ORGANIC LETTERS

2002
Vol. 4, No. 19
3301−3304

Regiochemistry of S-Alkyl-Substituted Alkynes in Pauson–Khand Reactions. Is a Correlation with X-ray Data and Charge Distribution Calculations of the $Co_2(CO)_6$-Alkyne Complexes Possible?

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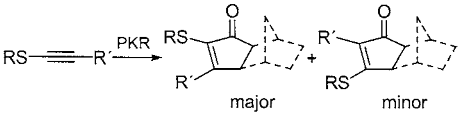
Received July 22, 2002

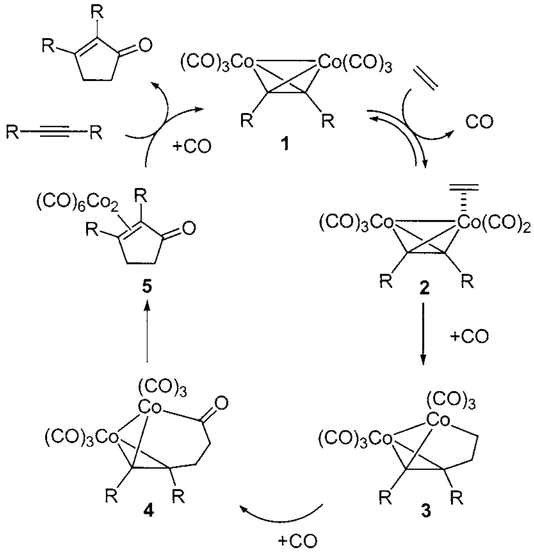
ABSTRACT



Pauson–Khand reactions (PKR) of RSC≡CR′ (6–10) yielded in all cases as the main product the regioisomer with the alkyl-S group disposed α to the CO group (16a–22a). Correlation of these results with X-ray data and charge distribution calculations of the corresponding dicobalthexacarbonyl complexes proves that a recently postulated “trans effect” in these complexes is not suitable for predicting the regiochemical outcome of the PKR unambiguously.

The Pauson−Khand reaction is a convenient procedure for generating cyclopentenone ring systems.[1,2] One equivalent of alkyne, alkene, and carbon monoxide can be assembled with $Co_2(CO)_8$ as a catalyst in a one-pot reaction. As a result of the one-pot nature of this protocol, there is a lack of information with respect to intermediates of this multistep reaction sequence. To rationalize the pathway,[3] it is generally assumed that as a first step the alkyne reacts with $Co_2(CO)_8$ to yield the dicobalthexacarbonyl complex **1** (Scheme 1). Subsequently, one CO unit in **1** is replaced by an olefin to afford **2**. This exchange is followed by irreversible insertion reactions, first to **3** and then to **4**. Finally, a reductive elimination yields the complex **5** from which cyclopentenone originates. By reaction with CO, the $Co_2(CO)_8$ is regenerated to form a catalytic cycle.[3]

Scheme 1. Assumed Mechanism for Pauson−Khand Reaction[3]



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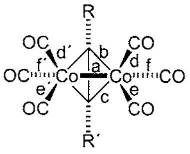
(1) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *Chem. Commun.* **1971**, 36; *J. Chem. Soc., Perkin Trans. 1* **1973**, 975−977.

(2) Reviews: Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855−5860. Pauson, P. L. In *Organometallics in Organic Synthesis*; de Meijere, A., tom Dieck, H., Eds.; Springer: Berlin, 1988; pp 233−246. Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M. Ed.; Pergamon: Oxford, 1991; pp 5, 1037−1064. Schore, N. E. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley & Sons: New York, 1991; pp 40, 1−90. Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; pp 12, 703−739. Geis, O.; Schmalz, H. G. *Angew. Chem., Int. Ed.* **1998**, *37*, 911−915.

(3) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861−5869.

10.1021/ol026578q CCC: $22.00

Recently, quantum chemical calculations have examined the mechanistic assumptions shown in Scheme 1 by calculating the energy of the assumed intermediates as well as the transition states.[4] Furthermore, the bonding properties of the alkyne−dicobalthexacarbonyl complex were investigated by DFT calculations,[5] in order to find out whether electronic effects could play a role in determining which CO ligand is substituted in the second step, from **1** to **2** (Scheme 1). Using the hybrid Hartree−Fock/DFT approach (B3LYP) and carrying out a population analysis, it was found that the bonding of the six CO groups in **1** is differently influenced by the substituents (**1a**, Figure 1).[5] The calculations reveal that the two pseudoaxial CO groups are bound stronger than the four pseudoequatorial ones. For R = H and R′ = CH_3, it is found that the pseudoequatorial CO groups that are positioned trans to R′ = CH_3 exhibit longer Co−CO bond lengths (*d* and *d*′) than the others. This has been explained by a polarization of the $Co_2(CO)_6$−alkyne complex by the substituents, meaning that the CH_3 substituent causes a positive polarization of the neighboring carbon atom, thus leading to the observed weakening of the trans-positioned Co−CO bond. For R = H and R′ = CO_2Me, the bond dissociation energies for all four pseudoequatorial groups are predicted to be about equal. As a consequence of the assumed mechanism, the bonding properties of **1a** (R = H, R′ = CH_3) should lead to the cyclopentenone with R′ disposed α to the CO group.



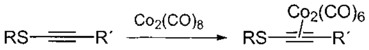
1a

Figure 1. $Co_2(CO)_6$−alkyne complex.

In connection with our interest in the structure of $Co_2(CO)_6$−alkyne complexes[6] and Pauson−Khand reactions of cyclic diynes,[7] we have prepared the alkyl-thiosubstituted alkynes **6**−**10** and reacted them with $Co_2(CO)_8$ to obtain the corresponding dicobalthexacarbonyl complexes **11**−**15** (Table 1).[8]

We used **6**−**10** because we assumed from our previous experience that most of the dicobalthexacarbonyl complexes should be solids. And indeed, for **11**−**14** we were able to grow single crystals that enabled us to investigate their structures in the solid state. In Table 2 we have listed the most relevant distances in the complexes. Our investigations revealed that the distances between the cobalt atoms (a in Figure 1) vary only slightly (2.46−2.47 Å) within the range reported for related complexes.[6] Larger variations are observed for the cobalt−carbon distances of the former alkyne unit (b and c in Figure 1). Most interesting with respect to the assumed regioselectivity in the Pauson−Khand reaction are the Co−CO distances of the pseudoaxial (*f* and *f*′ in Figure 1) and pseudoequatorial CO groups (*d* and *d*′; *e* and *e*′ in Figure 1). It is found that the average value for the pseudoaxial Co−CO distances $f^* = 0.5(f + f')$ is shorter than the average values *d** and *e**. The average value of the pseudoequatorial Co−CO distances cis to the MeS group (*d**) is found to be shorter than the trans distance (*e**) for **11**, **12**, and **14** (Table 2). In the case of **13**, *e** is found to be shorter than *d**.[9]

Table 1. Formation of $Co_2(CO)_6$−Alkyne Complexes[a]



alkyne	R	R′	complex
6	Me	Me	**11**
7	Me	^{t}Bu	**12**
8	Me	Ph	**13**
9	Me	CO_2Et	**14**
10	^{t}Bu	Me	**15**

[a] Reaction conditions: 1 equiv of alkyne, 3 equiv of $Co_2(CO)_8$, DCM, 8 h, from 0 °C to room temperature.

Table 2. Bond Lengths in $Co_2(CO)_6$−Alkyne Complexes[a]

complex R, R′	a^b [Å]	b^b [Å]	c^b [Å]	d^* [Å]	e^* [Å]	f^* [Å]
11 Me, Me	2.466	1.954	1.959	1.815	1.827	1.792
12 Me, ^{t}Bu	2.461	1.968	1.968	1.818	1.824	1.798
13 Me, Ph	2.470	1.962	1.980	1.830	1.823	1.792
14 Me, CO_2Et	2.470	1.965	1.942	1.817	1.834	1.801

[a] From crystallographic data. [b] Standard deviation varies between 0.0003 and 0.0019.

To correlate these values to the charge distribution in the complexes, we carried out a DFT (RB3LYP) single-point calculation based on the geometries of the X-ray structures (Table 3). Suprisingly, the calculations reveal that the expected trans relation between the positively polarized former alkyne carbon atom and the weakened pseudoequatorial Co−CO bonds exists only in complex **14** (R = Me, R′ = CO_2Et). For the others, **11** (R = CH_3, R′ = CH_3), **12** (R = CH_3, R′ = ^{t}Bu), and **13** (R = CH_3, R′ = C_6H_5), the positively polarized former alkyne carbon atom is positioned cis to the weakened pseudoequatorial Co−CO bonds.

If we assume that the longer (weaker) bond of the $Co_2(CO)_6$ complexes is cleaved first in the Pauson−Khand

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[4] Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2001**, *123*, 1703−1708.

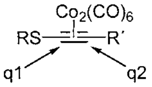
[5] Robert, F.; Milet, A.; Gimbert, Y.; Konya, D.; Green, A. E. *J. Am. Chem. Soc.* **2001**, *123*, 5396−5400.

[6] Rausch, B. J.; Gleiter, R.; Rominger, F. *J. Chem. Soc., Dalton Trans.* **2002**, 2219−2226.

[7] Rausch, B. J.; Becker, H.; Gleiter, R.; Rominger, F. *Synlett* **2002**, 723−726.

[8] Montenegro, E.; Poch, M.; Moyano, A.; Pericas, M. A.; Riera, A. *Tetrahedron* **1997**, *53*, 8651−8664.

Table 3. Charges in $Co_2(CO)_6$−Alkyne Complexes[a]

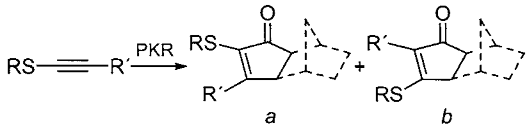


complex	R, R′	q1	q2
11	Me, Me	−0.445	−0.366
12	Me, ${}^tBu$	−0.472	−0.343
13	Me, Ph	−0.450	−0.510
14	Me, CO_2Et	−0.482	−0.499

[a] Atomic charges (e^-) from DFT (RB3LYP) single-point calculations based on the geometries of the X-ray structures.

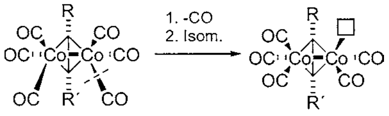
reaction and the “empty” position is replaced by the olefin (simple mechanism), we expect for the Pauson−Khand products in the cases of **6**, **7**, **9**, and **10** the regioisomers with configuration *a* and in the case of **8** configuration *b* (see Table 4). However, we might as well assume that an isomerization takes place after one Co−CO bond has been cleaved (see Scheme 2). In the resulting $Co_2(CO)_5$−alkyne complex, the “empty” position might be positioned trans to the positively polarized carbon of the former alkyne unit before it is replaced by the olefin (isomerization mechanism).

Table 4. Expected Regiochemistry, Simple vs Isomerization Mechanism



alkyne	complex	R, R′	simple mechanism	isomerization mechanism
6	**11**	Me, Me	*a*	*b*
7	**12**	Me, ${}^tBu$	*a*	*b*
8	**13**	Me, Ph	*b*	*a*
9	**14**	Me, CO_2Et	*a*	*a*
10	**15**	${}^tBu$, Me	*a*	*b*

Scheme 2. Isomerization Mechanism



In this case, we expect for the Pauson−Khand products of **8** and **9** the regioisomers with configuration *a* and in the cases of **6**, **7**, and **10** regioisomers with configuration *b* (see Table 4).

To probe these hypotheses, we have carried out the Pauson−Khand reaction with **6**−**10** using norbornene and ethylene as olefin components (Table 5). In the cases of **6**, **8**, and **10**, we were able to isolate cyclopentenone derivatives from the reaction with ethylene as well as norbornene, whereas for **9** only norbornene gave the desired Pauson−Khand product. Due most likely to steric hindrance, **7** did not react under Pauson−Khand conditions at all.

Table 5. Reactions, Yields, and Selectivities

alkyne	R, R′	olefin	reaction conditions[a]	yield [%] ratio of *a*:*b*[b]
6	Me, Me	ethylene	A	72 (**16**) 100:0
6	Me, Me	norbornene	B	64 (**17**) 100:0
8	Me, Ph	ethylene	A	32 (**18**) 100:0
8	Me, Ph	norbornene	B	69 (**19**) 100:0
9	Me, CO_2Et	norbornene	B	61 (**20**) 100:0
10	${}^tBu$, Me	ethylene	A	50 (**21**) 84:16
10	${}^tBu$, Me	norbornene	B	48 (**22**) 100:0

[a] Conditions A: 1 equiv of alkyne, 2 equiv of $Co_2(CO)_8$, 4 equiv of DMSO, 50 bar ethylene, 4 days at 100 °C, toluene. Conditions B: 1 equiv of alkyne, 1.2 equiv of $Co_2(CO)_8$, 10 equiv of norbornene, 3 days at 65 °C, toluene. [b] By ^1H NMR.

The isolated yields were good for **16**, **17**, **19**, and **20** (61−72%) and moderate for **18**, **21**, and **22** (32−50%). For **21**, we could isolate the two regioisomers (**21*a*** and **21*b***) in a ratio of 84:16, whereas for **16**−**20** and **22**, only the isomer with the alkyl-thio group in α-position relative to the CO group could be found. Our assignment of the structures of **16*a*** and **22*a*** is based on NMR experiments. We find a

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(9) **Crystal Structure Determination for 11:** $C_{10}H_6Co_2O_6S$; MW = 372.07; red; polyhedron; monoclinic; space group $P2_1/n$; $a = 6.9927(1)$ Å; $b = 13.8298(1)$ Å; $c = 14.7921(2)$ Å; $\beta = 90.808(1)$ °; $V = 1430.37(3)$ Å^3; $Z = 4$; $T = 200(2)$ K.; $d_{calcd} = 1.728$ g/cm^3; $F(000) = 736$; $\mu = 2.479$ mm^{-1}; 14 420 reflections collected; 3268 independent reflections ($R_{int} = 0.0328$); 2516 reflections observed ($I > 2\sigma(I)$); R(F) = 0.026; R(F^2) = 0.060; S (GOF) on $F^2 = 1.04$; $(\Delta\rho)_{max} = 0.33$ e/Å^3; $(\Delta\rho)_{min} = -0.41$ e/Å^3. **Crystal Structure Determination for 12:** $C_{13}H_{12}Co_2O_6S$; MW = 414.15; red; polyhedron; monoclinic; space group $P2_1/c$; $a = 8.2064(1)$ Å; $b = 8.2989(1)$ Å; $c = 25.1943(4)$ Å; $\beta = 93.466(1)$ °; $V = 1712.70(4)$ Å^3; $Z = 4$; $T = 200(2)$ K; $d_{calcd} = 1.606$ g/cm^3; $F(000) = 832$; $\mu = 2.080$ mm^{-1}; 17 120 reflections collected; 3913 independent reflections ($R_{int} = 0.0309$); 3371 reflections observed ($I > 2\sigma$ (I)); R(F) = 0.026; R(F^2) = 0.060; S (GOF) on $F^2 = 1.07$; $(\Delta\rho)_{max} = 0.22$ e/Å^3; $(\Delta\rho)_{min} = -0.52$ e/Å^3. **Crystal Structure Determination for 13:** $C_{15}H_8Co_2O_6S$; MW = 434.13; red; lamina; monoclinic; space group $C2/c$; $a = 27.7906(5)$ Å; $b = 8.0960(1)$ Å; $c = 15.2989(2)$ Å; $\beta = 96.431(1)$ °; $V = 3420.48(9)$ Å^3; $Z = 8$; $T = 200(2)$ K; $d_{calcd} = 1.686$ g/cm^3; $F(000) = 1728$; $\mu = 2.087$ mm^{-1}; 17 227 reflections collected; 3927 independent reflections ($R_{int} = 0.0670$); 2684 reflections observed ($I > 2\sigma(I)$); R(F) = 0.041; R(F^2) = 0.087; S (GOF) on $F^2 = 0.97$; $(\Delta\rho)_{max} = 0.74$ e/Å^3; $(\Delta\rho)_{min} = -0.48$ e/Å^3. **Crystal structure determination for 14**: $C_{12}H_8Co_2O_8S$; MW = 430.10; red; polyhedron; triclinic; space group P1; $a = 7.1307(3)$ Å; $b = 7.8746(3)$ Å; $c = 15.4358(6)$ Å; $\alpha = 99.689(1)$ °; $\beta = 101.569(1)$ °; $\gamma = 97.369(1)$ °; $V = 825.16(6)$ Å^3; $Z = 2$; $T = 200(2)$ K; $d_{calcd} = 1.731$ g/cm^3; $F(000) = 428$; $\mu = 2.170$ mm^{-1}; 8591 reflections collected; 3766 independent reflections ($R_{int} = 0.0272$); 3099 reflections observed ($I > 2\sigma(I)$); R(F) = 0.025; R(F^2) = 0.061; S (GOF) on $F^2 = 0.99$; $(\Delta\rho)_{max} = 0.33$ e/Å^3; $(\Delta\rho)_{min} = -0.32$ e/Å^3.

NOESY-coupling between the protons of the methyl group and the neighboring proton(s) of the cyclopentenone ring. For **18*a*** and **19*a***, the structures were established by X-ray investigations of the corresponding sulfoxides of **18*a*** and **19*a***. The structures of **17*a***, **20*a***, **21*a***, and **21*b*** followed from the crystal structures of **17*a***, **20*a***, and **21*a***.

Using the Co−CO length as a guide and assuming that the "weakest bound" CO is replaced by the olefin, we arrive at the correct regiochemistry for **6**, **9**, and **10**. Only in **8** is the regiochemistry of the major product not in accordance with the expected result. On the other hand, if we use the polarization of the former alkyne unit as an indicator, assuming that after CO dissociation the olefin coordinates trans to the positively polarized carbon of the former alkyne unit, we obtain the correct regiochemistry for **8** and **9**, whereas in the case of **6** and **10**, the correct regiochemical outcome of the Pauson−Khand reaction cannot be predicted.

From these results we conclude that it is not possible to predict the regiochemical outcome of the major Pauson−Khand product on the basis of structural data that represent the ground state of the corresponding dicobalthexacarbonyl complexes. Therefore, we believe that an extensive theoretical study is necessary in order to find out whether electronic effects in the transition states of the corresponding reaction steps influence the regiochemical outcome of the Pauson−Khand reaction of these compounds.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft (SFB 623), the Fonds der Chemischen Industrie, and the BASF Aktiengesellschaft Ludwigshafen.

Supporting Information Available: Experimental procedures and analytical and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL026578Q