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Reaction Mechanisms

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The Pauson–Khand Mechanism Revisited: Origin of CO in the Final Product**

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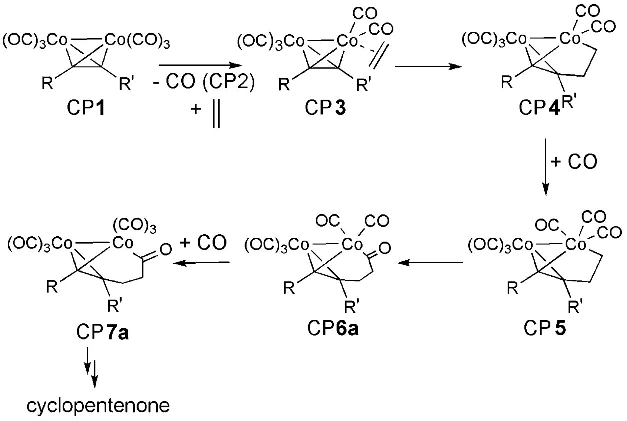
Dedicated to Professor Gérard Buono

***Abstract:** The mechanism of the Pauson–Khand reaction has been studied by mass spectrometry and it has been found, through ion-molecule reaction with ^{13}CO, that the carbon monoxide incorporated into the product cyclopentenone is one that has been retained within the complex. Theoretical and kinetic calculations support this finding, which provides a complementary explanation for the effect of Pauson–Khand promoters.*

The Pauson–Khand reaction (PKR), a dicobalt-octacarbonyl-mediated process for joining an alkene, an alkyne, and carbon monoxide to form a cyclopentenone, is a powerful tool for accessing complex molecules.[1] Given the importance of this transformation and the recent advances in theoretical chemistry, it is not surprising that considerable effort has been made over the past few years to establish its mechanism. In their pioneering paper in 2001, Yamanaka and Nakamura[2] presented a mechanistic pathway for the reaction using ethylene and acetylene as model organic partners (Scheme 1, R = R′ = H). This work provided the first theoretical support for the now widely accepted proposal made by Magnus and Principe in 1985.[3]

In their mechanistic pathway, the initially formed and often isolated alkyne dicobalt hexacarbonyl complex of type CP**1**, after loss of CO and coordination of the alkene, gives a complex of type CP**3**. The latter undergoes insertion of the alkene to give the key cobaltacycle of type CP**4**. After the return of the missing CO ligand (complex of type CP**5**) and insertion, the cobalt acyl complex of type CP**6a** is produced. The cyclopentenone is finally obtained after extrusion of a [Co(CO)$_3$] fragment from the cobaltacycle and cleavage of [Co$_2$(CO)$_6$].



Scheme 1. Proposed mechanistic pathway for the Pauson–Khand reaction (CP designation of Yamanaka and Nakamura[2]).

In 2003, we reported the first confirmation, by mass spectrometry, of the existence of the proposed intermediate of type CP**4**.[4] For that study, the easily deprotonated bridging ligand bis(diphenylphosphino)methane was placed on the neutral dicobalt species to enable facile observation of species in mass spectrometry ion-molecule experiments. A somewhat different approach has now been undertaken to delve into the apparently unquestioned, yet to us quite questionable, return of CO (CP**4**→CP**5**) in the postulated Magnus mechanism. We envisioned a novel study in which the putative incorporation of an external CO at this stage would be examined with ^{13}CO, again in mass spectrometry ion-molecule experiments. Herein, we disclose the results of this study, which has led to a new, more plausible interpretation of an important facet of the Pauson–Khand transformation.

To be able to observe the cyclopentenone final product in ion-molecule experiments, the cationic alkyne salt *N*-methyl-*N*-propargylpyrrolidinium hexafluorophosphate[5] appeared ideally suited. The positive ESI mass spectrum[6] of the complex MSCP**1** displayed an ion at *m*/*z* 410, accompanied by an abundant peak at *m*/*z* 382 (100%), MSCP**2**, corresponding to the reactive intermediate complex [MSCP**1**-CO] (Scheme 2). The ion at *m*/*z* 382, submitted to a collision activated reaction (CAR) with norbornene, introduced into the modified transfer hexapole H0, yielded an adduct ion at *m*/*z* 476, corresponding to [MSCP**1**-CO + norbornene]. After selection by Q1, this adduct was submitted to a second CAR with CO in the H2 collision cell (see the Supporting Information for experimental details).

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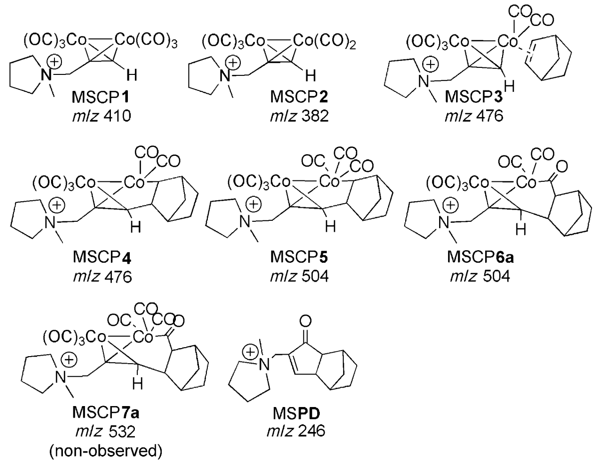


Scheme 2. Ions observed in CAR/CAR with norbornene in H0 and ^{12}CO in H2: *m/z* 476 [MSCP1-CO + norbornene] is selected by Q1 to give *m/z* 504 [MSCP1 + norbornene] in H2. (MS designates mass spectra results)

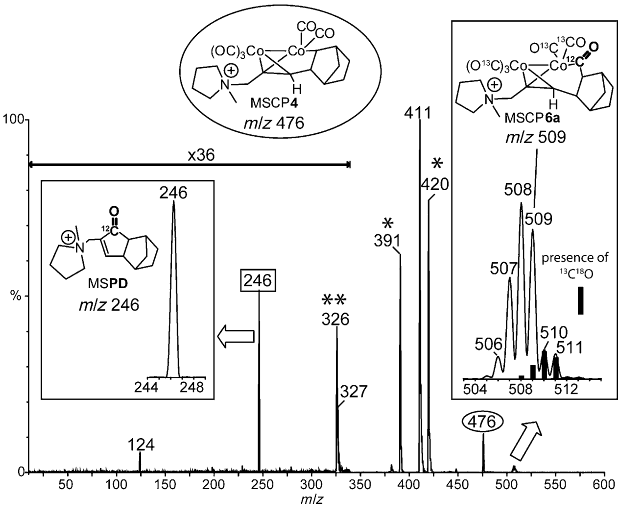


Figure 1. Consecutive CAR/CAR experiments using norbornene, then ^{13}CO: *m/z* 476 [MSCP1-CO + norbornene], formed by a first CAR in H0, is selected by Q1 to give ion-molecule reactions with ^{13}CO in H2. * The *m/z* 391 results from loss of *N*-methylpyrrolidine from *m/z* 476; *m/z* 420 corresponds to *m/z* 391 + ^{13}CO. ** Peak due to loss of norbornene and two CO ligands from *m/z* 476.

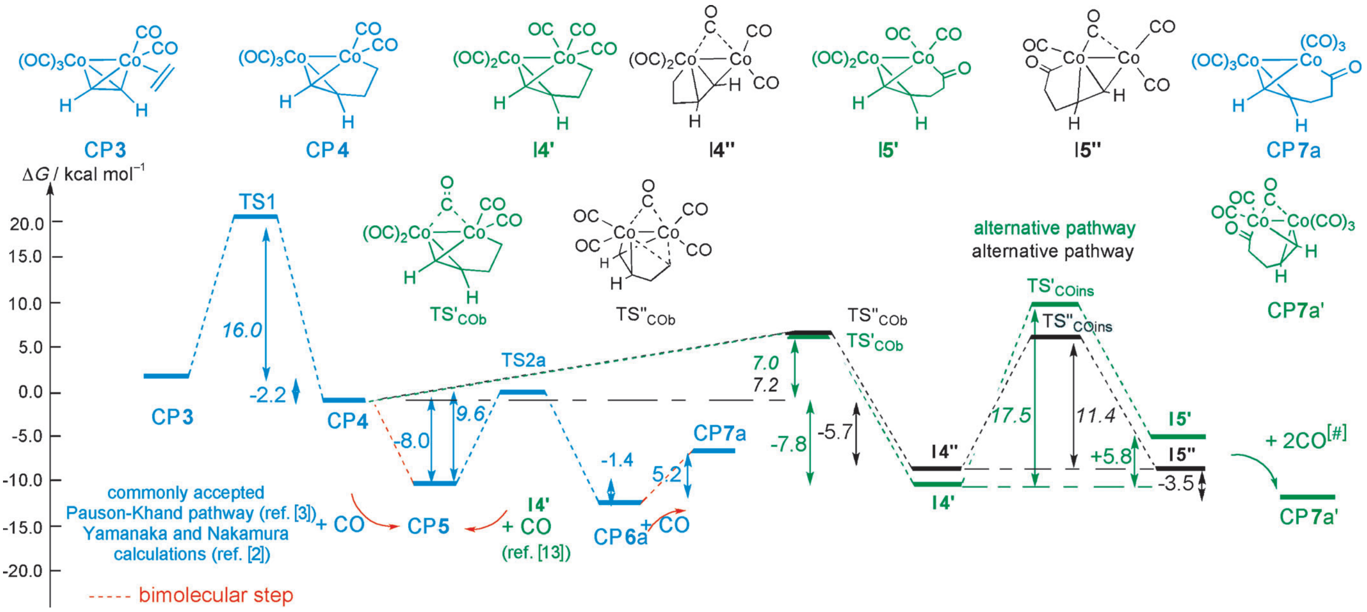
The structure of the ion at *m/z* 476 can be assumed to be MSCP**3**, possibly admixed with the cobaltacycle MSCP**4**. Ions at *m/z* 504 can be attributed to complexes MSCP**5** and/or MSCP**6a**, products of CO addition without or with subsequent insertion, respectively. DFT studies performed by Yamanaka and Nakamura strongly suggest that CO insertion can occur only after an exothermic uptake of CO by the complex CP**4** to give CP**5** (corresponding to MSCP**5**).[7] Interestingly, the ion *m/z* 532 for MSCP**7a** was not observed in spite of a reasonable stability previously calculated for this type of intermediate. The expected ion at *m/z* 246, corresponding to MS**PD**, was however produced.[8] Significantly, MS**PD** was not observed in collision-induced dissociation (CID) experiments with the ion at *m/z* 476 (MSCP**3** and/or MSCP**4**) using argon or nitrogen (see the Supporting Information). Saturation of the free coordination site on cobalt thus seems to be necessary prior to insertion of CO and/or reductive elimination to give the cyclopentenone.

This experiment was next repeated with ^{13}CO as the collision gas, and the following were observed: first, ions at *m/z* 410 were mainly shifted to *m/z* 411, as a result of norbornene–^{13}CO exchange during collisions in H2.[9] Secondly, ions at *m/z* 476 were not shifted although exchange with ^{13}CO might have been expected. A possible explanation is that the observed ions at *m/z* 476 are those with kinetic energy that is too high to allow CAR processes with ^{13}CO. Ions at *m/z* 476 with lower kinetic energy, though, can react with ^{13}CO several times, because of a longer resident time in H2 after the first collision, to yield ions with different extents of incorporation (Figure 1). Indeed, the *m/z* 505–509 distribution suggests that complexes MSCP**5** and/or MSCP**6a** can incorporate up to five ^{13}CO units.[10]

Most significantly, the peak corresponding to MS**PD** remained at *m/z* 246, thus there is no incorporation of ^{13}CO. This result is particularly revealing in that it reflects the origin of the CO in the final product. If complex MSCP**5** is an intermediate on the pathway to the cyclopentenone, a notion that is at present nearly universally accepted, then it is difficult if not impossible to understand the complete absence of ^{13}CO in MS**PD**. This absence can be understood, however, if there is an internal CO transfer (or bridging) before insertion and before collision with ^{13}CO (compare CP**4**→CP**5**).

Several often-used productive experimental protocols would also seem to argue for the intramolecularity of this process. Intuitively, the intramolecular transfer of a coordinated CO should occur more readily than the return of a CO in, for example, dilute solution at elevated temperature under an inert atmosphere (typically, toluene, 80 °C, Ar). The putative return of a CO unit to a CP**4**-type complex with the use of an amine oxide as a reaction promoter (typically, 3–6 equiv NMO, CH_2Cl_2, RT)[11] would appear to be particularly problematic since a "tertiary amine *N*-oxide could readily remove CO on [cobalt] oxidatively as carbon dioxide".[12]

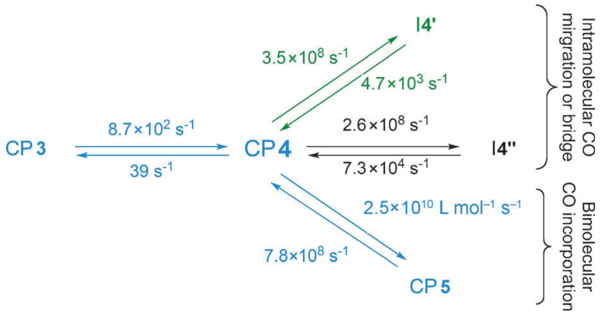
To examine more closely this previously unrecognized possibility—insertion of CO in the complex of type CP**4** or a derivative without first the incorporation of an external CO on the unsaturated cobalt—calculations were performed on Yamanaka and Nakamura's model reaction at the same level of theory (Scheme 3, blue pathway). Since CO insertion into the Co–C bond most likely involves a fully coordinated Co atom,[7] an intramolecular migration of CO in the complex CP**4** was first considered (green pathway). It was found that such a structure can indeed be formed through a bridged transfer of CO between cobalt atoms, as depicted in Scheme 3. The transition state ($TS'_{\mathbf{COb}}$), only 7.0 kcal mol^{-1} above CP**4** and thus easily accessible, engenders exothermically (7.8 kcal mol^{-1}) a new intermediate **I4′**.[13] The CO insertion in **I4′** to give **I5′** is energetically the most difficult in this new pathway (17.5 kcal mol^{-1}), but comparable to that required earlier for the formation of CP**4**. Another possible pathway (in black), however, also exists and involves translocation of the cobaltacycle through switching from



Scheme 3. Potential energy surfaces for Pauson–Khand transformation (B3LYP/631LAN, see Ref. [2] for full description of basis set used). The relative energies (in kcal mol^{-1} at $T = 353$ K) correspond to Gibbs free energies. The red dotted lines indicate bimolecular steps. Zero energy refers to CP4. [#] See the Supporting Information for details.

one Co to the other via TS″$_{\mathrm{COb}}$, located 7.2 kcal mol^{-1} above CP**4**. This migration involves the concomitant formation of a CO bridge between the two Co atoms, as depicted in **I4″**. The CO insertion in **I4″** to give **I5″** is now only 11.4 kcal mol^{-1}. Theoretical calculations thus indicate that alternative, somewhat higher energy but intramolecular pathways, which involve transfer or bridging of CO between cobalt atoms, are indeed feasible.

Kinetic simulations offer strong support. After coordination of the alkene (CP**3**) and formation of the cobaltacycle (CP**4**), the currently accepted mechanism proceeds by a bimolecular, barrierless association reaction that is diffusion controlled. However, the above-mentioned intramolecular alternatives now must also be considered. Starting from CP**4**, there are four possible events: 1) reversion to CP**3**, 2) return of a CO through a bimolecular process to form CP**5** (Yamanaka-Nakamura proposal), 3) intramolecular CO migration without structural change (TS′$_{\mathrm{COb}}$), and 4) CO bridging concomitant with formation of the alternative cobaltacycle (TS″$_{\mathrm{COb}}$). Kinetic rate constants for each have been calculated at $T = 353$ K (Scheme 4) by using the thermodynamic formulation of the transition-state theory $k = k_{\mathrm{B}}T/h\,e^{-\Delta G^{\neq}/RT}$, except for the bimolecular CP**4**→CP**5** step, which is diffusion controlled (rate determined by using a simple diffusion model in an apolar solvent combined with the van't Hoff equation[14]). Clearly, after formation of CP**4**, the reaction quickly proceeds toward products (reversion to CP**3** is not favorable). For the Yamanaka and Nakamura proposal to compete efficiently with intramolecular CO migration (or bridging), R in $R = k_{\mathrm{return}}[\mathrm{CO}]/k_{\mathrm{mig(or\ brid)}}$ must be ≥ 1, thus leading to $[\mathrm{CO}] \geq k_{\mathrm{mig(or\ brid)}}/k_{\mathrm{return}} \approx 10^{-2}$ M. This CO concentration level is not present in a typical Pauson–Khand reaction medium.



Scheme 4. Kinetic rate constants associated with possible CP**4** transformations (colors relate to those in Scheme 3).

In summary, CAR/CAR experiments with ^{13}CO strongly suggest that incorporation of an additional CO in a complex of type CP4 through a bimolecular process is not likely to occur, and theoretical calculations have validated alternatives in which the CO incorporated in the final cyclopentenone involves one that has been retained throughout in the complex. The currently accepted mechanism for this important transformation would thus seem to require revision.

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Keywords: cobalt · density functional calculations · gas-phase reactions · mass spectrometry · reaction mechanisms

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[7] Direct CO insertion in CP**4** to produce a cobalt acyl complex was modeled and gave the transition state CP**4**TS (see the Supporting Information), which is energetically disfavored (16.4 kcal mol^{-1} above CP**4**) compared with energy levels of other transition states.

[8] Others peaks corresponding to loss of *N*-methylpyrrolidine are also present. See the Supporting Information.

[9] Ions at *m*/*z* 412 and 413 are also detectable. The number of CO ligands exchanged depends on the time of residence of the initial ion in the collision cell H2.

[10] Six ^{13}CO units apparently cannot be incorporated. The structure MSCP**6a** is thus preferred to MSCP**5** for the ion at *m*/*z* 504. The ions at *m*/*z* 510 and 511 are due to a small amount of ^{13}C^{18}O contamination of ^{13}C^{16}O. See Figure SI5 and SI6 for details.

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[13] The possibility that **I4′** gives CP**5** ($\Delta G < 2$ kcal mol^{-1}) by incorporation of an external CO is unlikely because the intramolecular process yielding **I5′** should be kinetically favored.

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