Utility of the Tandem Pauson−Khand Reaction in the Construction of Tetracycles

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The scope of the tandem Pauson−Khand reaction has been explored for the regiospecific construction of [5.5.5.5]- and [5.6.6.5]tetracyclic systems via the photolytic method of Livinghouse. The rapid regiospecific entry into the two dicyclopentapentanoid systems **17** and **29** was accomplished from the key diene-diynes **11** and **19b**. A photochemically mediated catalytic tandem Pauson−Khand cyclization was employed to prepare the parent ring systems of dicyclopenta[*a*,*e*]pentalene (from **19b**) and dicyclopenta[*a*,*f*]pentalene (from **11**) in regiospecific fashion in a one-pot process. Under these conditions, conversion of acyclic diene-diyne **16** into tetracyclic system **17** was achieved in 74% yield, while a similar process was employed to convert **28** into tetracycle **29** in 90% yield. This is much improved over the previous conditions that employed NMO. Six carbon−carbon bonds were generated in this process constituting up to 98% yield for each carbon−carbon bond so formed. Furthermore, tetracyclic [5.6.6.5] systems such as dicyclopenta[*b*,*g*]decalins **37**, **38**, and **40** were prepared from similar diene-diyne precursors via the tandem Pauson−Khand cyclization. Importantly, acetal **36** provided the desired *cis*-fused [5.6.6.5] system **38a** (via **40a/b**) in stereospecific fashion. This reaction is unique in that it provides a *cis*-decalin ring system; moreover, the yield of each of the six carbon−carbon bonds formed in this process was at least 89%. The structure of *cis* diol **38a** was confirmed by X-ray crystallography.

Introduction

During the last two decades interest in the study of molecules that contain significant amounts of strain energy in their molecular structure has increased. The questions of bonding character, π overlap, and Hückel stabilization are of great importance to computational and organic chemists.[1−6] The desire to better understand the bonding character of carbon has prompted the study of the synthesis of a number of strained molecules termed polyquinenes.[7] Dicyclopenta[*a*,*e*]pentalene (**1**) and dicyclopenta[*a*,*f*]pentalene[8] (**2**) (Figure 1) have not been synthesized and have been discussed only from a computational point of view. Controversy exists as to whether these 14π annulenes are delocalized, exhibit aromatic Hückel-type stability, or exist as nonalternant hydrocarbons that behave as highly reactive olefins.[9−14]

Figure 1. Dicyclopenta[*a*,*e*]pentalene **1** and dicyclopenta[*a*,*f*]-pentalene **2**.

The parent ring systems of **1** and **2** have been prepared by Eaton,[15,16] McKervey,[17] Hafner,[18] Kotha,[19] Mehta,[20,21] and others, as well as in our laboratory;[22] however, the present approach was designed to employ a tandem Pauson−Khand reaction[23−27] to regiospecifically generate the tetracyclic framework of annulenes **1** and **2**. This would provide systems required for the construction of **1** and **2** in a higher oxidation state than previously

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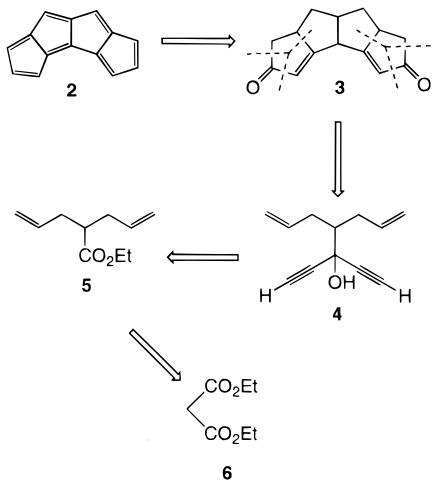
Scheme 1



achieved.[22] The newly incorporated functionality would permit further transformations toward the eventual synthesis of **1** and **2**.

Results and Discussion

The initial retrosynthetic strategy employed to gain entrance into the angular tetraquinane system is shown in Scheme 1. In the design of this approach the inherent symmetry present in both annulenes **1** and **2** was recognized. Because the Pauson−Khand reaction[28−33] has proven to be an effective means to generate fused five-membered rings, an appropriately functionalized substrate was constructed to attempt a tandem reaction. The tandem Pauson−Khand reaction,[23−27,34,35] which generates six carbon−carbon bonds in a one-pot process, is an ideal way to quickly increase molecular complexity, analogous to studies on the Diels−Alder and Weiss reactions reported by Bertz.[36,37] Moreover, the photochemically mediated catalytic Pauson−Khand cyclization developed by Livinghouse[38] was an attractive protocol for preparative synthesis of bicyclic enones. The key feature of this approach was the ease with which one can assemble an appropriately functionalized acyclic system such as diene-diyne **4** to set up a tandem Pauson−Khand reaction to generate the dicyclopentapentalene framework.

Consequently, after identification of diene-diyne **4** as the key substrate for the first model reaction, a simple synthetic sequence for its rapid construction from readily available diethyl malonate (**6**) was designed. As illustrated in Scheme 2, the addition of the sodium salt of diethyl malonate,[39] which was generated in situ by treating diethyl malonate (**6**) with sodium ethoxide in ethanol, to allyl bromide at 70 °C resulted in diallylation and furnished diethyl-2,2-diallylmalonate **7**. Monoester **5** was prepared directly from diester **7** by employing the conditions of Krapcho.[40] Diester **7** was stirred in dimethyl sulfoxide at reflux in the presence of lithium chloride. Treatment of ester **5** with excess lithium trimethylsilylacetylide smoothly furnished the desired alcohol **8**, and the silyl groups were removed with tetrabutylammonium fluoride to provide diene-diyne **4**.

Under the modified conditions of the Pauson−Khand reaction of Schreiber,[41] diene-diyne **4** was treated with 3.0 equiv of dicobalt octacarbonyl [$Co_2(CO)_8$] in CH_2Cl_2, and this was followed by addition of excess *N*-methylmorpholine-*N*-oxide monohydrate (NMO) to provide the tetracyclic diastereomers represented by **10** in 20% yield. Attempts to cyclize diene-diyne **8** directly under thermal conditions, as well as using NMO as a promoter, were not successful, presumably as a result of steric interactions between the bulky trimethylsilyl groups in the dicobalt hexacarbonyl functionalized intermediate and the corresponding dione (see **9**). Since this model sequence was successful, an approach to the more highly functionalized diol related to monoalcohol **4** was conceived. A modified retrosynthetic analysis was developed in which the diene-diyne **11** was functionalized as a diol, as shown in Scheme 3. The key diol **11** was synthesized from diethyl oxalate (**12**).

As shown in Scheme 4, a route to diol **11** from diethyl oxalate (**12**) by a two-step process was developed. Numerous attempts to synthesize **13** via the literature method of Saytzeff[42,43] proved too difficult to control on a large scale because of the exothermic nature of the process; consequently, milder conditions were sought. A modified procedure was developed utilizing THF as a solvent. In this vein, diethyl oxalate (**12**) in THF was added to a mixture of allyl bromide and zinc in THF to afford the α-hydroxy ester **13**.

Ester **13** was stirred with freshly prepared excess lithium trimethylsilylacetylide to provide the desired diol **11**. To determine if the tandem Pauson−Khand reaction would take place in the absence of a conformational restraint (i.e., an acetonide to provide a constrained geometry), the trimethylsilyl groups were removed from diol **11** on stirring with K_2CO_3 [44] in methanol to provide diene-diyne **14**. An attempt to cyclize diene-diyne **14** with 2.5 equiv of $Co_2(CO)_8$ in CH_2Cl_2 followed by addition of excess NMO[41] was unsuccessful. The lack of a conformational restraint to eclipse the diene-diyne moieties was felt to be a major factor that prevented the tandem cyclization toward the tetracyclic dione **15** from taking place. Constraint of the diol **11** in an eclipsed geometry, as shown in Scheme 4, was accomplished when diol **11** was treated with 2,2′-dimethoxypropane in refluxing chloroform in the presence of pTSA[45] to afford the desired

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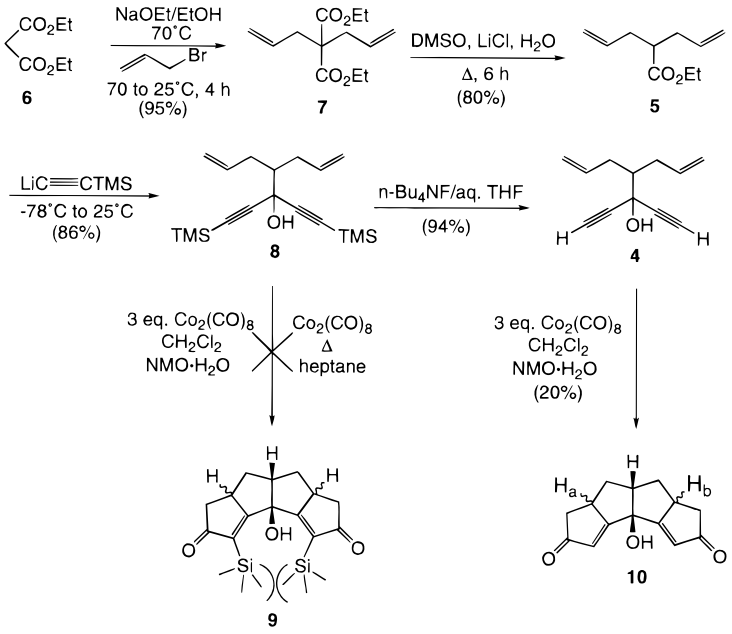
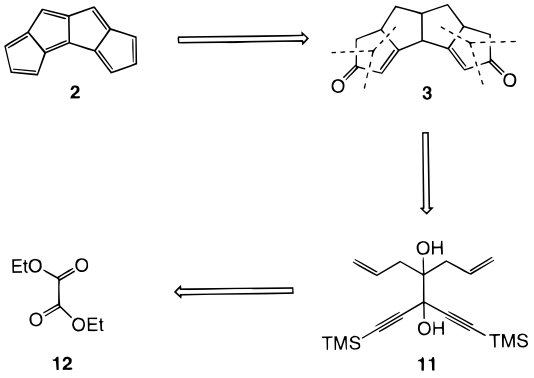
Scheme 2



Scheme 3



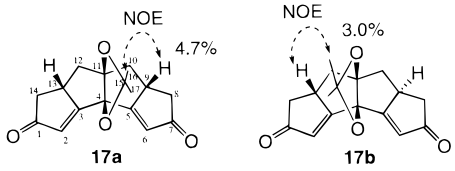


Figure 2. NOE enhancements observed for tetracycles **17a** and **17b**.

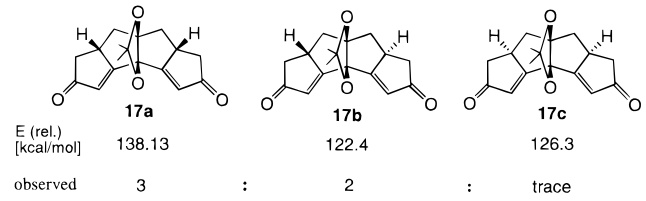


Figure 3. Calculated relative energies of tetracycles **17a**−**c**.

acetonide followed by removal of the silyl groups to provide diene-diyne **16**. Recently Keese[25,26] has reported a tandem Pauson−Khand reaction to furnish a [5.5.5.5]-fenestrane system obtained in a complex mixture of products under the modified conditions of Schreiber.[41] Using this procedure, acetonide **16** was stirred with 2.5 equiv of dicobalt octacarbonyl in CH_2Cl_2, followed by addition of excess *N*-methylmorpholine-*N*-oxide to provide the dicyclopentapentanoid systems represented by **17** in a one-pot process in 67% yield. The two major components (**17a** and **17b**) (Figure 2) were separated via selective recrystallization from heptane. A trace of another stereoisomer **17c** was found in the mother liquor, obtained in only small amounts.

The stereochemistry of each stereogenic center of these tetracycles was not considered critical. Both isomers **17a** and **17b** of the tetracyclic system should serve as functionalized precursors to an annulene such as **2**. The structures of all three isomers were assigned by high-resolution NMR spectroscopy including NOESY and 2D COSY experiments (see Supporting Information for details).

To rationalize the observed stereoselectivity of the three isomers formed in this process, MM2[46] calculations were employed to determine the relative energies of the three diastereomers **17a**−**c** (see Figure 3). The fact that the calculated energies do not correlate directly with the experimental results suggests that in the steps of the tandem Pauson−Khand reaction, steric effects in the metallocyclic intermediates[30,47−49] and kinetics of the insertion process are responsible for this observed stereoselectivity (see below).[50]

Attempts to effect the tandem cyclization of acetonide **16** under thermal conditions[32] led to yields of the tetracyclic systems represented by **17** in the range of 45−50%. The tandem Pauson−Khand reaction can be carried out on a 3 g level; however, large quantities of $Co_2(CO)_8$ (i.e., 13 g) were needed under these early stoichiometric conditions. Catalytic conditions were sought to generate the tetracyclic system on a preparative scale. This would render it much easier to purify the products from this process. Recently Livinghouse[38] has reported a photo-

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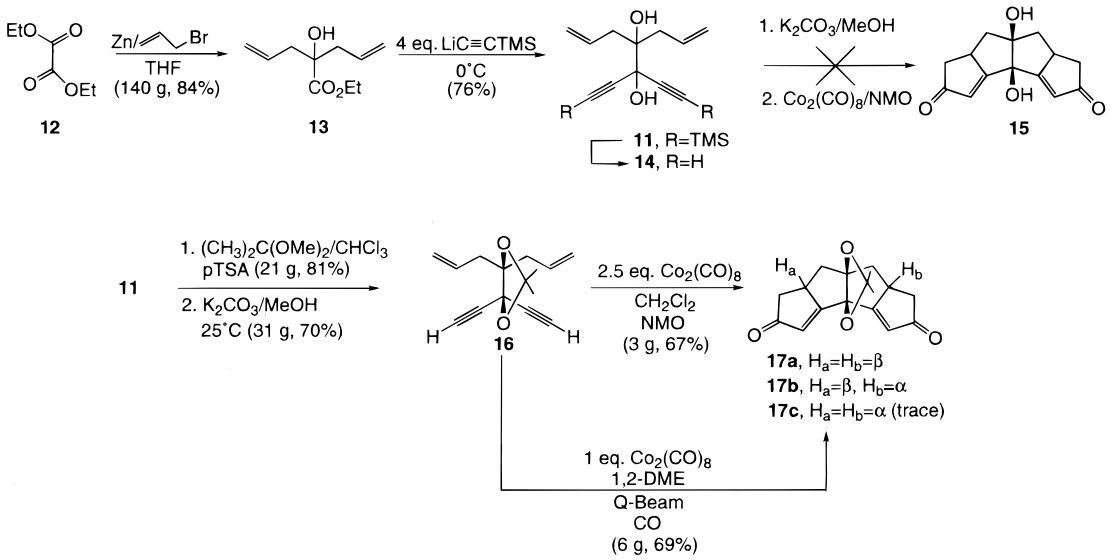
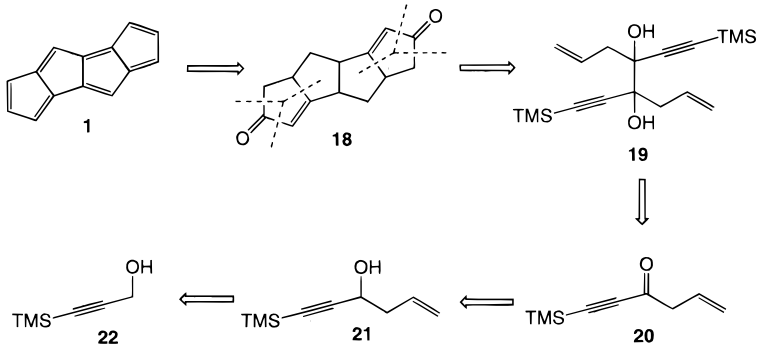
Scheme 4



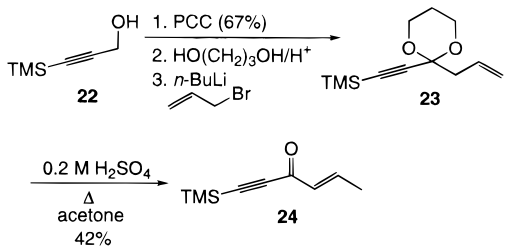
Scheme 5



chemically mediated catalytic intramolecular Pauson–Khand reaction in which 5–10 mol % of $Co_2(CO)_8$ was employed in the cyclization. Diene-diyne **16** (300-mg scale) was stirred with 9 mol % of $Co_2(CO)_8$ and irradiated with a Q-Beam MAX MILLION 100 W xenon spotlight[51] for 72 h at 50–55 °C under an atmosphere of CO. This process provided a mixture of tetracyclic systems represented by **17** in 74% yield. Attempts to carry out the reaction on multigram levels with 10 mol % of $Co_2(CO)_8$ resulted in prolonged reaction times. For preparative purposes, the photochemical cyclization was best carried out on a 6-g scale of diene-diyne **16** with 1 equiv (50 mol %) of $Co_2(CO)_8$ to provide the three tetracyclic systems **17a–c** in 69% yield in a ratio of 4.7:5.9:1, respectively (Scheme 4).[27] The ratio of dicyclopentapentanoids was determined by proton NMR and ^{13}C inverse gate NMR experiments. The observance of dione **17c** in slightly higher yield than with the cyclization carried out in the presence of NMO may result from a slower reaction rate resulting in greater thermodynamic control.[50]

This regiospecific catalytic tandem Pauson–Khand process has been expanded to include the synthesis of the parent ring system contained in the 14π annulene dicyclopenta[*a*,*e*]pentalene (**1**). The retrosynthetic analysis for the synthesis of diene-diyne **19** is illustrated in Scheme 5. The key diene-diyne **19** required for tandem Pauson–Khand cyclization must contain the *dl* stereochemistry. It was felt the diol **19** could be synthesized by a pinacol coupling reaction[52,53] from ketone **20**, which was readily available from propargyl alcohol **22**.

Scheme 6



An initial literature search for ketone **20** resulted in a four-step synthesis illustrated in Scheme 6.[54] Propargyl alcohol **22** was oxidized with pyridinium chlorochromate (PCC) to furnish the desired aldehyde, and this was followed by cyclic acetal formation with 1,3-propanediol in the presence of pTSA to give the 1,3-dioxane. Deprotonation of the acetal with *n*-BuLi was followed by addition of allyl bromide to provide the ene-yne **23**. Hydrolysis of the ketal in 0.2 M aqueous H_2SO_4 in refluxing acetone, however, did not provide the reported[54] desired ketone **20** but furnished the α,β-unsaturated ketone **24** instead (Scheme 6). The structure of this

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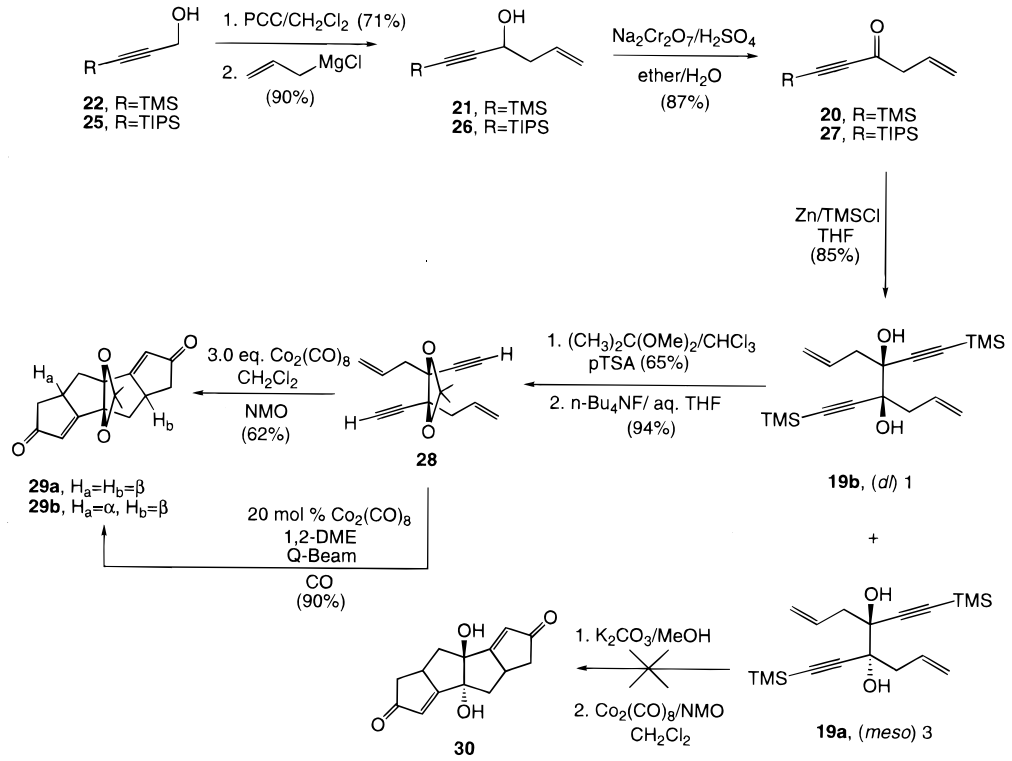
Scheme 7



ketone **24** was characterized;[50] however, numerous attempts to modify the conditions still did not provide the desired ketone **20**. It was believed the first component formed was the ketone **20**, but this olefin underwent rapid isomerization into the more stable enone system contained in α,*β*-unsaturated ketone **24**. Consequently, another route to this key ketone **20** was developed.

As illustrated in Scheme 7, alcohol **22** was oxidized with pyridinium chlorochromate (PCC) on a 50-g scale to provide the propargyl aldehyde, which was then reacted with allylmagnesium chloride to furnish the secondary alcohol **21**.[55] Under mild conditions at room temperature, the alcohol **21** was treated with $Na_2Cr_2O_7 \cdot 2H_2O$ in a biphasic system (ether/water) to afford ketone **20**. Attempts to purify this ketone on a silica gel wash column resulted in isomerization to the α,*β*-unsaturated enone **24**. The lability of this system and the cleanliness of the previous step prompted use of the crude ketone directly without purification.

The pinacol coupling reaction[52,53] has been demonstrated to be a versatile reaction in organic synthesis to prepare 1,2-diols. Typical metals employed in this process include titanium,[56,57] zinc,[58] and magnesium,[59] although this scope is expanding as newer metals are being exploited. The simplest conditions were sought to attempt a pinacol coupling of ketone **20**. The sensitivity of the functional groups contained in **20** were taken into account during evaluation of the various conditions. Consequently, as shown in Scheme 7, the ketone **20** was stirred in the presence of excess zinc dust and trimethylsilyl chloride.[58] This process furnished a mixture of *meso* **19a** and *dl* **19b** diols in a 3:1 ratio, respectively, in 85% yield, which were separated by flash column chromatography. The *dl* isomer **19b** was required for the future tandem Pauson−Khand cyclization (after acetonide formation) as opposed to the *meso* isomer **19a**, which would carry the alkene and alkyne moieties *cis* to one another when the diol was constrained.

If the *meso* diol was in the staggered conformation as expected, the diene-diyne units might be close enough to each other for the tandem cyclization to occur. *meso*-Diol **19a** was treated with K_2CO_3 in methanol to remove the trimethylsilyl groups, and the colbalt-mediated cyclization was attempted with $(Co)_2(CO)_8$/NMO. The Pauson−Khand cyclization in the *meso* case was presumably retarded as a result of the formation of a higher energy *trans* ring junction[60] of the tetraquinane **30** which would result (Scheme 7). Another possible explanation for the lack of success in the *meso* system is the lability of the propargylic functionality associated with diol **19a**. Since the earlier diene-diyne **4** employed for the synthesis of tetracyclic system **10** cyclized in poor yield (Scheme 2), it was not surprising that *meso*-diol **19a** did not afford tetracycle **30**. Similar observations with propargylic alcohols that did not undergo a Pauson−Khand cyclization were reported by Keese.[25,26]

The poor selectivity of *dl* to *meso* isomers may be rationalized on the basis of the bulkiness of the radical intermediates.[50] Alteration of the alkynyl trimethylsilyl groups to bulky triisopropylsilyl (TIPS) groups (**25** → **26** → **27**) to increase the stereoselectivity of *dl* formation did not help direct the pinacol coupling reaction to the desired *dl* product. Attempts to improve the stereoselectivity of **19b** to **19a** employing Cp_2TiCl_2/Zn,[61] SmI_2,[62,63]

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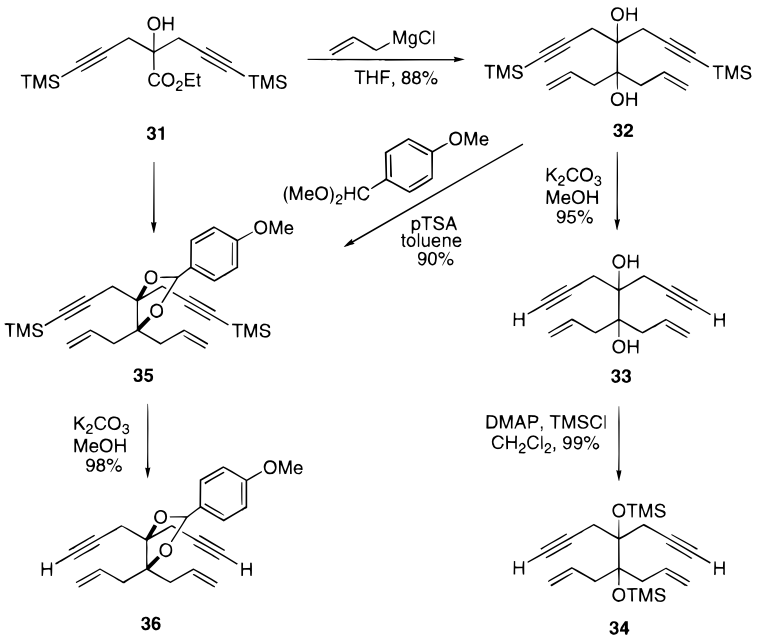
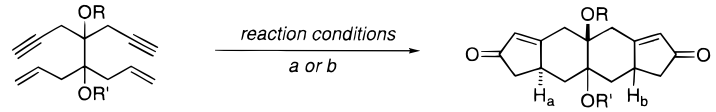
Scheme 8



Scheme 9



34 R, R' = TMS	38% *procedure a*	**37a** OR' = β, H_b = β (3.2) **37b** OR' = α, H_b = α (1)
	53% *procedure b*	**37a** OR' = β, H_b = β (4) **37b** OR' = α, H_b = α (1)
33 R, R' = H	26% *procedure a*	**38a** OR' = β, H_b = β (2.2) **38b** OR' = α, H_b = α (1)
	52% *procedure b*	**38a** OR' = β, H_b = β (2.3) **38b** OR' = α, H_b = α (1)

a =1 equiv. $Co_2(CO)_8$, DME, CO, hν
b =2.5 equiv. $Co_2(CO)_8$, NMO, CO, CH_2Cl_2

or other metals were not successful or resulted only in low yields of the diols. However, recently an alternative pathway to the desired **19b** (TIPS analogue) has been developed that provides the two isomers in a ratio of 5.5:1 (*dl*/*meso*).[64]

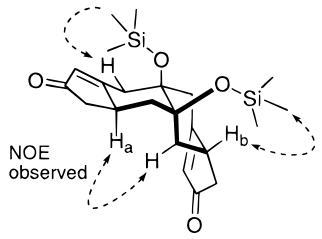
As shown in Scheme 7, the desired *dl* diol **19b** was stirred with 2,2′-dimethoxypropane in refluxing chloroform in the presence of pTSA[45] to furnish the acetonide. The silyl groups were removed from the acetonide on exposure to tetrabutylammonium fluoride to provide diene-diyne **28**. Acetonide **28** was stirred with 3 equiv of $Co_2(CO)_8$ in CH_2Cl_2. This process was followed by addition of NMO to provide the tetracyclic systems represented by **29** in 62% yield as a 1:1 mixture of diastereomers. Both stereoisomers **29a** and **29b** of the tetracyclic system should serve as functionalized precursors to a planar annulene such as **1**.

To explore the utility of the photochemically mediated catalytic tandem Pauson−Khand cyclization,[27,38] diene-diyne **28** was treated with 20 mol % of dicobalt octacarbonyl followed by irradiation[51] for 24 h at 50−55 °C under an atmosphere of CO. This process provided a mixture of tetracycles **29a** and **29b** in 90% yield in a ratio of 2:3, respectively.[27]

Recently, the tandem Pauson−Khand cyclization has been extended to generate the tetracyclic framework of the [5.6.6.5] carbon systems **37** or **38**.[34] Analogous to the method employed for the preparation of the previous [5.5.5.5]dicyclopentapentalene skeletons, this tandem Pauson−Khand strategy began from acyclic molecules (Scheme 8) but provided an internal *cis*-decalin within a [5.6.6.5]dicyclopenta[*b*,*g*]decalin tetracycle (Scheme 9).

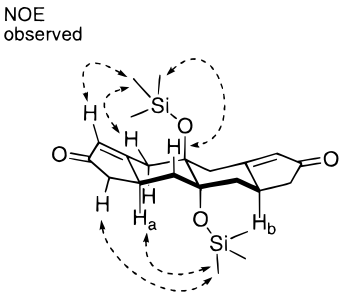
A straightforward sequence was developed for rapid construction of the diene-diyne required for this extension of the tandem Pauson−Khand reaction. Bisalkyne **31** was readily available by addition of diethyl oxalate to a stirred suspension of trimethylsilyl propargyl bromide and zinc in THF with a catalytic amount of mercury(II) chloride.[50] When the dialkyne ester **31** was treated with 3 equiv of

(61) Handa, Y.; Inanaga, J. *Tetrahedron Lett.* **1987**, *28*, 5717.
(62) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765.
(63) Namy, J. L.; Souppe, J.; Collin, J.; Kagan, H. B. *J. Org. Chem.* **1984**, *49*, 2045.
(64) Cao, H.; Cook, J. M., manuscript in preparation.



37a $H_a = \alpha$, $H_b = \beta$

Figure 4.



37b H_a, $H_b = \alpha$

Figure 5.

allylmagnesium chloride, diene-diyne **32** was obtained (Scheme 8). Removal of the silyl protecting groups from the alkyne functions in **32** occurred readily in the presence of K_2CO_3/MeOH[44] to afford the desired diol **33**. Protection of the hydroxyl groups via excess DMAP and TMSCl furnished the penultimate Pauson−Khand intermediate **34**.

The application of the Livinghouse photochemically mediated Pauson−Khand protocol[38] for the synthesis of the parent ring systems of the dicyclopentapentalenes[27] had previously provided a convenient, catalytic tandem reaction process. This success prompted the use of similar reaction conditions here for construction of the desired [5.6.6.5]tetracycle. Conversion of diene-diyne **34** into tetracyclic decalins **37a/b** was met with somewhat limited initial success (38% yield). The two tetracyclic diones **37a/b** (Figures 4 and 5) were obtained in a 3:1 ratio, easily separated by flash column chromatography, and fully characterized (see Supporting Information). The spectral data for the two [5.6.6.5]dicyclopenta[*b*,*g*]decalins was similar to that of the [5.5.5.5]dicyclopenta[*a*,*f*]pentalene systems discussed earlier (see Suporting Information for structural assignments based on NMR spectroscopy).

It is interesting to note that a *cis*-fused decalin system was preferentially formed in this tandem Pauson−Khand reaction. To rationalize the observed stereoselectivity of the two isomers formed in this process, MM2[65,66] calculations were employed to determine the relative energies of the potential diastereomeric [5.6.6.5] systems. The relative energies of tetracycles **37a/b** are shown in Scheme 10, as well as those for the other four possible isomers **37c**−**f** (not observed). Examination of the calculated energies indicated the two tetracycles obtained are clearly lower in energy than the other potential products. Although the tetracycle with a *trans*-fused 6−6 ring juncture **37b** was slightly lower in energy than the *cis* counterpart **37a** (2.5 kcal/mol), the *cis* compound was preferentially formed in a 3.2:1 ratio. While an unequivocal mechanistic hypothesis for the Pauson−Khand reaction has not been reported to date, the currently accepted pathway has relied on steric interactions in the metallocycle intermediate to determine product formation.[30,47−49] As mentioned in the case of the [5.5.5.5]dicyclopenta[*a*,*f*]-pentalene systems **17a**−**c** discussed previously, kinetics of the insertion process are also believed to be important, as evidenced by the isolation of **17a** as the predominant product rather than the lower energy **17b** or **17c**. Numerous factors may contribute to the observed stereochemical outcome for this [5.6.6.5] tandem Pauson−Khand system, but steric interactions in the proposed metallocycle intermediates are believed to play a significant role.

Recently, Castro et al.[49] have employed MMX force field calculations to evaluate the relative energies of the intermediary cobaltacycles in the Pauson−Khand reaction, which provides new evidence to support the proposed mechanism.[30,47,48] The configuration of the product formed was correlated to that of the most stable (product-determining) cobaltacycle. The intermediate cobaltacyclopentane ring fusion with a *trans* arrangement, which appeared to be severely strained, was shown to be more stable than the *cis* isomer.[49]

The studies of Castro et al.[49] permit the qualitative prediction of the stereochemical outcome of this tandem Pauson−Khand reaction. An illustration of the steric components involved in the metallocycle intermediates **39a**−**f** is shown in Scheme 10, accompanied by the six possible [5.6.6.5]dicyclopenta[*b*,*g*]decalin products **37a**−**f**. The hydrogen atom at the juncture between the two rings that are formed (here the 5−6 ring fusion) is shown on the face opposite of the bulky cobalt species. In this tandem Pauson−Khand reaction, formation of two sets of rings at once would create an unfavorable steric interaction between the two cobaltacycle moieties. This situation is further exacerbated by the presence of the two trimethylsiloxy groups. Examination of molecular models of the six diastereomers indicated that the two isomers that formed **37a** and **37b** (which have the lowest energies) should proceed through the least hindered metallocycle intermediates **39a** and **39b**.

Since *cis*-fused decalins were preferentially formed in this process, it was felt the trimethylsilyl groups in diene-diyne **34** may have retarded the reaction progress, resulting in low yields. Steric interactions from the bulky silyl groups would further promote a staggered arrangement of diene-diyne **34**, limiting the success of the tandem Pauson−Khand reaction. Proper alignment of the diene-diyne moieties would require an eclipsed conformation, which would appear to be much less favored in the presence of the trimethylsilyl protecting groups. For this reason, the tandem Pauson−Khand reaction of the unprotected diol **33** was then carried out (Scheme 9). Unfortunately, the method of catalytic photolysis furnished low yields of the [5.6.6.5]dicyclopenta[*b*,*g*]decalin tetracycles **38a**/**b** [(26%), Table 1, entry b] in a 2.2:1 ratio. This is in contrast to the [5.5.5.5]tetracyclic system en route to the dicyclopentapentalene framework, in which the tandem Pauson−Khand reaction of unconstrained diol **14** did not provide the desired tetracyclic product **15**. The structure of tetracyclic *cis*-decalin diol **38a** was

(65) MacroModel 6.0 was the program employed for calculations. MM2 force field and Monte Carlo methods were employed to conduct the conformational search.

(66) Harris, N.; Gajewski, J. *J. Am. Chem. Soc.* **1994**, *116*, 6121.

Scheme 10

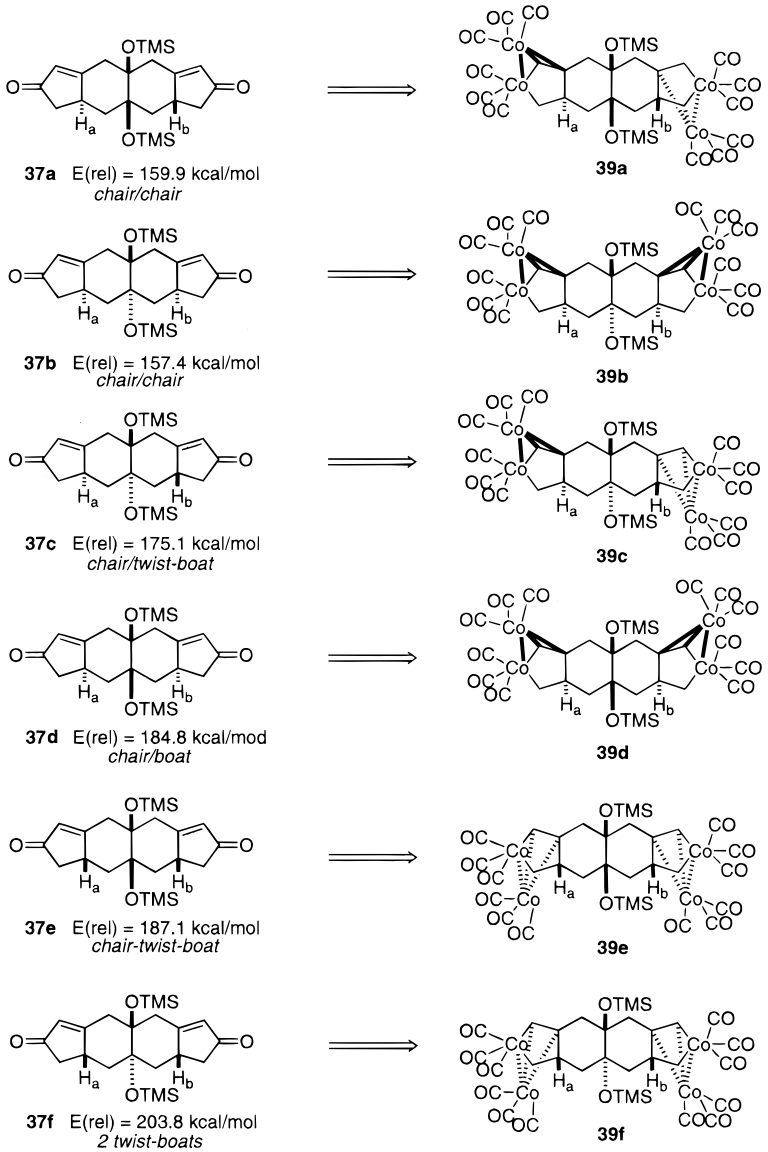


Table 1.

entry	substrate	reaction conditions[a]	yield (%)	product	ratio[b]
a	OTMS **34**	DME, hν	38	**37a/b**	3.2:1
b	diol **33**	DME, hν	26	**38a/b**	2.2:1
c	diol **33**	DME, 65 °C	31	**38a/b**	2.2:1
d	**OTMS 34**	**CH_2Cl_2, NMO**	**53**	**37a/b**	**4.0:1[c]**
e	**diol 33**	**CH_2Cl_2, NMO**	**52**	**38a/b**	**2.3:1**
f	diol **33**	CH_3CN, NMO	44	**38a/b**	2.2:1
g	diol **33**	CF_3CH_2OH, NMO	33	**38a/b**	2.1:1
h	diol **33**	1:1 heptane/CH_2Cl_2, NMO	<5	**38a/b**	
i	diol **33**	heptane, NMO	0	**38a/b**	
j	acetal **36**	CH_2Cl_2, NMO	43	**40a/b**	1.2:1
k	acetal **36**	DME, hν	45	**40a/b**	1.1:1

[a] All reactions were performed under an atmosphere of carbon monoxide. [b] Ratios are approximate and were determined by integration of the NMR spectra. [c] Isolated yield.

confirmed by a single-crystal X-ray analysis (see Supporting Information for details).

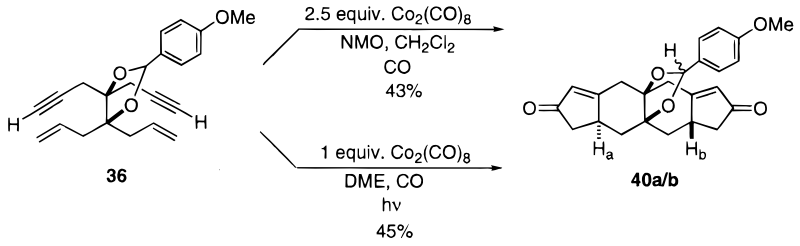
The *cis*:*trans* ratio of products **38a/b** from this reaction series (2.2:1) was slightly lower than that of the case of the bistrimethylsilyl-protected series (**37a/b**, 3.2:1). The tandem Pauson−Khand reaction of the diene-diol **33** must be effected by removal of this species. In the metallocycle related to minor isomer **38b**, where two cobalt species are on one face with a hydroxyl group, it was believed that steric interactions are somewhat reduced, and a slightly higher amount of the *trans* product was observed.

Removal of the silyl groups from the hydroxyl moieties in tetracyclic dione **37a** with tetrabutylammonium fluoride hydrate in THF provided diol **38a** in 89% yield. The spectral data obtained for this product were identical in all respects to the diol **38a** obtained via the tandem Pauson−Khand reaction of diol **33**.

As shown in Table 1, a variety of reaction conditions were investigated in attempts to increase the reaction yield from the initial photochemical process. Recently, Livinghouse[67] has reported that the thermal (60 °C) version of the catalytic Pauson−Khand procedure (entry c, Table 1) occurred in yields comparable to the photolytic catalytic method.[38] In the study outlined below, yields for the tetracyclic products were also similar to the light-promoted reactions. The modified conditions of Schreiber[41]

(67) Belanger, D. B.; O'Mahony, D. J. R.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7637.

Scheme 11



employed earlier in the route to the dicyclopentapentalene framework were successfully adapted here, and the yield of tetracycles **37a/b** was increased to 53% (4:1 ratio of diastereomers) (Scheme 9). Importantly, diol **33** was also submitted to the same reaction conditions, which provided tetracycle **38a/b** in 52% yield. Success with this approach prompted the study of other solvents (see Table 1, entries f−i), but CH_2Cl_2 remained the solvent of choice. It was felt the polarity of CH_2Cl_2 contributed to the near-homogeneous nature of the NMO reaction in contrast to the heterogeneous mixture present when heptane was employed.

Finally, the success of the tandem Pauson−Khand reaction (53%) in the sterically hindered case, coupled with no yield increase when the free diol **33** itself was employed, prompted the construction of a constrained diene-diyne conformation via a benzylidene acetal, which substantially reduced rotation about the diol carbon−carbon bond. Treatment of diol **32** with *p*-anisaldehyde dimethyl acetal in refluxing toluene with a catalytic amount of pTSA readily provided acetal **35** (Scheme 8). The trimethylsilyl groups were removed on stirring with K_2CO_3/MeOH[44] to afford diene-diyne **36**. This constrained, eclipsed diene-diyne was subjected to the conditions of NMO for the tandem Pauson−Khand reaction to provide the *cis*-fused decalin **40a/b** in 43% yield (Scheme 11), isolated as a 1.2:1 inseparable mixture of acetal isomers (Table 1, entry j). The spectral data provided evidence that only one tetracyclic core was formed but the material was diastereomeric at the benzylic carbon atom (see Supporting Information for details).

Reaction of *p*-methoxybenzylidene acetal **36** with dicobalt octacarbonyl under the conditions of the photochemically mediated Pauson−Khand process afforded 45% of the desired *cis*-decalin **40a/b** in a 1.1:1 ratio (Table 1, entry k and Scheme 11). Deprotection of the *p*-methoxybenzylidene acetal in this isomeric mixture was accomplished by heating the mixture of decalins **40a/b** in water (∼70 °C) in the presence of a catalytic amount of zinc chloride. This reaction exclusively afforded a single [5.6.6.5]diol **38a** in high yield, which confirmed that the diastereomers **40a/b** were isomeric at the benzylic carbon atom and not two diastereomeric tetracycles at H_b at the 5−6 ring fusion. When this process was scaled up, **40a/b** was accompanied by a trace amount of the symmetrical diastereomer (H_a and H_b on the same face) in an approximately 19:1 ratio. The Pauson−Khand reaction of diene-diyne acetal **36** has been shown to be a process that proceeds with high diastereoselectivity. This result again lends evidence to the steric arguments for metallocycle intermediates believed to play a role in product formation. The *p*-methoxybenzylidene protecting group occupies a larger volume on one face of the molecule than the trimethylsiloxy groups, which can rotate out of the way. The presence of two cobalt moieties on the same face (required for observation of a symmetrical isomer) was greatly reduced in the presence of the *p*-methoxybenzylidene protecting group; consequently only one diastereomer predominated. The process with the acetal protecting group is unique for it provides only the *cis*-fused decalin system, as expected.

Conclusion

The regiospecific entry into the two functionalized tetraquinanes, cyclopentapentalenes **17** and **29**, was made possible by the synthesis of the key diene-diynes **11** and **19b**, followed by a photochemically mediated tandem Pauson−Khand process. This permitted the facile regiospecific preparation of functionalized ring systems related to dicyclopenta[*a*,*e*]pentalene **1** and dicyclopenta-[*a*,*f*]pentalene **2** in 74% and 90% yields, respectively. This reaction is catalytic in some cases and stoichiometric in others, as illustrated here. Six carbon−carbon bonds were generated in this process, constituting a 95% and 98% yield for each carbon−carbon bond formed in **17** and **29**, respectively. In addition to the preparation of tetracyclic systems **17** and **29**, the scope of the tandem Pauson−Khand reaction has been extended to the [5.6.6.5] dicyclopenta[*b*,*g*]decalin ring system. A *cis*-fused decalin core **38a** was obtained in stereospecific fashion from the formation of six carbon−carbon bonds in this one-pot process when acetal **36** was employed. The tandem Pauson−Khand reaction is unique in that it provides a *cis*-decalin ring system. Moreover, the yield of each of the six carbon−carbon bonds formed in this procedure in some examples (see **37a/b**) was at least 89%. The extension of the cobalt-mediated process to this [5.6.6.5] system extends the utility of the tandem Pauson−Khand reaction for the generation of other novel tetracyclic diene diones.

Experimental Section

Melting points are uncorrected. Tetrahydrofuran was distilled from sodium−benzophenone ketyl. Diisopropylamine was dried by distillation over KOH. Dicobalt octacarbonyl was purchased from Strem Chemical Company. All air-sensitive reactions were kept under an inert atmosphere of nitrogen or argon. A Q-Beam MAX MILLION 100 W xenon spotlight was purchased from K-Mart and is distributed by Brinkmann, Inc.

4-(2-Propenyl)-1-(trimethylsilyl)-3-[(trimethylsilyl)-ethynyl]-6-hepten-1-yne-3-ol (8). A solution of trimethylsilylacetylene (11.5 g, 0.117 mol) in THF (50 mL) was cooled to 0° followed by addition of *n*-BuLi (43.0 mL, 2.5 M in hexanes). After 45 min, the ester[39] **5** (6.00 g, 0.035 mol) in THF (55 mL) was added dropwise. The solution that resulted was stirred for 1 h and quenched with an aqueous solution of saturated NH_4Cl (50 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude material was purified by flash chromatography

(silica gel, eluent 10% EtOAc/hexanes) to give diene-diyne **8** (10.0 g, 88%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.98−5.82 (m, 2H), 5.10−4.98 (m, 4H), 2.58−2.48 (m, 2H), 2.28−2.16 (m, 2H), 1.96−1.89 (m, 1H), 0.17 (s, 18H) hydroxy signal not resolved; ^{13}C NMR (63 MHz, $CDCl_3$) δ 137.58, 116.09, 104.69, 89.42, 68.02, 49.34, 34.51, −0.34; IR (neat) 3519, 3073, 1636 cm^{-1}; LRMS (CI) *m*/*z* relative intensity 319 (M + 1, 4), 223 (100). Anal. Calcd for $C_{18}H_{30}OSi_2$: C, 67.85; H, 9.50. Found: C, 67.53; H, 9.79.

3-Ethynyl-4-(2-propenyl)-6-hepten-1-yne-3-ol (4). A solution of the diene-diyne **8** (0.300 g, 0.94 mmol) was dissolved in THF (30 mL), treated with tetrabutylammonium fluoride (2.8 mL, 1.0 M solution in THF), and stirred at room temperature. After 20 min, the mixture was poured into water (30 mL) and extracted with EtOAc (2 × 25 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give the crude alcohol. Flash chromatography (silica gel, eluent EtOAc) provided alcohol **4** (0.155 g, 94%) as a golden colored oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.96−5.80 (m, 2H), 5.12−4.99 (m, 4H), 2.75 (broad s, 1H), 2.60 (s, 2H), 2.59−2.48 (m, 2H), 2.30−2.18 (m, 2H), 2.02−1.94 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 137.20, 116.52, 83.09, 73.05, 67.46, 48.78, 34.33; IR (neat) 3515, 3293, 3074, 1639 cm^{-1}. This material was used directly in the next step without further purification.

Reaction of Diene-Diyne 4 with $Co_2(CO)_8$ to Provide Tetracyclic Diones 10. To a stirred solution of the diene-diyne **4** (0.297 g, 1.71 mmol) in CH_2Cl_2 (15 mL) was added $Co_2(CO)_8$ (0.649 g, 1.90 mmol, 1.1 equiv) in one portion. A new nonpolar red spot was observed by TLC (silica gel) and assumed to be the monometallocycle complex. An additional 1 equiv of $Co_2(CO)_8$ (0.650 g) was added to the mixture, and a new upper red spot appeared on TLC that was believed to be the bismetallocycle complex. *N*-Methylmorpholine-*N*-oxide monohydrate (2.40 g, 17.8 mmol)[41] was then added in one portion, and the solution that resulted was stirred overnight. The mixture was passed through a plug of silica gel (eluent EtOAc) to provide a mixture of the tetracyclic diones represented by **10**. Attempts to scale this reaction to preparative levels were not successful. **10** (symmetrical isomer): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.21 (d, J = 2.2 Hz, 2H), 3.24−3.11 (m, 2H), 2.96 (t, J = 0.2 Hz, 1H), 2.74 (d, J = 6.4 Hz, 1H), 2.68 (d, J = 6.4 Hz, 1H), 2.20 (d, 2.7 Hz, 1H), 2.14−1.83 (m, 5H), hydroxy signal not resolved; ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.84, 188.60, 125.33, 83.82, 56.16, 43.73, 43.69, 38.78; LRMS (CI) *m*/*z* relative intensity 231 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{14}H_{14}O_3$ (M^+) 230.0942, found 230.0939. **10** (unsymmetrical isomer): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.23 (d, J = 2.0 Hz, 1H), 5.87 (d, J = 2.2 Hz, 1H), 3.75 (broad s, 1H), 3.44 (m, 1H), 3.02 (m, 2H), 2.74−2.58 (m, 3H), 2.20−2.11 (m, 2H), 2.07−1.88 (m, 1H), 1.60 (m, 1H), 1.03 (q, J = 9.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 209.92, 209.44, 188.36, 185.58, 125.60, 124.80, 81.07, 56.70, 45.03, 42.60, 42.50, 41.74, 38.02, 35.25; LRMS (CI) *m*/*z* relative intensity 231 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{14}H_{14}O_3$ (M^+) 230.0942, found 230.0940.

Ethyl-2-(2-propenyl)-2-hydroxy-4-pentenoate (13). To a three-neck 3-L round-bottom flask equipped with a mechanical stirrer, pressure equalizing dropping funnel, and reflux condenser was placed granular zinc metal (186 g, 2.84 mol, 20 mesh) in dry THF (600 mL) under nitrogen. Pure allyl bromide (202 mL in 200 mL of THF) was added dropwise (slowly), and about 100 mL of the solution was dispensed until the formation of the zinc Grignard was observed. This process is very exothermic, and great care should be taken to control the temperature. The remainder of the allyl bromide solution was then added slowly to maintain the internal temperature at 45 °C or lower. After complete addition (1.5 h) of the allyl bromide solution, the mixture was stirred for 1 h, followed by cooling in an ice bath to 0−5 °C. Diethyl oxalate (**12**) (138 g, 0.94 mol) in THF (100 mL) was added dropwise (slowly) to maintain the internal temperature at 30 °C or less. After stirring for 45 min, approximately 1.0 mL of the reaction mixture was removed and quenched with an aqueous solution of saturated NH_4Cl for analysis by NMR. Examination of the proton spectrum of the crude material revealed 30% of diethyl oxalate remained unreacted. An additional amount of zinc (24 g) was added in one portion followed by slow addition of allyl bromide (30 mL neat), and the proton spectrum was rechecked after 1 h. Examination of the proton spectrum at this time indicated the presence of only 8% unreacted diethyl oxalate remaining. Additional zinc (20 g) and allyl bromide (20 mL neat) were added again, and the slurry was stirred for 1 h. Examination again of the proton spectrum indicated complete consumption of diethyl oxalate. The reaction was then quenched slowly at 0−5 °C by dropwise addition of a saturated aqueous solution of NH_4Cl. A heavy precipitate formed, and ethyl acetate (400 mL) was added followed by rapid stirring for 10 min. The gelatinous material was removed by vacuum filtration and washed thoroughly with ethyl acetate. The solid gelatinous salts were dissolved in 5% aqueous HCl and extracted with EtOAc to remove additional product that had been trapped in the solids. The combined organic extracts were neutralized with aqueous saturated $NaHCO_3$, washed with brine and dried ($MgSO_4$). Concentration of the solvent under reduced pressure followed by vacuum distillation afforded **13** (145.0 g, 84%) as a colorless liquid: bp 62−63 °C, 3.5 mmHg (lit.[42] 208−209, 760 mmHg). The spectral characteristics for **13** are in agreement with the literature.[50]

4-(2-Propenyl)-1-(trimethylsilyl)-3-[(trimethylsilyl)-ethynyl]-6-hepten-1-yne-3,4-diol (11). A solution of trimethylsilylacetylene (0.968 g, 9.88 mmol) in THF (25 mL) was stirred at 0 °C (ice bath). *n*-BuLi (3.64 mL, 2.5 M in hexanes) was added, and the mixture that resulted was allowed to stir for 30 min. A second flask that contained ester **13** (0.413 g, 2.25 mmol) in THF (10 mL) was cooled to 0 °C. The freshly prepared lithium trimethylsilylacetylide solution was added by syringe into the second flask. After 2 h, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl (15 mL). The aqueous layer was extracted with ether (2 × 50 mL). The combined extracts were neutralized with a saturated aqueous solution of $NaHCO_3$, dried ($MgSO_4$), and concentrated under reduced pressure. The crude diol was purified by flash chromatography (silica gel, eluent 15% EtOAc/hexanes) to give **11** (0.565 g, 75.4%): mp 50.5−51.5 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.07−5.90 (m, 2H), 5.15−5.08 (m, 4H), 2.92 (s, 1H), 2.59 (sept, J = 7.2 Hz, 4H), 2.26 (s, 1H), 0.18 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 134.12, 118.32, 103.15, 90.98, 77.78, 71.07, 39.82, −0.50; IR (KBr) 3500, 3077, 2170, 1642 cm^{-1}; LRMS (CI) *m*/*z* relative intensity 335(2), 223 (100). Anal. Calcd for $C_{18}H_{30}O_2Si_2$: C, 64.61; H, 9.04. Found: C, 64.64; H, 9.09.

4-(2-Propenyl)-1-(trimethylsilyl)-3-[(trimethylsilyl)-ethynyl]-6-hepten-1-yne-3,4-diol (11) (preparative scale). A solution of trimethylsilylacetylene (100.02 g, 1.02 mol) in THF (500 mL) was stirred at 0 °C. *n*-BuLi (416 mL, 2.5 M in hexanes) was added via a pressure equalizing dropping funnel, and the mixture that resulted was stirred for 60 min. A solution of the ester **13** (48.08 g, 0.258 mol in 125 mL THF) was added dropwise via a pressure equalizing dropping funnel over a period of 60 min, and the mixture that resulted was allowed to stir for 2 h. An aqueous solution of saturated NH_4Cl (125 mL) was added dropwise. The mixture was diluted with ether (200 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The mixture was recrystallized from heptane to furnish a first crop of diol **11** (29.85 g). A second crop of the diol was recrystallized from the mother liquor to provide an additional 14.05 g. The mother liquor can be flash chromatographed (silica gel, eluent 25% EtOAc/hexanes) to provide additional diol if desired. The spectral characteristics of **11** were in agreement with those reported above in a previous experiment.

3-(Ethynyl)-4-(2-propenyl)-6-hepten-1-yne-3,4-diol (14). A solution of the diol **11** (1.01 g, 3.01 mmol) in MeOH (25 mL) was stirred at room temperature. Anhydrous K_2CO_3 (0.827 g, 5.98 mmol) was added portionwise. After 1 h, the mixture was diluted with ether (50 mL) and H_2O (50 mL). The aqueous layer was extracted with ether (2 × 50 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to afford **14** (0.567 g, 98%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.05−5.89 (m, 2H), 5.15 (d, J = 3.8 Hz, 2H), 5.10 (s, 2H), 3.20 (broad s, 1H), 2.71−2.51 (m, 6H),

2.4 (broad s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.64, 118.93, 81.80, 77.65, 74.30, 70.53, 39.66; IR (neat) 3505, 3297, 3077, 2116, 1639 cm^{-1}; LRMS (EI) *m*/*z* relative intensity 149 (10), 69 (100). This material was employed directly in the next step.

Attempted Pauson−Khand Reaction with Diene-Diyne 14. A solution of the diene-diyne **14** (0.238 g, 1.25 mmol) in CH_2Cl_2 (15 mL) was stirred at room temperature. Dicobalt octacarbonyl (1.02 g, 2.98 mmol) was added in one portion, and the mixture that resulted was stirred for 1.5 h. The 4-methylmorpholine-*N*-oxide (1.50 g, 12.75 mmol) was added to the mixture portionwise. When the reaction mixture was monitored by TLC (silica gel, EtOAc), no evidence of product formation was observed, and only baseline material was visualized. The reaction was stirred for an additional 24 h and rechecked with no change.

4,4-(Diethynyl)-2,2-dimethyl-5,5-(di-2-propenyl)-1,3-dioxolane (16). A solution of the diol **11** (23.02 g, 68.9 mmol), 2,2′-dimethoxypropane (16 mL), and dry pTSA (322 mg) was dissolved in $CHCl_3$ (1.4 L) and heated to reflux in a Soxhlet apparatus filled with 4 Å molecular sieves for 16 h. Analysis by TLC at this time indicated the presence of a small amount of unreacted starting material. The reaction mixture was cooled and concentrated under reduced pressure, followed by flash chromatography (silica gel, eluent 5% EtOAc/hexanes) to afford the acetonide (20.98 g, 81% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.0−5.8 (m, 2H), 5.15 (d, J = 2.5 Hz, 2H), 5.09 (d, J = 1.0 Hz, 2H), 2.60 (m, 4H), 1.51 (s, 6H), 0.16 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.17, 118.50, 110.70, 101.82, 92.23, 87.07, 75.19, 38.64, 28.63, −0.60; IR (neat) 3076, 2127, 1638 cm^{-1}; LRMS (EI$^+$) *m*/*z* relative intensity 374 (8), 206 (100); HRMS (EI$^+$) calcd for $C_{20}H_{31}O_2Si_2$ (M^+) 374.2097, found 374.2045. The recovered diol may be recycled for future use. The acetonide was employed directly in the next step.

To a stirred solution of the acetonide (31.29 g, 83.7 mmol) in MeOH (450 mL) was added K_2CO_3 (17.4 g, 0.129 mol) in one portion. The solution that resulted was stirred at room temperature for 30 min. The mixture was concentrated to one-half of its original volume under reduced pressure, diluted with $CHCl_3$ (200 mL), and washed with water (100 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 50 mL). The combined organic extracts were washed with brine (100 mL) and dried ($MgSO_4$). The solvent was concentrated under reduced pressure followed by storing in a freezer, which resulted in a tan solid. This material was recrystallized from heptane to afford diene-diyne **16** (13.3 g, 70%): mp 55−56 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.94−5.78 (m, 2H), 5.19−5.12 (m, 4H), 2.69 (s, 2H), 2.64 (d, J = 7.3 Hz, 4H), 1.53 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 132.56, 119.03, 111.04, 86.97, 80.23, 75.47, 74.34, 38.59, 28.58; IR (neat) 3273, 3072, 2121, 1641 cm^{-1}; LRMS (EI$^+$) *m*/*z* relative intensity 215 (10), 189 (100). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.21; H, 7.89. Found: C, 77.82; H, 7.92.

***cis*-6a,7,8,8a-Tetrahydro-10,10-dimethyl-(epoxymethanoxy)-dicyclopenta[*a*,*f*]pentalene-2,5(1*H*,6*H*)-dione (17a), *trans*-6a,7,8,8a-Tetrahydro-10,10-dimethyl-(epoxymethanoxy)-dicyclopenta[*a*,*f*]pentalene-2,5(1*H*,6*H*)-dione (17b), and *cis*-6a,7,8,8a-Tetrahydro-10,10-dimethyl-(epoxymethanoxy)-dicyclopenta[*a*,*f*]pentalene-2,5(1*H*,6*H*)-dione (17c).** A solution of the diene-diyne **16** (0.900 g, 3.91 mmol) and $Co_2(CO)_8$ (3.34 g, 9.76 mmol) in CH_2Cl_2 (45 mL) was stirred at room temperature under an atmosphere of CO. After 12 h, *N*-methylmorpholine-*N*-oxide (3.30 g, 28.01 mmol) was added portionwise to the mixture. Additional NMO was later added until no metal complexes were observed by TLC (silica gel). The purple solution was concentrated to one-half of its original volume under reduced pressure, loaded onto a silica gel column, and eluted (flash chromatography) with EtOAc to provide **17a** and **17b** (0.743 g, 67%) in a ratio of 2:1, respectively, accompanied by a trace of **17c**.

17a: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.20 (d, J = 2.3 Hz, 2H), 3.75 (m, 2H), 2.73 (dd, J = 6.7 Hz, 2H) 2.60 (dd, J = 8.5 Hz, 2H), 2.13 (dd, J = 3.2 Hz, 2H), 1.54 (s, 6H), 1.32 (dd, J = 11.5 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.30, 179.54, 128.57, 117.30, 106.97, 88.27, 46.05, 43.09, 42.95, 28.93; IR (KBr) 3084, 1709, 1635 cm^{-1}; HRMS (EI$^+$) calcd for $C_{17}H_{18}O_4$ (M^+) 286.1205, found 286.1201. Anal. Calcd for $C_{17}H_{18}O_4 \cdot {}^1/_8H_2O$: C, 70.76; H, 6.38. Found: C, 70.85, H, 6.41.

17b: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.36 (d, J = 2.2 Hz, 1H), 5.94 (d, J = 2.0 Hz, 1H), 3.4 (m, 1H), 2.94 (m, 1H), 2.79−2.64 (m, 3H), 2.48 (dd, J = 7.8 Hz, 1H), 2.27−2.13 (m, 2H), 1.71 (t, J = 12.5 Hz, 1H), 1.50 (s, 3H), 1.33 (s, 3H), 1.21 (t, J = 12.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.73, 208.17, 182.90, 181.48, 127.14, 126.65, 117.60, 104.13, 89.21, 44.14, 43.58, 42.96, 42.64, 42.39, 41.91, 28.62, 28.02; IR (KBr) 1713, 1641 cm^{-1}; LRMS (CI) *m*/*z* relative intensity 287 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{17}H_{18}O_4$ (M^+) 286.1206, found 286.1195.

17c: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.28 (d, J = 2.3 Hz, 2H), 3.40−3.28 (m, 2H), 2.74−2.54 (m, 4H), 2.23−2.13 (m, 2H), 1.85 (t, J = 12.7 Hz, 2H), 1.36 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 207.53, 183.40, 127.06, 120.88, 102.82, 92.31, 46.83, 44.82, 43.28, 29.26; LRMS (CI) *m*/*z* relative intensity 287 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{17}H_{18}O_4$ (M^+) 286.1205, found 286.1198. This process could be scaled up to the 3-g level with no loss in yield.

Photochemically Mediated Pauson-Khand Reaction of Acetonide 16 to Provide Tetracyclic System 17. A solution of the diene-diyne **16** (6.00 g 26.07 mmol) and $Co_2(CO)_8$ (8.94 g, 26.13 mmol, 1 mol equiv) in degassed 1,2-DME (300 mL) was stirred at room temperature under an atmosphere of CO. After 1 h, the reaction mixture was irradiated with a Q-Beam MAX MILLION spotlight.[51] During the course of the irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50 and 55 °C (approximately 2.5 ft distance between lamp and reaction flask). After 25 h, irradiation was discontinued, the mixture was cooled, and the solvent was concentrated under reduced pressure. The residual material that was isolated was purified by flash chromatography (silica gel, eluted twice, 70% EtOAc/hexane) to afford 5.15 g (69%) of a mixture of tetracyclic diones **17a**, **17b**, and **17c** in a ratio of 4.7:5.9:1, respectively. The spectral characteristics of these cyclopentapentalenes were identical to those reported in the previous experiment. When this process was run on 300-mg scale, a 74% yield of **17a**−**c** was realized.[50]

1-Trimethylsilyl-5-hexen-2-yne-3-ol (21). A solution of allylmagnesium chloride (190 mL, 2.0 M solution in THF) was cooled to 5 °C (ice bath) followed by addition of 3-trimethylsilyl-2-propynal[66] (32.9 g, 0.261 mol) dissolved in THF (60 mL). After stirring for 1 h, the mixture was quenched carefully with a saturated aqueous solution of NH_4Cl (125 mL) while the internal temperature was carefully kept at 25 °C or less. The mixture was diluted with ether (200 mL), and the aqueous layer was extracted with ether (2 × 50 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give the crude alcohol **21**. Vacuum distillation (water aspirator) of this material afforded **21** (42.37 g, 97%) as a colorless liquid: bp 86−87 °C, 15 mmHg; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.92−5.76 (m, 1H), 5.18−5.11 (m, 2H), 4.37 (t, J = 6.2 Hz, 1H), 2.43 (t, J = 6.5 Hz, 2H), 2.12 (broad s, 1H), 0.12 (s, 9H). The spectral characteristics of **21** are in agreement with those published earlier.[55]

1-Trimethylsilyl-5-hexen-2-yne-3-one (20). A solution of 1-trimethylsilyl-5-hexen-2-yne-3-ol **21** (5.00 g, 29.76 mmol) in ether (130 mL) was cooled to 0−5 °C and stirred vigorously. Another solution, which had been prepared from $Na_2Cr_2O_7 \cdot 2H_2O$ (10.0 g, 33.56 mmol) and concentrated H_2SO_4 (6 mL) dissolved in water (45 mL), was added dropwise via a dropping funnel. The temperature was maintained at 0 °C. After the addition was complete, the ice bath was removed, and the mixture was allowed to warm to room temperature. After 2 h, the reaction mixture was diluted with ether (100 mL). The organic layer was washed with a solution of saturated aqueous $NaHCO_3$, washed with brine, and dried ($MgSO_4$). Concentration of the solvent under reduced pressure furnished ketone **20** (4.17 g, 84%) as a pale yellow oil, and this material was used directly in the next step. [Note: avoid flash chromatography at this point; even a wash column on silica gel will isomerize the allyl group to the conjugated enone]. ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.01−5.84 (m, 1H), 5.23−5.13 (m, 2H), 3.29 (d, J = 7.0 Hz, 2H), 0.22 (s, 9H); ^{13}C NMR (63 MHz,

$CDCl_3$) δ 184.84, 129.16, 119.52, 101.69, 98.91, 49.67, −0.85; IR (neat) 3082, 2149, 1678, 1639 cm^{-1}; LRMS (EI^+) *m/z* relative intensity 125 (100).

4-(2-Propenyl)-1-(trimethylsilyl)-3-[(trimethylsilyl)-ethynyl)]-6-hepten-1-yne-3,4-diol (*meso*-19a and *dl*-19b). Ketone **20** (4.97 g, 29.94 mmol), activated zinc dust (19.6 g, 0.299 mol), and trimethylsilyl chloride (19.4 g, 0.299 mol) were added to THF (85 mL) at 5 °C (ice bath) and stirred under nitrogen. The mixture was warmed to room temperature. After 4 h, H_2O was added dropwise very carefully one drop at a time, which resulted in a moderate temperature rise. Ether (100 mL) was added, and the aqueous layer was extracted with ether (3 × 50 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give a mixture of *meso*-**19a** and *dl*-**19b** isomers (4.49 g, 89%) in a ratio of 3:1, respectively. Separation of the two isomers was achieved with flash chromatography (silica gel, eluent 30% EtOAc/hexanes).

19a (*meso*): ^1H NMR (250 MHz, $CDCl_3$) δ 6.12−5.95 (m, 2H), 5.20−5.13 (m, 4H), 2.60 (s, 2H), 2.54 (m, 4H), 0.16 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.52, 118.60, 105.22, 92.10, 76.13, 40.31, −0.22; LRMS (CI) *m/z* relative intensity 335 (M + 1, 15), 317 (100). Anal. Calcd for $C_{18}H_{30}O_2Si_2$; C, 64.61; H, 9.04. Found: C, 64.68; H, 9.13.

19b (*dl*): ^1H NMR (250 MHz, $CDCl_3$) δ 6.12−5.96 (m, 2H), 5.23−5.14 (m, 4H), 2.65 (m, 4H), 2.53 (s, 2H), 0.16 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.51, 119.26, 104.69, 92.12, 75.62, 41.74, −0.21; LRMS (CI) *m/z* relative intensity 335 (M + 1, 10), 317 (100). Anal. Calcd for $C_{18}H_{30}O_2Si_2$; C, 64.61; H, 9.04. Found: C, 64.75; H, 9.05.

1-Triisopropylsilyl-5-hexen-2-yne-3-ol (26). The 3-triisopropylsilylpropargyl alcohol **25** (16.0 g, 75.47 mmol), which had been dissolved in CH_2Cl_2 (75 mL), was added to a slurry of PCC (24.4 g, 113.0 mmol) in CH_2Cl_2 (330 mL) and stirred with an overhead stirrer at room temperature. After 1.5 h, observation of TLC (silica gel) indicated starting alcohol remained. Additional PCC (13.0 g) was added, and the mixture was allowed to stir for 3 h. The mixture was transferred to a wash column (silica gel) and eluted with CH_2Cl_2. The solvent was removed under reduced pressure while the bath temperature was kept at 25 °C or less until approximately 20 mL of solvent remained. Vacuum distillation (water aspirator) of the material afforded the aldehyde (11.4 g, 71%): bp 105 °C; ^1H NMR (250 MHz, $CDCl_3$) δ 9.18 (s, 1H), 1.09 (s, 21H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 176.28, 104.60, 100.57, 18.40, 11.00; IR (neat) 2147, 1667 cm^{-1}; HRMS (EI^+) calcd for $C_{12}H_{22}OSi$ (M^+) 210.1440, found 210.1441. This material was employed directly in the next step.

A solution of allylmagnesium chloride (50.0 mL, 2.0 M solution in THF) was cooled to 5 °C (ice bath) followed by addition of the aldehyde (11.0 g, 52.38 mmol), which had been dissolved in THF (30 mL). After 1 h, the mixture was quenched with a saturated solution of aqueous NH_4Cl (40 mL) while the internal temperature was carefully kept at 25 °C or less. The reaction mixture was diluted with ether (100 mL). The aqueous layer was extracted with additional ether (2 × 50 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to provide the crude alcohol **26**. Purification by vacuum distillation (water aspirator) afforded **26** (12.97 g, 97%) as a pale yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 5.97−5.80 (m, 1H), 5.21−5.13 (m, 2H), 4.42 (t, J = 6.0 Hz, 1H), 2.46 (t, J = 6.0 Hz, 2H), 1.81 (broad s, 1H), 1.04 (s, 21H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 133.04, 118.70, 108.23, 66.03, 62.17, 42.41, 18.56, 11.22; IR (neat) 3332, 3078, 2169, 1642 cm^{-1}; HRMS (EI^+) calcd for $C_{15}H_{28}OSi$ (M^+) 252.1909, found 252.1919. This material was employed directly in the next step.

1-Triisopropylsilyl-5-hexen-2-yne-3-one (27). A solution of 1-trimethylsilyl-5-hexen-2-yne-3-ol **26** (1.003 g, 3.98 mmol) in ether (20 mL) was cooled to 0−5 °C and stirred vigorously. A solution that had been prepared from $Na_2Cr_2O_7 \cdot 2H_2O$ (3.01 g, 10.10 mmol) and concentrated H_2SO_4 (2.3 mL) dissolved in water (15 mL) was added dropwise. After the addition was complete, the ice bath was removed, and the mixture was allowed to warm to room temperature. After 1 h, the mixture was diluted with ether (100 mL). The organic layer was neutralized with a saturated aqueous solution of $NaHCO_3$, washed with brine, and dried ($MgSO_4$). Concentration of the solvent under reduced pressure furnished ketone **27** (0.92 g, 96%) as a pale yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 6.02−5.86 (m, 1H), 5.24−5.13 (m, 2H), 3.30 (d, J = 6.9 Hz, 2H), 1.10 (s, 3H), 1.09 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 184.81, 129.35, 119.65, 103.96, 96.90, 50.10, 18.45, 11.04; IR (neat) 2147, 1678, 1636 cm^{-1}; LRMS (EI^+) *m/z* relative intensity 209 (96), 109 (100). This material was employed directly in the next step.

Attempted Pinacol Coupling of Ketone 27. A solution of the ketone **27** (0.92 g, 3.68 mmol), activated zinc dust (2.40 g, 36.70 mmol), and trimethylsilyl chloride (2.50 g, 23.15 mmol) dissolved in THF (20 mL) was cooled to 5 °C (ice bath) and stirred under nitrogen. The mixture was allowed to warm to room temperature. After 4 h, H_2O was added dropwise very carefully to quench the process one drop at a time. Ether was added to the mixture, and the aqueous layer was extracted with additional ether (2 × 50 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Analysis by TLC (silica gel) indicated a complex mixture of four to five components with the major spot exhibiting a similar R_f to alcohol **26**. Analysis of the proton NMR of this material indicated that reduction of the starting ketone to the alcohol **26** occurred, which suggested the intermediate transition state may be too bulky for pinacol coupling.

Attempted Pauson−Khand Cyclization with *meso*-Diol 19a. A solution of the *meso*-diol **19a** (1.018 g, 3.00 mmol) in 5% aqueous THF (20 mL) was stirred at room temperature. Tetrabutylammonium fluoride (9.0 mL, 1.0 M solution in THF) was added dropwise, and the mixture was stirred for 30 min. The reaction solution was washed with water (30 mL) and brine (30 mL) and dried ($MgSO_4$). Concentration of the solvent under reduced pressure afforded the crude diol, which was flash chromatographed (silica gel, eluent 25% EtOAc/hexanes) to provide the diol (0.454 g, 79%): ^1H NMR (250 MHz, $CDCl_3$) δ 6.13−5.97 (m, 2H), 5.25−5.18 (m, 4H), 2.68 (s, 2H) 2.61 (m, 4H), 2.56 (s, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 132.90, 119.58, 83.26, 75.36, 53.94, 40.36; IR (neat) 3527, 3292, 2113, 1641 cm^{-1}; LRMS (CI^+) *m/z* relative intensity 173 (50), 131 (100). This material was used directly in the next step. A solution of the diene-diyne diol (0.193 g, 1.01 mmol) in CH_2Cl_2 (11 mL) was stirred at room temperature. Dicobalt octacarbonyl (1.04 g, 3.04 mmol) was added in one portion, and the mixture that resulted was stirred for 2 h. The 4-methylmorpholine-*N*-oxide (1.50 g, 12.75 mmol) was then added to the mixture portionwise. When the reaction mixture was monitored by TLC (silica gel, EtOAc), no evidence of product formation was observed; only baseline material was visualized. The reaction was stirred for an additional 24 h and rechecked with no change.

***trans*-4,5-Diethynyl-2,2-dimethyl-4,5-di-2-propenyl-1,3-dioxolane (28).** A solution of the *threo*-diol **19b** (0.399 g, 1.19 mmol), 2,2′-dimethoxypropane (2.0 g mL), and dry pTSA (25 mg) in $CHCl_3$ (125 mL) was heated to reflux in a Soxhlet apparatus filled with 4 Å molecular sieves. After 6 h, analysis by TLC (silica gel) indicated an approximate ratio of acetonide to diol of 3:1. Additional 2,2′-dimethoxypropane (2.0 g) was added, and the reaction was heated for an additional 2 h. After 13 h of heating (total reaction time) the reaction mixture was cooled to room temperature and washed with a saturated aqueous solution of $NaHCO_3$ and brine and dried ($MgSO_4$). Concentration of the solvent under reduced pressure afforded the crude acetonide, which was chromatographed by a gravity column (silica gel, eluent 4% EtOAc/hexanes) to give the acetonide (0.288 g, 65% yield): ^1H NMR (250 MHz, $CDCl_3$) δ 6.02−5.86 (m, 2H), 5.19−5.12 (m, 4H), 2.77 (dd, J = 6.6 Hz, 2H), 2.53 (dd, J = 7.6 Hz, 2H), 1.52 (s, 6H), 0.15 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 132.82, 118.48, 110.64, 104.23, 94.33, 81.99, 42.60, 27.80, −0.34; IR (neat) 3079, 2167, 1642 cm^{-1}, LRMS (EI^+) *m/z* relative intensity 359 (8), 135 (100). This material was employed directly in the next step. A solution of the acetonide (0.278 g, 0.743 mmol) in 5% aqueous THF (5 mL) was stirred at room temperature. Tetrabutylammonium fluoride (3.71 mL, 1.0 M solution in THF) was added dropwise, and the mixture was stirred for 30 min. The reaction solution

was diluted with ether (40 mL), washed with water (20 mL) and brine (20 mL), and dried ($MgSO_4$). Concentration of the solvent under reduced pressure afforded the diene-diyne **28** (0.169 g, 98%) as a pale yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.05−5.88 (m, 2H), 5.23−5.15 (m, 4H), 2.86 (d, J = 6.6 Hz, 4H), 2.66 (s, 2H), 1.54 (s, 6H); ^{13}C NMR (63 MHz, C_6D_6) δ 132.98, 118.76, 111.13, 82.71, 82.23, 77.65, 43.03, 28.03; IR (neat) 3293, 3077, 2109, 1641 cm^{-1}; LRMS (EI$^+$) *m*/*z* relative intensity 215 (100); HRMS (EI$^+$) calcd for $C_{14}H_{15}O_2$ (M − 15) 215.1072, found 215.1071. This material was used directly in the next step.

(3b.α.,4a.α.,7b.α.,8a.α.)-4a,5,8,8a-Tetrahydro-10,10-dimethyl-3b,7b-(epoxymethanoxy)-dicyclopenta[*a*,*e*]pentalene-2,6(1*H*,4*H*)-dione (29a) and (3b.α.,4a.α.,7b.α.,8a.*β*.)-4a,5,8,8a-Tetrahydro-10,10-dimethyl-3b,7b-(epoxymethanoxy)-dicyclopenta[*a*,*e*]pentalene-2,6(1*H*,4*H*)-dione (29b). A solution of the diene-diyne **28** (0.058 g, 0.257 mmol) and $Co_2(CO)_8$ (0.282 g, 0.826 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature under an atmosphere of CO. After 1.5 h, *N*-methylmorpholine-*N*-oxide (1.0 g, 8.56 mmol) was added to the reaction mixture portionwise. Additional NMO was added until the metal complexes were no longer observed by TLC. The purple solution that remained was concentrated under reduced pressure to one-half of its original volume, and this material was loaded onto a silica gel column and eluted with EtOAc to provide **29a** and **29b** (0.044 g, 62%) in a ratio of 2:3, respectively: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.20 (d, J = 2.2 Hz, 1H), 6.16 (d, J = 2.0 Hz, 2H), 6.07 (d, J = 2.3 Hz, 1H), 3.79−3.72 (m, 2H), 3.56−3.45 (m, 1H), 2.97−2.90 (m, 1H), 2.83−2.61 (m, 6H), 1.80 (t, J = 12.7 Hz, 1H), 1.56 (s, 6H), 1.53 (s, 3H), 1.33 (s, 3H), 1.21 (dd, J = 7.1 Hz, 12.05 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.87, 208.57, 208.09, 185.98, 184.28, 183.18, 127.48, 126.09, 125.01, 117.43, 117.14, 98.21, 97.19, 94.25, 46.11, 42.70, 42.28, 42.23, 41.87, 40.72, 40.10, 39.18, 29.04, 28.48, 28.04 (two signals could not be resolved); LRMS (CI$^+$) *m*/*z* relative intensity 287 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{17}H_{18}O_4$ (M$^+$) 286.1205, found 286.1194.

Photochemically Mediated Pauson−Khand Reaction of Acetonide 28 to Provide Tetracyclic System 29. A solution of the diene-diyne **28** (0.196 g, 0.853 mmol) and $Co_2(CO)_8$ (0.060 g, 0.176 mmol, 0.2 mole equiv) in degassed 1,2-DME (7 mL) was stirred at room temperature under an atmosphere of CO. The reaction mixture was irradiated with a Q-Beam MAX MILLION spotlight.[51] During the course of the irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50 and 55 °C (approximately 2.5 ft distance between lamp and reaction flask). After 24 h, irradiation was discontinued, the mixture was cooled, and the solvent was concentrated under reduced pressure. The residual material that was isolated was purified by flash chromatography (silica gel, eluent 55% EtOAc/hexane) to afford (0.219 g, 90%) of a mixture of tetracyclic diones **29a** and **29b** in a ratio of 2:3, respectively. The spectral characteristics of these cyclopentapentalenes were identical to those reported in the previous experiment.

Synthesis of Diene-Diyne 32. A solution of ester **31**[50] (8.218 g, 25.36 mmol) in THF (100 mL) was stirred under N_2 and cooled with a water bath. Allylmagnesium chloride (2.0 M in THF, 38.0 mL, 76.0 mmol, 3 equiv) was added quickly via syringe, and the cooling bath was removed. After 1 h, a 0.25 mL aliquot was removed and quenched by an aqueous solution of saturated NH_4Cl for analysis by NMR. A small amount of starting material remained. An additional 6.0 mL of allylmagnesium chloride (12.0 mmol, 0.5 equiv) was added, and the mixture was stirred for 1 h to complete the reaction. The flask was cooled to 0 °C, and the reaction was quenched via dropwise addition of aqueous saturated NH_4Cl. The reaction mixture was diluted with 100 mL of H_2O and 100 mL of Et_2O. The aqueous layer was extracted with Et_2O (3 × 100 mL), and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to provide the crude diene-diyne. Flash chromatography (silica gel, eluent 5% EtOAc/hexanes) afforded **32** as a pale yellow oil (8.037 g, 88%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.04−5.87 (m, 2H), 5.12−5.06 (m, 4H), 2.97 (s, 1H), 2.86 (s, 1H), 2.69 (s, 4H), 2.51 (d, J = 7.4 Hz, 4H), 0.15 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 134.47, 117.64, 103.31, 69.35, 77.64, 76.81, 40.20, 28.08, −0.07; IR (thin film) 3529, 3074, 2174 cm^{-1}; LRMS (CI$^+$) *m*/*z* relative intensity 363 (M + 1, 27), 347 (100). Anal. Calcd for $C_{20}H_{34}O_2Si_2$: C, 66.24; H, 9.45. Found: C, 66.06; H, 9.40.

Deprotection of Diene-Diyne 32 to Provide Diene-Diyne 33. A solution of the diol **32** (7.86 g, 21.7 mmol) in MeOH (220 mL) was stirred at room temperature. Anhydrous K_2CO_3 (4.50 g, 32.6 mmol, 1.5 equiv) was added. After 1 h, the mixture was diluted with $CHCl_3$ (200 mL). Water was added to dissolve the excess K_2CO_3 (100 mL), and the aqueous layer was extracted with additional $CHCl_3$ (3 × 150 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to afford crude **33**. Flash chromatography (silica gel, eluent 15% EtOAc/hexanes) afforded **33** as a pale yellow oil (4.50 g, 95%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.02−5.85 (m, 2H), 5.15−5.09 (m, 4H), 2.72 (d, J = 2.6 Hz, 4H), 2.49 (d, J = 7.5 Hz, 4H), 2.12 (t, J = 2.6 Hz, 2H), OH signals were not resolved; ^{13}C NMR (65 MHz, $CDCl_3$) δ 134.20, 118.40, 80.61, 76.70, 72.19, 40.01, 26.24; IR (thin film) 3532, 2118, 1638 cm^{-1}; LRMS (CI$^+$) *m*/*z* relative intensity 219 (M + 1, 8), 201 (100); HRMS (EI$^+$) calcd for $C_{14}H_{18}O_2$ (M$^+$) 218.1307, found 218.1312. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.04; H, 8.31.

Protection of Diol 33 to Give Trimethylsilyl Derivative 34. To a solution of diol **33** (3.33 g, 15.3 mmol) in CH_2Cl_2 (100 mL) were added 4-(dimethylamino)pyridine (18.7 g, 153.4 mmol, 10 equiv) and trimethylsilyl chloride (18.5 mL, 145.8 mmol, 9.5 equiv). The reaction mixture was stirred for 20 h, and TLC indicated the absence of unreacted starting material and the presence of monoprotected diol, in an approximate ratio of 1:2 with diprotected product. An additional amount of DMAP (9.35 g, 76.6 mmol, 5 equiv) and TMSCl (9.2 mL, 72.5 mmol, 4.7 equiv) was added, and reaction mixture was stirred for 12 h. TLC indicated the presence of only the higher R_f diprotected diol. The reaction mixture was cooled to 0 °C and quenched via dropwise addition of H_2O (15 mL), followed by filtration through a pad of silica gel. The filter cake was rinsed with excess EtOAc, and the filtrates were concentrated under reduced pressure to provide crude **34**. Purification by flash chromatography (silica gel, eluent hexanes) afforded **34** as a colorless oil (5.46 g, 99%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.99−5.82 (m, 2H), 5.06−4.98 (m, 4H), 2.86 (dd, J = 17.0, 2.7 Hz, 2H), 2.66 (dd, J = 17.0, 2.7 Hz, 2H), 2.63−2.43 (m, 4H), 2.04 (t J = 2.8 Hz, 2H), 0.19 (s, 9H), 0.14 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 135.65, 116.63, 82.79, 82.63, 82.17, 71.54, 41.34, 26.62, 3.03, 2.65; IR (thin film) 3081, 3075, 2119 cm^{-1}; LRMS (EI$^+$) *m*/*z* relative intensity 321 (M$^+$ − C_3H_5, 9), 183 (100); HRMS (EI$^+$) calcd for $C_{20}H_{34}O_2Si_2$ (M$^+$ − C_3H_5) 321.1677, found 321.1706. Anal. Calcd for $C_{20}H_{34}O_2Si_2$: C, 66.24; H, 9.45. Found: C, 66.08; H, 9.47.

Protection of Diene-Diyne 32 To Give *p*-Methoxybenzylidene Acetal 35. A solution of diol **32** (2.91 g, 8.05 mmol), *p*-anisaldehyde dimethyl acetal (2.70 mL, 2 equiv) and dry pTSA (123 mg, 0.09 equiv) in toluene (260 mL) was heated to reflux in a Soxhlet apparatus filled with 4 Å molecular sieve pellets. After 40 min, the reaction mixture was cooled to room temperature, quenched via addition of aqueous saturated $NaHCO_3$ (100 mL), and diluted with Et_2O (200 mL). The aqueous layer was extracted with Et_2O (3 × 150 mL), and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to provide crude protected diol **35**. Purification by flash chromatography (silica gel, eluent 4% Et_2O/hexanes) afforded the benzylidene acetal **35** as an almost colorless oil (3.47 g, 90% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.08−5.87 (m, 2H), 5.99 (s, 1H), 5.18−5.03 (m, 4H), 3.80 (s, 3H), 3.06 (d, J = 17.1 Hz, 1H), 2.85−2.66 (m, 4H), 2.59−2.50 (m, 3H), 0.17 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.02, 133.72, 133.36, 131.02, 127.64 (2), 118.31, 118.03, 113.60 (2), 102.94, 102.34, 100.41, 88.00, 87.77, 85.54, 84.74, 55.27, 38.76, 36.74, 27.00, 24.83, 0.00; IR (thin film) 3076, 2177 cm^{-1}; LRMS (CI$^+$) *m*/*z* relative intensity 481 (M + 1, 45), 345 (100); HRMS (EI$^+$) calcd for $C_{28}H_{40}O_3Si_2$ (M$^+$) 480.2539, found 480.2516.

Anal. Calcd for $C_{28}H_{40}O_3Si_2$: C, 69.95; H, 8.39. Found: C, 69.65; H, 8.32.

Removal of Trimethylsilyl Groups of *p*-Methoxybenzylidene Acetal 35 To Afford 36. A solution of the benzylidene acetal **35** (1.06 g, 2.22 mmol) in MeOH (30 mL) was stirred at room temperature. Anhydrous K_2CO_3 (0.49 g, 3.56 mmol, 1.6 equiv) was added. After 2 h, TLC analysis of the reaction mixture indicated that a small amount of monoprotected alkyne remained. Additional K_2CO_3 (0.40 g, 1.3 equiv) was added, and the reaction mixture was stirred for 1 h. The mixture was concentrated under reduced pressure to a white paste, which was dissolved in 100 mL each of H_2O and Et_2O. The aqueous layer was extracted with Et_2O (3 × 100 mL). The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated under reduced pressure to afford crude **36**, which was purified by flash chromatography (silica gel, eluent 7% EtOAc/hexanes) to afford **36** as a colorless oil (0.73 g, 98%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.06−5.85 (m, 3H), 5.20−5.06 (m, 4H), 3.79 (s, 3H), 3.04 (dd, J = 17.0, 2.7 Hz, 1H), 2.82−2.70 (m, 4H), 2.57−2.53 (m, 3H), 2.11−2.07 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.15, 132.37, 132.07, 129.68, 126.73 (2), 117.61, 117.44, 122.72 (2), 99.56, 84.51, 83.65, 79.12, 78.75, 70.59, 70.51, 54.30, 37.66, 35.57, 24.50, 22.23; IR (thin film) 3291, 3073, 2119, 1612 cm^{-1}; LRMS (CI$^+$) *m*/*z* relative intensity 337 (M + 1, 27), 137 (100); HRMS (EI$^+$) calcd for $C_{22}H_{24}O_3$ (M$^+$) 336.1711, found 376.1725. Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.57; H, 7.16.

General Procedure A: Photochemical Catalytic Pauson−Khand Reaction of Diene-Diyne with $Co_2(CO)_8$ To Provide a [5.6.6.5]Tetracyclic Dione. A solution of the diene-diyne **34**, **33**, or **36** (1 equiv) and dicobalt octacarbonyl (1.05 equiv) in degassed 1,2-DME (∼0.10 M) was stirred at room temperature under an atmosphere of CO. After 1 h the reaction mixture was irradiated with a Q-Beam MAX MILLION spotlight.[51] During the course of the irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50 and 55 °C (approximately 2.5 ft distance between lamp and reaction flask). After 20 h, irradiation was discontinued, the mixture was cooled, and the solvent was concentrated under reduced pressure. The residual material that was isolated was purified by flash chromatography on silica gel to provide tetracycles **37a/b**, **38a/b**, or **40a/b**, respectively.

37a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.90 (s, 1H), 3.24−3.18 (m, 1H), 3.15 (d, J = 12.4 Hz, 1H), 2.81−2.74 (m, 1H), 2.68 (d, J = 12.4 Hz, 1H), 2.65 (d, J = 14.8 Hz, 1H), 2.64 (dd, J = 18.6, 6.6 Hz, 1H), 2.59 (dd, J = 18.6, 6.6 Hz, 1H), 2.48 (d, J = 14.8 Hz, 1H), 2.08 (dd, J = 12.6, 6.0 Hz, 1H), 2.03 (dd, J = 18.6, 3.0 Hz, 1H), 2.03 (dd, J = 12.0, 12.0 Hz, 1H), 2.02 (dd, J = 18.6, 3.0 Hz, 1H), 1.95 (dd, J = 12.0, 6.0 Hz, 1H), 1.73 (dd, J = 13.5, 12.5 Hz, 1H), 0.20 (s, 9H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.35, 207.71, 180.37, 179.63, 130.42, 129.16, 80.36, 77.20, 42.36, 41.58, 41.51, 41.48, 40.65, 40.31, 38.70, 36.95, 2.71, 2.53; LRMS (CI$^+$) *m*/*z* relative intensity 419 (M + 1, 100). Anal. Calcd for $C_{22}H_{34}O_4Si_2 \cdot {}^1/_4H_2O$; C, 62.44; H, 8.20. Found: C, 62.43; H, 8.23.

37b: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.92 (s, 2H), 3.08−3.00 (m, 2H), 2.97 (d, J = 14.1 Hz, 2H), 2.69 (d, J = 14.1 Hz, 2H), 2.57 (dd, J = 18.5, 6.5 Hz, 2H), 1.98 (dd, J = 18.5, 2.8 Hz, 2H), 1.90 (dd, J = 13.5, 6.0 Hz, 2H), 1.68 (dd, J = 13.0, 13.0 Hz, 2H), 0.23 (s, 9H), 0.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.93, 180.39, 130.03, 81.41, 77.53, 41.61, 40.26, 39.17, 37.02, 2.77, 2.49; LRMS (CI) *m*/*z* relative intensity 419 (M + 1, 100); HRMS (EI$^+$) calcd for $C_{22}H_{34}O_4Si_2$ (M$^+$) 418.2047, found 418.1996. When this reaction was run on a larger scale, sufficient quantities of **37b** were obtained that permitted the accurate structural assignment of the minor isomer as *trans* rather than the *cis* system previously implied.[34]

38a/b: ^{1}H NMR (300 MHz, D_2O) δ 6.08−6.04 (m, 4H), 3.34−3.23 (m, 2H), 3.04−3.00 (m, 2H), 3.02 (d, J = 13.3 Hz, 2H), 2.87 (d, J = 13.3 Hz, 2H), 2.81−2.63 (m, 8H), 2.21−1.91 (m, 10H), 1.79 (dd, J = 12.8, 12.8 Hz, 1H), 1.60 (dd, J = 13.1, 13.1 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) major isomer δ 213.24, 212.50, 183.62, 183.39, 127.59, 126.56, 75.23, 71.58, 40.14, 39.66, 39.29, 38.37, 37.37, 37.18, 36.96, 35.42; minor isomer δ 213.03, 184.66, 127.15, 75.09, 70.94, 39.80, 38.84, 37.66, 35.42; LRMS (CI) *m*/*z* relative intensity 275 (M + 1, 100). Anal. Calcd for $C_{16}H_{18}O_4 \cdot {}^1/_3H_2O$: C, 68.55; H, 6.71. Found: C, 68.46; H, 6.71. Major isomer **38a** was partially separated and characterized: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.96 (s, 2H), 3.75 (bs, 1H), 3.29 (m, 2H), 3.02 (d, J = 13.2 Hz, 1H), 2.79−2.52 (m, 5H), 2.40 (m, 1H), 2.20 (dd, J = 13.6, 6.1 Hz, 1H), 2.07−2.00 (m, 3H), 1.89−1.69 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 208.88, 208.44, 180.44, 179.53, 130.70, 129.00, 76.44, 73.06, 42.71, 42.02, 41.55, 41.17, 40.16, 38.94, 38.67, 36.78; LRMS (CI) *m*/*z* relative intensity 275 (M + 1, 100).

40a/b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.7 Hz, 2H), 6.93−6.87 (m, 4H), 6.25 (s, 1H), 6.16 (s, 1H), 6.04 (s, 3H), 5.87 (s, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.34−3.18 (m, 5H), 3.05 (d, J = 13.5, 1H), 2.85 (d, J = 13.0 Hz, 1H), 2.65−2.49 (m, 13H), 2.09−2.03 (m, 4H), 2.03−1.60 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.10, 205.97, 205.72, 205.50, 176.52, 176.24, 175.33, 175.06, 157.75 (2), 129.32, 128.90, 128.39, 127.94, 127.74, 126.98, 124.74 (2), 124.61 (2), 111.86 (2), 111.77 (2), 98.36, 98.01, 82.30, 80.50, 79.61; LRMS (CI) *m*/*z* relative intensity 393 (M + 1, 57), 137 (100); HRMS (EI$^+$) calcd for $C_{24}H_{24}O_5$ (M$^+$) 392.1624, found 392.1613. When this reaction was run on a larger scale, **40a/b** was accompanied by a trace amount of the symmetrical diastereomer (H_a and H_b on the same face) in an approximately 19:1 ratio.

Thermal Pauson−Khand Reaction of Diene-Diyne with $Co_2(CO)_8$ To Provide a [5.6.6.5]Tetracyclic Dione. A solution of the diene-diyne **33** (0.413 g, 1.89 mmol) and dicobalt octacarbonyl (0.681 g, 1.99 mmol, 1.05 equiv) in degassed 1,2-DME (18 mL) was stirred at room temperature under an atmosphere of CO. After 1 h, the reaction mixture was heated to an internal temperature of 65 °C via an oil bath and stirred for 17 h, at which time the reaction mixture was cooled, and the solvent was concentrated under reduced pressure. The residual material that remained was purified by flash chromatography (silica gel, eluent 5% MeOH/EtOAc) to afford of a mixture of tetracyclic diones **38a** and **38b** in a ratio of 2.2:1, respectively (0.161 g, 31%). The spectral characteristics of these tetracyclic diones were identical to those reported in a previous experiment.

General Procedure B: Pauson−Khand Reaction of Diene-Diyne with $Co_2(CO)_8$ and NMO To Provide a [5.6.6.5]Tetracyclic Dione. A solution of the diene-diyne **34**, **33**, or **36** (1 equiv) and dicobalt octacarbonyl (2.5 equiv) in the solvent indicated in Table 1 (∼0.07 M) was stirred at room temperature under an atmosphere of CO. After stirring for 2 h, the reaction mixture was diluted with additional solvent, and *N*-methylmorpholine-*N*-oxide was added to the reaction mixture portionwise. After stirring several hours, additional NMO was added until no metal complexes were observed by TLC (silica gel). The reaction solution was concentrated to one-half of its original volume, and the mother liquor was loaded onto a silica gel column and purified by flash chromatography to provide tetracycles **37a/b**, **38a/b**, or **40a/b**, respectively.

Deprotection of Silyl-Protected [5.6.6.5]Tetracycle 37a To Provide Tetracyclic Diol 38a. To a solution of [5.6.6.5]-tetracycle **37a** (42.9 mg, 0.103 mmol) in THF (1.0 mL) was added tetrabutylammonium fluoride hydrate (56.0 mg, 0.214 mmol, 2.1 equiv), turning the reaction solution deep red. The reaction mixture was stirred for 10 min and diluted with 15 mL each of H_2O, $CHCl_3$, and MeOH. The aqueous layer was extracted with additional $CHCl_3$ and MeOH (1:1 v/v, 4 × 20 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford crude diol **38a**, which was purified by flash chromatography (silica gel, eluent 6% MeOH/EtOAc) to afford **38a** as a white foam (24.2 mg, 89%). The spectral characteristics of diol **38a** were identical to those reported for diol **38a** in a previous Pauson−Khand experiment.

Deprotection of Benzylidene Acetal [5.6.6.5]Tetracycle 40a/b To Afford Tetracyclic Diol 38a. Approximately 6 mg of acetal **40a/b** and 0.5 mL of H_2O were placed in a micro test tube, and a few crystals of zinc chloride were added. The

heterogeneous reaction mixture was heated on a sand bath at 70 °C. The reaction mixture was monitored by TLC (silica gel, 10% MeOH/EtOAc), and evidence of product formation of lower Rf was observed within 30 min, identical to the tetracyclic diol **38a** by comparison to an authentic sample (R_f value = 0.23). Consumption of the starting material and conversion to diol **38a** was essentially complete after 10 h.

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Supporting Information Available: Detailed characterization and assignment of the structures of **17a**, **17b**; **29a**, **29b**; **37a**, **37b**; and **40a**, **40b** by NMR spectroscopy. Tables of crystallographic data, structure solution and refinement, atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for **38a**. Detailed experimental procedures for the syntheses of compounds **37a/b**, **38a/b**, and **40a/b** illustrated in Table 1. An X-ray crystallographic file is available in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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