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Stereoselectivity in the Intramolecular Pauson-Khand Reaction: Towards a Simple Predictive Model

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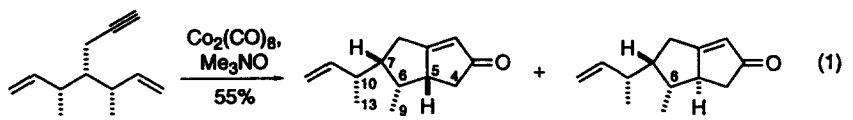
Abstract: The major product in the intramolecular Pauson-Khand reaction of 3,4-disubstituted 1,6-heptenynes to form bicyclo[3.3.0]octenones is highly dependent on the relative configurations of the two stereocenters of the substrate. For example, cycloaddition of the "*syn,syn*" stereoisomer of 3,5-dimethyl-4-propargyl-1,6-heptadiene gives predominantly an enone containing both substituents in more hindered *endo* orientations; the "*syn,anti*" stereoisomer, upon reaction across the "syn" linkage similarly gives mostly *endo* product, but upon reaction across the "anti" portion of the molecule affords almost exclusively an enone in which the C6 methyl group possesses *exo* stereochemistry. Parallel results obtain from enynes built upon cyclohexane frameworks. Calculated energies of pre-cycloaddition enynes, metallacycles presumed to be the penultimate intermediates in the cyclization mechanism, and the final products are examined in order to develop a reasonable predictive model. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Cyclopentenones; Mechanisms; Molecular modelling/mechanics; Pauson-Khand reactions

INTRODUCTION

In the intramolecular Pauson-Khand (PK) cyclization of 1,6-heptenynes to bicyclo[3.3.0]octenones, allylic and propargylic groups on the substrate normally end up on the *exo* face of the product.[1,2,3] We recently described a case in which the major product contained an *endo* methyl group at position C6 on the saturated ring (eq 1) and rationalized this result on the basis of conformational preferences about the allylic position.[4]



(1)

We have now examined three additional stereochemically defined dienynes specifically designed to probe these issues. Herein we present evidence that our earlier view, while helpful in defining systems that might lead to such results, is too limited to be of predictive value. However, by comparing experimental product ratios with calculated energies of presumed intermediates and products of these processes, we find that we can successfully rationalize not only our new results but also other work in this area, and perhaps provide a basis for at least qualitative prediction of stereochemical outcomes of related reactions.

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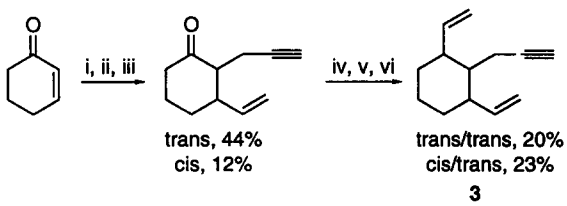
EXPERIMENTAL RESULTS

Pauson-Khand Cycloadditions of Stereochemically Defined Acyclic and Cyclic Dienynes

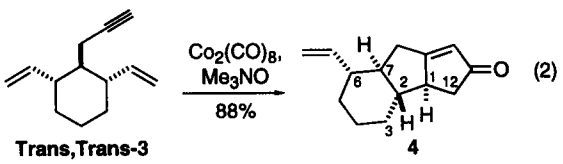
In order to expand the experimental basis of this study, we prepared a second acyclic substrate, **syn,anti-1**, by a route parallel to that used for **syn,syn-1**.[5,6] Because of the relative inaccessibility of the precursor to the corresponding **anti,anti-1** diastereomer,[7] we instead chose as alternatives two stereochemically defined, cyclohexane-based dienynes, **trans,trans-3** and **cis,trans-3**, whose preparations are shown in Scheme 1.[8] Characterization of the two stereoisomers of **3** was straightforward. Wittig reaction of *trans*-2-propargyl-3-vinylcyclohexanone with methoxymethylene ylide followed by hydrolysis gave a mixture of *trans,trans*- and *cis,trans*-2-propargyl-3-vinylcyclohexanecarbaldehyde, each of which was converted to the corresponding dienyne by Wittig olefination. A parallel sequence beginning with *cis*-2-propargyl-3-vinylcyclohexanone was also carried out in an attempt to obtain *cis,cis*-**3** via the *cis,cis*-aldehyde. However, the latter isomerized completely to its *cis,trans* isomer during the final Wittig reaction to give exclusively **cis,trans-3**, identical to one of the two products derived from *trans*-2-propargyl-3-vinylcyclohexanone, thus confirming its stereochemistry. Pauson-Khand cycloaddition results for each of these enynes follow.

Scheme 1



i. CH_2=CHMgBr, CuI; ii. HMPA; iii. HC≡$CHCH_2Br$, separate; iv. Ph_3PCH_2OMe, NaH, DMSO; v. Amberlite IR-120 resin, H_2O, DMSO, separate; vi. Ph_3PCH_3, NaH, DMSO.

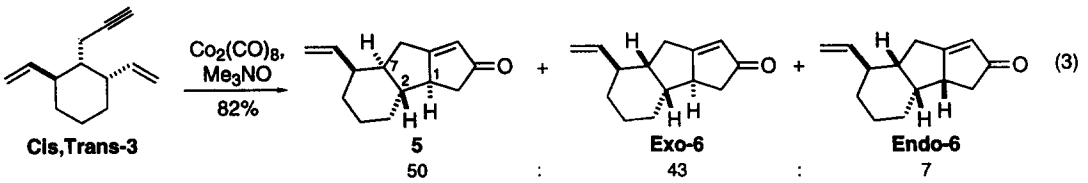
Trans,trans-3 cyclizes to give **4**[9] as *a single stereoisomerically pure product* in 88% yield,[10] with *exo* stereochemistry for the cyclohexane ring bond at C2 (eq 2).



Cis,trans-3 and **syn,anti-1** possess nonequivalent vinyl groups. Therefore, each may react by either of two distinct pathways that differ in the relative stereochemistry of the substituents on the linkage between the participating ene and yne functionalities. Each substrate was found to cyclize through both available pathways to give characteristically different stereochemical outcomes.

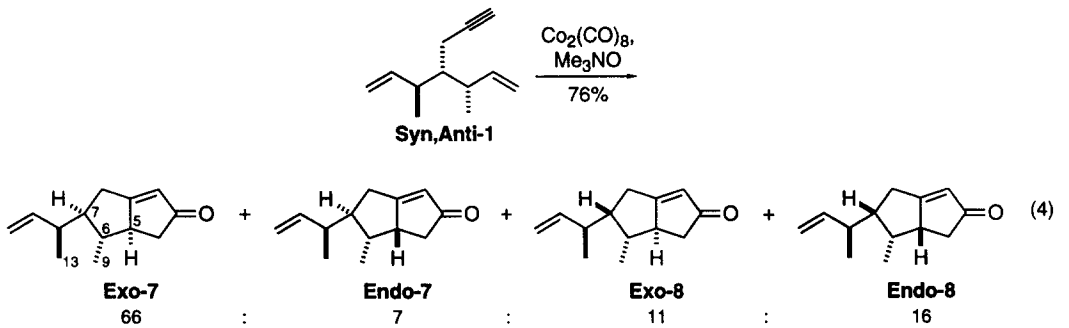
Cis,trans-3 cyclizes to give a mixture of three products (eq 3). Reaction involving the mutually *trans* propargyl and vinyl substituents proceeds in complete analogy with that of **trans,trans-3** to give a single *exo* enone **5**, differing from **4** only in the configuration of the remote vinyl group. Two enones arise from

cyclization between the mutually *cis* propargyl and vinyl moieties of **cis,trans-3**: **exo-6** and **endo-6**, with the former greatly predominating.



(3)

Cyclization of the last substrate, **syn,anti-1**, is the most complex, giving all four possible products (eq 4). **Exo-7** and **endo-7** arise from cyclization across the "anti" linkage. **Exo-7** is the major product, just as *exo* products **4** and **5** are the major products from the cycloadditions of **trans,trans-3** and **cis,trans-3**, respectively, across their "trans" junctions. Unlike its cyclic analogs, **syn,anti-1** also affords a small amount of *endo* product, **endo-7**, from the "anti" cyclization mode. Finally, similar to the cyclization of **syn,syn-1**, reaction of **syn,anti-1** across the "syn" bond gives more **endo-8** than **exo-8**. **Exo-7** was the only one of these four products isolable in pure form; the remaining three were obtained as mixture separable only on an analytical scale using HPLC; NMR data are thus incomplete for **endo-7** and **exo-8**, the minor components.



(4)

Characterizations of Stereoisomeric Enones 2, 4, 5, 6, 7, and 8

The elucidation of the structures of the enone products of the four Pauson-Khand processes described above was straightforward, being based upon a combination of 1D and 2D NMR data, and ultimately supported by two X-ray crystal structures. COSY and HETCOR measurements enabled signal assignment. Table 1 lists ^1H chemical shifts of protons diagnostic of the stereochemistry of the substitutent at C6 in the bicyclic and C2 in the tricyclic enones relative to both the adjacent ring fusion and to the stereocenter on the other side (note that the bicyclic and tricyclic enone numberings are different—see eq 1 and 2—but protons in comparable locations are listed together). The spectra of the bicyclic enones **2**, **7**, and **8** were better resolved in $CDCl_3$, whereas C_6D_6 proved to be superior for the tricyclics **4–6**, and the data were recorded using these solvents. For direct comparison, the data for **endo-2** in C_6D_6 are given in the last column. Only chemical shifts of signals for which we consider our assignments to be completely unambiguous are listed.

Table 1. Diagnostic ^1H Chemical Shifts for Enones **2** and **4–8**. Data in the left half of the table (bicyclic enones) were recorded in $CDCl_3$ solvent; those in the right half (tricyclics and **endo-2**) in C_6D_6.

Proton	Exo-2	Endo-2	Exo-7	Endo-7	Exo-8	Endo-8	*Proton*	Exo-4	Exo-5	Exo-6	Endo-6	Endo-2
4-endo	1.98	2.15	2.03			2.20	*12-endo*	1.84	1.73	1.64	1.88	1.95
4-exo	2.60	2.35	2.55			2.40	*12-exo*	2.38	2.28	2.28	2.11	2.14
5	2.72	3.11	2.59			3.15	*1*	2.08	1.90	2.38	2.37	2.44
6	*1.77*	2.22	*1.30*	2.25		2.32	*2*	*0.43*	*0.63*	*1.05*	2.03	1.69
9	1.17	*0.55*	1.13	*0.72*	1.18	*0.59*	*3* (1H)	0.78			*0.09*	*0.19*

Several points emerge with respect to the question of *exo* or *endo* stereochemistry at C6 (in **2**, **7**, and **8**) and C2 (in **4–6**). Protons and protons on alkyl groups at these positions exhibit upfield shifts when located on the *endo* face of the bicyclo[3.3.0] moiety (*italicized* entries in Table 1), relative to those nuclei on the *exo* face of the bicyclic system. In addition, the chemical shift difference between the diastereotopic methylene protons on the α-carbon of the enone (C4/C12) serves as an equally reliable diagnostic: $\Delta\delta\,(H_{exo} - H_{endo}) > 0.50$ ppm when the substituent at C6/C2 is *exo*, but $\Delta\delta\,(H_{exo} - H_{endo}) < 0.25$ ppm when that substituent is *endo*. In addition, the relative stereochemistry at C6 and C7 (in **2**, **7**, and **8**) and at C2 and C7 (in **4–6**) may be deduced from the chemical shifts of the protons at positions C6/C2 and C5/C1. *Endo* protons at C6/C2 are shifted upfield by about 0.5 ppm when the alkyl substituents at C6/C2 and at C7 are mutually *trans* (enones **4**, **5**, and **7**), relative to when they are *cis* (**2**, **6**, and **8**). A similar shift is found for the ring fusion (C5/C1) proton.

NOE-based methods provided supporting evidence. For example, in **exo-2** H5 shows NOE with CH_3-9 and CH_3-13 on the C7 side chain; in **exo-7** only NOE with C9 appears; in **endo-2** and **8** both are absent, replaced by NOE with H6. In the tricyclics, the analogous H1 shows NOE with H7 in **5** and **endo-6** (in **4** H7 is not resolved from other cyclohexane resonances), but not in **exo-6**. Because the stereochemistry of each dienyne precursor had been previously established, assignment of the configuration of the stereocenter on the side chain in the bicyclic enones and in the cyclohexane ring in the tricyclics was unambiguous.

We also determined X-ray crystal structures for both **4** and **exo-6**, which supported the foregoing assignments. Figure 1 displays images of the structures obtained for these two compounds; for additional details see the Supplementary Materials.

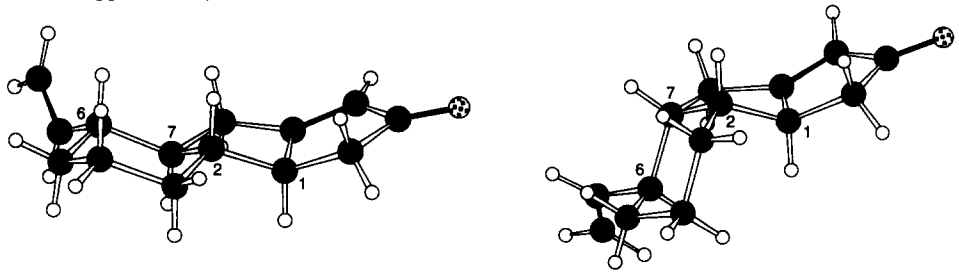


Figure 1. Depictions of X-ray crystal structures of **4** (left) and **exo-6** (right).

COMPUTATIONAL RESULTS AND DISCUSSION

Molecular Modeling Studies of Pauson-Khand Substrates, Products, and Possible Reaction Intermediates

Is it possible to rationalize the stereochemical pathways followed by these four reactions? Furthermore, can we identify characteristic benchmarks usable as (at least) qualitative predictors for the direction and degree of selectivity exhibited? To these ends we began by calculating relative energies for the substrates, products, and a key putative intermediate for the cycloaddition of **syn,syn-1** (Figure 2).

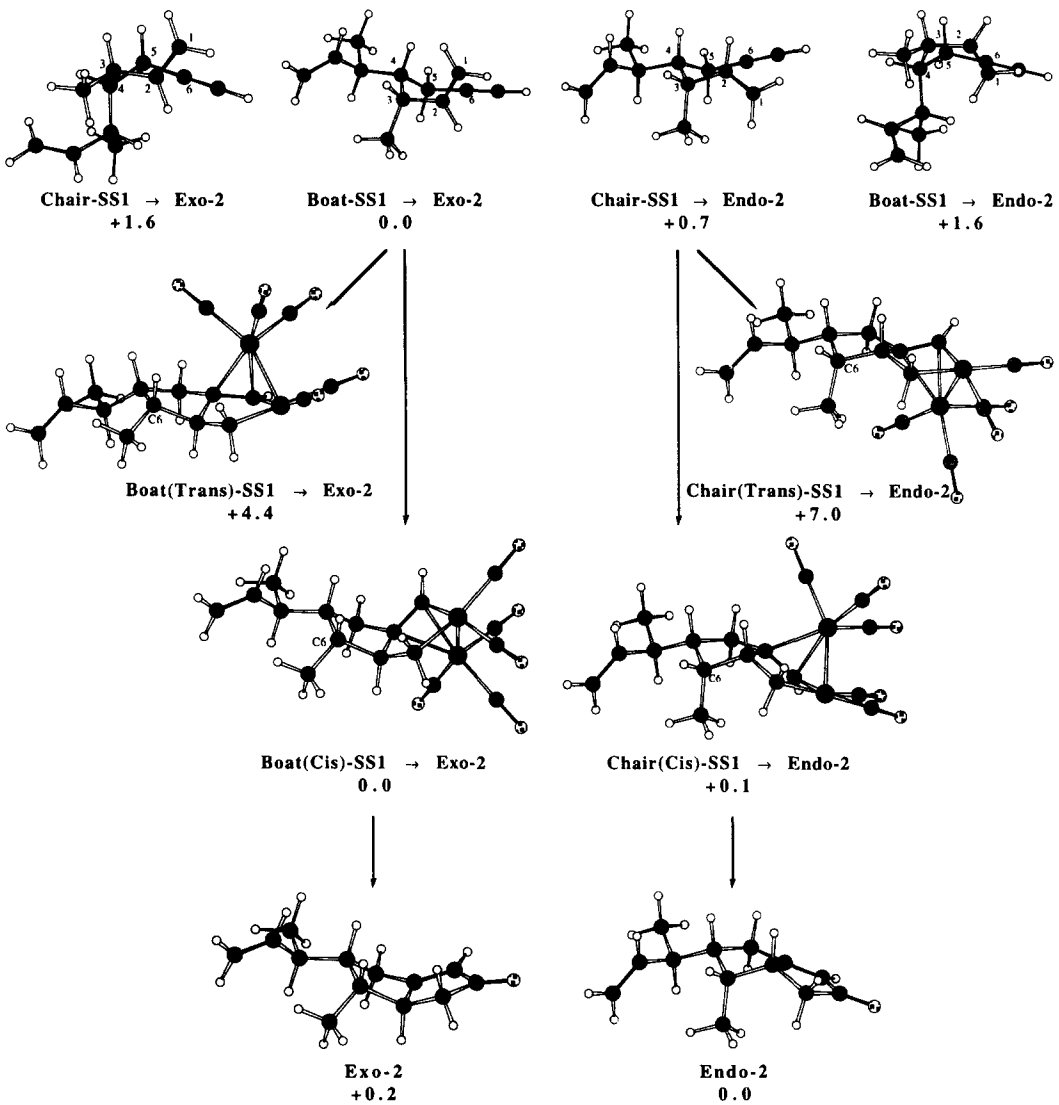


Figure 2. Minimized structures and relative energies (in kcal mol^{-1}) for four conformations of **syn,syn-1** (top), **exo-** and **endo-2** (bottom), and four possible diastereomeric metallacycle intermediates (middle). All species associated with **exo-2** are depicted in the left half of the scheme; those associated with **endo-2** are on the right.

Four conformations of the substrate, each a local energy minimum, were identified: two in which the relative orientation of the alkene function with respect to the stereocenter at C3 is such that the product after complexation and insertion would be **exo-2**, and two that would similarly lead to **endo-2**. For example, in the conformation at the upper left in Figure 2 (**Chair-SS1 → Exo-2**), the orientation of H2 (the ring-fusion proton upon bond formation between C2 and C6) defines the *exo* face of the bicyclic product; H2 in this conformation will end up *trans* to H3 and *cis* to the C3 methyl, which emerges with an *exo* orientation. Within each pair, one possesses a chair-like conformation of its C1–C6 fragment,[11] while the other is boat-like in shape. Relative energies (kcal mol^{-1}) are given below each structure. Below the enynes are illustrated four energy-minimized diastereomeric metallacyclic intermediates. Note that these four metallacycles appear to derive from only the two lower-energy enyne conformations; were the remaining two to react directly, they would merely give higher-energy conformations of the same four metallacycles due to steric interactions between the bulky pseudoaxial C4 side chain and the cobalt carbonyl portion of the molecule. The four metallacycles also break down into two pairs, distinguished by the stereochemistry of the product they afford (*exo* or *endo* methyl at C6—enone numbering) and of the ring fusion with respect to the newly-formed carbon–carbon bonds of the incipient bicyclic enone system (*cis* or *trans*). Metallacycle energies were calculated for $Co_2(CO)_5$ complexes, the presumed immediate products of alkene insertion, but the same energy trends are observed in the corresponding $Co_2(CO)_6$ complexes. Finally, the structures and relative energies of the two possible product enones are given.

Several points are immediately clear: (1) Energy differences between enyne conformations reflect steric interactions in a reasonable manner: in the two preferred conformations the large group at C4 is pseudoequatorial with respect to the C1–C6 fragment and *anti* to one of the two substituents on C3, whereas in the disfavored structures the group at C4 is pseudoaxial and *gauche* to *both* the methyl and vinyl groups at C3.

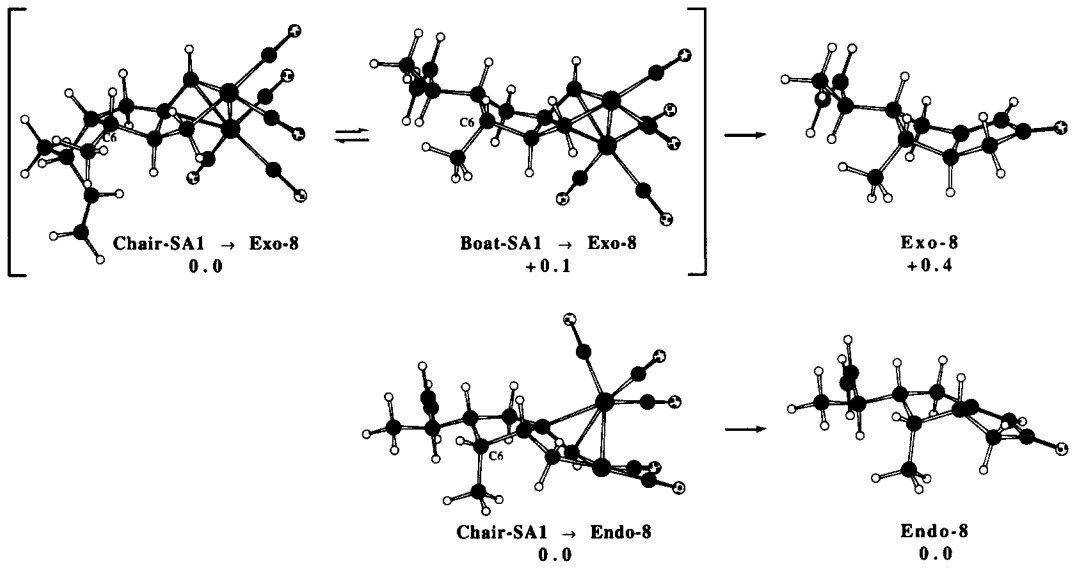


Figure 3. Minimized structures and relative energies (in kcal mol^{-1}) for **exo-** and **endo-8**, and possible metallacycle intermediates deriving from cycloaddition of **syn,anti-1** across its *syn* linkage.

(2) The *cis* metallacycles are significantly more stable than the *trans*. We find this to be generally the case: the *cis* metallacycles leading to **exo-7** and **endo-7** are 4.6 and 3.5 kcal mol^{-1} more stable, respectively, than the corresponding *trans* metallacycles, and the comparable energy differences between the *cis* and *trans* metallacycles leading to **exo-6** and **endo-6** are 6.1 and 7.1 kcal mol^{-1} , respectively. Therefore, we consider only *cis* metallacycles to be viable intermediates in this set of systems. (3) The (*cis*) metallacycles leading to the *exo* and *endo* products are similar in calculated energy, as are the final enones themselves.[12]

The cycloaddition of **syn,anti-1** across the "syn" bond (eq 4) is qualitatively similar to the cycloaddition of **syn,syn-1**: it gives more **endo-8** than **exo-8**, but the preference is small, consistent with the fact that, as for **syn,syn-1**, the two *cis* metallacycles associated with this mode of reaction are essentially identical in energy, as are the two products (Figure 3, previous page). In the case of the metallacyclic precursor to **exo-8** two local minima were found, one similar to the precursor to **exo-2**, and the other differing by a partial ring flip.

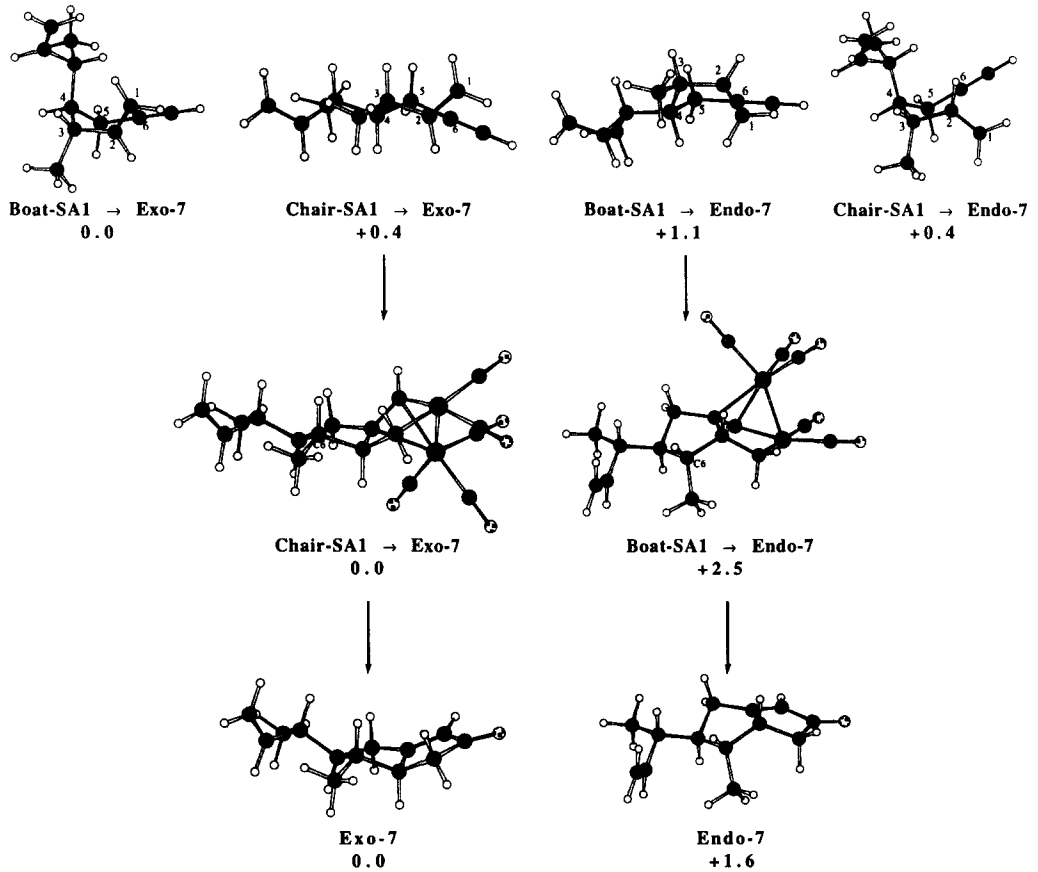


Figure 4. Minimized structures and relative energies (in kcal mol^{-1}) for four conformations of **syn,anti-1** set up for cycloaddition across its *anti* linkage (top), **exo**- and **endo-7** (bottom), and two possible *cis* metallacycle intermediates (middle). Species associated with **exo-7** are depicted in the left half of the scheme; those associated with **endo-7** are on the right.

Exo-7 and **endo-7** arise from cyclization of **syn,anti-1** across the "anti" linkage. Figure 4 illustrates four conformations of the starting enyne, all local energy minima, that place the appropriate alkene function within reacting distance of the triple bond. Two *cis* metallacycles and the two products are also shown. Note that direct reaction from the two lower-energy enyne structures (with the bulky groups at C3 and C4 mutually *anti*) would lead to higher energy metallacycle conformations than those shown, because of the pseudoaxial orientation of the substituents. In contrast to reactions across "syn" bonds, this process not only displays both a substantial experimental preference (10:1) for formation of the *exo* product but also a significant calculated energetic preference for the *exo*-metallacycle and enone (but *not* the enyne precursor).

Similar results, both experimentally and computationally, obtain from cycloadditions of **trans,trans-3** and of **cis,trans-3** across its "trans" linkage, to give **4** and **5**, respectively (Figures 5 and 6). Both these processes afford *exo* products exclusively, and, again, the calculated energies are consistent, substantially favoring both the corresponding metallacycles and enones.

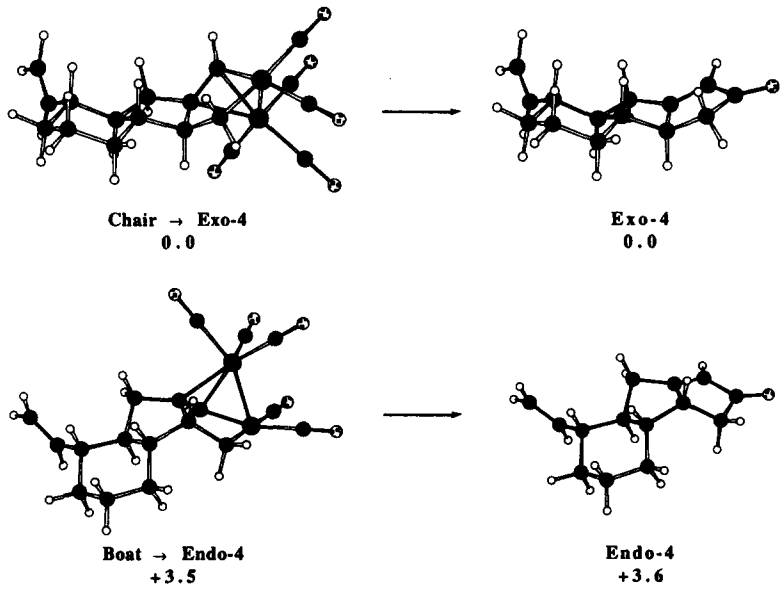


Figure 5. Minimized structures and relative energies (in kcal mol^{-1}) for **exo-** and **endo-4**, and possible metallacycle intermediates deriving from cycloaddition of **trans,trans-3**.

Finally, reaction of **cis,trans-3** across its "cis" linkage completes the picture. While the analogous cyclizations of the two corresponding acyclic substrates proceeded to give small excesses of *endo* products, in this case a 7:1 preference for **exo-6** is observed. Figure 7 reveals the cyclohexane ring to be the origin of this effect: in both **exo-6** and its metallacyclic precursor, two of the three substituents on this ring are equatorial, while the pathway to **endo-6** forces two into axial positions. A cyclohexane ring flip in either the metallacyclic precursor to **endo-6** or in the enone itself restores equatorial orientations to two groups, but at the cost of introducing severe eclipsing interactions in the now boat-like remainder of the molecule, that raise the overall energy by 1.7 kcal mol^{-1} for the metallacycle and 1.9 kcal mol^{-1} for the enone.

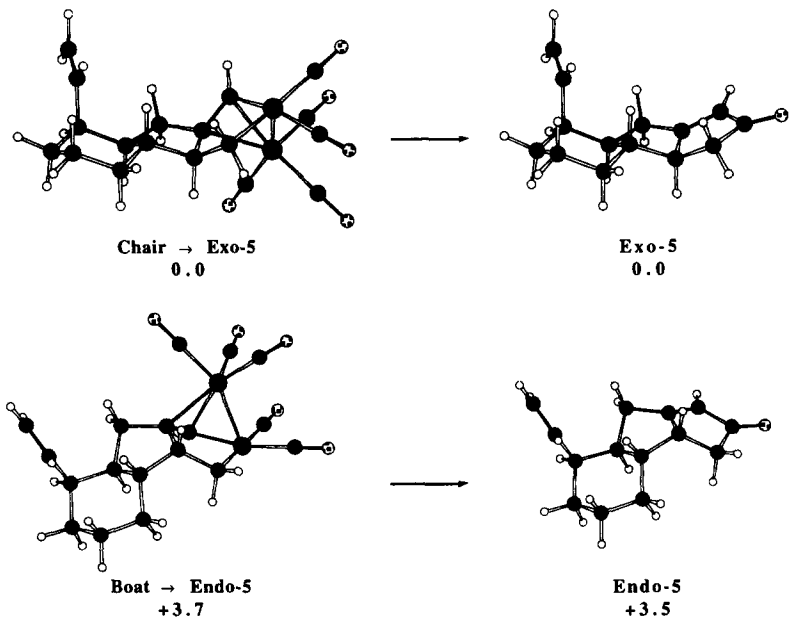


Figure 6. Minimized structures and relative energies (in kcal mol^{-1}) for **exo-** and **endo-5**, and possible metallacycle intermediates deriving from cycloaddition of **cis,trans-3** across the *trans* bond.

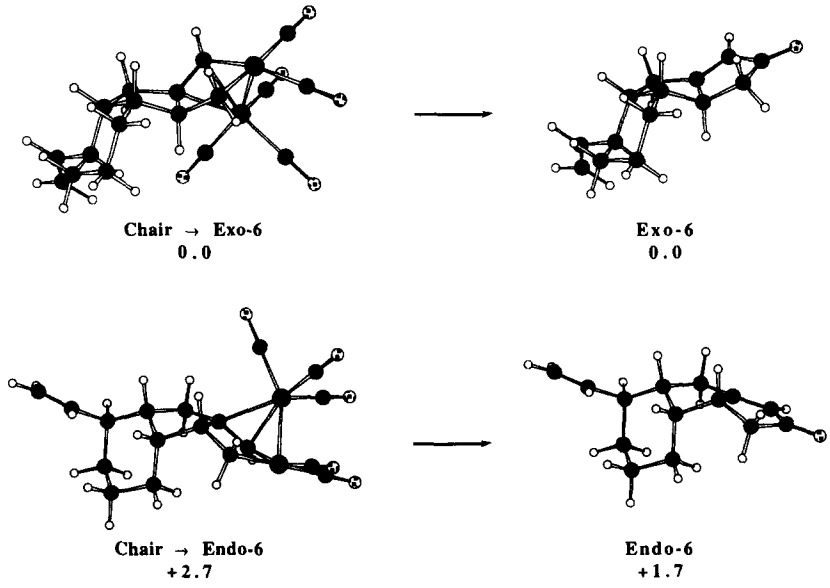


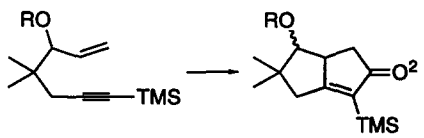
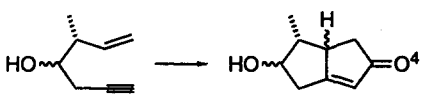
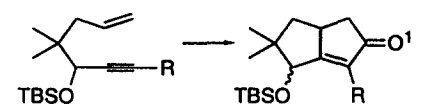
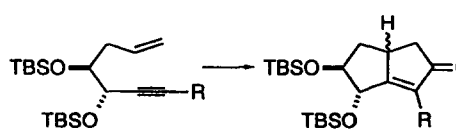
Figure 7. Minimized structures and relative energies (in kcal mol^{-1}) for **exo-** and **endo-6**, and possible metallacycle intermediates deriving from cycloaddition of **cis,trans-3** across the *cis* bond.

Mechanistic Implications and Prediction of Stereochemistry

The results presented above suggest that experimental product ratios correlate at least semiquantitatively with metallacycle energy differences and, to a lesser extent, those of the enone products. The correlation is better when the stereoselectivity is larger, as in the cases of **4**, **5**, **exo-6**, and **exo-7**. The two *endo*-selective situations, **endo-2** and **endo-8**, show low stereoselectivity experimentally. The calculated energy differences are small, consistent with the low selectivity, if not large enough to be predictive of its direction.

Mechanistically, there is no experimental evidence for reversibility of any of the carbon–carbon bond forming steps in the Pauson-Khand reaction. Thus any correlation between calculated product energies and experimental product ratios is fortuitous and an artifact of the conformational similarities between the enones and their metallacyclic precursors. The stereoselectivity is likely kinetic in origin and governed by differences in transition state energy at the stage of metallacycle formation, making differences in metallacycle energies the closest to being of potential predictive value.[13] However, a predictive method based upon examination of either substrate or product structures would be of greater *practical* value. As our data indicate, enone energies do correspond semiquantitatively to observed product ratios, even being consistent with the preferred directions of the two *endo*-selective systems. Is this generally the case? Turning to several systems in the literature we find good correlations between energy differences between *exo* and *endo cis*-metallacycles and experimental *exo*:*endo* product ratios on the one hand, and *exo* and *endo* product energy differences on the other (Table 2).[14]

Table 2. Comparison of experimental product ratios with metallacycle and product energies (kcal mol^{-1}).

Reaction[Ref]	Experimental *exo*:*endo* ratio (at C6 or C8)	$\Delta H_{endo} - \Delta H_{exo}$ (metallacycles)	$\Delta H_{endo} - \Delta H_{exo}$ (products)
	(R = H) 72 : 28	0.3	0.1
	(R = MOM) 100 : 0	1.5	1.8
	(syn/cis) 92 : 8	1.9	2.5
	(anti/trans) 75 : 25	2.1	1.7
	(R = H) 39 : 61[a]	−1.1	0.6
	(R = Me) 77 : 23	1.2	1.2
	(R = TMS) 96 : 4	3.1	4.8
	(R = H) 50 : 50	−0.2	0.9
	(R = TMS) 100 : 0	3.7	1.7

[a] ±6%; average of three runs under different reaction conditions (M. E. Krafft and C. Hirosawa, unpublished results).

Note that these examples include reactions of enynes substituted at the propargylic (C5) and allylic (C3) carbon atoms, as well as both mono- and disubstituted at C4. The correlation between the energy differences in the enone products and the precursor metallacycles is closer for the allylic-substituted systems (better than ±1 kcal mol^{-1}) than for propargylic-substituted examples (up to ±2 kcal mol^{-1} discrepancies). Even in the latter, however, the trends are encouragingly consistent with experiment, including the response of the system to substitution at the alkyne terminus. The correlations hold even despite the wide variety of experimental conditions used (thermal, amine oxide activated, etc.).

Finally, with respect to the particular substrates described in this work, we note that one situation that appears to favor formation of a C6 *endo*-substituted enone as the major product is that in which the substrate exhibits *syn* relative stereochemistry at C3/C4 *and the group at C4 is more sterically bulky than that at C3*. Note that reversal of the relative steric requirements of the two groups reverses the outcome: *syn*-3-methyl-4-hydroxy systems give *higher exo:endo ratios* than do the *anti* (Table 2, 2nd pair of entries).[4,16] When the C3 and C4 substituents are identical, variable ratios are obtained, sensitive both to the steric bulk of the group at the alkyne terminus and the reaction conditions (Table 2, last entries).[17] The computational data reproduce these results rather well, the correlation with metallacycle energy differences generally being better. Given the accuracy limits in the latter,[12] one cannot expect clear-cut predictions in systems exhibiting low (ca. ≤ 3:1) selectivity, although trends in structurally related systems are reproduced well. While direct experimental evidence bearing on the detailed mechanistic course of the Pauson-Khand reaction continues to remain elusive, our results lend strong support to the metallacycle model as the most generally applicable working hypothesis.

EXPERIMENTAL SECTION

General Procedures. All air and/or water sensitive reactions were carried out using oven dried glassware under an inert atmosphere of argon gas. Solvents and reagents were purified and/or dried according to common procedures.[18] Trimethylamine *N*-oxide (TMANO) was prepared according to the procedure by Soderquist.[19] Trimethylamine *N*-oxide, dicobalt octacarbonyl, and lithium acetylide were stored and weighed out in a Vacuum Atmospheres DriLab.

(3*R,4*r**,5*S**)-3,5-Dimethyl-4-(*p*-toluenesulfonyloxymethyl)-1,6-heptadiene (Syn,syn isomer).** Following literature procedures (3*R**,4*r**,5*S**)-3,5-dimethyl-4-(hydroxymethyl)-1,6-heptadiene[5,20] was prepared by $LiAlH_4$ reduction of (3*R**,4*r**,5*S**)-3,5-dimethyl-1,6-heptadiene-4-carboxylic acid.[21] To a solution of tosyl chloride (3.63 g, 19.0 mmol, 1.25 eq) in pyridine (23 mL) at 0° C was added via cannula a solution of (3*R**,4*r**,5*S**)-3,5-dimethyl-4-(hydroxymethyl)-1,6-heptadiene (2.350 g, 15.24 mmol) in 6.5 mL of pyridine. After 1 h at 0° C the reaction was allowed to proceed for 2 d at rt, quenched with ice, and extracted with 3 x 50 mL Et_2O. The combined extracts were washed with 60 mL satd aq NaCl, evaporated to near-dryness, treated with 20 mL heptane and 25 mL Et_2O, and dried over Na_2SO_4. Evaporation of solvent gave the product as a yellow oil, which was purified by chromatography (SiO_2, 1:9 Et_2O:hexane) to give 4.3 g (91% yield) of tosylate as a colorless oil. FTIR (neat) 3078(m), 3034(w), 2973(s), 2928(s), 2880(m), 1638(m), 1597(m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (d, J = 6.8 Hz, 6H), 1.49 (m ,1H), 2.38 (m, 2H), 2.43 (s, 3H), 3.99 (d, J = 4.5 Hz, 2H), 4.86–4.93 (m, 4H), 5.62 (m, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 21.5, 37.1, 46.6, 69.0, 114.1, 127.9, 129.7, 132.9, 142.6, 144.6; Anal: calcd for $C_{17}H_{24}SO_3$ C, 66.20%, H, 7.84%; found: C, 66.45%. H, 8.20%.

(3*R,5*R**)-3,5-Dimethyl-4-(*p*-toluenesulfonyloxymethyl)-1,6-heptadiene (Syn,anti isomer).** Using the procedure described above, (3*R**,5*R**)-3,5-dimethyl-1,6-heptadiene-4-carboxylic acid[21] was reduced to the corresponding alcohol[5,20] and tosylated to give the product as a colorless oil in 81% yield.

FTIR (neat) 3075(m), 2963(s), 2922(s), 2876(s), 1639(m), 1598(s), 1363(s), 1176(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (d, J = 6.9 Hz, 3H), 0.98 (d, J = 7.0 Hz, 3H), 1.44–1.51 (m, 1H), 2.31–2.45 (m, 2H), 2.44 (s, 3H), 3.96 (dd, J = 9.9, 5.2 Hz, 1H), 4.03 (dd, J = 9.9, 4.4 Hz, 1H), 4.89–4.95 (m, 4H), 5.55–5.71 (m, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 18.8, 21.6, 37.1, 37.4, 47.2, 69.3, 114.4, 114.8, 127.9, 129.7, 133.0, 140.7, 142.4, 144.6.

(3*R,4*r**,5*S**)-3,5-Dimethyl-4-(2-propynyl)-1,6-heptadiene (Syn,syn-1).** A solution of (3*R**,4*r**,5*S**)-3,5-dimethyl-4-(*p*-toluenesulfonyloxymethyl)-1,6-heptadiene (4.302 g, 13.95 mmol) in 15 mL DMSO under Ar was cannulated onto solid (90%) lithium acetylide ethylene diamine complex (1.86 g, 18.13 mmol) precooled to 0° C. After removal of the ice bath the reaction was stirred overnight, quenched with satd aq NH_4Cl, and extracted with 3 x 15 mL Et_2O. The extracts were washed with 20 mL satd aq NaCl and dried over $CaSO_4$. Filtration and solvent removal at 0° C gave 1.81 g (80% yield) of crude **syn,syn-1** as a yellow oil. Preparative GC (7% FFAP Chrom W, AW, DMCS N, 140° C, flow rate 80 mL/min) gave **syn,syn-1** pure enough for characterization (NMR indicated the presence of 0.2–0.3 eq water). FTIR (neat) 3311(s), 3079(s), 2974(s), 2929(s), 2878(s), 2118(m), 1641(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, J = 6.8 Hz, 6H), 1.47 (m, 1H), 1.92 (t, J = 2.7 Hz, 1H), 2.16 (dd, J = 5.5, 2.8 Hz, 2H), 2.46 (m, 2H), 4.95–5.03 (m, 4H), 5.75 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 16.7, 38.9, 46.4, 69.3, 84.5, 113.6, 143.6; Anal: calcd for $C_{12}H_{18}$•0.2H_2O C, 86.89%, H, 11.18%; found: C, 86.98%. H, 10.87%.

(3*R,5*R**)-3,5-Dimethyl-4-(2-propynyl)-1,6-heptadiene (Syn,anti-1).** The same procedure was followed as for **syn,syn-1**. The product was isolated as a yellow oil in 75% yield. Preparatory GC similarly afforded pure **syn,anti-1**. FTIR (neat) 3310(s), 3078(m), 2965(s), 2929(s), 2877(m), 2117(w), 1637(m), 1461(w), 1422(w), 1375(w), 998(m), 912(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, J = 6.9 Hz, 3H), 1.06 (d, J = 6.9 Hz, 3H), 1.42–1.49 (m, 1H), 1.94 (t, J = 2.7 Hz, 1H), 2.14 (ddd, J = 17.4, 6.3, 2.7 Hz, 1H), 2.23 (ddd, J = 17.4, 5.5, 2.7 Hz, 1H), 2.41–2.56 (m, 2H), 4.97–5.05 (m, 4H), 5.73–5.87 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7, 17.2, 18.9, 38.8, 39.2, 69.2, 84.7, 113.9, 114.3, 141.8, 143.3.

(5*R,6*R**,7*S**)-6-Methyl-7-[(1*R**)-1-methyl-2-propenyl]bicyclo[3.3.0]oct-1-en-3-one (Endo-2) and (5*R**,6*S**,7*R**)-6-Methyl-7-[(1*S**)-1-methyl-2-propenyl]bicyclo[3.3.0]oct-1-en-3-one (Exo-2).** A solution of 0.188 g (1.16 mmol) **syn,syn-1** in 6 mL CH_2Cl_2 was added rapidly via cannula to a flask charged with 0.475 g (1.39 mmol) $Co_2(CO)_8$ at 0° C under Ar. After 8 h the flask was purged with O_2 and a solution of 0.609 g TMANO (8.11 mmol) in 9 mL CH_2Cl_2 slowly added. After 2 h the flask was exposed to the air and ca. 1 mL H_2O and ca. 1 mL Et_2O added. The reaction was allowed to stir until the purple colored material had turned to a brown solid. The mixture was then filtered through a plug containing celite, silica, and $MgSO_4$. Solvent removal gave a yellow oil which was purified on silica using 20% Et_2O in hexane to give 0.20 g (90% yield) of **2** as a colorless oil. The isomers were separated preparatively on MPLC [Lobar® A (240-10) column]. Retention time for **exo-2** was 68 min and for **endo-2**, 81 min. The isomers were also separated by HPLC (25 cm normal phase SiO_2, 10.0 mm id, 8 μ particle size, flow rate 3 mL/min). The solvent used was 20% *t*-butyl methyl ether in hexane with 1% 2-propanol. Retention time for **endo-2** was 19 min and for **exo-2**, 16 min. For **endo-2**: FTIR (neat) 3075(w), 2963(s), 2929(s), 2871(m), 1708(vs), 1628(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.55 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 5.8 Hz, 3H), 2.10–2.18 (m, 3H), 2.16 (m, 1H), 2.23 (m, 1H), 2.35 (dd, J = 18.2, 6.3 Hz, 1H), 2.76 (m, 1H), 3.1 (bs, 1H), 4.95 (dd, J = 10.3, 1.3 Hz, 1H), 5.03 (dd, J = 17.2, 1.6 Hz, 1H), 5.71 (ddd, J = 17.4, 10.1, 7.5 Hz, 1H), 5.84 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.7, 19.8, 29.8, 34.9, 37.6, 39.2, 50.6, 51.8, 113.5, 125.3, 142.7, 189.7, 211.2. For **exo-2**: FTIR (neat) 3068(w), 2962(m), 2909(m), 2876(m), 1708(s), 1632(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, J = 6.8 Hz, 3H), 1.17 (d, J = 7.1 Hz, 3H), 1.77 (ddq, J = 11.0, 8.7, 7.1 Hz, 1H), 1.98 (dd, J = 17.5, 3.0 Hz, 1H), 2.35 (dddd, J = 8.4, 8.4, 5.6, 5.6 Hz, 1H), 2.45 (dd, J = 17.6, 5.8 Hz, 1H), 2.52 (m, 1H), 2.60 (ddd, J = 17.7, 6.2, 0.5 Hz, 1H), 2.64 (ddd, J = 17.7, 8.1, 1.0 Hz, 1H), 2.72 (bs, 1H), 5.00 (m, 1H), 5.01 (m, 1H), 5.80 (ddd, J = 17.8, 10.1, 6.4 Hz, 1H), 5.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 16.5, 29.3, 37.2, 41.8, 42.5, 46.6, 51.9, 113.3, 124.4, 143.6, 189.7, 210.6.

(5*R,6*S**,7*S**)-6-Methyl-7-[(1*R**)-1-methyl-2-propenyl]bicyclo[3.3.0]oct-1-en-3-one (Exo-7), (5*R**,6*R**,7*R**)-6-Methyl-7-[(1*S**)-1-methyl-2-propenyl]bicyclo[3.3.0]oct-1-en-3-one (Endo-7), (5*R**,6*S**,7*R**)-6-Methyl-7-[(1*R**)-1-methyl-2-propenyl]bicyclo[3.3.0]oct-1-en-3-one (Exo-8), and (5*R**,6*R**,7*S**)-6-Methyl-7-[(1*S**)-1-methyl-2-propenyl]bicyclo-[3.3.0]oct-1-en-3-one (Endo-8).** The same procedure was followed as for **2**. The purified product mixture was isolated as a colorless oil in 76% yield. Partial separation could be achieved by HPLC using the same conditions as for **2**. An inseparable mixture of **exo-7**, **endo-7**, and **exo-8** had a retention time of 14 min. Pure **endo-8** eluted at 17 min. Isomer ratios were obtained from capillary GC (DB-WAX 30m column, 180° C, flow rate 100 kPa). Retention time for **exo-7** was 10.9 min, for **endo-7**, 12.8 min, for **exo-8**, 13.5 min, and for **endo-8**, 16.5 min. The product mixture contained 65.8% **exo-7**, 6.7% **endo-7**, 11.0% **exo-8**, and 16.5% **endo-8**. FTIR (neat,) : 3075(w), 2961(s), 2925(s), 2871(s), 1708(s), 1645(s) cm^{-1}. For **exo-7**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J = 6.85 Hz, 3H), 1.13 (d, J = 6.36 Hz, 3H), 1.3 (m, 1H), 1.99 (m, 1H), 2.01–2.05 (m, 1H), 2.31 (m, 1H), 2.37 (ddd, J = 18.8, 10.5, 1.7 Hz, 1H), 2.50–2.57 (m, 1H), 2.60 (bs, 1H), 2.72 (m, 1H), 4.97 (dd, J = 10.3, 1.1 Hz, 1H), 5.00 (dd, J = 17.2, 1.4 Hz, 1H), 5.76 (ddd, J = 17.3, 10.1, 7.1 Hz, 1H), 5.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 18.2, 29.9, 39.6, 41.1, 43.2, 52.0, 54.3, 113.4, 124.7, 142.9, 189.5, 210.5. For **endo-8**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.59 (d, J = 7.1 Hz, 3H), 1.06 (d, J = 6.1 Hz, 3H), 2.00–2.15 (m, 3H), 2.20 (dd, J = 18.2, 3.6 Hz, 1H), 2.32 (m, 1H), 2.40 (ddd, J = 18.1, 6.4, 1.1 Hz, 1H), 2.67 (m, 1H), 3.15 (bs, 1H), 4.94 (dd, J = 10.2, 1.8 Hz, 1H), 5.03 (dd, J = 17.2, 1.8 Hz, 1H), 5.68 (ddd, J = 17.1, 10.0, 7.9 Hz, 1H), 5.86 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.8, 19.0, 30.5, 34.3, 37.6, 39.9, 50.2, 52.0, 113.5, 125.4, 143.2, 190.1, 211.4.

***Cis*- and *trans*-3-Ethenyl-2-(2-propynyl)cyclohexanone.** A mixture of anhydrous CuI (2.09 g, 11.0 mmol) in 10 mL THF was cooled to –15° C and treated with 20 mL of 1M vinylmagnesium bromide in THF. After 10 min the mixture was cooled to –78° C and 0.968 mL (10.0 mmol) cyclohexenone was added dropwise by syringe. The mixture was warmed to –30° C, stirred for 30 min, cooled to –78° C, and treated first with 10 mL HMPA and then 4.76 g (40.0 mmol) propargyl bromide. The mixture was slowly warmed to –20° C, stirred for 3 h, and then quenched with 5 mL MeOH, diluted with 30 mL Et_2O, and treated with 40 mL satd aq NH_4Cl. After 30 min at rt the layers were separated, the aq phase washed with 3 x 40 mL Et_2O, and the combined organic layers dried ($MgSO_4$). Repeated flash chromatography (SiO_2, 16:1 hexane:Et_2O) gave 1.16 g *cis* (12% yield) and 5.49 g *trans* (44% yield) ketones as colorless oils. For ***cis*-3-ethenyl-2-(2-propynyl)cyclohexanone**: ^1H NMR (300 MHz, C_6D_6) δ 1.39 (m, 3H), 1.75 (m, 2H), 2.17 (m, 4H), 2.62 (m, 1H), 2.88 (m, 1H), 4.89 (dd, J = 9.9, 1.2 Hz, 1H), 5.01 (dd, J = 16.8, 1.2 Hz, 1H), 5.33 (ddd, J = 16.8, 9.9, 7.5 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 16.7, 22.7, 30.8, 41.2, 45.1, 51.9, 69.5, 82.3, 117.7, 135.4, 207.9. For ***trans*-3-ethenyl-2-(2-propynyl)cyclohexanone**: ^1H NMR (300 MHz, C_6D_6) δ 1.14 (m, 2H), 1.43 (m, 2H), 1.78 (m, 3H), 2.15 (m, 2H), 2.36 (m, 2H), 4.87 (dd, J = 10.5, 1.2 Hz, 1H), 4.93 (dd, J = 16.1, 1.2 Hz, 1H), 5.33 (ddd, J = 16.1, 10.5, 8.0 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 16.6, 25.5, 32.0, 41.2, 48.1, 53.0, 69.5, 82.9, 115.6, 140.7, 207.2; Anal: calcd for $C_{11}H_{14}O$ C, 81.43%, H, 8.69%; found: C, 80.31%. H, 8.61%; HRMS: calcd for $C_{11}H_{14}O$ (M+) 162.1045, found 162.1052.

***Trans*-1-Ethenyl-3-(methoxymethylidene)-2-(2-propynyl)cyclohexane.** DMSO (11 mL) was added to 0.410 g (10.2 mmol) NaH under Ar and the mixture slowly warmed to 75° C for 1 h. After cooling to rt a solution of 4.68 g (13.2 mmol) (methoxymethyl)triphenylphosphonium chloride in 17 mL DMSO was added dropwise by cannula followed by a solution of 0.554 g (3.40 mmol) *trans*-3-ethenyl-2-(2-propynyl)cyclohexanone in 3 mL DMSO. The solution was warmed to 70° C for 1 h, cooled, and extracted with 6 x 20 mL hexane. The extracts were washed with 30 mL satd aq NH_4Cl, 30 mL satd aq NaCl, and dried (Na_2SO_4). Flash chromatography (SiO_2, hexane) yielded 0.518 g (82% yield) *trans* enol ether, which was used without further purification. ^1H NMR (300 MHz, C_6D_6) δ 1.23 (m, 2H), 1.52 (m, 2H), 1.81 (m, 3H), 2.22 (m, 2H), 2.34 (m, 1H), 2.48 (m, 1H), 3.22 (s, 3H), 4.92 (d, J = 12.0 Hz, 1H), 5.00 (d, J = 17.3 Hz, 1H),

5.64 (m, 1H), 5.89 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.6, 24.0 (2), 30.6, 42.7, 45.6, 58.5, 70.0, 82.7, 104.4, 114.3, 141.1, 142.2; HRMS: calcd for $C_{13}H_{18}O$ (M+) 190.1358, found 190.1363.

***Trans,trans*- and *cis,trans*-3-Ethenyl-2-(2-propynyl)cyclohexanecarbaldehyde.** A solution of 1.23 g (6.9 mmol) *trans*-enol ether in 50 mL DMSO (50 ml) was added via cannula to a mixture of 20 g Amberlite IR-120(plus) ion exchange resin (Aldrich) and 6 mL water under Ar. The heterogeneous mixture was stirred for 18 h and filtered. The filtrate was treated with 30 mL chloroform and 20 mL ice cold satd aq $NaHCO_3$, the organic phase separated, washed with ice water and satd aq NaCl, and dried (Na_2SO_4). Excess solvent was removed *in vacuo* and the crude product chromatographed immediately (SiO_2, 70:1 hexane:Et_2O) to afford 0.410 g all *trans* aldehyde (36% yield) and 0.441 g (39% yield) *cis,trans* aldehyde. These aldehydes are quite unstable and were used immediately in the next step. For ***trans,trans*-3-ethenyl-2-(2-propynyl)cyclohexanecarbaldehyde**: ^1H NMR (300 MHz, C_6D_6) δ 0.88 (m, 1H), 1.25 (m, 2H), 1.52 (m, 4H), 1.83 (t, J = 2.6 Hz, 1H), 2.04 (m, 1H), 2.31 (m, 3H), 4.99 (d, J = 11.9 Hz, 1H), 5.09 (d, J = 18.1 Hz, 1H), 5.31 (m, 1H), 9.39 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 19.9, 24.3, 26.0, 32.3, 38.2, 44.2, 51.9, 70.9, 81.1, 115.3, 141.4, 202.0. For ***cis,trans*-3-ethenyl-2-(2-propynyl)cyclohexanecarbaldehyde**: ^1H NMR (300 MHz, C_6D_6) δ 0.8–1.5 (m, 5H), 1.70 (m, 1H), 1.75 (t, J = 2.6 Hz, 1H), 2.14 (m, 1H), 2.35 (m, 3H), 2.75 (d, J = 2.5 Hz, 1H), 4.84 (m, 2H), 5.19 (m, 1H), 9.47 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.6, 21.8, 25.3, 32.4, 41.3, 43.6, 48.3, 70.5, 83.0, 115.3, 142.1, 202.8.

***Trans,trans*- and *cis,trans*-1,3-Diethenyl-2-(2-propynyl)cyclohexane (Trans,trans-3 and cis,trans-3).** A solution of dimsyl anion sodium salt was prepared from 0.382 g (9.50 mmol) NaH and 8.5 mL DMSO as previously described. A solution of 4.18 g methyltriphenylphosphonium bromide in 12.7 mL DMSO was added dropwise at rt by cannula, followed by addition of a solution of 0.335 g (1.9 mmol) *cis,trans*-aldehyde in 2.1 mL DMSO. The mixture was slowly warmed to 70° C, stirred for 2 h, cooled, and extracted with 6 x 20 mL hexane. The extracts were washed with 30 mL satd aq NH_4Cl, 30 mL satd aq NaCl, and dried (Na_2SO_4). Flash chromatography (SiO_2, hexane) yielded 0.121 g (72% yield) **cis,trans-3** as a colorless oil. **Trans,trans-3** was similarly prepared from *trans,trans*-aldehyde in 68% yield. For **trans,trans-3**: ^1H NMR (300 MHz, C_6D_6) δ 0.69 (tt, J = 3.9, 11.0 Hz, 1H), 1.00 (app dq, splittings = 3.2, 12.4 Hz, 2H), 1.20 (m, 1H), 1.52 (dt, J = 12.9, 3.5 Hz, 1H), 1.62 (br d, J = 12.4 Hz), 1.75 (t, J = 2.4 Hz, 1H), 2.29 (m, 4H), 4.98 (dd, J = 1.0, 10.2 Hz, 2H), 5.19 (dd, J = 1.0, 17.4 Hz, 2H), 5.42 (m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.2, 25.1, 33.1 (2), 43.4, 44.7 (2), 70.1, 81.7, 114.7 (2) , 142.5 (2). For **cis,trans-3**: ^1H NMR (300 MHz, C_6D_6) δ 0.97 (app br q, splitting = 11.5 Hz, 1H), 1.33 (m, 3H), 1.53 (m, 3H), 1.77 (m, 2H), 1.80 (m, 1H), 2.28 (dd, J = 1.8, 16.8 Hz, 1H), 2.81 (m, 1H), 4.82 (m, 2H), 5.07 (d, J = 10.5 Hz, 1H), 5.21 (d, J = 18.2 Hz, 1H), 5.32 (m, 1H), 5.77 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.8, 21.2, 31.5, 33.0, 40.5, 42.9, 43.8, 69.7, 83.7, 114.4, 116.8, 137.8, 142.9; Anal: calcd for $C_{13}H_{18}$ C, 89.59%, H, 10.41%; found: C, 88.63%. H, 10.30%; HRMS: calcd for $C_{13}H_{18}$ (M+) 174.1409, found 174.1413.

(1*R,2*S**,6*S**,7*S**)-6-Ethenyltricyclo[7.3.0.0^{2,7}]dodec-9-en-11-one (4).** A solution of 0.102 g (0.59 mmol) **trans,trans-3** in 2 mL CH_2Cl_2 was added to a solution of 0.289 g (0.73 mmol) $Co_2(CO)_8$ in 2 mL CH_2Cl_2 and the mixture stirred for 1.5 h and then cooled to 0° C. A solution of 0.308 g (4.1 mmol) TMANO in 4.1 CH_2Cl_2 mL was added dropwise over a period of 15 min. The reaction mixture was stirred for 3 h while it slowly warmed to rt. It was then diluted with 5 mL ether, filtered through celite/SiO_2, the solvent evaporated, and the product chromatographed (SiO_2, 4:1 hexane:Et_2O) to afford 0.104 g (88% yield) **4** as a crystalline solid, mp 66-67° C; ^1H NMR (300 MHz, C_6D_6) δ 0.43 (app dq, splittings = 3.2, 11.4 Hz, 1H), 0.78 (app dq, splittings = 3.4, 12.0 Hz, 1H), 0.97–1.15 (m, 3H), 1.55–1.77 (m, 5H), 1.84 (ddd, J = 0.6, 3.6, 17.4 Hz, 1H), 2.08 (m, 1H), 2.36 (m, 1H), 2.38 (m, 1H), 4.99 (m, 2H), 5.57 (m, 1H), 5.83 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 25.7, 29.9, 31.5, 33.0, 40.7, 47.5, 50.1, 50.3, 52.1, 113.5, 125.8, 142.4, 187.8, 208.1.

(1*R,2*S**,6*R**,7*S**) - 6 - Ethenyltricyclo[7.3.0.0^{2,7}]dodec - 9 - en - 11 - one (5), (1*R**,2*S**,6*R**,7*R**) -6- Ethenyltricyclo[7.3.0.0^{2,7}]dodec - 9 - en - 11 - one (Exo-6), and (1*R**,2*R**,6*S**,7*S**)-6-Ethenyltricyclo[7.3.0.0^{2,7}]dodec-9-en-11-one (Endo-6).** Via a similar procedure a mixture of **5**, **exo-6**, and **endo-6** in a ratio of approximately 50:43:7 was obtained in a total yield of 82%. Separation by careful chromatography afforded **5** and **endo-6** as colorless oils, and **exo-6** as a crystalline solid, mp 105-106° C. For **5**: ^{1}H NMR (300 MHz, C_6D_6) δ 0.63 (m, 1H), 1.28 (m, 4H), 1.56 (m, 2H), 1.73 (dd, J = 2.5, 15.8 Hz, 1H), 1.90 (m, 2H), 2.04 (m, 2H), 2.24 (m, 1H), 2.28 (dd, J = 7.0, 15.8 Hz, 1H), 4.91 (d, J = 17.1 Hz, 1H), 5.01 (d, J = 10.5 Hz, 1H), 5.63 (m, 1H), 5.73 (br s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 21.4, 29.5, 31.1, 32.3, 40.6, 41.3, 44.6, 49.0, 52.3, 116.9, 125.8, 137.5, 187.6, 207.8. For **endo-6**: ^{1}H NMR (300 MHz, C_6D_6) δ 0.09 (m, 1H), 0.85 (m, 1H), 1.09 (m, 3H), 1.27 (m, 2H), 1.56 (m, 1H), 1.75 (m, 1H), 1.88 (dd, J = 2.7, 17.7 Hz, 1H), 2.03 (m, 2H), 2.11 (dd, J = 8.1, 17.7 Hz, 1H), 2.37 (m, 1H), 4.94 (d, J = 18.9 Hz, 1H), 5.01 (d, J = 10.0 Hz, 1H), 5.77 (m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 18.8, 20.9, 25.2, 29.2, 34.7, 36.8, 38.5, 43.4, 51.4, 113.4, 125.7, 142.3, 187.2, 208.5. For **exo-6**: ^{1}H NMR (300 MHz, C_6D_6) δ 0.83 (m, 1H), 1.05 (m, 1H), 1.20 (m, 4H), 1.38 (m, 1H), 1.44 (m, 1H), 1.52 (m, 1H), 1.64 (dd, J = 3.0, 17.1 Hz, 1H), 2.09 (br s, 2H), 2.28 (dd, J = 6.3, 17.1 Hz, 1H), 2.38 (m, 1H), 4.84 (d, J = 18.6 Hz, 1H), 4.94 (d, J = 8.4 Hz, 1H), 5.36 (m, 1H), 5.73 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.6, 25.7, 32.3, 32.5, 41.3, 43.4, 43.8, 45.1, 45.9, 114.3, 125.8, 142.9, 188.4, 208.0; Anal: calcd for $C_{14}H_{18}O$ C, 83.12%, H, 8.69%; found: C, 83.22%. H, 9.02%; HRMS: calcd for $C_{14}H_{18}O$ (M+) 202.1358, found 202.1343.

Calculations. Structure minimizations were carried out using Molecular Mechanics available in the CAChe system (Oxford Molecular Group) version 4.0. The CAChe Mechanics application implements Allinger's standard MM2 force field[22] augmented by estimates of force field parameters for situations not addressed by MM2, enabling minimization calculations to be carried out for square planar, trigonal-bipyramidal, and octahedral atoms. Minimizations employed a second-derivative (Block Diagonal Newton Raphson) method. For freely rotating side chains the energy of the molecule was mapped as a function of the appropriate dihedral angles. For acyclic systems **syn,syn-1** and **syn,anti-1** the C2–C6 distance was set at 2.5Å (the nominal 1–3 distance in cyclohexane); small variations in this value in either direction had no effect on the calculated energy differences.

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Supplementary Material Available: X-ray crystal structure data for compounds **4** and **exo-6** (14 pages). See any current masthead page for ordering and Internet access information.

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[10] Characterized crystallographically. For **4**: monoclinic, $P2_1/a$, colorless plates, a = 9.236(7) Å, b = 10.556(5) Å, c = 11.954(4) Å, β = 98.82(4)°, V = 1151.6(11) Å^3, Z = 4, R = 0.0746. For **exo-6**: triclinic, $P\bar{1}$, colorless parallelpipeds, a = 6.6543(19) Å, b = 7.555(2) Å, c = 11.938(3) Å, α = 94.79(2)°, β = 99.19(2)°, γ= 109.28(2)°, V = 553.2(3) Å^3, Z = 2, R = 0.0475.

[11] Not the proper compound numbering. These substances are 3,5-dimethyl-4-(2-propynyl)-1,6-heptadienes.

[12] Mechanics calculations were carried out using the CAChe system's augmented MM2 force field, for which agreement of calculated ΔH_f° with experimental values is normally within ± 0.7 kcal mol^{-1} (see Experimental Section). The qualitative validity of the structures calculated for enones **4** and **exo-6** is supported by their virtual superimposibility on the X-ray structures. In further support for the calculated enone structures, the largest upfield ^{1}H NMR shifts for protons at C6/C2 and C5/C1 (Table 1) occur where the calculated structure reveals a chair-like conformation for the bicyclo[3.3.0] fragment with the proton in question pseudoaxial and vicinal to a pseudoequatorial alkyl moiety. This general phenomenon is elaborated in detail in Curtin, H.; Dalling, D. K.; Grant, D. M. *J. Org. Chem.* **1986**, *51*, 136. We thank one of the referees for directing our attention to this extremely useful reference.

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