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The Nature of Cyclopentyne from Different Precursors

John C. Gilbert,* Everett G. McKinley,[1] and Duen-Ren Hou

Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, TX 78712

Abstract: The ratio of [2+2] and [2+4] cycloaddition products from reaction of spiro[4.2]hepta-1,3-diene with cyclopentyne depends on the source of the cyclopentyne. A mechanistic rationale for the phenomenon is presented.
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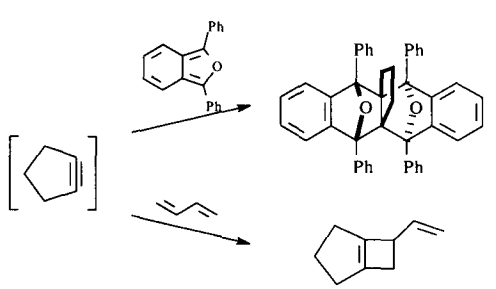
Introduction

There are two general types of experimental entries into cyclopentyne (**1**),[2] *viz.*, rearrangements, as in the ring-expansion of cyclobutylidenecarbene (**2**), derived by geminal elimination of nitrogen[3] or bromine,[4] from **3** and **4**, respectively, and vicinal elimination, such as that involving 1,2-dibromocyclopentene (**5**).[5] Definitively characterizing this highly reactive intermediate remains elusive, although there is some evidence for its existence under matrix isolation conditions.[6a] In solution, the half-life of **1** is estimated to be less than *one* second at -78 °C.[6b]

1 **2** **3** **4** **5** **6**

a. R = *n*-BuO
b. R = Cl

The chemistry of cyclopentyne is characterized by processes involving addition of nucleophiles across the in-plane π-bond. For example, 1-butanol and lithium chloride add to **1** providing **6a**[3a] and **6b**,[5a] respectively, after hydrolysis. Carbon-carbon π-bonds also function as nucleophiles toward **1**, affording both [2+4]-[5] and [2+2]-cycloadducts,[3,4] as illustrated in Equation 1. It is such cycloaddition reactions that are the subject of the present paper.

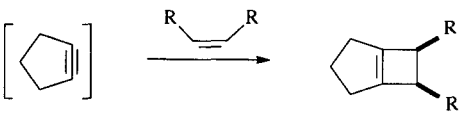


(1a)

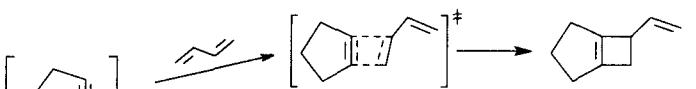
(1b)

Results

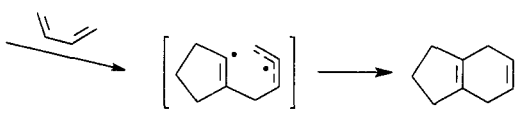
Our studies were stimulated by an AM 1-based calculation of the reaction path for the cycloaddition of **1** and 1,3-butadiene (Eq. 1b).[7] Such computations were themselves prompted by a calculation that found an allowed pathway for the [2+2]-cycloaddition of cyclopentyne and ethylene,[8] a result commensurate with experimental observations of the stereospecificity of this process (Eq. 2).[3a,4a] With the diene as ynophile, two reaction channels are predicted, an allowed, concerted [2+2] process (Eq. 3a), and a forbidden, stepwise [2+4]-cycloaddition (Eq. 3b). The calculated $\Delta\Delta H^{\ddagger}$ is less than 2 kcal/mol, with $\Delta H^{\ddagger}$ for the allowed reaction being lower.[7]



(2)

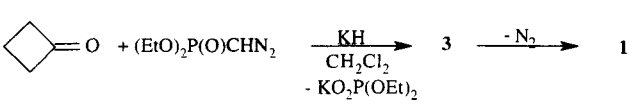


(3a)

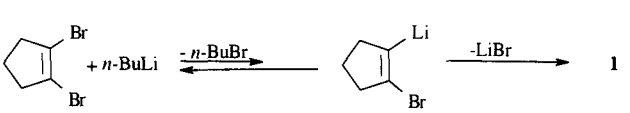


(3b)

Previous experimental investigations of the reaction of **1** with dienes revealed only exclusive [2+4] or [2+2] cycloaddition pathways, rather than a combination of both.[4a,5] However, interpretation of the results in terms of possible competition between the two processes is complicated by the thermodynamic driving force to achieve aromaticity in the former instance (Eq. 1a) and the preference for the *s-trans* conformation in the latter (Eq. 1b). To circumvent such complications, we addressed the issue of competing modes of cycloaddition by using the *s*-cis-locked aliphatic diene, spiro[4.2]-hepta-1,3-diene (**7**).[9] Cyclopentyne was prepared from two different precursors, **3** and **5**. Diazocompound **3** was itself derived as a transient intermediate from the base-promoted reaction of diethyl diazomethylphosphonate (DAMP)[10] with cyclobutanone (Eq. 4) and undergoes loss of dinitrogen to provide carbene **2**, the director precursor of **1**.[3] Debromination of **5** was effected with *n*-butyllithium by way of the transmetallated species **8** (Eq. 5).[11]



(4)

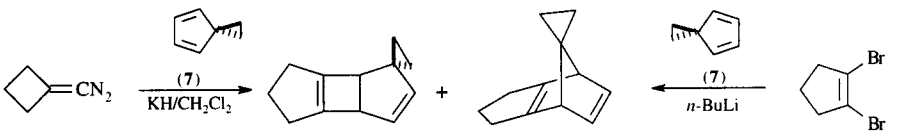


5 8

(5)

Producing **3** in the presence of diene **7** afforded an approximately 1:3 mixture of **9** and **10** (Scheme 1), the [2+2]- and [2+4]-cycloadducts, respectively. The results are among the few in which a strained π-system

Scheme 1



3 **9** **10** **5**

simultaneously undergoes these two types of cycloadditions.[12] The isomers, whose structures were proven spectroscopically (see Experimental Section), were formed in a combined isolated yield of up to 10%, based on the amount of ketone used and the temperature at which the ring expansion was performed (Table 1). Moreover, the ratio of the two products was basically *independent* of temperature over the range of -50 to +25 °C, although the relatively low yields of cycloadducts resulted in rather large experimental errors.

Run	Source of Cyclopentyne	T (°C)	Yield (%)[a]	Ratio 9:10[b]
1	**3**	-40	5	1:2.9
2	**3**	-25	-	1:3.6
3	**3**	0	5	1:2.7
4	**3**	25	2	1:3.4
5	**5**	0	-	60:1[c]
6	**5**	25	-	20:1
7	**5**	60	-	11:1
8	**5**	80	20	9.4:1

[a] Isolated yield

[b] Average of two or more runs

[c] Owing to the small amounts of **10** formed, this ratio is subject to considerable experimental error

Table 1. Product ratios as a function of precursor and temperature.

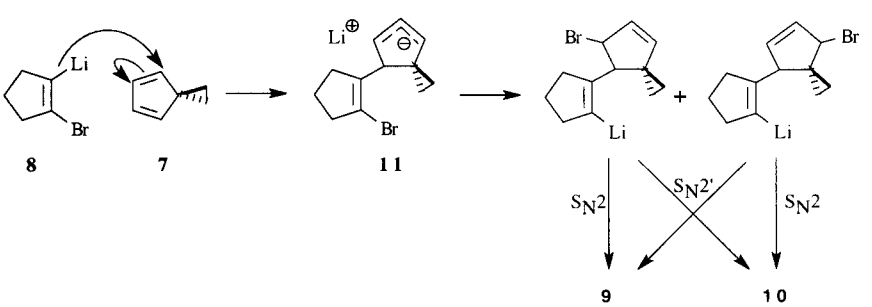
The analogous reaction of **5** with *n*-butyllithium at -40 °C, to produce **8**, followed by warming to effect elimination[13] in the presence of **7**, again afforded a mixture of **9** and **10** in up to 20% isolated yield. However, not only was the proportion of isomers observed in this case dramatically different from the previous reaction, now strongly favoring the [2+2] adduct **9**, but the ratio of the two cycloadducts showed a significant temperature-*dependence* as well (Table 1).[14] Control experiments showed that **9** and **10** are stable to the reaction conditions, ensuring that the observed ratios of products represented kinetic rather than thermodynamic phenomena. With respect to the ring-expansion route (Eq. 4), for example, kinetic control is signaled by the insensitivity of product ratio to temperature and time of reaction. The key control experiments demonstrating kinetic control for the vicinal elimination method (Eq. 5) involved analyzing aliquots removed periodically from a reaction mixture heated at 100

°C; an unchanging ratio of **9**:**10** was observed over a time-period of 45 min. Consequently, the isomers are thermally stable up to 100 °C in the presence of LiBr.

An additional control experiment was performed to test whether the LiBr formed in the vicinal elimination route to cyclopentyne might somehow be suppressing the formation of **10**. This experiment involved adding 0.1 equivalent of the anhydrous salt under the protocol of Equation 4 at a temperature of -40 °C. Although the yield of cycloadducts decreased to about 1%, the observed ratio of **9**:**10** was 1:2.5, a value within experimental error of that observed in the absence of LiBr. In short, kinetic control is operative with both methods for generating cyclopentyne, and *exogenous* LiBr[15] does not affect the partitioning between the [2+2] and [2+4] pathways.

The experimental results clearly exclude a common reactive intermediate, *e.g.*, free cyclopentyne (**1**), as being directly responsible for the cycloaddition reactions of Scheme 1, and it is necessary to explore alternative mechanistic options for forming the cycloadducts **9** and **10**. One possibility is that **8** does not eliminate bromide to form **1** (Eq. 5), but instead adds to **7** to afford the allylic anion **11** (Scheme 2). Intramolecular transmetallation and subsequent S_N2 and/or S_N2' reaction of the resulting species could afford **9** and **10**.[16] Wittig and Heyn previously had shown that the rate of disappearance of anion **8** in diethyl ether was independent of the concentration of 2,5-diphenylisobenzofuran (Eq. 1a),[5a] a precedent that counters the bimolecular nature of the pathway in Scheme 2. However, these investigators also found indications of second-order processes involving **8** when the solvent was THF. If the tendency of the organolithium to react via bimolecular rather than unimolecular pathways extends to hydrocarbon media, a sequence like that outlined in Scheme 2 is more plausible.

Scheme 2



Exploring the molecularity of the transition state for the disappearance of anion **8** is complicated by the fact that treating 1,2-dibromocyclopentene (**5**) with one equivalent of *n*-butyllithium establishes a pseudo-equilibrium between **5** and **8** in which **5** predominates at the temperatures required for forming cycloadducts (Eq. 5). For example at 0 °C, K_{eq} ~ 0.1. It is about 0.2 at -20 °C, a temperature at which **8** does not eliminate LiBr. In any case, if the equilibration is fast relative to further reaction of **8**, the resulting pre-equilibrium does not affect the prediction that the rate of disappearance of **8** according to Scheme 2 would show a first-order dependence on the concentration of **7**, whereas this rate would be independent of diene concentration according to the route involving generation of **1** (Eq. 5).

The results of qualitative kinetic studies of the effect of diene concentration on the rate of disappearance of **5**, and hence **8**, are depicted in Figure 1 as first-order plots. Each kinetic run encompasses at least 1.5 half-lives for the reaction. Although there is scatter in the data, particularly for the runs involving higher concentrations of

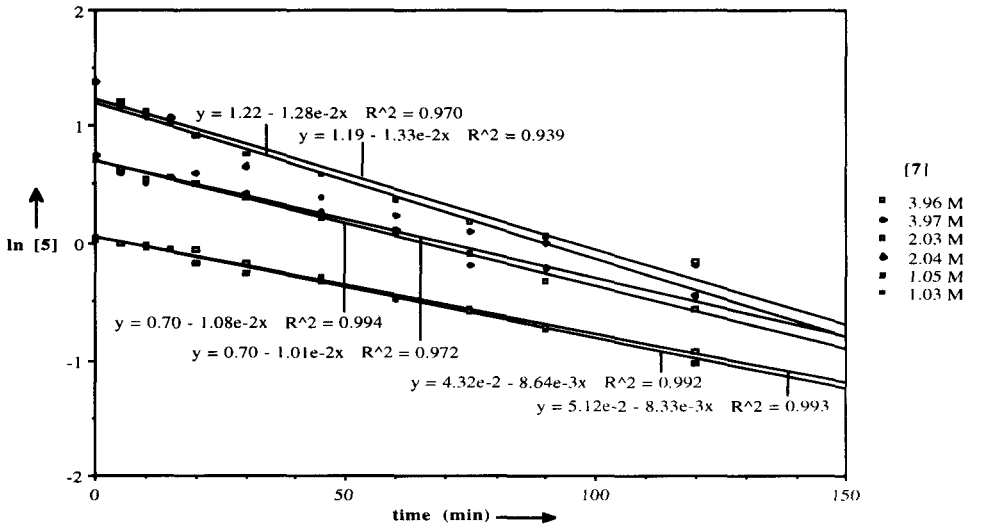


Figure 1. Rate of disappearance of 5 as function of the concentration of 7

diene **7**, the measured rate constants increase by only 50% (1.41×10^{-4} sec^{-1} to 2.1×10^{-4} sec^{-1}) as a function of a four-fold change in [**7**]. These results might signal incursion of bimolecular processes such as that of Scheme 2 for consuming **8**, but their contribution to the fate of **8** is minor at best. The modest rate increases observed could also be associated with other factors of course, such as changes in the solvating properties of the reaction medium. In any case, the primary mechanistic mode for forming cycloadducts **9** and **10** appears *not* to involve rate-determining addition of **8** to diene **7**, instead presumably involving a prior unimolecular decomposition of **8** to cyclopentyne (**1**). This result mirrors that of Wittig and Heyn.[5a]

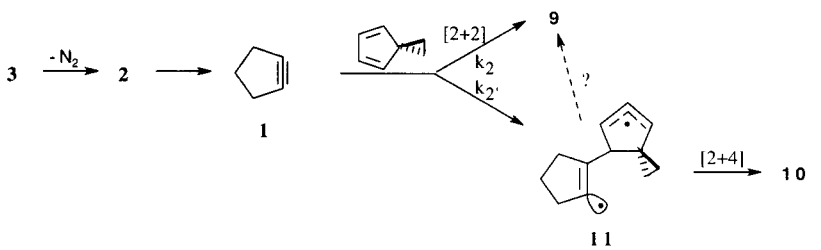
Discussion

Regardless of its mode of preparation, reaction of cyclopentyne with **7** produces two cycloaddition products as shown in Scheme 2. This is a highly provocative result because theoretical considerations preclude both the [2+2] and [2+4] processes from being allowed as concerted thermal processes involving suprafacial participation of the two π-systems: The theory of orbital symmetry (OS)[17] would predict the two modes of reaction to be stepwise and concerted, respectively, whereas that of orbital isomerism (OI)[18,19] would predict just the opposite mechanistic scenario. Stereoelectronic considerations make any antarafacial participations most improbable as well. Although the absence of stereochemical information in the present results does not allow an unambiguous choice between the two theoretical motifs, the previously reported stereospecificity of [2+2]-cycloadditions (Eq. 2)[3b,4b] argues for OI as controlling the mechanistic course of the cycloadditions. Consequently, the following interpretation will use that theoretical construct.

In the context of OI, the results when **3** is the precursor of **1** are shown in Scheme 3. To rationalize the predominance of **10** in the reaction (Table 1), the stepwise reaction channel involving intermediate **11** is preferred

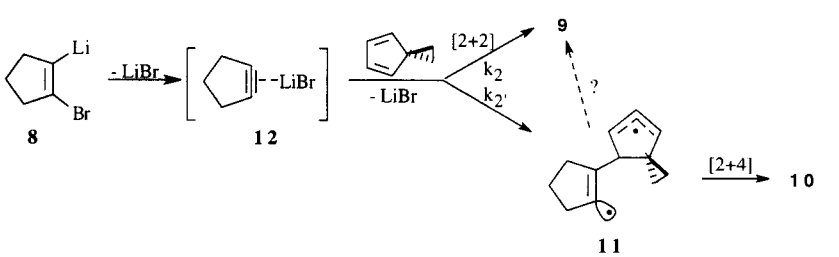
over the concerted pathway, i.e., $k_{2'} > k_2$. The experimentally observed near invariance with temperature of the ratio of **9:10** requires that $\Delta\Delta H^{\ddagger}$ be about 0 kcal/mol for the two different bimolecular transition states defining these rate constants.[20] If this be true, partitioning between the stepwise and concerted pathways is entropy controlled. The constancy of the product ratio as a function of temperature also places constraints on the enthalpies for the transition states defining the partitioning of biradicaloid **11** between the cycloadducts **9** and **10:** They too would have to be essentially identical, an unlikely possibility in terms of the differing stereoelectronic factors involved. A preferred scenario, in our opinion, is that **11** collapses exclusively to the thermodynamically more stable [2+4]-cycloadduct **10**.[21,22]

Scheme 3



An explanation distinct from that of Scheme 3 is needed for the results when dibromide **5** is used as the potential source of **1**. One hypothesis that accounts for the temperature-dependence of the ratio of **9:10** (Table 1) and posits a different reactive intermediate for the cycloaddition is that the elimination of lithium bromide from **8** produces a cyclopentyne-LiBr complex **12** (Scheme 4) rather than free cyclopentyne itself.[23] It is this complex that then reacts with **7** to afford the cycloadducts via concerted and stepwise pathways for which $\Delta\Delta H^{\ddagger} \neq 0$. As noted above, attempting to probe for the intervention of a species such as **12** by adding exogenous LiBr to a reaction involving generation of **3** fails because of the low solubility of the salt in the medium and the exceedingly short lifetime of **1**.

Scheme 4



Conclusions

Elimination reactions involving diazocompound **3** and dibromide **5** in the presence of spiro[4.2]hepta-1,3-diene (**7**) afford both [2+2]- and [2+4]-cycloadducts but *not* through a common reactive intermediate. We believe

that free cyclopentyne (**1**) is formed from **3**, whereas a complexed form, **12**, of the cycloalkyne is produced from **5**. The present results are the first in which systems known to generate cyclopentyne undergo two competing modes of cycloaddition, one of which is presumably allowed as a thermal process, whereas the other is stepwise.[24]

Further studies are underway to define the fascinating pericyclic chemistry of this and related cycloalkynes and to explore the intriguing role that lithium ion may be playing when vicinal and geminal elimination of bromine from **4** and **5**, respectively, occurs.

Experimental Section

All cyclopentyne reactions were performed under an atmosphere of dry nitrogen in one-neck flame-dried flasks. Low-temperature baths other than 0 °C and -78 °C were obtained with a Neslab CC-100 II Cryocool immersion cooler using acetone as the bath liquid. Dry-ice/acetone was used for -78 °C baths. Solvents were dried by distillation, under an atmosphere of N_2, using the drying agents sodium/benzophenone ketyl for tetrahydrofuran (THF) and CaH_2 for dichloromethane (CH_2Cl_2). Unless otherwise noted, concentration of solutions was accomplished by rotary evaporation at water aspirator pressures.

Preparative GC purifications were performed with a GOW-MAC 500P gas chromatograph equipped with a 10% SE-30 3-ft x 1/8-inch column (SGE, Inc.) using helium as the carrier gas (30 mL/min) and a thermal conductivity detector. HPLC purifications were performed on a Waters 6000A instrument equipped with a Waters Radial Compression Module with a 2.5 x 10-cm Prep-Pak silica gel cartridge and a refractive index detector.

GC/MS analyses were performed using a Varian 3400 gas chromatograph equipped with a 12-m x 0.22-mm GB-5 (95% dimethyl-, 5% diphenylpolysiloxane) capillary column using helium as the carrier gas (1.0 mL/min) and interfaced with a Finnigan 700 electron impact ion trap detector (EI-ITD) mass spectrometer. These analyses involved temperature programming from 80 °C (t = 0) to 200 °C at a ramp-rate of 25 °C/min. High-resolution MS analyses were obtained with a VG-ZAB 2E instrument operating in the EI mode at 70 eV.

In non-kinetic runs, quantitative GC analyses of cycloadducts were obtained on a Hewlett-Packard (HP) 5890A analytical gas chromatograph interfaced with an HP 3390A Recording Integrator and equipped with a 25-m x 0.25-mm AT-1 (100% dimethylpolysiloxane) capillary column using helium as the carrier gas (0.6 mL/min) and a flame-ionization detector (FID); temperature programming was the same as for GC/MS analyses except that the ramp-rate was 15 °C/min. For kinetic analyses, the same conditions were used with the exception that the flowrate of helium was 1.2 mL/min.

With the exception of COSY and APT spectra, which were recorded on a General Electric QE-500 instrument operating at 500 (^1H) and 125 (^{13}C) MHz, all ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, on a General Electric QE-300 instrument. All chemical shifts are referenced to C_6D_6, the solvent for NMR analyses.

Cyclopentyne from Cyclobutanone

General Procedure Potassium hydride dispersion (530 mg of a 30% KH in mineral oil, 4 mmol of KH) was placed in a dry 25-mL flask equipped with a stirbar and septum. Under a continuous flow of dry nitrogen, the dispersion was washed with hexanes (3 x 4 mL) to remove the mineral oil. Dry CH_2Cl_2 (1 mL) was added by syringe. The resulting slurry was cooled to -78 °C. A solution of DAMP[10] (780 mg, 4.38 mmol) and dry CH_2Cl_2 (0.5 mL) was transferred into the slurry by cannulation. After this solution was stirred for 10 min,

spiro[4.2]hepta-1,3-diene[9] (1.80 g, 19.6 mmol) was added by syringe and the mixture was stirred for 10 min. Cyclobutanone[24] (0.25 g, 3.57 mmol) was added by syringe, and the mixture was stirred at -78 °C for 0.5 h.

A. Preparative Runs The -78 °C bath was replaced by a -30 °C bath to effect formation and decomposition of **3.** Reaction was complete after 15 min, as evidenced by a color change from yellow to reddish and cessation of gas evolution. A solution of maleic anhydride (1.92 g, 19.6 mmol) in CH_3CN (*ca.* 10 mL) was added to the reaction mixture. The bath was removed, and the mixture was allowed to warm to room temperature, where it was stirred for at least 1 h. It was then extracted with pentane (3 x 25 mL). The organic layer was dried ($MgSO_4$ or Na_2SO_4), filtered, and concentrated to about 10 mL. This solution was passed through a short silica plug using pentane as eluant until TLC (100% pentane eluant) showed that no more compounds were eluting

GC isolation The eluant was concentrated to approximately 1 mL and subjected to preparative gas chromatography. GC conditions: injector temperature, 200 °C, helium flow rate, 30 mL/min, initial column temperature, 100 °C. Compounds were collected from the GC into pre-weighed collection tubes. After an injection, the initial temperature was held until the first peak, which contained solvent and **7**, had eluted. The temperature was ramped at 10 °C/min to 120 °C, where it was held until compound **10** (44.1 mg, 7%) eluted, after which it was ramped at 10 °C/min to 140 °C, and kept there until compound **9** (19.6 mg, 3%) eluted. Finally, the temperature was ramped to 200 °C to effect elution of the dimer of **7**. The condensates were washed with C_6D_6 from the collection tubes and passed through a 1 cm silica plug. The silica plug was flushed with C_6D_6 (1–2 mL) until TLC (100% pentane eluent) showed that no more of the adduct was eluting. The C_6D_6 solutions were concentrated to *ca.* 0.6 mL with a stream of dry nitrogen and used for NMR analyses.

HPLC isolation The eluent was concentrated as in the procedure for GC purification, and the residue was purified by HPLC, using 100% pentane as eluent. Compound **9** (15.7 mg) eluted before compound **10** (32.6 mg) and were obtained in a combined yield of 9%. The dimer of **7** was also isolated.

Spectral data for **9**. ^{1}H NMR: δ 5.85 (dd, J = 5.6, 2.3 Hz, 1H, C(3)-H), 5.03 (d, J = 5.8 Hz, 1H, C(2)-H), 3.92 (br s, 1H, C(4)-H), 3.04 (br s, 1H, C(5)-H), 2.33-2.15 (m, 4H, C(8)-H and C(10)-H), 1.92-1.83 (m, 2H, C(9)-H), 0.86 (m, 1H, cyclopropyl), 0.63 (m, 1H, cyclopropyl), 0.50 (m, 2H, cyclopropyl); ^{13}C NMR: δ 158.0 (vinylic), 151.7 (vinylic), 138.4 C(2), 130.1 C(3), 54.2 C(4), 50.7 C(5), 30.3 (allylic cyclopentene), 30.1 (allylic cyclopentene), 27.7 C(1), 26.4 C(9), 15.4 (cyclopropyl), 9.3 (cyclopropyl); HRMS: *m/z* calcd for $C_{12}H_{14}$ (M^+) 158.1096, found 158.1090.

Spectral data for **10**. ^{1}H NMR: δ 6.81 (t, J = 1.8 Hz, 2H, C(1)-H), 2.64 (br s, 2H, C(2)-H), 2.51-2.43 (m, 2H, C(4)-H), 2.16-2.03 (m, 2H, C(4)-H), 2.03-1.90 (m, 2H, C(5)-H), 0.56 (m, 2H, cyclopropyl), 0.52 (m, 2H, cyclopropyl); ^{13}C NMR: δ 158.4 C(3), 142.6 C(1), 68.4 C(6), 54.8 C(2), 30.5 C(4), 28.3 C(5), 10.5 (cyclopropyl), 9.9 (cyclopropyl); HRMS: *m/z* calcd for $C_{12}H_{14}$ (M^+) 158.1096, found 158.1090.

B. Variable Temperature Experiments The general procedure described above was followed.

i. -50 °C Trapping. After the 0.5 h at -78 °C, the flask was placed in a -50 °C bath, where it remained for 5.5 h. Work-up and GC purification provided **9** and **10** in a combined yield of 5%. Analytical GC analysis showed the ratio of **9**:**10** to be 1:2.9.

ii. -25 °C Trapping. Procedure was as in **B.**i. above except that after the 30 min at -78 °C, the flask was placed in a -25 °C bath, where it remained 0.5 h. Analytical GC analysis showed the ratio of **9:10** to be 1:3.6.

iii. 0 °C Trapping. The general procedure described above was followed to the point where the DAMP solution is added to the KH/CH_2Cl_2 slurry. Cyclobutanone and **7** were added to a separate dry flask that had

been pre-cooled to 0 °C and the solution was stirred magnetically. The solution of the DAMP anion was then added to this solution by cannulation, and immediate and vigorous gas evolution was observed. Work-up and GC purification provided **9** and **10** in a combined yield of 5%. Analytical GC analysis showed the ratio of **9**:**10** to be 1:2.7.

iv. Room Temperature Trapping. The procedure of **B.**iii above except that the flask to which cyclobutanone and **7** were added was at room temperature. Work-up and GC purification provided **9** and **10** in a combined yield of 2%. Analytical GC analysis showed the ratio of **9**:**10** to be 1:3.4.

C. Spiking Experiment with Lithium Bromide The general procedure given above for preparing DAMP anion was followed, and the same relative amounts of reagents were used. A dry 25-mL Schlenk flask containing a stirbar and lithium bromide (9.0 mg, 0.10 mmol, 0.1 eq relative to cyclobutanone) was evacuated (oil pump) and flame-dried to ensure that the LiBr was anhydrous. The flask was allowed to cool to room temperature, restored to atmospheric pressure with dry nitrogen and placed in a -40 °C bath. Diene **7** was added, and the slurry was stirred at -40 °C for 10 min. The solution of DAMP anion was then transferred by cannulation to the **7**/LiBr slurry, and cyclobutanone was added. The reaction mixture was stirred at -40 °C for 1 h and then warmed to -30 °C, where it remained for 18 h. The mixture was diluted with pentane (100 mL), washed with deionized water (25 mL), and layers were separated. The organic layer was dried (Na_2SO_4), and GC/MS analysis of this crude solution showed **9** and **10** in a ratio of 1:2.5. Purification by HPLC provided the cycloadducts in a combined yield of 1%.

Cyclopentyne from 1,2-Dibromocyclopentene.

General Procedure 1,2-Dibromocyclopentene (515 mg, 2.28 mmol) and diene **7** (1.80 g, 19.6 mmol) were added to a dry 25-mL flask equipped with a stirbar and a reflux condenser and protected from atmospheric moisture. The flask was then immediately cooled in a -40 °C bath, and its contents were stirred for 10 min, after which a solution of *n*-BuLi (1.90 mL of a 1.50 *M* solution in hexanes, 2.85 mmol) was added. The resulting solution was held at -40 °C for 0.5 h, and then heated under reflux (95–100 °C) for 5 min.

A. Preparative Runs The reaction mixture was cooled to room temperature, and a solution of maleic anhydride (1.92 g, 19.6 mmol) in CH_3CN (*ca.* 10 mL) was added. The resulting mixture was stirred magnetically at room temperature for at least 1 h, and then extracted with pentane (3 x 50 mL). Following concentration to a volume of about 10 mL, this solution was passed through a short silica plug using pentane as eluent until TLC (100% pentane eluent) showed that no more compounds were eluting. This pentane solution was concentrated to approximately 1 mL. HPLC purification of this solution yielded **9** as a clear, colorless oil in 20% yield.

B. Analytical Runs The reaction mixture was cooled to room temperature, quenched with water, diluted with pentane (50 mL), and washed with water (25 mL). The organic layer was dried (Na_2SO_4), filtered, and passed through a short silica plug using pentane as eluent until TLC (100% pentane eluent) showed that no more compounds were eluting. The resulting solution was examined by analytical gas chromatography without concentration. Three different runs gave an average ratio of **9**:**10** of 9.4:1.

C. Variable Temperature Experiments The general procedure above was followed except that after being held at -40 °C for 0.5 h, the flask was placed in a bath at the appropriate temperature for 0.5 h. Work-up according to the analytical protocol provided the samples for GC analysis.

D. Adduct Stability 1,2-Dibromocyclopentene (250 mg, 1.11 mmol) and **7** (0.9 g, 9.8 mmol) were added to a dry 10-mL flask equipped with a stirbar and a reflux condenser. The solution was cooled to -40 °C bath and after 15 min a solution of *n*-BuLi (1.3 *M* in hexanes, 1.3 mL, 1.69 mmol) was added. The reaction mixture was stirred for 15 min at -40 °C and subsequently heated under reflux. At intervals of 1, 3, 8, 15, 25, and 45 min, *ca.* 0.1-mL aliquots were removed and diluted in pentane (2 mL). The aliquots were examined by analytical GC and found to have a ratios of **9:10** of 8.9:1, 8.7:1, 8.4:1, 8.5:1, 9.0:1, and 8.3:1, respectively.

E. Kinetics 1,2-Dibromocyclopentene, spiro[4,2]hepta-1,3-diene and hexane were combined in a 5-mL flask equipped for magnetic stirring and introduction of dry nitrogen. The stirred solution was cooled to -78 °C and after 5 min *n*-BuLi (1.1 *M* in hexanes, 1.39 mmol) was added. This solution was stirred for an additional 5 min, and then the flask was transferred to an ice-water bath with continued stirring. At 5, 10, 15, 20, 30, 45, 60, 75, 90 and 120 min, 100-μL aliquots were removed and quenched in a 1:10 water-pentane mixture (0.5 mL) at 0 °C. The organic solution was filtered through a cotton plug before GC analysis.

Solutions having three different concentrations of diene **7** and having identical total volumes of 2.42 mL were prepared as follows.

3.96 *M*: 1,2-Dibromocyclopentene (250 mg, 1.11 mmol), spiro[4,2]hepta-1,3-diene (883.6 mg, 9.59 mmol) and *n*-BuLi (1.26 mL of 1.1 *M* solution in hexanes, 1.39 mmol).

2.03 *M:* 1,2-Dibromocyclopentene (250 mg, 1.11 mmol), spiro[4,2]hepta-1,3-diene (448.0 mg, 4.86 mmol), hexane (0.50 mL) and *n*-BuLi (1.26 mL of 1.1 *M* solution in hexanes, 1.39 mmol).

1.05 *M:* 1,2-Dibromocyclopentene (250 mg, 1.11 mmol), spiro[4,2]hepta-1,3-diene (234.0 mg, 2.54 mmol), hexane (0.76 mL) and *n*-BuLi (1.26 mL of 1.1 *M* solution in hexanes, 1.39 mmol).

The concentration of 1,2-dibromocyclopentene as a function of time was determined by its relative ratio to an internal standard, which was an unreactive impurity originally present in the spiroheptadiene **7**.

F. Equilibrium between 5 and 8 To a 10-mL flask equipped for magnetic stirring and introduction of dry nitrogen and containing *n*-BuLi (1.12 *M* in hexanes, 1.11 mmol) at -78 °C was added 1,2-dibromocyclopentene (100 mg, 0.886 mmol). After being stirred for 5 min at -78 °C, the solution was placed in a -20 °C bath. Over a period of four hours, 50-μL aliquots were removed and quenched in a 3:10 water-pentane mixture (0.5 mL) at 0 °C. The organic solution was filtered through a cotton plug before GC analysis. The ratio of **8:5** remained approximately 1:6.5 over the course of the experiment.

Performing this experiment for a two-hour period at 0 °C and in the presence of spiroheptadiene **7** afforded an average ratio of 0.1 for the ratio of **8:5**.

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References and Footnotes

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11. As reflected in the yield of adducts **9** and **10**, *n*-BuLi was found to be more effective than *t*-BuLi for the dehalogenation.
12. For example, such behavior is reported for benzyne (Wittig, G.; Dürr, H. *Liebigs Ann. Chem.* **1964**, *672*, 55–62; Crews, P.; Beard, J. *J. Org. Chem.* **1973**, *38*, 522–532), for 1,2-dehydro-*o*-carborane (Ghosh, T.; Gingrich, H. L.; Kam, C. K.; Mobraaten, E. C.; Jones Jr., M. J. *J. Am. Chem. Soc.* **1991**, *113*, 1313–1318), and is proposed for 1,2,4-cyclohexatriene (Christl, M.; Braun, M.; Müller, G. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 473–476). We thank a referee for bringing the latter reference to our attention.
13. In our hands, reaction mixtures containing 1-lithio-2-bromocyclopentene (**8**) are stable to *ca.* -20 °C. The requirement of higher temperatures to effect elimination is precedented by the known kinetics for decomposition of **8** in ethereal media: Wittig, G.; Weinlich, J.; Wilson, E. R. *Chem. Ber.* **1965**, *98*, 458–470; also see reference 5a.
14. Recent studies using a different spirodiene confirm that the ratios of [2+2]- and [2+4]-cycloadducts are independent of temperature when **3** is the precursor of **1**, but dependent on temperature with **5** as the precursor; moreover, the experimental error observed when **3** is used is considerably lower than in the present case: Hou, D.-R. unpublished results.
15. Because lithium bromide has low solubility in the reaction medium, this control experiment does not precisely mimic the situation wherein this salt is being generated directly in the presence of cyclopentyne by vicinal elimination of **5**. This issue is under investigation.
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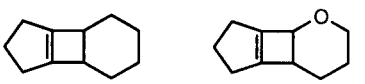
19. A referee has commented that the *ab initio* calculations of Johnson (Johnson, R.; Daoust, K. J. *J. Am. Chem. Soc.*, **1995**, *117*, 362–367) have "effectively demolished" the idea of orbital isomerism. We do not share this opinion. In contrast to our AM 1 investigations,[18] the *ab initio* studies do not explore the entire potential energy surface for the reactions of strained cycloalkynes. Were they to do so, we believe that our conclusions regarding the potential for concerted [2+2]-cycloadditions and electrocyclic reactions of such

systems would be vindicated, although we now believe it is the symmetrical rather than the unsymmetrical form of cyclopentyne that is responsible for this reaction channel.[7]

20. Although this could reflect diffusion control of the reaction between **1** and **7**, we think it does not, based on the fact that generating **1** from **3** in the presence of equimolar amounts of cyclohexene and dihydropyran produces a 1:3 ratio of the corresponding [2+2]-cycloadducts **i** and **ii**: Hou, D.-R., unpublished results.



i **ii**

21. Detailed AM 1 computational studies show that the potential energy surface for the [2+4]-cycloaddition is complex but definitely consistent with a forbidden process.[7]
22. The recent report of a stepwise component for the [2+4]-cycloreversion of norbornene lends credence to the intervention of **11** on the pathway to **10**: Zewail, A.; Horn, B.A.; Herek, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 8755–8756.
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24. We are unable at this time to exclude the possibility that *both* **9** and **10** are produced by stepwise addition of **3** to **7** to afford biradicaloid **11**; collapse of the biradicaloid to the cycloadducts would require a $\Delta\Delta H^{\ddagger}$ of about 0 kcal/mol to account for the temperature-independence of the product ratio.
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