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Unprecedented Highly *cis*-Diastereoselective Olefin Cyclopropanation Using Copper Homoscorpionate Catalysts

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

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

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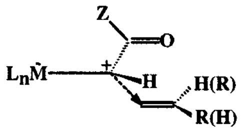
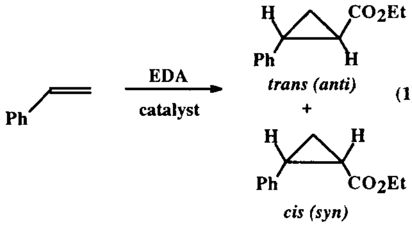
Among the metal-based catalysts examined for the intermolecular olefin cyclopropanation reaction, those of rhodium and copper have been preferentially employed in the past decade.[1,2] Rhodium catalysts are usually derived from $Rh_2(OAc)_4$, and complexes containing chiral ligands such as carboxylates or carboxamidates have induced high enantioselection in this transformation.[3] Porphyrin−rhodium complexes have also shown remarkable catalytic activity and asymmetric induction.[1,3] Copper(I) complexes with chiral salicylaldimines, bis(oxazolines), semicorrines, and bipyridines have shown similar effect, and high ee's have been reported.[1−3] In contrast to these results, there is still one elusive goal: the diastereocontrol of the reaction. The influence of the structure (catalyst, olefin) in diastereoselectivity is not high, a fact that has been rationalized by assuming that the high reactivity of the metal−carbene complex results in an early transition state (**A**) in which the olefin is still a significant distance from the metal center. Because of this, steric influences are not important in the induction of diastereomeric excesses (de), unless very bulky reactants (diazoacetate and olefin) are employed. The cyclopropanation of styrene with ethyl diazoacetate (EDA) has been studied as a model for this reaction (eq 1). Most catalysts lead to *cis:trans* ratios in the range 50:50 to 25:75.[1−3] Only a few examples are known that have provided high *trans* diastereoselectivities. The catalyst $RuCl_2$(pybox) gave[4] a 9:91 *cis:trans* ratio, and the porphyrin osmium Os(TPP) (TPP = tetraphenylporphyrin) moved that ratio to 1:13 (*cis:trans*).[5] On the other hand, few catalysts favor the formation of the *cis* isomer,[1] the maximum diastereoselectivity corresponding to Hossain's iron-based catalyst, $[Cp(CO)_2Fe(THF)]^+$,[6] (84:16 *cis:trans* ratio, 40% yield). The use of copper-catalysts have not provided better results: the highest *cis* selectivity has been reported by Brunner and co-workers using a chiral, camphor-derived tetrakispyrazolylborate copper (I) complex, (74:26, *cis:trans*).[7] The situation with other olefins is quite similar, and only high *trans* diastereoselectivities have been induced by means of very bulky diazoacetates. The menthyl or the BHT derivatives have provided a noticeable amount of the *trans* isomer of the corresponding cyclopropanes for 1-alkenes.[8] 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. Previous reports on this reaction gave preferentially *trans* diastereoselectivity when the aforementioned bulky diazoacetates where employed. Masamune[9] reported 16:84 *cis:trans* formation with a copper-based catalyst and menthyl diazoacetate. Doyle later provided a 6:94 *cis:trans* ratio when using rhodium acetate and BDA as the carbene source. To our knowledge, a catalyst that generates a diastereomeric excess on the *cis* isomer with EDA as the carbene source and 1-alkenes or 2,5-dimethyl-2,4-hexadiene is yet unknown.





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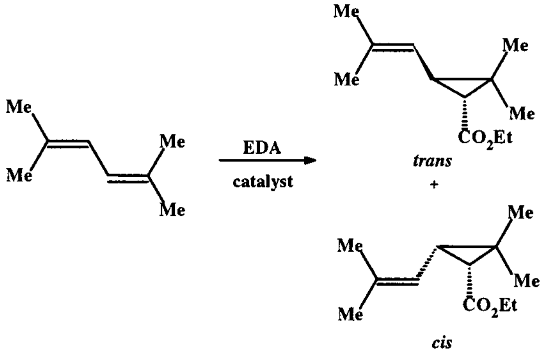

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We have recently reported[10] the use of bispyrazolylborate−copper complexes as catalysts for the olefin cyclopropanation reaction. An earlier report showed[11] that the complex Tp*Cu (**1**; Tp* = hydrotris(3,5-dimethylpyrazolyl)borate) catalyzed the conversion of olefins into the corresponding cyclopropanes, with a 55:45 *cis:trans* selectivity. In this contribution we present the results of the olefin cyclopropanation reaction with a series of in situ generated copper(I) complexes of general formula Tp^XCu, in which the groups attached to the pyrazolyl rings have been varied to probe steric effects on the catalytic reaction.

The catalyst precursors were prepared in situ upon reacting CuI with the thalium (or potassium) salt of the corresponding

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[*] Author correspondence. E-mail: perez@dqcm.uhu.es.

[†] Universidad de Huelva.

[‡] University of Delaware.

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

(2) 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.

(3) (a) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919. (b) Pfaltz, A., Yamamoto, H., Jacobsen, E. N., Eds.; *Comprehensive Asymmetric Catalysis*; Springer-Verlag 1999; Chapter 16.

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

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

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

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

(8) (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) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6008. (c) Aratani, T. *Pure Appl. Chem.* **1985**, *57*, 1839.

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

(10) Díaz-Requejo, M. M.; Nicasio, M. C.; Pérez, P. J. *Organometallics* **1998**, *17*, 3051.

(11) (a) Pérez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1993**, *12*, 261. (b) Diaz-Requejo, M. M.; Pérez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1997**, *16*, 4399.

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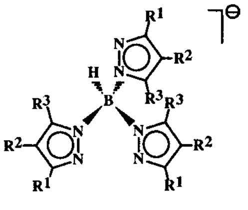
Table 1. Olefin Cyclopropanation[a] Using the Tris(pyrazolyl^X)borate−Copper(I) System

olefin	ligand[b]	yield[c,d]	*cis*:*trans*[c]
styrene	Tp^{Ph}	80	80:20
	Tp$^{Ph,4-Me}$	86	82:18
	Tp$^{Ph,4-Pr}$	86	85:15
	Tp$^{\alpha-Nt}$	87	82:18
	Tp^{Ms}	97	>98:2
1-hexene	Tp^{Ph}	65	44:56
	Tp$^{Ph,4-Me}$	63	50:50
	Tp$^{Ph,4-Pr}$	63	54:46
	Tp$^{\alpha-Nt}$	73	49:51
	Tp^{Ms}	84	77:23
2,5-dimethyl, 2,4-hexadiene	Tp^{Ph}	99	42:58
	Tp$^{Ph,4-Me}$	99	51:49
	Tp$^{Ph,4-Pr}$	99	55:45
	Tp$^{\alpha-Nt}$	80	60:40
	Tp^{Ms}	97	78:22

[a] For experimental details, see ref 14. [b] Ligands were prepared as described in the literature (ref 12). [c] Determined by GC after total consumption of EDA. [d] Percentage of cyclopropanes at the end of the reaction (diethyl fumarate and maleate accounted until 100% of EDA).

Tp^X ligand,[12] in a similar procedure to that reported for the synthesis of Tp*Cu.[13] These precatalysts were treated with a mixture of ethyl diazoacetate and styrene ([Cu]:[EDA][styrene] = 1:50:250, 0.05 mmol of Cu).[14] The results are shown in Table 1. The *cis* diastereomer was the major product observed in most cases; the diastereomeric excesses strongly depended on the pendant groups in the pyrazolyl rings. In the case of styrene, the 3-phenyl derivative induced a 60% de (80:20 *cis*:*trans*), thus improving the best result known to date with any copper catalyst, the already mentioned Brunner's system (52% de). Moreover, that value moved up to 64 and 70 when introducing alkyl substituents as R^2 in the 3-Ph ligand. But the use of the mesityl derivative (2,4,6-trimethylphenyl) provided the best result ever achieved for this transformation: a >98:2 *cis:trans* selectivity. We believe that this is related to the restriction on phenyl rotation that these methyl groups enforce in the mesityl case, restricting the mesityl ring to an essential orthogonal orientation with respect to the pyrazolyl plane. This geometry would provide the smallest catalytic pocket, which may be responsible for high *cis* selectivity.



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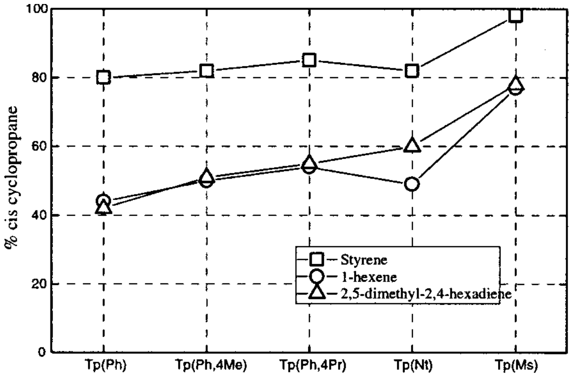

Figure 1. Trends of the *cis* diastereoselectivity in the olefin cyclopropanation reation catalyzed by Tp^{X}Cu complexes.

The results presented show a remarkable diastereoselectivity for the Tp^{Ms}−Cu(I) catalyst in the styrene cyclopropanation reaction. This exceptional feature of the mesityl-based catalyst is also applicable to other olefins. Table 1 shows the results of the cyclopropanation of 1-hexene and 2,5-dimethyl-2,4-hexadiene. The Tp^{Ms}Cu catalyst provides nearly identical *cis:trans* ratios for 1-hexene (77:23) and for the trisubstituted olefin (78:22). As mentioned above, no report on noticeable, preferential *cis* cyclopropanation has appeared to date for these olefins. In our case, the achievement of the *cis* orientation is accompanied of a quite remarkable de, since 3:1 *cis:trans* mixtures are obtained with these substrates.

It is also worth mentioning the similar trend observed for the three olefins with the copper-based catalysts employed, as shown in Figure 1. Thus, the effect of the incorporation of alkyl groups in R^2 in terms of de is identical for the three olefins. The maximum corresponds, also in the three cases, to the mesityl derivative. We interpret these similarities as a consequence of the capabilities of this family of catalysts, operating in such a way that only the olefin nature seems to influence the final cyclopropanation results.

In conclusion, we have discovered an excellent soluble catalyst for the cyclopropanation of olefins using ethyl diazoacetate as the carbene source since this system exhibits moderate to high rates and yields as well as an unprecedented level of *cis* diastereoselectivity. The modifications of these catalysts to increase the *cis* diastereoselectivity for general olefins to the levels achieved for styrene is currently underway in our laboratory.

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(12) Trofimenko, S. *Scorpionates, The Coordination Chemistry of Polypyrazolylborate Ligands*; Imperial College Press: River Edge, NJ, 1999.

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

(14) Experimental procedures: 0.05 mmol of CuI and an equimolar amount of the MTp′ salt were dissolved in CH_2Cl_2 and the mixture was stirred for 2−3 h, and then filtered. The filtrate was charged with styrene (1.3 g, 12.5 mmol, 500 equiv), and 50 equiv of EDA were added in one portion (0.285 g, 2.5 mmol). The reaction was completed in 1 h (GC). In the case of 2,5-dimethyl-2,4-hexadiene, EDA (dissolved in 20 mL of dichloroethane) was added with a syringe pump for 20 h (yields not optimized). In a scale-up experiment, a 1:500:2500 [Cu]:[EDA]:[styrene] (3 g, 25 mmol of EDA) mixture was monitored by GC. After 2 h, no more EDA remained in solution, leading to a TOF value of 250 M h^{-1}. All reactions were performed at room temperature. Caution: for higher scales, EDA should be added portionwise to avoid explosions.