J|A|C|S
ARTICLES

Copper(I)−Homoscorpionate Catalysts for the Preferential, Kinetically Controlled Cis Cyclopropanation of α-Olefins with Ethyl Diazoacetate

M. Mar Díaz-Requejo,[†] Ana Caballero,[†] Tomás R. Belderraín,[†] M. Carmen Nicasio,[†]
Swiatoslaw Trofimenko,[‡] and Pedro J. Pérez*,[†]

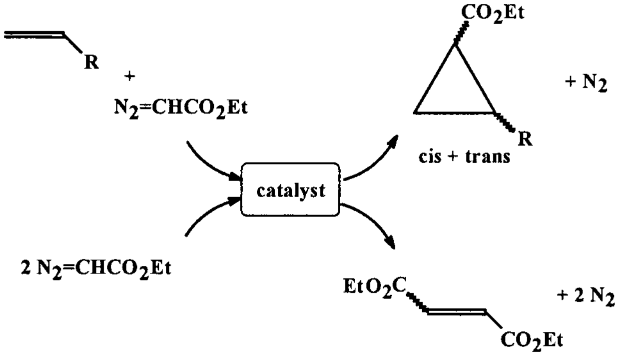
Contribution from Departamento de Química y Ciencia de Materiales, Universidad de Huelva,
Carretera de Palos de la Frontera s/n 21819-Huelva, Spain, and Department of Chemistry and
Biochemistry, University of Delaware, Newark, Delaware 19716

Received August 6, 2001

Abstract: In situ prepared copper catalysts Tp^XCu (Tp^X = homoscorpionate) catalyze the olefin cyclopropanation reaction using ethyl diazoacetate as the carbene source. Very high values of both activity and diastereoselectivity toward the cis isomer have been obtained for styrene, α-methylstyrene, 1-hexene, 1-octene, vinyl acetate, *n*-butyl vinyl ether, 2,5-dimethyl-2,4-hexadiene, and 3,3-dimethyl-1-butene. The effect of the temperature in the diastereoselectivity was almost negligible within the range −10 to +30 °C. Kinetic studies have allowed us to propose that the homoscorpionate ligand might act in a dihapto form during the catalytic process. This transformation seems to operate under kinetic control, where the formation of the cis isomer would govern the reaction rate.

Introduction

Scheme 1. The Olefin Cyclopropanation Reations



The olefin cyclopropanation reaction constitutes a nice example to evaluate the different orientations that a metal-based catalyst can induce.[1] Since the mid 1960s this transformation has been traditionally performed by reacting a diazo compound reagent, which acts as the carbene precursor, and an olefin (Scheme 1), with the intermediacy of a transition-metal complex.[2] A nondesired side reaction, the decomposition of the diazo reagent, also takes place simultaneously. With monosubstituted olefins, the former reaction leads to the formation of two cyclopropane diastereomers, cis and trans, as a consequence of the existence of two stereogenic centers. The variables that could be optimized in the olefin cyclopropanation reaction are (i) the minimization of the diazo compound decomposition reaction, (ii) the diastereoselectivity, and (iii) the enantioselectivity. The first one has usually been avoided by means of slow addition devices, the diazo compound concentration being maintained at low levels compared to that of the olefin, although this method supposes the use of long reaction times. On the other hand, control of the enantioselectivity has been extensively studied and maximum levels of enantioselection have already been achieved. The most efficient catalysts for this reaction are based on copper or rhodium, although some others of ruthenium and cobalt have also been reported.[2] The ligands employed vary from one metal to another. Thus, semicorrines,[3] bisoxazolines,[4] or bipyridines[5] have been attached to copper whereas carboxylates[6] or carboxamidates[6] are the ligands of choice with the rhodium(II) Rh_2L_4-type catalysts. Other ligands such as porphyrins[7]

---

* Corresponding author. E-mail: perez@dqcm.uhu.es.
[†] Universidad de Huelva.
[‡] University of Delaware.

(1) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, U.K., 1995; Vol 12, p 387.

(2) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York 1998.

(3) (a) Leutenegger, U.; Umbricht, G.; Fahrni, C.; Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143-2156. (b) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553−1565.

(4) (a) Evans, D. A.; Woerpel, K. A.; Himman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726−728. (b) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005−6008

(5) (a) Ito, K.; Katsuki, T. *Chem Lett.* **1994**, 1857−1860. (b) Ito, K.; Katsuki, T. *Tetrahedron Lett.* **1993**, *34*, 2661−2664. (c) Kwong, H.-L.; Lee, W.-S.; Ng, H.-F.; Chiu, W.-H.; Wong, W.-T. *J. Chem. Soc., Dalton Trans.* **1998**, 1043−1046.

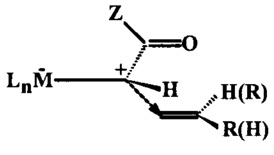
(6) (a) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919. (b) Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc., Chem. Commun.* **1990**, 361−362. (c) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897−6907. (d) Doyle, M. P.; Zhou, Q.-L. *Tetrahedron Lett.* **1996**, *37*, 4129−4132. (e) Doyle, M. P.; Winchester, W. R.; Hoorn, J. A. A.; Lynch, V.; Simonsen, S. H.; Ghosh, R. *J. Am. Chem. Soc.* **1993**, *115*, 9968−9978.

(7) Maxwell, J. L.; O'Malley, S.; Brown, K. C.; Kodadek, T. *Organometallics* **1992,** *11*, 645−652.

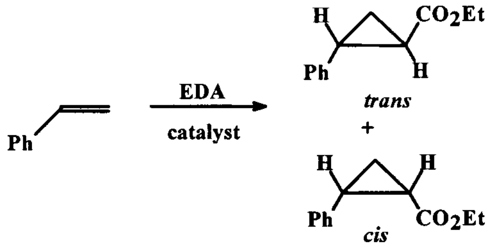
10.1021/ja011895y CCC: $22.00

(rhodium), pybox (ruthenium),[8] or salen (cobalt,[9] ruthenium[9,10]) have also provided noticeable enantiomeric excesses.

In contrast to the aforementioned advance in enantioselectivity, diastereocontrol of this transformation has remained somewhat elusive. The number of catalysts reported to date that induce a noticeable degree of diastereomeric excess (de) is relatively small in number compared with those providing large ee's. This fact has been explained in terms of the small influence of the structure of the catalyst in the diastereoselectivity due to the existence of an early transition state (**A**) in which the olefin is sufficiently far from the metal center to be affected by steric effects.[2] These steric influences are not therefore decisive in the induction of de's, although some good results have been obtained by means of very bulky diazo compounds, olefins, or both. The cyclopropanation of styrene has been frequently employed as a probe to test the catalytic potential of a transition-metal complex toward this transformation (eq 1). The vast majority of reported catalysts have provided cis/trans ratios within the range 50:50−25:75. Beyond these limits, a catalyst could be described as unusually diastereoselective. A few examples are known to preferentially promote the formation of the trans diastereomer. Complex $RuCl_2$(Pybox-*ip*) provided a 9:91 cis/trans ratio.[8] The porphyrin osmium complex Os(TPP) (TPP = tetraphenylporphyrin) enhanced the trans selectivity up to 1:13 (cis/trans),[11] whereas the iron analogue decreased that ratio to 1:9.[12] The cobalt complex Co(salen)I also favored that isomer, leading to a 2:98 cis/trans ratio.[9]



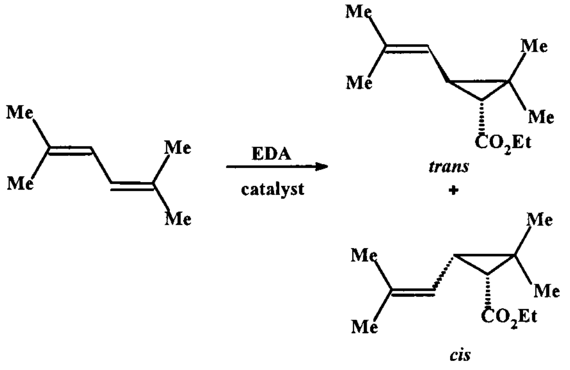
A



(1)

On the other hand, cis diastereoselectivity is still rare[1] in such a way that the maximum values reached when we started our work on this topic corresponded to Hossain's iron-based catalyst, $[Cp(CO)_2Fe(THF)]^+$,[12] (84:16 cis/trans ratio, 40% yield). The well-known copper and rhodium catalysts had not provided better results. Only a modest 74:26, cis/trans ratio had been reported by Brunner and co-workers using a chiral, camphor-derived tetrakis(pyrazolyl)borate copper(I) complex.[13] In a work developed simultaneously to ours, Katsuki and co-workers achieved both highly cis and trans diastereoselectivities with Co−salen complexes by modifying the groups attached to the salen ligand.[14] In their preliminary communication,[14a] a 98:2 cis/trans ratio was reported for styrene cyclopropanation using the bulkier *tert*-butyl diazoacetate as the carbene source, a Co(II)−salen complex as the catalyst, and *N*-methylimidazole as an additive. Later, this work was extended to ethyl diazoacetate, with similar results and conditions, and 24 h as the total reaction time.[14b] Finally, Mezzetti et al.[15] recently reported high cis diastereoselectivities with the five-coordinated $[RuClPNNP)]^+$ complexes, although yields are quite low (12% yield for a 95:5 cis/trans ratio).

The situation with α-olefins is somewhat simple: only a few catalysts have induced trans diastereoselectivities and *none*, to our knowledge, has been reported to promote cis diastereoselectivity in noticeable yield. The menthyl or the BHT diazo derivatives have provided excesses of the trans isomer in the 1-alkene cyclopropanation reaction.[16] More interesting is the cyclopropanation of 2,5-dimethyl-2,4-hexadiene to give the chrysanthemate ester (eq 2), due to its use in pesticide industry.



(2)

With those sterically demanding diazo compounds, preferentially trans diastereoselectivity has been already published: Masamune[17] reported 16:84 cis/trans formation with a copper-based catalyst and menthyl diazoacetate whereas Doyle later provided a 6:94 cis/trans ratio when using rhodium acetate and BDA as the carbene source.[16a] Only the already mentioned Mezzetti's catalyst $[RuClPNNP)]^+$ has afforded excesses of the cis isomer, but only in a 18% yield.[15]

The above information constitutes the starting point of this work, part of which has already been communicated:[18] the development of a cis diastereoselective catalyst for the general cyclopropanation reaction of styrene as well as for α-olefins.

Results and Discussion

α -Olefin Cyclopropanation Reaction Catalyzed by Tp^X-Cu. We previously reported the catalytic capabilities of the complex $Tp^*Cu(C_2H_4)$ or its 16-e derivative Tp*Cu (Tp* = hydrotris(3,5-dimethylpyrazolyl)borate toward the conversion

---

(8) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S.-B.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223

(9) Fukuda, T.; Katsuki, T. *Synlett* **1995**, 825−826.

(10) (a) Uchida, T.; Irie, R.; Katsuki, T. *Synlett* **1999**, 1163−1165. (b) Uchida, T.; Irie, R.; Katsuki, T *Tetrahedron* **2000**, *56*, 3509.

(11) Smith, D. A.; Reynolds, D. N.; Woo, L. K. *J. Am. Chem. Soc.* **1993**, *115*, 2511

(12) Seit, W. J.; Saha, A. K.; Hossain, M. M. *Organometallics* **1993**, *12*, 2604.

(13) Brunner, H.; Singh, U. P.; Boeck, T.; Altmann, S.; Scheck, T.; Wrackmeyer, B. *J. Organomet. Chem.* **1993**, *443*, C16−C18.

(14) (a) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 3647−3651. (b) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Adv. Synth. Catal.* **2001**, *343*, 79−88.

(15) Bachmann, S.; Furler, M.; Mezzetti, A. *Organometallics* **2001**, *20*, 2102−2108.

(16) (a) Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906. (b) Aratani, T. *Pure Appl. Chem.* **1985**, *57*, 1839.

(17) Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.* **1991**, *32*, 7373.

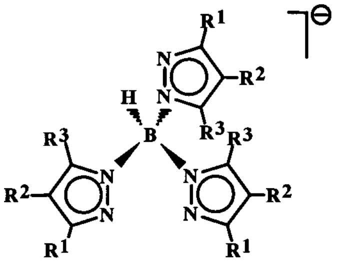
(18) Díaz-Requejo, M. M.; Belderrain, T. R.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 3167−3168.

Table 1. α-Olefin Cyclopropanation Reaction Catalyzed by $Tp^{X}Cu^{a}$

	$Tp^{Ph}Cu$		$Tp^{\alpha-Nt}Cu$		$Tp^{Ph,4-Me}Cu$		$Tp^{Ms}Cu$		
olefin	% yield[b]	cis:trans[c]	% yield[b]	cis:trans[c]	% yield[b]	cis:trans[c]	% yield[b]	cis:trans[c]	de
3,3′-dimethyl-1-butene[d]	61	25:75	28	26:74	78	28:72	82	65:35	30
2,5-dimethyl, 2,4-hexadiene[d]	99	42:58	80	60:40	99	51:49	97	78:22	56
1-hexene	65	44:56	73	49:51	63	50:50	84	77:23	54
1-octene	69	44:56	72	47:53	66	51:49	80	75:25	50
vinyl acetate[d]	66	45:55	47	52:48	30	54:46	87	92:8	84
n-butyl vinyl ether	93	46:54	93	59:41	92	57:43	97	79:21	58
styrene	80	80:20	87	82:18	86	82:18	>98	98:2	96
α-methylstyrene	91	82:18	92	84:16	87	86:14	98	97:3	94

[a] See Experimental Section [b] Determined by GC after total consumption of EDA. [c] Percentage of cyclopropanes at the end of the reaction (diethyl fumarate and maleate accounted for 100% of EDA). [d] Carried out with syringe pumps.

of olefins into cyclopropanes,[19] the diastereoselectivity achieved in the cyclopropanation of styrene being modest, but favoring the cis isomer (55:45). These catalysts have also promoted the conversion of olefins into aziridines[19a] and epoxides,[20] as well as of alkynes into cyclopropenes.[21] Given the availability of a considerable number of Tp^{X} ligands,[22] we have tested their catalytic capabilities in the cyclopropanation reaction of α-olefins when coordinated to a copper center. The procedure employed was identical in all cases. The catalyst precursor was generated in situ upon mixing equimolar amounts of CuI and the potassium or the thalium salt of the corresponding ligand Tp^{X}. The resulting catalyst-containing solution was charged with a 1:5 mixture of ethyl diazoacetate and the olefin (1:50:250, [Cu]:[EDA]:[olefin]) and stirred at room temperature until no EDA was detected by GC. The olefins studied included aromatic or aliphatic, linear or branched, as well as O-containing substituents. Table 1 displays the results with four different catalysts (Tp^{Ph}, $Tp^{Ph,4Me}$, $Tp^{\alpha Nt}$, Tp^{Ms}), the most efficient, from a diastereoselective point of view, being with no doubt $Tp^{Ms}Cu$. The phenyl derivative only induced cis excesses for the styrene derivatives, whereas the trans isomer was the major product for the other six olefins. When moving to the $Tp^{Ph,4Me}$-containing catalyst, only the bulky 3,3-dimethyl-1-butene olefin gave excesses in the trans isomer. Very similar values were obtained with the α-naphthyl derivative. The use of the mesityl derivative gave, with no exceptions, cis diastereomeric excesses for the array of olefins studied. The cis diastereoselectivity was clearly increased following the sequence $Tp^{Ph} < Tp^{Ph,4Me} < Tp^{\alpha Nt} < Tp^{Ms}$. In addition, it is also possible to establish a similar order for the olefins. The 3,3-dimethyl-1-butene substrate provided, in all cases, the lowest cis diastereoselectivity. A group formed by 2,5-dimethyl-2,4-hexadiene, 1-hexene, 1-octene, vinyl acetate, and *n*-butyl vinyl ether provided similar values of cis/trans for each catalyst. This is important since 1-hexene seems to be an excellent model for the rest of those olefins. Finally, the styrenes gave the highest values for the cis isomer. A possible interpretation for these data could be related to the restriction on phenyl rotation that the ortho methyl groups induce in the Tp^{Ms} case, which would force the mesityl rings to occupy an essential orthogonal orientation with respect to the pyrazolyl plane. Tolman and co-workers prepared the complex $Tp^{Ms}Cu(THF)$,[23] its X-ray structure being in good accord with this proposition. A geometry that would present this characteristic, together with the transient noncoordinated third pyrazolyl ring as a cap during the catalytic cycle, would provide the smallest catalytic pocket, which may be responsible for high cis selectivity. To our knowledge, there is no previous report on a catalyst that induces such diastereoselection in this range of olefins toward the cis isomer using ethyl diazoacetate. As mentioned above,[15] a recent work by Mezzetti et al. described a ruthenium-based catalyst that, despite its high diastereoselectivity, presents a very low activity (yields <20%), even with the aid of slow-addition devices. Katsuki's remarkable cobalt catalyst,[14] which gives both high diastereoselectivity and activity for styrene, has not yet been reported to work with other olefins.



Tp^{x}

An important feature of these catalysts, in addition to the preferentially cis diastereoselectivity, is their high activity toward the cyclopropanation reaction, with very small amounts of the EDA decomposition products being obtained. Most of the experiments carried out in Table 1 were run without resorting to slow-addition devices, thus shortening the reaction times. Particularly interesting is the result obtained in a scale-up experiment carried out with styrene, in which a 1:500:2500 [Cu]/[EDA]/[styrene] ratio (3 g, 25 mmol of EDA, added portionwise due to the explosive nature of the diazo compound) was employed. The diazo compound was consumed in 2 h, leading to a TOF value of 250 mmol h^{-1}. Despite the high concentration of EDA, the yield in cyclopropanes was >98%, the cis/trans diastereoselectivity being maintained as >98:2.

We have also performed catalytic competition experiments with several olefins to establish the relative reactivity of those substrates in our catalytic systems. Styrene, α-methylstyrene, 1-hexene, and 2,5-dimethyl-2,4-hexadiene have been reacted in

---

(19) (a) Pérez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1993**, *12*, 261. (b) Díaz-Requejo, M. M.; Pérez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1997**, *16*, 4399. (c) Díaz-Requejo, M. M.; Belderrain T. R.; Nicasio, M. C.; Pérez, P. J. *Organometallics* **2000**, *19*, 285−289.

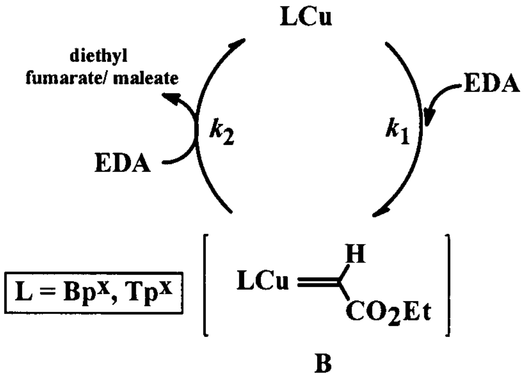
(20) Díaz-Requejo, M. M.; Belderrain, T. R.; Pérez, P. J. *Chem. Commun.* **2000**, 1853−1854.

(21) Díaz-Requejo, M. M.; Mairena, M. A.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Chem. Commun.* **2001**, 1804.

(22) Trofimenko, S. *Scorpionates, The Coordination Chemistry of Polypyrazolylborate Ligands*; Imperial College Press: London, 1999.

(23) Schneider, J. L.; Carrier, S. M.; Ruggiero, C. E.; Young, V. G.; Tolman, W. D. *J. Am. Chem. Soc.* **1998**, *129*, 11408−11418.

Scheme 2



couples, using a 1:25:250 [Cu]/[EDA]/[olefin] ratio (125 equiv of each olefin). The relative reactivity order obtained was 322:154:20:1 for styrene/α-methylstyrene/1-hexene/diene, respectively. These data must be taken into account in a cyclopropanation experiment, since those less reactive olefins would be better cyclopropanated by means of a syringe pump, to optimize the overall yields.

Kinetic Studies. Mechanistic studies[24] carried out recently with the model complex BpCu (Bp = dihydrobis(pyrazolyl)-borate) have led us to propose that the active species that reacts with the diazo compound to generate the metal−carbene intermediate must accomplish a 14-electron geometry. It was also demonstrated that the olefin inhibited the consumption of EDA, due to the formation of copper−olefin complexes. In addition, the presence of other N-donor ligands also induced the same effect, i.e., a decrease in the concentration of the active catalytic species. After these results, and given the exceptional catalytic capabilities of the Tp^{X}Cu system, we decided to compare, from a kinetic point of view, the catalytic properties of the complexes Bp^{X}Cu and the related Tp^{X}Cu (Bp^X =Bp; Bp = Bp*, dihydridobis(3,5-dimethylpyrazolyl)borate; Tp^X = Tp, hydrotris(pyrazolyl)borate; Tp = Tp*). Thus, the disappearance of EDA with time was monitored for each of those catalysts, upon varying their concentrations, in a set of experiments carried out in the absence of olefin (see Experimental Section). In all cases, first-order kinetics were observed, indicating that the formation of the metal−carbene intermediate is the rate-determining step. Scheme 2 displays a simple reaction mechanism that would explain these data. It can be readily seen that the rate of EDA consumption should be given by eq 3, and the value of k_{obs} should be that of eq 4:

$$\frac{-\mathrm{d[EDA]}}{\mathrm{dt}} = 2k_1[\mathrm{Cu}]_{\mathrm{tot}}[\mathrm{EDA}] \tag{3}$$

$$k_{obs} = 2k_1[\mathrm{Cu}]_{\mathrm{tot}} \tag{4}$$

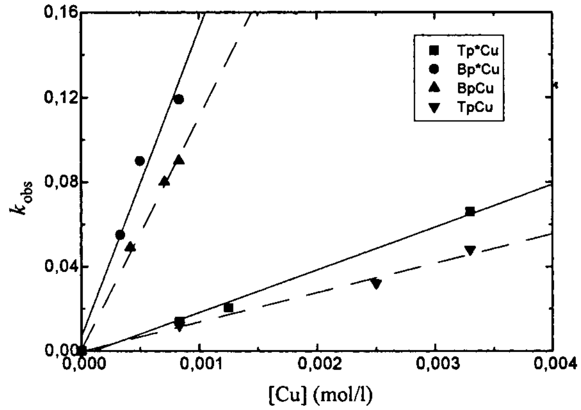


Figure 1. Variation of the rate constant (k_{obs}) vs catalyst concentration for EDA decomposition catalyzed by complexes Bp^{X}Cu and Tp^{X}Cu.

Scheme 3

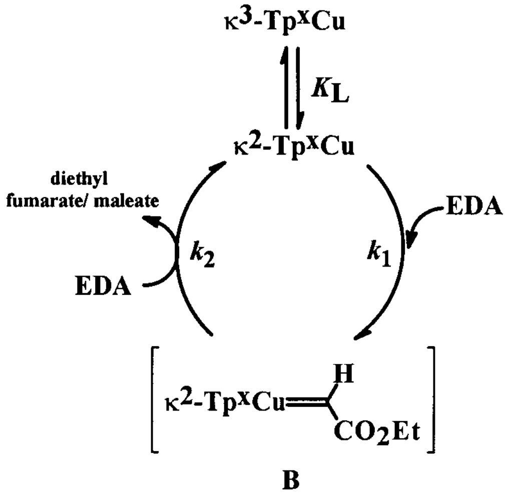


Figure 1 shows the variation of k_{obs} versus $[\mathrm{Cu}]_{\mathrm{tot}}$ for the four catalysts referred to above. A significant difference appeared between the bis- and the tris(pyrazolyl)borate derivatives. Both catalysts with two N-donors showed a similar variation in the reaction rate, the same similarity being observed with the couple of three N-donor ligands. But a considerable difference is established between the two and three N-donor ligands. A possible explanation for the trend observed in Figure 1 would invoke the existence of a dihapto−trihapto equilibrium in the Tp^X complexes, in such a way that the active catalytic species to react with EDA would be the dihapto form. If we assume this, then Scheme 2 would convert in Scheme 3, and the value of k_{obs} should now include the equilibrium constant K_L (eq 5).

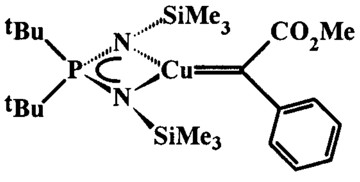
$$k_{obs} = \frac{2k_1[\mathrm{Cu}]_{\mathrm{tot}}K_L}{1 + K_L} \tag{5}$$

Our previous studies with the model system of BpCu have shown values of K_L that indicated the 14-electron species are less favored in the equilibrium. This would explain the observed decrease in the k_{obs} values when moving from Bp^{X}Cu to Tp^{X}Cu as the catalysts. It seems reasonable to believe that the catalytic active species when using the complexes Tp^{X}Cu as the catalyst precursors would be a dihapto species, with a third pyrazolyl ring uncoordinated. This κ^2-Tp^{X}Cu would react with EDA to give the corresponding carbene intermediate (**B** in Scheme 3). This proposal finds support in a very recent contribution from Straub and Hoffman,[25] in which they have detected for the first time a copper(I)−carbene complex that is active in the olefin cyclopropanation reaction. This carbene complex (**C**) contains an iminophosphanamide ligand, the LCu moiety accounting for 14 electrons and being isoelectronic to the κ^2-Tp^{X}Cu fragment.

---

(24) Díaz-Requejo, M. M.; Belderrain T. R.; Nicasio, M. C.; Prieto, F.; Pérez, P. J.; *Organometallics* **1999**, *18*, 2601−2609.

(25) Straub, B. F.; Hofmann, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1288.



C

Also, García and co-workers[26] reported a theoretical study on the copper-catalyzed cyclopropanation reaction, in which they have demonstrated that the carbene moiety is attached to a 14-e metal center prior to its interaction with the olefin. In addition, the existence of a copper−olefin complex has also been proposed as the resting state.

We believe that the third pyrazolyl ring in κ^2-Tp^{X}Cu could not be "innocent" during the cyclopropanation process: on the other hand, its proximity to the metal center could have a certain influence in the induction of diastereoselectivity. We have obtained some relevant information after comparing the values of diastereoselectivity induced by several Bp^{X}Cu and Tp^{X}Cu complexes. The results are shown in Table 2. The existence of a third pyrazolyl ring in the Tp^X ligands induced the enhancement of the amount of the cis isomer in the three cases. We interpret all the above results as follows: the Tp^X ligand acts in a dihapto form during the carbene-transfer reaction, but the noncoordinated ring is responsible for a certain degree of the preferentially cis isomer formation.

Thermodynamic and Kinetic Considerations. We performed several experiments at different temperatures in order to test the influence of this variable in the catalyst-induced diastereoselection. In the case of styrene, a similar trend was observed for the group of Tp$^{\alpha-\mathrm{Nt}}$-, Tp$^{\mathrm{Ph,4Me}}$-, Tp$^{\mathrm{Ph,4Et}}$-, and Tp$^{\mathrm{Ph,4Pr}}$-containing catalysts: the amount of the cis isomer was slightly enhanced (5%) along the temperature range from +50 to −10 °C. In the case of the Tp$^{\mathrm{Ms}}$Cu catalyst, the percentage of the cis isomer remained constant within the range of temperature studied. We believe this is a consequence of the existence of the already mentioned rigid geometry for the latter and a somewhat less rigid conformation for the others, so that rotation of the phenyl ring is diminished as the temperature decreases. We also studied the same effect with 1-hexene, but no detectable changes in diastereoselectivity were observed with the above catalysts. Since 1-hexene presents a considerably less sterically demanding geometry compared to styrene, it seems that the observed effect of the temperature in the conformation of the phenyl rings in the Tp^X ligands has no parallelism in the 1-hexene case, a fact that could be applied to the rest of olefins.

From the above results, it seems that the diastereoselectivity induced by a given catalyst and a certain olefin shows almost no dependence with respect to temperature. This could be interpreted as a consequence of a small or no thermodynamic control in this transformation, which obviously must be related to a kinetically controlled catalytic process. We have monitored the disappearance of ethyl diazoacetate in the cyclopropanation of styrene using four different catalysts that also differ in the diastereoselectivity that induces to the reaction: Tp* (16% de), Tp$^{\beta-\mathrm{Nt}}$ (34% de), Tp$^{\mathrm{Ph}}$ (60% de), and Tp$^{\mathrm{Ms}}$ (96% de). After total consumption of EDA, first-order kinetics were observed, from which the values of k_{obs} were obtained. Figure 2 shows the plot of k_{obs} versus the percentage of *cis*-cyclopropane, where a linear dependence is observed. We believe that this observation is in accord with our proposal of a kinetically controlled process. Therefore, the cis isomer is the kinetic isomer whereas the trans isomer is the thermodynamically favored. We might conclude that, in this system, the generation of the cis isomer governs the overall reaction rate.

Table 2. *cis/trans*-Cyclopropane Ratio Obtained with Bp^{X}Cu and Tp^{X}Cu Complexes

R^1	R^2	R^3	Bp^X	Tp^X
H	H	H	25:75	42:58
Me	H	Me	40:60	55:45
^{t}Bu	H	H	40:60	62:38

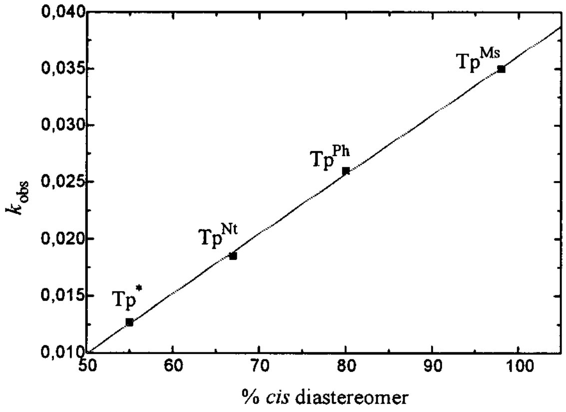


Figure 2. Plot of k_{obs} vs percentage for the cis isomer in the styrene cyclopropanation reaction.

Conclusions

A family of catalysts of general formula Tp^{X}Cu, generated in situ, catalyzes the cyclopropanation of terminal olefins, including aryl, alkyl with O-containing substituents, and the industrially important 2,5-dimethyl-2,4-hexadiene substrate, using the readily available ethyl diazoacetate as the carbene source. The mesityl derivative, Tp$^{\mathrm{Ms}}$Cu, provides exceptionally high levels of diastereoselectivity toward the *cis*-cyclopropane for all the olefins studied and with very high yields that are, in some cases, almost quantitative. Kinetic studies have revealed that the Tp^X ligands act in a dihapto form during the carbene-transfer reaction, with the noncoordinated pyrazolyl ring playing a substantial role in the induction of the diastereoselectivity. These studies have also shown that the transformation seems to proceed under kinetic control, in which the formation of the kinetic isomer, the *cis*-cyclopropane, regulates the reaction rate.

Experimental Section

General Methods. All preparations and manipulations were carried out under an oxygen-free nitrogen atmosphere using conventional Schlenk techniques. The solvents employed for all preparations were degassed before use. Olefins and ethyl diazoacetate were purchased from Aldrich and employed without further purification. The homoscorpionate ligands were prepared according to literature methods[22] as well as the complexes Bp^{X}Cu[27] and Tp^{X}Cu.[28] GC data were collected with

---

(26) Fraile, J. M.; García, J. I.; Martínez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **2001**, *123*, 7616.

(27) (a) Bruce, M. I.; Walsh, J. D. *Aust. J. Chem.* **1979**, *32*, 2753. (b) Houser, R. P.; Tolman, W. B. *Inorg. Chem.* **1995**, *34*, 1632.

(28) Mealli, C.; Arcus, C. S.; Wilkinson, J. L.; Marks, T. J.; Ibers, J. A. *J. Am. Chem. Soc.* **1975**, *98*, 711.

a Varian GC-3350 instrument. NMR experiments were run in a Varian Mercury 400-MHz spectrometer.

General Cyclopropanation Reaction of Styrene. (a) A total of 0.05 mmol of CuI and an equimolar amount of the MTp′ salt (M = K, Tl) were suspended in CH_2Cl_2, and the mixture was stirred for 2−3 h. The salts were removed by filtration, and the filtrate was charged with styrene (1.3 g, 12.5 mmol, 500 equiv) and 50 equiv of EDA (0.285 g, 2.5 mmol). Both reagents were added in one portion. The consumption of EDA was monitored by GC, the reaction time ranging from 1 to 3 h. The effect of temperature in the diastereoselectivity was studied upon performing the above transformation inside a thermostatic bath of $t \pm 0.1$ °C. (b) A scale-up experiment was carried out with the $Tp^{Ms}Cu$ catalyst, using a 1:500:2500 [Cu]/[EDA]/[styrene] ratio (3 g, 25 mmol of EDA). In this case, EDA was added portionwise to avoid explosions. After 2 h, no EDA was detected in the reaction mixture. The yield in cyclopropanes was >97%, with a 98:2 cis/trans diastereoselectivity. (c) For other olefins, the procedure was identical. For the less reactive olefins, the yields were optimized by means of a syringe pump. In this case, a solution of EDA in 20 mL of dichloroethane was added at a 2 mL/h rate into the olefin and catalyst-containing solution. The results are shown in Table 2.

Cyclopropanation Competition Experiments with Several Olefins. The catalyst was generated in situ following the aforementioned procedure. The solution containing the catalyst was charged with 250 equiv (12.5 mmol) of an equimolar mixture of styrene and α-methylstyrene. Ethyl diazoacetate (0.142 g, 1.25 mmol) was immediately added, in one portion, to the above solution. A 0.48 ratio of cyclopropane (α-methylstyrene)/cyclopropane (styrene) products was determined by GC after total consumption of EDA. Following the same procedure, experiments with equimolar mixtures of 1-hexene/styrene and 1-hexene/2,5-dimethyl-2,4-hexadiene gave the respective ratio of products 0.063 and 20.21.

Kinetic Experiments. All the kinetics experiments reported in this contribution were carried out by following the same procedure. The required amount of the precatalyst was dissolved in 1,2-dichloromethane, and then olefin, EDA, or both were added to the stirred solution in the corresponding ratio. The consumption of EDA was monitored at 25 °C by GC. The initial conditions, concentration versus time tables, and corresponding plots are given in the Supporting Information.

Acknowledgment. We thank the Dirección General de Enseñanza Superior (Proyectos PB98-0958 and 1FD97-0919-CO2-O2) and the Universidad de Huelva (Plan Propio de Investigación and Servicio de Resonancia Magnética Nuclear).

Supporting Information Available: Derivation of kinetic eqs 3−5. Concentration vs time tables and the corresponding plots for all the kinetic data referred in the text. This material is available free of charge via the Internet at http://pubs.acs.org. See any current masthead page for ordering information and Web access instructions.

JA011895Y