Reaction Mechanisms

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Lewis Base Promoters in the Pauson–Khand Reaction: A Different Scenario**

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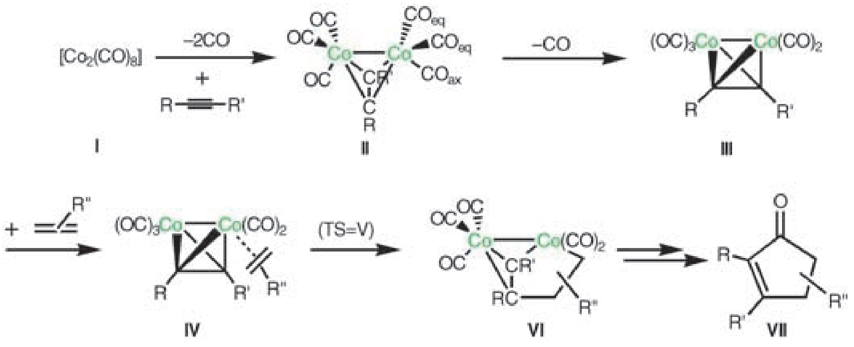
The Pauson–Khand reaction,[1] a dicobalt octacarbonyl mediated process for joining an olefin and an acetylene to produce a cyclopentenone (Scheme 1), is enjoying increased application in synthesis because of recent improvements that permit a broad range of substrates to be used successfully.[2–5] Spectacular rate and yield increases in both the intra- and intermolecular versions of the reaction have been found to result, in particular, from the addition of Lewis bases,[6] such as amines[3] and thioethers[4] as well as alcohols, ethers, and water.[5]



Scheme 1. Pauson–Khand mechanism.

Although the fundamental role of these Lewis base additives has received little study, it has been widely assumed that they function by accelerating the departure of a second CO ligand from the acetylene cobalt complex to create the requisite vacant site for olefin coordination, and in this way overcome the putative limiting factor.[6] Current reports abound with statements such as "[certain] Lewis bases in low-valent organotransition-metal complexes make the existing ligands labile and produce the reactive complexes"[6b] and "when amines coordinate to low-valent organotransition metals, the existing ligands on the metal become labile".[6a] However, do these spectacular increases really derive from a facilitated departure of a CO ligand to liberate a site for olefin coordination? We questioned this interpretation as it seemed clear that the obligatory loss of the first CO ligand would be energetically the same in the absence or presence of the promoter;[7] the fact that similar temperatures[8] are required for the reaction with and without a promoter being present provides evidence for this reasoning. Moreover, simple Lewis bases, essentially σ donors, should increase backdonation toward the remaining CO ligands by electronic enrichment of the metal, thus making the loss of the second CO ligand at best comparable, if not more difficult.[9] Herein, the prevailing view is shown to be incorrect and a new interpretation based on theoretical studies at the DFT level is outlined.

Yamanaka and Nakamura[10a] and our group[10b] have described the Pauson–Khand reaction pathway at the DFT level. Three particularly important findings resulted: First, the step that requires the most energy (ca. 26.4 kcal mol^{-1}) is decarbonylation,[10c] which occurs at the outset of the reaction (**II**→**III**, Scheme 1); second, equatorial (eq; $\mathbf{IV}_{eq}$) and axial (ax; $\mathbf{IV}_{ax}$) olefin coordination modes are possible (Figures 1 and 2), with the energies of activation for the formation of the cobaltacycle (**VI**) in the range 10.0–14.4 kcal mol^{-1} (the lowest-energy transition state is $\mathbf{V}_{ax}$);[10b] third, the formation of the cobaltacycle is reversible.[11]

In the present study, a CO ligand in complex **II** was replaced with a molecule of water, which occupies a lower-energy equatorial position ($\Delta E = 5$ kcal mol^{-1}, complex $\mathbf{III}_{H_2O}$; Figure 3, blue data).[13] Based on examination of the Co–CO bond lengths in $\mathbf{III}_{H_2O}$, extraction of a second

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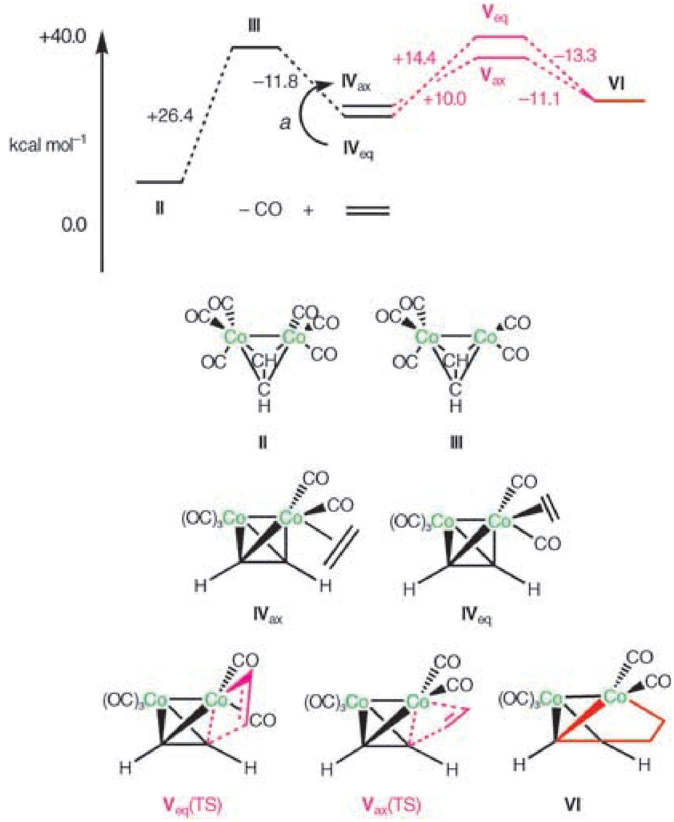

Figure 1. Energy barrier for formation of **VI** without a promoter. *a*) See Figure 2 for the transformation of $\mathbf{IV}_{eq}$ into $\mathbf{IV}_{ax}$. TS = transition state.

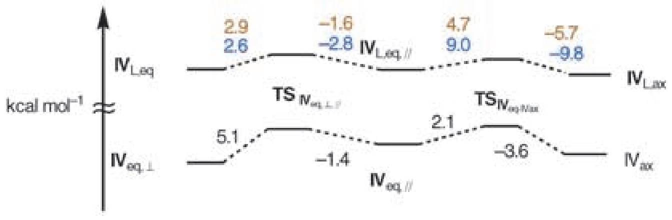

Figure 2. Transformation of $\mathbf{IV}_{eq}$ into $\mathbf{IV}_{ax}$. L = Ligand; ⊥, // are perpendicular and parallel coordination modes, respectively (with respect to the Co–Co axis).

molecule of CO from $\mathbf{III}_{H_2O}$ was found to engender complex $\mathbf{III}_{H_2O\text{-}CO}$, in which the CO ligand has been lost from the remaining equatorial position on the water-associated cobalt atom (24.7 versus 31.5 kcal mol^{-1} for removal of a CO ligand from the next lowest-energy position, which is in the *trans*-equatorial position on the water-free cobalt atom). It is perfectly clear that water does not facilitate the loss of a second CO ligand, as only 1.6 kcal mol^{-1} separates the loss of the first and second CO ligands.[14] Next, association of complex $\mathbf{III}_{H_2O\text{-}CO}$ with ethylene at the vacant site on the water-associated cobalt atom produced complexes $\mathbf{IV}_{H_2O,ax}$ and $\mathbf{IV}_{H_2O,eq}$ (Figure 3).[15] The former confronts an activation-energy barrier of 8.4 kcal mol^{-1} for the formation of cobaltacycle $\mathbf{VI}_{H_2O}$ via transition-state $\mathbf{V}_{H_2O,ax}$, whereas the latter must overcome an activation-energy barrier of 22.6 kcal mol^{-1} via $\mathbf{V}_{H_2O,eq}$. Thus, it can be assumed that

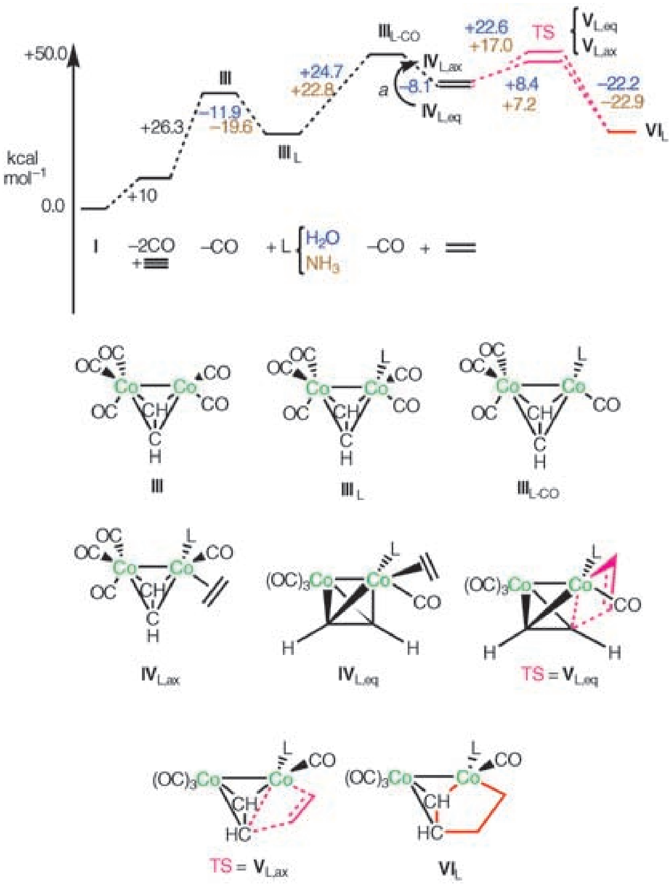

Figure 3. Energy barrier for formation of **VI** with promoter. *a*) See Figure 2 for the transformation of $\mathbf{IV}_{L,eq}$ into $\mathbf{IV}_{L,ax}$.

olefin insertion in the presence of water occurs from the axial position with an activation-energy barrier of 8.4 kcal mol^{-1}. This activation-energy barrier is lower than when the water is absent (then the olefin insertion is 10.0 kcal mol^{-1} from an axial position and 14.4 kcal mol^{-1} from an equatorial),[10b,16] but is nevertheless too high to explain the substantial acceleration of the reaction in its presence. A comparison of Figures 1 and 3, however, clearly reveals the remarkable ability of the promoter to stabilize the cobaltacycle: $\mathbf{VI}_{H_2O}$ is more than 22 kcal mol^{-1} lower than the transition state $\mathbf{V}_{H_2O,ax}$. As only 8.4 kcal mol^{-1} is required to reach this transition state in the forward direction, the formation of the cobaltacycle is in essence irreversible[17] in the presence of water. This irreversibility is the major effect of this promoter in the Pauson–Khand reaction.

Ammonia has also been studied at the DFT level to probe the remarkable accelerating effect of amines in the Pauson–Khand reaction, and the results have been found to parallel those obtained above with water as the promoter. Once again, removal of a second CO ligand from the complex ($\mathbf{III}_{NH_3}$) is energetically comparable to removal of the first ligand (Figure 3, brown data). The lower activation energy leading to the cobaltacycle transition state $\mathbf{V}_{NH_3}$ in the forward direction is 7.2 kcal mol^{-1} (Figure 3) and starting from the cobaltacycle $\mathbf{VI}_{NH_3}$, the activation energy is 22.9 kcal mol^{-1}, which effectively makes the insertion, as before, irreversible.

In conclusion, it has been shown for the first time that most simple Lewis base promoters are likely to achieve their dramatic rate effects in the Pauson–Khand reaction by imposing irreversibility on olefin insertion, rather than by facilitating the departure of a CO ligand to create a vacant site for olefin coordination, as previously believed. This discovery may help in the design of new ligands for improved efficacy and/or asymmetric induction in this important transformation.

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[7] It is important to point out that there is apparently no pathway (eventually of lower energy) that involves a concerted exchange[12] or direct attack of the promoter on a CO ligand.

[8] For example, the Pauson–Khand reaction of 1-(hept-6-en-1-ynyl)benzene in the presence of cyclohexylamine required 3 days at 25 °C to obtain the expected adduct in 46 % yield, whereas at 83 °C, typical thermal conditions, the reaction was complete after 5 min and afforded the adduct in 99 % yield.[3b]

[9] Although phosphines and phosphites can be considered Lewis bases, as they coordinate to the metal center through σ donation, the relatively low-energy phosphorus d orbitals, which permit overlap with the metal d orbitals, also make them π acceptors. For this reason, they cannot be treated in the present context as simple Lewis bases. Thioethers, which are also π acceptors although weaker than phosphines, appear from preliminary results to behave as H_2O and NH_3, namely, as pure σ donors (A. Milet, C. Perez del Valle, unpublished results).

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[11] Reversibility seems probable on closer examination, although the contrary was assumed[10b] based on earlier work.[1c,10a] This possibility is supported by a subsequent mass-spectrometric study[12] that detected in two separate experiments the insertion product prior to incorporation of any of the CO present and follows from the low CO concentration generally present in the Pauson–Khand reaction medium. (Reversibility does not affect the conclusion given in reference [10b].)

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[14] This finding is fully consistent with recent calculations (supported by X-ray structure determinations) carried out by Frenking et al. on the octahedral complexes $[M(CO)_6]$ and $[M(CO)_5L]$ ($M = Cr, Mo, W$; $L = H_2O, NH_3$). In this investigation, it was shown that replacing a CO ligand with a Lewis base (L) significantly shortens the M−CO bond *trans* to L and slightly shortens those *cis*. On the reasonable assumption that the length of a M−CO bond reflects its strength, the results of Frenking et al. imply that removal of a second CO ligand from $[M(CO)_5L]$ is at best no easier than removal of the first; see: G. Frenking, S. Dapprich, T. Meisterknet, J. Uddin, *Metal–Ligand Interactions in Chemistry, Physics and Biology* (Eds.: N. Russo, D. R. Salahub), Kluwer, Dordrecht, **2000**, pp. 73–89.

[15] Pseudorotation[10b] in the equatorially coordinated olefin complex $\mathbf{IV}_{H_2O,eq}$ to give the axially coordinated complex $\mathbf{IV}_{H_2O,ax}$ was determined to be energetically feasible (see Figure 2).

[16] This lowering of the energy of activation is because of a reduction in the gap energy between the highest occupied molecular orbital (HOMO) of the alkyne–$Co_2(CO)_4H_2O$ fragment and the lowest unoccupied molecular orbital (LUMO) of ethylene in $\mathbf{IV}_{H_2O}$ (0.211 versus 0.224 eV in the complex without the promoter, **IV**). As this interaction is involved in the formation of the new C–C bond of the cobaltacycle, it follows that the better overlap in $\mathbf{IV}_{H_2O}$ should translate into a lower activation energy.

[17] For a discussion on the effect of imposing irreversibility on a step in a reversible, multistep transformation, see: T. Baer, W. L. Hase in *Unimolecular Reaction Dynamics* (Eds.: M. L. H. Green, J. Halpem, S. V. Ley, T. Mukaiyama, J. P. Simons), Oxford University Press, Oxford, **1996**.