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Pauson-Khand Reaction of Activated Olefins.

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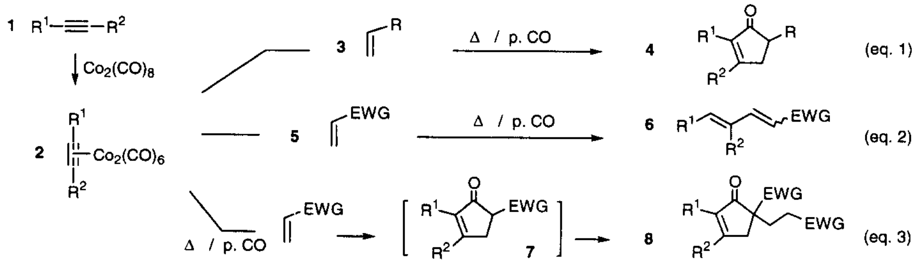
Abstract

The cobalt-mediated Pauson-Khand reaction of alkynes with electron deficient olefins was shown to be promoted by N-methylmorpholine oxide at 0-20°C and led to 5-functionalized cyclopent-2-enones.

Key words : Pauson-Khand reactions, cycloadditions, cobalt complexes, activated olefins

The cobalt-mediated cycloaddition [2+2+1] of an alkyne **1** and an alkene **3** (eq. 1), known as the Pauson-Khand reaction, has become a widely used synthetic method for the preparation of cyclopent-2-enones **4**, in particular in intramolecular reactions.[1,2] Its synthetic value has been recently enhanced by the use of milder conditions which involve promoters such as silica,[3] tertiary amine N-oxides[4] or DMSO,[5] and allow the cycloaddition to be carried out at room temperature. However, reactions with activated olefins **5** have been shown to follow a competitive pathway leading to conjugated dienes **6** via a β-hydrogen elimination process (eq. 2).[6]



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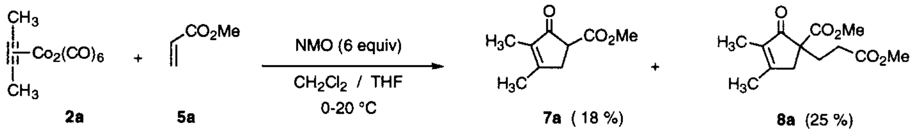
More recently, the reaction of an olefin **5** bearing an electron-withdrawing group (EWG = CO_2Me, CN) was revisited and shown to give rise to a substituted cyclopentenone **8**, formally via the ketone **7**, as the result of a coupled Pauson-Khand/Michael-type reaction (eq. 3).[7,8]

We report herein our own results on the reactivity of electron deficient olefins in the Pauson-Khand reaction. These demonstrate that 5-functionalized cyclopent-2-enones **7** may be obtained when alkyne-hexacarbonyldicobalt complexes **2** are reacted with activated olefins **5** in the presence of N-methylmorpholine oxide (NMO) as a promoter.

An initial experiment with complex **2a** and 6 equivalents of methyl acrylate **5a** in CH_2Cl_2-THF (2 :1) at 0-20°C/4 h in the presence of NMO (6 equiv) gave the expected cyclopentenone **7a** (18%). The diketoester **8a** (25%) was also obtained arising from subsequent reaction of ketoester **7a**.



The indesired Michael addition could be minimised by using a smaller amount of methyl acrylate: reaction with only 2 equivalents of the conjugated ester **5a** led to cyclopent-2-enone **7a** in 59% yield (Table, entry 1).

The reactivity of other activated olefins (conjugated esters, ketones, nitriles and sulfones) with several alkyne-hexacarbonyldicobalt complexes **2a-c** were then examined (Table). Under similar conditions[9] dicobalt complexes **2b** and **2c** reacted with methyl acrylate to afford cyclopentenones **7c** and **7f** (entries 4 and 7). Substituted acrylates turned out to be very unreactive; α-methylacrylate **5b** did not react under these conditions (entry 2) and β-methylacrylate **5c** gave cyclopentenone **7d** in a low yield (8%) (entry 5). These latter results were not totally unexpected since the Pauson-Khand reaction is known to be very sensitive to steric effects.[2] Unsaturated ketones as methylvinylketone, cyclopent-2-enone and cyclohex-2-enone were also unreative.

The reactions of phenylvinylsulfone **5d** with complexes **2a,b** were also tested and shown to be effective, with 5-phenylsulfonylcyclopent-2-enones **7b** and **7e** obtained in 50-70% yield (entries 3 and 6). The reactivity of acrylonitrile was more difficult to control. Under the conditions employed, reaction of dicobalt complex **2a** with acrylonitrile gave a complex mixture of products : 5-cyanocyclopent-2-enone **7g** (28%), dicyanocyclopentenone **8b** (4%) and the subtituted 2-norbornanone **9** (7%) were isolated.[11] The formation of ketones **8b** and **9** may be easily rationalised by a Michael-type addition of the cyclopentenone **7g** to acrylonitrile and a further intramolecular such 1,4-addition leading to ketone **9**.[12]

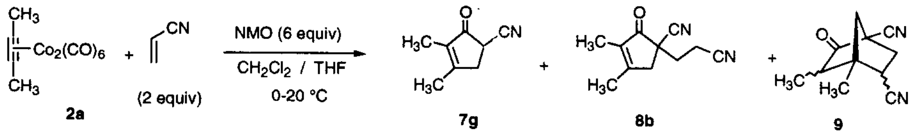
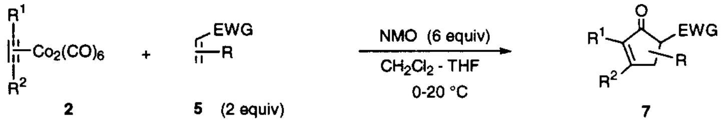
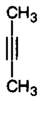
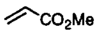
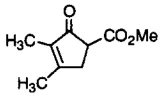
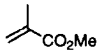
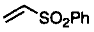
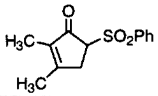
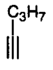
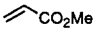
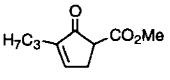
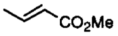
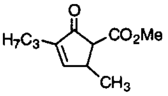
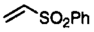
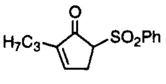
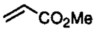
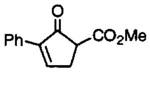


Table. Cobalt-mediated cycloaddition of alkynes with electron deficient olefins



Entry	Alkyne **1**	Activated Olefin **5**	Cyclopentenone **7**	Yield %
1	 **1a**	 **5a**	 **7a**	59
2		 **5b**	no reaction	-
3		 **5d**	 **7b**	71
4	 **1b**	 **5a**	 **7c**	47
5		 **5c**	 **7d**	8
6		 **5d**	 **7e**	49
7	 **1c**	 **5a**	 **7f**	41

In summary we have shown that the carbonylative cocyclisation of alkynes and electron deficient olefins can be controlled at 0-20 °C by using a tertiary amine N-oxide (N-methylmorpholine oxide) as a promoter of the cycloaddition. 5-Functionalized cyclopent-2-enones may then be obtained with moderate to fair yields.

Acknowledgments

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References and Notes

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7. Costa, M.; Mor, A. *Tetrahedron Lett.* **1995**, *36*, 2867-2870.
8. In previous work, cyclopentenone **8** was obtained as the major product (15-53% yield) together with the intramolecular Michael addition product generated from **8** and alkyne cyclotrimerization products.
9. **A typical procedure is as follows** (Table, entry 1) : To a stirred solution of (but-2-yne)-$Co_2(CO)_6$ **2a** (680 mg, 2 mmol) and freshly distilled methyl acrylate **5a** (344 mg, 4 mmol) in 2:1 CH_2Cl_2-THF (15 mL) at 0°C was added N-methyl-morpholine oxide (6 equiv). The reaction was allowed to warm to room temperature and then stirred overnight. The reaction was passed through a small plug of silica gel and the filtrate concentrated *in vacuo*. Flash-chromatography (Petroleum ether/Et_2O 50:50, $R_f = 0.37$) over silica gel afforded methyl 3,4-dimethyl-2-oxo-3-cyclopentene-1-carboxylate **7a** (59 %) as white cristals. **M.P** = 59-60°C (lit[10] : 60-61°C). **I.R** (film) : 1735, 1700, 1650, 1435, 1390, 1330, 1160, 700 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ ppm: 1.68 (br s, 3H, C=C(CO)-$\mathrm{C}\mathit{H}_3$); 2.06 (s, 3H, CO-C=C-$\mathrm{C}\mathit{H}_3$); 2.67 (br dd, 1H, J_{AB} = 17.6 Hz and J = 7 Hz, C=CCH*H*); 2.87 (br d, 1H, J_{AB} = 17.6 Hz, C=C-C*H*H); 3.40 (dd, 1H, J = 7 Hz and J = 3 Hz, CO-C*H*-CO_2Me); 3.73 (s, 3H, O-$\mathrm{C}\mathit{H}_3$). **^{13}C NMR** ($CDCl_3$, 75 MHz) δ ppm : 8.1 (C=C(CO)-*C*H3), 17.1 (CO-C=C-$\mathit{C}H_3$), 35.6 ($\mathit{C}H_2$), 51.0 (CO-O$\mathit{C}H_3$), 52.5 (CO-*C*H-CO_2Me), 134.6 (C=*C*(CO)), 169.9 (*C*=C-CO), 170.1 (*C*O-OMe), 202.1 (*C*=O). **M.S** (EI, 70 eV): *m/z* 168 (100, $M^{+\cdot}$), 137 (22, $[M-OCH_3]^{+\cdot}$), 108 (48, $[M-1-CO_2CH_3]^{+\cdot}$), 80 (25), 65 (13), 59 (18, $[CO_2CH_3]^{+\cdot}$), 55 (51).
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11. 2-Norbornanone **9** was isolated as a mixture of two stereoisomers in a 95/5 ratio determined by ^{1}H NMR.
12. This type of intramolecular Michael addition product has also been observed as coproduct from reaction of methyl acrylate in previous work by Costa et al.[7,8]