

Review

Copper, silver and gold-based catalysts for carbene addition or insertion reactions

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Received 31 May 2005; accepted 8 July 2005
Available online 31 August 2005

Abstract

Two families of catalysts containing trispyrazolylborate (Tp^x) or *N*-heterocyclic carbenes (NHC) with the group 11 metals have proven useful for several reactions involving the transfer of the $:\text{CHCO}_2\text{Et}$ group from ethyl diazoacetate to saturated and unsaturated substrates.

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Keywords: Carbene transfer; Homogeneous catalysis; Copper; Silver; Gold; Trispyrazolylborate; *N*-heterocyclic carbenes; Cyclopropanation; C–H functionalization

Contents

1. Introduction	5441
2. Results and discussion	5442
2.1. Trispyrazolylborate-containing catalysts	5442
2.1.1. Olefin cyclopropanation: a diastereoselective catalyst for the <i>cis</i> isomer	5442
2.1.2. Carbene insertion into carbon–hydrogen bonds	5443
2.1.3. Functionalization of polyolefins	5446
2.1.4. Miscellaneous additions and insertions reactions	5446
2.2. <i>N</i> -heterocyclic carbene-containing catalysts	5448
3. Conclusions	5449
Acknowledgements	5450
References	5450

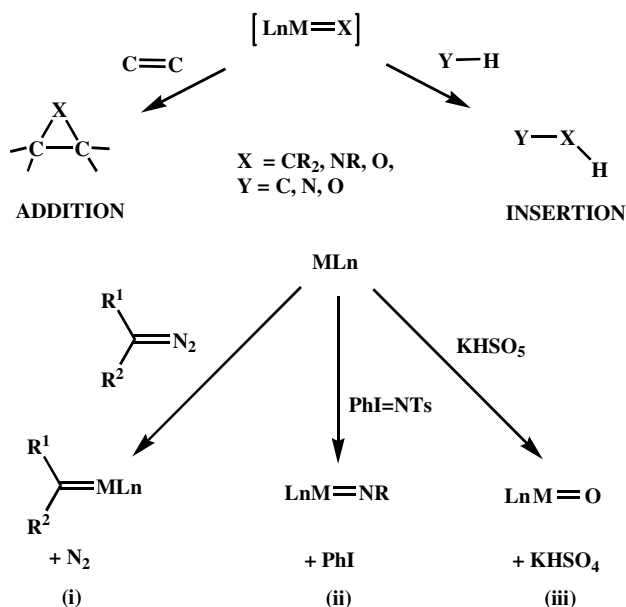
1. Introduction

The conversion of small, accessible molecules into others with a certain added value constitutes one of

the main challenges at the beginning of this century [1]. One of the strategies employed for such goal is the transfer, in a catalytic manner, of carbene, nitrene or oxo units (from the appropriate sources) to saturated or unsaturated substrates (Scheme 1, top) with the intermediacy of a transition metal complex as the catalyst [2]. The addition of those units to carbon–carbon double bonds affords cyclopropanes, aziridines or epoxides,

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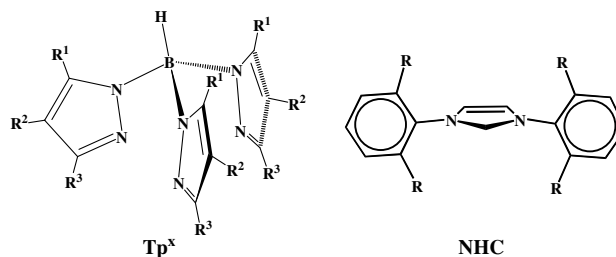


Scheme 1. (Top) Reactivity of metallo-carbenes, -nitrenes and -oxo intermediates. (Bottom) Generation of the species $L_nM = X$ for the transfer of carbene, nitrene and oxo groups.

respectively. It is also possible to use this methodology to insert such fragments into several, saturated X–H bonds ($X = N, O$ or C , among others) [2].

The development of catalytic systems for the reactions shown in Scheme 1 requires the availability of sources for the X group as well as the design of the appropriate ML_n complex that would react with those sources to give the $L_nM = X$ species. These are quite electrophilic in nature, short-lived and very reactive, a set of properties that ensure the viability of a catalytic cycle. Diazo compounds have been extensively employed as the source for carbene transfer reactions, in the most common example of this type of processes (Scheme 1, bottom). However, the interest in the formation of carbon–nitrogen bonds has led to the study of the related nitrene transfer reactions [3]. In this case, the most common source for the nitrene group is $PhI = NTs$ ($Ts = tosyl$) and related. The main drawbacks are the formation of iodobenzene as byproduct and the limitation to *N*-tosyl aziridines. Regarding the former, a new trend is emerging in the use of the haloamines-T $NaXNTs$ ($X = Cl$, chloramines; $X = Br$, bromamine) that only produces more environmentally benign NaX as side-products upon nitrene transfer. Regarding the oxo transfer process, a number of catalytic systems have been described using oxone ($KHSO_5$) as the oxo source for olefin epoxidation reactions [4].

Since the mid 1990s we have been involved in the development of copper-based catalysts for the above transformations. The use of bis-(Bp^x) and trispyrazolylborate (Tp^x) ligands [5] (Scheme 2) allowed the development of catalytic systems for olefin cyclo-



Scheme 2. Trispyrazolylborate (Tp^x) and *N*-heterocyclic carbene (NHC) ligands.

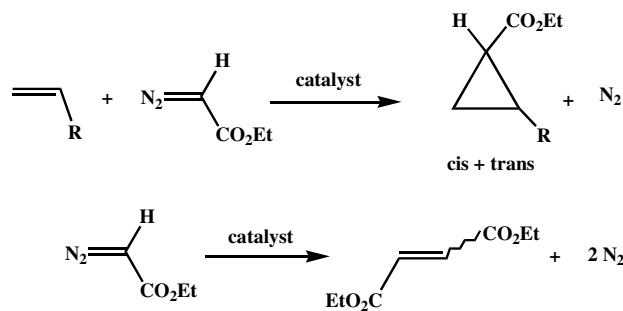
propanation [6a,6b,6c], aziridination [6d] and epoxidation [4], as well as for alkyne cyclopropanation [7]. These results were reviewed in the previous volume dedicated to metal-carbenes [8]. In the last few years, we have focused our research into the development of group 11 metal-based catalysts for the transfer of the carbene $:CHCO_2Et$ from ethyl diazoacetate to several saturated and unsaturated fragments. In addition to the already mentioned Tp^x -containing complexes, we have also prepared new catalysts where the metal atom is bonded to a *N*-heterocyclic carbene ligand (NHC, Scheme 2). In this contribution, we present the results obtained with these two families of catalysts in carbene transfer reactions from ethyl diazoacetate to saturated and unsaturated fragments.

2. Results and discussion

2.1. Trispyrazolylborate-containing catalysts

2.1.1. Olefin cyclopropanation: a diastereoselective catalyst for the *cis* isomer

The catalytic transfer of carbene groups from diazo compounds to olefins to yield cyclopropane products (Scheme 3) have been extensively employed in the last decades [2]. Although very active and enantioselective catalysts had been reported for this transformation, the control of the diastereoselection, i.e., the preferential formation of the *cis* or the *trans* isomer of the cyclopropane



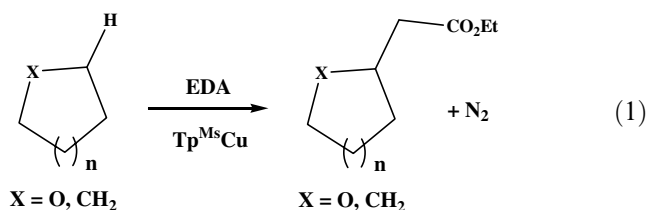
Scheme 3. (Top) Olefin cyclopropanation of terminal olefins with ethyl diazoacetate. (Bottom) Side reaction, coupling of ethyl diazoacetate.

had been elusive. At the beginning of our work, some specific catalysts for the *trans* isomer had been reported [2], but for the *cis* case the maximum diastereomeric excess (de) corresponded to 84% for styrene, whereas no de had been reported for other olefins different from styrene. We had earlier reported the use of the complex Tp^*Cu as a catalyst for the conversion of olefins and ethyl diazoacetate into cyclopropanes [6d,9]. Given the availability of a certain number of Tp^x ligands with distinct electronic and steric properties, we decided to screen the effect of the Tp^x ligand, when bonded to copper, for this reaction. Several Tp^xCu complexes (Table 1) were used, with a group of terminal olefins, the results being shown in Table 2. It is clearly observable that there is a dramatic effect of the Tp^x ligand employed in each catalyst. The $\text{Tp}^{\text{Ms}}\text{Cu}$ complex gave the highest diastereomeric excesses, that in the case of styrene was ca. 96% [10]. More interestingly, excesses of the *cis* isomer were obtained with the array of olefins employed, converting this compound as a general catalyst for the preferential *cis*-cyclopropanation of terminal olefins [11]. In addition, it is worth to mention that this is also a very chemoselective catalyst since the amounts of diethyl fumarate and maleate, formed from the catalytic coupling of ethyl diazoacetate, were quite low.

2.1.2. Carbene insertion into carbon–hydrogen bonds

The discovery of the catalytic properties of $\text{Tp}^{\text{Ms}}\text{Cu}$ for the above transformation led us to test it for the insertion of ethyl diazoacetate into carbon–hydrogen

bonds. Only a few examples based in copper had been described: the use of this methodology for such purposes has been mainly developed with rhodium (II) catalysts [12]. In spite of this, we found that $\text{Tp}^{\text{Ms}}\text{Cu}$ was capable of inducing the insertion of EDA into the C–H bonds of cycloalkanes with moderate yield, as well as in the α -C–H bonds of cyclic ethers in high yields (Eq. (1)) [13]. However, in the case of regular alkanes (hexane and 2-methylbutane) the yields were quite low.



The availability of many trispyrazolylborate ligands prompted us to try other Tp^x , with an obvious question: among the nearly 150 ligands, which criteria should we use to choose the appropriate ligand? Since the electrophilic nature of the metalcarbene intermediates shown in Scheme 1 is well established [2,12], it was planned to test Tp^x ligands with electron-withdrawing capabilities. We chose $\text{Tp}^{\text{Br}3}$ as a candidate and prepared the complex $\text{Tp}^{\text{Br}3}\text{Cu}(\text{NCMe})$, which X-ray structure is shown in Fig. 1. A previous evaluation of electron density at metal center could be foreseen in terms of the comparison of the $\nu(\text{CO})$ values for $\text{Tp}^{\text{Ms}}\text{Cu}(\text{CO})$ and $\text{Tp}^{\text{Br}3}\text{Cu}(\text{CO})$, 2079 and 2105 cm^{-1} , respectively. In good accord with

Table 1
 Tp^x ligands employed in this work

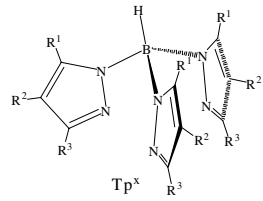
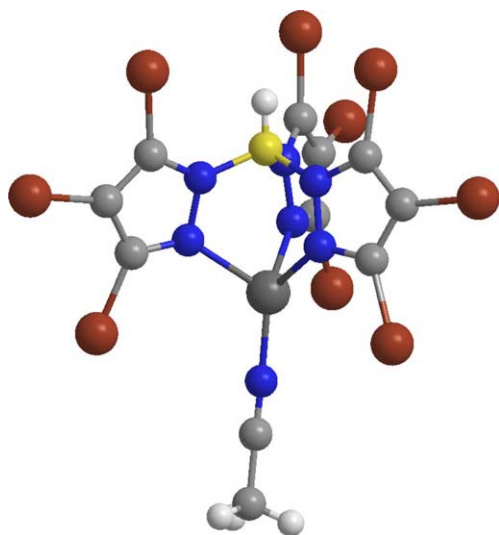
	Ligand	R ¹	R ²	R ³
	Tp^*		CH ₃	H
Tp^{Cy}		H	H	C ₆ H ₁₁
Tp^{Ph}		H	H	C ₆ H ₅
Tp^{Ms}		H	H	Mesityl
$\text{Tp}^{\text{Br}3}$		Br	Br	Br
$\text{Tp}^{\text{Ph,4-Me}}$		H	CH ₃	C ₆ H ₅
$\text{Tp}^{\alpha\text{-Nf}}$		H	H	α -Naphthyl

Table 2
 Olefin cyclopropanation reaction catalyzed by Tp^xCu

Olefin	$\text{Tp}^{\text{Ph}}\text{Cu}$		$\text{Tp}^{\alpha\text{-Nf}}\text{Cu}$		$\text{Tp}^{\text{Ph,4-Me}}\text{Cu}$		$\text{Tp}^{\text{Ms}}\text{Cu}$		<i>De</i> ^a
	Yield	<i>cis:trans</i>	Yield	<i>cis:trans</i>	Yield	<i>cis:trans</i>	Yield	<i>cis:trans</i>	
3,3'-Dimethyl-1-butene	61	25:75	28	26:74	78	28:72	82	65:35	30
2,5-Dimethyl-2,4-hexadiene	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	66	45:55	47	52:48	30	54:46	87	92:8	84
<i>n</i> -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 Diastereomeric excess for the $\text{Tp}^{\text{Ms}}\text{Cu}$ case.

Fig. 1. Molecular structure of $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$.

this difference, the reaction of EDA and cyclohexane in the presence of $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$ led to nearly quantitative conversion into ethyl cyclohexylacetate, whereas under the same conditions only 50% yields were previously obtained with $\text{Tp}^{\text{Ms}}\text{Cu}$. The improvement of the catalytic capabilities was established in the study carried out with several alkanes, with the results shown in Table 3 [14].

Several trends can be extracted from these data. Insertion takes place into secondary and tertiary sites, but not into primary C–H bonds. The values of the regioselectivity toward the tertiary C–H bonds ranged within the 87–99% interval (after statistic correction). In the

Table 3
Insertion of ethyl diazoacetate into C–H bonds of alkanes catalyzed by $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$

Alkane	Products	Yield	Select
	 80:20	53	91 ^a
	 62:38	73	87 ^a
	 —	56	>99 ^a
	 —	71	>99 ^a
	 78:22	50	64 ^b
	 76:24	60	76 ^b

^a Selectivity for tertiary sites, normalized for the relative number of hydrogen atoms.

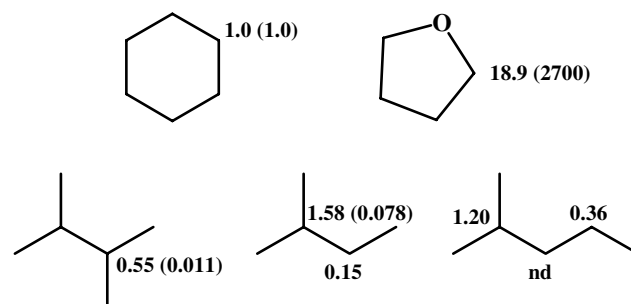
^b Selectivity for C2 secondary sites, also normalized.

case of the linear alkanes, pentane or hexane, EDA was preferentially inserted into the less hindered positions. Since the tertiary sites correspond to the more sterically demanding positions as well as to the lower in energy C–H bonds, it is reasonable to assume that electronic factors predominate in these transformations. Only when the bond energies were similar (e.g., secondary sites in pentane and hexane), the steric pressure seems to govern the regioselectivity.

We have also performed intermolecular competition experiments with several substrates with the aim of establishing the relative reactivity of distinct reaction sites [15]. Cyclohexane was chosen as the reference, the results are shown in Scheme 4, where they are compared with the reported, related data described with $\text{Rh}_2(\text{S-DOSP})_4$ as the catalyst and $\text{N}_2\text{C}(\text{Ph})\text{CO}_2\text{Et}$ as the carbene source [16]. We could conclude that the $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$ catalyst displays a different chemoselectivity toward non-activated C–H bonds, i.e., for hydrocarbon molecules, than the rhodium system.


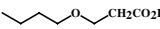
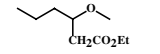

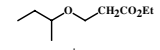

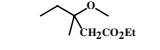
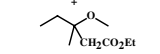

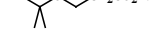

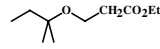
The lack of observation of any insertion into primary sites moved us to focus on such goal. First, we took advantage of the easiness to activate the α -positions in ethers and investigated the insertion of EDA into a series of methyl-alkyl ethers, and with three different catalysts [15]. The insertion of the $:\text{CHCO}_2\text{Et}$ groups (from EDA) into the methyl group was observed in most cases (Table 4), with yields and selectivities that depended of the catalyst employed.

However, the activation of methyl groups of regular alkanes was not achieved with any of the $\text{Tp}^{\text{X}}\text{Cu}$ catalysts employed. On the basis of a work by Zhou and co-workers [17] that demonstrated that for $\text{M}(\text{CO})\text{Cl}$ compounds ($\text{M} = \text{Cu}, \text{Ag}$) the silver center displayed a lower electron density, we prepared the Tp^{Br^3} -silver analogue to $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$. The reaction of silver triflate and $\text{TiTp}^{\text{Br}^3}$ in acetone gave $[\text{Tp}^{\text{Br}^3}\text{Ag}]_2 \cdot (\text{CH}_3\text{COCH}_3)$ [18a], that readily converted into $\text{Tp}^{\text{Br}^3}\text{Ag}(\text{thf})$ in tetrahydrofuran solutions. The decrease in electron density when moving from copper to silver was again evaluated



Scheme 4. Relative reactivity of hydrocarbons toward the carbene insertion (from EDA) into C–H bonds using $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$ as the catalyst. Values between parentheses are for $\text{Rh}_2(\text{S-DOSP})_4$ and $\text{N}_2\text{C}(\text{Ph})\text{CO}_2\text{Et}$ as the carbene source.

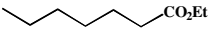
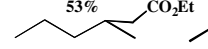
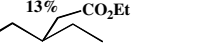
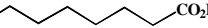
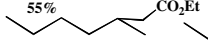
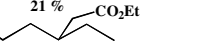

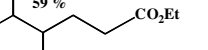
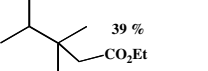

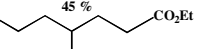
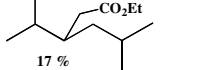
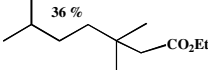

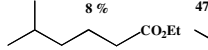
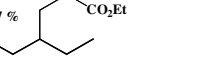
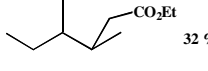
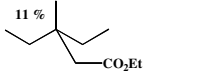

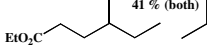
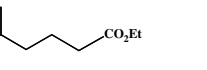
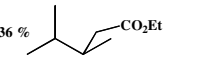
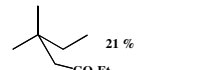

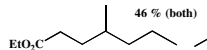
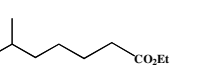
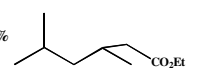
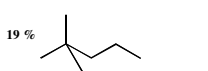

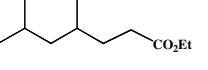
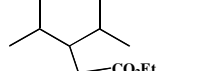
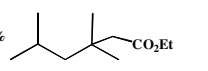
Table 4
Regioselectivity values for the activation of C–H bonds of alkyl-methyl ethers via carbene insertion with Tp^{Cu} as the catalyst

Substrate	Product	$\text{Tp}^{\text{Br}^3}\text{Cu}$	$\text{Tp}^{\text{M}^5}\text{Cu}$	$\text{Tp}^{\text{Cy}}\text{Cu}$
	 + 	23	41	9
		65	77	21
	 + 	35	23	79
		>99	–	–
		>99	–	–

with the aid of the carbonyl $\text{Tp}^{\text{Br}^3}\text{Ag}(\text{CO})$, that showed an absorption centred at 2157 cm^{-1} (2110 cm^{-1} for the Cu case). Table 5 displays the results obtained with this silver catalyst, for which the desired insertion into the primary C–H bonds of alkanes has been observed. A

similar catalyst reported by Dias et al. [18b] did not unexpectedly provide any primary insertion. When available, secondary and tertiary sites were also activated. In all cases, very low yields in the EDA-coupling products were detected, as a consequence of the high chemoselectivity of this catalyst toward the insertion into the carbon–hydrogen bonds. What makes the difference between the Cu- and Ag-containing catalysts to explain their behaviours? One could argue that the differences in the metal size could affect the regioselectivity of this process; however, when those catalysts were used in the styrene cyclopropanation reaction, a 58:42 *cis:trans* ratio of cyclopropanes was observed in the copper case, whereas the silver analogue gave equimolar amounts of both isomers. Since steric factors are known to control this transformation, the observation of a nearly identical *cis:trans* ratio (actually lower for silver) indicates that the volume of the catalytic pocket are quite similar, or slightly higher in the case of Ag. Therefore, the activation of primary sites by the silver catalysts cannot be explained as a consequence of a higher steric effect, but mainly to the increase in the electrophilic character of the metal center.

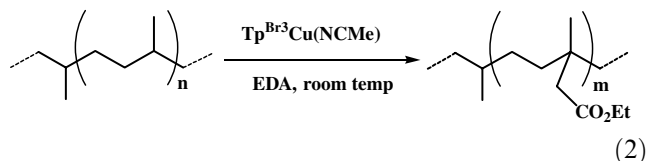
Table 5
Functionalization of carbon–hydrogen bonds of hydrocarbons by insertion of ethyl diazoacetate using $[\text{Tp}^{\text{Br}^3}\text{Ag}]_2 \cdot (\text{CH}_3\text{COCH}_3)$ as the catalyst

Substrate	Primary C–H active	Secondary C–H active	Tertiary C–H active	Others ^a
n-pentane	27% 	53%  13% 	–	7%
n-hexane	22% 	55%  21% 	–	2%
	59% 	–	39% 	2%
	45% 	17% 	36% 	2%
	8%  47% 	32% 	11% 	2%
	41% (both)  	36% 	21% 	2%
	46% (both)  	36% 	19% 	8%
	79% 	6% 	13% 	2%

^a Diethyl fumarate and maleate, and ethyl glycolate as byproducts.

2.1.3. Functionalization of polyolefins

It is well known the importance of polyolefins containing polar groups in polymer chemistry. However, the synthesis of those materials is quite difficult, since most of the common olefin polymerization catalysts are somewhat incompatible with many polar groups of the co-monomers. Because of this, we decided to investigate the potential of the carbene insertion methodology to the field of polyolefin modification [19], with the idea of inserting polar groups in the chains a posteriori, that is, after the polymer has been prepared. We started with a sample of polybutene [20], a very stereoregular polymer (one methyl branch every four carbons), and $\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$ as the catalyst. After completion of EDA addition, NMR studies revealed that the $:\text{CHCO}_2\text{Et}$ fragments were exclusively incorporated into the tertiary C–H bonds of the polyolefin, in a ratio of ca. 10 CO_2Et groups per 1000C, in a process carried out at room temperature (see Eq. (2)).



Polymer analyses revealed another important attribute of this system: the values of M_w , M_n and PDI of the modified polymers were quite similar to those of the starting, unmodified polyolefins. We believe that this must be interpreted as the result of a chain scission-free functionalization process, where none of very few C–C bond cleavage takes place. This is of interest since this method provides a tool to insert polar groups into the polyolefin chain without substantial modification of the initial polymer microstructure. This feature has been observed not only with polybutene but also with commercial samples of polyethylene-co-1-octene (40% w/w in 1-octene). Table 6 shows the values of GPC analyses for the latter polymer, where it is clearly observable the already commented similarities in M_w , M_n and PDI. In addition, we have also found that it is possible to exert a certain control in the degree of incorporation, the main variable being the polymer to EDA ratio. Fig. 2 shows the variation of the number of CO_2Et groups per 1000C added as a function of the polymer:EDA ratio.

Table 6

GPC data for the modified polymers compared with those of the respective starting materials (ethylene-co-1-octene)

Polymer (M_w , M_n and PDI)	Pol:EDA ratio	CO_2Et per 1000C incorp.	Modified polymer (M_w , M_n and PDI)
63, 30, 2.08	1:1.5	5.1	66, 32, 2.05
63, 30, 2.08	1:3	10.7	67, 33, 2.04
63, 30, 2.08	1:6	17.5	66, 31, 2.14
63, 30, 2.08	1:12	31.7	100, 57, 1.76

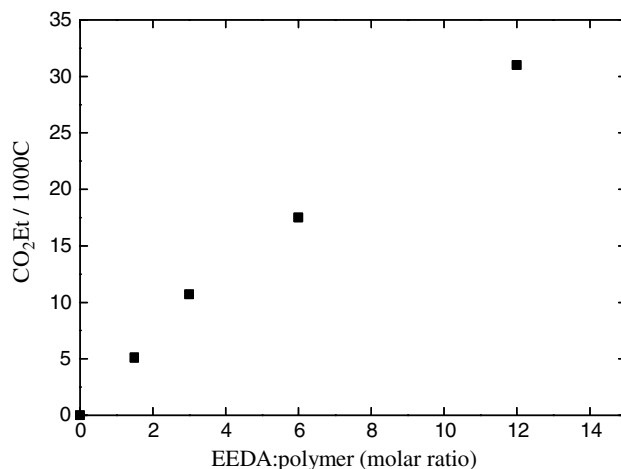
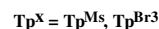
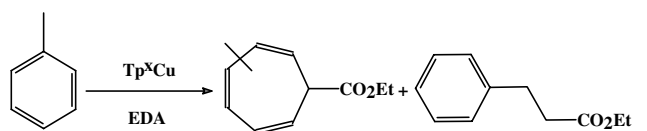
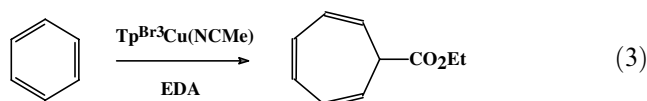


Fig. 2. Dependence of the degree of incorporation with the polymer:EDA ratio employed. Polymer: polyethylene-co-1-octene.

2.1.4. Miscellaneous additions and insertions reactions

Arenes and furans have also been treated with EDA in the presence of Tp^xCu complexes as the catalyst. In the case of benzene, a cycloheptatriene derivative was



(4)

formed due to the addition of the $:\text{CHCO}_2\text{Et}$ group to the aromatic double bond and to the subsequent expansion of the bicyclic intermediate (Eq. (3)). But when alkyl-benzenes were studied, this reaction competed with that of the insertion of EDA in the C–H bonds of the alkyl groups (Eq. (4)). We also found that the ratio of addition:insertion was affected by the nature of the Tp^x ligand (Table 7) [21].

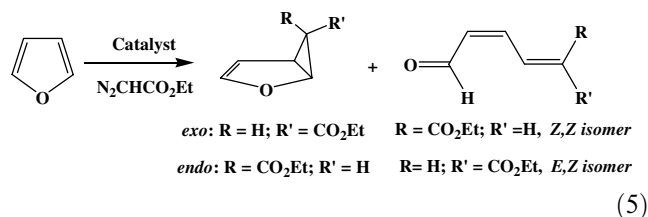
Table 7

Reactions of ethyl diazoacetate with alkylaromatic substrates with Tp^xCu as the catalysts

Substrate	$\text{Tp}^{\text{Br}^3}\text{Cu}(\text{NCMe})$		$\text{Tp}^{\text{Ms}}\text{Cu}$	
	% Insertion ^a	% Addition ^a	% Insertion ^a	% Addition ^a
Toluene	8	62	20	nd
Mesitylene	12	75	30	<5
Ethylbenzene	30	18	56	nd
Ethyltoluene	45	nd	58	nd

^a Determined by GC, diethyl fumarate and maleate accounted for 100%.

The reaction of EDA and furan in the presence of dirhodium tetraacetate, followed by addition of elemental iodine, has been employed for years as a route for the formation of dienes (Eq. (5)). We have studied this reaction in the presence of Tp^xCu as the catalyst and found that this copper-based system can be employed as an alternative to $\text{Rh}_2(\text{OAc})_4$ [22]. Two different products, cyclopropanes and dienes, are formed in this reaction, the *endo* cyclopropane being observed for the first time in this case. The use of different Tp^x ligands have the corresponding effect in the ratio of products and isomers obtained, as shown in Table 8. But more important, the activity of these catalysts are, at least, comparable to that of dirhodium tetraacetate, a feature also observed for substituted furans such as 2-methylfuran or 2,5-dimethylfuran. We have also studied a model reaction for the synthesis of osto-panic acid. It consists in the reaction of 2-hexylfuran with EDA, that led to a mixture of the desired dienes in very high yield.



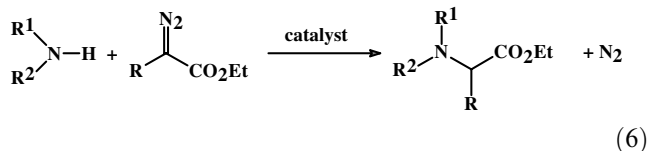
On the other hand, we have studied the insertion of EDA into polar bonds, such as the cases of amines (N–H) or alcohols (O–H). The insertion of ethyl dia-

Table 8
 Tp^xCu -catalyzed reaction of ethyl diazoacetate (EDA) and furan^a

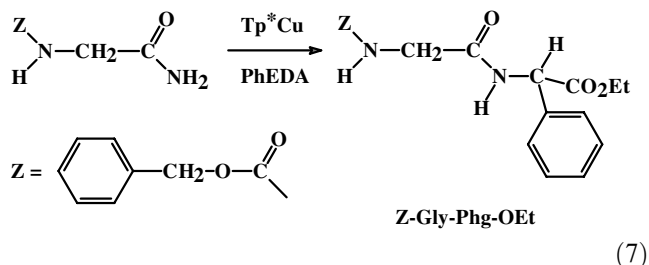
	Tp^xCu	$\text{Tp}^{\text{Cy}}\text{Cu}$	$\text{Tp}^{\text{Ms}}\text{Cu}$	Br^3Cu	$\text{z}(\text{OAc})_4$
	32	38	30	30	34
	7	6	6	5	nd
	3	3	9	8	10
	11	9	32	43	20
	nd	nd	nd	nd	2
Yield	53	56	77	86	66

^a EDA-based yields, determined by NMR using biphenyl as internal standard. Diethyl maleate and fumarate accounted for 100% of initial EDA.

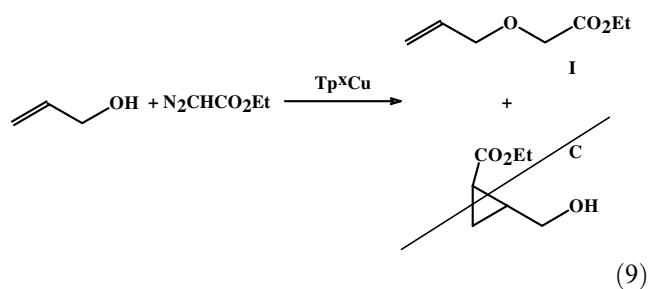
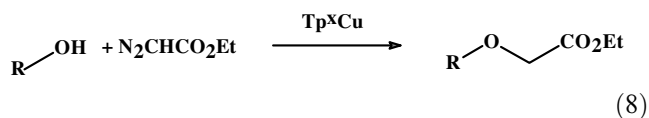
zoacetate in the nitrogen–hydrogen bond of amines leads to the formation of glycine derivatives. In general, we have found that the use of $\text{RC}(\text{N}_2)\text{CO}_2\text{Et}$ diazo compounds and amines, in the presence of catalytic amounts of Tp^*Cu , produces the corresponding aminoacid derivatives in nearly quantitative yields (Eq. (6)) [23].



This methodology has also been applied to the synthesis of dipeptides, in the reaction of a protected aminoacid (amido form) and the appropriate diazo compound, e.g., $\text{PhC}(\text{N}_2)\text{CO}_2\text{Et}$ (PhEDA). In this case, the exclusive insertion of the diazo compound into one of the amido N–H bonds provided the dipeptide Z-gly-Phg-OEt in high yields (Eq. (7))



Several saturated and unsaturated alcohols have also been employed as the substrates in their reaction with EDA, using Tp^xCu complexes as the catalyst [24]. In all cases, the conversion of the alcohol into the resultant ether was observed in nearly quantitative yield. As representative examples, Eqs. (8) and (9) show the reactions of *n*-alcohols as well as allylic alcohol with EDA. In addition to the observed high yields, it is of value to point that no addition, i.e., formation of cyclopropanes (C), of the double bond was observed with the unsaturated alcohol; only the insertion product (I) was obtained, an attribute of this copper-based system that has not been described for other systems



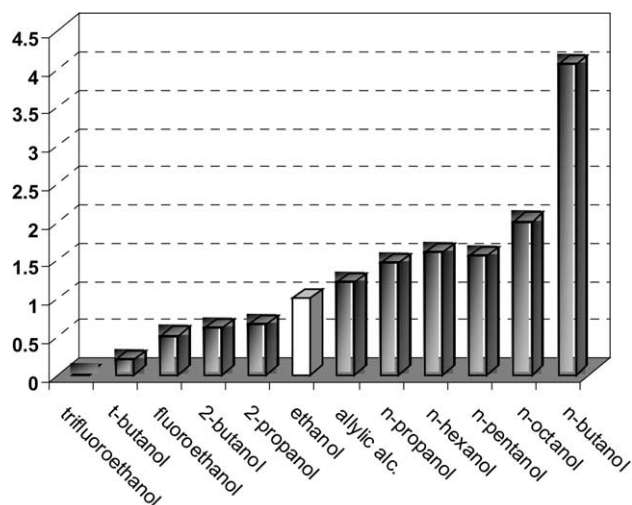


Fig. 3. Relative reactivity of alcohols toward carbene insertion catalyzed by Tp^*Cu .

In spite of the high yields, we have found that the relative reactivity of the group of alcohols employed is quite different. By means of intermolecular competition experiments we have built a scale of reactivity, with ethanol as the reference. Fig. 3 shows these results, from which we can highlight the following trends: (i) linear alcohols of higher chains are more reactive than ethanol; (ii) for a series of identical general formula alcohols, e.g., $C_4H_{10}O$, the higher the branching the lower the reactivity (n -butanol $>$ *sec*-butanol $>$ *tert*-butanol) and (iii) the existence of electron-withdrawing atoms diminishes the reactivity (ethanol $>$ 2-fluoroethanol \gggg 2,2,2-trifluoroethanol).

2.2. *N*-heterocyclic carbene-containing catalysts

We have recently initiated the study of complexes containing *N*-heterocyclic carbenes for carbene transfer reactions (from EDA) and the successive addition or insertion of such fragment to organic substrates. Our first attempts were made with the complex $I\text{Pr}CuCl$ ($I\text{Pr}$: 1,3-bis(diisopropylphenyl)imidazole-2-ylidene) and

were quite disappointing: the solutions of this complex did not catalyze EDA decomposition, a facet that satisfy nearly all copper (I) complexes [2]. However, we found that the addition of styrene to those solutions not only induced the copper-catalyzed EDA decomposition but also gave the expected cyclopropanes in very high yields (Scheme 5) [25]. We monitored this transformation by GC, as shown in Fig. 4. In the absence of styrene, $[\text{EDA}]$ remained constant for the length of the experiment. But the addition of styrene caused $[\text{EDA}]$ consumption, following first-order kinetics. This observation was found not only for styrene, but also for a set of olefins, amines and alcohols. In all cases, the addition of the substrate was the requirement for the reaction to start [25].

Since those substrates that induced EDA decomposition are, to a higher or lower extend, good donors, we believe that this behaviour must be related to the formation of any copper–substrate complex that would be the real catalyst, therefore the complex $I\text{Pr}CuCl$ being inactive to such purpose. De-coordination of the chloride would be crucial in this proposal and the active catalyst should present a cationic nature. In good accord with this, we prepared the complex $[I\text{Pr}Cu(\text{NCMe})_3]\text{BF}_4$ and tested it for EDA decomposition:

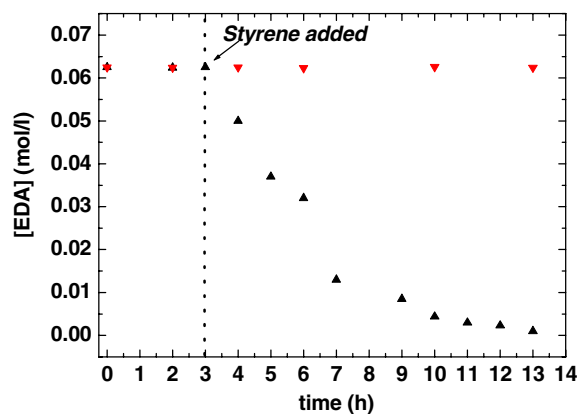
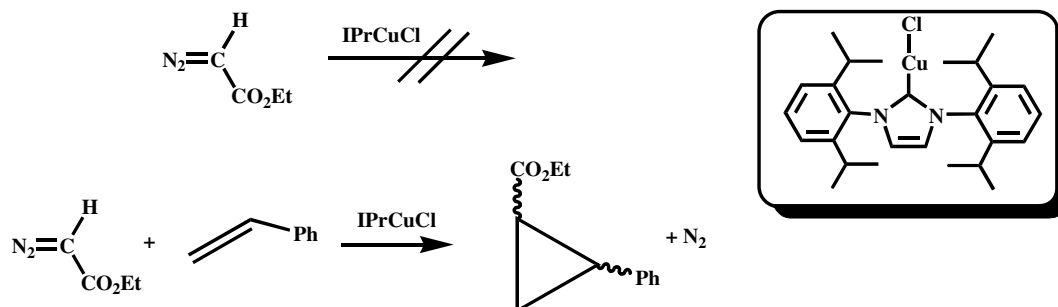


Fig. 4. EDA decomposition in the presence of $I\text{Pr}CuCl$. (▼) EDA as the sole reagent. (▲) Styrene added at 3 h.



Scheme 5. Reactions of EDA in the presence of $I\text{Pr}CuCl$.

the methylene chloride solutions of this complex decomposed EDA instantaneously without the need of any substrate in the reaction medium.

The above copper-based catalysts are the first system capable of transferring EDA but that is not prone to EDA dimerization. At the time we were studying the catalytic properties of this complex, we were also working in the already discussed $\text{Tp}^{\text{Br}^3}\text{Ag}$ system, where we found the activation of the primary sites of hydrocarbons. We considered of interest to evaluate the activity of the complexes IPrMCl toward this carbon–hydrogen activation methodology, using the three group 11 metals, Cu, Ag and Au. We prepared the silver and gold complexes, which X-ray structures are shown in Fig. 5, and examined their catalytic capabilities in the direction of inserting EDA into the C–H bonds of a model substrate, cyclohexane (Scheme 6). As expected, none of the three complexes catalyze the EDA decomposition in cyclohexane solutions, since the proposed chloride decoordination and formation of a cationic species is not favoured in this reaction medium. But the addition of one equivalent, with respect to the metal complex, of NaBAR'_4 ($\text{Ar}' = 3,5\text{-C}_6\text{H}_3(\text{CF}_3)_2$), induced the carbene transfer and the formation of ethyl cyclohexylacetate in high yields for the three metal-based catalysts. This has supposed the discovery of gold for this kind of transformations, since this metal remained unknown as a catalyst for diazo compound decomposition processes [26].

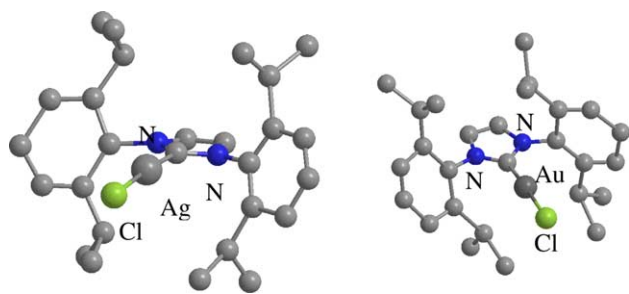
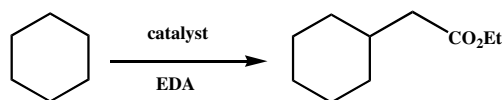


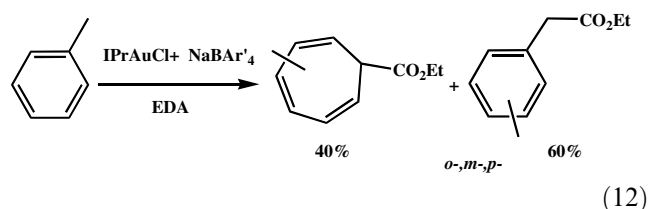
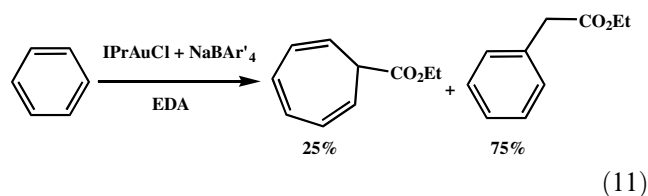
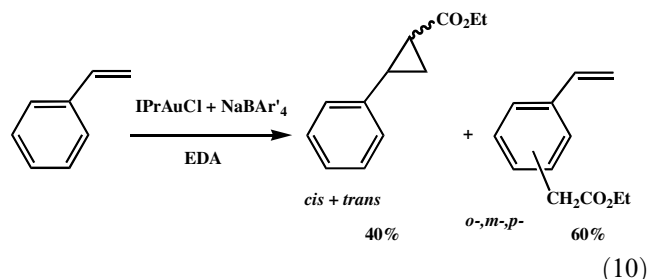
Fig. 5. Solid-state structures of the complexes IPrAgCl (left) and IPrAuCl (right).



Catalyst	Yield
IPrMCl (Cu, Ag, Au)	No reaction
$\text{IPrCuCl} + \text{NaBAR}'_4$	80
$\text{IPrAgCl} + \text{NaBAR}'_4$	74
$\text{IPrAuCl} + \text{NaBAR}'_4$	84

Scheme 6. Reaction of cyclohexane and EDA in the presence of IPrMCl .

The later finding prompted us to study the catalytic properties of the gold-based complex [26]. The somewhat trivial styrene cyclopropanation reaction revealed the unusual behaviour of this catalyst. We found that the expected cyclopropanes were not the major product from the reaction of styrene and EDA in the presence of $\text{IPrAuCl} + \text{NaBAR}'_4$. In addition, three products identified as the *ortho*, *meta* and *para* isomers of styryl acetate were obtained (Eq. (10)). The formation of these compounds can be rationalized in terms of a *formal* insertion of the $:\text{CHCO}_2\text{Et}$ unit into the aromatic C–H bond, a process that was unknown for the intermolecular version. But this reaction seems to be general for those substrates containing aryl C–H bonds. As shown in Eqs. (11) and (12), benzene and toluene also underwent this transformation. In both cases, the insertion products were accompanied by the cycloheptatrienes obtained upon double bond cyclopropanation and subsequent ring expansion.



3. Conclusions

The $\text{Tp}^x\text{-M}$ ($\text{M} = \text{Cu}, \text{Ag}$) and NHC-M ($\text{M} = \text{Cu}, \text{Ag}, \text{Au}$) systems display interesting catalytic capabilities toward the addition and/or insertion of ethyl diazoacetate to many saturated or unsaturated substrates. Both the nature of the ligand and the metal used promote certain differences in the catalytic activities, providing a tool-box to adjust the nature of the catalyst to the desired product.

Acknowledgements

We thank MEC (and former MCYT) and Junta de Andalucía for funding (PB98-0958, BQU2002-01114, INV97-0066, Programa Ramón y Cajal). Dr. M.C. Nicasio, Dr. T.R. Belderrain, Dr. A. Caballero, Dr. M.E. Morilla, Mr. M.R. Fructos and Mr. J. Urbano are also acknowledged.

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