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Extension of the Tandem Pauson-Khand Reaction to [5.6.6.5]Tetracycles: A Unique Entry into *cis*-Fused Decalins.

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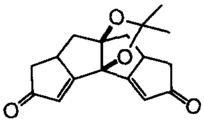
Abstract: The tandem Pauson-Khand reaction has been extended to the synthesis of [5.6.6.5]dicyclopenta[*b,g*]decalins. This approach provides a unique entry into a *cis*-fused decalin-based ring system *via* an acyclic precursor.

The intramolecular Pauson-Khand reaction[1,2] is one of the most versatile tools for the construction of bicyclo[3.3.0]octen-ones. Previous interest in the tandem version of this reaction has resulted in the synthesis of the parent [5.5.5.5]enone ring systems such as **1**; potential intermediates en route to 14π polyquinenes represented by dicyclopenta[*a,f*]pentalene (**2**) and dicyclopenta[*a,e*]pentalene.[3] We wish to report the first extension of this dicobalt octacarbonyl-mediated *tandem* process which has permitted facile entry into [5.6.6.5]dicyclopenta[*b,g*]-decalins (see **3**) with a *cis*-fused decalin core.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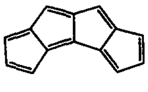
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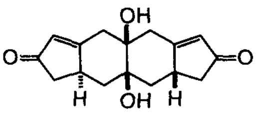

3

There are several methods utilized for the formation of *cis*-fused decalin rings. Most commonly, inter- and intramolecular[4] Diels-Alder reactions are employed, as well as anionic cycloadditions;[5] samarium diiodide-promoted constructions are also known.[6] In addition, *cis*-decalins have also been prepared *via* an intramolecular aldol reaction[7] and an asymmetric Heck-type reaction.[8] In contrast, this tandem Pauson-Khand strategy begins from acyclic molecules in which 6 carbon-carbon bonds are formed in a one-pot process, while providing an internal cis-decalin within the tetracyclic system.

The synthesis of the diene-diyne required for the tandem Pauson-Khand reaction began with bisalkyne **4**, 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.[9] When the dialkyne ester **4** was stirred with allylmagnesium chloride the diene-diyne **5** was furnished in 88% yield (Scheme 1). The desired diol **6** was obtained by stirring **5**

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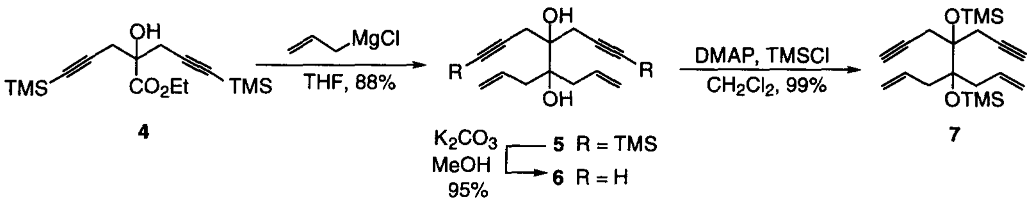
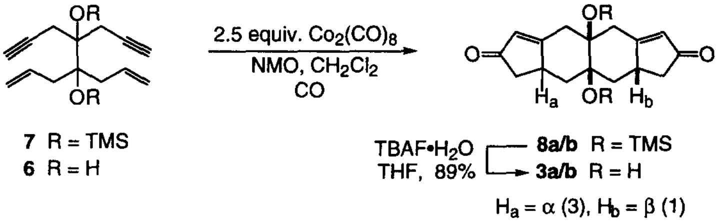
with K_2CO_3/MeOH (95%) and this was followed by protection of the hydroxyl groups *via* DMAP and TMSCl to furnish the seco-Pauson-Khand intermediate **7** (99%).

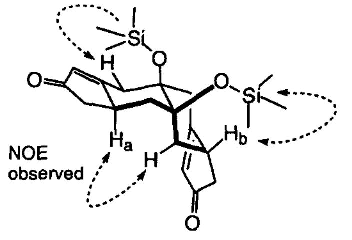
Scheme 1



Application of the Livinghouse photochemically-mediated Pauson-Khand protocol[10] to the synthesis of the parent ring system of the dicyclopentapentalenes had previously provided a convenient, semi-catalytic tandem reaction sequence. Similar reaction conditions were employed here [1 equiv. $Co_2(CO)_8$ added to a 0.10 M solution of **7** in DME under a CO atmosphere, irradiation with Q-Beam for 12 h][3c] to convert **7** into *cis*-decalin **8** with somewhat limited success (38% yield). The stereochemistry of the trimethylsilyl protected diol **8** at the 6-6 ring fusion was determined to be exclusively *cis* *via* 2D NMR techniques (Figure 1).[11] Removal of the silyl groups in **8** with TBAF hydrate in THF provided diol **3** in 89% yield.



Since only *cis*-fused decalins were formed in this process, it was felt the trimethylsilyl groups in **7** may have retarded the reaction progress. For this reason, the Pauson-Khand reaction of the unprotected diol **6** was then carried out. Unfortunately, the method of catalytic photolysis furnished low yields of the [5.6.6.5]dicyclopenta[*b*,*g*]decalin tetracycle **3a/b** [(26%), Table 1, entry *b*].



8a H_a, H_b, trans

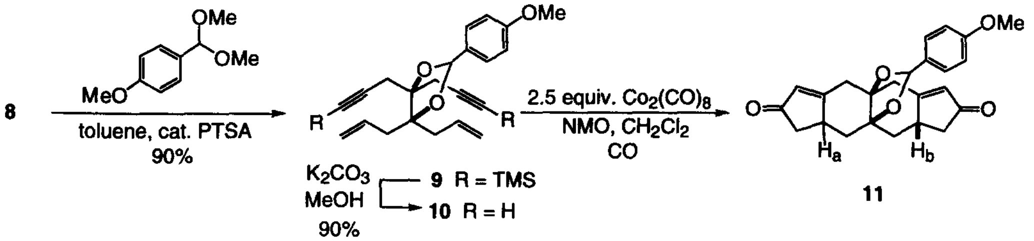
Figure 1

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[12] 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.[10] In the study outlined below, yields for the tetracyclic products were also similar to the light-promoted reactions. The modified conditions of Schreiber,[13] [2.5 equivalents of $Co_2(CO)_8$ followed by excess N-methylmorpholine-N-oxide (NMO) in CH_2Cl_2] employed earlier in our laboratory,[3a,b] were successfully employed here and the yield of **8** was increased to 53% (3:1 ratio of diastereomers at H_a). Importantly, diol **6** was also submitted to the same reaction conditions which provided tetracycle **3** 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 the solvent.

Table 1

Entry	Substrate	Reaction Conditions	% Yield	Product
a	OTMS **7**	DME, hv	38	**8**
b	diol **6**		26	**3**
c	diol **6**	DME, 65°C	31	**3**
d	**OTMS 7**	**CH_2Cl_2, NMO[14]**	**53**	**8**
e	**diol 6**		**52**	**3**
f	diol **6**	CH_3CN, NMO	44	**3**
g	diol **6**	CF_3CH_2OH, NMO	33	**3**
h	diol **6**	1:1 heptane/CH_2Cl_2, NMO	<5	**3**
i	diol **6**	heptane, NMO	0	**3**
j	acetal **10**	CH_2Cl_2, NMO	30	**11**
k	acetal **10**	DME, hv	45	**11**

Finally, the success of the tandem Pauson-Khand reaction (53%) in the sterically hindered case, coupled with no yield increase when the diol itself was employed, prompted the construction of a fixed diene-diyne conformation *via* a benzylidene acetal, which substantially reduced rotation about the diol carbon-carbon bond. Treatment of diol **5** with *p*-anisaldehyde dimethyl acetal in refluxing toluene, (catalytic amount of PTSA), readily provided acetal **9** in 90% yield. The trimethylsilyl groups were removed on stirring with K_2CO_3/MeOH (90%) to afford diene-diyne **10**. This constrained, eclipsed diene-diyne was subjected to the NMO conditions for the tandem Pauson-Khand reaction to provide the *cis*-fused decalin **11** in 30% yield, isolated as a 1.2:1 mixture of acetal isomers (entry *j*). Similarly, reaction of acetal **10** *via* the photochemically-mediated Pauson-Khand procedure afforded 45% of the desired decalin **11** in a 1:1 ratio (entry *k*).



In summary, 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 was obtained exclusively from the formation of 6 carbon-carbon bonds in this one-pot process. This 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 is at least 89%.

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11. Major NOEs are shown here. Complete NMR results will be published elsewhere, in preparation.
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14. A typical procedure is as follows: A solution of the diene-diyne **7** (0.255 g, 0.704 mmol) and dicobalt octacarbonyl (0.602 g, 1.76 mmol, 2.5 equiv) in CH_2Cl_2 (10 mL) was stirred at rt under an atmosphere of carbon monoxide. After stirring for 2 h, examination of TLC indicated an absence of starting material and the reaction mixture was diluted with CH_2Cl_2 (10 mL) and N-methylmorpholine-N-oxide (0.825 g, 7.04 mmol, 10 equiv) was added portionwise. After stirring 6 h, additional NMO was added (0.400 g, 3.41 mmol) until no metal complexes were observed by TLC. The purple solution was concentrated to one-quarter of its original volume under reduced pressure and loaded onto a silica gel column and eluted (flash chromatography) with 55% EtOAc/hexane to provide tetracycles **8a** and **8b** (3:1) as off-white solids, 0.156 g (53%). **8a**: ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.3, 207.7, 180.4, 179.6, 130.4, 129.2, 80.4, 77.2, 42.4, 41.6, 41.51, 41.48, 40.7, 40.3, 38.7, 37.0, 2.7, 2.5; LRMS (CI) m/z relative intensity 419 (M+1, 100), 329 (72). **8b**: ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 180.2, 129.7, 81.1, 77.2, 41.3, 39.9, 38.9, 36.7, 2.6, 2.2; LRMS (CI) m/z relative intensity 419 (M+1, 100), 329 (25).