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Pauson-Khand Reaction with Allenic Compounds II : Reactivity of Functionalized Allenes.

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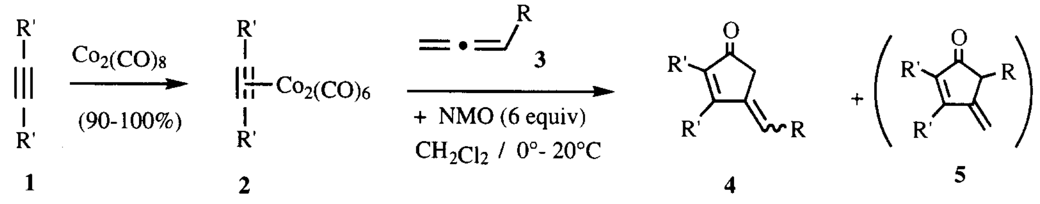
Abstract : The cobalt-mediated cycloaddition of alkynes with functionalized allenes were shown to lead to different 4- and 5-alkylidenecyclopent-2-enones **4-6**. Regioselectivity depends on both steric and electronic effects of the substituents. © 1997 Published by Elsevier Science Ltd.

The octacarbonyldicobalt-mediated cycloaddition of an alkyne and an alkene with carbon monoxide to cyclopent-2-enone (Pauson-Khand reaction[1]) has found wide interest for the synthesis of five-membered ring compounds.[2] This synthetic interest has been enhanced by the discovery of quite milder conditions ; indeed, the use of tertiary amine N-oxides[3], DMSO[4] or silica[5] as promoters allows the reaction to be performed at room temperature.

Recently we took advantage of these milder experimental conditions and described that allenic compounds can be introduced as unsaturated partners in the Pauson-Khand reaction.[6] Thus allenic hydrocarbons **3** (R = H, alkyl) react with alkyne-hexacarbonyldicobalt complexes **2** in the presence of N-methylmorpholine oxide NMO and lead to 4-alkylidenecyclopent-2-enones **4** (scheme 1).[6]



scheme 1

The reaction was shown to be highly regioselective to cyclopent-2-enone **4** ; however new experiments have demonstrated that the regiomer 4-alkylidenecyclopent-2-enone **5** may be also isolated in very small amounts (≤ 5%) in some few cases.[7]

We have now found that functionalized allenes **3** (Y = functional group) may be used as well in this cycloaddition and report herein our results on the regioselectivities to cyclopent-2-enones **4-6** encountered with these allenic substrates (see Table).

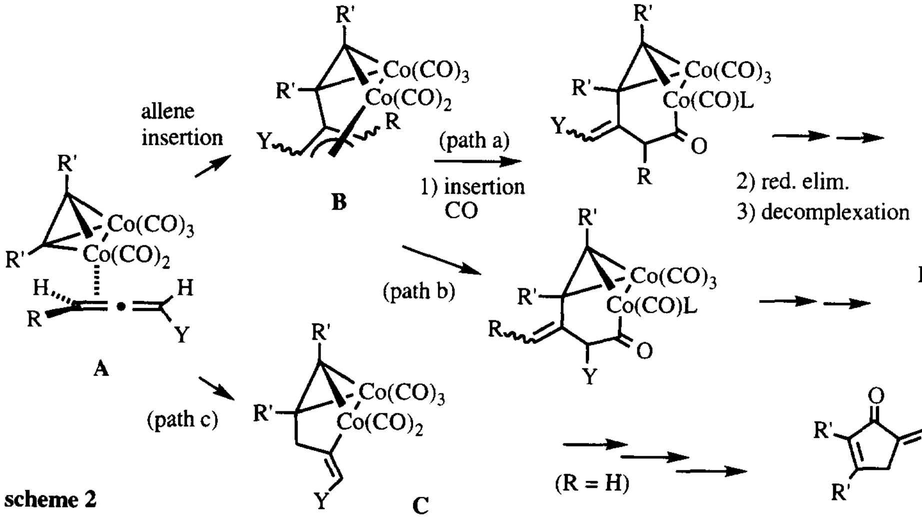
The cycloadditions of alkyne-hexacarbonyldicobalt complexes **2a** (R' = CH_3) and **2b** (R' = n-C_3H_7) [quantitatively obtained from alkynes **1a,b** and $Co_2(CO)_8$] with the selected functionalized allenes **3a-f** were realized in the presence of NMO (6 equiv) in THF-CH_2Cl_2 (1:1)[8] between -78°C and 20°C (see Table).[9]

We first selected tert-butoxyallene **3a** which reacted very vigorously with complex **2a** in THF-CH_2Cl_2 (1:1) when NMO was added at 0°C and led to a low 10% yield of cyclopentenone (E)-**4a**. The yield increased to 30% by carrying out the reaction from -78°C to 20°C (Table, entry 1). Dimethylphenylsilylallenes **3b** and **3c** (entries 2 and 3) and tributylstannylallene **3d** (entry 4) all led to a mixture of the two 4-alkylidene-cyclopent-2-enones (E)-**4** and **5** from which the former one was by far the major regioisomer.

We then looked at the reactivity of allenes **3e,f** which bear an electron-withdrawing group. Ethyl buta-2,3-dienoate **3e** and phenylsulfonylallene **3f** led to 4-alkylidenecyclopent-2-enones (E)-**4e** and (E)-**4f** respectively (entries 5 and 6) ; they also led to other cyclisation products, the regiomer 5-alkylidene-cyclopent-2-enones (E)-**6e** and (E)-**6f** (ratio **5/6** = 70/30 in both cases).

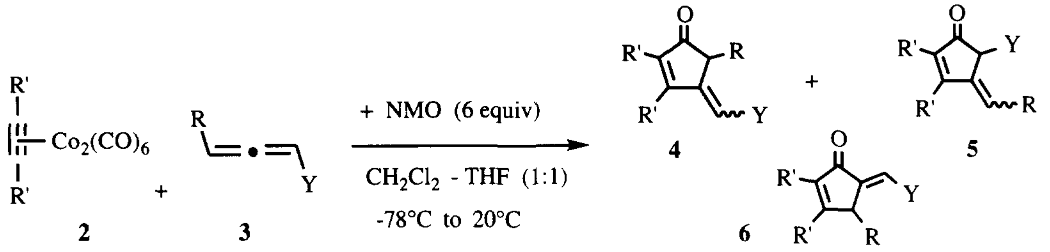
This set of experiments with functionalized allenes **3a-f** and our previous results with allenic hydrocarbons[6] demonstrate that several pathways might be involved according to the electronic effect of the allenic substituent. The following mechanistic rationale from a first association alkyne-$Co_2(CO)_5$-allene complex **A** may account for the observed regioselectivities to cyclopent-2-enones **4-6** (scheme 2) :

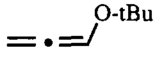
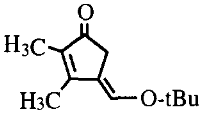
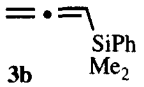
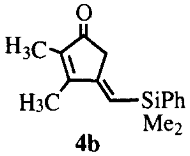
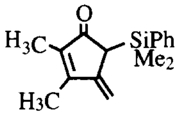
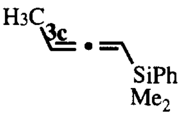
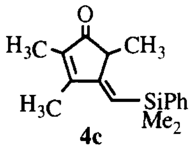
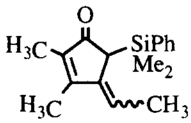
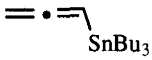
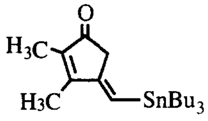
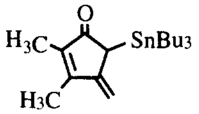
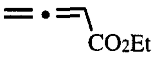
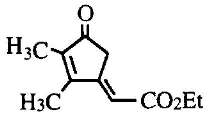
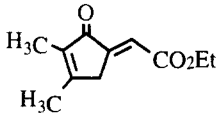
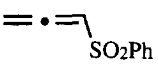
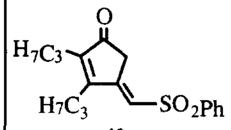
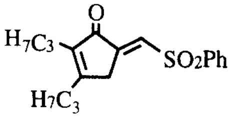
- with an electron-releasing group (Y = alkyl, OR, SiR_3, SnR_3), the insertion of allene **3** in one of the formal C-Co bonds of complex **A** would occur via the central carbon atom of the allenic unit and lead to a common π-allyl organocobalt intermediate **B** from which 4-alkylidenecyclopent-2-enones **4** (path a) and **5** (path b) would be formed after the generally accepted further steps of the Pauson-Khand reaction[2,10] : CO insertion into the allylic C-Co bonds which turns out to be favoured on the less sterically hindered pole of the π-allylic system (**4** is the major product), reductive elimination and decomplexation.
- with an electron-withdrawing group (Y = CO_2R, SO_2Ph), insertion of the allenic unit might also take place within its more electron-rich double bond and lead to the σ-vinyl organocobalt intermediate **C** from which 5-alkylidenecyclopent-2-enone **6** would be obtained via the same typical steps.



scheme 2

Table : Pauson-Khand cycloaddition of alkynes **1** with functionalized allenes **3**.

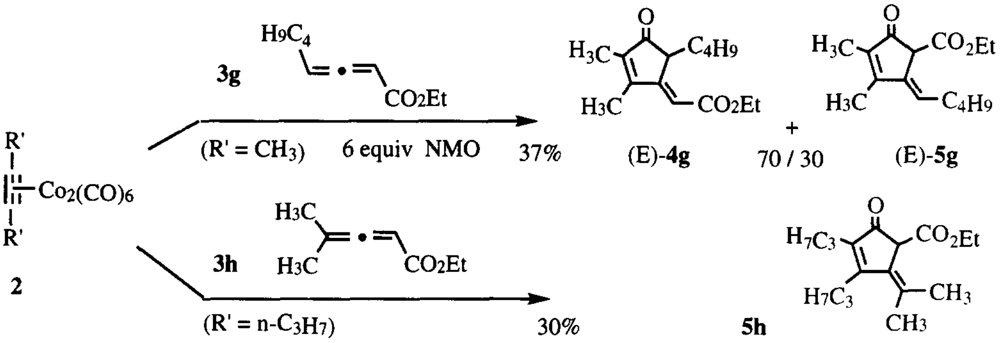


Entry	Alkyne **1**	Allenic Compounds **3** *	Cyclopent-2-enones ** **4** , **5** , **6**	Yield **4+5+6**	Ratio **4/5** **4/6**
1	 **1a**	 **3a**	 **4a**	30 % (10 % at 0°C)	
2			 **4b**  **5b**	74%	95/5
3			 **4c**  (E/Z = 54/46) **5c**	75%	70/30
4		 **3d**	 **4d**  **5d**	26%	72/28
5	1a	 **3e**	 **4e**  **6e**	47%	70/30
6	 **1b**	 **3f**	 **4f**  **6f**	35%	70/30

* Cycloadditions were carried out using 1-1.2 equiv of hexacarbonyldicobalt complex **2** with respect to allene **3**, except in entry 1 (**2a/3a** = 1/2).

** Cyclopentenones **4**, **5** and **6** were obtained as pure materials isolated through flash-chromatography.

Two other α-allenic esters **3g,h** were also studied in order to get further insight into the respective influence of steric and electronic effects on the cycloaddition. Ethyl octa-2,3-dienoate **3g** gave a 70/30 mixture of cyclopent-2-enones (E)-**4g** and (E)-**5g**, while trisubstituted allenic ester **3h** led to the single cyclopent-2-enone **5h**. These two last experiments show that steric effect of substituents is overwhelming electronic effect, since path c is then no more operating.



As a summary, we have shown that functionalized allenes can enter into the Pauson-Khand reaction with alkynes and lead to 4- and 5-alkylidenecyclopentenones **4-6**. This study also allowed to propose a mechanistic rationale according to the steric and electronic effects of the allenic substituents.

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7. Ahmar M.; Antras, F.; Cazes, B., unpublished results.
8. The use of THF as coordinating cosolvent has been shown to accelerate the rate of the Pauson-Khand reaction : Kraft, M.E.; Scott, I.L.; Romero, R.H.; Feibelmann, S.; Van Pelt, C.E. *J. Am. Chem. Soc.* **1993**, *115*, 7199-7209.
9. **Typical procedure is as follows** (entry 5) : To a stirred solution of the $Co_2(CO)_6$-(but-2-yne) **2a** (2.25 mmol, 1.2 equiv) and ethyl buta-2,3-dienoate **3e** (1.9 mmol) in 1:1 CH_2Cl_2-THF (10 mL) at -78°C was added N-methylmorpholine oxide (6 equiv). The reaction was stirred 0.5 h at -78°C and then allowed to return to room temperature in 2-3 h. The resulting mixture was passed through a small plug of silicagel. The filtrate was concentrated in vacuo to a brown oil. Purification was effected by flash-chromatography (Petroleum ether/Et_2O 70:30) and gave ketones (E)-**4e** (R_f = 0.26 ; 33%) and (E)-**6e** (R_f = 0.30 ; 14%) as chromatographically homogeneous clear oils.

   (E)-**4e** : ^1H NMR ($CDCl_3$; 200 MHz) δ ppm 1.32 (t, J = 7.1 Hz, 3H); 1.90 (s, 3H); 2.11 (s, 3H); 3.39 (s, 2H); 4.23 (q, J = 7.1 Hz, 2H); 5.95 (s, 1 H).

   (E)-**6e** : ^1H NMR ($CDCl_3$; 200 MHz) δ ppm 1.30 (t, J = 7.1 Hz, 3H); 1.80 (s, 3H); 2.13 (s, 3H); 3.47 (s, 2H); 4.24 (q, J = 7.1 Hz, 2H); 6.53 (s, 1 H).
10. For a recent publication on the mechanistic aspects of Pauson-Khand reaction see reference 8.

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