

Carbenoid insertions into benzylic C-H bonds with heterogeneous copper catalysts

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The copper complexes with bis(oxazoline) or azabis(oxazoline) ligands, once supported on laponite clay by electrostatic interactions, are able to catalyze the insertion of carbenoids in benzylic C-H bonds. In contrast with rhodium catalysts, they are more active with tertiary than with secondary bonds, through a similar mechanism as shown by Hammett correlation. Enantioselectivities are only moderate, with values up to 50% ee. The immobilized catalysts are partially recoverable and the best results are obtained in the case of reactions with high chemoselectivity.

1. Introduction

The development of new synthetic methodologies for the functionalization of C-H bonds is currently a subject of great interest. The use of carbene insertion reactions is a well-established methodology that provides new C-C bonds in a controllable way.¹ Intramolecular carbene insertions were first developed, using dirhodium carboxylates as catalysts, whereas the usefulness of the intermolecular version arrived with the use of donor/acceptor diazocompounds.² This discovery can be considered as a milestone that changed the vision of the carbene insertion reactions as a tool in the synthesis of compounds with a certain structural complexity. Since then many examples of the reaction using dirhodium catalysts have been described, in many cases using chiral carboxylates, which lead to very high enantioselectivities.³

Nevertheless the use of other metals as catalysts for carbene insertions is still rather scarce. Complexes of coinage metals (gold, silver, and copper) have been described as useful catalysts for insertions,⁴ even in the case of the poorly reactive methane molecule.⁵ Copper remains as the most attractive catalyst for this kind of reaction, given its availability and low price. In the enantioselective version of the reaction the examples with copper catalysts are even less abundant. The initial poor results obtained in the intramolecular C-H insertion of diazoesters^{6,7} have been only recently improved using α -diazosulfones, leading from high to excellent enantioselectivities depending on the size of the formed cycle and its substituents.^{8,9}

Regarding copper catalyzed enantioselective intermolecular reactions, carbene insertions into O-H bonds were first described,¹⁰ whereas results were improved and extended to other X-H bonds by using *spiro*-bis(oxazoline) ligands.¹¹ After an early attempt of enantioselective intermolecular insertion into C-H bonds, with poor results,¹² our group described for the first time a successful intermolecular insertion into THF,¹³ extended to other cyclic ethers with enantioselectivities from low to moderate depending on the structure of the substrate.¹⁴ In fact a good part of this moderate success is due to the use of complexes immobilized by electrostatic interactions¹⁵ on a synthetic clay (laponite) able to modulate not only the catalytic activity but also the stereochemical course of the catalyzed reaction.¹⁶ Other approaches to heterogeneous catalysts, with or without chiral modification, have been also attempted.¹⁷

In this paper we describe the extension of the same methodology to the carbene insertion reactions into benzylic C-H bonds, using copper complexes with different bis(oxazoline) ligands (Figure 1) both in homogeneous phase and supported on laponite clay by cationic exchange.

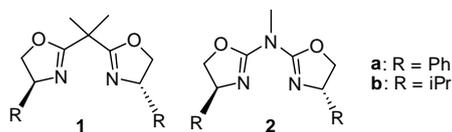


Figure 1. Bis(oxazoline) (1) and azabis(oxazoline) (2) ligands used in this work.

2. Results and Discussion

2.1. Preparation of the immobilized catalysts

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Laponite was the support chosen for the preparation of the immobilized catalysts. It is a synthetic clay with ideal formula $(\text{Na}_{0.5} \cdot n\text{H}_2\text{O})[(\text{Mg}_{5.5}\text{Li}_{0.5}\text{Si}_8(\text{OH})_4\text{O}_{20})]$. The magnesio-silicate platelets (each platelet is composed by one octahedral MgO_6 layer between two tetrahedral SiO_4 layers) are nanodiscs of around 0.03 μm diameter, negatively charged due to the isomorphous substitution of part of Mg by Li. The clay particles (tectoids) are piles of platelets with compensating hydrated sodium cations in the interlamellar spaces (side view in Figure 2).¹⁸ The cationic exchange with the complex $\text{L}^*\text{Cu}(\text{OTf})_2$ takes place in a polar medium (methanol) able to dissolve the leaving salt, NaOTf in this case. The bulkiness of the new cations produces a certain degree of disorder in the final material (Figure 2) as well as some expansion in the interlayer space (detectable by a decrease in the intensity and a shift to lower angles of the 001 diffraction peak in X-ray diffraction patterns of oriented samples¹⁹) which confers a high degree of accessibility to the catalytic sites.

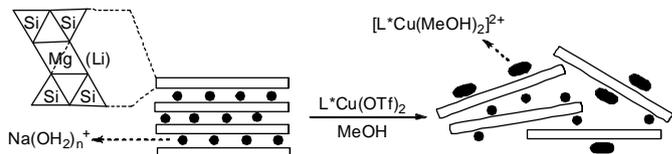
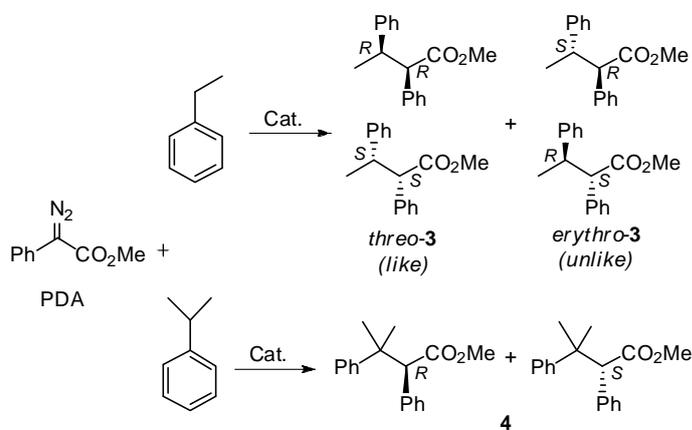


Figure 2. Cationic exchange process (side view of the nanodiscs of laponite).

2.2. Reactions of cumene and ethylbenzene with phenyldiazoacetate

The insertion into simple benzylic substrates, such as ethylbenzene and cumene, has shown some interesting features in the $\text{Rh}_2(\text{S-DOPS})_4$ catalyzed reaction. Ethylbenzene is more reactive than cumene (5:1 ratio) with *p*-bromophenyldiazoacetate (pBrPDA),²⁰ presumably due to steric reasons. The lower reactivity of cumene promotes the low chemoselectivity of insertion with respect to the competitive double cyclopropanation in the aromatic ring, with an insertion/cyclopropanation selectivity of 60/40 with pBrPDA and 30/70 with phenyldiazoacetate (PDA).²¹ In parallel with reactivity, enantioselectivity obtained with cumene is also much lower (50% ee with pBrPDA and <10% ee with PDA) than the excellent value obtained with ethylbenzene (86% ee with pBrPDA²⁰). In the case of copper catalysts, the most demanding reactions with PDA were tested (Scheme 1), using each benzylic substrate as reaction solvent, and the results are gathered in Table 1.



Scheme 1. Reactions of PDA with ethylbenzene and cumene.

As can be seen, homogeneous copper catalysts lead to very poor results at temperatures up to 65°C, with yields always lower than 5%. Rhodium acetate was tested for the sake of comparison, and yield was much higher with ethylbenzene (22%), whereas reactivity of cumene was much lower, as expected from previous results.²⁰ Results were clearly better when heterogeneous catalysts were used. First of all it is remarkable that cyclopropanation products were not detected, so the chemoselectivity for insertion is complete. The only by-products came from dimerization of the diazo compound. Yields in the range of 20-25% were obtained in the reaction of ethylbenzene with **2b**-Cu complex immobilized on laponite between 50 and 80°C. Diastereoselectivity was always over 80:20, similar or even higher than that obtained with $\text{Rh}_2(\text{S-DOSP})_4$ with pBrPDA.²⁰ With regard to enantioselectivity it is always moderate, with values ranging 45-50% ee with both **1a** and **2b** ligands. The effect of temperature on enantioselectivity is completely different in both cases, with a decrease at higher temperatures, as expected, in the case of **1a**, but constant enantioselectivity up to 80°C, in the case of **2b**. Unfortunately recovery is not very efficient. Lap-Cu**1a** was analyzed after reactions with cumene and ethylbenzene at 65°C. The analysis of the fresh catalyst (0.23 mmol Cu/g, N/Cu ratio = 2.4, C/N ratio = 10.6) was in good agreement with previous results.²² After reaction the amount of copper was slightly reduced (0.19 mmol/g after cumene reaction, 0.22 mmol/g after

ethylbenzene reaction), with a similar N/Cu ratio (2.3 and 1.7, respectively) but much higher C/N ratio (around 19 in both cases). This seems to indicate that deactivation is probably due to poisoning, as it was observed in the analogous cyclopropanation reactions,²³ favoured by the formation of dimerization by-products given the rather low chemoselectivity of the insertion reaction.

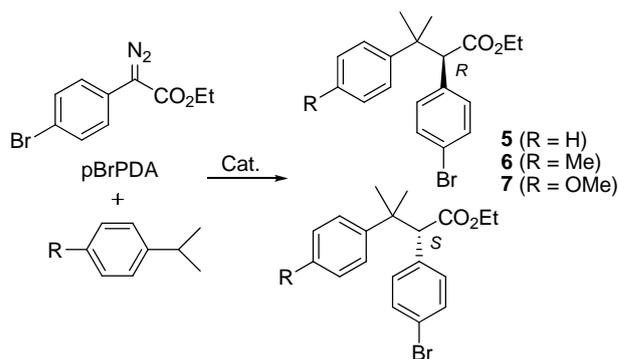
Table 1. Results of the reaction between methyl phenyldiazo-acetate (PDA) and benzylic substrates (ethylbenzene and cumene).^a

Substrate	Catalyst	T (°C)	Yield (%)	<i>threo/erythro</i>	ee ^b (%)	
Et-benz.	Cu(OTf) ₂	50	1	n.d.	–	
	2b -Cu(OTf) ₂	50	1	n.d.	n.d.	
	Rh ₂ (OAc) ₄	50	22	72/28	–	
	Lap-Cu	50	15	73/27	–	
	Lap-Cu 1a	50	8	83/17	45	
		65	19	81/19	34	
		80	17	77/23	28	
	Lap-Cu 2b	50	20	81/19	50	
		65	23	83/17	50	
		80	21	83/17	53	
		(2 nd run)	50	6	83/17	15
	Cumene	Cu(OTf) ₂	65	3	–	–
1a -Cu(OTf) ₂		65	2	–	n.d.	
2b -Cu(OTf) ₂		65	3	–	n.d.	
Rh ₂ (OAc) ₄		65	7	–	–	
Lap-Cu		65	26	–	–	
Lap-Cu 1a		65	40	–	21	
Lap-Cu 1b		65	78	–	21	
		80	67	–	8	
(2 nd run)		65	73	–	12	
(3 rd run)		65	60	–	10	
Lap-Cu 2b		65	31	–	45	
		80	27	–	40	
(2 nd run)		65	26	–	23	
Rh ₂ (<i>S</i> -DOSP) ₄ ^c	50	21 ^d	–	<10		
	50	37 ^{e,f}	–	50 ^e		

^a Substrate used as reaction solvent. ^b Enantioselectivity of the major diastereomer. ^c Ref. 21. ^d 48% yield of dicyclopropanation product in the aromatic ring is also obtained. ^e Results in the reaction with pBrPDA. ^f 24% yield of dicyclopropanation product in the aromatic ring is also obtained.

In contrast with Rh catalysts, cumene is more reactive than ethylbenzene with heterogeneous copper catalysts. The competitive reaction with Lap-Cu showed a ratio between cumene and ethylbenzene insertion products close to 2:1. At 65°C yields depend on the ligand present in the catalyst, from 26% without ligand up to 78% with **1b**. Enantioselectivity is also highly dependent on the structure of the ligand, from 21% ee obtained with both bis(oxazolines) **1a** and **1b**, up to 45% ee reached with **2b**, a value much better than that described in the same reaction for Rh₂(*S*-DOSP)₄²¹ and similar to that obtained with pBrPDA.²⁰ The behaviour with respect to recovery is slightly better than in the case of ethylbenzene, in agreement with the better chemoselectivity of this reaction. Yields are kept almost constant in one or two recycles, but in all cases enantioselectivity significantly drops. As expected from the reactivity order, the primary benzylic position of toluene was completely inactive to insertion, in contrast with Rh catalysts.^{20,24,25}

2.3. Reactions of *p*-substituted cumenes



Scheme 2. Reactions of pBrPDA and *p*-substituted cumenes.

Davies has described the positive effect of *para* substitution to protect benzene ring,^{20,21,24} and at the same time electron donating groups have shown to activate ethylbenzene.²⁰ In view of that, the effect of substitution has been studied in the case of cumene with pBrPDA using heterogeneous copper catalysts (Scheme 2). First of all the electronic effect on the reactivity was studied by competitive reactions catalyzed by Lap-Cu**1b**. Cumenes substituted with donor groups (R = Me, OMe) were much more reactive than unsubstituted cumene. The Hammett analysis (Figure 3) shows a better correlation with σ^+ ($r^2 = 0.99$) than with σ_p ($r^2 = 0.87$), with a ρ value of -1.55 , indicating a certain development of a positive charge in the insertion step. This result is analogous to that obtained with Rh catalysts for ethylbenzene²⁰ ($\rho = -1.27$), pointing to a similar reaction mechanism. Differences seem to indicate a more asynchronous transition state in the cumene reactions, probably with a higher charge development.

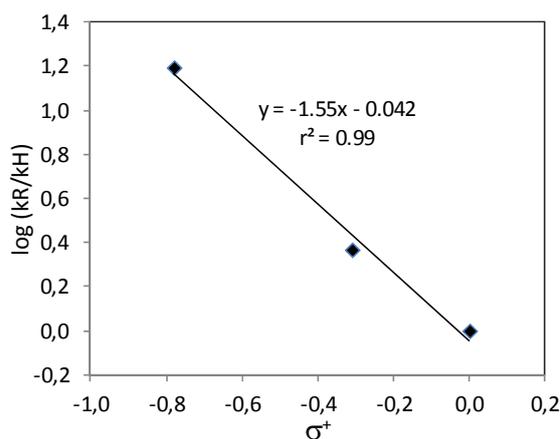


Figure 3. Hammett correlation in the reaction of pBrPDA and substituted cumenes.

In view of that results, the reaction of pBrPDA with *p*-isopropylanisole (R = OMe) was tested in petroleum ether as a solvent (Table 2), instead of the own aromatic compound. Results in homogeneous phase were again very poor ($\leq 6\%$ yield), in spite of the higher reactivity of *p*-isopropylanisole. On the contrary, yields with heterogeneous catalysts (35-40%) were similar or even better than those obtained with cumene used as a solvent. The only exception is Lap-Cu**1b**, which already led to very high yields with cumene. Enantioselectivity also reached similar values, 20% ee with the phenyl substituted ligand **1a** and 35-40% ee with the isopropyl substituted ligand **1b**. In this case the catalysts was recovered and reused, with similar results in the second cycle but an almost complete deactivation in the third one. This effect has been attributed to the irreversible adsorption of chelating by-products, typically in reactions of diazocompounds with low chemoselectivity. Yield and enantioselectivity obtained with Lap-Cu**1b** are comparable to the results described for the reaction of PDA with *p*-isopropylanisole catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$, whereas the use of $\text{Rh}_2(\text{S-PTAD})_4$ leads to better yield but lower enantioselectivity.²¹

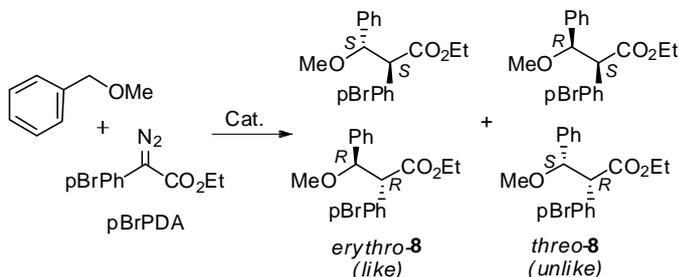
Table 2. Results of the reaction between ethyl *p*-bromophen-yl diazoacetate (pBrPDA) and *p*-isopropylanisole.^a

Catalyst	Yield (%)	% ee
Cu(OTf) ₂	5	–
Lap-Cu	36	–
1a -Cu(OTf) ₂	6	n.d.
1b -Cu(OTf) ₂	4	n.d.
Lap-Cu 1a	41	20
Lap-Cu 1b	35	36
(2 nd run)	36	39
(3 rd run)	4	n.d.
Rh ₂ (<i>S</i> -DOSP) ₄ ^b	48	48
Rh ₂ (<i>S</i> -PTAD) ₄ ^b	81	11

^a In petroleum ether as a solvent, under reflux (68°C). ^b Result with PDA (ref. 21) at 50°C.

2.4. Reaction of methyl *p*-bromophenyldiazoacetate with benzyl methyl ether

In principle a secondary benzylic C-H bond in α position of an oxygen atom should be more reactive than the analogous bond in ethyl benzene. Thus benzyl methyl ether was envisaged as a better substrate for carbene insertion and it was made react with pBrPDA in solution (Scheme 3).



Scheme 3. Reaction of pBrPDA and benzyl methyl ether.

The two diastereomers *erythro-8* (*like*) and *threo-8* (*unlike*) were identified by comparison of their ¹H NMR spectrum with that of the analogous *erythro* and *threo* methyl 2,3-diphenyl-3-methoxypropionate,²⁶ and other related compounds.²⁷ The higher coupling constant in the CH-CH system (10.4 vs 9.6 Hz) and the higher chemical shift of the methoxy group (3.22 vs 3.07 ppm) are in agreement with the *threo* configuration. Moreover this identification is also in agreement with the shielding effect of the aromatic groups in the most stable antiperiplanar conformation (Figure 4).²⁸

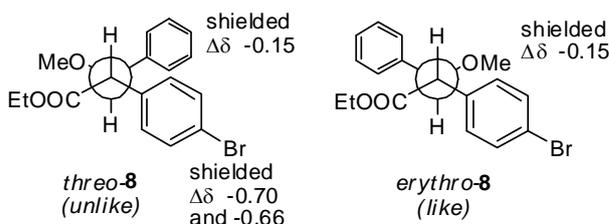


Figure 4. Newman projections of *unlike* and *like* compounds of insertion of pBrPDA in benzyl methyl ether.

As expected, yields were better than those obtained with ethylbenzene as a solvent (Table 3). In fact, even the homogeneous complex **1a**-Cu(OTf)₂ was able to promote the reaction, albeit with low yield (20%).

An important effect of the nature of the ligand was observed, as the reaction did not take place with **1b**-Cu(OTf)₂. Immobilization on laponite again significantly improves the chemoselectivity of the process, leading to higher yields than the homogeneous catalysts, and nearly as good as Rh₂(OAc)₄. The same ligand effect was present in the heterogeneous catalysts, with an improvement from 31% yield with **1b** to 87% yield with **1a**.

With regard to stereoselectivities, both diastereo- and enantioselectivity were always low. The *threo* (*unlike*) diastereomer was always slightly favoured over the *like* one, with diastereomeric ratios in the range of 60/40 to 70/30. Values around 25% ee were obtained with **1a** as a ligand, both in solution and in solid phase. Moreover, the catalyst Lap-Cu**1a** was recoverable at least twice, in agreement with the higher chemoselectivity of this reaction. In this case the catalyst Lap-Cu**1b** was analyzed after reaction, with similar results to those of Lap-Cu**1a** (see above). The copper content was only slightly lower than that of the fresh catalyst (0.19 vs 0.21 mmol/g), with similar N/Cu ratio (2.1 vs 2.3) and a significant increase in the carbon content (C/N ratio 17.6 instead of the starting 7.7), pointing again to the poisoning with by-products.²³

These poor stereoselectivity results, mainly in comparison with the higher enantioselectivity obtained with cyclic ethers,^{13,14} are probably due to the lack of bulky groups in both reactants and to the conformational freedom of the open chain ether. To the best of our knowledge this reaction had not been described in the literature. The most similar example involves the reaction of PDA with benzyl *tert*-butyldimethylsilyl ether, catalyzed by rhodium complexes.²⁹ In that case the typical Rh₂(*S*-DOSP)₄ catalyst led to high yield (83%) and diastereoselectivity (95/5), but low enantioselectivity (17% ee). Interestingly this and other Rh catalysts favoured the *syn* (*like*) diastereomer. The bulkiness of the silyl group, in contrast with the small size of the methyl one, may account for this difference in diastereoselectivity.

Table 3. Results of the reaction between ethyl *p*-bromophenyldiazoacetate (pBrPDA) and benzyl methyl ether.^a

Catalyst	Yield (%)	<i>threo/erythro</i>	ee ^b (%)
Lap-Cu	24	61/39	–
1a -Cu(OTf) ₂	22	60/40	26
1b -Cu(OTf) ₂	2	n.d.	n.d.
Lap-Cu 1a	87	68/32	22
(2 nd run)	53	68/32	28
(3 rd run)	77	70/30	17
Lap-Cu 1b	31	68/32	12
Rh ₂ (OAc) ₄	90	57/43	–

^a In petroleum ether as a solvent, under reflux (68°C). ^b Enantioselectivity of the major diastereomer.

3. Conclusions

Immobilization by electrostatic interactions improves the efficiency of copper complexes with chiral bis(oxazoline) and azabis(oxazoline) ligands for carbenoid insertions into benzylic C-H bonds. Although the exact reasons are not clear, immobilized catalysts may expose the catalytic sites to the reaction medium better than the complexes, as these are insoluble in the non-polar medium of the insertion reaction. Moreover, site isolation and mainly the change of anion, from triflate to a bulkier non-coordinating solid anion (in a similar way to the effect of BArF anion³⁰), may also play an important role in this improvement.

The reaction mechanism seems to be similar to that of the rhodium catalyzed reactions, as shown by the Hammett correlation, but the reactivity of tertiary vs secondary C-H bonds is the opposite. Up to 78% yield can be reached with cumene, used as reaction solvent, but the best enantioselectivity (45% ee) is obtained with a less chemoselective catalyst. Slightly higher enantioselectivity can be reached with ethylbenzene (50-53% ee) albeit with lower yields. The most reactive substrate is benzyl methyl ether (up to 87% yield with only 2:1 substrate/diazocompound ratio), but low enantioselectivity is obtained, in contrast with cyclic ethers, probably due to the high conformational freedom of this substrate.

To sum up, chiral heterogeneous copper catalysts can be highly efficient for this kind of reactions, but new ligands have to be designed to improve enantioselectivities.

4. Experimental section

The preparation and characterization of the heterogeneous copper catalysts have been described elsewhere.¹⁴

4.1. Carbene insertion in ethylbenzene and cumene.

A suspension of dried heterogeneous catalyst (100 mg, around 0.02 mmol Cu) in anhydrous substrate (ethylbenzene or cumene, 10 mL) with n-decane (100 mg) as internal standard was heated at the required temperature under an inert atmosphere. A solution of methyl phenyldiazoacetate (176 mg, 1 mmol) in anhydrous substrate (10 mL) was slowly added over 4h with a syringe pump. Once the addition had finished, the reaction mixture was stirred and heated at the same temperature for 4 h. The catalyst was filtered off and washed with anhydrous dichloromethane (5 mL). Yield and diastereoselectivity were determined by GC and enantioselectivities were determined by HPLC. The catalyst was dried under vacuum and reused under the same conditions.

The insertion products were purified by flash chromatography on silica using hexane/ethyl acetate or hexane/isopropanol mixtures as eluents. The two isomers of methyl 2,3-diphenylbutanoate were identified according to the literature.³¹⁻³³

Methyl erythro-2,3-diphenylbutanoate (erythro-3). ¹H NMR (400 MHz, CDCl₃): 7.47–6.95 (m, 10H), 3.72 (d, 1H, J = 11.1 Hz), 3.46 (m, 1H), 3.37 (s, 3H), 1.02 (d, 3H, J = 7.0 Hz). **Methyl threo-2,3-diphenylbutanoate (threo-3).** ¹H NMR (400 MHz, CDCl₃): 7.47–6.95 (m, 10H), 3.71 (d, 1H, J = 11.1 Hz), 3.71 (s, 3H), 3.46 (m, 1H), 1.39 (d, 3H, J = 6.8 Hz).

Methyl 3-methyl-2,3-diphenylbutanoate (4).³⁴ HRMS (ESI): calculated (C₁₈H₂₀O₂Na) 291.1355, found: 291.1318. ¹H NMR (400 MHz, CDCl₃): 7.34–7.20 (m, 10H), 3.82 (s, 1H), 3.37 (s, 3H), 1.44 (s, 3H), 1.27 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): 173.0, 147.3, 135.6, 130.2, 128.0, 127.8, 127.3, 126.6, 126.2, 62.5, 51.4, 41.4, 26.5, 25.0.

4.2. Competitive insertions.

A suspension of dried Lap-Cu (60 mg, around 0.04 mmol Cu) in a solution of the substrates (10 mmol each) in anhydrous petroleum ether (10 mL) was heated under reflux (68°C) and under an inert atmosphere. A solution ethyl *p*-bromophenyldiazoacetate (268 mg, 1 mmol) in petroleum ether (10 mL) was slowly added over 4h with a syringe pump. Once the addition had finished, the reaction mixture was stirred and heated at the same temperature and the reaction was monitored by GC-FID. The insertion products were identified by GC-MS (*m/z*: ethyl 2-(4-bromophenyl)-3-methyl-3-phenyl-butanoate (**5**) 360; ethyl 2-(4-bromophenyl)-3-methyl-3-(4-methylphenyl)-butanoate (**6**) 374; ethyl 2-(4-bromophenyl)-3-(4-methoxyphenyl)-3-methyl-butanoate (**7**) 390; in all cases the isotopic distribution was in agreement with the molecular formula).

4.3. Carbene insertion in *p*-isopropylanisole and benzyl methyl ether.

A suspension of dried heterogeneous catalyst (100 mg, around 0.02 mmol Cu) in a solution of the substrate (2 mmol) in anhydrous petroleum ether (10 mL) with n-decane (100 mg) as internal standard was heated under reflux (68°C) and under an inert atmosphere. A solution ethyl *p*-bromophenyldiazoacetate (268 mg, 1 mmol) in petroleum ether (10 mL) was slowly added over 4h with a syringe pump. Once the addition had finished, the reaction mixture was stirred and heated at the same temperature for 4 h and it was treated in the same way as described above.

The insertion products were purified by kugelrohr distillation to eliminate the unreacted substrate, followed by flash chromatography on silica.

Ethyl 2-(4-bromophenyl)-3-(4-methoxyphenyl)-3-methyl-butanoate (7).³⁵ HRMS (ESI): calculated (C₂₀H₂₃BrO₃Na) 413.0723, found: 413.0723. ¹H NMR (400 MHz, CDCl₃): 7.34 (d, 2H, J = 8.5 Hz), 7.18 (d, 2H, J = 9.0 Hz), 7.07 (d, 2H, J = 8.5 Hz), 6.80 (d, 2H, J = 9.0 Hz), 3.94 (m, 2H), 3.79 (s, 3H), 3.77 (s, 1H), 1.46 (s, 3H), 1.31 (s, 3H), 1.04 (t, 3H, J = 7.6 Hz). ¹³C NMR (100 MHz, CDCl₃): 172.3, 158.0, 139.0, 134.8, 131.9, 130.8, 127.7, 121.5, 113.3, 62.1, 60.4, 55.4, 40.9, 26.3, 25.4, 14.1.

Ethyl threo-2-(4-bromophenyl)-3-methoxy-3-phenyl-propanoate (threo-8). ¹H NMR (400 MHz, CDCl₃): 7.25 (d, 2H, J = 8.4 Hz), 7.19-7.14 (m, 3H), 7.06-7.01 (m, 2H), 6.97 (d, 2H, J = 8.4 Hz), 4.63 (d, 1H, J = 10.5 Hz), 4.22 (m, 2H), 3.76 (d, 1H, J = 10.5 Hz), 3.22 (s, 3H), 1.27 (t, 3H, J = 7.2 Hz). ¹³C NMR (100 MHz, CDCl₃): 172.3, 138.2, 134.0, 131.5, 130.7, 130.6, 128.3, 127.6, 121.7, 85.9, 61.3, 59.2, 57.1, 14.3. HRMS (ESI): calculated (C₁₈H₁₉BrO₃Na) 385.0410, found: 385.0410. *Erythro* isomer (from a *threo/erythro* mixture): ¹H NMR (400 MHz, CDCl₃): 7.91 (d, 2H, J = 8.8 Hz), 7.67 (d, 2H, J = 8.8 Hz), 7.36-7.23 (m, 5H), 4.69 (d, 1H, J = 9.6 Hz), 3.88 (m, 2H), 3.84 (d, 1H, J = 9.6 Hz), 3.07 (s, 3H), 0.96 (t, 3H, J = 7.2 Hz).

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