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Pauson-Khand Cycloaddition of α,ω-Allenynes.

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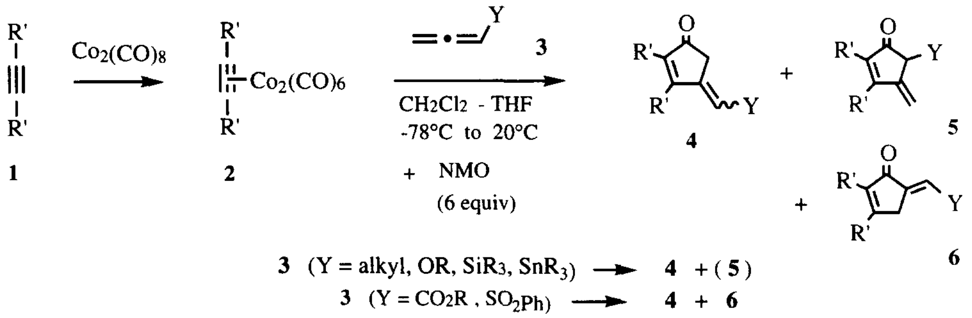
Abstract : The intramolecular cobalt-mediated reaction of α,ω-allenynes **8** leads to bicyclic dienones **10** and α-alkylidenecyclopentenones **11** ; regioselectivity depends on the substitution pattern of the allenic moiety. © 1997 Published by Elsevier Science Ltd.

The Pauson-Khand reaction - cobalt-mediated carbonylative cycloaddition of an alkyne and an alkene to cyclopent-2-enone - is presently considered as one of the most synthetically interesting reactions for the preparation of five-membered ring compounds.[1] Particularly, the intramolecular version of this cycloaddition has been widely used for the synthesis of numerous polycyclic compounds[1,2] from α,ω-enynes. Moreover it has been realized enantioselectively, which opened new routes to enantiopure natural products.[3]

We recently described[4] that allenic compounds **3** can be used as "olefinic" partners with alkynes **1** in the Pauson-Khand reaction if this one is promoted by N-methylmorpholine oxide NMO.[6] This new [2+2+1] cycloaddition of allenes leads at low temperature (-78°C to 20°C) to 4- and 5-alkylidenecyclopent-2-enones **4-6** according to the electronic and steric nature of the allenic substituents (scheme 1).[4,5]

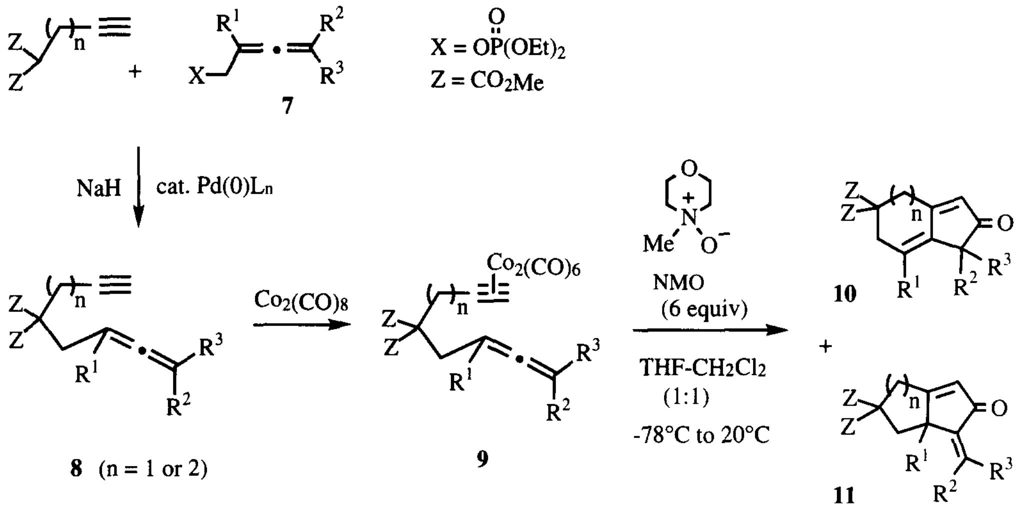


3 (Y = alkyl, OR, SiR_3, SnR_3) → **4** + (**5**)
3 (Y = CO_2R , SO_2Ph) → **4** + **6**

Scheme 1

An intramolecular carbonylative cycloaddition to bicyclic unsaturated ketones **10** and/or **11** could be easily envisioned from α,ω–allenynes **8** (scheme 2). However the overall result of this reaction might be impeded in its first step, the formation of the hexacarbonyldicobalt complex **9** from **8**, because $Co_2(CO)_8$ is known to promote the polymerization of allenic compounds.[7] We report here the results of our first investigations in this field.

The synthesis of several α,ω-allenynes **8** [1,2-dien-7-ynes **8a-d** (n =1) and 1,2-dien-8-ynes **8e,f** (n = 2)] required for this study was realized via the palladium-catalysed substitution of the phosphates **7** of α-allenic alcohols[8] by acetylenic malonates as depicted in scheme 2.

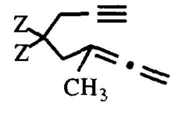
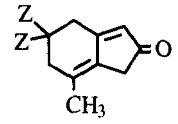
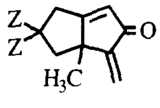
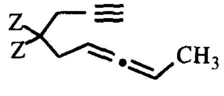
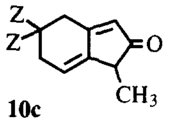
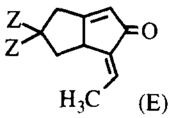
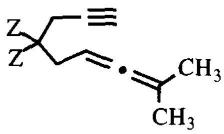
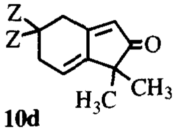
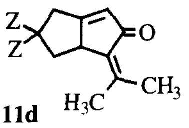
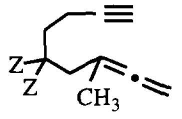
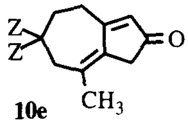
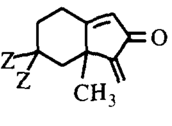
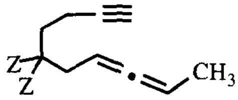
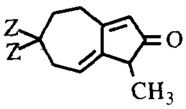
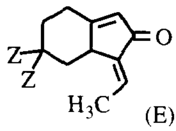


scheme 2

An initial experiment was carried out with the simplest unsubstituted allenyne **8a** ($R^1 = R^2 = R^3 = H$). Its treatment under the experimental conditions developed previously[4,5] (addition of 6 equivalents of NMO into a 1:1 CH_2Cl_2-THF solution of allenyne **8** at -78°C) led to no defined products, while this allenyne was unrecovered. This unsuccessful reaction could be explained by the afore-mentioned polymerization of the allenic moiety which might be faster than the formation of the hexacarbonyldicobalt complex **9a**. This was likely to occur since it turned out that allenynes **8b-f** (n = 1 or 2) for which the allenic moieties are more sterically hindered and less prone to interact with $Co_2(CO)_8$ led effectively to the expected bicyclic ketones **10b-f** and **11b-f** (see Table).[9]

With gem-disubstituted allenes **8b** and **8e**, ketones **10b** and **10e** were obtained very regioselectively but with rather low yields (entries 1 and 4). Further reactions with allenynes **8c,d,f** which are substituted on both ends of the allenic unit led more efficiently to bicyclic ketones **10** and **11**[10] (entries 2,3 and 5). Regioselectivity was shown to depend on the substitution pattern of allenynes. 1,3-Disubstitution of the allenic moiety led to about equal amounts of ketones **10c,f** and **11c,f** (entries 2 and 5) while regioselectivity was enhanced towards dienone **10d** with a trisubstituted allene (entry 3).

Table : N-Methylmorpholine oxide-promoted Pauson-Khand cycloaddition of α,ω-allenynes **8**.

Entry	α,ω-Allenynes **8** (Z = CO_2Me)	Bicyclic cyclopentenones **10**, **11**	Ratio* **10/11**	Yield % ** **10 + 11**
1	**8b** 	 **10b**  **11b**	90/10	22
2	**8c** 	 **10c**  (E)-**11c**	50/50	31
3	**8d** 	 **10d**  **11d**	80/20	45
4	**8e** 	 **10e**  **11e**	100/0	10
5	**8f** 	 **10f**  (E)-**11f**	45/55	50

* Ratios **10/11** were estimated from GLC and/or ^1H NMR analysis of the mixtures of both isomers **10** and **11** which were inseparable via classical flash-chromatography.

** Yields (**10** + **11**) refer to materials isolated through flash-chromatography

This work has demonstrated for the first time the feasibility of performing the tertiary amine oxide-promoted Pauson-Khand cycloaddition of α,ω-allenynes[11] the synthetic value of which is currently prospected in our group. It complements recent studies about related metal-mediated cycloaddition procedures which lead to bicyclic dienones (type **10**)[12] or α-methylenecyclopentenones (type **11**).[11]

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9. **Typical procedure is as follows** (entry 3) : allenyne **8d** (1 mmol) was added to a solution of $Co_2(CO)_8$ (1.2 mmol) in CH_2Cl_2 (10 mL) at 0°C. This solution was stirred at room temperature for 2 hours and filtered through a small plug of celite® ; washing with ether and evaporation of solvents gave the crude dicobalt complex **9d**. This complex was diluted in CH_2Cl_2-THF (1:1) (20 mL) and treated at -78°C with N-methylmorpholine oxide NMO (6 equiv with respect to the starting material **8d**). The mixture was allowed to return to room temperature in 1 hr and stirred again 2 hrs. After filtration over celite®, washing with ether and evaporation of solvents, flash-chromatography on silicagel (petroleum ether/ether 50/50) gave an oil (Rf = 0.25, 45% yield) composed of the two isomers **10d** and **11d** which were inseparable ; their ratio **10d/11d** = 80/20 was mesured via GLC and ^{1}H NMR.

   10d : ^{1}H NMR ($CDCl_3$, 200 MHz) δ ppm, 1.07 (s, 6H); 2.91 (d, ^3J = 4.4 Hz, 2H); 3.23 (d, $^4J_{allyl}$ = 1.3 Hz, 2H); 3.72 (s, 6H); 5.84 (dt, ^5J = 1.6 Hz and ^3J = 4.4 Hz, 1H); 5.91 (broad s, 1H)

   11d : ^{1}H NMR ($CDCl_3$, 200 MHz) δ ppm, 1.92 (s, 3H); 2.26 (s, 3H); 1.15-1.3 (m, 1H); 1.6-1.8 (m, 1H); 2.95 (dd, ^3J = 12.8 Hz and ^3J = 8 Hz); 3.27 (broad s, 2H); 3.74 (s, 3H); 3.81 (s, 3H); 6.03 (broad s, 1H).

10. α-Ethylidenecyclopent-2-enone **11c** (as well as ketone **11f**) was obtained as the E-stereoisomer as shown by the downfield vinyl hydrogen atom at δ = 6.61 ppm (qd, ^3J = 7.2 Hz and J_{allyl} = 1.8 Hz) and upfield allyl methyl group at δ = 1.9 ppm (t, ^3J = 7.2 Hz). For ^{1}H NMR data about α-methylene cyclopent-2-enones, see : Jacobi, P.A.; Brielmann, H.L.; Cann, R.G. *J. Org. Chem.* **1994**, *59*, 5305-5316.

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