Bromo-3-phenylpropane-2,2,3,3-d_4. A 1000-mL round-bottomed flask equipped with a pressure-equalizing addition funnel was charged with a solution of *N*-bromosuccinimide (38.8 g, 0.218 mol) in CH2Cl2 (350 mL). The stirred solution was cooled to 0 °C in an ice bath, and a solution of triphenylphosphine (53.3 g, 0.203 mol) in CH_2Cl_2 (150 mL) was placed in the addition funnel and was added dropwise to the reaction flask. Stirring was continued for 5 min upon completion of the addition, and pyridine (7.33 g, 7.5 mL, 93 mmol) was added to the reaction mixture. A solution of 3-phenyl-1-propanol-2,2,3,3-d_4 (10.0 g, 71.3 mmol) in CH_2Cl_2 (150 mL) was added over a period of 20 min. The reaction mixture was stirred for 20 h at room temperature and was diluted with pentane (50 mL). After removal of the precipitated triphenylphosphine oxide and succinimide by suction filtration, the solution was concentrated to a volume of 30 mL on a rotary evaporator. Additional pentane (10 mL) was added, and the solution was again filtered. The solvent was again removed on a rotary evaporator, and the residue was dissolved in pentane (25 mL). After cooling to 0 °C, the solution was filtered and concentrated on a rotary evaporator. The crude bromide was distilled (35 Torr, 122 °C) through a short-path condenser to provide pure 1-bromo-

3-phenylpropane-2,2,3,3-d_4 (9.50 g, 46.8 mmol) in 66% yield. ^{1}H NMR (200 MHz, CDCl3): δ 3.34 (s, 2 H), 3.10–3.38 (m, 5 H).

Methyl 2-Oxo-1-(3-phenylpropyl)cyclopentanecarboxylate. Into a 100-mL round-bottomed flask were placed methyl 2-oxocyclopentanecarboxylate (7.1 g, 50 mmol), DMSO (50 mL), and LiOH·H_2O (2.1 g, 50 mmol). The solution was stirred for 10 min while a solution of 1-iodo-3-phenylpropane (10.7 g, 43.4 mmol) in DMSO (5 mL) was added. Stirring at room temperature under a N_2 atmosphere was continued for 18 h. The reaction mixture was then transferred to a separatory funnel and was partitioned between saturated aqueous NaCl (100 mL) and diethyl ether (50 mL). The organic layer was separated, and the aqueous phase was extracted with two additional portions of ether (2 × 50 mL). The combined organic extracts were washed successively with H_2O (5 × 100 mL) and saturated aqueous NaCl (100 mL). After drying over $MgSO_4$, the solvent was removed on a rotary evaporator to give the crude alkylation product (10.57 g). Analysis by ^{1}H NMR showed that the product was a mixture of isomers resulting from the desired C-alkylation (81%) and O-alkylation (19%). A 300-mL round-bottomed flask equipped with a reflux condenser was charged with a solution of the crude alkylation product in 93% EtOH (130 mL). Girard's reagent T (13.0 g, 78 mmol) and glacial acetic acid (10 mL) were added to the solution, and the mixture was heated at reflux for 40 min. Upon cooling to room temperature, the solution was transferred to a separatory funnel containing saturated aqueous NaCl (100 mL). The mixture was extracted with three 50-mL portions of diethyl ether, and the ethereal extracts were discarded. The aqueous phase was transferred to an Erlenmeyer flask, acidified with concentrated HCl (20 mL), and heated at 65 °C for 10 min. After cooling to room temperature, the solution was then extracted with diethyl ether (3 × 50 mL), and the combined ethereal extracts were washed successively with H_2O (2 × 100 mL), saturated aqueous $NaHCO_3$ (2 × 50 mL), and saturated aqueous NaCl (50 mL). The solution was dried over $MgSO_4$, and the solvent was removed on a rotary evaporator to give methyl 2-oxo-1-(3-phenylpropyl)cyclopentanecarboxylate (6.41 g, 24.6 mmol) as a pale yellow oil in 57% yield. Typical yields for the purified product ranged between 21% and 57%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.40–1.75 (m, 3 H), 1.80–2.10 (m, 4 H), 2.20–2.40 (m, 4 H), 2.45–2.70 (m, 3 H), 3.68 (s, 3 H), 7.10–7.33 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.57, 26.70, 32.68, 33.55, 35.98, 37.93, 52.21, 60.41, 125.83, 128.30, 141.69, 171.40, 214.83. LPMS: *m/e* 242, 228, 200, 183, 172, 142, 117 ,104, 91 (base peak), 40.

Methyl 2-Oxo-1-(3-bromo-3-phenylpropyl)cyclopentanecarboxylate. A solution of methyl 2-oxo-1-(3-phenylpropyl)cyclopentanecarboxylate (3.00 g, 11.5 mmol) in CCl_4 (75 mL) was placed in a 200-mL round-bottomed flask equipped with a reflux condenser. *N*-Bromosuccinimide (2.05 g, 11.5 mmol) and benzoyl peroxide (50 mg) were added, and the suspension was heated at reflux for 10 h. The reaction flask was cooled to 0 °C in an ice bath, and the succinimide was removed by suction filtration. The solvent was removed on a rotary evaporator, and the crude orange oil was dissolved in 1:1 diethyl ether–pentane (100 mL). The solution was washed successively with H_2O (2 × 75 mL), saturated aqueous $NaHCO_3$ (2 × 50 mL), and saturated aqueous NaCl (50 mL), and the organic phase was dried over $MgSO_4$. The diethyl ether–pentane was removed *in vacuo* to give crude methyl 2-oxo-1-(3-bromo-3-phenylpropyl)cyclopentanecarboxylate (3.90 g, 11.5 mmol) as a mixture of diastereomers in 99% yield. Yields for the bromination averaged 81% over four runs. Analysis by ^{1}H NMR indicated that no purification was necessary; however, purification may be achieved by column chromatography (70 × 50 mm silica gel pad in a glass frit). An R_f value of 0.28 was observed for the bromide when 20% EtOAc in hexanes was employed as the eluent. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.70–2.60 (m, 10 H), 3.72, 3.71 (s [for each diastereomer], 3 H), 4.89 (t, 1 H), 7.25–7.40 (m, 5 H).

Methyl 2-Oxo-1-(3-iodo-3-phenylpropyl)cyclopentanecarboxylate. A solution of methyl 2-oxo-1-(3-bromo-3-phenylpropyl)cyclopentanecarboxylate (3.90 g, 11.5 mmol) in acetone (45 mL) was placed in a 125-mL Erlenmeyer flask. Sodium iodide (3.50 g, 23 mmol) was added, and the solution was stirred for 6 h at room temperature. The reaction mixture was poured into a separatory funnel containing H_2O (100 mL) and was extracted with three 50-mL portions of diethyl ether. The combined ethereal extracts were washed successively with saturated aqueous $NaHSO_3$ (100 mL) and H_2O (100 mL). After drying over $MgSO_4$, the crude product was purified by column chromatography. Elution from a silica gel column with 30% EtOAc in hexanes provided pure methyl 2-oxo-1-(3-iodo-3-phenylpropyl)cyclopentanecarboxylate (2.1 g, 5.44 mmol) in 47% yield. The iodide is light and heat sensitive and will begin to discolor within several hours if precautions are not observed. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.55–2.60 (m, 10 H), 3.67, 3.70 (s [for each diastereomer], 3 H), 5.03 (t, 1 H), 7.17–7.42 (m, 5 H).

5-Carbomethoxy-2-phenylbicyclo[3.3.0]octan-1-ol. A three-necked 300-mL round-bottomed flask was fitted with a glass stopper, a septum inlet, and a vacuum adapter. The reaction apparatus was evacuated to 0.01 Torr and was filled with dry Ar. A 0.1 M solution of SmI_2 in THF (87 mL, 8.7 mmol) was transferred into the reaction flask via cannula. The solution was concentrated *in vacuo* to an approximate volume of 40 mL and was cooled to −30 °C in a dry ice–ethylene glycol bath. A solution of methyl 2-oxo-1-(3-iodo-3-phenylpropyl)cyclopentanecarboxylate (1.6 g, 4.14 mmol) in THF (5 mL) was transferred via cannula to the reaction flask. Stirring was continued for 90 min while the bath temperature was maintained between −30 and −20 °C. The reaction flask was then warmed to room temperature, and the mixture was stirred for an additional 15 min. The reaction mixture was then transferred to a separatory funnel and partitioned between saturated aqueous K_2CO_3 (50 mL) and diethyl ether (50 mL). The organic phase was removed, and the aqueous phase was extracted with two additional portions of ether. The extracts were combined, washed successively with H_2O (2 × 50 mL) and saturated aqueous NaCl (50 mL), and dried over $MgSO_4$. Purification by chromatography on silica gel with 20% EtOAc in hexanes provides 5-carbomethoxy-2-phenylbicyclo[3.3.0]octan-1-ol (0.89 g, 3.42 mmol) as a mixture of *exo* and *endo* phenyl isomers in 82% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20–2.10 (m, 7 H), 2.35–2.60 (m, 3 H), 2.85 (br s, 1 H), 3.15–3.30 (m, 1 H), 3.76 (s, 3 H), 7.20–7.45 (m, 5 H). LRMS: *m/e* 242, 228, 200, 183, 172, 142, 104 (base peak), 91, 42.

Methyl *endo*-8-Phenylbicyclo[3.3.0]oct-1-ene-5-carboxylate and Methyl 2-Phenylbicyclo[3.3.0]oct-1-ene-5-carboxylate. A solution of a mixture of *exo* and *endo* isomers of 5-carbomethoxy-2-phenylbicyclo[3.3.0]octan-1-ol (0.97 g, 3.73 mmol) in pyridine (8 mL) was placed in a 25-mL round-bottomed flask equipped with a reflux condenser. 4-(Dimethylamino)pyridine (30 mg) was added, and the solution was blanketed with dry N_2. Phosphorus oxychloride (2.47 g, 1.5 9 mL, 16.1 mmol, 4.3 equiv) was transferred to the reaction flask via syringe, and the solution was heated at reflux for 8 h. After cooling to 0 °C, H_2O (2 mL) was added dropwise to quench excess phosphorus oxychloride, and the mixture was transferred to a separatory funnel. The mixture was neutralized with saturated aqueous $NaHCO_3$ (20 mL) and was extracted with four 100-mL portions of diethyl ether. The organic extracts were combined and washed successively with H_2O (2 × 100 mL), 10% aqueous hydrochloric acid (100 mL), saturated aqueous $NaHCO_3$ (100 mL), and saturated aqueous NaCl (100 mL). Drying the extracts over $MgSO_4$ and removal of the solvent on a rotary evaporator provided a clear yellow oil (0.62 g) identified by ^{1}H NMR as a mixture of dehydration products. Purification by elution down a silica gel column with 20% EtOAc in hexanes provided 0.46 g (1.90 mmol) of the isomeric alkenes (R_f = 0.23) in 51% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.60–2.65 (m), 2.70–2.93 (m), 3.10–3.20 (m), 3.68, 3.73 (s, 3 H), 5.13 (m), 7.18–7.48 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 25.38, 28.12, 34.40, 35.48, 35.61, 36.46, 38.34, 38.56, 43.15, 51.88, 52.01, 65.30, 67.89, 123.17, 126.14, 126.73, 127.13, 127.99, 128.21, 128.26, 132.61, 136.32, 143.87, 147.39, 156.32, 176.79, 176.89.

Methyl *endo*-4-Phenylbicyclo[3.3.0]octane-1-carboxylate. A mixture of methyl *endo*-8-phenylbicyclo[3.3.0]oct-1-ene-5-carboxylate and methyl 2-phenylbicyclo[3.3.0]oct-1-ene-5-carboxylate (0.46 g, 1.90 mmol) was dissolved in MeOH (10 mL) and placed in a high-pressure bottle. A catalytic amount of 10% Pd/C (approximately 50 mg) was added, and the mixture was shaken under H_2 (55 psi) for 18 h on a Parr high-pressure apparatus. The suspension was diluted by the addition of MeOH (20 mL) and was filtered through Celite to remove the catalyst. The solvent was then removed on a rotary evaporator to give methyl *endo*-4-phenylbicyclo[3.3.0]octane-1-carboxylate (0.46 g, 1.88 mmol) in 99% yield. No purification of the product was required. The product may be purified by elution down a silica gel column with 10% EtOAc in hexanes. Methyl *endo*-4-phenylbicyclo[3.3.0]octane-1-carboxylate displayed an R_f value of 0.50 with this chromatographic system. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.85–1.08 (m, 1 H), 1.20–2.05 (m, 7 H), 2.15–2.22 (m, 1 H), 2.30–2.45 (m, 1 H), 3.04 (q, 1 H), 3.29–3.42 (m, 1 H), 3.72 (s, 3 H), 7.15–7.35 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.02, 27.78, 29.79, 36.70, 39.51, 47.94, 52.01, 53.17, 59.35, 125.76, 127.84, 127.97, 139.11, 179.16.

(*endo*-4-Phenylbicyclo[3.3.0]octyl)-1-methanol. A 50-mL round-bottomed flask equipped with a reflux condenser was charged with a solution of methyl *endo*-4-phenylbicyclo[3.3.0]octane-1-carboxylate (0.75 g, 3.07 mmol) in anhydrous diethyl ether (20 mL). The stirred solution was cooled to 0 °C under dry N_2, and lithium aluminum hydride (0.57 g,

15.02 mmol, 4.9 equiv) was added against a N_2 counterflow. The stirred suspension was allowed to warm to room temperature over a period of 4.5 h. The reaction mixture was then transferred to a separatory funnel, and excess lithium aluminum hydride was carefully quenched by the addition of H_2O (20 mL). Additional ether was added (20 mL) followed by acidification with 10% aqueous HCl until the solid had dissolved. The ethereal layer was removed, and the aqueous phase was extracted with two 20-mL portions of ether. The combined organic extracts were washed successively with H_2O (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL). After drying over $MgSO_4$, the ether was removed on a rotary evaporator to give crude (*endo*-4-phenylbicyclo[3.3.0]octyl)-1-methanol (0.62 g 2.87 mmol) as a colorless oil in 94% yield. Yields for the reduction averaged greater than 75%. The reaction proceeded cleanly, and no purification was required for subsequent steps. The product could be obtained in analytical purity, however, by column chromatography on silica gel utilizing 20% EtOAc in hexanes as the eluent. The alcohol eluted with an R_f value of 0.29 and could be visualized with a 4% solution of phosphomolybdic acid in EtOH. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.75–1.10 (m, 1 H), 1.15–1.47 (m, 3 H), 1.50–1.75 (m, 4 H), 1.80–2.00 (m, 3 H), 2.38 (q, J = 8.5 Hz, 1 H), 3.18 (q, J = 8.5 Hz, 1 H), 3.50 (d, J = 9.8 Hz, 1 H), 3.55 (d, J = 9.8 Hz, 1 H), 7.10–7.35 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 26.35, 27.68, 30.00, 35.69, 38.02, 47.86, 50.61, 55.31, 70.47, 125.56, 127.82, 127.89, 142.80.

(*endo*-4-Phenylbicyclo[3.3.0]octyl)-1-methanol *p*-Toluenesulfonate. Into a 50-mL round-bottomed flask were placed THF (20 mL) and a small crystal (approximately 2 mg) of 1,10-phenanthroline. (*endo*-4-Phenylbicyclo[3.3.0]octyl)-1-methanol (0.62 g 2.87 mmol) was added, and the stirred solution was cooled to 0 °C under an atmosphere of dry N_2. Butyllithium (approximately 3.0 mL of a 1.6 M solution in hexanes) was added until the red color of the butyllithium–1,10-phenanthroline charge-transfer transfer complex persisted. The solution was stirred for 5 min, and *p*-toluenesulfonyl chloride (0.76 g, 4 mmol, 1.4 equiv) was added as a solid. The cooling bath was removed, and the solution was allowed to warm to room temperature over a period of 5.25 h. The solution was then poured into a separatory funnel containing H_2O (50 mL) and was extracted with three 30-mL portions of diethyl ether. The combined organic extracts were washed successively with H_2O (4 × 50 mL), saturated aqueous $NaHCO_3$ (4 × 50 mL), H_2O (1 x 50 mL), and saturated aqueous NaCl (50 mL). The extracts were then dried over $MgSO_4$ with decolorizing carbon, and the solution was concentrated *in vacuo* to give the crude tosylate contaminated with unreacted *p*-toluenesulfonyl chloride. Purification was accomplished by chromatography on a 40 mm × 40 mm silica gel column incorporating 10% EtOAc in hexanes as the eluent. The tosylate eluted with an R_f value of 0.40. (*endo*-4-Phenylbicyclo[3.3.0]octyl)-1-methanol *p*-toluenesulfonate (0.93 g, 2.51 mmol) was obtained in 87% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.77–1.00 (m, 1 H), 1.10–2.00 (m, 6 H), 2.33 (q, J = 8.5 Hz, 1 H), 2.46 (s, 3 H), 3.13 (q, J = 8.5 Hz, 1 H), 3.89 (dd, J = 10.0 Hz, 1 H), 3.92 (dd, J = 10.0 Hz, 1 H), 7.10–7.30 (m, 5 H), 7.36 (d, J = 8.8 Hz, 2 H), 7.82 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.67, 26.15, 27.48, 29.83, 35.73, 38.13, 47.50, 50.85, 53.04, 76.92, 125.72, 127.74, 127.89, 127.93, 129.85, 133.10, 142.11, 144.68.

1-Methyl-*endo*-4-phenylbicyclo[3.3.0]octane (4n). A solution of (*endo*-4-phenylbicyclo[3.3.0]octyl)-1-methanol *p*-toluenesulfonate (0.90 g, 2.43 mmol) in THF (25 mL) was placed in a 50-mL round-bottomed flask. The flask was fitted with a reflux condenser, and lithium alumnium hydride (0.5 g, 13.2 mmol, 5.4 equiv) was added. The stirred suspension was heated for 10 h at reflux under an atmosphere of dry N_2. After cooling to room temperature, the reaction mixture was transferred to a separatory funnel, and excess lithium alumnium hydride was quenched by the addition of H_2O (5 mL). A 10% aqueous HCl solution was added to dissolve the aluminate salts, and the resulting solution was extracted with three 50-mL portions of diethyl ether. The combined ethereal extracts were washed successively with H_2O (5 × 50 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL). The extracts were dried over $MgSO_4$, and the ether was removed on a rotary evaporator. The crude hydrocarbon (R_f = 0.54) was purified by elution down a 40 mm × 40 mm silica gel column with neat hexanes. Pure 1-methyl-*endo*-4-phenylbicyclo[3.3.0]octane (0.37 g, 1.85 mmol) was obtained in 76% yield. Yields for the reduction averaged 70%. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.83–1.05 (m, 1 H), 1.19 (s, 3 H), 1.24–1.77 (m, 7 H), 1.82–1.97 (m, 2 H), 2.23 (q, J = 10 Hz, 1 H), 3.28 (q, J = 10 Hz, 1 H), 7.10–7.35 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 26.21, 28.37, 29.73, 30.55, 40.63, 42.89, 47.65, 49.40, 55.26, 125.38, 127.82, 127.86, 143.37. LRMS: m/e 200, 143, 117, 104 (base peak), 81, 65, 39. HRMS: m/e found 200.1564, calculated for $C_{15}H_{20}$ 200.1565.

1-Methyl-*exo*-4-phenylbicyclo[3.3.0]octane (4x). A 10-mL round-bottomed flask was charged with potassium *tert*-butoxide (60 mg, 0.55 mmol) and pentane (5 mL). The stirred suspension was cooled to 0 °C under an atmosphere of dry N_2, and butyllithium (0.6 mL of a 1.6 M solution in hexanes, 0.96 mmol) was introduced via syringe. Stirring was continued for 10 min at 0 °C, and a solution of 1-methyl-*endo*-4-phenylbicyclo[3.3.0]octane (10 mg, 0.05 mmol) in pentane (0.2 mL) was introduced via syringe. The reaction mixture was stirred for 4.5 h at room temperature and was quenched by the addition of H_2O (1 mL). The contents of the reaction flask were transferred to a separatory funnel, and the crude mixture was extracted with two 5-mL portions of pentane. The combined pentane extracts were washed with H_2O (2 × 5 mL) and saturated aqueous NaCl (5 mL). After drying over $MgSO_4$, the pentane was removed on a rotary evaporator, and the mixture was analyzed by gas chromatography. Three compounds were present in a 1:1.1:5.2 ratio with the major component identified as 1-methyl-*endo*-4-phenylbicyclo[3.3.0]octane. The mixture was further analyzed by GC/MS, allowing the two remaining products to be tentatively identified as 1-methyl-*exo*-4-phenylbicyclo[3.3.0]octane (m/e = 200) and an unknown unsaturated isomer (m/e = 198), perhaps arising from a reaction with adventitious oxygen or from LiH elimination.

(*E*)-2-Methyl-2-butenal Cyclohexylimine.[45] Into a 50-mL round-bottomed flask were placed benzene (30 mL), (*E*)-2-methyl-2-butenal (2.0 g, 23.8 mmol), and cyclohexylamine (2.36 g, 2.72 mL, 23.8 mmol). The reaction flask was fitted with a reflux condenser and a Dean–Stark trap, and the solution was heated for 6 h at reflux. After cooling to room temperature, the benzene was removed under reduced pressure to give (*E*)-2-methyl-2-butenal cyclohexylimine (3.60 g, 21.8 mmol) in 92% yield. The imine was used without subsequent purification. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.10–1.90 (m, 16 H), 2.97 (m, 1 H), 5.88 (q, 1 H), 7.79 (s, 1 H).

2-Methyl-2-(3-phenylpropyl)-3-butenal. A three-necked 100-mL round-bottomed flask was fitted with a thermometer/thermometer adapter in the center neck. The remaining necks were fitted with a rubber septum and a glass stopper, and the reaction flask was charged with diisopropylamine (1.56 g, 2.18 mL, 15.6 mmol) and THF (30 mL). The stirred solution was cooled to 0 °C under a blanket of dry N_2, and butyllithium (9.73 mL of a 1.6 M solution in hexanes, 15.6 mmol) was introduced to the reaction flask via syringe. Stirring was continued for 5 min, and the solution was cooled to –78 °C in a dry ice–acetone bath. A solution of (*E*)-2-methyl-2-butenal cyclohexylimine (2.56 g, 15.6 mmol) in THF (5 mL) was added dropwise via syringe at a rate that maintained the reaction temperature at or below –68 °C. After stirring for 5 min, 1-bromo-3-phenylpropane (2.80 g, 2.13 mL, 14 mmol) was added via syringe at a rate that again maintained the reaction temperature below –68 °C. Upon completion of the addition, the reaction mixture was stirred at –78 °C for 3 h and was warmed to room temperature over a period of 5 h. A solution of oxalic acid (10 g) in H_2O (50 mL) was then added, and the crude reaction mixture was stirred overnight. The product was steam distilled, and the distillate was extracted with three 50-mL portions of ether. The extracts were washed successively with H_2O (2 × 50 mL), 10% aqueous HCl (2 × 20 mL), H_2O (50 mL), and saturated aqueous $NaHCO_3$ (2 × 50 mL). After drying over $MgSO_4$, the solvent was removed on a rotary evaporator to give the crude C2 and C4 alkylation products. Purification was achieved by column chromatography on silica gel using 17% EtOAc in hexanes to elute the products. The desired 2-methyl-2-(3-phenylpropyl)-3-butenal eluted first (R_f = 0.60) to give 1.19 g (5.89 mmol) of pure material in 42% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.17 (s, 3 H), 1.48–1.70 (m, 4 H), 2.67 (t, J = 7.62, 2 H), 5.10 (d, J = 17.2 Hz, 1 H), 5.26 (d, J = 10.8 Hz, 1 H), 5.78 (dd, J = 10.8 Hz, J = 17.2 Hz, 1 H), 7.10–7.35 (m, 5 H), 9.37 (s, 1 H).

3-Methyl-3-(3-phenylpropyl)-1,4-pentadiene (5). A 100-mL round-bottomed flask equipped with a reflux condenser was charged with methyltriphenylphosphonium bromide (2.12 g, 5.94 mmol, 1.1 equiv) and anhydrous diethyl ether (40 mL). The suspension was stirred under an atmosphere of dry N_2, and butyllithium (3.71 mL of a 1.6 M solution in hexanes, 5.94 mmol) was added to the reaction flask via syringe. The bright yellow solution was stirred at room temperature for 10 min and was cooled to 0 °C. A solution of 2-methyl-2-(3-phenylpropyl)-3-butenal (1.09 g, 5.4 mmol) in diethyl ether (10 mL) was transferred to the reaction flask via cannula. After stirring at room temperature for 1 h, additional

(45) Crawford, R. J.; Lutener, S.; Tokunaga, H. *Can. J. Chem.* **1977**, *55*, 3951.

ether (20 mL) was added, and the mixture was heated to reflux. After 12 h, the reaction flask was cooled to room temperature, and the contents were transferred to an Erlenmeyer flask and diluted with pentane (120 mL). The reaction mixture was filtered through a 1-cm Celite pad and was concentrated on a rotary evaporator to give a yellow oil. The crude product (R_f = 0.8) was purified by column chromatography on silica gel employing 5% EtOAc in hexanes as the eluting agent. Pure 3-methyl-3-(3-phenylpropyl)-1,4-pentadiene (0.8 g, 4.0 mmol) was obtained as a colorless oil in 74% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.12 (s, 3 H), 1.45–1.70 (m, 4 H), 2.62 (t, J = 7.5 Hz, 2 H), 4.97 (dd, J = 1.1 Hz, J = 12.1 Hz, 2 H), 5.04 (dd, J = 1.1 Hz, J = 8.8 Hz, 2 H), 5.86 (dd, J = 11.4 Hz, J = 17.3 Hz, 2 H), 7.15–7.40 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.68, 26.33, 36.56, 40.48, 42.95, 111.81, 125.15, 128.24, 128.37, 142.58, 145.72. LRMS: m/e 200, 185, 172, 131, 104, 91 (base peak), 65, 41. HRMS: m/e found 200.1564, calculated for $C_{15}H_{20}$ 200.1565.

2-(Hydroxymethyl)-2-(3-phenylpropyl)cyclopentanol. A 100-mL round-bottomed flask equipped with a reflux condenser was charged with a solution of methyl 2-oxo-1-(3-phenylpropyl)cyclopentanecarboxylate (1.50 g, 5.76 mmol) in diethyl ether (50 mL). The solution was cooled to 0 °C under a N_2 atmosphere, and lithium aluminum hydride (0.87 g, 23 mmol, 4 equiv) was added in portions against a N_2 counterflow. The suspension was stirred for 5 min at 0 °C and was heated at reflux for 1 h. After cooling to room temperature, the reaction mixture was transferred to a separatory funnel, and unreacted lithium aluminum hydride was destroyed by the careful addition of H_2O (20 mL). After acidification with 10% aqueous HCl (50 mL), the solution was extracted with three 25-mL portions of diethyl ether. The combined extracts were washed successively with H_2O (2 × 20 mL), saturated aqueous $NaHCO_3$ (20 mL), and saturated aqueous NaCl (20 mL) and were dried over $MgSO_4$. After removal of the solvent on a rotary evaporator, the crude colorless oil was further dried under vacuum (0.02 Torr) for 1 h. The crude diol was purified by column chromatography. Elution down a 50 mm × 45 mm silica gel pad with 40% hexanes in EtOAc (R_f = 0.43) provided 2-(hydroxymethyl)-2-(3-phenylpropyl)cyclopentanol (0.78 g, 3.34 mmol) as a single isomer in 58% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.02–1.40 (m, 2 H), 1.40–1.83 (m, 7 H), 1.83–2.12 (m, 3 H), 2.65 (t, J = 7.3 Hz, 2 H), 3.32 (d, J = 10.5 Hz, 1 H), 3.63 (d, J = 10.5 Hz, 1 H), 4.01 (t, J = 8 Hz, 1 H), 7.10–7.43 (m, 5 H).

3-(Chloromethyl)-3-(3-phenylpropyl)cyclopentene. A 25-mL round-bottomed flask equipped with a reflux condenser was charged with 2-(hydroxymethyl)-2-(3-phenylpropyl)cyclopentanol (0.43 g, 1.84 mmol) and pyridine (10 mL). 4-(Dimethylamino)pyridine (40 mg) and phosphorus oxychloride (1.32 g, 0.8 mL, 8.6 mmol, 5 equiv) were added, and the stirred solution was heated at reflux for 26 h under a N_2 atmosphere. After cooling to room temperature, the solution was transferred to a separatory funnel, and excess phosphorus oxychloride was destroyed by the careful addition of H_2O (10 mL). After acidification with 10% aqueous HCl (100 mL), the solution was extracted with three 25-mL portions of diethyl ether. The combined ethereal extracts were washed successively with H_2O (50 mL), 10% aqueous HCl (50 mL), H_2O (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL). The extract was dried over $MgSO_4$, and the ether was removed on a rotary evaporator to give the crude chloride as a pale yellow oil. Purification by elution down a silica gel column with neat hexanes (R_f = 0.36) gave pure 3-(chloromethyl)-3-(3-phenylpropyl)cyclopentene (0.170 g, 0.73 mmol) in 40% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.5–1.62 (m, 4 H) 1.62–1.90 (m, 2 H), 2.36 (m, 2 H), 2.61 (m, 2 H), 3.45 (d, J = 1.0 Hz, 2 H), 5.50 (dt, J = 5.7 Hz, J = 2.2 Hz, 1 H), 5.79 (dt, J = 5.7 Hz, J = 3.3 Hz, 1 H), 7.10–7.35 (m, 5 H). IR (neat) cm^{-1}: 2997, 1603, 1495, 1453, 749, 690.

1-(Chloromethyl)-1-(3-phenylpropyl)cyclopentane. A solution was prepared by dissolving 3-(chloromethyl)-3-(3-phenylpropyl)cyclopentene (0.49 g, 2.09 mmol) in 5% AcOH in EtOH (20 mL). The solution was transferred to a high-pressure bottle, and approximately 10 mg of 10% Pd/C was added. The bottle was placed in a Parr hydrogenator and was shaken for 20 h under 55 psi of H_2. The solution was diluted with diethyl ether (10 mL) and was filtered through a 1-cm Celite pad. The filtrate was transferred to a separatory funnel and was extracted with three 20-mL portions of pentane. The extracts were combined and were washed successively with H_2O (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and saturated aqueous NaCl (20 mL). After drying over $MgSO_4$, the solvent was removed on a rotary evaporator to provide 1-(chloromethyl)-1-(3-phenylpropyl)cyclopentane (0.41 g, 1.73 mmol) in 83% yield. No purification was required. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3–1.7 (m, 12 H), 2.60 (t, 2 H), 3.42 (s, 3 H), 7.12–7.38 (m, 5 H).

1-Methyl-1-(3-phenylpropyl)cyclopentane. A solution of 1-(chloromethyl)-1-(3-phenylpropyl)cyclopentane (0.41 g, 1.73 mmol) in benzene (10 mL) was placed in a 25-mL round-bottomed flask. Tri-*n*-butyltin hydride (1.01 g, 0.94 mL, 3.46 mmol, 2 equiv) and AIBN (10 mg) were added, and the reaction flask was fitted with a reflux condenser. The stirred solution was heated at reflux for 8 h under an atmosphere of dry N_2. After cooling to room temperature, the solvent was removed on a rotary evaporator, and the residue was purified on a silica gel column employing neat pentane as the eluent (R_f = 0.8). Pure 1-methyl-1-(3-phenylpropyl)cyclopentane (0.21 g, 1.04 mmol) was obtained in 60% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (s, 3 H), 1.20–1.40 (m, 6 H), 1.50–1.75 (m, 6 H), 2.58 (t, J = 7.7 Hz, 2 H), 7.10–7.38 (m, 5 H) ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 24.88, 26.38, 27.90, 37.35, 39.84, 42.70, 42.74, 125.97, 128.63, 128.78, 143.40. LRMS: m/e 202, 187, 145, 120, 104, 91, 83 (base peak), 55, 41. HRMS: m/e found 202.1713, calculated for $C_{15}H_{22}$ 202.1722.

1-Methyl-1-(3-bromo-3-phenylpropyl)cyclopentane. A solution was prepared by dissolving 1-methyl-1-(3-phenylpropyl)cyclopentane (0.20 g, 0.99 mmol) in carbon tetrachloride (25 mL) in a 50-mL round-bottomed flask equipped with a reflux condenser. Benzoyl peroxide (10 mg) and *N*-bromosuccinimide (0.185 g, 1.04 mmol, 1.05 equiv) were added, and the solution was heated for 10 h at reflux under a N_2 atmosphere. The reaction flask was cooled to 0 °C in an ice bath, and the succinimide was removed by suction filtration. The solvent was removed on a rotary evaporator, and the crude residue was dissolved in pentane (20 mL). The solution was cooled in an ice bath, and additional precipitated succinimide was removed by suction filtration. The fitrate was transferred to a separatory funnel and was washed successively with H_2O (20 mL), saturated aqueous $NaHSO_3$ (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and saturated aqueous NaCl (20 mL). The extract was dried over $MgSO_4$, and the pentane was removed on a rotary evaporator to give 1-methyl-1-(3-bromo-3-phenylpropyl)cyclopentane (0.25 g, 0.89 mmol) as a pair of diastereomers in 90% yield. No purification was required. ^{1}H NMR (200 MHz, $CDCl_3$): (2 diastereomers) δ 0.92, 0.97 (2 s, 3 H), 1.1–1.8 (m, 10 H), 2.20–2.40 (m, 2 H), 4.90 (t, 2 H).

(*E*)-3-(1-Methylcyclopentyl)-1-phenylpropene (6). A solution of 1-methyl-1-(3-bromo-3-phenylpropyl)cyclopentane (0.25 g, 0.89 mmol) in DMSO (10 mL) was placed in a 25-mL round-bottomed flask. Potassium *tert*-butoxide (0.2 g, 1.78 mmol, 2 equiv) was added, and the solution was stirred under a N_2 atmosphere at room temperature for 2 h. The reaction mixture was then transferred to a separatory funnel containing H_2O (100 mL) and was extracted with three 20-mL portions of pentane. The combined hydrocarbon extracts were washed with H_2O (5 × 20 mL) and saturated aqueous NaCl (20 mL) and were dried over $MgSO_4$. After removal of the solvent on a rotary evaporator, the crude product was purified by elution down a silica gel column with neat pentane to give (*E*)-3-(1-methylcyclopentyl)-1-phenylpropene (31 mg, 0.154 mmol) in 17% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (s, 3 H), 1.10–1.80 (m, 8 H), 2.19 (d, J = 6.6 Hz, 2 H), 6.15–6.45 (m, 2 H), 7.10–7.45 (m, 5 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 24.97, 27.01, 39.45, 43.06, 45.93, 126.36, 127.17, 128.86, 129.16, 131.94, 138.35. LRMS: m/e 200, 128, 118, 115, 91, 83, 55, 41. HRMS: m/e found 200.1558, calculated for $C_{15}H_{20}$ 200.1565.

Isolation and Characterization of Hydrocarbon 7. Thirty-two kinetic samples were combined and chromatographed on a 40 mm × 45 mm silica gel column, utilizing neat pentane as the eluent. Approximately 3 mg of compound 7 (R_f = 0.91) was obtained. Analysis of the major chromatographic fraction by GC showed only one volatile compound to be present. Analysis by ^{1}H NMR spectroscopy, however, indicated a greaselike hydrocarbon impurity. Repeated chromatography failed to separate the impurity. The hydrocarbon was dissolved in methylene chloride (1 mL) in a 5-mL round-bottomed flask, and a solution of 4-phenyl-1,2,4-triazoline-3,5-dione (5 mg) in methylene chloride (2 mL) was added dropwise until the red color of the solution persisted. The solvent was removed on a rotary evaporator, and the crude Diels–Alder adduct was recrystallized from hexane (approximately 0.75 mL) to provide 800 μg of pure material. Diene (incomplete): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95 (s, 3 H), 1.78 (br s, 1 H), 2.89 (br s, 1 H), 5.10–5.22 (m, 1 H), 5.30–5.45 (m, 1 H), 5.69–5.79 (m, 2 H). Adduct: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 3 H), 2.45 (br s, 1 H), 1.1–1.85 (m, 12 H), 4.62 (dd, J = 1.6 Hz, J = 5.5 Hz, 1 H), 4.93 (m, 1 H), 6.36 (ddd, J = 6.8 Hz, J = 6.8 Hz, J = 1.6 Hz, 1 H), 6.57 (ddd, J = 6.9 Hz, J = 6.8 Hz, J = 2.0 Hz, 1 H), 7.20–7.55 (m, 5 H). LRMS: m/e 375, 227, 199, 143, 129, 119, 104 (base peak), 95, 91, 81, 67, 55, 40. HRMS: m/e found 375.1935, calculated for $C_{23}H_{25}N_3O_2$ 375.1947.

Sample Tube Preparation for Kinetic Studies. Lead-glass tubing (7

mm × 1.08 m) was obtained from a commercial neon-sign supplier (Glantz and Sons; Buffalo, New York). The tubing was cut into 250-mm lengths, and one end was sealed in a hot methane–oxygen flame. The open end was fire polished, and a constriction was placed approximately 110 mm from the sealed end. The tubes were then annealed for 12 h at 435 °C in an annealing oven. After cooling, the tubes were filled with distilled water and were allowed to stand for 8 h. The water was removed, and the tubes were rinsed successively with distilled water (2 mL) and reagent grade acetone (2 mL). After drying overnight in a glassware oven at 140 °C, the tubes were stored in a desiccator until needed.

Sample Preparation for Kinetic Studies. A stock solution was prepared by placing **2** (0.312 g) (or **2**-d_4 (0.246 g)) and cyclododecane (1 mL of a 3.156 mg/mL solution in pentane) in a volumetric flask and diluting to 50 mL with pentane. Kinetic samples were prepared by transferring 0.5 mL of stock solution to the lead-glass tubes. The pentane was removed by rotating the tubes at a near-horizontal inclination while a heat gun was used to gently evaporate the solvent. The sample tubes were connected to a vacuum manifold assembly via 0.25-in. Cajon fittings modified to accept 7-mm OD tubing and were subjected to full vacuum for 5 s to remove residual pentane. The tubes were then cooled in liquid N_2 and underwent one freeze–pump–thaw cycle. After recooling in liquid N_2, the tubes were evacuated to approximately 0.005 Torr and were sealed at the constriction with a hot methane–oxygen flame. The seal was then annealed for approximately 30 s with a cool methane flame. In order to protect the relatively fragile lead glass from thermal shock, each sample tube was sealed *in vacuo* within a 10-mm OD Pyrex tube. The sample tubes were stored at −20 °C in a freezer until their use. One tube containing undeuteriated material was cracked after sealing and was analyzed by gas chromatography. The tube was calculated to contain (versus the internal standard) 3.41 mg of material. The tube of deuteriated reactant was similarly calculated to contain 2.76 mg of the bicyclopentane. Since these figures are higher than the actual amounts of reactants added, it is apparent that there was some selective loss of internal standard during sample preparation. However, since all reactions studied exhibited first-order kinetic behavior, the exact masses of reactant were not required.

The samples prepared as described above were heated in a bath[46] employing a 1:1 mixture of molten KNO_3–$NaNO_2$ as the medium. The molten salt mixture was contained in a stainless-steel bucket, insulated on the sides and bottom by 6 in. of vermiculite and on the top by six 1-in.-thick sheets of Marinite. Heating was achieved with an MIS Chromalox heating cable (Niagara Electric Sales Co.) wound spirally against the bucket interior. Efficient mixing of the medium was achieved with a three-blade, 2-in.-diameter propeller connected to a Universal Electric Co. Series 1GA 75995 Model AA2H136 overhead stirrer, via an 18 in. × $^5/_{16}$ in. stainless-steel shaft, inserted through the Marinite cover. Samples were placed into stainless-steel sleeves that allowed for flow-through of the medium. The sleeves were introduced into the eutectic through slots in the Marinite cover. The temperature of the medium was maintained to ±0.1 °C with a Bayley Instrument Company Model 124 precision temperature controller employing a platinum resistance thermometer and was measured with a type K thermocouple. The temperaure was registered with a SynconWeston Model 2427 thermocouple panel meter and was calibrated against a digital multimeter at the conclusion of the kinetic studies. The sample tubes were heated at six temperatures between 268 and 328 °C for times up to 5 half-lives. At the end of each kinetic run, the sample tubes were scored and cracked, and the contents were transferred to clean vials with three 0.25-mL portions of pentane.

Analysis of the Kinetic Samples by Gas Chromatography. The pyrolysate was analyzed by gas chromatography utilizing a Hewlett-Packard 5880A Series gas chromatograph equipped with a Level Four terminal/integrator and employing a flame-ionization detector. Separations were performed on 12 m × 0.2 mm ID fused-silica methyl silicone deactivated Carbowax 20 M column. The GC was operated with a 0.8 mL/min flow of He as the carrier gas. The oven was programmed to maintain an initial temperature of 110 °C for 1 min and then to implement a 1 °C/min temperature ramp for 13 min, whereupon all volatile products had eluted. Injections of 1 μL for each sample were made in triplicate.

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