

Exclusive Aromatic vs Aliphatic C-H Bond Functionalization by Carbene Insertion with Gold-based Catalysts

Ivan Rivilla, B. Pilar Gómez-Emeterio, Manuel R. Fructos, M. Mar Díaz-Requejo, Pedro J. Pérez**

Laboratorio de Catálisis Homogénea, Departamento de Química y Ciencia de los Materiales, Unidad Asociada al CSIC, Centro de Investigación en Química Sostenible (CIQSO). Universidad de Huelva, 21007-Huelva, Spain

AUTHOR EMAIL ADDRESS : perez@dqcm.uhu.es mmdiaz@dqcm.uhu.es

RECEIVED DATE (to be automatically inserted after your manuscript is accepted if required according to the journal that you are submitting your paper to)

TITLE RUNNING HEAD Gold-catalyzed arene C-H bonds functionalization by carbene insertion.

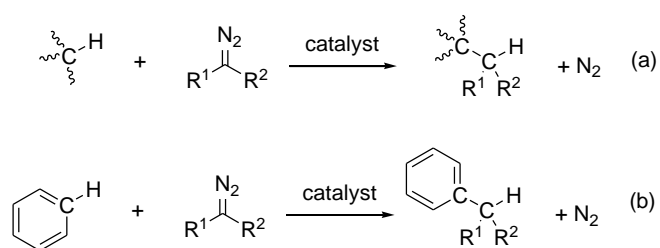
ABSTRACT. The direct functionalization of aromatic C-H bonds by carbene insertion from diazocompounds catalyzed by gold complexes with N-heterocyclic ligands is described. The reaction is completely selective toward the C_{sp}²-H bonds, other C_{sp}³-H bonds remaining unreacted. A study with a several NHC ligands in Au(I) and Au(III) complexes has been performed. A potential application in profen derivatives has also been developed.

KEYWORDS : Gold catalysis, Carbene transfer, C-H functionalization, NHC ligands, Diazo compounds

Introduction

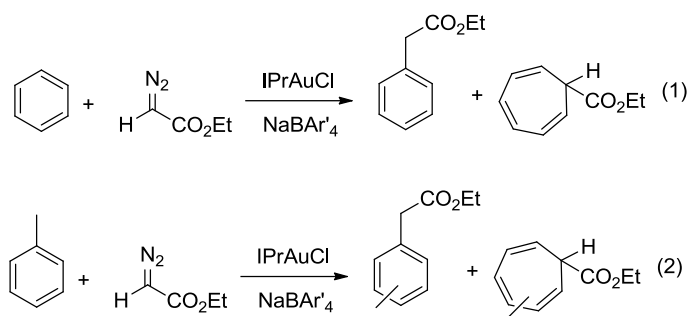
The functionalization of carbon-hydrogen bonds throughout a formal metal-mediated carbene insertion using diazo compounds as the carbene source (Scheme 1a) constitutes a synthetic tool that is growing in interest in the last decades.^{1,2} Both the inter-³ and intramolecular² versions have been described for C_{sp}³-H bonds. While the functionalization of *aromatic* C_{sp}²-H bonds with this strategy is

Scheme 1. The functionalization of C-H bonds by carbene insertion from diazocompounds.



somewhat developed for intramolecular processes, the intermolecular version is yet quite rare (Scheme 1b). Examples are reduced to independent work by Shechter⁴ and Livant⁵ with dirhodium acetate as the catalyst and elaborated diazo compounds led to the direct functionalization of benzene or anisole. After those reports, we described⁶ the first example of this intermolecular aromatic C-H bond functionalization by carbene insertion with commercial ethyl diazoacetate (EDA), and based in a gold catalyst. The complex IPrAuCl (**1**) (IPr = 1,3-bis(diisopropylphenyl) imidazol-2-ylidene) in the presence of one equivalent of NaBAr'₄ (Ar' = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate) as halide scavenger promoted the conversion of benzene and ethyl diazoacetate (EDA) into a 3:1 mixture of ethyl 2-phenylacetate and ethyl cyclohepta-2,4,6-trienecarboxylate (eq 1), at variance with other reported catalytic systems that exclusively provided the cycloheptatriene product.⁷ The aromatic C-H bond functionalization of toluene was also described using EDA as carbene source and the same gold catalytic precursor (eq 2). In this case, we found a mixture 4:1 mixture of products derived from the formal

insertion of the carbene group into the aromatic C-H bond and the cycloheptatriene derivative, respectively.



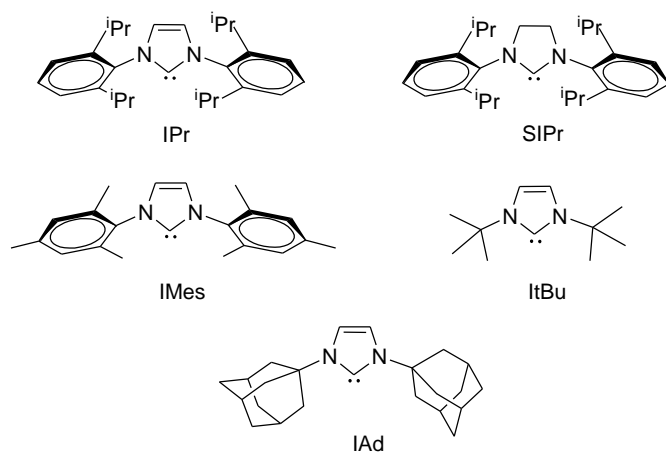
In a separate work from our laboratory, complexes of composition $(\text{NHC})\text{AuCl}$ were found to catalyze the functionalization of alkane C-H bonds by carbene insertion.⁸ A significant effect of the NHC ligand was observed both in the chemo- and regioselectivity of the reaction. On the basis of this, we have wondered about the existence of a similar effect in the functionalization of aromatic C-H bonds. In this contribution, we describe the catalytic capabilities of a series of Au(I) and Au(III) complexes toward the aromatic C-H bond functionalization using several diazo compounds as the carbene source. We have found that the appropriate choice of metal oxidation state, NHC ligand and diazo source allows a certain control in the selectivity of this transformation, with a preferential insertion of the carbene moiety into the $\text{C}_{\text{sp}}^2\text{-H}$ bonds, even when other $\text{C}_{\text{sp}}^3\text{-H}$ were available. We have also applied this methodology to the synthesis several profen derivatives.

Results and discussion

The catalytic activity of NHC-containing Au(I) and Au(III) complexes.

A series of complexes of general formula (NHC)AuCl and (NHC)AuBr₃ were prepared following literature methods,^{9,10} using the set of NHC ligands shown in Scheme 2. We have first targeted benzene

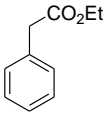
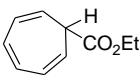
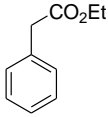
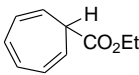
Scheme 2. NHC-ligands employed in this work.



as the substrate to be functionalized using EDA as the carbene source (see eq 1) with an array of ten gold complexes as the catalyst precursor, and using one equiv of NaBAR₄ to in situ remove the chloride ligand and generate the cationic Au(I) or Au(III) catalytic species.^{6,11} The reactions were performed using benzene as the solvent, at room temperature, and adding the EDA in one portion, avoiding the use of slow addition devices, a technique frequently employed in these transformations involving diazo compounds. The results are shown in Table 1, from which we can extract some interesting observations. First, most complexes induced high to very high conversions, intended as the percentage of EDA converted into products. It is worth mentioning that a secondary, non-desired reaction leading to the formation of diethyl fumarate (DEF) and maleate (DEM) usually constitutes the main drawback for diazo compound-based transformations, although in our case the amounts of DEF and DEM are not high (with the exception of the IMes derivative). Second, the insertion product, i. e., ethyl 2-phenylacetate,

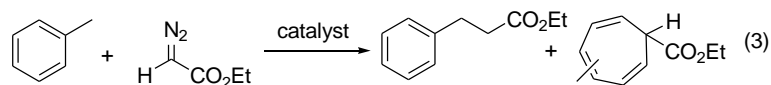
was the major product in all cases, the highest selectivity toward this compound being provided by the IPr(Au)-containing catalyst.

Table 1. Reaction of Benzene and EDA in the presence of (NHC)AuCl and (NHC)AuBr₃ as catalyst precursors.^a

Entry	NHC	(NHC)AuCl			(NHC)AuBr ₃		
		Conv. (%) ^b	% Insertion Product 	% Addition Product 	Conv. (%) ^b	% Insertion Product 	% Addition Product 
1	IPr	99	75	25	98	60	40
2	SIPr	99	65	35	81	56	44
3	IMes	64	70	30	85	54	46
4	IAd	99	45	55	85	55	45
5	IPr	90	65	35	99	69	31

^aCatalyst loading = 0.025 mmol, 0.5 mmol of diazocompound in 3 mL of benzene, room temperature. ^bPercentage of initial EDA converted into products. The remaining up to 100% of initial EDA was converted into diethyl fumarate and maleate.

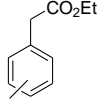
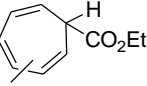
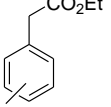
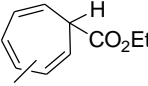
In order to gain information about the effect of the presence of alkylic C-H bonds as substituents in the aromatic ring, we have also studied toluene as the substrate. In the previously reported catalytic systems for carbene transfer from diazo compounds to toluene, or other alkyl-aromatic substrates, the reaction provides mixtures of the functionalization product derived from the insertion into the alkyl group,^{7b,12,13} as well as to the cycloheptatrienes (eq 3):



Following a similar experimental procedure to that commented for benzene, we have carried out the study with the ten catalyst precursors (Table 2). To our delight, we have observed that in no case the functionalization of the methyl group took place. On the other hand, the formal insertion of the carbene

group into the aromatic C-H bond was the preferred path. We have also found that the Au(III) complexes

Table 2. Reaction of toluene and EDA in the presence of (NHC)AuCl and (NHC)AuBr₃ as catalyst precursors.^a

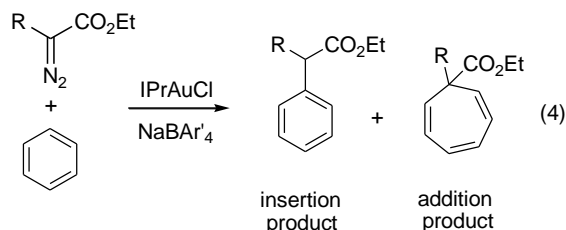
Entry	NHC	(NHC)AuCl			(NHC)AuBr ₃		
		Conv. (%) ^b	% Insertion Product  <i>o m p</i>	% Addition Product 	Conv. (%) ^b	% Insertion Product  <i>o m p</i>	% Addition Product 
1	IPr	99	80 46 21 33	20	75	>99 50 22 28	-
2	SIPr	64	78 48 21 31	20	90	>99 50 19 31	-
3	IMes	72	72 44 27 29	28	87	70 44 26 30	30
4	IAd	89	78 47 16 37	22	96	80 47 25 28	30
5	IBu	95	60 44 25 31	40	97	77 42 27 31	23

^aCatalyst loading = 0.025 mmol, 0.5 mmol of diazocompound in 3 mL of the substrate at room temperature. ^bPercentage of initial EDA converted into products. The remaining up to 100% of initial EDA was converted into diethyl fumarate and maleate.

bearing IPr or SIPr ligands *exclusively* provided the insertion product, with none of the seven-member cycle. The presence of the methyl group in the aromatic ring also induces the formation of the three *ortho*, *meta* and *para* isomers. Table 2 also contains the regioselectivities observed, with slight variations. It seems that for this diazo compound the *o:m:p* ratio is not significantly influenced by the catalyst.

Diazocompound screening.

The lack of observation a significant effect of the NHC ligand in the *o:m:p* regioselectivity in the reaction of EDA with toluene led us to employ a set of different diazocompounds. In a first series of experiments, benzene was reacted with ethyl 2-diazopropionate, ethyl α -diazo- α -(trimethylsilyl) acetate and ethyl 3,3,3-trifluoro-2-diazopropionate in the presence of catalytic amounts of IPrAuCl + NaBAR'₄ (eq 4). As inferred from the results shown in Table 3, this transformation strongly depended of the



nature of the diazo compound.

Whereas the previously reported reaction with EDA led to the consumption of the diazocompound at room temperature after a few hours, the use of ethyl 2-diazopropionate originated a change in the course of the reaction: after 3 d at 60 °C, only 20% of the initial diazo compound was consumed with 10% of the corresponding insertion product being obtained. Similar results were found with the trifluoromethyl diazo analogue, ethyl 3,3,3-trifluoro-2-diazopropionate (Table 3, entry 3).

Table 3. Reaction of benzene and different diazo compounds in the presence of IPrAuCl + NaBAR'₄ as the catalyst.^a

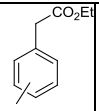
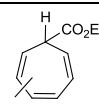
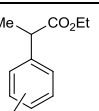
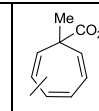
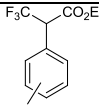
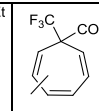
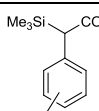
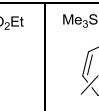
Entry	R ^b	Temp/ Time (°C/h)	Conv. (%) ^c	% Insertion Product	% Addition Product
1	H	20/6	>99	75	25
2	CH ₃	60/72	20	10	nd
3	CF ₃	60/3	15	>99	nd
4	Me ₃ Si	60/24	>99	85	15

^aCatalyst loading = 0.025 mmol, 0.5 mmol of diazocompound in 3 mL of the substrate. ^bR as in eq 3. ^cPercentage of initial diazocompound converted into products. The remaining up to 100% of initial EDA was converted into diethyl fumarate and maleate.

However, a quite interesting result was obtained with ethyl α -diazo- α -(trimethylsilyl) acetate as the carbene source: after 24 h at room temperature, quantitative conversions into a 85:15 mixture of the respective insertion and addition products were observed (Table 3, entry 4). No products derived from the coupling of the carbene groups were detected.

The study was expanded to toluene as the substrate, but also introducing the variable of the oxidation state of gold. Thus, both IPrAuCl or IPrAuBr₃ complexes were employed as the catalyst precursor, in the presence of one equiv of NaBAR⁴. Table 4 contains the conversions and distribution of products observed. It is noteworthy that in no case the methyl group of toluene was functionalized, again demonstrating the selectivity of this catalytic system toward the aromatic C-H bond functionalization.

Table 4. Reaction of toluene with several diazo compounds in the presence of IPrAuCl and IPrAuBr₃ as the catalyst precursors.^{a,b}

Catalyst	H-C(=N ₂)-CO ₂ Et			Me-C(=N ₂)-CO ₂ Et			F ₃ C-C(=N ₂)-CO ₂ Et			Me ₃ Si-C(=N ₂)-CO ₂ Et		
			Conv (%) ^c			Conv (%) ^c			Conv (%) ^c			Conv (%) ^c
IPrAuCl	80% ^e 46:21:33	20% ^e	>99 ^d	50% ^e 31:36:33	50% ^e	28 ^d	95% ^e 33:35:32	nd ^e	29 ^d	90% ^e 40:27:33	10% ^e	>99 ^d
IPrAuBr ₃	100% ^e 50:22:28	nd ^e	70 ^d	100% ^e 32:37:31	nd ^e	30 ^d	nr	nr	nr	100% ^e 30:31:29	nd ^e	90 ^d

^aCatalyst loading = 0.025 mmol, 0.5 mmol of diazocompound in 3 mL of toluene. Temperature: 60 °C, except for EDA (RT). ^bReaction times: EDA: 12 h; ethyl 2-diazopropionate, 72 h; ethyl 3,3,3-trifluoro-2-diazopropionate: data correspond to 3h, catalyst decomposition being observed after that time; ethyl 2-(trimethylsilyl)-2-phenylacetate, 24 h. ^cDetermined by NMR with internal standard at the end of the reaction. XX:XX:XX corresponds to the *ortho:meta:para* distribution of products. ^dBased on initial diazocompound, the remaining up to 100% corresponded to fumarate or maleate derivatives or unreacted diazocompound. ^eDistribution of products; nd : not detected; nr = no carbene transfer reaction observed.

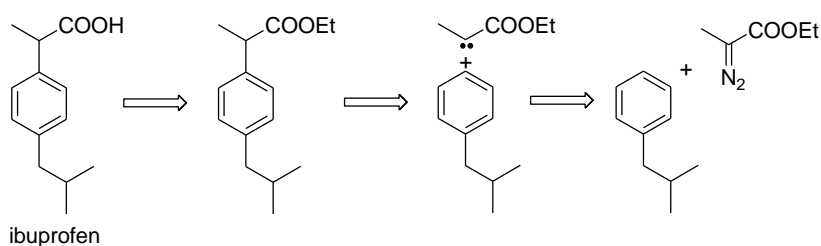
EDA as well as the SiMe₃-containing diazo compound provided high to very high conversions, whereas the CH₃- or CF₃-derived diazo reagents displayed a much lower reactivity, in spite that the reactions were performed at 60 °C except in the case of EDA. In the case of the more reactive reagents, the Au(III) catalyst precursor gave *exclusively* the insertion product, the cycloheptatriene being not detected in the

reaction mixture (some fumarate and maleate were also present due to the side reaction). Finally, the *o:m:p* selectivity did not vary significantly neither with the catalyst nor with the carbene source.

On the way to profen derivatives: isobutylbenzene as substrate.

Once we learnt that other diazo compounds were compatible with this gold-based catalytic system, we focussed our attention in the expansion of this methodology. As shown in Scheme 3, profens such as ibuprofen could be ideally prepared by the direct insertion of a given carbene unit into the C-H bond of an aromatic hydrocarbon.

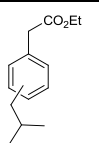
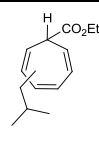
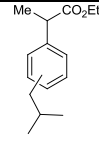
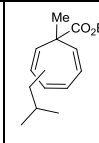
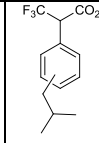
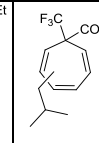
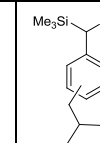
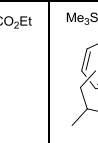
Scheme 3. Strategy for the synthesis of ibuprofen by carbene insertion.



After the results presented above, we decided to study the use of several diazocompounds using isobutylbenzene as ibuprofen precursor. Again, IPrAuCl and IPrAuBr₃ were employed as the catalyst precursor. The results of this study are shown in Table 5. Ethyl diazoacetate and ethyl α -diazo- α -(trimethylsilyl)acetate provided the best conversions, all the diazo reagent being consumed and the coupling products remaining below 10%. On the other hand, ethyl 2-diazopropionate and ethyl 3,3,3-trifluoro-2-diazopropionate gave low to moderate conversions. Reactions were carried out at 60° C for 24 h with the more reactive diazo compounds. The chemoselectivity, intended as the insertion: addition products ratio is favored when using the Au(III) catalyst, that induced the completely selective formation of the insertion products with EDA or Me₃SiC(N₂(CO₂Et)). *It is noteworthy that in no case the insertion of the carbene group took place into the carbon-hydrogen bonds of the alkyl-substituents.* As mentioned in the Introduction, this is at variance with other reported catalytic systems for carbene transfer from diazo compounds that, when applied to alkyl-aromatic substrates, led to the functionalization of the alkyl group,^{7b,11,12} as well as to the cycloheptatrienes. In our case, the selectivity

induced by the gold catalyst toward aromatic functionalization is complete with RC(N₂)CO₂Et (R = H, SiMe₃). In addition, the complex IPrAuBr₃ also enhanced the formation of the *para*-isomer, that reached 63 % and 56 % for EDA and the trimethylsilyl-derivative.

Table 5. Reaction of isobutylbenzene with several diazo compounds in the presence of IPrAuCl and IPrAuBr₃ as the catalyst precursors.^{a,b}

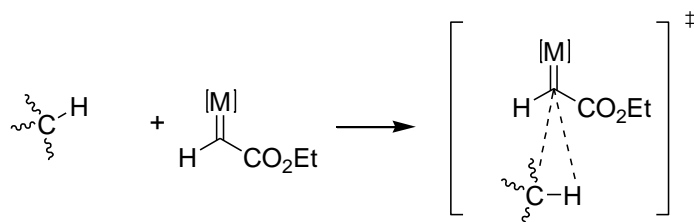
Catalyst	H-C(=N ₂)-CO ₂ Et			Me-C(=N ₂)-CO ₂ Et			F ₃ C-C(=N ₂)-CO ₂ Et			Me ₃ Si-C(=N ₂)-CO ₂ Et		
			Conv (%) ^c			Conv (%) ^c			Conv (%) ^c			Conv (%) ^c
IPrAuCl	88% ^e 43:25:32	12% ^e	>99 ^d	60% ^e 42:27:31	40% ^e	35 ^d	95% ^e 38:39:23	nd ^e	76 ^d	81% ^e 48:24:28	19% ^e	>99 ^d
IPrAuBr ₃	100% ^e 18:19:63	nd ^e	>99 ^d	100% ^e 31:44:25	nd ^e	30 ^d	nr	nr	nr	95% ^e 23:21:56	5% nd ^e	90 ^d

^aCatalyst loading = 0.025 mmol, 0.5 mmol of diazocompound in 3 mL of isobutylbenzene. Temperature: 60 °C, ^bReaction times: EDA: 12 h; ethyl 2-diazopropionate, 72 h; ethyl 3,3,3-trifluoro-2-diazopropionate: data correspond to 3h, catalyst decomposition being observed after that time; ethyl 2-(trimethylsilyl)-2-phenylacetate, 24 h. ^cDetermined by NMR with internal standard at the end of the reaction. XX:XX:XX corresponds to the *ortho:meta:para* distribution of products. ^dBased on initial diazocompound, the remaining up to 100% corresponded to fumarate or maleate derivatives or unreacted diazocompound. ^eDistribution of products; nd : not detected; nr = no carbene transfer reaction observed.

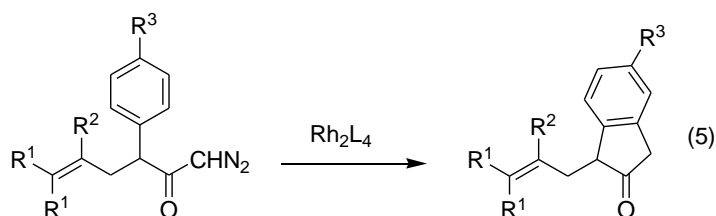
Some comments about the mechanism governing this transformation.

In the case of the functionalization of C_{sp}³-H bonds by this methodology, it is commonly accepted that such transformation occurs after the interaction of a metallacarbene intermediate with the C-H bond

Scheme 4. Commonly accepted explanation for the functionalization of C_{sp}³-H by carbene insertion.



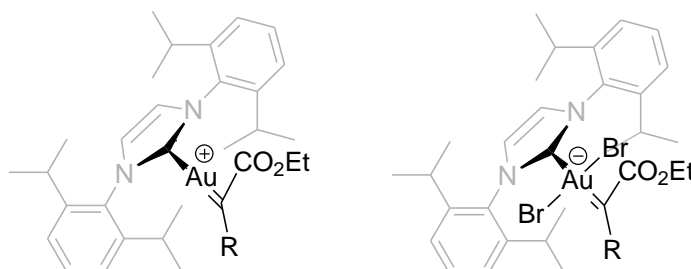
through a transition state involving exclusively carbenic carbon atom and the C-H bond (Scheme 4).¹⁴ This is in good agreement with the experimental observation that the observed trend in reactivity, in all reported systems, follows the order tertiary > secondary > primary sites, i. e., the bond dissociation energy (BDE) order.¹⁵ However, this assumption can be hardly applied to the results described in this contribution. In the molecule of isobutylbenzene, quite distinct C-H bonds relative to BDE values, are present: aromatic (ca 115 kcal/mol), benzylic (ca 90 kcal/mol), aliphatic tertiary (ca 95 kcal/mol) and aliphatic primary (ca 98 kcal/mol). Since in no case the functionalization of other C-H bond different than the aromatics are observed, and given that these are, by far, the more stable (in terms of BDE values) of the entire molecule, it seems reasonable to propose that this transformation cannot be explained by the pathway shown in Scheme 4. A possible description of the mechanistic pathway could be based in a previous work that employed rhodium diacetate catalysts for intramolecular C-H insertion reactions. Padwa, Doyle and co-workers described¹⁶ the reaction shown in eq. (5) as the result of the electrophilic addition of the metallocarbene intermediate to the aromatic ring, followed by a 1,2-hydride migration step. We believe that a similar process could take place in our system, therefore accounting for the observed exclusive selectivity toward the aromatic C-H bonds.



The observation of the enhancement toward the *para*-isomer when using Au(III) also deserves some comments. The addition of the halide scavenger and subsequent interaction with ethyl diazoacetate must afford transient gold-carbene species (Scheme 5). The geometry around the metal center must be similar to the starting complexes, i. e., linear for Au(I) and square-planar for Au(III). The assignment of the trans disposition of both the NHC ligand and the diazo-derived carbene ligand is based in a previous observation from our laboratory in a methylation reaction.¹¹ On the basis of those geometries, it is reasonable to propose that the interaction of the carbene CRCO₂Et with the aromatic

ring would be more constrained in the case of the square-planar geometry. However, the volume of the

Scheme 5. Plausible Gold-carbene intermediates.



diazo compound also influences the selectivity, the formation of the *para*-isomer being reduced when increasing the size of the R substituent. This is in agreement with data in table 4, where the *para*-isomer is increased when moving from Au(I) to Au(III) and decreased when moving from EDA to Me₃SiC(N₂)CO₂Et.

Conclusion.

We have found that the aromatic carbon-hydrogen bonds of alkyl-substituted benzenes can be directly functionalized under mild conditions using the methodology carbene transfer from several diazocompounds with gold-based catalysts, in a process that discriminates between aromatic and aliphatic C-H bonds in favor of the formers. The precatalyst IPrAuBr₃ has been found to promote the best values of chemo- and regioselectivity. This strategy has been applied for the direct synthesis of profen derivatives. Work aimed to develop more efficient and selective catalyst for this transformation is currently underway in our laboratory.

Experimental Section

General Methods. All experiments requiring a dry atmosphere were performed using conventional vacuum line and Schlenk techniques or in a dry box. The reagents were purchased from Sigma Aldrich. Complexes IPrAuCl and IPrAuBr₃ were prepared following literature procedures,^{9,10} as well as the diazocompounds¹⁷ and NaBAr'₄ (Ar' = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate).¹⁸ NMR solvents were stored over molecular sieves under nitrogen. NMR data were recorded at 298 K using Varian Mercury 400. ¹⁹F NMR chemical shifts were referenced relative to an external CFCl₃ standard. IR spectra were recorded on a Varian 1000 FT-IR. GC data were collected on Varian 3900 and 3800 instruments.

General Catalytic Experiment. The catalyst (0.025 mmol) was dissolved in 3 mL of the corresponding substrate (benzene, toluene, isobutylbenzene), and one equiv. of NaBAr'₄ was added to the solution. After 15 min of stirring, (R)C(N₂)CO₂Et (R = H, Me, SiMe₃, CF₃, 0.5 mmol) was added in one portion. Upon stirring at 60°C for 72 h (except for R = H that was performed at room temperature), the volatiles were removed and the residue dissolved in CDCl₃. NMR studies revealed the formation of two products: the cycloheptatrienes formed via the Buchner reaction and phenylacetates produced through the formal insertion of the carbene into the aromatic C-H bond. See Tables for results and Supporting Information for more details. We have not performed the chromatographic separation of the *o*, *m* and *p*- isomers, determining their ratio by NMR studies.

ACKNOWLEDGMENTS. We wish to thank DGI (CTQ2008-00042BQU and Consolider Ingenio 2010, Grant CSD2006-0003) and Junta de Andalucía (P07-FQM-02870) for funding.

SUPPORTING INFORMATION PARAGRAPH. Experiment details and spectroscopic data for the insertion and addition compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

References.

- 1) Davies, H. M. L.; Manning, J. R., *Nature* **2008**, *451*, 417-424.
- 2) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. *Chem. Rev.* **2010**, *110*, 704-724.
- 3) Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Pérez, P. J. *Dalton Trans.* **2006**, 5559-5566.
- 4) Rosenfeld, M. J.; Shankar, B. K.; Shechter, H. *J. Org. Chem.* **1988**, *53*, 2699-2705.
- 5) Yang, M.; Webb, T. R.; Livant P. *J. Org. Chem.* **2001**, *66*, 4945-4949.
- 6) Fructos, M. R.; Belderrain, T. R.; de Frémont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 5284-5288.
- 7) (a) Doyle, M. P.; McKervey M. A. and Tao Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, John Wiley & Sons, New York **1998**. (b) Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Hubert, A. J.; Petiniot, N.; Teyssie, P. H. *J. Chem. Soc., Chem. Commun.* **1980**, 765-766. (c) Morilla M. E.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S. Pérez, P. J.; *Organometallics* **2004**, *23*, 293-295. (d) Lovely, C. J.; Browning, G.; Badarinarayana, V.; Dias, H. V. R. *Tetrahedron. Lett.* **2005**, *46*, 2453-2455.
- 8) Fructos M. R.; de Fremont, P.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Organometallics*, **2006**, *25*, 2237-2241.
- 9) de Fremont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411-2418.
- 10) de Fremont, P.; Singh, R.; Stevens, E. D.; Petersen, L.; Nolan, S. P. *Organometallics* **2007**, *26*, 1376-1385.

- 11) Urbano, J.; Hormigo, J.; de Fremont, P.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Chem. Commun.* **2008**, 759-761.
- 12) (a) Callot, H. J.; Metz, F. *Nov. J. Chem.* **1985**, *9*, 167-171. (b) Davies, H. M. L.; Jin, Q. *Tetrahedron Asymmetry* **2003**, *14*, 941-949. (c) Davies, H. M. L.; Jin, Q.; Ren, P.; Kovalevsky, A. Y. *J. Org. Chem.* **2002**, *67*, 4165-4169.
- 13) Morilla, M. E.; Díaz-Requejo, M. M.; Belderraín, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Organometallics* **2006**, *25*, 293-295.
- 14) See: Braga, A. A. C.; Maseras, F.; Urbano, J.; Caballero, A.; Díaz-Requejo, M. M.; Pérez, P. J. *Organometallics* **2006**, *25*, 5292-5300, and references cited therein.
- 15) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255-263.
- 16) Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669-8680.
- 17) (a) Ethyl 3,3,3-trifluoro-2-diazopropionate: Shi, G.; Xu, Y. *J. Org. Chem.* **1990**, *55*, 3385-3388. (b) Ethyl α -diazomethylacetate: Bachmann, S.; Fielenbach, D.; Jorgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044-3049. (c) Ethyl α -diazo- α -(trimethylsilyl)acetate: Fronda, A.; Maas, G. *J. Organomet. Chem.* **1985**, *290*, 33-39.
- 18) (a) Brookhart, M.; Grant, B.; Volpe, A. F. *Organometallics* **1992**, *11*, 3920-3922; (b) Iwamoto, H.; Sonoda, T.; Kobayashi, H. *Tetrahedron Lett.* **1983**, *24*, 4703-4706.

Exclusive Aromatic vs Aliphatic C-H Bond Functionalization by Carbene Insertion with Gold-based Catalysts

Ivan Rivilla, B. Pilar Gómez-Emeterio, Manuel R. Fructos, M. Mar Díaz-Requejo,* Pedro J. Pérez*

