

Intermetallic coinage metal-catalyzed functionalization of alkanes with ethyl diazoacetate: Gold as a ligand

M. Ángeles Fuentes^a, María Rodríguez-Castillo^b, Miguel Monge^b, M. Elena Olmos^b,
Jose M. López-de-Luzuriaga^{b,*}, Ana Caballero^{a,*}, Pedro J. Pérez^{a,*}

^aLaboratorio de Catálisis Homogénea, Departamento de Química y Ciencia de los Materiales, Unidad Asociada al CSIC, Centro de Investigación en Química Sostenible (CIQSO),

Campus de El Carmen s/n, Universidad de Huelva, 21007-Huelva, Spain

^bDepartamento de Química, Grupo de Síntesis Química de La Rioja, UA-CSIC, Complejo Científico-Tecnológico, Universidad de La Rioja, 26004-Logroño, Spain

ARTICLE INFO

Article history:

Available online 15 January 2011

Dedicated to Prof. Robert G. Bergman

Keywords:

C–H functionalization

Diazocompounds

Carbenes

Coinage metals

ABSTRACT

The complexes $[\text{Au}_2\text{M}_2(\text{C}_6\text{F}_5)_4(\text{NCMe})_2]_n$ ($\text{M} = \text{Cu}$, **1**; $\text{M} = \text{Ag}$, **2**) have been tested as catalysts for the functionalization of alkanes by the carbene insertion methodology, using ethyl diazoacetate as the carbene source. Moderate to high conversions have been obtained. The observed selectivities seem to favor the proposal that the active metal for catalysis is the Cu/Ag center, the $\text{Au}(\text{C}_6\text{F}_5)_2$ unit acting as a spectator ligand in both cases.

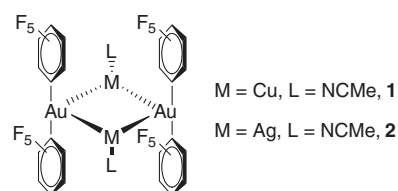
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1. Introduction

The functionalization of alkane carbon–hydrogen bonds still constitutes a challenge in modern chemistry [1,2]. One of the strategies developed in the last decades is based in the metal-catalyzed transfer of a carbene group from a diazo compound to the C–H bond of the alkane, a process that effectively affords functionalized products (Scheme 1) [3,4]. This transformation takes place without the intermediacy of any interaction between the metal center and the C–H bond, precluding the formation of stable organometallic species and therefore favoring the existence of a catalytic cycle. Rhodium- [5] and coinage metal-based [6] complexes have been reported to promote this transformation. Seminal work by Teyssié and co-workers [7] described the use of rhodium acetate-like complexes for the insertion of the CHCO_2Et unit (from ethyl diazoacetate, EDA) into the C–H bonds of alkanes such as pentane or hexane, among others. In the late 1990s, Davies and co-workers resuscitated this strategy providing, for the first time, the asymmetric functionalization of alkanes by carbene insertion [8]. Regarding the use of coinage metals, seminal work in the 1970s by Scott and DeCicco [9a] and Wulfsberg and co-workers [9b] gave very low yields with cyclic substrates. Several years ago, our group rediscovered the potential of group 11 metal-based catalysts for

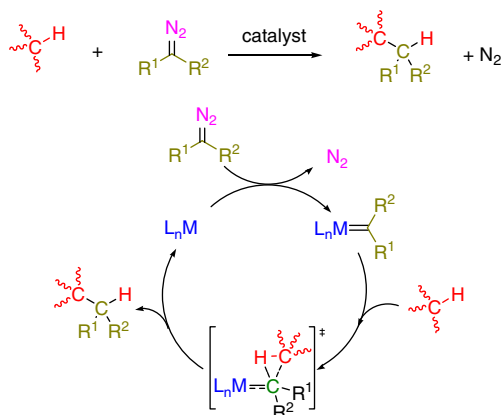
this transformation, first with copper, and later with silver and gold, using either trispyrazolylborate (Tp^x) [10], trispyrazolylmethane (Tpm^x) [11] or N-heterocyclic carbene (NHC) [12] ligands (Fig. 1). Dias, Lovely and co-workers have also described other Tp^xAg complexes as catalysts for this transformation [13].

Given the potential of the three coinage metal to promote the transfer of carbene units from EDA to the C–H bonds of alkanes [6], we wondered about the ability of the complexes $[\text{Au}_2\text{M}_2(\text{C}_6\text{F}_5)_4(\text{NCMe})_2]_n$ ($\text{M} = \text{Cu}$, **1**; $\text{M} = \text{Ag}$, **2**) [14] for such transformation, given the co-existence of gold and copper or silver in the same catalyst precursor. In this contribution, we present the results obtained with complexes **1** and **2** as catalysts for the reaction of EDA with several linear, branched and cyclic alkanes. High to quantitative conversions have been obtained, with moderate selectivities. The comparison of the observed regioselectivities with those previously reported for each metal supports the proposal that gold acts as a spectator ligand in these compounds, the real catalytic center being the copper or silver ion.



* Corresponding authors.

E-mail addresses: josemaria.lopez@unirioja.es (J.M. López-de-Luzuriaga), ana.caballero@dqcm.uhu.es (A. Caballero), perez@dqcm.uhu.es (P.J. Pérez).



Scheme 1. C–H bond functionalization by metal-catalyzed carbene insertion from diazo compounds.

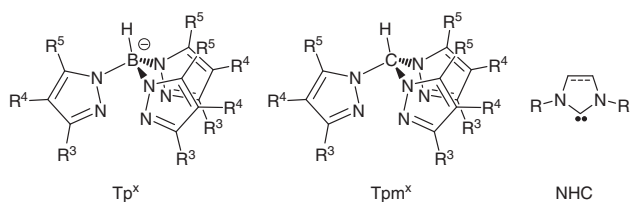
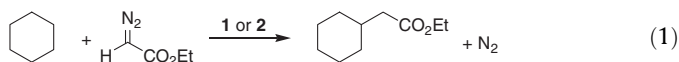


Fig. 1. Some ligands employed in the coinage metals-catalyzed C–H bond functionalization by carbene insertion from diazo compounds.

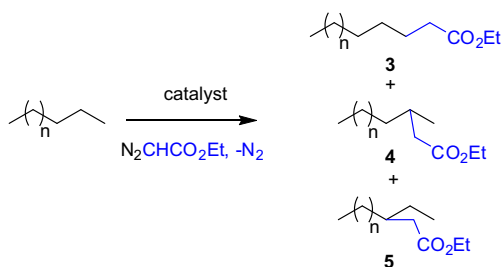
2. Results and discussion



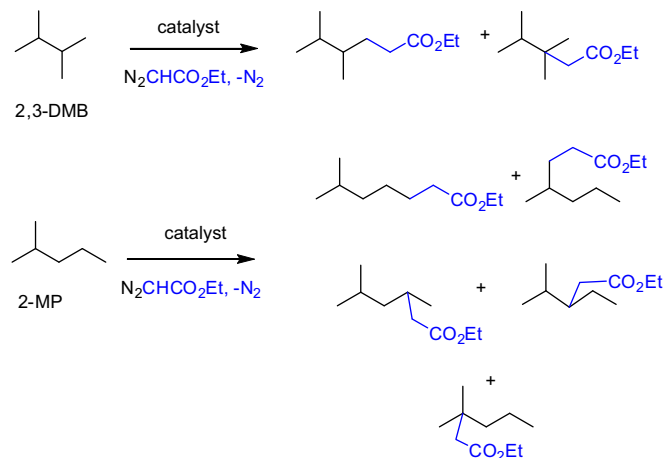
2.1. Alkane functionalization

As a probe reaction, cyclohexane was reacted with ethyl diazoacetate in the presence of complexes **1** or **2** as the catalyst, (Eq. (1)). A solution of either **1** or **2** (0.0125 mmol) in cyclohexane (10 mL) was prepared under a dinitrogen atmosphere. Ethyl diazoacetate (0.5 mmol, dissolved in 10 mL of cyclohexane) was added with the aid of a syringe pump for 12 h. The functionalized product, ethyl 2-cyclohexylacetate, was obtained in 92 and 99% yields, respectively, with **1** or **2** as the catalyst. It is worth mentioning that in the case of the silver catalyst, EDA could be added in one portion, thus avoiding the need of a slow addition device (yield: 72%).

Once demonstrated that both compounds could catalyze the transfer of the carbene moiety to C–H bonds of cyclohexane, we moved onto the use of linear alkanes such as pentane and hexane. In a similar manner to the procedure employed with cyclohexane (see Section 5), these C5 and C6 alkanes were reacted with EDA



Scheme 2. Functionalization of pentane and hexane with EDA and **1** or **2** as the catalyst.



Substrate	Catalyst	Conv ^a	%		
			primary ^b	secondary ^b	tertiary ^b
2,3-DMB	1	88	6	---	94
2,3-DMB	2	95	16	---	84
2-MP	1	87	21	24	55
2-MP	2	81	45	22	33

^aDetermined by GC, diethyl fumarate and maleate accounted for 100% of initial EDA. ^bDistribution of products, determined by GC.

Scheme 3. Functionalization of 2,3-dimethylbutane and 2-methylpentane with EDA and **1** or **2** as the catalyst.

in the presence of compounds **1** and **2**. As shown in Scheme 2, the Au–Cu intermetallic catalyst precursor provided a mixture of two products derived from the exclusive insertion of the carbene group into the secondary sites of the hydrocarbons, the methyl C–H bonds remaining unchanged. At variance with these results, compound **2** containing the Au–Ag unit induced not only the insertion in those secondary sites but also in the primary C–H bonds of both pentane and hexane. Yields were high in both cases, although as indicated above, the carbene precursor, EDA, was added with the aid of a syringe pump when **1** as the catalyst, whereas it was added in one portion in those experiments carried out in the presence of **2** as the catalyst.

Two other substrates were also tested in this study, 2,3-dimethylbutane (2,3-DMB) and 2-methylpentane (2-MP), in order to further evaluate the regioselectivity toward different C–H bonds within the same alkane. As shown in Scheme 3, all available C–H bonds were functionalized, with conversions into the functionalized products higher than 80% (based on initial EDA).

3. The effect of the metal: regioselection

As mentioned above, we have previously described the use of coinage-metal based catalyst for the functionalization of alkane

Catalyst	n	Conv ^a	% 3 ^b	% 4 ^b	% 5 ^b
1	1	90	nd	75	25
1	2	84	nd	61	39
2	1	99	25	64	11
2	2	80	26	42	32

^aDetermined by GC, diethyl fumarate and maleate accounted for 100% of initial EDA. ^bDistribution of products, determined by GC.

Table 1

Regioselectivity^a observed for the functionalization of pentane with EDA in the presence of several coinage metal catalysts.

Catalyst	Regios. 1ry C1	Regios. 2ry C2	Regios. 2ry C3	Reference
1	–	1.50	1.00	This work
2	1.00	8.70	6.8	This work
Tp ^{Br3} Cu(NCMe)	–	1.77	1.00	[10b]
[Tp ^{Br3} Ag] ₂	1.00	2.94	1.44	[10d]
IPrAuCl + NaBAR' ₄	1.00	3.17	2.19	[12a]

^a Values normalized for the relative number of C–H bonds of each type.

Table 2

Regioselectivity^a observed for the functionalization of 2,3-dimethylbutane with EDA in the presence of several coinage metal catalysts.

Catalyst	Regios. 1ry C–H	Regios. 3ry C–H	Reference
1	1.00	94.0	This work
2	1.00	31.0	This work
Tp ^{Br3} Cu(NCMe)	–	1.00	[10b]
[Tp ^{Br3} Ag] ₂	1.00	3.97	[10d]
IPrAuCl + NaBAR' ₄	1.00	1.23	[12a]

^a Values normalized for the relative number of C–H bonds of each type.

Table 3

Regioselectivity^a observed for the functionalization of 2-methylpentane with EDA in the presence of several coinage metal catalysts.

Catalyst	Regios. 1ry C–H	Regios. 2ry C–H	Regios. 3ry C–H	Reference
1	1.00	2.57	55.0	This work
2	1.00	1.10	33.0	This work
Tp ^{Br3} Cu(NCMe)	–	1.00	6.52	[10b]
[Tp ^{Br3} Ag] ₂	1.00	1.76	3.70	[10d]
IPrAuCl + NaBAR' ₄	1.00	1.92	2.06	[12a]

^a Values normalized for the relative number of C–H bonds of each type.

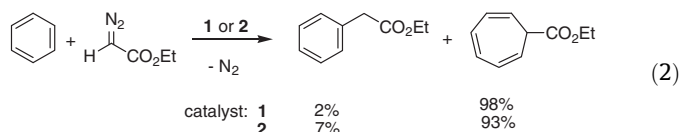
by the carbene insertion methodology, using EDA as the carbene source. Those studies showed that the order of reactivity follows the order tertiary > secondary > primary C–H bonds [15], that is, the same trend that the C–H bond dissociation energy [16]. In order to compare the regioselectivity induced by compounds **1** and **2**, the distribution of products shown in Schemes 2 and 3 must be normalized with the number of hydrogens of each type (primary, secondary, tertiary). Tables 1–3 contains such values for three representative examples, pentane, 2,3-dimethylbutane and 2-methylpentane. In addition of the values obtained with **1** and **2**, and for the sake of comparison, the regioselectivities previously described with three other coinage metal catalysts are also included.

In all cases, the aforementioned trend of reactivity matching the bond dissociation energy has also been found with these intermetallic Au–M (M = Cu, Ag) compounds: tertiary sites are more prone to functionalization as inferred for the highest value of the regioselectivity with no a single exception. When pentane as the substrate, the lack of tertiary sites made secondary positions as the most favorable and, among them, those of C2. Since the BDEs of both C2 and C3 C–H bonds do not differ much, this could be explained as the result of the steric effect, that plays a secondary but somewhat relevant role in this reaction. The same behavior and explanations apply to hexane as the substrate.

The copper-containing compound **1** seems to favor the insertion of the carbene group into secondary and/or tertiary sites, whereas the primary C–H bonds are less prone to undergo this transformation. This is in good agreement with the previous work carried out with copper-based catalysts such as Tp^{Br3}Cu(NCMe) [10b], that led

exclusively to tertiary sites functionalized derivatives. In the case of the Au–Ag compound **2**, a remarkably high selectivity toward the tertiary sites is observed. Thus, with 2,3-dimethylbutane as the substrate a 1:31 regioselectivity for primary:tertiary sites has been found. Such ratio is similar to that with 2-methylpentane (1:33), but quite different from that previously reported with [Tp^{Br3}Ag]₂ (1:3.97 and 1:3.70, respectively, for 2,3DMB and 2MP) [10d]. A comparison with the gold-based catalytic system [IPr–AuCl] + NaBAR'₄ would not explain those values: the latter catalyst clearly favored the insertion into primary sites, the regioselectivity for the tertiary sites being the lowest known to date (1:1.23, primary:tertiary, for 2,3-dimethylbutane and 1:2.06, also primary:tertiary, for 2-methylpentane) [12]. Therefore, data available indicate that in compounds **1** and **2**, the active catalytic center are copper and silver, respectively, the gold center not participating in the catalytic transformation. A second feature of this system is that the silver catalyst induces an exceptionally high regioselectivity toward tertiary sites, in contrast with previous work from our as well as Rasika Dias's groups [10d,13b].

In the search for additional evidences to support the role of gold as an spectator in this catalytic system, we have carried out the reaction of benzene and ethyl diazoacetate in the presence of **1** and **2** as the catalyst. The reaction of benzene and ethyl diazoacetate, the so-called Büchner reaction, usually provides a mixture of cycloheptatrienes. But in the presence of an appropriate transition metal catalyst (rhodium-, copper-, or silver-based), only one cycloheptatriene is formed in a selective manner [17]. Recently, we discovered IPrAuCl + NaBAR'₄ for the catalytic transfer of carbenes from ethyl diazoacetate, using benzene as the substrate [18]. In this reaction, and in addition to the expected cycloheptatriene, the major product was ethyl 2-phenylacetate, the product derived from the formal insertion of the carbene group into the benzene C–H bond. When complexes **1** and **2** were employed in this reaction, very low yields of the insertion product were observed, the major product being, by far the cycloheptatriene (Eq. (2)) [19]. We believe that, again, the catalytic results are in agreement with the role of gold as a “ligand” for copper or silver, with no participation at all in the catalytic reaction.



4. Conclusion

We have found that the complexes [Au₂M₂(C₆F₅)₄(NCMe)₂]_n (M = Cu, **1**; M = Ag, **2**) catalyze the functionalization of several alkanes, linear or branched, by means of the insertion of :CHCO₂Et, generated from ethyl diazoacetate, into the carbon–hydrogen bonds. Data available seems to favor the proposal that the active catalytic centers are copper or silver, with the gold Au(C₆F₅)₂ acting as a ligand that affects the course of the catalytic transformation.

5. Experimental

5.1. 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 purified using a BRAUN-SPS system and were degassed before use. The hydrocarbons and ethyl diazoacetate were purchased from Aldrich and employed without further purification. The complexes **1** and **2**

were prepared as previously described. [14] GC data were collected with a Varian GC-3350 instrument. NMR experiments were run in a Varian Mercury 400 MHz spectrometer.

5.2. General catalytic experiment

0.0125 mmol of complex **1** or **2** were dissolved in 10 mL of the substrate, adding 1–2 mL of dichloromethane in the case that it does not completely dissolve in the neat hydrocarbon. Ethyl diazoacetate (0.5 mmol, 40 equiv.) was added in one portion or with the aid of a syringe pump, in the latter case dissolved in 10 mL of the alkane, and with an addition time of 12 h. The consumption of EDA was monitored by GC, the reaction time being 12 h. At that time, volatiles were removed under vacuum at 0 °C and the products identified and quantified by NMR, using an internal standard.

Acknowledgments

We wish to thank the DGI for funding (CTQ2008-00042/BQU and CTQ2010-20500-C02-02) and for a FPI studentship (MAF).

References

- [1] (a) R.G. Bergman, *Nature* 446 (2007) 391;
(b) B.A. Arndtsen, R.G. Bergman, T.A. Mobley, T.H. Peterson, *Acc. Chem. Res.* 28 (1995) 154.
- [2] J.A. Labinger, J.E. Bercaw, *Nature* 417 (2002) 507.
- [3] H.M.L. Davies, J.R. Manning, *Nature* 451 (2008) 417.
- [4] M.M. Díaz-Requejo, T.R. Belderrain, M.C. Nicasio, P.J. Pérez, *Dalton Trans.* 5999 (2006).
- [5] M.P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, *Chem. Rev.* 110 (2010) 704.
- [6] M.M. Díaz-Requejo, P.J. Pérez, *Chem. Rev.* 108 (2008) 3379.
- [7] A. Demonceau, A.F. Noels, A. Hubert, P. Teyssié, *J. Chem. Soc., Chem. Commun.* 688 (1981).
- [8] H.M.L. Davies, R.E.J. Beckwith, *Chem. Rev.* 103 (2003) 2861.
- [9] (a) L.T. Scott, G.J. DeCicco, *J. Am. Chem. Soc.* 96 (1974) 322;
(b) D.S. Wulfman, R.S. McDaniel, B.W. Peace, *Tetrahedron* 32 (1976) 1241.
- [10] Tp^*Cu catalysts: (a) M.M. Díaz-Requejo, T.R. Belderrain, M.C. Nicasio, S. Trofimenko, P.J. Pérez, *J. Am. Chem. Soc.* 124 (2002) 896;
(b) A. Caballero, M.M. Díaz-Requejo, T.R. Belderrain, M.C. Nicasio, S. Trofimenko, P.J. Pérez, *J. Am. Chem. Soc.* 125 (2003) 1446;
(c) A. Caballero, M.M. Díaz-Requejo, T.R. Belderrain, M.C. Nicasio, S. Trofimenko, P.J. Pérez, *Organometallics* 22 (2003) 4145;
 Tp^*Ag catalysts: (d) J. Urbano, T.R. Belderrain, M.C. Nicasio, S. Trofimenko, M.M. Díaz-Requejo, P.J. Pérez, *Organometallics* 24 (2005) 1528;
(e) J. Urbano, A.A.C. Braga, F. Maseras, E. Álvarez, M.M. Díaz-Requejo, P.J. Pérez, *Organometallics* 28 (2009) 5968.
- [11] (a) P. Rodríguez, E. Álvarez, M.C. Nicasio, P.J. Pérez, *Organometallics* 26 (2007) 6661;
(b) P. Rodríguez, A. Caballero, M.M. Díaz-Requejo, M.C. Nicasio, P.J. Pérez, *Org. Lett.* 8 (2006) 557.
- [12] (a) M.R. Fructos, P. de Frémont, S.P. Nolan, M.M. Díaz-Requejo, P.J. Pérez, *Organometallics* 25 (2006) 2237;
(b) P. de Frémont, E.D. Stevens, M.R. Fructos, M.M. Díaz-Requejo, P.J. Pérez, S.P. Nolan, *Chem. Commun.* (2006) 2045.
- [13] (a) H.V.R. Dias, R.G. Browning, S.A. Richey, C.J. Lovely, *Organometallics* 23 (2004) 1200;
(b) H.V.R. Dias, R.G. Browning, S.A. Richey, C.J. Lovely, *Organometallics* 24 (2005) 5784.
- [14] E.J. Fernández, A. Laguna, J.M. López-de-Luzuriaga, M. Monge, M. Montiel, M.E. Olmos, M. Rodríguez-Castillo, *Organometallics* 25 (2006) 3639.
- [15] A.A.C. Braga, F. Maseras, J. Urbano, A. Caballero, M.M. Díaz-Requejo, P.J. Pérez, *Organometallics* 25 (2006) 5292.
- [16] S.J. Blanksby, G.B. Ellison, *Acc. Chem. Res.* 36 (2003) 255.
- [17] (a) A.J. Anciaux, A. Demonceau, A.F. Noels, A.J. Hubert, N. Petiniot, P.H. Teyssié, *J. Chem. Soc., Chem. Commun.* (1980) 765;
(b) M.E. Morilla, M.M. Díaz-Requejo, T.R. Belderrain, M.C. Nicasio, S. Trofimenko, P. Pérez, *J. Organometallics* 23 (2004) 293;
(c) C.J. Lovely, G. Browning, V. Badarinarayana, H.V. Rasika Dias, *Tet. Lett.* 46 (2005) 2453.
- [18] M.R. Fructos, T.R. Belderrain, P. Frémont, N.M. Scott, S.P. Nolan, M.M. Díaz-Requejo, P.J. Pérez, *Angew. Chem., Int. Ed.* 44 (2005) 5284.
- [19] The reaction of EDA and benzene in the presence of $\text{IPrMCl} + \text{NaBAR}'_4$ ($M = \text{Cu, Ag}$) provides the insertion product in 3–8% yield, the major product being the cycloheptatriene. Unpublished results from this laboratory.