Chelation Isomerism in (Allylamino)carbene Complexes and Its Impact on Stereoselection: A Study of Coordination Equilibrium by Dynamic HPLC

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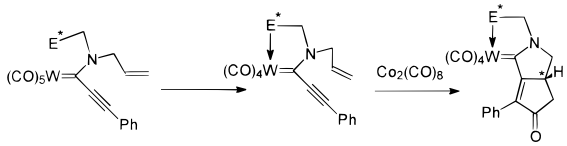
Abstract: A study related to isomerism brought about by the two different chelation modes of the residual double bond resulting from the intramolecular Pauson−Khand reaction in [(diallylamino)alkynylcarbene]tungsten complexes was undertaken. The presence of a stereogenic center on the carbene ligand in the cycloadduct caused a clear difference in energy between the two diastereomeric forms resulting from alkene chelation. The energy barrier involved in their interconversion was determined by means of dynamic HPLC (D-HPLC) experiments, and its relative high value was related to the difficulty of the inversion at the nitrogen center due to structural rigidity.

The use of transition metals in organic synthesis and the search for more efficient enantioselective processes are predicted among the most thrusting fields of organic synthesis in the oncoming years, especially taking into consideration that metal-mediated processes are often liable to be turned into catalytic processes.[1] Most of the approaches in this merging field have been based on the selective introduction of a stereogenic center to control the formation of the new stereocenters in the reaction course. Excellent results have been obtained by the use of chelating ligands such as in the Sharpless, Noyori, and Jacobsen systems.[2] A different and promising approach in enantioselective synthesis is the accomplishment of intramolecular reactions (Diels−Alder, Michael, Pauson−Khand, ...) within a preformed substrate which includes a metal center able to join chemical activation to chiral restrictions provided it is involved in an asymmetric chelate ring. Different aspects of the effect of chelate species in some C−C-forming intermolecular reactions through transition metal complexes have been analyzed.[3]

We have recently studied a transition metal carbene system able to undergo Pauson−Khand cycloaddition without any external activation.[4] In this reaction a stereogenic center is formed. We reasoned that by building up a chelate ring in an enantioselective fashion we were creating a chiral surrounding able to induce selectivity on the formation of the bridgehead center (Scheme 1). Support for this assumption was found in the diastereofacial selectivity displayed by cyclic α-heterocycloenones in their catalytic hydrogenation (these compounds may be formally related with heteroatom-chelated transition metal carbene complexes).[5]

Scheme 1



The most trivial way to achieve chirality in a metal carbene complex is just by simple chelation of a distal double bond since it generates helicity in an octahedral environment. This may be exploited in stereoselective synthesis provided there is no equilibration between the two possible coordination modes, namely, that of the metal to each one of the olefin faces. We thought that the study of the aspects involved in either the formation and the opening of the chelate ring and the mutual interconversion of the two possible chelated isomers were of the utmost importance for our purposes. The thermodynamic and kinetic parameters corresponding to these species in equilibrium and their interconversion could be easily determined by nonchiral means provided a noninverting stereogenic center was present in the complex, as a marker, to convey diastereodifferentiation in the interconverting chelates. To gain such an insight into the nature of the chelative bond was considered fundamental concerning the possibility of the enantioselective preparation of one of the substrates or, alternatively, the

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(1) Seebach, D. *Angew. Chem.* **1990**, *102*, 1363−1409; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1320−1367.

(2) (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; J. Wiley: New York, 1994. (b) Ojima, I. *Catalytic Asymmetric Synthesis*; VCH Pub. Inc.: New York, 1993. (c) Fuji, K. *Chem. Rev.* **1993**, *93*, 7−2066. (d) Khota, S. *Tetrahedron* **1994**, *50*, 3639−3662.

(3) Reetz, M. T., *Acc. Chem. Res.* **1993**, *26*, 462−468.

(4) (a) Camps, F.; Moretó, J. M.; Ricart, S.; Viñas, J. M. *Angew. Chem., Int. Ed Engl.* **1991**, *30*, 1470−1472. (b) Dötz, K. H.; Christoffers, J. *J. Organomet. Chem.* **1992**, *426*, C58−C61. (c) Jordi, L.; Moretó, J. M.; Ricart, S.; Viñas, J. M.; Mejias, M.; Molins, E. *Organometallics* **1992**, *11*, 3507−3510. (d) Jordi, L.; Segundo, A.; Camps, F.; Ricart, S.; Moretó, J. M. *Organometallics* **1993**, *12*, 2556−2564. (e) Jordi, L.; Ricart, S., ; Viñas, J. M.; Moretó, J. M. *Organometallics* **1997**, *16*, 2808−2818.

(5) Sato, M.; Kuroda, H.; Kaneko, C.; Furuya, T. *J. Chem. Soc., Chem. Commun.* **1994**, 687−688.

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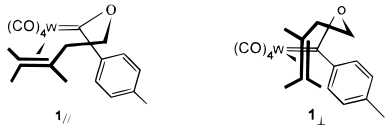
Scheme 2. Parallel and Perpendicular Conformers of Tungsten Complex **1**



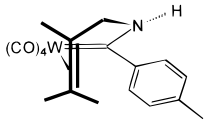
separation of both enantiomers prior to their further application to the mentioned strategy in stereoselective synthesis.

Here, we report one of such studies using a tungsten−carbene complex bearing a chiral allylamino bicyclic structure as the carbene component. With such a compound we prove that the presence of an asymmetric carbon on the carbene ligand stabilizes one of the two diastereomeric forms resulting from alkene chelation.

Results and Discussion

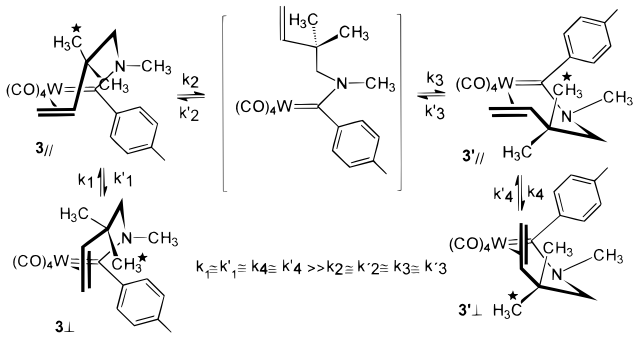
Early, Casey et al. reported the detection of two different [(homoallyloxy)carbene]tungsten tetracarbonyl species, having a distal double bond chelated onto the metal, and supposed that they were transient complexes to finally afford the products of intramolecular cyclopropanation.[6] Their signals obtained in solution in the corresponding NMR and IR spectra were thought to arise from the parallel and perpendicular modes of coordination of the double bond to the metal related to the metal−carbene bond (Scheme 2).

Later, they also reported the easy chelation of the allylamino analogue giving a very stable complex (**2**) unable to evolve further to the corresponding aminocyclopropane. The same behavior was described by Rudler et al. in their studies related to the synthesis and reactivity of aminocarbene complexes.[7]



The solid-state structure of **2** was resolved by X-ray diffractometry and found to contain the complex in a perpendicular arrangement exclusively.[8] Furthermore, even though similar energies were anticipated for both conformations, the perpendicular complex was the only one to be detected in solution. Allyloxy- and 3-butenylamino-chelated analogues of compound **2** were reluctant to be prepared: the first one decomposed before chelation was accomplished while the second one evolved to the corresponding allyl-chelated 2-butenylamino complex after isomerization. This isomerization could be prevented by placing a *gem*-dimethyl group at the allyl site, and so the corresponding compound **3** with a larger chelate ring was synthesized.[9] This compound was stable enough to give crystals, the structure of which was established by X-ray diffraction, and also its dynamic behavior in solution could be studied since there was diastereotopicity in the aromatic protons which was thought to result from a hindered aryl rotation, due mainly to the substitution of

Scheme 3. Dynamic Equilibrium in Solution for Carbene−Tungsten Complex **3** As Postulated by Casey et al.



the amino proton with a methyl group, with an energy barrier of $\Delta G^{\ddagger}_{298} = 16.6\ (\pm 0.7)$ kcal·mol^{-1}; ($\Delta H^{\ddagger} = 11.3\ (\pm 0.7)$ kcal·mol^{-1}; $\Delta S^{\ddagger} = -18\ (\pm 2)$ cal·K^{-1}·mol^{-1}).[9c]

On the basis of theoretical studies assigning similar energies to both the parallel and the perpendicular double bond coordination[10] and especially due to the presence of both species in approximately the same abundance in the solid state of complex **3**, the authors did not hesitate to assume their presence also in solution.[9a] Since no doubling of resonance signals was observed in the NMR spectra, the authors proposed that both species should be interconverting fast enough on the NMR scale (i.e., k_1, k'_1, k_4, $k'_4 \gg 10^{-2}$ s^{-1}) so that they were separately undetectable even at low temperatures. The loss of diastereotopicity in the *gem*-dimethyl and in the α-amino methylene protons of complex **3** was only observed at very high temperatures because of the high barrier inherent to this process ($\Delta G^{\ddagger}_{298} = 18.8\ (\pm 0.6)$ kcal·mol^{-1} ; $\Delta H^{\ddagger} = 18.5\ (\pm 0.6)$ kcal·mol^{-1}; $\Delta S^{\ddagger} = -1\ (\pm 1)$ cal·K^{-1}·mol^{-1}).[9c] Casey et al. proposed that the change in chemical environment for the proton takes place by a decoordination of the double bond to give a 16 electron species and subsequent recoordination by the opposite olefin face (Scheme 3). That nitrogen substitution had some consequence in rising the rotation barrier for the aryl ring around the carbene−aryl bond was indicated by the increase of this barrier for complex **2** after *N*-methylation ($\Delta G^{\ddagger}_{298} = 11.9\ (\pm 1.2)$ kcal·mol^{-1}; $\Delta H^{\ddagger} = 8.9\ (\pm 0.9)$ kcal·mol^{-1}; $\Delta S^{\ddagger} = -10\ (\pm 4)$ cal·k^{-1}·mol^{-1}).[9c] Despite the fact that the barrier for the *N*-methyl derivative of **2** was lower than that for **3** and it might otherwise depend on the size of the chelated ring and on the degree of pyramidalization at the nitrogen in both rings,[11] *no association was made between the inversion of the chelative ring (inversion at nitrogen) and the flapping of the aromatic ring.* However, this might be the case, and by forming a chelate ring the nitrogen atom would be forced to pyramidalize. As a consequence, stabilization of the carbene center would thus be provided, by the aromatic ring whose conformational freedom would thus be partially restricted. The neat negative charge developed on the metal would efficiently be delocalized on its five π-acidic ligands, i.e., the four carbonyls and the perpendicularly coordinated double bond. Thus, the bond order for the W−C bond will approach that of a single bond and, therefore, be able to rotate. As we increase the temperature to overpass the aryl rotation barrier, the electronic demand of the carbene center will render the metal more positive, and therefore, the parallel chelation mode may be approached.[10] Thus, the

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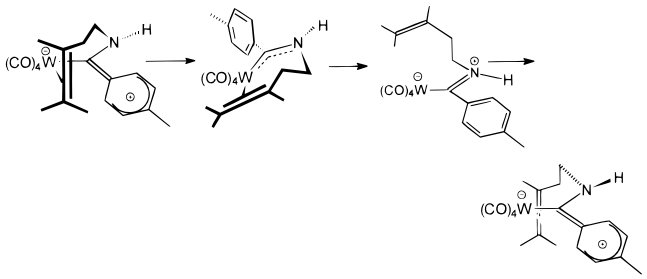
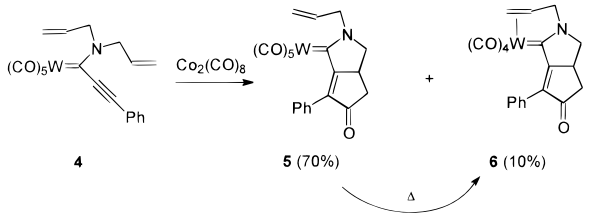
(10) Eisenstein, O.; Hoffmann, R.; Rossi, A. R. *J. Am. Chem. Soc.* **1981**, *103*, 5382−5384.

(11) There is a substantial difference in the values of pyramidalization between six and five-membered cyclic enamines (formally related to carbene−amino complexes). See: Anderson, B. A.; Wulff, W. D.; Rahm, A. *J. Am. Chem. Soc.* **1993**, *115*, 4602−4611.

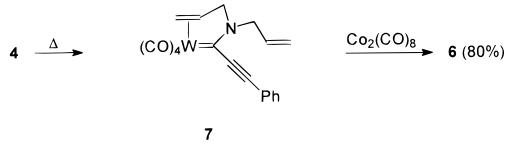
Scheme 4. Flattening of the Chelative Ring and Decoordination Process Proposed for Complexes Related to **3**



Scheme 5



Scheme 6



heteroatom will now contribute with more π donation to the carbene center with concomitant less pyramidalization at the N. The limit of this conformational motion is the flattening of the chelative ring, decoordination of the double bond, and loss of diastereotopicity in the aromatic ring (Scheme 4). As a consequence, the more substituted is the nitrogen, or more pyramidalized within the structure of the carbene ligand, the higher will be the barrier for inversion of the chelate ring through this chelation, decoordination, and rechelation process.[12] To confirm this, it is necessary however to perform detailed studies with appropriate tungsten complexes that have similar structural and electronic characteristics.

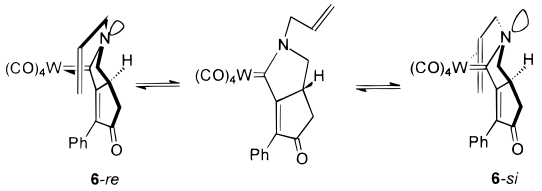
In our studies of the Pauson−Khand (P−K) carbonylative cycloaddition on (diallylamino)alkynylcarbene complexes **4,** we observed the formation of the chelated tetracarbonyl complex **6** as a side product (Scheme 5).

By heating the starting complex **4** in the absence of $Co_2(CO)_8$, the corresponding chelated enyne **7** was obtained. This complex was treated under the Pauson−Khand reaction conditions, and the complex **6** was exclusively obtained (Scheme 6). Also, heating of **5** led to extensive formation of **6.**

Product **6,** displaying the four CO bands in the infrared typical for a tetracarbonyl octahedral complex, had, in $CDCl_3$ solution, a double set of signals in its ^{1}H NMR and also in the corresponding ^{13}C NMR spectra, both sets being in an approximate 1.2/1 ratio. We interpreted this result as the consequence of the simultaneous presence of two isomeric forms that differed only in the mutual arrangement of the chelated

(12) In agreement with the potential stabilizing role displayed by conjugated π electronic systems, very recently, Templeton et al. have reported that the two possible stereoisomers (*E* and *Z*) of a, chiral at the metal, enolate carbene species were found not to interconvert on the ^{1}H NMR time scale despite the presence of an electron-donating heteroatom adjacent to the carbene center: Brent Gunnoe, T.; White, P. S.; Templeton, J. L. *Organometallics* **1997**, *16*, 370−377.

Scheme 7



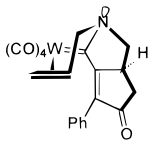
double bond and the bridgehead stereogenic center that in our case was not invertible. Nevertheless, unexpectedly, either heating or cooling the probe, we did not observe any shift, widening, or collapsing of the NMR signals. These facts led us to think initially that we were facing the existence of true diastereomers, and therefore we decided to apply a chromatographic technique, such as HPLC, to resolve them. Indeed, the use of SiO_2, as the stationary phase, and *n*-hexane/EtOAc (20/80), as the mobile phase, allowed us not only to distinguish both isomers but also to achieve their complete separation provided the column temperature was set low enough (253 K). We also determined their relative abundance which turned out to be 1.3/1 at room temperature.[13] We observed that the initially separated *"isomers"* remained unchanged in solution for as long as their temperature was kept at 253 K but both of them independently and slowly restored the initial isomer ratio if the solution was left at room temperature. From these observations we were convinced that the two *"diastereomers"* were in practice conformers which differ in their free energies and have a relatively high rotation barrier at least in terms of the NMR time scale (Scheme 7).

We dismissed the presence of the parallel coordination mode in this complex, **6//**, as a low energy state since (a) we were dealing with five-membered chelate allyl complexes for which there were no precedents of the parallel conformer, (b) only two sets of signals (instead of three or four) were recorded in the ^{1}H and ^{13}C NMR spectra and only two peaks in the HPLC chromatogram profile were observed, and (c) a theoretical calculation, based on an empirical force field (MM2), showed that the corresponding energy for the parallel arrangement should lay far above that for perpendicular **6**-*re*.[14]

Since there was no possibility to assess the values of the thermodynamic parameters for the equilibrium by dynamic NMR (D-NMR) experiments, we turned our attention to the dynamic HPLC (D-HPLC) technique. This technique has been recently used for the study of some slow molecular dynamic processes and the determination of their thermodynamic and kinetic parameters.[15−18] Attractive features of this new technique for our purposes are the absence of any special require-

(13) We could only detect one UV absorption maximum in the spectrum of compound **6**. This result may be expected from the relatively large distance and low electronic interaction between the chromophore and the chelated double bond.

(14) An empirical calculation (MM2) of the energy corresponding to both parallel and perpendicular conformers of **6** showed a considerable lower stability for the parallel conformer **6//**. A MM2 calculation performed by PC-Model 6.0 gives a MMXE for the *re* isomer of 77.4 kcal·mol^{-1} while the same MM2 calculation performed for the parallel isomer **6//-***si* ascribes a MMXE of 102.0 kcal·mol^{-1}.



6// *re*

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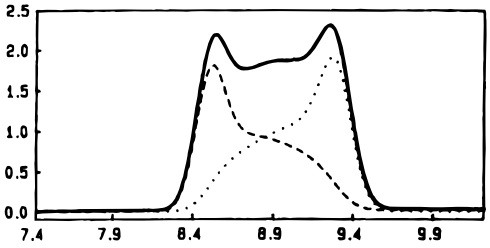

Figure 1. An example of a simulated chromatogram showing the curve (solid line) resulting from the sum of the two ideal individual chromatographic curves for injections of pure isomer A (dashed line) or B (dotted line).

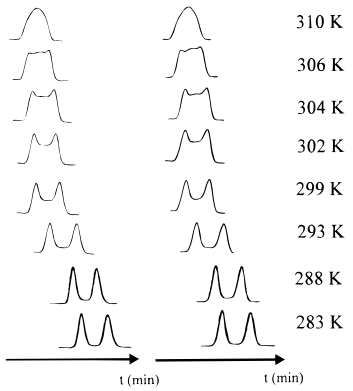

Figure 2. Experimental D-HPLC chromatograms of complex **6** (left) in the temperature range of 283−310 K at a constant flow rate using a μ-Porasil silica column (particle size 10 μm, 30 cm × 4 mm (inner diameter)) and UV detector at 270 nm, and simulated chromatograms (right): $N_A = N_B = 8000 \pm 500$; $C_B^0/C_A^0 = 1.30$, assuming that $\epsilon_B/\epsilon_A = 1.0$, and the parameters given in Table 1.

ment for the chromatographic phases and the studied process as well as the typical working temperatures (from 200 to 380 K) which enable the study of processes with energy barriers ranging from 15 to 30 kcal·mol^{-1} that are beyond the range of the classical D-NMR technique. The simplest dynamic chromatographic experiment involves two resolvable species that are interconvertible on the separation time scale (minutes). In this case, typical peak shape deformations (see Figures 1 and 2) resembling those encountered in D-NMR spectroscopy are produced by changing the temperature and/or the flow rate of the chromatographic experiment.[19] Consequently, the resulting peak shapes contain all the thermodynamic and kinetic parameters concerning the adsorption equilibria of the two interconverting species between the mobile and stationary phases (primary equilibria) as well as those parameters corresponding to the exchange process between the two species occurring both in the mobile phase and in the stationary one. Recently, two distinct methods, based on the simulation of experimental elution profiles, have been developed for studying interconverting processes occurring during chromatography. One of such methods uses a discontinuous plate model[16] while the other utilizes the stochastic one;[15] the latter provides both the kinetic and thermodynamic parameters of the dynamic process. Thus, the simulation of the elution profiles of two resolvable and interconverting species, A and B, at any experimental conditions (flow rate and temperature) with the stochastic method yields the apparent rate constants for the overall forward, $k^{\rightarrow} = k(A \rightarrow B)$, and reverse $k^{\leftarrow} = k(B \rightarrow A)$, processes[20] and the classical chromatographic parameters of the two interconverting species (i.e., retention times, t_A and t_B, and theoretical plate numbers, N_A and N_B) as well as the molecular ratio of the two species, C_B^0/C_A^0 at the injection temperature provided that their relative response at the detector, ϵ_B/ϵ_A, is known. This stochastic method also affords the equilibrium constant in the mobile phase, $K_m = k_m^{\rightarrow}/k_m^{\leftarrow}$, by using the following relationship: $K_m = k^{\rightarrow}t_A/k^{\leftarrow}t_B$.[16] Figure 2 shows the experimental chromatograms of a series of D-HPLC experiments performed at different temperatures and at constant flow rate with the tungsten complex **6** together with the simulated chromatograms using the stochastic method and the parameters given in Table 1.

Table 1. Chromatographic, Kinetic, and Thermodynamic Data Obtained from the Simulation of the Experimental Elution Profiles at Different Temperatures for D-HPLC Experiments with Complex **6**

T (K)	t_A (min)	t_B (min)	k(A→B) (s^{-1})	k(B→A) (s^{-1})	K_m[a]
263	11.6	13.0	*b*	*b*	
268	11.0	12.3	*b*	*b*	
273	10.5	11.7	*b*	*b*	
278	10.1	11.2	*b*	*b*	
283	9.7	10.8	*b*	*b*	
288	9.4	10.3	3.3×10^{-4}	1.9×10^{-4}	1.57
293	9.1	10.0	5.7×10^{-4}	3.7×10^{-4}	1.40
299	8.5	9.3	1.3×10^{-3}	8.8×10^{-4}	1.30
302	8.5	9.2	1.8×10^{-3}	1.4×10^{-3}	1.14
304	8.5	9.2	2.4×10^{-3}	2.1×10^{-3}	1.07
306	8.4	9.1	3.0×10^{-3}	2.5×10^{-3}	1.10
310	8.2	9.0	4.8×10^{-3}	4.4×10^{-3}	1.02

[a] Equilibrium constants in the mobile phase of the dynamic equilibrium between the least retained, A, and the most retained, B, diastereoconformers of complex **6**. [b] Apparent rate constants lower than 1.5×10^{-4} s^{-1}.

Using the retention times and the apparent rate constants, obtained in the temperature range of 288−310 K, we found $\Delta H° = -3.5 \pm 0.3$ kcal·mol^{-1} and $\Delta S° = -12 \pm 1$ cal·K^{-1}·mol^{-1} for the equilibrium between the diastereoconformers of complex **6**. Such data indicate that the most retained isomer is enthalpically favored while it is entropically disfavored. Therefore, this result clearly shows that the presence of an asymmetric carbon atom on a rigid bicyclic compound that acts as a carbene ligand in a tungsten−carbene−alkene complex promotes a stereoinduction during the alkene chelation. The apparent rate constants at 288−310 K were also used to determine an approximate energy barrier for the interconversion of diastereoconformers of complex **6**.[15] Using the apparent rate constants for the reverse process we found $\Delta G^{\ddagger}_{298} = 21.6 \pm 0.6$ kcal·mol^{-1} ($\Delta H^{\ddagger} = 24.8 \pm 0.6$ kcal·mol^{-1} and $\Delta S^{\ddagger} = +11 \pm 2$ cal·K^{-1}·mol^{-1}) as the energy barrier for interconverting the most retained isomer, B, into the least one. This barrier is considerably high, being similar to those obtained for some strained small heterocycles[21] and a series of polysubstituted aziridines and diaziridines whose energy barriers are mainly due to the inversion of pyramidal nitrogen atoms.[16,22]

(17) Gasparini, F.; Lunazzi, L. Misiti, D.; Villani, C. *Acc. Chem. Res.* **1995**, *28*, 163 and references therein.

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(19) For representative examples of such behaviors see: (a) Sinjc, V.; Oklobzija, M.; Lisini, A.; Sega, A.; Kajfea, F. *Tetrahedron* **1979**, *35*, 2531. (b) Schurig, V.; Bürkle, W. *J. Am. Chem. Soc.* **1982**, *104*, 7573. (c) Lebl, M.; Gut, V. *J. Chromatogr.* **1984**, *288*, 1. (d) Eiglsperger, A.; Kastner, F.; Mannschreck, A. *J. Mol. Struct.* **1985**, *126*, 421. (e) Moriyasu, M.; Yamagami, C.; Kato, A.; Hashimoto, Y.; Takao, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1539. (f) Mannschreck, A.; Andert, D.; Eiglsperger, A.; Gmahl, E.; Büchner, H. *Chromatographia* **1988**, *25*, 182. (g) Mannschreck, A.; Kiessl, L. *Ibid.* **1989**, *28*, 263.

(20) The apparent rate constants, $k^{\rightarrow}$ and $k^{\leftarrow}$, determined by this method are in fact related to those involved in the actual equilibria occurring in the mobile phase, $k_m^{\rightarrow}$ and $k_m^{\leftarrow}$, and in the stationary phase, $k_s^{\rightarrow}$ and $k_s^{\leftarrow}$. Although such apparent rate constants need not be equal to the rate constants of the interconverting processes occurring in the mobile and stationary phases, in practice they can be used to determine an approximate energy barrier for the studied dynamic process.

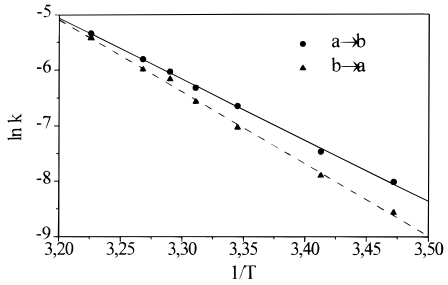


Figure 3. Van't Hoff diagram: ln *k* as a function of 1/*T* for the calculated values.

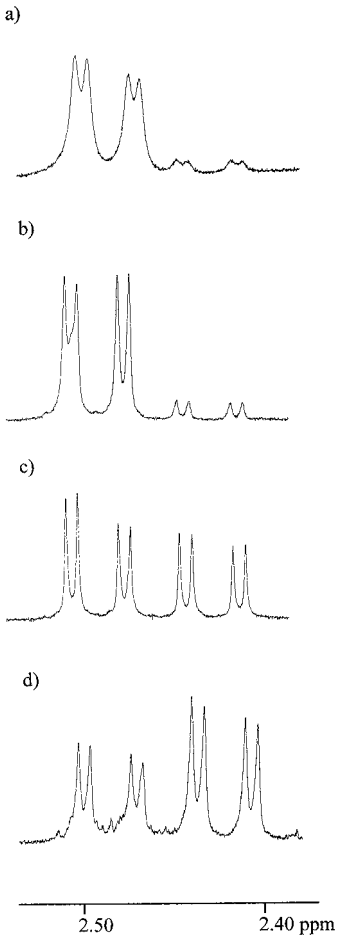


Figure 4. ^{1}H NMR signals almost exclusive of one isomer (a) at 223 K, (b) at 273 K, (c) at 293 K after waiting for 30 min at this temperature, and (d) after 12 h at 293 K, when the equilibrium has been achieved (solvent $CDCl_3$).

The univocal characterization and assignation of the two conformers could be made by a preparative HPLC separation of one of the conformers (the less retained of them named A) and the immediate performance of its ^{1}H NMR at −50 °C. We saw only one set of signals (see Figure 4).

In the spectrum of the isolated isomer we could single out a signal at δ 4.55 which was assigned to the pseudo*equatorial* proton H_e of the *re* isomer (this proton appears more shielded in its *si* counterpart, at δ 4.26), while the pseudo*axial* proton H_a in the same conformer appears as the most shielded of all

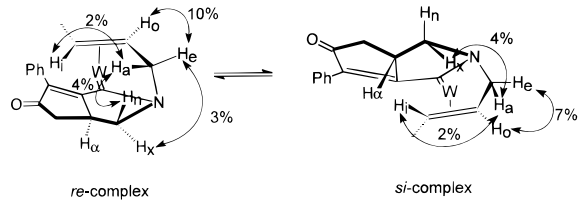
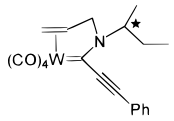


Figure 5.

allylic protons at δ 3.70 (Figure 5). We interpret the strong magnetic anisotropy between the two allylic protons in the *re* isomer as arising from the pseudo-cis ring fusion geometry which is placing one of the allylic hydrogens (H_a) pointing inward to the concave side of the tricyclic system and very probably within the region influenced by the conjugated system. As a complementary identification we could appreciate NOE effects between the high-field methylene olefin proton H_i and the more shielded allylic proton H_a on one side and the olefin methylene H_o and the low-field allylic proton on the other (in both species). This correlation is only compatible with a perpendicular chelation geometry. The parallel coordination would have led this last proton, H_o, to the neighborhood of H_a instead. Therefore, the least retained isomer A turned out to have the metal chelated at the *re* face of the allyl substituent.

Following our interest in the stereochemistry of chelation in the starting alkynyl carbenes, we further prepared the complex **8** to study the influence exerted by the triple bond on the chelative system.



8

In the present case we have a triple bond always adjacent to the carbene center, a carbene−metal bond with a low content of double bond character, and the heteroatom in a single chelative five membered ring with no further steric restrictions and liable only to marginal pyramidalization. Complex **8** as compared to **6** may be expected to display an electronically richer metal center, and therefore chelation would be disfavored (despite the fact that complex **8** could be analyzed, characterized, and subjected to NMR and HPLC techniques, it proved to be much more labile than **6**, a possible indication of an easy dissociation of the chelated double bond to give the corresponding unsaturated species).[23] Although these features should facilitate the inversion of the chelative ring again, by NMR, we could detect two rotamers in $CDCl_3$ at 293 K.[24] However, their interconversion was much faster since they could not be resolved by HPLC even at low temperatures (233 K). Presumably the facility for inversion in this case was falling in the range between those complexes studied by Casey and the ones reported above.

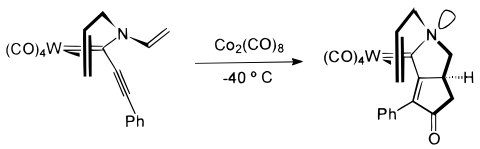
(21) (a) Klarner, F.-G.; Schroer, D. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1294. (b) Stephan, B.; Zinner, H.; Kastner, F.; Mannschreck, A. *Chimia* **1990**, *44*, 336. (c) Schurig, V.; Jung, M.; Schleiner, M.; Klarner, F.-G. *Chem. Ber.* **1992**, *125*, 1301.

(22) Mintas, M. Mannschreck, A. *Chem. Ber.* **1979**, *112*, 2028. Schurig, V.; Leyrer, V. *Tetrahedron: Asymmetry* **1990**, *1*, 865.

(23) Chelation of σ basic heteroatoms has been found quite general for other kinds of carbene complexes. See for instance: (a) Dötz, K. H.; Sturm, W.; Popall, M.; Riede, J. *J Organomet. Chem.* **1984**, *277*, 267−275. (b) Dötz, K. H.; Rau, A.; Harms, K. *Chem. Ber.* **1992**, *125*, 2137−2142. c.*)* Dötz, K. H.; Larbig, H.; Harms, K. *Chem. Ber.* **1992**, *125*, 2147−2148. (d) Dötz, K. H.; Rau, A.; Harms, K. *J. Organomet. Chem.* **1992**, *439*, 263−277. (e) Grotjahn, D. B.; Kroll, F. E. K.; Schäfer, T.; Harms, K.; Dötz, K. H. *Organometallics* **1992**, *11*, 298−310. (f) Dötz, K. H.; Kroll, F.; Harms, K. *J. Organomet. Chem.* **1993**, *459*, 169−176. (g) Powers, T. S.; Shi, Y.; Wilson, K. J.; Wulff, W. D.; Rheingold, A. L. *J. Org. Chem.* **1994**, *59*, 6882−6884. Nevertheless, we were unable to achieve efficient σ-chelation in alkynylcarbene complexes by either thermical or photochemical methods.

(24) When D-NMR was tried in $Cl_4C_2D_2$ at 383 K, the complex decomposed before any interconversion could be recorded.

Scheme 8



7 **6**-*re*

As stated at the beginning, it was also our interest to investigate whether a determined geometry for chelation might bring in any selectivity in the formation of the stereogenic bridgehead center in a P−K cycloaddition. Provided that chelation could be frozen throughout the relatively long times required for the accomplishment of the P−K cycloaddition at low temperature, the steric demands displayed by a chelative ring and a substituted nitrogen could convey some degree of stereoinduction. Thus, when the reaction was performed on pure chelated starting complex **7**, as the substrate, and $Co_2(CO)_8$ at 233 K, we found that a single diastereomer (the higher in energy **6**-*re*) was produced as indicated by HPLC (Scheme 8). However, when this product was allowed to warm to room temperature, the equilibrium ratio for these conditions was reached after a few hours.

Conclusions

The presence of a stereogenic center on a tungsten (allylamino)carbene complex originates the formation of two diastereomeric chelation products whose interconversion energy depends on the degree of pyramidalization of the N-center imposed by the inherent carbene structure and the size of the chelate ring. This energy, in particular cases, can approach that of separable isomers and be determined by means of dynamic HPLC (D-HPLC) techniques. Conversely, the presence of a chelate ring in a carbene complex can lead to strong discrimination in the formation of a stereogenic center in an intramolecular cycloaddition.

Experimental Section

Unless otherwise stated all common reagents were used as obtained from commercial suppliers without further purification.

NMR spectra were recorded on a Bruker DRX-500 or a Varian XL-300 apparatus. All samples of carbene complexes were filtered through a pad of Celite and EDTA prior to recording the spectra. IR spectra were recorded on a Bomem FT-IR M-120 spectrophotometer. Elemental analyses were performed using a Carlo-Erba 1106 apparatus. HPLC chromatography was performed on a Perkin-Elmer Series LC-235 spectrometer equipped with a diode array detector, a PE Nelson Series 900 interface coupled to an external computer, and a Perkin-Elmer Series 410 pump system. For the dynamic HPLC studies a μ-Porasil column from Waters (silica particle size 10 μm, 30 cm × 4 mm) was used as the stationary phase and EtOAc/hexane (90:10) mixtures with a flow rate of 0.8 mL·min^{-1} were used as the mobile phase. The column was thermostated at the different working temperatures with a glass homemade jacket using a F3 Haake ultrathermostat. Solvents for HPLC were degassed previously. Flash column chromatography was performed with "flash grade" silica (SDS 230−400 mesh). Solvents were distilled and dried prior to use.

All the reactions were carried out under argon using previously dried solvents. Pentacarbonyl[(diallylamino)(phenylethynyl)carbene]tungsten(0) **(4)** was prepared by a literature procedure.[24]

Preparation of *cis*-Tetracarbonyl(3-η^2-allyl-3-aza-8-phenylbicyclo-[3.3.0]oct-8-en-2-ylidene)tungsten(0) (6). To a stirred solution of 1.01 g (2.00 mmol) of tetracarbonyl[(diallylamino)(phenylethynyl)carbene]-tungsten(0) (**7**) in 50 mL of dry toluene was added 0.82 g (2.40 mmol) of $Co_2(CO)_8$. After 30 min of stirring at room temperature, a control by TLC showed the disappearance of the starting complex. Evaporation followed by chromatography (hexane/EtOAc = 1/1) afforded 0.90 g (84%) of **6** in an isomer mixture with a 1/1.2 ratio. IR (CCl_4): ν 2027, 1947, 1934, 1897, 1720 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): (*re* isomer) δ 2.46−2.51 (dd, J = 17.8, 4.0 Hz, 1H, CH_2), 2.84−2.89 (dd, J = 17.8, 6.5 Hz, 1H, CH_2), 3.29−3.31 (d, J = 12.9 Hz, 1H, CH_2), 3.51−3.57 (m, J = 15.5, 6.5, 4.0, 3.5, Hz, 3H, CH_2, C*H*), 3.89−3.93 (dd, J = 15.5, 3.5 Hz, 1H, CH_2), 3.66−3.70 (dd, J = 14.5, 6.0 Hz, 1H, CH_2), 4.51−4.55 (dd, J = 14.5, 5.0 Hz, 1H, CH_2), 4.55−4.67 (m, J = 12.9, 5.0 Hz, 1H, CH_2), 7.41−7.46 (m, 5H, Ph); (*si* isomer) δ 2.39−2.43 (dd, J = 18.0, 4.2 Hz, 1H, CH_2), 2.81−2.83 (d, J = 12.3 Hz, 1H, CH_2), 2.83−2.88 (dd, J = 18.0, 7.0 Hz, 1H, CH_2), 2.98−3.00 (d, J = 9.2 Hz, 1H, CH_2), 3.39−3.43 (dd, J = 11.8, 7.9 Hz, 1H, CH_2), 3.51−3.57 (ddd, J = 4.2, 7.9, 8.4 Hz, 1H, C*H*), 3.87−3.91 (dd, J = 11.8, 8.4 Hz, 1H, CH_2), 4.13−4.16 (d, J = 15.3 Hz, 1H, CH_2), 4.22−4.26 (dd, J = 15.3, 5.0 Hz, 1H, CH_2), 4.55−4.67 (m, J = 12.3, 9.2, 6.0, 5.0 Hz, 1H, C*H*), 7.41−7.46 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$, 75.4 MHz) (*re* + *si* isomers): δ 40.5 (t), 43.3 (d), 43.6 (d), 54.9 (t), 58.1 (t), 59.7 (t), 61.4 (t), 61.9 (t), 68.1 (d), 72.9 (d), 128.0 (d), 128.1 (d), 128.5 (d), 128.6 (d), 130.2 (d), 130.4 (d), 130.5 (s), 130.6 (s), 142.9 (s), 143.5 (s), 177.8 (s), 177.9 (s), 202.8 (s), 203.3 (s), 203.6 (s), 203.8 (s), 207.1 (s), 207.6 (s), 208.7 (s), 208.9 (s), 209.6 (s), 214.5 (s), 239.0 (2C, C═W). EM (FAB+): m/e 533 (M^+, 100), 505 (23), 449 (75), 421 (45). Anal. Calcd for $C_{20}H_{15}NO_5W$: C, 45.04; H, 2.81; N, 2.63. Found: C, 45.28; H, 3.07; N, 2.60.

Preparation of *cis*-tetracarbonyl[(η^2-allyl-(*S*)-isobutylamino)-(phenylethynyl)carbene]tungsten(0) (8). A solution of 0.328 g (0.60 mmol) of pentacarbonyl[(*N*-allyl-(*S*)-isobutylamino)(phenylethynyl)-carbene]tungsten(0) in 20 mL of toluene was heated to 80 °C for 2 h. After evaporation and chromatography (hexane/CH_2Cl_2 = 3/1) 0.225 g (72%) of the expected product **8** in an isomer ratio of 1/1 was obtained. UV (ethanol): λ 292.9, 321.0 nm. IR (CCl_4): ν 2175, 2024, 1932, 1910 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.96 (t, J = 7.5 Hz, 3H, CH_3), 1.28 (d, J = 6.6 Hz, 3H, CH_3), 1.38 (d, J = 6.6 Hz, 3H, CH_3), 1.54−1.73 (m, J = 7.5, 7.0 Hz, 4H, CH_2), 3.26−3.74 (m, J = 16.8, 11.7, 7.5, 7.0, 6.6 Hz, 6H, C*H*, CH_2), 4.43−4.68 (m, 6H, CH_2, C*H*), 7.36−7.60 (m, 5H, Ph). ^{13}C NMR (acetone-d_6, 75 MHz): δ 11.3 (q), 11.4 (q), 19.3 (q), 19.5 (q), 29.0 (t), 29.4 (t), 56.2 (t), 56.6 (t), 61.7 (t), 62.8 (t), 65.5 (d), 65.7 (d), 75.0 (d), 76.5 (d), 90.9 (s), 123.0 (d), 124.8 (s), 129.7 (d), 131.3 (d), 133.1 (s), 203.3 (s), 203.5 (s), 203.8 (s), 204.0 (s), 210.5 (s), 210.8 (s), 212.6 (s), 213.2 (s), 232.5 (C═W), 233.1 (C═W). Anal. Calcd for $C_{20}H_{19}NO_4W$: C, 46.09; H, 3.67; N 2.69. Found: C, 45.93; H, 3.65; N, 2.65.

Dynamic HPLC Experiments. Several chromatograms at different temperatures (283−310 K) were recorded, using a μ-Porasil silica column (particle size 10 μm, 30 cm × 4 mm (inner diameter)), EtOAc/hexane (90/10) mixtures with a flow rate of 0.8 mL·min^{-1}, and UV detector at 270 nm. The glass jacket around the column was connected to a F3 Ultra Haake thermostat and before each chromatogram was recorded, the column was stabilized for 30 min at a set temperature. The HPLC tube at the entrance of the column was looped and was placed in a jacket, so that the solvent could be precooled before entering the column. All other connections had to be as short as possible to minimize dead volume in the chromatographic system.

Separation and Univocal Assignment of the Two Isomers of 6 by HPLC. A μ-Porasil silica column (particle size 10 μm, 30 cm × 4 mm (inner diameter)) was used as the stationary phase for separation. EtOAc/hexane (90/10) mixtures with a flow rate of 0.8 mL·min^{-1} were used as the mobile phase. The first isomer could be isolated in pure form when only one-third of the first fraction was collected and the signal of the UV detector (270 nm) increased. Evaporation at 233 K afforded only the *re* isomer which was dissolved in $CDCl_3$ precooled to 233 K to run its ^{1}H NMR spectra at different temperatures (223 K up to room temperature).

HPLC Studies on *cis*-Tetracarbonyl[(η^2-*N*-allyl-*(S)*-isobutylamino)(phenylethynyl)carbene]tungsten(0) (8) at Different Temperatures. Several chromatograms at different temperatures (233−273 K) were recorded, using a μ-Porasil silica column (particle size 10 μm, 30 cm × 4 mm (inner diameter)) and a UV detector at 293 nm. As eluents of the HPLC, mixtures of $CHCl_3$/hexane and EtOAc/hexane were used. Separation of the two isomers could never be obtained.

Cyclization of Tetracarbonyl[(diallylamino)(phenylethynyl)-carbene]tungsten(0) (7) at 233 K. A solution of 1.00 g (2.00 mmol)

of tetracarbonyl[(diallylamino)(phenylethynyl)carbene]tungsten(0) (**7**) in 20 mL of dry THF was cooled to 233 K, and 0.82 g (2.40 mmol) of $Co_2(CO)_8$ was added. After 12 h the solvent was removed at 233 K under high vacuum and the sample was dissolved in the eluent, which was previously cooled to 233 K. Only one isomer (*re* with the lower retention time) could be detected using a μ-Porasil silica column (particle size 10 μm, 30 cm $\times$ 4 mm (inner diameter)), EtOAc/hexane (90/10) mixtures with a flow rate of 0.8 mL·min^{-1} as eluent, and a UV detector at 270 nm. The system was cooled previously with the glass jacket to 233 K.

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Supporting Information Available: Experimental procedures, analytical and spectral data for compounds **7** and precursors of **8** (3 pages). See any current masthead page for ordering information and Web access instructions.

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