J. Am. Chem. Soc. **1998,** *120,* 6871−6876

Study of a Vinylidenecarbene−Cycloalkyne Equilibrium in the *D*$_3$-Trishomocubyl Ring System

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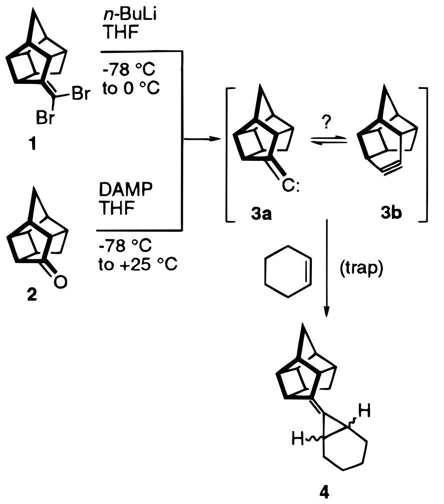
Received December 22, 1997. Revised Manuscript Received May 14, 1998

Abstract: The same cage-annulated vinylidenecarbene, **7a**, could be generated and subsequently trapped in situ by cyclohexene via either of the following methods: (i) low-temperature reaction of 4-(dibromomethylene)-pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**6**) with *n*-BuLi−THF and (ii) low-temperature reaction of 5-bromopentacyclo[7.3.0.0^{2,7}.0^{3,11}.0^{6,10}]dodec-4-ene (**12**) with LDA−THF. These results, together with the corresponding results of site-specific ^{13}C-labeling experiments performed on **6**-C(4)═^{13}CBr$_2$ and **12**-^{13}C(5), provide evidence for the thermodynamic stability of **7a** *vis-à-vis* **7b**. In addition, the results of semiempirical and ab initio MO calculations demonstrate the relative kinetic as well as thermodynamic preference for **7a** *vis-à-vis* **7b**.

Introduction

Cycloalkanylidenecarbene−cycloalkyne rearrangements have been the subject of numerous experimental[1−3] and theoretical[2d,4] investigations. Among carbocyclic species, whereas cyclobutyne has been reported to rearrange to cyclopropanylidenecarbene,[2g,4b] higher cycloalkyne homologues do not exhibit similar behavior. Instead, higher cycloalkyne homologues generally are preferred thermodynamically; with some notable exceptions,[5b] they frequently are formed via spontaneous rearrangement of the corresponding cycloalkanylidenecarbenes.[1,2a−f,5a] Interestingly, a cage-annulated cyclopentanylidenecarbene has been generated recently that does *not* display any tendency to rearrange to the corresponding cycloalkyne.[3a] Thus, the reactive intermediate produced either (i) via reaction of 8-(dibromomethylene)pentacyclo-[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**1**) with *n*-BuLi−THF or (ii) via base-promoted reaction of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one (**2**) with diethyl diazomethylphosphonate (DAMP) has been shown to be vinylidenecarbene **3a** rather than the corresponding cycloalkyne, **3b** (see Scheme 1).[3a] We now report the results of a corresponding study of the reactive intermediate produced via reaction of 4-(dibromomethylene)pentacyclo-[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**6**) with *n*-BuLi−THF.

Scheme 1



Results and Discussion

Dibromomethylenation[6] of pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecan-4-one (**5**)[7] afforded **6** in excellent yield (91%) (Scheme

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(8) (a) Interestingly, we observed that only one of two possible “vinylidenecarbene dimers”, **9** (i.e., *meso* or *d,l*), was formed in this reaction. However, despite many attempts, we were unable to obtain a good-quality single crystal of this material for X-ray structural analysis. Hence, the identity of the single isomer formed in this reaction remains unestablished. (b) When **6** was allowed to react with *n*-BuLi−THF in the absence of cyclohexene (trap), the isolated yield of **9** increased marginally (i.e., from 9% to 13%). In addition, **9** was obtained in low yield (6%) when **12** was allowed to react with LDA−THF in the absence of cyclohexene. When the latter reaction was performed in the presence of added cyclohexene, **9** was not detected among the reaction products.

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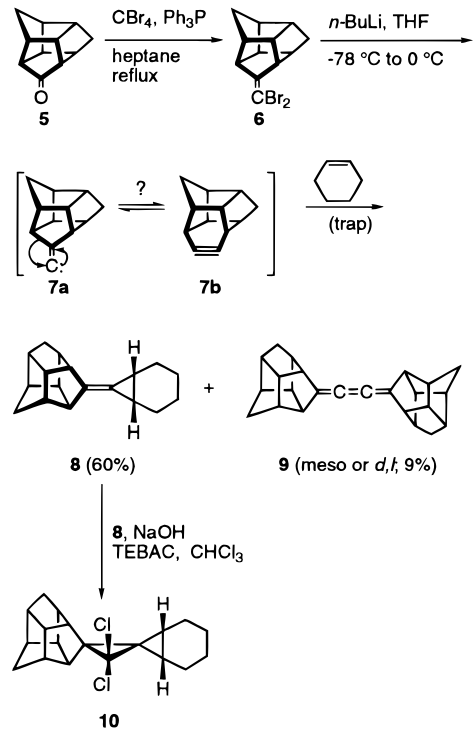
S0002-7863(97)04313-8 CCC: $15.00

Scheme 2



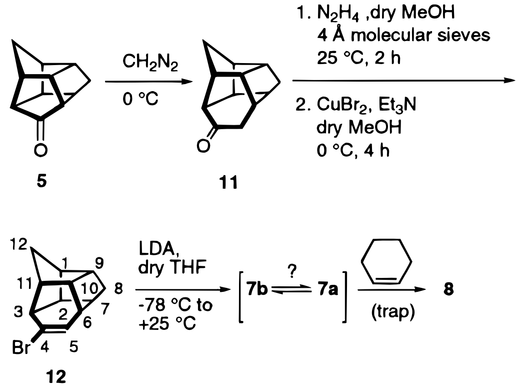
2). The structure of **6** was established unequivocally via application of X-ray crystallographic methods. Subsequent low temperature reaction of **6** with *n*-BuLi−THF, when performed in the presence of excess cyclohexene (trap), afforded cycloadduct **8** (Scheme 2) in 60% yield along with a cumulene, **9** (9%), that might have been formed either via dimerization of vinylidenecarbene **7a** or, alternatively, via reaction of an intermediate vinyl anion with either vinylidenecarbene **7a** or the starting dibromide (**6**).[8]

The cycloadduct **8** thereby obtained was reacted with dichlorocarbene (generated under phase-transfer conditions).[9] Crystallization of the resulting crude product afforded the dichlorospirocyclic adduct **10** (Scheme 2), whose structure was established unequivocally via application of X-ray crystallographic methods.

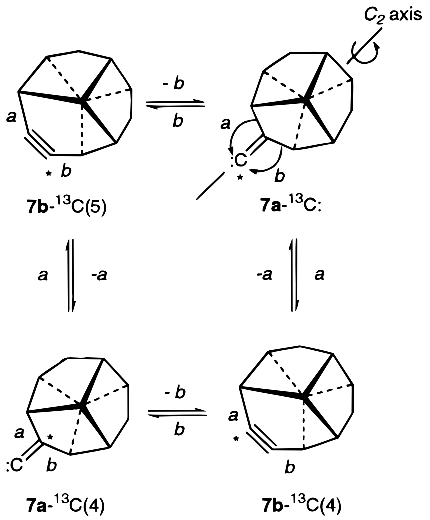
The foregoing result is consistent with the formation and subsequent in situ trapping of an intermediate vinylidenecarbene (i.e., **7a**) and provides no evidence for the intermediacy of the corresponding cycloalkyne, **7b**. To gain additional evidence concerning the potential incursion of **7b** in this reaction, a method was devised whereby **7a** and/or **7b** might be accessed from the "cycloalkyne side" of the equilibrium. The synthetic methodology that was employed for this purpose is shown in Scheme 3. Thus, diazomethane-promoted ring expansion of **5**[10] afforded **11** (94% yield). Attempted conversion of **11** into the corresponding geminal dibromide[11] under the conditions shown in Scheme 3 proceeded with concomitant elimination of HBr, thereby affording a cage-annulated bromoalkene, **12**.

An attempt was made to generate cycloalkyne **7b** directly via low-temperature reaction of **12** with lithium diisopropylamide (LDA) in dry THF. However, when this reaction was performed in the presence of added cyclohexene, only cycloadduct **8** was isolated. We conclude that, if **7b** is formed at all via this reaction, it rearranges spontaneously and very rapidly to the corresponding vinylidenecarbene (**7a**), the only reactive intermediate that is capable of being trapped in situ by cyclohexene.

Scheme 3



Scheme 4



Results of ^{13}C-Labeling Studies. To further address the issue of the potential intermediacy of **7b** in these reactions, two separate site-specific ^{13}C-labeling studies were performed. In the first study, reaction of **6**-C(4)=^{13}CBr$_2$ (enriched with 5 atom % ^{13}C) with *n*-BuLi at low temperature in the presence of cyclohexene (trap) afforded the corresponding ^{13}C-labeled cycloadduct **8** along with the corresponding ^{13}C-labeled "vinylidenecarbene dimer", i.e., **9** (vide supra).

Carbon-13-labeled cycloadduct **8** was converted into **10** via reaction with :CCl$_2$, and the gated-decoupled ^{13}C NMR spectrum of **10** was integrated carefully. Analysis of the integrated ^{13}C NMR spectrum established that no scrambling of the^{13}C label had occurred, as would be required by the incursion of cycloalkyne **7b** (see Scheme 4). We conclude from this result that **7b** is not energetically accessible via the corresponding vinylidenecarbene (**7a**) and that there is no incursion of the former species on the reaction profile by which **7a** is formed via *n*-BuLi-promoted α-elimination of bromine from **6**.

In the second site-specific ^{13}C-labeling study, ring expansion of **5**,[10] when performed via the method shown in Scheme 3 by using ^{13}CH$_2$N$_2$, afforded **11**-^{13}C(5) (enriched with 5 atom % ^{13}C). Subsequently, this material was converted into **12**-^{13}C-(5) by using the procedure shown in Scheme 3. Then, **12**-^{13}C-(5) was reacted with LDA−THF at low temperature in the presence of cyclohexene (trap), thereby affording the corresponding ^{13}C-labeled cycloadduct **8**. Finally, this material was converted into **10** via reaction with dichlorocarbene (see Scheme 2), and the gated-decoupled ^{13}C NMR spectrum of **10** was integrated carefully. Analysis of the integrated, gated-decoupled ^{13}C NMR spectrum established that the ^{13}C label had become

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Table 1. Results of Semiempirical and Ab Initio Calculations

computational method	alkanylidene−carbene (**7a**)	cycloalkyne (**7b**)	transition-state energy
AM1 (kcal mol^{-1})[a]	153.8 [0][d]	174.9 [0]	193.1 [1]
relative energies (kcal mol^{-1})	(0.0)	(21.1)	(39.3)
HF/6-31G(*)[b] (hartrees)	−461.26696 [0]	−461.22317 [0]	−461.22217 [1]
relative energies (kcal mol^{-1})	(0.0)	(27.5)	(28.1)
ZPVE[c] (kcal-mol^{-1})	139.6	139.5	139.3
B3LYP/6-31G(*)// HF/6-31G(*) (hartrees)	−464.33482	−464.32155	−464.31646
relative energies (kcal mol^{-1})	(0.0)	(8.3)	(11.5)

[a] Heats of formation, ΔH_f, in kcal mol^{-1}. [b] Absolute energies in hartrees. [c] Zero-point vibrational energies in kcal mol^{-1}. [d] Number of calculated imaginary frequencies are given in brackets.

scrambled over *both* vinyl carbon positions in **8**, as would be required by the incursion of cycloalkyne **7b** (see Scheme 4). This result confirms the fact that **7b**-^{13}C(5) is formed directly in this reaction [via base-promoted elimination of HBr from **12**-^{13}C(5)]. However, prior to being trapped in situ by cyclohexene, this cycloalkyne intermediate rearranges very rapidly to the corresponding vinylidenecarbene. Due to the fact that both **7a** and **7b** possess C_2 symmetry, cycloalkyne−vinylidenecarbene rearrangement in this system proceeds via two equally probable competing pathways that result in scrambling of the ^{13}C label between the two vinyl carbon atoms in the trapping product, **8**.[12]

Results of Theoretical Calculations. The energetics of rearrangement of vinylidenecarbene **7a** to the corresponding cycloalkyne, **7b**, were investigated by using (i) semiempirical MO computational methods (AM1 Hamiltonian)[13] and (ii) ab initio calculations at the HF/6-31G(*) and B3LYP/6-31G(*)//HF/6-31G(*) levels of theory. The results thereby obtained are shown in Table 1.

All of the computational results contained therein clearly reflect the thermodynamic preference for **7a** *vis-à-vis* **7b**. Interestingly, the results of HF/6-31G(*) calculations indicate a thermodynamic preference for **7a** similar to that which was obtained at the AM1 level of theory. However, the kinetic barrier calculated at the higher level of theory is predicted to be substantially less than that predicted by semiempirical calculations. An even more striking change is seen when the results of a single-point calculation performed at the B3LYP/6-31G(*)//HF/6-31G(*) level of theory[14] are compared with the corresponding HF/6-31G(*) calculated results. The results of the Becke[14] calculations indicate that the thermodynamic preference for **7a** is reduced by ca. 20 kcal-mol^{-1} and the kinetic barrier for the **7a**−**7b** interconversion is reduced by >15 kcal mol^{-1} relative to the corresponding values that were calculated at the HF/6-31G(*) level of theory. A similar influence of electron correlation on the energetics of cycloalkanylidenecarbene−cycloalkyne rearrangements has been reported previously.[4]

In the case of the corresponding *monocyclic* systems, the results of ab initio calculations performed at the MP4SDTQ/6-31G(*) level of theory[4b] suggest that cyclohexyne is preferred thermodynamically to cyclopentanylidenecarbene by 16.0 kcal mol^{-1}. For purposes of comparison, we have performed HF/6-31G(*) calculations with full geometry optimization on cyclopentanylidenecarbene and cyclohexyne. The results of a single-point calculation performed at the B3LYP/6-31G(*) level of theory[14] with HF/6-31G(*) geometry optimization suggests that cyclohexyne is preferred thermodynamically to cyclopentanylidenecarbene by 11.0 kcal mol^{-1}. Both species are predicted to display the preferred C_2 symmetry.

In addition, the "perturbed" cyclopentanylidenecarbene and cyclohexyne moieties contained within the **7a** and **7b** molecular frameworks, respectively, have been partially optimized at the HF/6-31G(*) level of theory. The C−H bond distances, bond angles, and torsion angles in each "monocyclic moiety" were optimized by freezing the HF/6-31G(*)-calculated positions of the carbon atoms in the cyclopentanylidenecarbene moiety in **7a** and again in the cyclohexyne moiety in **7b**. This approach provides a potential method to evaluate the role of steric effects associated with the constraints imposed by the cycloannulating cage framework upon the relative thermodynamic stabilities of "monocyclic" cyclopentanylidenecarbene and "monocyclic" cyclohexyne in **7a** and **7b**, respectively. The results of a single-point B3LYP/6-31G(*)//HF/6-31G(*) calculation performed for these "perturbed monocyclic" cyclopentanylidenecarbene and cyclohexyne moieties contained within **7a** and **7b** suggest that the latter species is destabilized relative to the former by 1.5 kcal mol^{-1}. This result is in qualitative agreement with experiment and suggests that the observed destabilization of **7b** *vis-à-vis* **7a** may be due at least in part to the geometric constraints imposed by cage annulation upon these two, potentially equilibrating, reactive intermediates.

Overall, our computational results confirm the experimentally observed thermodynamic instability of **7b** *vis-à-vis* **7a**. The thermodynamic driving force in the monocyclic system that favors cyclohexyne in the cyclopentanylidenecarbene−cyclohexyne equilibrium is clearly reversed in the case of the corresponding equilibrium in our cage annulated systems, **7a**,**b**.

Conclusions

Entry into the **7a**−**7b** manifold from either the "vinylidenecarbene side" (Scheme 2) or the "cycloalkyne side" (Scheme 3) of this putative equilibrium leads to products that result exclusively via in situ trapping of **7a**. The thermodynamic and kinetic inaccessibility of **7b** from **7a** is confirmed by the results of semiempirical and ab initio MO calculations and receives further confirmation via the results of site-specific ^{13}C-labeling studies.

Experimental Section

Melting points are uncorrected. Elemental microanalytical data were obtained by personnel at M−H−W Laboratories, Phoenix, AZ. Low-resolution electron impact (EI) mass spectra were obtained by using a Varian Saturn 3 ion trap GC/MS system that was operated at 70 eV. High-resolution mass spectral data for **8** were obtained at the Mass

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(12) A reviewer noted that symmetrization that results in ^{13}C scrambling between the two vinyl carbon atoms when **12**-^{13}C(5) is treated with LDA−THF might occur at the vinyl anion stage. In an effort to obtain additional information in this regard, **12**-^{13}C(5) was allowed to react with LDA−THF at −78 °C during 2 h. The reaction mixture was warmed to 0 °C and allowed to stir at that temperature for ca. 2 h, during which time the progress of the reaction was monitored via thin layer chromatographic (TLC) analysis. During this time, the formation of a small quantity of **9** was detected by TLC analysis. The reaction was quenched via addition of excess D_2O. Careful analysis of the ^{1}H and ^{13}C spectra of recovered **12**-^{13}C(5) (thereby recovered in 68% yield) revealed that (i) no scrambling of the ^{13}C label had occurred and (ii) no deuterium had become incorporated into recovered **12**-^{13}C(5). Although these results provide no additional insight into the question of symmetrization in the vinyl anion, they are nevertheless consistent with the interpretation that LDA-promoted anion formation in **12**-^{13}C(5) proceeds irreversibly.

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Spectrometry Facility at the Department of Chemistry and Biochemistry, University of Texas at Austin, by using a ZAB-E double-sector high-resolution mass spectrometer (Micromass, Manchester, England) that was operated in the chemical ionization mode. Specifically ^{13}C-labeled materials needed for this study, i.e., **6**-C(4)=^{13}CBr$_2$ and **11**-^{13}C(5) (both enriched with ca. 5 atom % ^{13}C) were prepared via the procedures described below by starting with isotopically enriched ^{13}CBr$_4$ and ^{13}C-Diazald (precursor to ^{13}CH$_2$N$_2$), respectively. The ^{13}C-labeled precursors needed for this purpose were purchased from the Aldrich Chemical Co., Milwaukee, WI, and were used as obtained therefrom.

4-(Dibromomethylene)pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (6). A mixture of **5**[7] (320 mg, 2.0 mmol), CBr$_4$ (995 mg, 3.0 mmol), and Ph$_3$P (1.57 g, 6.0 mmol) in dry heptane (40 mL) under argon was refluxed with stirring for 48 h. The reaction mixture was allowed to cool to ambient temperature and then was filtered. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel by eluting with pentane. The product thereby obtained was recrystallized from hexane to afford pure **6** (578 mg, 91%) as a colorless microcrystalline solid: mp 81−83 °C; IR (KBr) 2980 (s), 2951 (s), 2870 (m), 1460 (m), 1281 (m), 1169 (m), 1049 (w), 806 (s), 764 (m), 625 cm^{-1} (w); ^{1}H NMR (CDCl$_3$) δ 1.45 (q, $J = 10.6$ Hz, 4 H), 2.25 (m, 6 H), 2.55 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 34.0 (t), 43.0 (d), 45.8 (d), 47.2 (d), 53.4 (d), 70.2 (s), 155.5 (s); EI mass spectrum (70 eV), m/z (relative intensity) 316 (molecular ion, 8), 237 (25), 155 (34). Anal. Calcd for C$_{12}$H$_{12}$Br$_2$: C, 45.61; H, 3.83. Found: C, 45.36; H, 4.16. The structure of **6** was established unequivocally via application of X-ray crystallographic methods (vide infra).

Reaction of 6 with *n*-BuLi−THF in the Presence of Cyclohexene (Trap). A solution of **6** (432 mg, 1.37 mmol) and cyclohexene (1.12 g, 13.7 mmol) in dry THF (10 mL) under argon was cooled to −78 °C via application of an external dry ice−acetone bath. To this cold solution was added with stirring *n*-BuLi (1.32 mL of a 2.5 M solution of *n*-BuLi in hexane, 3.29 mmol). After the addition of the organometallic reagent had been completed, the reaction mixture was stirred at −78 °C for 1 h, at which time the external cold bath was replaced by an ice−water bath, and the reaction mixture was allowed to warm gradually to 0 °C during 3 h. The reaction was quenched via addition of ice-cold water (10 mL), and the resulting aqueous suspension was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The organic layer was dried (Na$_2$SO$_4$) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by eluting with pentane.

Workup of the first chromatography fraction afforded pure 4-(bicyclo[4.1.0]hept-7′-ylidene)pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**8**, 196 mg, 60%), which was thereby obtained as a colorless oil: IR (film) 2944 (s), 2855 (s), 1462 (m), 1292 (m), 1096 (w), 806 cm^{-1} (w); ^{1}H NMR (CDCl$_3$) δ 0.75−0.95 (m, 2 H), 1.10−1.30 (m, 4 H), 1.38 (*A*B, $J_{AB} = 12.0$ Hz, 4 H), 1.50−1.80 (m, 4 H), 1.92−2.16 (m, 6 H), 2.26−2.40 (m, 2 H); ^{13}C NMR (CDCl$_3$) δ 12.6 (d), 12.8 (d), 21.5 (2 C, t), 23.3 (t), 23.4 (t), 34.1 (2 C, t), 42.7 (d), 42.8 (d), 46.6 (d), 47.0 (d), 47.4 (2 C, d), 49.9 (d), 50.1 (d), 114.3 (s), 136.0 (s); CI mass spectrum (70 eV), m/z (relative intensity) 239 [(M + H)$^+$, 56], 238 (molecular ion, 100.0), 237 (72); HRMS calcd for C$_{18}$H$_{22}$ 238.1722, found 238.1714.

Continued elution of the chromatography column afforded a second fraction which, when concentrated in vacuo, afforded pure **9** (a single isomer, 38 mg, 9%)[8] as a colorless microcrystalline powder: mp 158−160 °C; IR (KBr) 2974 (s), 2874 (m), 2365 (w), 2334 (m) 1643 (w), 1458 (w), 1402 (w), 1292 (w), 1086 cm^{-1} (w); ^{1}H NMR (CDCl$_3$) δ 1.45 (m, 8 H), 2.20−2.55 (m, 16 H); ^{13}C NMR (CDCl$_3$) δ 34.0 (t), 43.2 (d), 47.2 (d), 47.3 (d), 53.6 (d), 124.0 (s), 147.3 (s); EI mass spectrum (70 eV), m/z (relative intensity) 314 ([M + 2]$^+$, 21), 313 ([M + 1]$^+$, 80), 312 (molecular ion, 100), 311 (16), 247 (12), 161 (7); HRMS calcd for C$_{24}$H$_{24}$ 312.1878, found 312.1872.

Dichlorocyclopropanation of 8. To a solution of **8** (150 mg, 0.625 mmol) and benzyltriethylammonium chloride (TEBAC, 28.5 mg, 0.125 mmol) in CHCl$_3$ (5 mL) was added 50% aqueous NaOH (5 mL), and the resulting mixture was stirred at ambient temperature for 24 h. The layers were separated, and the aqueous layer was extracted with CHCl$_3$ (2 × 10 mL). The combined organic layers were washed successively with 10% HCl (2 × 5 mL), saturated aqueous NaHCO$_3$ (2 × 5 mL), and water (2 × 5 mL). The organic layer was dried (Na$_2$SO$_4$) and filtered, and the filtrate was concentrated in vacuo. The residue was triturated with acetone (3 × 5 mL) to afford **10** (148 mg, 75%). Recrystallization of this material from hexane afforded pure **10**: mp 135−136 °C; IR (KBr) 2972 (s), 2941 (s), 2863 (s) 1501 (m) 1451 (m), 1287 (s), 1167 (m), 1065 (m), 1015 (m), 885 (s), 816 (s), 698 cm^{-1} (m); ^{1}H NMR (CDCl$_3$) δ 1.24 (m, 2 H), 1.38 (m, 6 H), 1.58 (m, 4 H), 1.76 (m, 1 H), 1.95 (m, 2 H), 2.03 (m, 1 H), 2.14 (m, 3 H), 2.31 (q, $J = 6.0$ Hz, 1 H), 2.49 (m, 1 H), 2.63 (m, 1 H); ^{13}C NMR (CDCl$_3$) δ 19.5 (d), 20.4 (t), 20.6 (t), 20.7 (d), 21.8 (t), 22.0 (t), 33.1 (t), 34.1 (t), 36.5 (s), 42.7 (d), 43.5 (d), 45.9 (d), 47.1 (d), 47.6 (d), 48.6 (d), 49.6 (s), 51.9 (2C, d), 70.6 (s). Anal. Calcd for C$_{19}$H$_{22}$Cl$_2$: C, 71.03; H, 6.90. Found: C, 71.10; H, 7.12. The structure of **10** was established unequivocally via application of X-ray crystallographic methods (vide infra).

Pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]dodecan-11-one (11).[10] A suspension of **5**[7] (2.60 g, 16.3 mmol) in Et$_2$O (100 mL) was cooled to 0 °C via application of an external ice−water bath. To this cooled suspension was added dropwise with stirring a solution of CH$_2$N$_2$ in Et$_2$O that had been generated via reaction of *p*-toluenesulfonylmethylnitrosamide (Diazald, 52.3 g, 244 mmol). After all of the ethereal CH$_2$N$_2$ solution had been added, the resulting mixture was stored at 0 °C for 56 h. Excess CH$_2$N$_2$ then was decomposed via careful, dropwise addition of glacial HOAc until the yellow color of CH$_2$N$_2$ had disappeared (ca. 13 mL). The resulting mixture was washed sequentially with saturated aqueous NaHCO$_3$ solution (20 mL) and water (20 mL), dried (Na$_2$SO$_4$), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography on silica gel by eluting with 10% Et$_2$O−pentane. Workup of the chromatographic eluate afforded **11** (2.66 g, 94%). Analytically pure **11**, prepared via vacuum sublimation of the material that had been purified via column chromatography was obtained as a colorless microcrystalline solid: mp 133−134 °C (lit.[10] mp 132−133 °C); ^{13}C NMR (CDCl$_3$) δ 33.8 (t), 34.2 (t), 36.3 (d), 37.0 (t), 39.88 (d), 39.93 (d), 40.5 (d), 40.7 (d), 47.1 (d), 48.2 (d), 55.0 (d), 216.3 (s). The IR and proton NMR of **11** obtained in this study are essentially identical to the corresponding spectra that have been reported previously for **11**.[10]

4-Bromopentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]dodec-4-ene (12). To a stirred suspension of previously dried 4 Å molecular sieves (3 g) in dry MeOH (20 mL) at ambient temperature was added anhydrous hydrazine (1.92 g, 60 mmol). After all of the hydrazine had been added, the reaction was stirred at ambient temperature for an additional 20 min. A solution of **11** (522 mg, 3.0 mmol) in MeOH (10 mL) then was added dropwise with stirring to the reaction mixture, and the resulting mixture was stirred at ambient temperature for 2 h. The reaction mixture was filtered, and the residue (molecular sieves) was washed with Et$_2$O (100 mL). The combined filtrates were concentrated in vacuo, and excess hydrazine was removed from the residue via gentle heating in vacuo. The crude product (hydrazone of **11**, 564 mg, ca. 100%) was used as obtained in the next synthetic step without additional purification or characterization.

To a solution of CuBr$_2$ (4.02 g, 18 mmol) in MeOH (20 mL) was added with stirring Et$_3$N (910 mg, 9.0 mmol) at ambient temperature. After all of the Et$_3$N had been added, the resulting mixture was stirred for an additional 10 min. The reaction mixture then was cooled to 0 °C via application of an external ice−water bath. A solution of the crude hydrazone of **11** (564 mg, 3.0 mmol, vide supra) in MeOH (10 mL) was added dropwise with stirring to the cooled reaction mixture during 10 min. Gentle evolution of N$_2$ was observed during this period. After all of the hydrazone had been added, the reaction mixture was stirred at 0 °C for an additional 4 h. The reaction was quenched via addition of 15% aqueous NH$_4$OH (100 mL), and the resulting aqueous suspension was extracted with CH$_2$Cl$_2$ (3 × 30 mL). The organic extracts were washed with brine (10 mL), dried (Na$_2$SO$_4$), and filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting with pentane. Pure **12** (519 mg, 73%) was thereby obtained as a colorless oil: IR (film) 2957 (s), 2878 (m), 1667 (w), 1634 (w), 1470 (w), 1300 (m), 1051 (w), 860 (w), 787 (m), 750 cm^{-1} (m); ^{1}H NMR (CDCl$_3$) δ 1.19−1.50 (m, 4 H), 1.58−1.70 (m, 1 H), 1.72−1.82 (m, 2 H), 1.91−2.01 (m, 1

Table 2. X-ray Data Collection and Processing Parameters for **6** and **10**

compd	**6**	**10**
formula	$C_{12}H_{12}Br_2$	$C_{19}H_{22}Cl_2$
size (mm)	0.22 × 0.41 × 0.52	0.21 × 0.22 × 0.51
space group	$P\bar{1}$	$P\bar{1}$
a (Å)	6.549(4)	8.9521(7)
b (Å)	9.443(3)	9.0587(9)
c (Å)	9.914(8)	10.5821(8)
α (deg)	84.15(5)	112.215(7)
β (deg)	71.40(5)	102.551(6)
γ (deg)	70.92(4)	92.167(7)
V (Å^3)	549.2(5)	768.7(1)
Z value	2	2
D_{calcd} (g cm^{-3})	1.911	1.388
μ (cm^{-1})	72.68	4.13
T (K)	295	295
$2\theta_{max}$ (deg)	44	50
total no. of reflns	1340	2702
no. of unique reflns	1340	2702
R_{int}	—	—
$I \geq 3\sigma(I)$	721	2031
no. of parameters	127	190
R, R_w	0.0530, 0.0699	0.0400, 0.0406
$(\Delta/\sigma)_{max}$	<0.01	<0.01
ρ_{max}; ρ_{min} (e Å^{-3})	0.79; −0.77	0.49; −0.34

H), 2.14−2.34 (m, 3 H), 2.38−2.47 (m, 1 H), 6.20−6.29 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 32.9 (t), 33.3 (t), 36.4 (d), 36.9 (d), 47.0 (d), 47.3 (d), 48.2 (d), 49.5 (2 C, d), 54.1 (d), 119.8 (s), 129.5 (d); EI mass spectrum (70 eV), m/z (relative intensity) (no molecular ion), 236 ([M − H]$^+$, 0.8), 157 (6), 91 (13). Anal. Calcd for $C_{12}H_{13}Br$: C, 60.78; H, 5.53. Found: C, 60.67; H, 5.67.

Reaction of 12 with LDA−THF in the Presence of Cyclohexene (Trap). A solution of **12** (119 mg, 0.5 mmol) and cyclohexene (411 mg, 5.0 mmol) in THF (5 mL) was cooled to −78 °C via application of a dry ice−acetone cold bath. To this cold solution was added with stirring LiN(i-Pr)$_2$ (LDA, 1 mL of a 1.5 M solution in cyclohexane, 1.5 mmol). After all of the LDA had been added, the resulting mixture was stirred at −78 °C for an additional 2 h, at which time the external dry ice−acetone bath was replaced by an ice−water bath, and the reaction mixture was allowed to warm gradually to 0 °C during 1 h. The reaction mixture was then stirred at 0 °C for an additional 3 h, at which time the external ice−water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring overnight. The reaction mixture then was cooled to 0 °C via application of an external ice−water bath, the reaction was quenched via dropwise addition of saturated aqueous NH_4Cl (1 mL), and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL), dried (Na_2SO_4), and filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting with pentane. Pure **8** (43 mg, 36%) was thereby obtained as a colorless oil. The ^{1}H and ^{13}C NMR spectra of this material were essentially identical with the corresponding spectra of **8** that had been obtained previously via reaction of **6** with n-BuLi, which had been performed in the presence of cyclohexene trap (vide supra).

X-ray Crystal Structures of 6 and 10. All data were collected on an Enraf-Nonius CAD-4 diffractometer by using the $\omega-2\theta$ scan technique, Mo Kα radiation (λ = 0.710 73 Å) and a graphite monochromator. Standard procedures used in our laboratory for this purpose have been described previously.[15] Pertinent X-ray data are given in Table 2. Data were corrected for Lorentz and polarization effects but not for absorption. The structures were solved by direct methods (**6** was solved by using SHELXS-86,[16] whereas SIR[17] was employed to solve structure **10**) and difference maps, and the model was refined by using full-matrix least-squares techniques. All non-hydrogen atoms were refined by using anisotropic thermal parameters. Hydrogen atoms were located on difference maps and then were included in the model in idealized positions [U(H) = $1.3B_{eq}$(C)] and allowed to ride upon the attached carbon atom. All computations other than those specified were performed by using MolEN.[18] Scattering factors were taken from the usual sources.[17]

^{13}C-Labeling Studies. Specifically ^{13}C-labeled compounds used in this study (see text) were prepared via the methods described above for the syntheses of the corresponding normal (unlabeled) materials. The extent of ^{13}C enrichment in the various reaction products thereby obtained was assessed via analysis of the corresponding gated-decoupled ^{13}C NMR spectra.[20]

Prior to performing ^{13}C NMR gated-decoupling experiments, spin−lattice relaxation times (i.e., T_1 values) were determined for all ^{13}C nuclei in each specifically ^{13}C-labeled molecule under investigation. Then, to ensure that efficient relaxation of all carbon nuclei had occurred before further pulses were applied, the pulse delay time employed for the gated-decoupling experiment was set ≥5 times the longest observed ^{13}C T_1 value.

^{13}C NMR gated-decoupling experiments were performed on ca. 0.1 M solutions of substrates in $CDCl_3$ in the absence of added spin-relaxation agents. The percentage of ^{13}C enrichment was estimated by averaging the results of careful multiple integrations of the gated-decoupled ^{13}C NMR spectrum in each case. The extent of ^{13}C-label scrambling concomitant with each reaction was ascertained by comparing the integrated, gated-decoupled ^{13}C NMR spectrum of each product with that of the corresponding, specifically ^{13}C-labeled reactant in each case.

Spectral integrations were performed a total of six times for each sample studied, and the standard deviation was calculated for each set of integrations (see Table 3). Comparison of the integration values for recovered **12**-^{13}C(5)[12] with those for **12**-^{13}C(5) "as synthesized" provides one measure of the error in the NMR method for estimating ^{13}C content and distribution. Another measure of error in the method is provided by the ratio of peaks: δ 49.6:δ 36.5 = (1.10 ± 0.02):1.00 that was measured for unlabeled **10**. Finally, note the quality of agreement between the ratio of peaks: δ 70.2:δ 155.5 = (5.41 ± 0.05): 1.00 for **6**-C(4)$=^{13}$CBr$_2$ and that of the corresponding ratio of peaks: δ 49.6:δ 36.5 = (5.32 ± 0.09):1.00 for **10** which contains one ^{13}C label (no label scrambling).

When potential sources of integration error, noted above, are taken into account, the distribution of label in **10** which contains two ^{13}C labels (due to label scrambling) suggests that complete symmetrization of the intermediate formed via reaction of **12**-^{13}C(5) with strong base may not have taken place. We are unable to specify the exact nature of this species on the basis of the experimental data that presently is available to us. Nevertheless, we can state with some certainty that the apparent lack of complete symmetrization in **10**, which contains two ^{13}C labels, is *not* due to the operation of competitive anionic rearrangement from **12**-^{13}C(5). Indeed, rearrangement of the anion formed from **12**-^{13}C(5) must proceed exclusively to afford **7a**-^{13}C:, which ultimately would result in the isolation of **10** that contains additional ^{13}C enrichment at the resonance signal that appears at δ 36.5, contrary to experimental observation.

Computational Methods. Semiempirical calculations (AM1 Hamiltonian)[13] and ab initio calculations were performed on an SGI INDIGO2 platform (UNIX operating system). AM1 calculations were performed by using SPARTAN software (version 5.0).[21a] Gaussian 94[21b] was employed for ab initio calculations. Ground-state geometries of

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Table 3. Results of ^{13}C NMR Spectral Integrations[a]

compd	resonance signals integrated (δ)	integration ratio
unlabeled **6**	155.5, 70.2	δ 155.5:δ 70.2 = 1.00: (1.06 ± 0.01)
6-C(4)=^{13}CBr$_2$	155.5, 70.2	δ 155.5:δ 70.2 = 1.00: (5.41 ± 0.05)
unlabeled **10**	49.6, 36.5	δ 49.6:δ 36.5 = (1.10± 0.02): 1.00
10 which contains one ^{13}C label (no label scrambling)	49.6, 36.5	δ 49.6:δ 36.5 = 1.00: (5.32± 0.09)
10 which contains two ^{13}C labels (due to label scrambling)	49.6, 36.5	δ 49.6:δ 36.5 = (1.34 ± 0.01): 1.00
unlabeled **12**	129.5, 119.8	δ 129.5:δ 119.8 = 1.00: (1.04 ± 0.01)
12-^{13}C(5), as synthesized	129.5, 119.8	δ 129.5:δ 119.8 = (4.81 ± 0.03): 1.00
recovered **12**-^{13}C(5)[b]	129.5, 119.8	δ 129.5:δ 119.8 = (5.27 ± 0.04): 1.00

[a] Carbon-13 NMR spectral integrations were performed on ca. 0.1 M solutions of substrates in CDCl$_3$ in the absence of added spin-relaxation agents. Spectral integrations were performed a total of six times for each sample studied, and the standard deviation was calculated for each set of integrations. [b] After having been treated with LDA at −78 °C, then warmed to 0 °C, and finally quenched via addition of D$_2$O (quench).

vinylidenecarbene **7a** and cycloalkyne **7b** and the corresponding transition state for their interconversion were optimized at the AM1 and HF/6-31G(*) levels of theory without any symmetry constraints having been imposed. In addition, B3LYP hybrid HF-DFT calculations[14] which employed a 6-31G(*) basis set were used to calculate thermodynamic and kinetic barriers to the interconversion of **7a** and **7b** for HF/6-31G(*) optimized geometries. Stationary points were characterized via complete vibrational frequency analyses as minima or saddle points.

Acknowledgment. We thank the Office of Naval Research (Grant N00014-98-1-0478 to A.P.M.), the Robert A. Welch Foundation (Grants B-963 to A.P.M. and B-1202 to S.G.B.), and the University of North Texas Faculty Research Committee (S.G.B.) for financial support of this study. We also thank Mr. Huang He, Department of Chemistry, University of North Texas, for assistance in obtaining the gated-decoupled ^{13}C NMR spectral results reported herein. In addition, we thank Professor Jennifer S. Brodbelt (Department of Chemistry, University of Texas at Austin) for having kindly obtained high-resolution chemical ionization mass spectral data for **8** and **9**. Finally, we thank Ms. Debra Dolliver, Department of Chemistry, Texas Woman's University, for having kindly obtained the low-resolution electron impact mass spectral data reported herein.

Supporting Information Available: Tables of positional parameters and their estimated standard deviations, general displacement parameter expressions (*U* values), bond distances, bond angles, torsion angles, and intermolecular contacts (less than 3.70 Å) for **6** and **10**, integrated gated-decoupled ^{13}C NMR spectra of **6**-C(4)=^{13}CBr$_2$, ^{13}C-enriched **10**, and **12**-^{13}C(5), and ^{13}C NMR spectra of normal (unlabeled) and ^{13}C-enriched **10** (31 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA974313E

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