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# Mechanistic and stereochemical aspects of the asymmetric cyclocarbonylation of 1,6-enynes with rhodium catalysts

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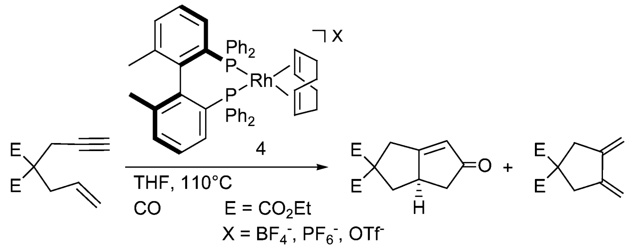
**NMR and kinetic investigations of the cyclocarbonylation of 1,6-enynes with cationic rhodium(I) catalysts, modified with atropisomeric diphosphines, disprove the involvement of carbonyl species for 1,6-enyne activation; low-temperature catalysis, with molecular sieves as the carbon monoxide reservoir, is highly enantioselective (ee up to 97%).**

A great deal of research has been devoted to asymmetric homogeneously catalyzed carbonylation reactions for the direct synthesis of valuable, optically active oxygenates. In recent years the [2 + 2 + 1] cycloaddition of an alkyne, an alkene and CO (Pauson–Khand-type reaction), both in the intra- and intermolecular forms, has been performed catalytically using titanocenes and ruthenium, cobalt, rhodium and iridium systems.[1] In particular rhodium(I) catalysts, when used in the presence of the atropisomeric diphosphine ligand Binap, give high optical yields.[2,3] However, these catalysts are efficient at high temperatures (*e.g.* 90–130 °C in the case of rhodium), at which the asymmetric discrimination of the ligand systems usually becomes limited.



1 2 3

The results for the catalyst formed *in situ* from $[Rh(cod)Cl]_2$, (*R*)-Biphemp and silver triflate were not reproducible due to the partial racemization of the product, caused by silver salts, especially AgOTf.[2] We recently reported positional anion effects in the new salts of Rh(I), [Rh(1,5-cod)Biphemp]X, X = $BF_4^-$, **4a**, $PF_6^-$, **4b** and $OTf^-$, **4c** studied by PGSE diffusion and $^1H$–$^{19}F$-HOESY NMR methods.[4] Each anion showed selectivity in its approach towards the cation and the three salts showed different amounts of ion pairing in $CD_2Cl_2$ in the order of **4b** > **4a** > **4c**.[5] These results correlate well with the observed anion effect using the abovementioned catalysts in the cyclocarbonylation of 4,4-bis(carboethoxy)hept-6-en-1-yne **1** with carbon monoxide. **4c** has the highest catalytic activity but the lowest amount of ion pairing (Fig. 1).

To extend the applicability of this interesting transformation, we investigated the dependence of the kinetics of the cyclocarbonylation of **1** on carbon monoxide, using cationic **4c** as the catalyst precursor. CO pressure negatively affects the kinetics of rhodium systems.[6] There was a clear minus 2 order with respect to the partial pressure of carbon monoxide in the range of $p_{CO}$ = 0.75–2.55 bar at 110 °C in THF as the solvent. Under those conditions, the enantioselectivity of the reaction is between 85.4 and 78.8%. Furthermore, the reaction is first order with respect to the enyne and the catalyst concentration.

Based on these kinetic results, we suggest two preliminary CO-dissociation steps, starting from the biscarbonyl species **5** before the 1,6-enyne binds to the cationic center **7** (Scheme 1). This proposal was checked by model studies. Exposing a tetradeuteromethanol solution of **4c** to hydrogen at room temperature in an NMR tube, the $^{31}P$-NMR spectrum showed the methanol complex **7** only;[7] this reacts with an understoichiometric amount of **1** at −70 °C to give two diastereomeric adducts at a molar ratio of 7 : 1. The nature of this adduct (probably **8**) was not determined exactly due to the broadness of the $^1H$- and $^{13}C$-NMR spectra. Adding CO to this solution at −70 °C resulted in a rapid enantioselective cyclocarbonylation with an enantiomeric excess of 90% and the formation of a mixture of the mono- and biscarbonyl species $[Rh(P^\circ P)(CO)(CD_3OD)]^+$ **6** and $[Rh(P^\circ P)(CO)_2]^+$ **5**. Addition of **1** to a mixture of both carbonyl species did not lead to the formation of the abovementioned enyne complex adduct **8** or to an adduct with a coordinated CO-ligand **11**.[2]

Molecular sieves 4 Å (M.S.) were introduced as promoters in the catalytic Pauson–Khand reaction with $Co_2(CO)_8$ and were used here as a CO reservoir to generate very low CO concentrations in solution.[8] We found that small solvent molecules, such as dichloromethane or methanol, displace the gas from the pores, whereas in toluene, THF and diglyme CO is retained by the molecular sieves for several hours. The reactions listed in Table 1 were carried out with pretreated molecular sieves, which were dried at 190 °C under high vacuum for three hours and cooled in a CO atmosphere.[8b] The solvent and substrate were added and a stream of argon was used to replace the CO atmosphere. At the same time the dissolved catalyst precursor **4** was activated in a separate flask by bubbling hydrogen to form **7**. The addition of **7** to the M.S./substrate mixture started the reaction. Compared to the control experiment (Entry 1) under normal conditions, reactions with

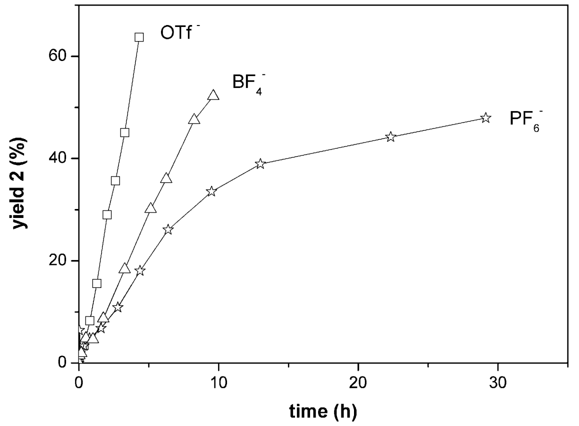


**Fig. 1** Anion effect in the cyclocarbonylation of **1** with [Rh(1,5-cod)Biphemp]X, X = $BF_4^-$, **4a**, $PF_6^-$, **4b** and $OTf^-$, **4c**. Reaction conditions: 2 mol% catalyst, 110 °C, THF and 4.6 bar reaction pressure.

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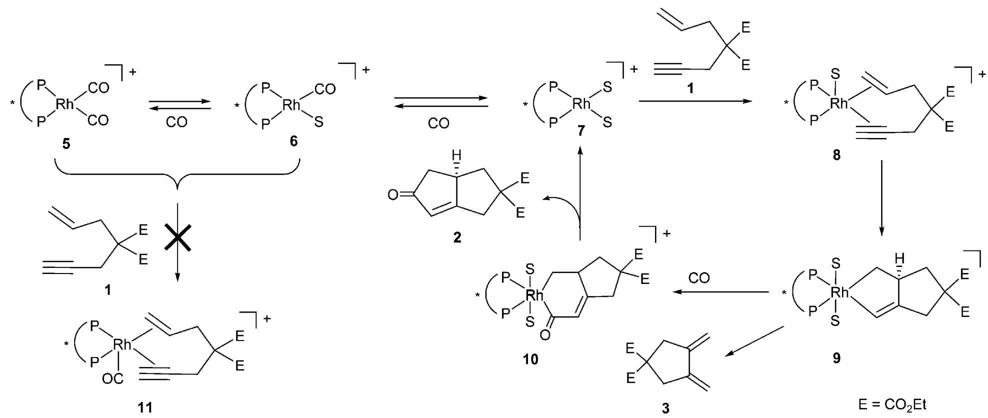

**Scheme 1** Proposed mechanism of the cationic Rh(I)-catalyzed asymmetric Pauson–Khand-type reaction.†

**Table 1** Rh(I)-catalyzed cyclocarbonylation of **1** with **4c** and molecular sieves as the CO reservoir[a]

| Entry | CO source | $T$ (°C) | Time (h) | Yield **2**/ Conversion (%) | Ee[b] (%) |
|---|---|---|---|---|---|
| 1 | 1 bar CO[c] | 90 | 90 | 72/85 | 79 |
| 2 | M.S. | 25 | 1 | 53/98 | 96 |
| 3 | M.S. | 0 | 4 | 33/99 | 97 |

[a] Reaction conditions: 2 mol% catalyst in 5 ml toluene, 0.0027 mmol **1**, tenfold weight amount (0.65 g) of molecular sieves (4 Å, powder) with respect to the substrate, pretreated with carbon monoxide. [b] Estimated by GC analysis. [c] Control experiment without M.S.

pretreated molecular sieves have not only much shorter reaction times, but also clearly higher enantioselectivities. To the best of our knowledge these are the first catalytic Pauson–Khand reactions of a 1,6-enyne carried out at such low temperatures.

More important, however, are the mechanistic results of the NMR and kinetic studies, which were used to develop a new protocol for the catalytic reaction. Therefore, the assumption that **7** is the catalytically active species was confirmed. Since the reaction proceeds catalytically, **10**, which forms **7** after the reductive elimination, may not have any coordinated CO.

The yields of **2** in the low-temperature reactions (Entries 2 and 3) were small, but the formation of the known main byproduct **3** was suppressed at these temperatures (10% at 25 °C; 0% at 0 °C).[3] Various dimer byproducts were generated instead.

In summary, NMR and kinetic studies clarified the substrate complexation step of 1,6-enynes with cationic Biphemp rhodium(I) complexes and showed that the active catalyst is a CO-free complex.

## Notes and references

† $^{31}$**P-NMR** (202 MHz, CD$_3$OD, 223 K) **4**: 26.4 (d, $J_{\text{Rh–P}} = 145.2$), **5**: 23.2 (d, $J_{\text{Rh–P}} = 124.4$), **6**: 49.8 (dd, $J_{\text{Rh–P}} = 163.0$, $J_{\text{P–P}} = 45.9$), 24.6 (dd, $J_{\text{Rh–P}} = 136.3$, $J_{\text{P–P}} = 45.9$), **7**: 55.3 (d, $J_{\text{Rh–P}} = 202.9$), **8**: major 47.2 (dd, $J_{\text{Rh–P}} = 191.1$, $J_{\text{P–P}} = 14.8$), 12.6 (dd, $J_{\text{Rh–P}} = 75.6$, $J_{\text{P–P}} = 14.8$), minor 50.8 (dd, $J_{\text{Rh–P}} = 191.1$, $J_{\text{P–P}} = 14.8$), 11.6 (dd, $J_{\text{Rh–P}} \approx 74$, $J_{\text{P–P}} \approx 14$).

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