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Regioselectivity in the Pauson–Khand reaction of allenic hydrocarbons

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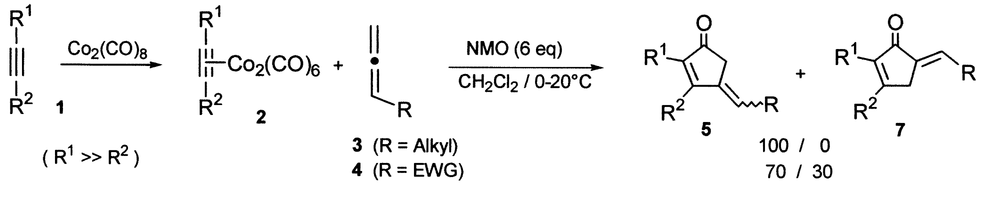
Abstract—The regioselectivity of the cobalt-mediated cocyclisation of alkynes with allenic hydrocarbons leading to 4- and 5-alkylidenecyclopentenones was shown to depend on the substitution pattern of both the acetylenic and allenic components. An initial pseudoaxial coordination of the allenic hydrocarbon may account for the formation of the 5-alkylidenecyclopentenone from acetylene. © 2001 Elsevier Science Ltd. All rights reserved.

The $Co_2(CO)_8$-mediated Pauson–Khand reaction[1] (PKR)—carbonylative cocyclisation of an alkyne with an olefin to cyclopent-2-enones—is considered as one of the most powerful syntheses of five-membered ring compounds.[1,2] Particularly, its intramolecular version has been widely used for the synthesis of polycyclic cyclopentenones.[2] Furthermore, mild experimental conditions at room temperature using tertiary amine *N*-oxides as initiators were described for this cycloaddition [2+2+1].[3]

Recently, we reported an analogous cycloaddition of alkynes with allenic hydrocarbons **3** which leads, with high regioselectivity, to 4-alkylidenecyclopent-2-enone **5** under these mild conditions using *N*-methylmorpholine *N*-oxide NMO as the initiator.[4] However, the reaction displayed an important electronic effect from the allenic part since the reactions of electron deficient allenes **4** (R = EWG) were later shown to lead to two isomeric cyclopentenones **5** and **7** (**5**/**7** = 70/30) (Scheme 1).[5]

Our initial work was mainly carried out with symmetrically disubstituted alkynes.[4] During an extensive exploration of this new cycloaddition, it turned out that its regioselectivity was more complex and depends on the nature of the acetylenic **1** and allenic hydrocarbons **3** used. We report herein the results of our investigations.

A reinvestigation of the cycloaddition of the disubstituted alkyne complex **2a** with 1,2-nonadiene **3a** demonstrated that it was not totally regioselective as previously reported. Thus, the regioisomeric 4-methylene-5-alkylcyclopentenone **6aa** was also produced in very small amounts (<5% molar ratio) whatever the conditions A or B used (Table 1, entries 1 and 2). However, the reaction of a *gem*-disubstituted allene such as vinylidenecyclohexane **3b** afforded the cyclopentenone **5ab** as a sole product (entries 3 and 4). It is noteworthy that the reactions carried out in CH_2Cl_2 and THF as cosolvent[6] (conditions B, temperature −78 to 20°C) gave in most cases higher yields of



Scheme 1.

Keywords: Pauson–Khand reaction; allene; cycloaddition; cyclopentenone; cobalt complex.

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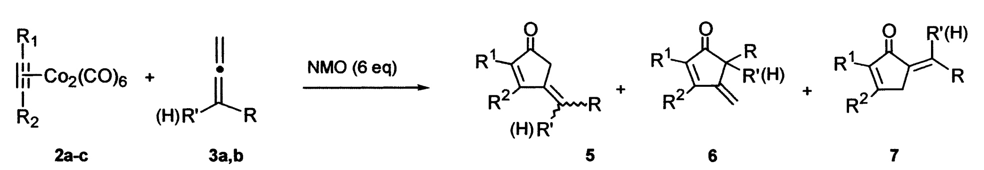
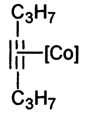
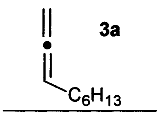
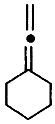
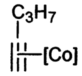
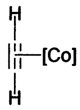
Table 1. Cycloadditions [2+2+1] of alkyne–dicobalt complexes **2** with allenic hydrocarbons **3**



Entry	Alcyne-[Co][a] 2	Allene 3	Conditions[b]	Ketone 5-7	Isomer ratio[c] 5 (E/Z)	6	7	Total Yield (%)[d]
1	 **2a**	 **3a**	A	**aa**	96 (100/0	4	-	71
2			B	”	97 (100/0)	3	-	77
3		 **3b**	A	**ab**	100	-	-	61
4			B	”	100	-	-	75
5	 **2b**	**3a**	B	**ba**	85 (71/29)	15	-	80
6		**3b**	B	**bb**	100	-	-	75
7	 **2c**	**3a**	C	**ca**	85 (70/30)	8	7	78
8			D (4 h)	”	90 (73/27)	3	7	79
9			D (6 h)	”	85 (75/25)	2	13	82
10		**3b**	C	**cb**	96	-	4	51
11			D (4 h)	”	80	-	20	52
12			D (6 h)	”	72	-	28	64

[a] [Co] = $Co_2(CO)_6$

[b] Conditions (A): CH_2Cl_2 / 0-20°C / 6-15h ; (B): CH_2Cl_2-THF (1:1) / -78°C to 20°C within 1 h, 3-4 h at r.t ; (C): CH_2Cl_2-THF (1:1) / 20°C / 2 h ; (D): CH_2Cl_2-THF (1:1) / -78°C to 20°C / within 4 or 6 h.

[c] Ratio of isomers determined by GLC analysis before purification.

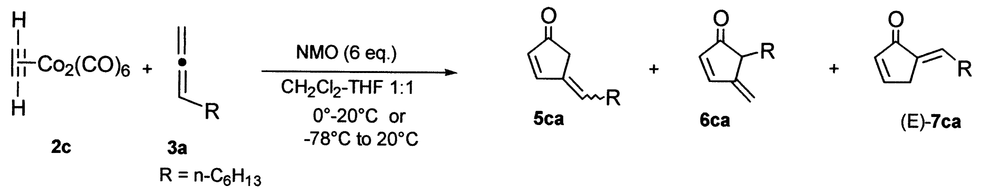
[d] Total yield (**5**+**6**+**7**) of purified products after flash-chromatography.

cyclopentenones than those in CH_2Cl_2 at 0–20°C (conditions A; compare entries 1/2 and 3/4).

The reaction of the monosubstituted dicobalt complex **2b** with allene **3a** was less regioselective and yielded a larger amount of 4-methylene-5-alkylcyclopentenone **6ba** (**5ba**/**6ba** = 85/15), while the one with vinylidenecyclohexane **3b** gave only one product, the cyclopentenone **5bb** (entries 5 and 6).

The acetylene–$Co_2(CO)_6$ complex **2c** reacted with allene **3a** in a quite different manner, since we could isolate a mixture of the three isomeric cyclopentenones **5ca**, **6ca** and (*E*)-**7ca** (Scheme 2, entries 7–9 of Table 1). The ratio of isomers **5**/**6**/**7** seemed to depend on the temperature. Indeed, the amount of ketone **7ca** was larger when the reaction was carried out at a lower temperature (slow warming up from −78 to 20°C within 6 h/entry 9).

A similar reaction of complex **2c** with allene **3b** gave also the isomeric 5-alkylidenecyclopentenone **7cb** (entries 10–12) and the same temperature effect was observed (compare entries 10/11/12).



Scheme 2.

In light of these results, a mechanistic rationale for the formation of the different cyclopentenones **5**–**7** can be proposed (Fig. 1). The mechanism of PKR of olefins is assumed to start by the loss of a CO ligand from one of the cobalt atoms followed by olefin coordination on this atom. For steric reasons, this coordination should be favoured *anti* to the larger substituent of the alkyne.[7,8]

Thus, complexation of the less substituted double bond of the allenic hydrocarbon **3** to the alkyne–dicobalt complex **2** would preferentially occur *anti* to the R^1 group ($R^1 \gg R^2$) and also *anti* to the allenic substituent R through the less hindered half-space defined by the allenic unit. This coordination would lead to the π-complex **A**. Next, the insertion of the allene into the adjacent formal C–Co bond would give the σ-allyl complex **B** (path a), from which the cyclopentenone **5** would be yielded after the further elemental steps of the PKR (CO insertion into the allylic C–Co bond, reductive elimination and decomplexation). The high *E*-stereoselectivity ($E/Z = 100/0$ when $R^2 \neq H$ and $E/Z = 75/25$ when $R^2 = H$) is derived from the large steric interaction between the R and R^2 groups. The formation of the regioisomeric cyclopentenone **6** could be explained from another less favoured π-complexation (complex **C**) of the allene through its more substituted double bond (path b). Insertion of the allene would lead to complex **D** and finally to ketone **6**. However, an alternative pathway which would involve the direct formation a π-allyl cobalt complex **E**, eventually within an equilibrium with complexes **B** and **D**, can also be envisioned (path c). Formation of the isomeric cyclopentenone **7** should emerge from the third π-complex **F**, through the insertion of the allene into the C–Co bond leading to the σ-vinyl cobalt complex **G**, followed by the further three final steps (path d).

However, the real reasons for the formation of ketones (*E*)-**7ca** and **7cb**, which are obtained only in the reactions of the acetylene–dicobalt complex **2c**, are not totally clear. Indeed, the understanding of the different behavior of complexes **2b** ($R^1 = n\text{-}C_3H_7$) and **2c** ($R^1 = H$) with allene **3a** (or **3b**) should involve some interaction between the group R^1 (or H) and the allenic hydrocarbon **3** and its substituents R or R′. This is not the case if the initial coordination of the allenic unit takes place *anti* to the R^1 group, and should rule out the π-complex **F** as a plausible intermediate.

So, we envisioned that this coordination may occur on a pseudoaxial vacant ligand site (referred to the Co–Co bond) of the cobalt atom, as has been already suggested in recent studies in the literature.[9,10] Such coordination would give rise to a set of π-complexes in dynamic equilibrium via rotation around the allene–Co π-bond (**H**, for example, Fig. 2). Among them, π-complex **I** seems to be the only one which presents: (i) steric interactions between the R^1 and R′ (or H) groups and (ii) a suitable disposition of the alkyne carbon–Co bond and the allenic double bond for the allene insertion; this last one would give complex **G** (path e) from which ketone **7** would be yielded. Furthermore, this last pathway may explain the *E*-configuration of cyclopentenone **7ca**, since the R^1 (=H) and R groups should be *anti* during the coordination step leading to π-complex **I** in order to minimise steric interactions between these two groups.

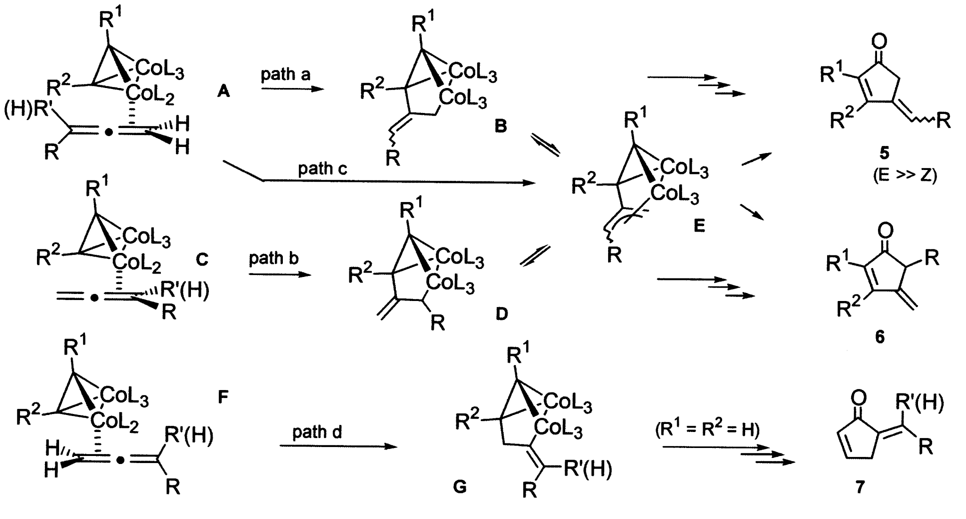


Figure 1.

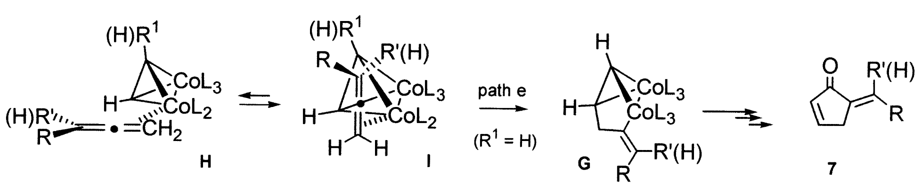


Figure 2.

In summary, this study has shown that the regioselectivity of the PKR of alkynes with allenic hydrocarbons depends on the substitution pattern of both the acetylenic and allenic partners. Competitive mechanistic pathways to the cyclopentenones **5**–**7** have been proposed from several allene–cobalt π-complexes. Particularly, 5-alkylidenecyclopentenones **7** are formed only from acetylene, which might be explained by an initial pseudoaxial coordination of the allenic unit to cobalt.

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