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Theoretical Study of the Regiochemistry-Determining Step of the Pauson−Khand Reaction

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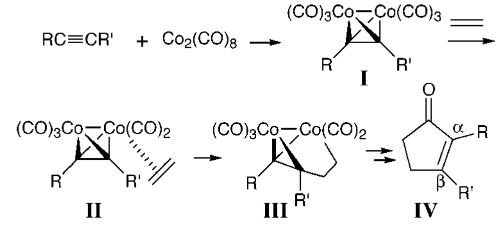
The Pauson−Khand reaction (PKR), a cobalt-mediated joining of an alkyne, an olefin, and carbon monoxide to yield a cyclopentenone (Scheme 1), has been the subject of a multitude of synthetic studies over the past 30 years.[1] In contrast, there has to date been a remarkable dearth of high-level computational studies of this important, yet still not intimately understood, reaction.[2,3] Herein we present a detailed B3LYP study[4] of the regiochemistry-determining event in the PKR, i.e., the formation of the cobaltacycle **III** from the olefin-coordinated dicobalt complex **II**,[5] with ethylene as the olefin and propyne as a prototypical nonsymmetric alkyne.

As seen in the propyne−dicobalt hexacarbonyl complex **1** (Figure 1), an axial (ax) and two equatorial positions, trans (eq_{tr}) and cis (eq_{cis}) with respect to the methyl group, are potentially available for parallel or perpendicular olefin coordination.[6] In the case of ethylene, the perpendicular coordination mode is favored by 3.4 kcal·mol^{-1} for the eq_{tr} position (3.3 kcal·mol^{-1}, eq_{cis}), with a barrier for the rotation ($TS_{tr//,\perp}$) calculated to be 4.7 kcal·mol^{-1} (Figure 2). The barrier for the pseudorotation of a CO and ethylene can easily be overcome at room temperature, since $TS_{eq,ax}$ lies only 2.3 and 2.9 kcal·mol^{-1} higher than the minima for $eq_{tr//}$ and ax coordination, respectively. Assuming that the barriers for the two other pseudorotations (ax $\rightleftharpoons$ eq_{cis} and eq_{tr} $\rightleftharpoons$ eq_{cis}) are similar, it can be concluded that ethylene does not occupy a unique coordination site at room (or elevated) temperature,[7] but moves easily from one position to another. In that the energy barriers for cobaltacycle formation range, as will be seen, from 11.0 to 16.8 kcal·mol^{-1},[8] *it is apparent that the initial coordination position of ethylene (and other olefins when pseudorotation is relatively facile) does not determine the regiochemistry in the PKR.*

Scheme 1



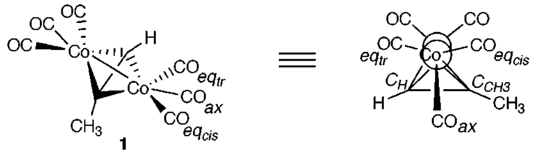


Figure 1. Possible olefin coordination sites (replacing a CO).

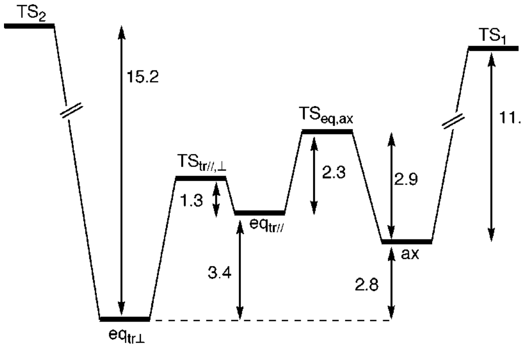


Figure 2. B3LYP/LANL2DZ* potential energy surface of the rotation of ethylene coordinated at the eq_{tr} position and the pseudorotation between $eq_{tr//}$ and ax coordination (energies in kcal·mol^{-1}).

Four transition states leading from the three most stable reactive complexes **2eq**$_{\mathbf{tr}\perp}$, **2eq**$_{\mathbf{cis}\perp}$, and **2ax** to the two cobaltacycles **3a** and **3b** have been characterized (Figure 3).[9] The two equatorial isomers **2eq**$_{\mathbf{cis}\perp}$ and **2eq**$_{\mathbf{tr}\perp}$ are more stable than **2ax** by 2.2 and 2.8 kcal·mol^{-1}, respectively.[10] Complex **2ax** has the shortest distance for the C−C bond formation, $r(C-C_H) = 2.816$ Å; the distance in **2eq**$_{\mathbf{tr}\perp}$ is $r(C-C_H) = 2.935$ Å and in **2eq**$_{\mathbf{cis}\perp}$ $r(C-C_{CH3}) = 2.955$ Å. Essentially the opposite is observed for the transition states for C−C bond formation from **2ax**: **TS1** has the longest distance, $r(C-C_H) = 1.953$ Å, followed by **TS3**, $r(C-C_{CH3}) = 1.980$ Å. Since the reaction **2ax** → **TS1** → **3a** is more

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(1) For reviews, see: (a) Schore, N. E. *Org. React.* **1991**, *40*, 1−90. (b) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297−341. (c) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263−3283. (d) Fletcher, A. J.; Christie, S. D. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1657−1668.

(2) For a DFT study of a trans effect, see: Robert, F.; Milet, A.; Gimbert, Y.; Konya, D.; Greene A. E. *J. Am. Chem. Soc.* **2001**, *123*, 5396−5400.

(3) For a recent DFT study of the PKR pathway, see: Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2001**, *123*, 1703−1708. It should be noted that in this work *only* acetylene was studied, thus the importance of the electronic effects that result from polarization of the acetylenic bond could not be evaluated and *only* equatorial olefin coordination was considered, although experimental data have suggested that axial olefin coordination may be involved (see: Derdau, V.; Laschat, S.; Jones, P. G. *Eur. J. Org. Chem.* **2000**, *4*, 681−689).

(4) Computational details: All calculations were performed with the Gaussian 98 suite of programs[4a] using a restricted B3LYP functional[4b,c] and the LANL2DZ[4d] for Co and a D95 split valence[4e] basis set for C, O, and H, with an augmentation of *d* polarization functions on C and O. The basis set is denoted as LANL2DZ*. All energies refer to zero point corrected energies. Net atomic charges have been calculated using natural population analysis from the NBO program[4f] at the same level of theory as for the optimizations. (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A6; Gaussian, Inc.: Pittsburgh, PA, 1998. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789. (d) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270−283. (e) Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; Plenum: New York, 1976; pp 1−28. (f) For a review, see: Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899−926.

(5) It is assumed that the initial C−C bond formation is irreversible and, from this point on, the regiochemistry is inalterable. See refs 1b and 3.

(6) The coordination mode is parallel/perpendicular with respect to the Co−Co axis. For axially coordinated ethylene, only one rotamer could be found. See Supporting Information for the optimized structures.

(7) PKR temperatures of ≥70 °C are common.

(8) This is in agreement with the work of Yamanaka and Nakamura,[3] in which a barrier of 14.4 kcal·mol^{-1} (from the eq position) was found with an analogous basis set.

(9) Cobaltacycle formation from **2eq**$_{\mathbf{tr//}}$ or **2eq**$_{\mathbf{cis//}}$ is highly unlikely since the shortest $r(C_{ethylene}-C_H) = 3.193$ and $r(C_{ethylene}-C_{CH3}) = 3.173$ Å, respectively.

(10) Such differences in stability cannot be explained solely by steric effects because both of the acetylenic substituents are rather small. The smallest close contact involving the ethylene moiety was found for eq_{cis} $r(H-H_{CH_3}) = 2.419$ Å.

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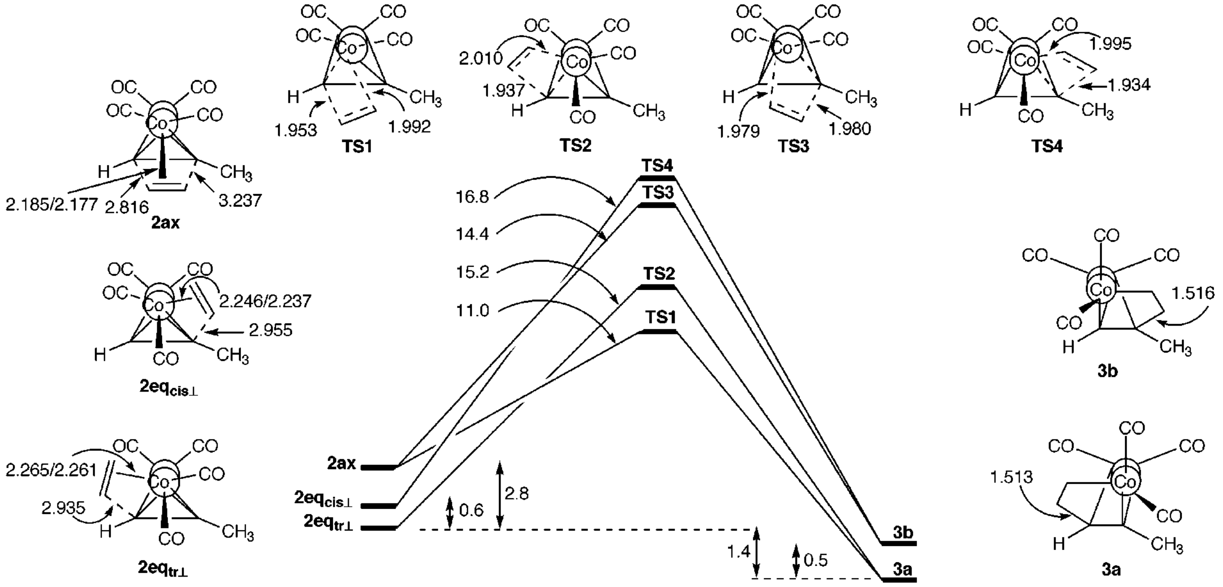

Figure 3. B3LYP/LANL2DZ* potential energy surface for the formation of the cobaltacycles (distances in Å and energies in kcal·mol^{-1}).

exothermic than **2eq**$_{\mathbf{tr}\perp}$ → **TS2** → **3a**, **TS1** should be found earlier on the bond formation reaction coordinate than **TS2** ($\delta r = 0.863$ vs 0.998 Å)[11] and, in addition, the more exothermic reaction should have the lower activation energy (11.0 vs 15.2 kcal·mol^{-1}),[12] and these phenomena are, in fact, observed. It can be noted that the reaction **2ax** → **TS3** → **3b** is more exothermic than **2eq**$_{\mathbf{cis}\perp}$ → **TS4** → **3b** and has a lower activation energy, yet **TS3** is found later than **TS4** ($\delta r = 1.257$ vs 1.021 Å); this is probably due to the long $C-C_{CH_3}$ in **2ax**. Additionally, there are strong indications that the polarization in the "acetylenic" C−C bond has an important influence on the stability of the transition states. The acetylenic carbon atom acts as a donor of electrons for the new C−C bond, therefore the transitions states involving C_H (-0.4 e$^-$) are more favorable than those involving C_{CH_3} (-0.2 e$^-$) (cf. **2eq**$_{\mathbf{tr}\perp}$ → **TS2** and **2eq**$_{\mathbf{cis}\perp}$ → **TS4**, where the distances between the reacting carbon atoms are nearly equal initially and in the transition states).

The important conclusion to be drawn from the above is that the reaction pathway **2ax** → **TS1** → **3a** is the most favorable: reactant **2ax** can, energetically, readily be formed from **2eq** and has substantially the lowest energy barrier for formation of the cobaltacycle.[13,14] Only **TS1** and **TS2**, significantly more stable than **TS3** and **TS4**, lead to **3a**, which is the cobaltacycle that affords the experimentally expected[1] cyclopentenone, with the methyl group at the α-position with respect to the carbonyl. It is noteworthy that cobaltacycle **3a** is slightly more stable than **3b** (Figure 3).

In summary, ethylene does not appear to react principally from an equatorial position but, through facile pseudorotation, from an axial position, the one of lowest activation energy for C−C bond formation. It is now clear that productive axial coordination of an olefin must be considered in theoretical as well as synthetic PKR studies.

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Supporting Information Available: Cartesian coordinates (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] (a) Bell, R. P. *Proc. R. Soc. London* **1936**, *A154*, 414−429. (b) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* **1938**, *34*, 11−24.

[13] Significantly, we have found that the analogous pathway is also of lowest energy for ethylene and unsubstituted (nonpolarized) acetylene. Axial coordination was not considered in ref 3.

[14] The interpretation in ref 2 remains reasonable where pseudorotation is energetically more demanding.