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Bornane-2,10-sultam: a highly efficient chiral controller and mechanistic probe for the intermolecular Pauson–Khand reaction

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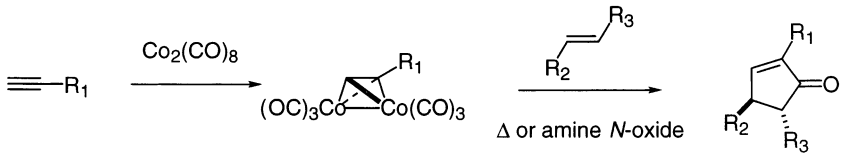
Abstract—The origin of the essentially complete diastereoselectivity observed in the intermolecular Pauson–Khand reactions of *N*-(2-alkynoyl)bornane-2,10-sultam derivatives has been studied by a combination of experimental and theoretical techniques. PM3(tm) calculations show that the corresponding dicobalthexacarbonyl complexes have only two stable conformations that are geometrically very similar. The CD spectra of these complexes are in accordance with these calculations. Finally, a PM3(tm)//DFT study of the putative intermediates in the Pauson–Khand cycloaddition of complex **5b** with norbornadiene shows that an oxygen atom of the sultam moiety of the auxiliary can selectively chelate one of the cobalt atoms of the initially formed alkyne–dicobalt-pentacarbonyl complex, and that the coordination of the olefin to the same cobalt in a well-defined orientation is also the energetically preferred option. This chelation effect leads to an extremely efficient chirality transfer to the C_2Co_2 tetrahedral core of the alkyne–dicobaltcarbonyl complex and completely determines the diastereoselectivity of the process. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The cobalt-mediated 2-cyclopentenone synthesis first disclosed in the early 1970s by Pauson, Khand and co-workers[1,2] (Scheme 1) now occupies a prominent place among transition-metal promoted cycloaddition reactions.[3] The wide acceptance of this reaction is attributable to factors such as its experimental simplicity, its compatibility with a wide range of functional groups, its predictable regio- and stereochemical outcome,[2] and the development of catalytic[1b,4] and asymmetric versions. In this respect, it is worth noting that whereas in the last 15 years a number of practical approaches to enantioselective intramolecular Pauson–Khand reactions have appeared in the chemical literature,[5,6] the achievement of high levels of enantiocontrol in intermolecular Pauson–Khand reactions in a general fashion still appears to be a challenging task.[7–9]

Some of the best results, both in terms of yields and diastereoselectivities, have been achieved through the use of chiral 2-alkynoic acid derivatives.[10–12] In particular, unprecedented high stereoselectivities are observed in the Pauson–Khand cycloaddition of *N*-(2-alkynoyl)bornane-2,10-sultam derivatives **1a**–**2d** with norbornadiene or norbornene (Scheme 2 and Table 1).[12] The *exo*-1,4-dicarbonyl regioisomers **2a**–**2d** and **3a** are the exclusive (for R = Ph or Me_3Si) or the major (R = Me or CH_2OMe) products of the reaction, and are consistently formed in high diastereoisomeric purity (from 125:1 to more than 800:1 diastereoisomeric ratios, rigorously established by HPLC). It is thus clear



Scheme 1.

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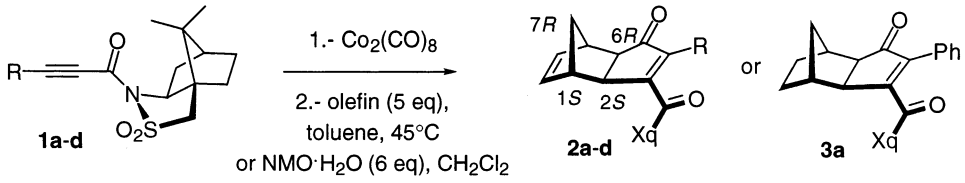


Scheme 2.

Table 1. Diastereoselective intermolecular Pauson–Khand reactions of *N*-(2-alkynoyl)bornane-2,10-sultam derivatives

Alkyne	Olefin	Reaction conditions	Product (yield, d.r.)
1a (R = Ph)	Norbornadiene	CH_2Cl_2, 6 equiv. NMO·H_2O, 0°C to rt, 1 h	**2a** (93%, >800:1)
1a (R = Ph)	Norbornene	CH_2Cl_2, 6 equiv. NMO·H_2O, 0°C to rt, 1 h	**3a** (54%, 125:1)
1b (R = $SiMe_3$)	Norbornadiene	CH_2Cl_2, 6 equiv. NMO·H_2O, 0°C to rt, 18 h	**2b** (78%, >800:1)
1c (R = Me)	Norbornadiene	Toluene, 45°C, 12 h	**2c** (55%, 318:1)[a]
1d′ (R = CH_2OMe)[b]	Norbornadiene	Toluene, 45°C, 12 h	**2d′** (52%, >800:1)[c]

[a] 24% of the regioisomeric 1,3-dicarbonyl adduct (as a non-separable 1.7:1 diastereoisomer mixture) was also obtained.
[b] The (1*S*,5*R*,7*R*)-bornane-2,10-sultam was used in this case, leading to **2d′** with (1*R*,2*R*,6*S*,7*S*)-configuration.
[c] 23% of the regioisomeric 1,3-dicarbonyl adduct (as a non-separable 1.1:1 diastereoisomer mixture) was also obtained.

that in several instances the bornane-2,10-sultam moiety imparts a high stereochemical bias to the reaction, leading to the practically exclusive formation of a single diastereoisomer (starting from (1*R*,5*S*,7*S*)-bornane-2,10-sultam affords the (1*S*,2*S*,6*R*,7*R*)-diastereoisomer). If we make the assumption that the stereoselectivity of the process is determined by the free-energy difference between a single pair of diastereoisomer transition states, this implies that this energy gap must be (at 0°C) higher than 15.2 kJ mol^{-1} (3.6 kcal mol^{-1}). Given the relatively high steric hindrance of the starting alkynes, the low temperatures at which the reactions take place is also remarkable.

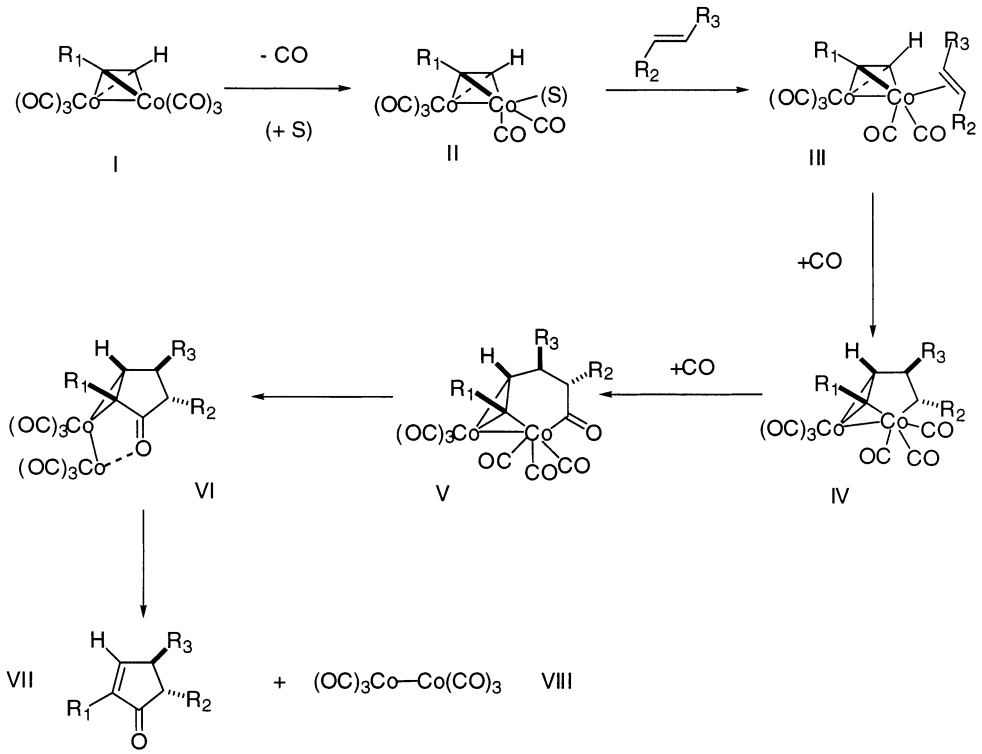
The outstanding stereoselectivity of the Pauson–Khand reaction of *N*-(2-alkynoyl)bornane-2,10-sultams prompted us to take a close look at the conformational properties of the corresponding dicobalthexacarbonyl complexes, and to obtain, by theoretical means, the structures and energies of the proposed intermediates of the reaction, in order to clarify the origin of the stereochemical bias induced by the bornanesultam moiety. We disclose herein the results of this study, which not only allows a rationalization of the observed diastereoselectivities, but also provides some clues on the general mechanism of the intermolecular Pauson–Khand reaction.

2. Results and discussion

2.1. Setting out the problem: mechanistic background of the Pauson–Khand reaction

The usually accepted mechanism of the Pauson–Khand reaction[13–15] is summarized in Scheme 3. Starting from the alkyne–dicobalt hexacarbonyl complex **I**, the first step involves the loss of a carbonyl ligand to give a pentacarbonylic species **II**, that is probably solvent coordinated. This transient species subsequently gives rise to an olefin-bonded complex **III**. The third step involves insertion of the π-complexed olefin into a carbon–cobalt bond of the cluster, and leads to the formation of the cobaltacycle **IV**. In this step, the first of the three single carbon–carbon bonds created in the reaction is formed, and both the regio- and stereochemistry of the cyclopentenone adduct are determined. It is important to recall here that in the transition state for this step the olefinic bond and the carbon–cobalt bond in which the insertion takes place must reach a syn-periplanar orientation. The next step involves insertion of a carbon monoxide ligand into the newly created carbon–cobalt bond and generates an acyl–cobalt complex **V**, that through reductive elimination of cobalt affords the complexed enone **VI**. Another reductive cobalt elimination gives the final product **VII** and a dicobaltcarbonyl fragment **VIII**. Under the appropriate reaction conditions, **VIII** can regenerate the starting complex **I** from the corresponding alkyne, leading to an overall catalytic process in dicobalt octacarbonyl.[4] Under the most commonly used reaction conditions, however, **VIII** undergoes irreversible decomposition and the overall process is stoichiometric in cobalt.

The carbon monoxide dissociation from the alkyne complex **I** is a highly endothermic step; the binding energies of the CO ligands in alkyne–dicobalthexacarbonyl complexes are of the order of 35–45 kcal mol^{-1},[15] and only a fraction of this energy can be recovered through coordination with the solvent. This initial dissociation can be promoted thermally (cf. heating in a hydrocarbon solvent), photochemically,[4b,16] oxidatively (by using a tertiary amine *N*-oxide that converts a metal-bound carbonyl into carbon dioxide),[17] or by the presence of a coordinating species.[18] In his mechanistic proposal for the Pauson–Khand reaction, Magnus[13] assumed that the cobaltacycle-forming step (from **III** to **IV**) was rate-determining and that the formation of the olefin-bound complex **III** from **I** was a reversible process. While this is probably true when the reaction is performed under thermal conditions and in an atmosphere of carbon monoxide, it is more likely that when



Scheme 3.

the reaction conditions are such that the carbon monoxide loss from **I** is irreversible the formation of **III** is the rate- and product-determining step.

When the starting alkyne is chiral, the two cobalt atoms of the hexacarbonyl complex **I** become diastereotopic, so that for a prochiral olefin with two stereoheterotopic faces, even assuming a fluxional behaviour of the ligands at each cobalt, at least four different kinds of olefin-coordinated complexes **III** have to be taken into account when trying to rationalize the stereochemical outcome of the reaction. Nevertheless, during our studies on the inter- and intramolecular Pauson–Khand reactions of chiral substituted alkynes, we have found that the absolute configuration of the major adducts obtained from the cyclization can be accurately predicted by analyzing the conformational behaviour of the starting dicobalthexacarbonyl complex (with the assumptions that the olefin coordinates preferentially to the less hindered cobalt atom and with an orientation that minimizes the steric interactions in the resulting complex). Our initial goal was therefore to evaluate the conformational preferences of the dicobalthexacarbonyl complexes of *N*-(2-alkynoyl)bornane-2,10-sultams, in order to see if this simplified approach could account for the very high diastereoselectivities of their intermolecular Pauson–Khand cyclizations.

2.2. Theoretical conformational study of the dicobalthexacarbonyl complex 5b

We began our study with a theoretical evaluation of the conformational behaviour of the alkyne–dicobalthexacarbonyl complex derived from **1b**, which as we have already seen shows an essentially complete diastereoselectivity (>800:1 d.r.) in its reaction with norbornadiene. Given the size of this system, we decided to perform the geometry optimizations with the semiempirical PM3(tm) procedure, which incorporates parametrization for transition metals to the original PM3 method,[19] as implemented in the SPARTAN package of programs.[20] In order to check the reliability of this procedure for alkynoic acid-derived complexes, we calculated the most stable geometries of both the acetylenedicarboxylic acid–dicobalthexacarbonyl complex **4a** and the dimethyl acetylenedicarboxylate–dicobalthexacarbonyl complex **4b** (Fig. 1), and the results were compared with the experimental (X-ray diffraction) geometries reported for these compounds.[21] As can be seen from the data gathered in Table 2, the agreement between the calculated and the experimental geometrical parameters is rather good, the only significant differences being that the PM3(tm) procedure slightly overestimates the cobalt–cobalt and the carbon–carbon bond lengths of the cluster by 0.06 and 0.16 Å, respectively.

Having thus established the ability of the PM3(tm) method to reproduce the geometry of the dicobalthexacarbonyl complexes of electron-deficient alkynes, we

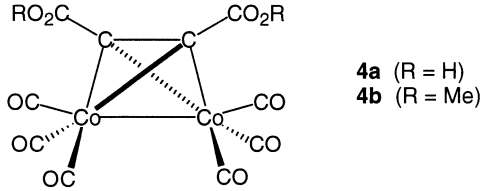


Figure 1. Complexes **4a** and **4b**.

Table 2. Selected calculated (PM3(tm)) and experimental[21] (X-ray) geometrical parameters of the $C_2Co_2(CO)_6$ moiety of complexes **4a** and **4b** (see Fig. 1)

	4a		**4b**	
	Experimental[21a]	Calculated	Experimental[21b]	Calculated
Bond lengths (Å)				
Co–Co	2.47	2.54	2.48	2.54
Co–C	1.93–1.95	1.96–1.97	1.91–1.93	1.96–1.98
Co–CO	–	1.80–1.82	1.70–1.80	1.81–1.82
C–CO_2R	–	1.47–1.48	1.40–1.44	1.48–1.49
C–C	1.35	1.51	1.33	1.51
Bond angles (°)				
Co–C–Co	79.3–79.7	80.6–80.9	79.7–80.7	80.0–80.4
C–Co–Co	50.0–50.3	49.5–49.7	–	49.9–50.0
C–Co–C	40.9–41.0	45.2	40.5–40.7	44.9–45.0
OC–Co–CO	–	98.7–100.0	104–105	98.1–99.5

applied it to the determination of the most stable geometries of the dicobalthexacarbonyl complex **5b**, derived from (1*R*,5*S*,7*S*)-*N*-(3-trimethylsilylpropiolyl)-bornane-2,10-sultam **1b**. After an exhaustive search, we located only two stable conformers for this compound, which we shall refer to as **5b**-I and **5b**-II, and whose structures, viewed from the side opposite to the $Co_2(CO)_6$ moiety, are shown in Fig. 2. Whereas **5b**-I is slightly more stable (ca. 1 kcal mol^{-1}) than **5b**-II, they are geometrically very similar, since in both cases the amide carbonyl is roughly eclipsed with the trimethylsilyl group; the values of the dihedral angles between the C=O and the C–Si bonds for **5b**-I and **5b**-II are +21.2 and −23.4°, respectively. On the other hand, the N–SO_2 bond of the sultam presents in both cases a strict antiperiplanar disposition with the amide carbonyl, in accordance with X-ray diffraction studies of other *N*-acyl sultams.[22] It is worth noting here that we have previously found that *N*-(2-alkynoyl)oxazolidinone derived complexes present a similar lowest energy conformation, in which the amide carbonyl also eclipses the other alkyne substituent, while the oxazolidinone carbonyl adopts an *anti* relationship with respect to it.[11]

In both **5b**-I and in **5b**-II the camphor moiety of the auxiliary is relatively far away from the $C_2Co_2(CO)_6$

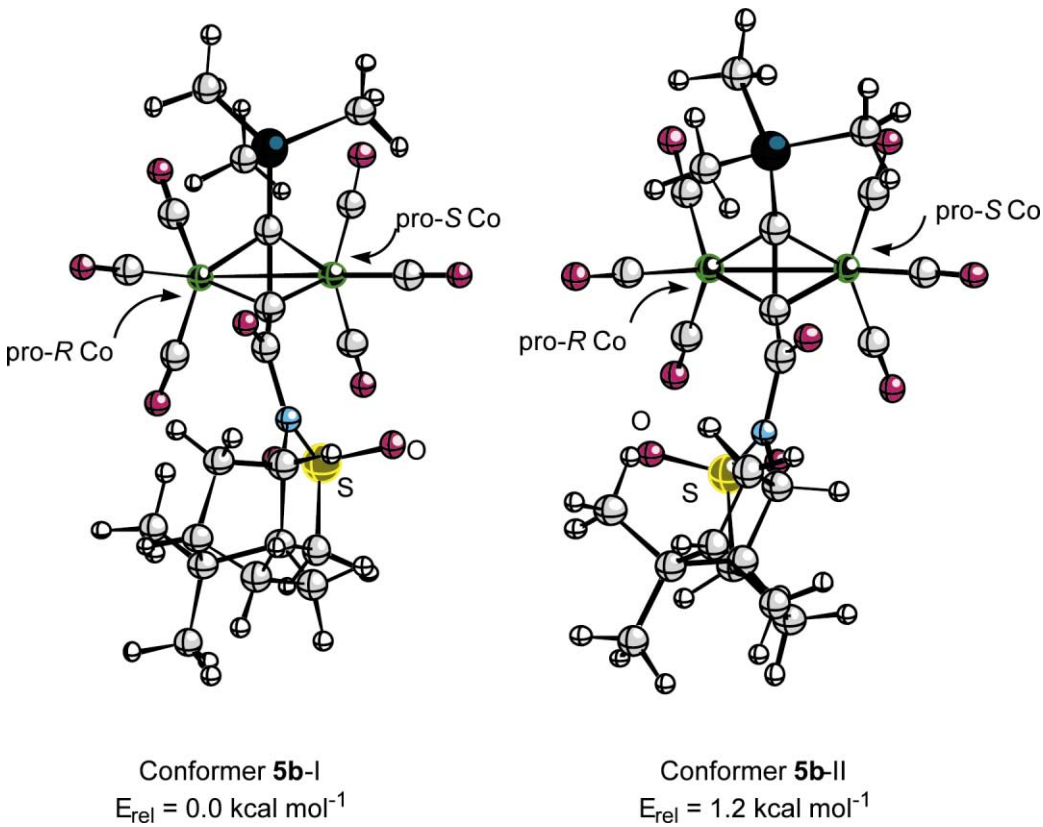


Figure 2. PM3(tm)-optimized minimum energy conformers of complex **5b**.

core, and does not appear to be able to exert a strong directing effect on the coordination of the olefin. On the other hand, the sultam ring is disposed in the vicinity of the $Co_2(CO)_6$ fragment: in the **5b**-I conformer, the SO_2 group is oriented close to the pro-*S* cobalt atom, so that the olefin should coordinate to this conformer preferentially by the pro-*R* cobalt (Fig. 3). It can be readily seen however that the situation is just the opposite for the less stable conformer **5b**-II; in this case, the SO_2 is close to the pro-*R* cobalt, therefore directing the olefin to the pro-*S* cobalt. Given the small calculated energy difference between the two conformers, it is not clear that the preferential coordination of the olefin to the pro-*R* cobalt can account for the essentially complete stereochemical bias shown by the reaction, which as we have seen requires free-energy differences between competing transition states higher than 3.6 kcal mol^{-1}. We decided therefore to perform further experiments and calculations on this system.

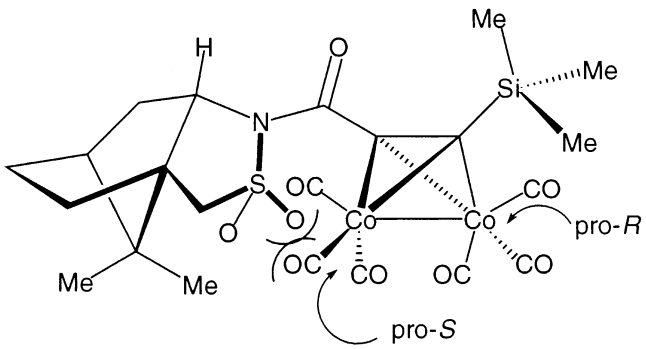


Figure 3. Schematic representation of conformer **5b**-I, showcasing the shielding of the pro-*S* $Co(CO)_3$ moiety by the SO_2 group.

2.3. Chiroptical study of 2-alkynoic acid-derived dicobalthexacarbonyl complexes

The circular dichroism (CD) spectra of the dicobalthexacarbonyl complexes of chiral acetylenes show several bands in the 300–600 nm zone that can be assigned to chirally perturbed UV transitions of the $C_2Co_2(CO)_6$ moiety. After analysing the CD spectra of a number of chiral (alkyne)dicobalthexacarbonyl complexes of known absolute configuration, Pályi et al. derived a quadrant rule for the 'upper' or 'acetylenic' zone of the complex that can be correlated with the sign of the first low-energy (λ>300 nm) CD band (Fig. 4).[23]

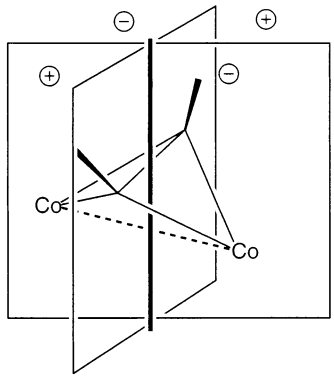


Figure 4. Upper sector quadrant rule of the $C_2Co_2(CO)_6$ chromophore.

We have also recently shown that the sign of the CD absorption at ca. 500 nm can be correlated to the absolute configuration of the chiral $C_2Co_2(CO)_5L$ moiety in phosphine–monosubstituted (1-alkyne)dicobaltpentacarbonyl complexes.[8g] We measured therefore the CD spectra of the complexes **5a** (derived from (1*R*,5*S*,7*S*)-*N*-(3-phenylpropiolyl)bornane-2,10-sultam **1a**) and **5b**, hoping to get some information about their conformational behaviour in solution (Fig. 5). We also obtained the CD spectrum of the *N*-(2-butynoyl)-oxazolidinone-derived complex **6**. It is interesting to note that for this complex, even though the absolute configuration of the camphor moiety is opposite to that of **5a** and **5b**, theoretical calculations predict a conformational behaviour very similar to that of **5b**, because in this case the eclipsing of the amide carbonyl with the other alkyne substituent disposes the camphor moiety of the oxazolidinone in the vicinity of the pro-*S* cobalt atom (corresponding to the pro-*R* cobalt in **5b**). The degree of similarity between the CD spectra of complexes **5a**, **5b** and **6** should then be a reliable test for the theoretical conformational analysis of the preceding section.

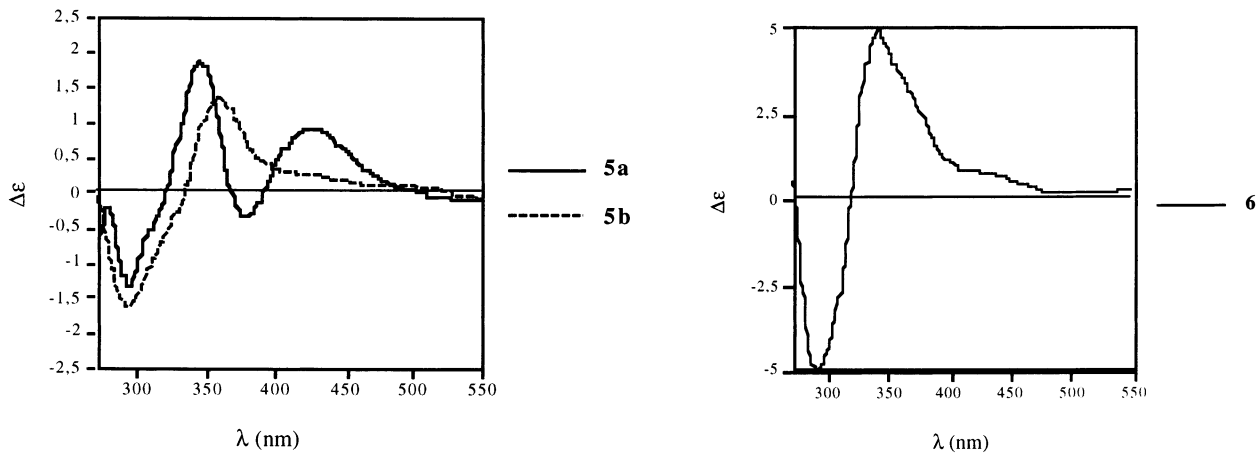


Figure 5. CD spectra of dicobalthexacarbonyl complexes **5a**, **5b** and **6** (dichloromethane, 25°C).

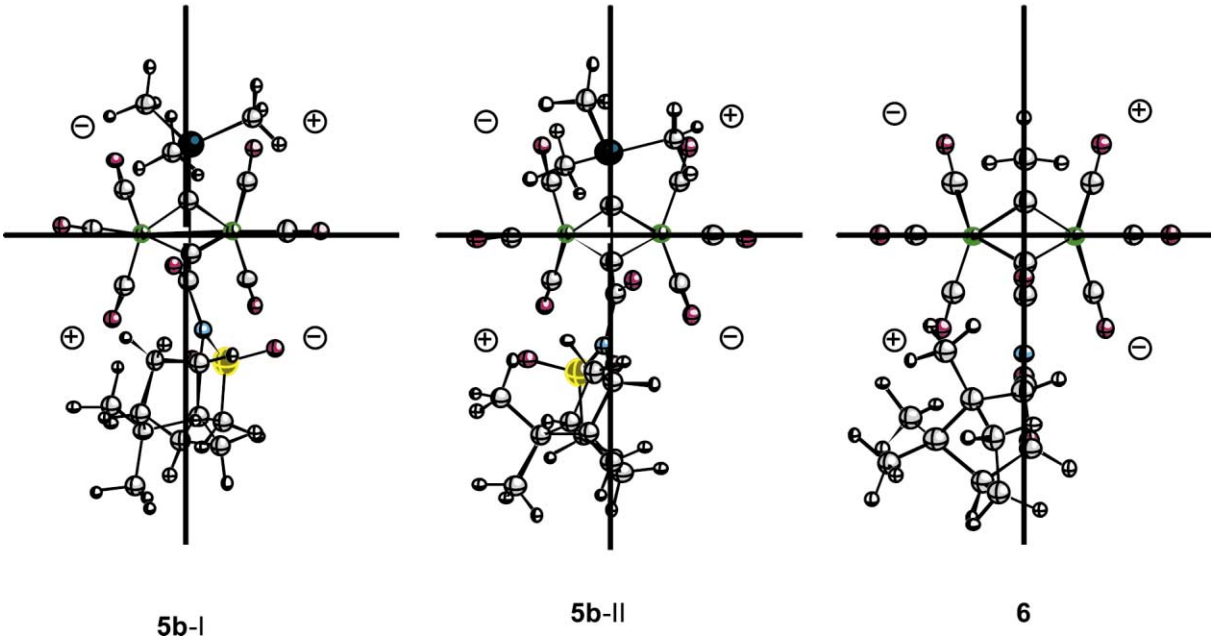
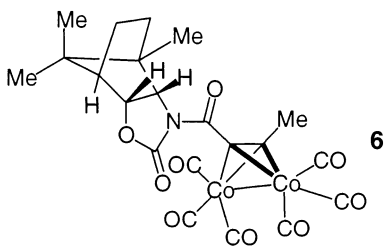


Figure 6. Quadrant rule projection (upper sectors) of conformers **5b**-I, **5b**-II and **6**.



Both **5a**, **5b** and **6** show a maximum positive dichroism at ca. 350 nm. In fact, the only significant difference (leaving aside the presence of a secondary maximum at 425 nm in the CD spectrum of **5a**, attributed to the phenyl substituent) between the spectra of these complexes lies in the different $\Delta\varepsilon$ values, that are much higher for **6** than for both **5a** and **5b**. The quadrant rule projections (upper sectors) of conformers **5b**-I and **5b**-II and of the low-energy conformation of **6** (according to PM3(tm) calculations) are depicted in Fig. 6. As can be readily seen, both in **5b**-II and in **6** the chiral auxiliary mainly occupies a positive quadrant, while in the case of conformer **5b**-I a significant proportion of the camphor moiety is disposed in the vicinal negative sector. The observed trends in the CD spectra are therefore in good accordance with the calculated conformations, and give support in particular to the hypothesis that the contribution of conformer **5b**-I to the equilibrium conformational mixture of complex **5b** in solution is the major one or at least non-negligible.

2.4. Theoretical study of the Pauson–Khand reaction between complex 5b and norbornadiene

Since the analyses of the conformational preferences of the *N*-(2-alkynoyl)bornane-2,10-sultam-derived complexes did not afford a clear-cut explanation for the very high stereoselectivities of their Pauson–Khand cyclization reactions with strained olefins, we turned our attention to the theoretical determination of the energies and structures of the most relevant intermediates along the reaction path, according to the mechanistic hypothesis summarized in Scheme 3. In doing so we hoped to identify a pair of diastereoisomer intermediates leading to opposite enantiomers of the final product, and whose energetic difference would be significant enough (ideally higher than 3.5 kcal mol^{-1}) to attribute to the preferential formation of one of them, the ultimate reason for the strong stereochemical bias exhibited by the reaction. In order to do so, we decided to examine a real case, i.e. the cocyclization of the alkyne **1b** (via the dicobalthexacarbonyl complex **5b**) with norbornadiene. As in Section 2.2, we decided to perform the geometry optimizations with the PM3(tm) method of the SPARTAN package programs,[20] complemented if necessary with single point calculations at density functional theory (DFT) level, as implemented in the ADF 2.0.1 code,[24] using the Vosko–Wilk–Nusair (VWN) local exchange correlation potential[25] with Perdew–Wang 91 nonlocal exchange and nonlocal correlation corrections.[26] The basis set used was a double-ζ STO, augmented to a triple-ζ STO in the 3d shell of Co atoms, that treats the $1s^2 2s^2 2p^6$ electrons of Co atoms and the $1s^2$ electrons of C and O atoms with the 'frozen-core' approximation according to the procedure of Baerends et al.[24a] This basis set is termed II(DZ)-SC in the ADF program.

Initially, we set out to characterize the dicobaltpentacarbonyl complexes derived from **5b**. Since, as we have already mentioned, the initial CO loss is a highly endothermic process, in doing so we wanted to evaluate the possibility that a first chiral discrimination, favoring the CO dissociation from one of the two diastereotopic cobalt centres, could take place at this initial stage of the reaction (see Scheme 3). In fact, all of the six CO ligands are non-equivalent in a C_1-symmetric alkyne–

dicobalt complex, so that six different pentacarbonyl complexes are possible. The corresponding six CO *relative* dissociation energies (calculated as the energy differences between conformer **5b**-I and the energy-minimized geometries of the six possible pentacarbonyl complexes) are given in Fig. 7.

According to the PM3(tm) calculations, the initial CO loss from the hexacarbonyl complex should take place preferentially from one of the equatorial positions which are proximal to the camphorsultam moiety, a result which can be easily understood on the basis of the steric interactions between the sultam ring and the CO ligands located in these positions. While the smallest dissociation energy appears to correspond to the pro-*S* cobalt, we thought that this stability order could be reversed if the SO_2 group (that as we have seen is placed closely to the two equatorial proximal to the acyl moiety) could act as an internal ligand, thus stabilizing the coordinatively unsaturated pentacarbonyl complexes. We were pleased to find that after a small geometrical distortion, the two most stable pentacarbonyl complexes led to the chelated intermediates **7**-I and **7**-II (Fig. 8).

As it can be seen, one of the oxygens of the sulfone can act as a ligand to the cobalt upon the loss of an equatorial carbon monoxide, facilitating the formation of the pentacarbonyl complex that, as we have discussed in Section 2.1, is the rate-determining step of the process. The intermediacy of these internally chelated species would then explain the relatively low temperatures at which the intermolecular Pauson–Khand reactions of the bornane-2,10-sultam-substituted alkynoates **1a**–**1d** take place. Moreover, the fact that intermediate **7**-II, in which the chelated cobalt is the pro-*R* one, is much more stable (by 6.7 kcal mol^{-1}) than intermediate **7**-I should strongly direct the coordination of the olefin to the $eq_{\alpha R}$ site of complex **5b**, therefore exerting a first stereodiscriminating step. The Co–O_2S bonding energy

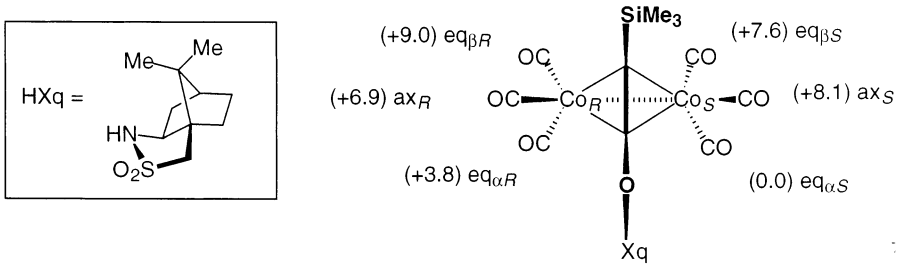


Figure 7. Calculated relative dissociation energies (kcal mol^{-1}, PM3(tm) method) of the CO ligands in complex **5b**. The six non-equivalent coordination sites around the metals are designated according to the following codes: eq, equatorial (*cis* to the Co–Co bond); ax, axial (*trans* to the Co–Co bond); α, β, proximity to the α,β alkyne positions; *R*, *S*, topicity of the Co atom in the tetrahedral prostereogenic C_2Co_2 core.

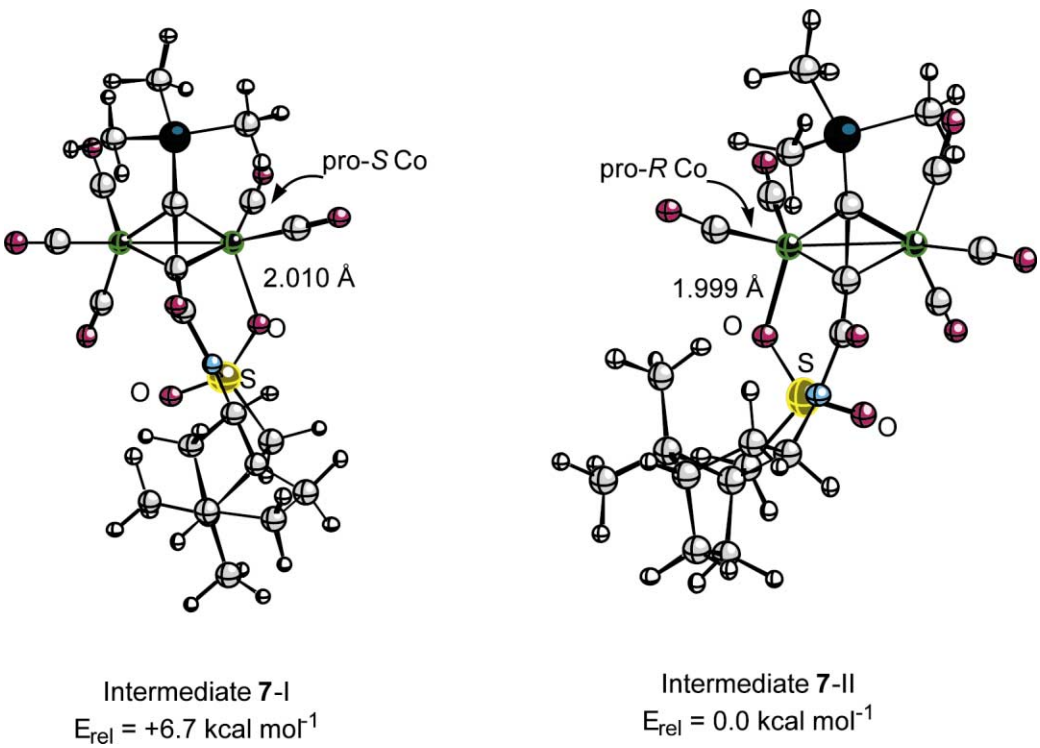


Figure 8. PM3(tm)-optimized internally chelated pentacarbonyl complexes derived from **5b**.

in **7**-II is 35.1 kcal mol^{-1}, according to PM3(tm). A more reliable estimation for this value, obtained by single-point DFT calculations on the PM3(tm) optimized geometries of **7**-II and of the corresponding non-chelated pentacarbonyl complex, is 24.8 kcal mol^{-1}. At the same level of theory, a PMe_3 ligand in the equatorial position of the dicobaltcarbonyl complex derived from ethyne has a binding energy of 43.7 kcal mol^{-1}.[15a] The oxygen atom of the sultam moiety acts therefore as a weakly coordinating ligand, while it does not lead to the formation of an isolable chelated pentacarbonyl complex, this effect strongly directs the coordination of the olefin to a precise cobalt atom.

We then turned our attention to the olefin-bonded intermediates subsequently involved in the reaction (structure III in Scheme 3), in order to see if in this case the bornane-2,10-sultam fragment exerted an important

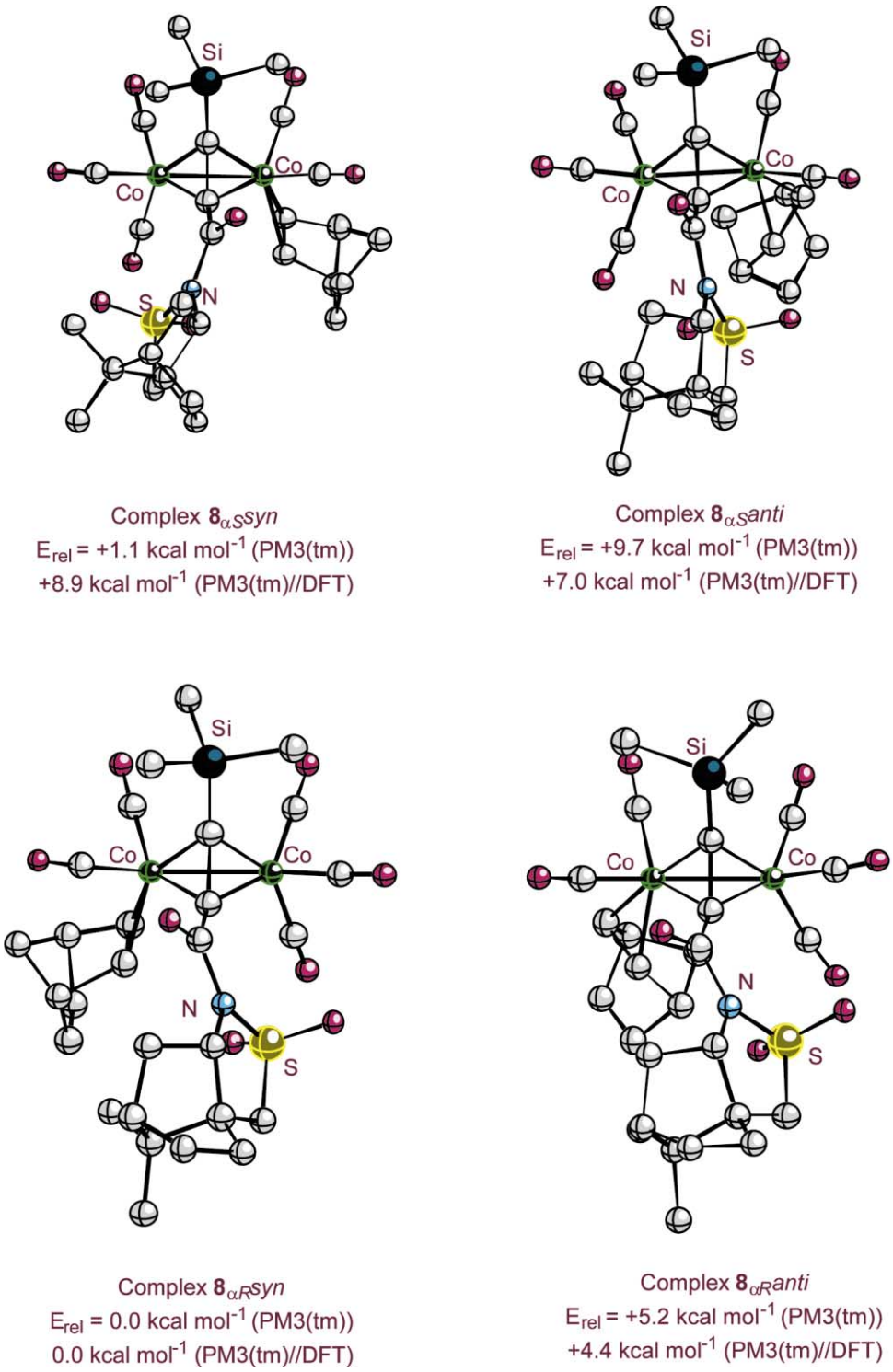
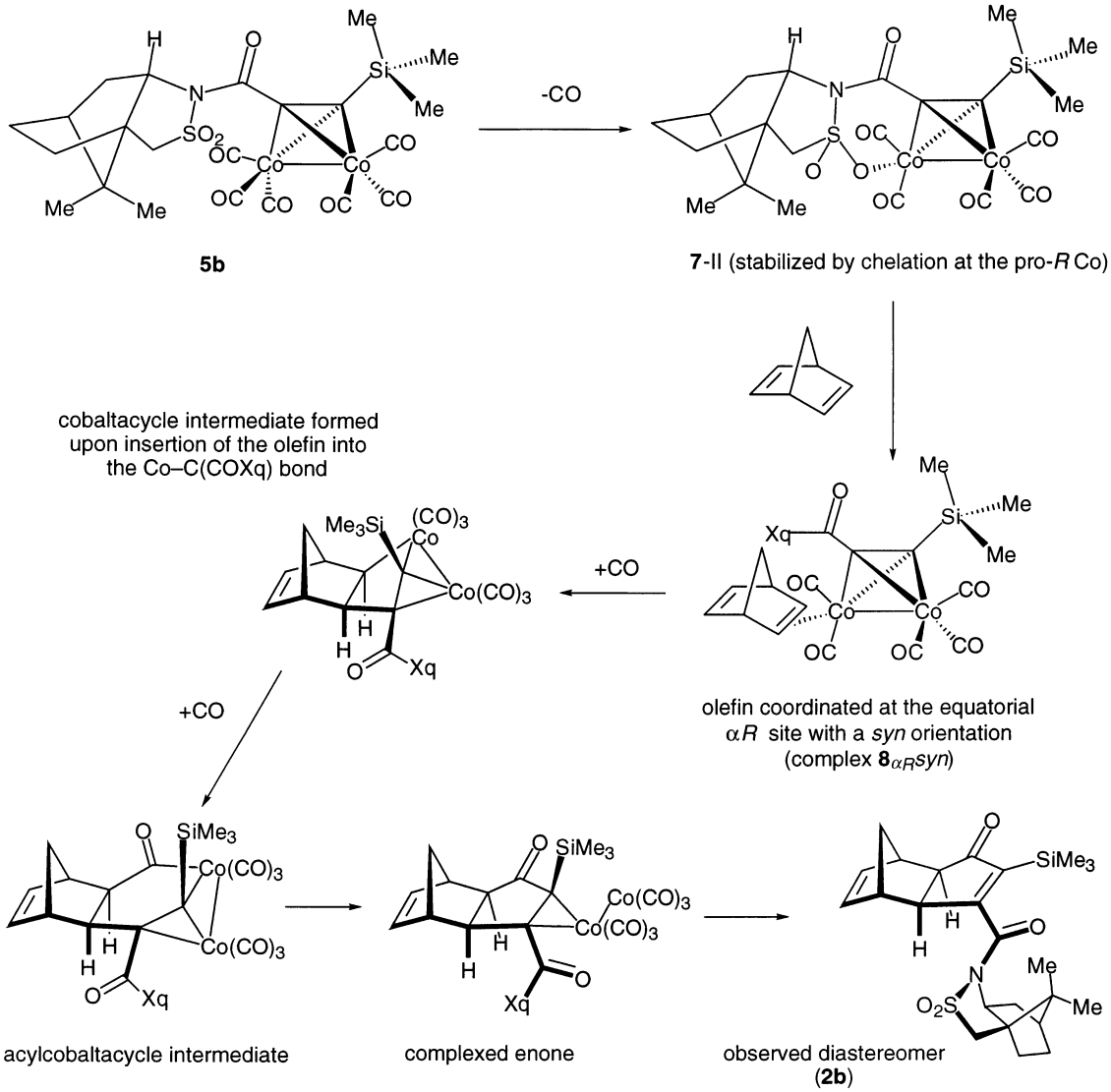


Figure 9. Structures and energies of the four possible intermediate complexes arising from coordination of norbornadiene at the eq_{α} positions of **5b**. Hydrogen atoms have been omitted for clarity.

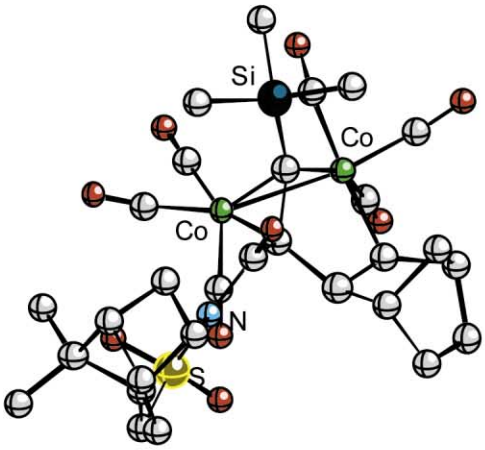
stereodiscriminating effect. Assuming that norbornadiene will coordinate preferentially to the SO_2-labilized eq_α sites, and since there are two possible orientations for a coordinated norbornadiene molecule (*anti*, in which the methylene bridge points away from the alkyne substituents; *syn*, in which the methylene bridge points towards the alkyne substituents) we must consider four possible different complexes of this type, which we shall refer to as $\mathbf{8}_{\alpha R}$*syn*, $\mathbf{8}_{\alpha S}$*syn*, $\mathbf{8}_{\alpha R}$*anti* and $\mathbf{8}_{\alpha S}$*anti*. The corresponding PM3(tm)-optimized geometries are shown in Fig. 9. In this case, the energies were calculated both at the PM3(tm) and at the PM3(tm)//DFT levels of theory. Both methods agree in conclusion that the most stable olefin-bonded intermediate is the $\mathbf{8}_{\alpha R}$*syn* one, which together with $\mathbf{8}_{\alpha S}$*anti* lead to the formation of the experimentally observed adduct **2b**.[27]

Therefore in both the pentacarbonyl complexes **7** and the olefin-coordinated intermediates **8**, the bornane-2,10-sultam chiral auxiliary appears to efficiently control the stereochemistry of the reaction. The calculated energy differences (at the PM3(tm)//DFT level of theory) between the diastereoisomer intermediates are at least 4.4 kcal mol^{-1}, a magnitude which is in accordance with the observed diastereoselectivities (Scheme 4).

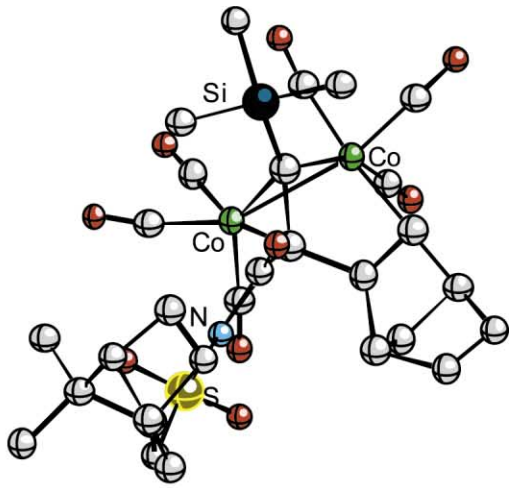
Since according to the original mechanistic hypothesis by Magnus[13] the predominant diastereoisomer should also correspond to the most stable cobaltacycle intermediate (see Scheme 4 and structure IV in Scheme 1), we optimized the geometries corresponding to the four possible cobaltacycles ($\mathbf{9}_{\alpha R}$*syn*, $\mathbf{9}_{\alpha S}$*syn*, $\mathbf{9}_{\alpha R}$*anti* and $\mathbf{9}_{\alpha S}$*anti*) arising from **8** upon olefin insertion in the Co–C(acylsultam) bond and CO uptake, in order to fill the vacant coordination site at the cobalt generated in the insertion step (Fig. 10). However, in this case the calculated energies (either at the PM3(tm) or at the PM3(tm)//DFT levels of theory) do not match with the stereochemical outcome of the reaction, since although the most stable cobaltacycle ($\mathbf{9}_{\alpha R}$*syn*) is the one leading to the observed adduct **2b**, cobaltacycle $\mathbf{9}_{\alpha S}$*syn*, that leads to the opposite diastereoisomer, has an almost identical energy at the more reliable PM3(tm)//DFT



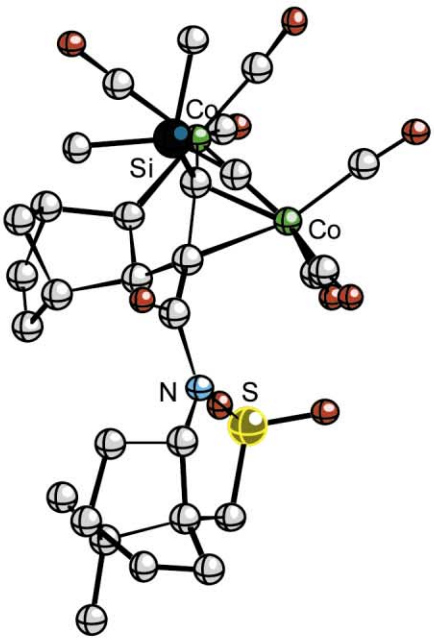
Scheme 4. Proposed preferred reaction path for the Pauson–Khand cycloaddition of complex **5b** with norbornadiene.



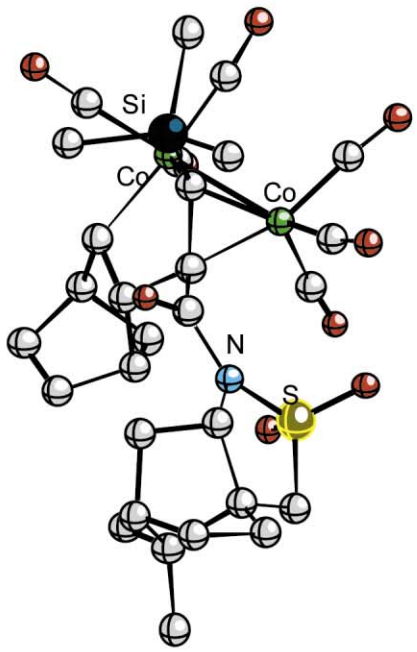
Complex $\mathbf{9}_{\alpha S}$*syn*
E_{rel} = +3.8 kcal mol^{-1} (PM3(tm))
+0.02 kcal mol^{-1} (PM3(tm)//DFT)



Complex $\mathbf{9}_{\alpha S}$*anti*
E_{rel} = +7.6 kcal mol^{-1} (PM3(tm))
+13.4 kcal mol^{-1} (PM3(tm)//DFT)



Complex $\mathbf{9}_{\alpha R}$*syn*
E_{rel} = 0.0 kcal mol^{-1} (PM3(tm))
0.0 kcal mol^{-1} (PM3(tm)//DFT)



Complex $\mathbf{9}_{\alpha R}$*anti*
E_{rel} = +6.4 kcal mol^{-1} (PM3(tm))
+13.8 kcal mol^{-1} (PM3(tm)//DFT)

Figure 10. Structures and energies of the four possible intermediate cobaltacycles resulting from olefin insertion in the norbornadiene-bonded complexes shown in Fig. 9. Hydrogen atoms have been omitted for clarity.

level. We would conclude therefore that in this case the product-determining step is not the formation of the cobaltacycle, but the formation of the olefin-bound intermediate.

3. Conclusion

In summary, the present results strongly suggest that the very high stereoselectivity of the intermolecular

Pauson–Khand reactions of *N*-(2-alkynoyl)bornane-2,10-sultams **1a–d** with norbornene or norbornadiene can be rationalized by assuming that the sultam auxiliary can selectively chelate one of the cobalt atoms of the initially formed alkyne–dicobaltpentacarbonyl complex, thus directing the coordination of the olefin to this internally activated cobalt. This fact, together with the strong preference of the norbornadiene to adopt a *syn* orientation in this product-determining complex, allows an extremely efficient chirality transfer to the C_2Co_2 cluster and completely secures the diastereoselectivity of the process. Oppolzer's camphorsultam auxiliary behaves therefore in a similar way to the 10-(alkylthio)isoborneols and 10-(alkylthio)isobornanethiols previously reported by us, in which the asymmetric induction also relies on the intermediate formation of a chelation-stabilized coordinatively unsaturated cobalt species.[7a,7f–g]

4. Experimental

4.1. General methods

Optical rotations were measured at room temperature (23°C) on a Perkin–Elmer 241 MC polarimeter (concentration in g/100 mL). Melting points were determined on a Gallenkamp apparatus and have not been corrected. Infrared spectra were recorded on a Perkin–Elmer 681 instrument. NMR spectra were acquired on a Varian Unity-300 instrument. ^{1}H NMR spectra were obtained at 300 MHz (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and b = broad) and ^{13}C NMR spectra were obtained at 75 MHz. Carbon multiplicities have been assigned by DEPT experiments. Mass spectra were recorded on a Hewlett–Packard 5890 instrument at 70 eV ionising potential; ammonia was used for chemical ionisation (CI). UV spectra were obtained on a Lambda 5 Perkin–Elmer apparatus. CD spectra were recorded at the Serveis Científico-Tècnics de la Universitat de Barcelona. Elemental analyses were performed by the Servei d'Anàlisis Elementals del CSIC de Barcelona. Exact mass measurements (HRMS) were performed by the Servicio de Espectrometría de Masas de la Universidad de Córdoba. Chromatographic analyses were performed on a Helwett–Packard 1050 HPLC instrument equipped with a Nucleosil 120 5C18 (25 cm) column. *N*-(2-Alkynoyl)bornane-2,10-sultams **1a–1d** were prepared as previously described.[28] Experimental procedures for the intermolecular Pauson–Khand reactions of compounds **1a–1c** and characterization data for the corresponding adducts **2a–2c** can be found in the supporting information in Ref. 12.

4.2. General procedure for the preparation of dicobalt hexacarbonyl complexes

To a solution of the *N*-(2-alkynoyl)oxazolidinone or *N*-(2-alkynoyl)bornane-2,10-sultam (0.07 mmol) in dichloromethane (2 mL) was added $Co_2(CO)_8$ (0.03 g, 0.08 mmol). After stirring for 1 h at room temperature the reaction mixture was filtered through Celite and purified by column chromatography on silica gel.

4.2.1. Dicobalt hexacarbonyl complex of (1*R*,5*S*,7*S*)-1-(10,10-dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decan-4-yl)-3-phenyl-3-propyn-1-one, 5a.

Obtained by the general procedure from the alkyne **1a** (0.010 g, 0.040 mmol) in 83% yield. IR (NaCl film): 3070, 2964, 2103, 2067, 2034, 1636, 1337, 1283, 1243, 1165, 1117, 612 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): 0.20 (s, 3H), 0.32 (s, 3H), 0.40–0.50 (m, 1H), 0.60–0.70 (m, 1H), 0.80–1.23 (m, 3H), 1.90–2.00 (m, 2H), 2.54–4.58 (d, J = 14 Hz, 1H), 2.62–2.66 (d, J = 14 Hz, 1H), 3.70–3.80 (m, 1H), 6.80–7.10 (m, 3H), 7.84–7.87 (d, 7 Hz, 2H). ^{13}C NMR (75 MHz, C_6D_6): 19.5 (CH_3), 21.1 (CH_3), 26.3 (CH_2), 32.7 (CH_2), 39.1 (CH_2), 45.1 (CH), 47.5 (C), 47.8 (C), 53.2 (CH_2), 66.8 (CH), 128.4 (CH), 128.9 (CH), 129.1 (CH), 138.0 (C), 160.0 (C), 199.0 (br, CO); the two signals corresponding to Co-bound carbons were too weak to be observed. UV–vis (CH_2Cl_2, 9.4×10^{-5} M): λ_{max} = 355 nm (ε = 3142), 315 nm (ε = 8697). CD (CH_2Cl_2, 2.5×10^{-4} M): λ_{max} = 425 nm ($\Delta\varepsilon$ = 0.91), 343 nm ($\Delta\varepsilon$ = 1.88).

4.2.2. Dicobalt hexacarbonyl complex of (1*R*,5*S*,7*S*)-1-(10,10-dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decan-4-yl)-3-trimethylsilyl-3-propyn-1-one, 5b.

Obtained by the general procedure from the alkyne **1b** (0.070 g, 0.19 mmol) in 81% yield. ^{1}H NMR (300 MHz, C_6D_6): 0.46 (s, 3H), 0.55 (s, 9H), 0.40–0.65 (m, 1H), 0.70–0.85 (m, 1H), 1.17 (s, 3H), 1.10–1.20 (m, 1H), 1.30–1.45 (m, 2H), 1.90–2.15 (m, 2H), 2.68–2.73 (d, J = 14 Hz, 1H), 2.77–2.82 (d, J = 14 Hz, 1H), 3.78–3.82 (dd, J = 8 Hz, J' = 5 Hz, 1H). ^{13}C NMR (75 MHz, C_6D_6): 1.23 ($3CH_3$), 19.5 (CH_3), 20.9 (CH_3), 26.3 (CH_2), 32.5 (CH_2), 38.8 (CH_2), 44.9 (CH), 47.5 (C), 48.0 (C), 53.1 (CH_2), 66.5 (CH), 160.0 (C), 199.0 (br, CO); the two signals corresponding to Co-bound carbons were too weak to be observed. CD (CH_2Cl_2, 5.0×10^{-4} M): λ_{max} = 360 nm ($\Delta\varepsilon$ = 1.30).

4.2.3. Dicobalt hexacarbonyl complex of (1*S*,2*R*,6*S*,7*R*)-7,10,10-trimethyl-5-(2-butynoyl)-3-oxa-5-azatricyclo-[5.2.1.0^{2,6}]decan-4-one, 6.

Obtained by the general procedure from the corresponding alkyne[28] (0.040 g, 0.07 mmol) in 82% yield. IR (NaCl film): 2970, 2100, 2060, 2020, 1775, 1660, 1380, 1280, 1270, 1200, 1090, 1060, 760 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): 0.29 (s, 3H), 0.47 (s, 3H), 0.60–1.20 (m, 7H), 1.60–1.62 (d, J = 4.8 Hz, 1H), 2.69 (s, 3H), 3.67–3.69 (d, J = 8.1 Hz, 1H), 4.08–4.10 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6): 1.4 (CH_3), 11.8 (CH_3), 19.4 (CH_3), 22.5 (CH_3), 22.8 (CH_2), 33.2 (CH_2), 46.4 (C), 47.7 (CH), 50.1 (C), 66.4 (CH), 81.2 (CH), 97.5 (C), 153.8 (C), 167.7 (C), 200 (br, CO); one of the two signals corresponding to Co-bound carbons was to weak to be observed. UV–vis (CH_2Cl_2, 1.0×10^{-4} M): λ_{max} = 360 nm (ε = 2982), 314 nm (ε = 5862). CD (CH_2Cl_2, 3.0×10^{-4} M): λ_{max} = 341 nm ($\Delta\varepsilon$ = 4.84).

4.3. Intermolecular Pauson–Khand reaction of 1a with norbornene

To a stirred solution of the *N*-(2-alkynoyl)bornane-2,10-sultam **1a** (0.100 g, 0.29 mmol) in anhydrous dichloromethane (5 mL) was added dicobaltoctacarbonyl (0.110 g, 0.32 mmol) in one portion and the resulting dark-coloured solution was stirred at room temperature for 1 h, after which time the formation of the dicobalt hexacarbonyl complex was complete (TLC). The mixture was purged with nitrogen and a solution of norbornene (0.273 g, 2.91 mmol) in dichloromethane (5 mL) was added dropwise. The mixture was externally cooled with ice, solid *N*-methylmorpholino-*N*-oxide monohydrate (0.245 g, 1.80 mmol) was added in one portion and the reaction mixture was allowed to warm to room temperature by removal of the cooling bath. After stirring at room temperature until the complete disappearance of the complex, the mixture was filtered through Celite and submitted to column chromatography on silica gel, eluting with 15–20% hexane/diethyl ether mixtures to afford adduct **2a** ((0.073 g, 54%); d.r. = 125:1, HPLC).

4.4. (1*S*,2*R*,6*S*,7*R*)-5-((1*R*,5*S*,7*S*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.$0^{1,5}$]decane-4-carbonyl)-4-phenyltricyclo[5.2.1.$0^{2,6}$]dec-4-en-3-one, 3a

Colourless solid. Mp 125–127°C (hexane–methylene chloride). IR (KBr): 3060, 2960, 2880, 1700, 1665, 1335, 1270, 1240, 1170, 1060, 755, 695 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 0.89 (s, 3H), 1.20–2.61 (m, 17H), 2.80–3.20 (m, 5H), 3.80–4.00 (m, 1H), 7.20–7.40 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): 19.8 (CH_3), 20.3 (CH_3), 26.5 (CH_2), 28.6 (CH_2), 28.8 (CH_2), 32.0 (CH_2), 32.8 (CH_2), 38.0 (CH_2), 38.0 (CH), 39.9 (CH), 44.8 (CH), 47.8 (C), 48.9 (C), 49.6 (CH), 52.8 (CH), 54.2 (CH_2), 64.7 (CH), 128.0 (CH), 128.7 (CH), 129.1 (CH), 130.4 (C), 143.5 (C), 160.3 (C), 166.6 (C), 207.8 (C). $[\alpha]_D^{25} = -18.8$ (c = 0.63, $CHCl_3$). MS (CI): 466 ($[M+1]^+$, 11%), 483 ($[M+18]^+$, 100%). HRMS (EI) calcd for $C_{27}H_{31}NO_4S$: 465.1974. Found: 465.1962. HPLC (Nucleosil C-18) = 23.80 min ($\varnothing$ = 0.8 mL/min, MeOH/H_2O, 70:30, λ = 240 nm).

4.5. Intermolecular Pauson–Khand reaction of 1d′ with norbornadiene

To a stirred solution of (1*S*,5*R*,7*R*)-1-(10,10-dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.$0^{1,5}$]dec-4-yl)-4-methoxy-2-butyn-1-one **1d** (0.146 g, 0.47 mmol) in anhydrous toluene (10 mL), dicobaltoctacarbonyl (0.172 g, 0.50 mmol) was added in one portion, and the resulting dark-coloured solution was stirred at room temperature for 1 h, after which time the formation of the dicobalthexacarbonyl complex was complete (TLC). The mixture was purged with nitrogen and a solution of norbornadiene (4.7 mmol) in toluene (5 mL) was added dropwise, then the reaction mixture was stirred at 45°C for 12 h (complete disappearance of the complex), filtered through Celite and submitted to column chromatography on silica gel, eluting with 15–20% hexane/diethyl ether mixtures. In this way, diastereoisomerically pure **2d′** (0.104 g, 52%); d.r. >800:1, HPLC was obtained. The regioisomeric 1,3-dicarbonyl adduct (1.13:1 diastereoisomer mixture, HPLC) was also isolated (0.047 g, 23%).

4.6. (1*R*,2*R*,6*S*,7*S*)-5-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5.2.1.$0^{1,5}$]decan-4-carbonyl)-4-methoxymethyltricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one, 2d′

Colourless solid. Mp 176–178°C (hexane–methylene chloride); IR (NaCl film): 2960, 2940, 2880, 1705, 1670, 1645, 1460, 1345, 1280, 1220, 1170, 1110, 960, 740, 695 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 0.99 (s, 3H), 1.21 (s, 3H), 1.20–1.45 (m, 5H), 1.90–2.00 (m, 2H), 2.00–2.15 (m, 2H), 2.40–2.50 (d, J = 5.6 Hz, 1H), 2.80–2.90 (m, 1H), 2.95–3.05 (m, 1H), 3.15–3.20 (m, 1H), 3.26 (s, 3H), 3.41–3.45 (d, J = 12 Hz, 1H), 3.47–3.51 (d, J = 12 Hz, 1H), 3.90–4.00 (m, 1H), 4.08–4.18 (d, J = 13 Hz, 1H), 4.18–4.23 (d, J = 13 Hz, 1H), 6.18–6.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 19.8 (CH_3), 20.3 (CH_3), 26.4 (CH_2), 32.6 (CH_2), 37.8 (CH_2), 41.9 (CH_2), 42.5 (CH), 44.0 (CH), 44.4 (CH), 47.8 (CH), 48.0 (C), 49.5 (C), 52.8 (CH_2), 53.1 (CH), 58.8 (CH_3), 64.8 (CH), 65.2 (CH_2), 137.6 (CH), 138.2 (CH), 145.8 (C), 162.0 (C), 165.5 (C), 207.0 (C); MS (CI): 432 ($[M+1]^+$, 13%), 449 ($[M+18]^+$, 100%); $[\alpha]_{435}^{25} = +111.2$ (c = 0.34, $CHCl_3$); anal. calcd for $C_{23}H_{29}NO_5S$ = C, 64.01; H, 6.77; N, 3.25; S, 7.43. Found = C, 63.88; H, 6.81; N. 3.27; S, 7.29; HPLC (Nucleosil C-18) = 20.22 min ($\varnothing$ = 0.8 mL/min, MeOH/H_2O, 65:35, λ = 240 nm).

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References

1. (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Chem. Commun.* **1971**, 36; (b) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977–981; (c) Intramolecular version: Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436–5438.
2. Leading reviews on the Pauson–Khand reaction: (a) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2–14; (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855–5860; (c) Schore, N. E. *Org. React.* **1991**, *40*, 1–90; (d) Schore, N. E. In *Comprehensive Organic Synthesis II*; Hegedus, S. L., Ed.; Pergamon Press: Oxford, 1995; Vol. 12, pp. 703–739; (e) Geis, O.; Schmalz, H. G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 911–914; (f) Buchwald, S. L.; Hicks, F. A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. II, pp. 491–510; (g) Sugihara, T.; Yamaguchi, M.; Nishizawa, M. *Recent Res. Dev. Organomet. Chem.*

1999, *2*, 13–43; (h) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297–341; (i) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263–3283; (j) Sugihara, T.; Yamaguchi, M.; Nishizawa, M. *Chem. Eur. J.* **2001**, *7*, 1589–1595.

3. For representative examples of metal mediated cyclocondensations leading to five-membered carbocycles, see: [**Ti**] (a) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688–11689; (b) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450–9451; [**Zr**] (c) Agnel, G.; Negishi, E.-I. *J. Am. Chem. Soc.* **1991**, *113*, 7424–7426; [**Mo**] (d) Jeong, N.; Lee, S. J.; Lee, B. Y.; Chung, Y. K. *Tetrahedron Lett.* **1993**, *34*, 4027–4030; (e) Kent, J. L.; Wan, H. H.; Brummond, K. M. *Tetrahedron Lett.* **1995**, *36*, 2407–2410; (f) Cao, H.; Van Ornum, S. G.; Cook, J. M. *Tetrahedron Lett.* **2000**, *41*, 5313–5316; [**W**] (g) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154–1156; (h) Shiu, Y.-T.; Madhushaw, R. J.; Li, W.-T.; Lin, Y.-C.; Lee, G.-H.; Peng, S.-M.; Liao, F.-L.; Wang, S.-L.; Liu, R. S. *J. Am. Chem. Soc.* **1999**, *121*, 4066–4067; (i) Barluenga, J.; Tomás, M.; Ballesteros, A.; Santamaría, J.; Brillet, C.; García-Granda, S.; Piñera-Nicolás, A.; Vázquez, J. T. *J. Am. Chem. Soc.* **1999**, *121*, 4516–4517; [**Fe**] (j) Pearson, A. J.; Dubbert, R. A. *Organometallics* **1994**, *13*, 1656–1661; [**Ru**] (k) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187–6188; (l) Kondo, T.; Nakamura, A.; Okada, T.; Suzuki, N.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2000**, *122*, 6319–6320; (m) Morisaki, Y.; Kondo, T.; Mitsudo, T. *Org. Lett.* **2000**, *2*, 949–952; [**Ni**] (n) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539–546; (o) Pagés, L.; Llebaria, A.; Camps, F.; Molins, E.; Miravitlles, C.; Moretó, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449–10461; (p) Zhang, M. H.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498–4499; (q) García-Gómez, G.; Moretó, J. M. *J. Am. Chem. Soc.* **1999**, *121*, 878–879; [**Rh**] (r) Ojima, I.; Fracchiolla, D. A.; Donovan, R. J.; Banerji, P. *J. Org. Chem.* **1994**, *59*, 7594–7595; (s) Matsuda, I.; Ishibashi, H.; Ii, N. *Tetrahedron Lett.* **1995**, *36*, 241–244; (t) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1999**, *121*, 4130–4135; (t) Kobayashi, T.; Koga, Y.; Narasaka, K. *J. Organomet. Chem.* **2001**, *624*, 73–87.
4. (a) Belanger, D. B.; Omahony, D. J. R.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7637–7640; (b) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285–2286; (c) Rautenstrauch, V.; Mégard, P.; Conesa, J.; Küster, W. *Angew. Chem.* **1990**, *102*, 1441–1443; (d) Jeong, N.; Hwang, S. H.; Lee, Y. Y.; Chung, K. *J. Am. Chem. Soc.* **1994**, *116*, 3159–3160; (e) Lee, B. Y.; Chung, Y. K.; Jeong, N.; Lee, Y.; Hwang, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 8793–8794; (f) Jeong, N.; Hwang, S. H.; Lee, Y. W.; Lim, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10549–10550; (g) Van Ornum, S. G.; Bruendl, M. M.; Cook, J. M. *Tetrahedron Lett.* **1998**, *39*, 6649–6650; (h) Belanger, D. B.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7641–7644; (i) Sugihara, T.; Yamaguchi, M. *Synlett* **1998**, *12*, 1384–1386; (j) Krafft, M. E.; Hirosawa, C.; Bonaga, L. V. R. *Tetrahedron Lett.* **1999**, *40*, 9177–9181; (k) Krafft, M. E.; Bonaga, L. V. R.; Hirosawa, C. *Tetrahedron Lett.* **1999**, *40*, 9171–9175; (l) Comely, A. C.; Gibson, S. E.; Stevenazzi, A.; Hales, N. J. *Tetrahedron Lett.* **2001**, *42*, 1183–1185.
5. Pauson–Khand cyclization of enynes with pendant, removable chiral auxiliaries: (a) Poch, M.; Valenti, E.; Moyano, A.; Pericàs, M. A.; Castro, J.; DeNicola, A.; Greene, A. E. *Tetrahedron Lett.* **1990**, *31*, 7505–7508; (b) Castro, J.; Sorensen, H.; Riera, A.; Morin, C.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Am. Chem. Soc.* **1990**, *112*, 9388–9389; (c) Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A.; Greene, A. E.; Piniella, J. F.; Alvarez-Larena, A. *J. Organomet. Chem.* **1992**, *433*, 305–310; (d) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A.; Greene, A. E. *Tetrahedron: Asymmetry* **1994**, *5*, 307–310; (e) Tormo, J.; Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1996**, *52*, 14021–14040; (f) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A.; Greene, A. E.; Alvarez-Larena, A.; Piniella, J. F. *J. Org. Chem.* **1996**, *61*, 9016–9020; (g) Tormo, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 4851–4856; (h) Stolle, A.; Becker, H.; Salaün, J.; de Meijere, A. *Tetrahedron Lett.* **1994**, *35*, 3521–3524; (i) Adrio, J.; Carretero, J. C. *J. Am. Chem. Soc.* **1999**, *121*, 7411–7412.
6. Intramolecular enantioselective Pauson–Khand and related cyclizations: (a) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688–11689; (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026–7033; (c) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Lett.* **2000**, *41*, 891–895; (d) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron: Asymmetry* **2000**, *11*, 797–808; (e) Jeong, N.; Sung, B. K.; Choi, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 6771–6772; (f) Shibata, T.; Takagi, T. *J. Am. Chem. Soc.* **2000**, *122*, 9852–9853.
7. Asymmetric intermolecular Pauson–Khand reactions of chiral auxiliary-containing alkynes: (a) Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A.; Bernardes, V.; Greene, A. E.; Alvarez-Larena, A.; Piniella, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 2153–2154; (b) Bernardes, V.; Verdaguer, X.; Kardos, N.; Riera, A.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *Tetrahedron Lett.* **1994**, *35*, 575–578; (c) Bernardes, V.; Kann, N.; Riera, A.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Org. Chem.* **1995**, *60*, 6670–6671; (d) Balsells, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1575–1580; (e) Montenegro, E.; Poch, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1997**, *53*, 8651–8664; (f) Montenegro, E.; Poch, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1998**, *39*, 335–338; (g) Verdaguer, X.; Vázquez, J.; Fuster, G.; Bernardes-Génisson, V.; Greene, A. E.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 7037–7052; (h) Montenegro, E.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvarez-Larena, A.; Piniella, J.-F. *Tetrahedron: Asymmetry* **1999**, *10*, 457–471; (i) Balsells, J.; Vázquez, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **2000**, *65*, 7291–7302.
8. Chiral-phosphine mediated enantioselective intermolecular Pauson–Khand reactions: (a) Bladon, P.; Pauson, P. L.; Brunner, H.; Eder, R. *J. Organomet. Chem.* **1988**, *353*, 449–454; (b) Brunner, H.; Niedernhuber, A. *Tetrahedron: Asymmetry* **1990**, *1*, 711–714; (c) Park, H.-J.; Lee, B. Y.; Kang, Y. K.; Chung, Y. K. *Organometallics* **1995**, *14*, 3104–3107; (d) Hay, A. M.; Kerr, W. J.; Kirk, G. G.; Middlemiss, D. *J. Organometallics* **1995**, *14*, 4986–4988; (e) Gimbert, Y.; Robert, F.; Durif, A.; Averbuch, M. T.;

Kann, N.; Greene, A. E. *J. Org. Chem.* **1999**, *64*, 3492–3497; (f) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvarez-Larena, A.; Piniella, J. F. *J. Organomet. Chem.* **1999**, *585*, 53–58; (g) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvarez-Larena, A.; Piniella, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 7944–7952; (h) Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A.; Maestro, M. A.; Mahía, J. *J. Am. Chem. Soc.* **2000**, *122*, 10242–10243.

9. Other approaches: (a) Kerr, W. J.; Kirk, G. G.; Middlemiss, D. *Synlett* **1995**, 1085–1086; (b) Derdau, V.; Laschat, S.; Jones, P. G. *Heterocycles* **1998**, *48*, 1445–1453; (c) Kerr, W. J.; Lindsay, D. M.; Rankin, E. M.; Scott, J. S.; Watson, S. P. *Tetrahedron Lett.* **2000**, *41*, 3229–3233; (d) Rutherford, D. T.; Christie, S. D. R. *Tetrahedron Lett.* **1998**, *39*, 9805–9808; (e) Fletcher, A. J.; Rutherford, D. T.; Christie, S. D. R. *Synlett* **2000**, 1040–1042.
10. Fonquerna, S.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1995**, *51*, 4239–4254.
11. Fonquerna, S.; Rios, R.; Moyano, A.; Pericàs, M. A.; Riera, A. *Eur. J. Org. Chem.* **1999**, 3459–3478.
12. (a) Fonquerna, S.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Am. Chem. Soc.* **1997**, *119*, 10225–10226; (b) Balsells, J.; Moyano, A.; Riera, A.; Pericàs, M. A. *Org. Lett.* **1999**, *1*, 1981–1984.
13. (a) Magnus, P. C.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5859–5861; (b) Magnus, P. C.; Principe, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851–4854.
14. References on mechanistic aspects of the Pauson–Khand reaction: (a) La Belle, B. E.; Knudsen, M. J.; Olmstead, M. M.; Hope, H.; Yanuck, M. D.; Schore, N. E. *J. Org. Chem.* **1985**, *50*, 5215–5222; (b) Montaña, A.-M.; Moyano, A.; Pericàs, M. A.; Serratosa, F. *Tetrahedron* **1985**, *41*, 5995–6003; (c) Casalnuovo, J. A.; Scott, R. W.; Harwood, E. A.; Schore, N. E. *Tetrahedron Lett.* **1994**, *35*, 1153–1156; (d) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1995**, *51*, 6541–6556; (e) Thommen, M.; Veretenov, A. L.; Guidetti-Grept, R.; Keese, R. *Helv. Chim. Acta* **1996**, *79*, 461–476; (f) Corlay, H.; James, I. W.; Fouquet, E.; Schmidt, J.; Motherwell, W. B. *Synlett* **1996**, 990–993; (g) Kowalczyk, B. A.; Smith, T. C.; Dauben, W. G. *J. Org. Chem.* **1998**, *63*, 1379–1389; (h) Krafft, M. E.; Wilson, A. M.; Dasse, O. A.; Bonaga, L. V. R.; Cheung, Y. Y.; Fu, Z.; Shao, B.; Scott, I. L. *Tetrahedron Lett.* **1998**, *39*, 5911–5914; (i) Corlay, H.; Fouquet, E.; Magnier, E.; Motherwell, W. B. *Chem. Commun.* **1999**, 183–184; (j) Breczinski, P. M.; Stumpf, A.; Hope, H.; Krafft, M. E.; Casalnuovo, J. A.; Schore, N. E. *Tetrahedron* **1999**, *55*, 6797–6812; (k) Kennedy, A. R.; Kerr, W. J.; Lindsay, D. M.; Scott, J. S.; Watson, S. P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4366–4372; (l) Robert, F.; Milet, A.; Gimbert, Y.; Konya, D.; Greene, A. E. *J. Am. Chem. Soc.* **2001**, *123*, 5396–5400.
15. For density functional studies on the Pauson–Khand reaction, see: (a) Vázquez, J. Ph.D. Thesis, Universitat de Barcelona, 1999; (b) Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2001**, *123*, 1703–1708; (c) Pericàs, M. A.; Balsells, J.; Castro, J.; Marchueta, I.; Moyano, A.; Riera, A.; Vázquez, J.; Verdaguer, X. *Pure Appl. Chem.*, in press.
16. Gordon, C. M.; Kiszka, M.; Junkin, I. R.; Kerr, W. J.; Scott, J. S.; Gebicki, J. *J. Organomet. Chem.* **1998**, *554*, 147–154.
17. (a) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289–5292; (b) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S. *Synlett* **1991**, 204–206; (c) Brown, D. S.; Campbell, E.; Kerr, W. J.; Lindsay, D. M.; Morrison, A. J.; Pike, K. G.; Watson, S. G. *Synlett* **2000**, 1573–1576.
18. (a) Hoye, T. R.; Suriano, J. A. *J. Org. Chem.* **1993**, *58*, 1659–1660; (b) Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220–223; (c) Stumpf, A.; Jeong, N.; Sunghee, H. *Synlett* **1997**, 205–207; (d) Sugihara, T.; Yamada, M.; Yamaguchi, M.; Nishizawa, M. *Synlett* **1999**, *6*, 771–773.
19. Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209–220.
20. SPARTAN, version 4.1.1, Wavefunction, Inc., 18401 Von Karman Ave., Suite 370, Irvine, CA, 92612.
21. (a) Baert, F.; Guelzim, A.; Coppens, P. *Acta Crystallogr.* **1984**, *B40*, 590–595; (b) Gregson, D.; Howard, J. A. K. *Acta Crystallogr.* **1983**, *C39*, 1024–1027.
22. McLaren, A. B.; Sweeney, J. B. *Synlett* **2000**, 1625–1627.
23. Kajtár, M.; Kajtár-Miklós, J.; Giacomelli, G.; Gaál, G.; Váradi, G.; Horváth, I. T.; Zucchi, C.; Pályi, G. *Tetrahedron: Asymmetry* **1995**, *6*, 2177–2194.
24. (a) Baerends, E. J.; Ellis, D. E.; Ros, P. E. *Chem. Phys.* **1973**, *2*, 41–51; (b) Versluis, L.; Ziegler, T. *J. Chem. Phys.* **1988**, *88*, 322–328; (c) Fan, L.; Ziegler, T. *J. Chem. Phys.* **1991**, *95*, 7401–7408; (d) teVelde, G.; Baerends, E. J. *J. Comput. Phys.* **1992**, *99*, 84–98.
25. Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200–1211.
26. Perdew, J. P.; Chevary, J. A.; Vosko, S. H.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, *46*, 6671–6687.
27. Coordination of norbornadiene at the axial sites of **5b** leads to two other complexes ax_R*anti* and ax_S*anti*, that are also less stable than the $\mathbf{8}_{\alpha R}$*syn* one by 2.3 and 3.0 kcal mol^{-1}, respectively (PM3(tm)//DFT values).
28. Fonquerna, S.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1685–1691.