

Gold-Catalyzed Intermolecular Formal Insertion of Aryldiazo Esters into Cp-H Bonds of Cp₂M (M = Fe, Ru)

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Dedicated to the memory of Professor José Barluenga

Abstract: The reaction of ferrocene (and ruthenocene) with aryldiazo acetates in the presence of gold catalysts provided new functionalized metallocenes resulting from a C-H bond functionalization process. This process is believed to proceed through initial decomposition of the diazo component with formation of an electrophilic gold carbene intermediate, which would be subsequently involved in an electrophilic aromatic substitution. The gold-catalyzed functionalization of ruthenocene exhibited a broad scope and a notable functional-group tolerance. Interestingly, the functionalized ferrocene derivatives were found to react with molecular oxygen to yield α -aryl- α -ferrocenyl- α -hydroxyacetates. Adsorption on silica gel was found to be essential for this dioxygen activation/C(sp³)-H bond functionalization sequence. The methodologies reported herein provide a simple and efficient approach to functionalized metallocene derivatives difficult-to-access through conventional organic functional group transformations.

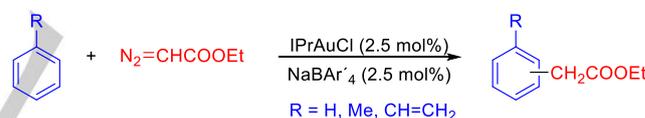
Introduction

Since the seminal report on the gold-catalyzed decomposition of ethyl diazoacetate and the subsequent trapping of the resulting gold-carbenoid species by Nolan, Díaz-Requejo, Pérez et al in 2005,^[1] the number of synthetic applications based on the gold chemistry of diazo compounds has been growing steadily.^[2] Among the synthetically useful transformations developed in this field, the reaction with arenes has attracted considerable interest as a means to access functionalized benzene derivatives featuring a non-trivial substitution pattern. Some of these gold-catalyzed arene C-H bond functionalization transformations proceeded with chemoselectivities previously unattainable using other metal complexes. In fact, in the above mentioned contribution, using ethyl diazoacetate as the carbene source, the authors already reported that the formal insertion of the carbene unit into the aromatic C-H bond was the preferred path not only for benzene but also for toluene and styrene (Scheme 1, a). In a follow-up study, the same group found a similar selectivity profile for other substituted arenes and diazo compounds.^[3]

In 2014, two research groups concurrently reported the selective C-H bond functionalization of electron-rich arenes (Scheme 1, b). Thus, Liu, Zhang and coworkers reported the gold-catalyzed C-H bond functionalization of phenols (or *N*-acylanilines) with α -aryl- α -diazoacetates.^[4] Notably, this process occurred with complete chemo- and site-selectivity toward *para* C-H functionalization, with none of the corresponding ether (or amide) derivatives arising from the O-H (or N-H) bond insertion reaction. Independently, Lan, Shi and coworkers reported a similar selectivity while investigating the reactivity of electronically activated arenes with α -aryl- α -diazoacetates in the presence of gold-catalysts. As in the previously discussed contribution, this aromatic C-H bond functionalization process was compatible with arenes bearing carbene-sensitive functional groups such as phenol, alkene and alkyne.^[5]

All these gold-catalyzed transformations have been proposed to proceed through an electrophilic aromatic substitution mechanism, in which a gold carbene intermediate resulting from the decomposition of the initial diazo compound would act as the electrophilic partner.^[6]

a) Seminal report on a new reactivity pattern^[1]



b) Extension to electron rich arenes^[4,5]



Scheme 1. Gold-catalyzed C-H bond functionalization of arene derivatives involving gold carbenoids from diazo compounds

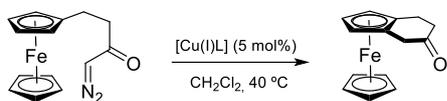
Surprisingly, despite the well-recognized electron-rich aromatic character of ferrocene and the fact that many functionalized ferrocene derivatives have found multiple applications in a number of important areas,^[7] the functionalization of ferrocene through catalytic carbene transfer remains a largely unsolved issue. Indeed, to the best of our knowledge, the only contribution in this field was communicated by Siegel and Schmalz, who in 1997 reported the intramolecular carbene insertion into the Cp-H bond of ferrocene derivatives in the presence of rhodium and copper catalysts (Scheme 2).^[8] In this seminal contribution, the authors also reported that the cyclization products accessed by this methodology were sensitive towards oxidation decomposing

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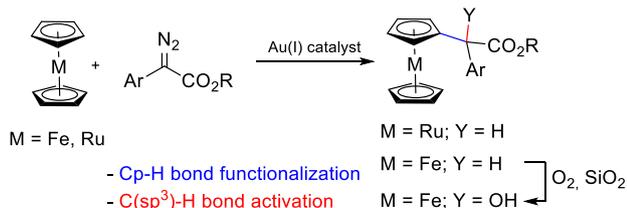
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upon exposure to air, generating 1,2-diketones or dimeric compounds.

C-H bond functionalization of ferrocene involving carbene intermediates^[8]



This work



Scheme 2. C-H bond functionalization of ferrocene derivatives involving metal carbene intermediates derived from diazo compounds

In 2014, our group disclosed the intermolecular gold-catalyzed reaction of vinyl diazo compounds and ferrocene to provide functionalized ferrocene derivatives.^[9] This reaction was proposed to occur by means of an electrophilic vinylgold carbene intermediate, which would react with the metallocene through the vinyllogous position rather than through the carbenic carbon atom.^[10] Continuing with the interest of our group in the synthesis of functionalized ferrocene derivatives based on metal-carbene chemistry,^[11] we envisioned that ferrocene might intercept the electrophilic gold carbenoid, generated from simple diazo compounds. Consequently, herein we report the intermolecular C-H bond functionalization of ferrocene and ruthenocene with α -aryl- α -diazoacetates under gold catalysis. An aerobic oxidation of the functionalized ferrocene derivatives to give α -aryl- α -ferrocenyl- α -hydroxyacetates is also reported. Adsorption on silica gel was found to be essential for this unusual dioxygen activation/C(sp³)-H bond functionalization sequence.

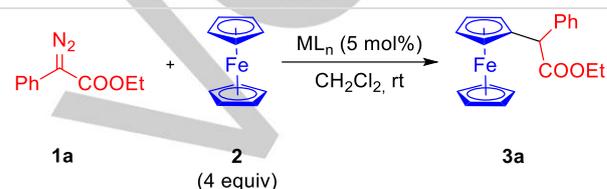
Results and Discussion

Formation of functionalized ferrocene derivatives. We began our study investigating the reaction of ferrocene and the simplest and most popular stabilized diazo compound, namely ethyl diazoacetate, in the presence of an array of gold catalysts. Unfortunately, we were not able to isolate in a synthetically useful yield the desired C-H bond functionalization product. In most cases, the reaction gave a complex mixture of products from which only trace amounts (< 5%) of the corresponding functionalized ferrocene derivative (ethyl ferrocenylacetate) could be isolated.^[12]

We next turned our attention to the use of aryl substituted diazo compounds. Thus, using ethyl 2-diazo-2-phenylacetate

(**1a**) as model substrate and an excess of ferrocene, after screening of several gold complexes (Table 1, entries 1-4), [Au(IPr)(MeCN)][SbF₆] (5 mol%) in dichloromethane at room temperature turned out to be the optimal catalyst providing the corresponding functionalized ferrocene **3a** in excellent yield (entry 4, 92 % by NMR using 1,1,2,2-tetrachloroethane as internal standard). Other gold complexes displayed inferior (entries 1 and 2) or similar (entry 3) performance. Noteworthy, copper and rhodium complexes (entries 5 and 6), which are the most common catalysts in transformations involving diazo compounds, were much less efficient in this C-H bond functionalization process.^[13]

Table 1. Summary of catalyst screening^[a]



entry	ML _n	3a (%) ^[b]
1	(2,4- <i>t</i> Bu ₂ C ₆ H ₃ O) ₃ PAuNTf ₂	38
2	JohnPhosAuNTf ₂	41
3	IPrAuNTf ₂	88
4	[IPrAu(CH ₃ CN)][SbF ₆]	92
5	[Cu(CH ₃ CN) ₄][PF ₆]	-
6	Rh ₂ (OAc) ₄	40

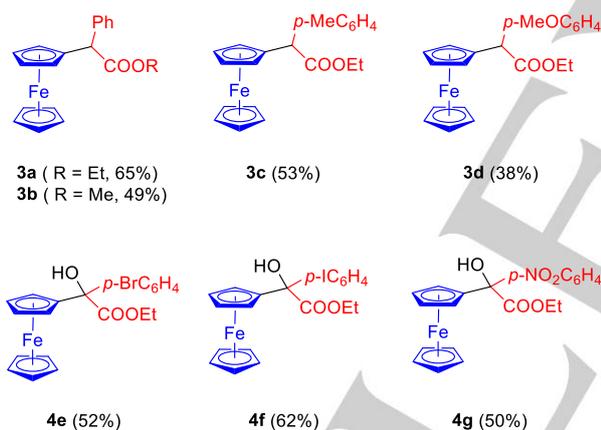
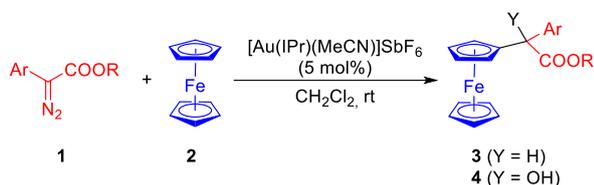
[a] Unless otherwise stated, these exploratory experiments were performed on a 0.2 mmol scale. [b] Yield determined by ¹H-NMR spectroscopy in CDCl₃, using 1,1,2,2-tetrachloroethane as internal standard.

Surprisingly, column chromatography purification of ferrocene **3a** using silica gel as the stationary phase and a 20:1 mixture of hexanes/ethyl acetate as the eluent resulted in a drastic drop in the yield (35%). Based on previous observations by us and others,^[14] this behavior could be very likely ascribed to a low stability of ferrocene **3a** towards aerobic oxidation during the chromatographic treatment. Trying to circumvent this problem, alternative stationary phases were investigated. Thus, whereas alumina did not improve substantially the yield of **3a**, the use of Florisil allowed its isolation in a satisfactory yield (65%).

With suitable reaction conditions in hand, we then focused on whether this gold-catalyzed process tolerates some variation of the diazo partner. As shown in Scheme 3, the reaction outcome was found to be highly dependent on the electronic nature of the starting diazo compound. Indeed, we observed that ethyl α -(4-methylphenyl)- α -diazoacetate was also a competent substrate in this transformation. Mimicking the situation found for the model reaction, the coupling product **3b** is somewhat sensitive and, as a result, it was isolated in moderate yield after chromatographic purification (49%). It was also demonstrated that a strong

electron-releasing group renders the process rather unproductive. Thus, although ethyl α -(4-methoxyphenyl)- α -diazooacetate behaved similarly, it gave the corresponding ferrocene derivative **3c** in lower yield.

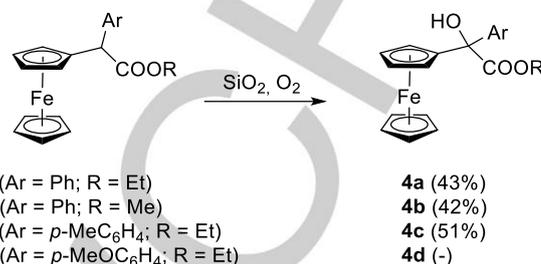
In contrast, attempts to prepare the corresponding ferrocene derivatives from α -aryl- α -diazooacetates featuring electron-withdrawing substituents on the aryl group failed. Apparently, the ferrocene derivatives arising from these aryldiazooacetates are more susceptible to oxidation and the only products isolated after chromatography (even using Florisil as the stationary phase) were alcohols **4** resulting from the aerobic oxidation of the α -position. Indeed, α -aryl- α -diazooacetates bearing bromo and iodo substituents at the *para*-position of the aryl group, furnished ferrocene derivatives **4e** (52%) and **4f** (62%), respectively. A similar result was found when ethyl α -(4-nitrophenyl)- α -diazooacetate was subjected to the above reaction conditions, thus rendering alcohol **4g** in 50% as the only isolable reaction product.



Scheme 3. Gold-catalyzed reaction of aryl diazoacetates **1** and ferrocene. Reaction conditions: **1** (0.5 mmol), **2** (2.0 mmol), $[\text{Au}(\text{IPr})(\text{CH}_3\text{CN})]\text{SbF}_6$ (5 mol%), CH_2Cl_2 (0.1 M), rt. Values within parentheses represent yields of the isolated products after column chromatography (Florisil, hexanes/ethyl acetate mixtures).

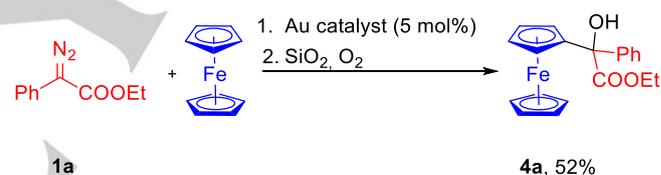
Next, in order to determine the actual role of the gold catalyst in the oxidation process we investigated the behavior of ferrocene **3a** towards oxygen. Thus, it was demonstrated that when a sample of ferrocene derivative **3a** was adsorbed on silica gel under vacuum and subsequently exposed to oxygen a clean oxidation took place allowing the isolation of hydroxyester **4a** in moderate yield (Scheme 4). This outcome suggests that the gold catalyst did not play any significant role in the formation of the oxidation products **4e-f**. Similarly, ferrocene derivatives **3b, c**

were transformed into the hydroxyesters **4b, c** with similar efficiency. The oxidation of *p*-methoxyphenyl-substituted ferrocene **3d** under otherwise similar reaction conditions was also attempted, but formation of desired product **4d** was not observed; instead a complex mixture of products was formed.



Scheme 4. Aerobic oxidation of ferrocene derivatives **3**.

Hydroxyester **4a** was also available through a one-pot procedure (Scheme 5). Thus, initial treatment of ethyl 2-diazo-2-phenylacetate (**1a**) with ferrocene (**2**) in the presence of the gold catalyst in dichloromethane, followed by addition of silica gel, concentration of the resulting mixture and final exposure to oxygen delivered the desired α -hydroxyester in moderate yield after chromatography.



Scheme 5. One-pot synthesis of ferrocene derivative **4a**.

The structures of ferrocene derivatives **3** and **4** were ascertained by NMR methods. In addition, single crystals of ferrocenes **3b** and **4b** suitable for X-ray structure analysis were obtained from pentane/dichloromethane at -20°C by the diffusion method, thus confirming unambiguously the initially proposed structures (Figure 1).^[15]

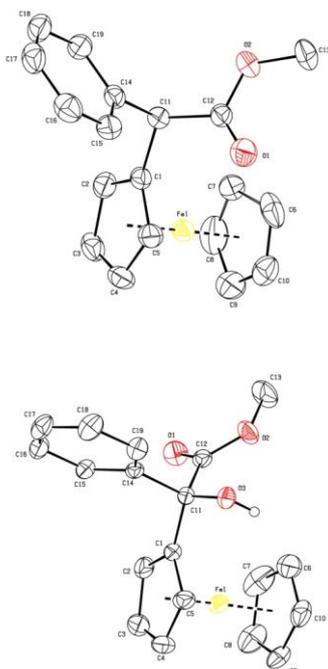
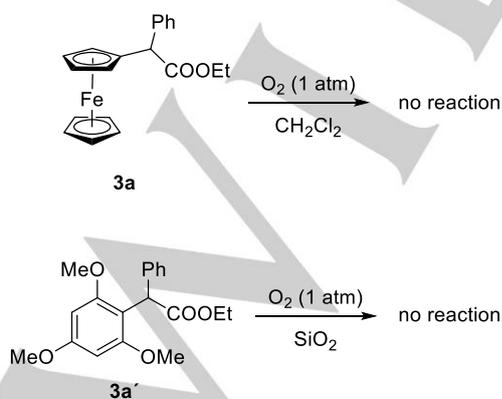


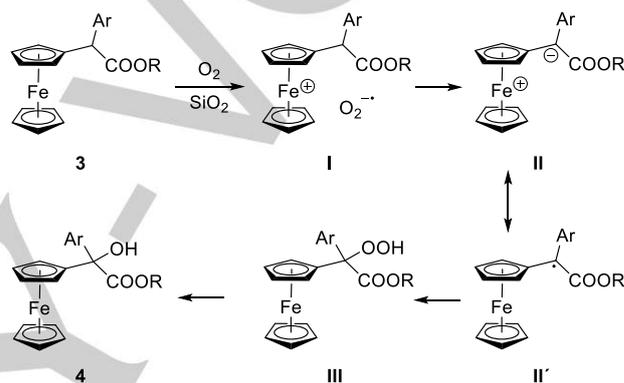
Figure 1. X-ray structures of ferrocene derivatives **3b** (top) and **4b** (bottom). Thermal ellipsoids are drawn at the 30% probability level.

Next, we performed some control experiments aimed to gain insight into this aerobic oxidation involving dioxygen activation (Scheme 6). First, we found that exposing to oxygen (1 atm) a solution of ferrocene derivative **3a** in dichloromethane proved ineffective since starting ferrocene was the only product observed in the reaction crude. On the other hand, when the diaryl-substituted ester **3a'** in lieu of ferrocenyl **3a** was subjected to the dry state aerobic oxidation conditions no reaction was observed at all, even after prolonged reaction time (3 days). Taken together, these control experiments show that both the ferrocene moiety and the adsorption on silica gel are crucial for a successful oxidation.



Scheme 6. Control experiments.

Although the chemistry of metallocenes adsorbed on silica gel has been barely investigated,^[16] very recently Cluff and Blümer studied the adsorption of ferrocene on silica gel by solid-state NMR methods and they found that in the presence of air adsorbed ferrocene is oxidized to ferrocenium salts at acidic surface silanol sites.^[17] Based on this observation, we hypothesize that our aerobic oxidation could proceed through initial electron transfer from iron to a dioxygen molecule with formation of ferrocenium ion **I** and superoxide radical anion intermediate, $O_2^{\cdot-}$, followed by deprotonation of the acidic α -CH proton (Scheme 7).^[18] The resulting neutral ferrocene species **II** could also be regarded as a carbon-centered radical **II'** which would evolve to the final oxygenated products **4** probably through hydroperoxide intermediate **III**.^[19]



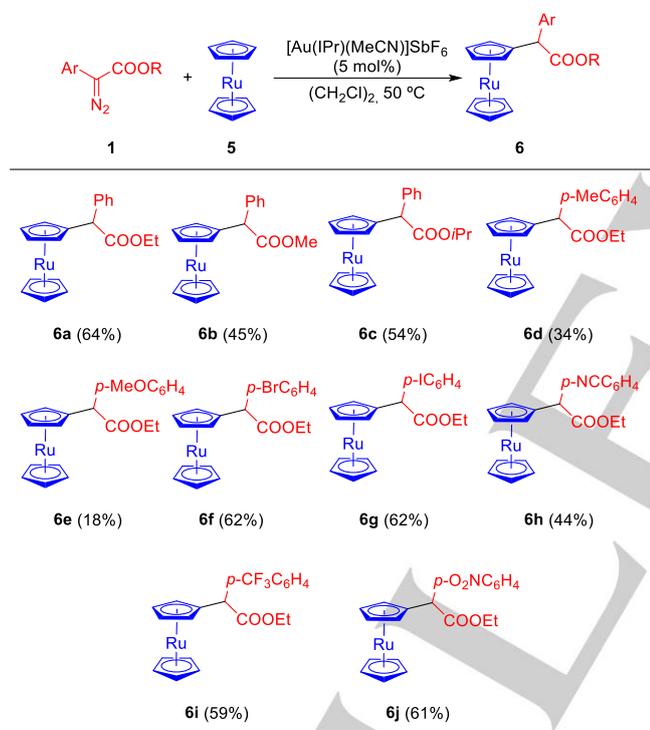
Scheme 7. Proposed mechanism for the aerobic oxidation of ferrocene derivatives **3**.

Although preliminary, these results on the aerobic oxidation of ferrocene derivatives adsorbed on silica could open up new synthetic opportunities for the development of new C-H bond activation methods involving dioxygen as the oxidant, a challenging issue in contemporary catalysis. Moreover, these results suggest that the adsorption of ferrocene derivatives on silica gel, a virtually unexplored research field, could provide unusual reactivity modes expanding the repertoire of available synthetic methodologies for the preparation of densely functionalized ferrocenes, an important goal in preparative organometallic chemistry.

Synthesis of functionalized ruthenocene derivatives 5. The results obtained in the gold-catalyzed reaction of ferrocene and α -aryl- α -diazoacetates encouraged us to further expand this C-H bond functionalization process to ruthenocene. Based on the general assumption that ruthenocenes are more difficult to oxidize than their isostructural ferrocene counterparts,^[20] we surmised that the reaction with ruthenocene could provide more stable products offering a solution to the inherent stability issues encountered for the ferrocene derivatives and, in an indirect way, supporting the participation of ferrocenium ions in the aerobic oxidation reported in the previous section.

For that purpose, we initially studied the reaction of ethyl 2-diazo-2-phenylacetate (**1a**) and an excess (4 equiv) of

ruthenocene (**5**) in the presence of a series of gold catalysts. The lower reactivity of ruthenocene in electrophilic aromatic substitution reactions is well-established in the literature and, consequently, in this model reaction very low conversions were observed under otherwise identical reaction conditions to those applied for the preparation of the ferrocene analogues (5 mol%, CH₂Cl₂, rt). To our delight, we found that heating at 50 °C in 1,2-dichloroethane led in some cases to the corresponding functionalized ruthenocene derivative. Once again, the best result was obtained with [Au(IPr)(MeCN)]SbF₆ as the catalyst, delivering the desired ruthenocene **6a** in an acceptable 66% yield by NMR (using 1,1,2,2-tetrachloroethane as internal standard). As anticipated, this yield was not substantially altered after chromatographic purification on silica gel, thus confirming our hypothesis of the higher robustness of the ruthenocene derivative, compared to the ferrocene analogue. Having found satisfactory reaction conditions for the C-H bond functionalization of ruthenocene, we then explored the substrate scope of this transformation (Scheme 8).



Scheme 8. Gold-Catalyzed Reaction of Aryl Diazo Derivatives **1** and Ruthenocene. Reaction conditions: **1** (0.5 mmol), **5** (2.0 mmol), [Au(IPr)(CH₃CN)]SbF₆ (5 mol%), (CH₂Cl)₂ (0.1 M), 50 °C. Values within parentheses represent yields of the isolated products after column chromatography (silica gel, hexanes/ ethyl acetate mixtures).

First, we found that the nature of the ester substituent does not play any significant role in the reaction outcome. In fact, the more sterically hindered isopropyl ester gave even a higher yield than the less hindered methyl ester.

Next, to determine the effect of the electronic properties of the substituents on the coupling process, an array of *para*-

substituted α -aryl- α -diazoacetates were subjected to the optimized conditions.

Substrates with electron-donating groups, such as methyl and methoxy, provided the corresponding coupling products **6d** and **6e**, respectively, in lower yields. Very likely, the *para* electron-donating substituent decreases the electrophilic character of the postulated gold carbene intermediate thereby rendering the coupling process more challenging. In line with this assumption, this effect is more pronounced for the substrate with a strong electron-releasing group such as methoxy.

In contrast, α -aryl- α -diazoacetates bearing electron-withdrawing substituents were found to be proficient substrates in this gold-catalyzed transformation. As shown in Scheme 8, this gold-catalyzed transformation was compatible with α -aryl- α -diazoacetates bearing halogen substituents at the *para*-position of the aryl group, and the corresponding functionalized ruthenocene derivatives **6f** and **6g** were isolated in moderate yield. The resultant bromo and iodo moieties could be subsequently handled through well-established methodologies towards the synthesis of new functionalized derivatives. A cyano group at the *para*-position was also tolerated affording ruthenocene derivative **6h**, albeit in somewhat lower yield (44%).

Ethyl α -diazo- α -(*p*-trifluoromethylphenyl)acetate also performed well in the reaction providing ruthenocene derivative **6i** in moderate yield. Finally, the presence of a strong electron-withdrawing nitro group posed no problems and ruthenocene derivative **6j** was isolated in an acceptable yield (61%).

As in the case of ferrocene analogues, the structure of metallocenes **6** was ascertained by NMR spectroscopy.

Additionally, a X-ray crystal structure analysis of ruthenocene derivative **6b** unambiguously confirmed the initially proposed structure (Figure 2).^[15]

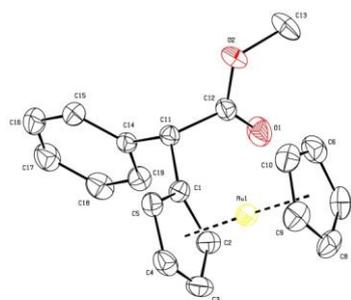
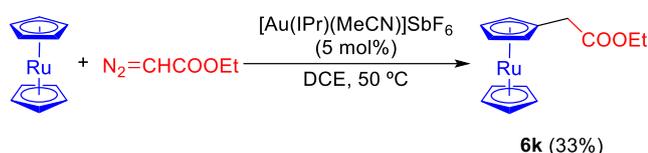


Figure 2. X-ray structure of alcohol **6b**. Thermal ellipsoids are drawn at the 30% probability level.

In light of the much broader scope of the C-H bond functionalization of ruthenocene involving gold carbenoids and the higher stability of the resulting products, we finally investigated the behaviour of ethyl diazoacetate, a challenging substrate in the reaction with ferrocene as stated before. Thus, it was gratifying to find that stirring a mixture of ethyl diazoacetate, ruthenocene (4 equiv) and 5 mol% of

[Au(IPr)(MeCN)]SbF₆ in dichloroethane at 50 °C led to the formation of ethyl ruthenocenylacetate **6k** in pure form, albeit in moderate yield (Scheme 9).



Scheme 9. Gold-catalyzed reaction of ruthenocene and ethyl diazoacetate.

Conclusions

In summary, we have developed the intermolecular formal carbene insertion into the Cp-H bond of ferrocene and ruthenocene in the presence of gold-catalysts. Starting from readily available α -aryl- α -diazoacetates, this C-H bond functionalization protocol allows for the synthesis of functionalized metallocene derivatives with difficult-to-access substitution patterns. Somewhat surprisingly, ferrocene derivatives are quite sensitive. Indeed, upon exposure to oxygen they are prone to undergo an aerobic oxidation of the α -position leading to tertiary substituted ferrocenyl alcohols. Control experiments demonstrated that adsorption on silica gel was found to be essential for this unusual dioxygen activation/C(sp³)-H bond functionalization sequence. These results together with those previously reported by Siegel and Schmalz demonstrate that the aerobic oxidation of functionalized ferrocenes cannot be exclusively regarded as an undesired reaction but it could turn into an appealing alternative to traditional synthetic approaches based on conventional organic functional group transformations. Not surprisingly the ruthenium analogues were found to be substantially more stable and the reaction tolerated a number of functional groups, highlighting the broad scope of this gold-catalyzed C-H bond functionalization.

Taken collectively, the results reported in this contribution represent a new demonstration of the synthetic potential of gold-carbenoid chemistry and set the stage for further applications of electrophilic metal carbenoids in the C-H bond functionalization of metallocenes, an underexplored research field.

Experimental Section

General Procedure for the Synthesis of Compounds **3a-d** and **4e-g**.

To a solution of [Au(IPr)(CH₃CN)]SbF₆ (21.6 mg, 0.025 mmol, 5 mol%) and ferrocene (**2**, 370 mg, 2 mmol) in CH₂Cl₂ (5 mL) was slowly added over 1.5 h (via a syringe pump) a solution of the corresponding diazoacetate **1** (0.5 mmol) in CH₂Cl₂ (2 mL). After the addition was complete, the resulting mixture was stirred at room temperature for an additional hour. The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (Florisil, hexanes/ethyl acetate 40:1). Elution produced 2 major fractions. The first one was unreacted ferrocene and the second fraction was found to be pure functionalized ferrocene derivatives **3a-d** and **4e-g**.

Aerobic Oxidation of Ferrocene Derivatives **3a-c.** To a solution of the corresponding ferrocene derivative **3a-c** (0.1 mmol) in a few mL of CH₂Cl₂ was added silica gel (1.8 g). The resulting suspension was stirred at room temperature for a while and then the solvent was evaporated under reduced pressure to dryness. The Schlenk flask was then charged with oxygen and allowed to stand at room temperature. After 1 day (for **3a** and **3b**) or 3 days (for **3c**) CH₂Cl₂ was added (10 mL) and the silica gel was removed by filtration and the crude product was purified by flash chromatography (SiO₂, hexane/ethyl acetate 20:1) to afford α -ferrocenyl- α -hydroxyester derivatives **4a-c**.

One-pot Procedure for the Synthesis of Hydroxyester **4a.** To a solution of [Au(IPr)(CH₃CN)]SbF₆ (21.6 mg, 0.025 mmol, 5 mol%) and ferrocene (**2**, 370 mg, 2 mmol) in CH₂Cl₂ (5 mL) was slowly added over 1.5 h (via a syringe pump) a solution of ethyl 2-diazo-2-phenylacetate (**1a**, 95 mg, 0.5 mmol) in CH₂Cl₂ (2 mL). After the addition was complete, the resulting mixture was stirred at room temperature for an additional hour. Then, silica gel (8 g) was added and the resulting suspension was stirred at room temperature for a while and the solvent was evaporated under reduced pressure to dryness. The Schlenk flask was then charged with oxygen and allowed to stand at room temperature. After 24 h, CH₂Cl₂ was added (20 mL) and the silica gel was removed by filtration and the crude product was purified by flash chromatography (SiO₂, hexane/ethyl acetate 20:1) to afford α -ferrocenyl- α -hydroxyester derivative **4a** (95 mg, 52%).

General Procedure for the Synthesis of Ruthenocene Derivatives **6**.

To a solution of [Au(IPr)(CH₃CN)]SbF₆ (21.6 mg, 0.025 mmol, 5 mol%) and ruthenocene (**5**, 460 mg, 2 mmol) in DCE (5 mL) at 50 °C was slowly added over 2 h (via a syringe pump) a solution of the corresponding diazoacetate **1** (0.5 mmol) in DCE (2 mL). After the addition was complete, the resulting mixture was stirred at 50 °C for an additional hour. The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (SiO₂, hexane/ethyl acetate 40:1) to yield functionalized ruthenocene derivatives **6**.

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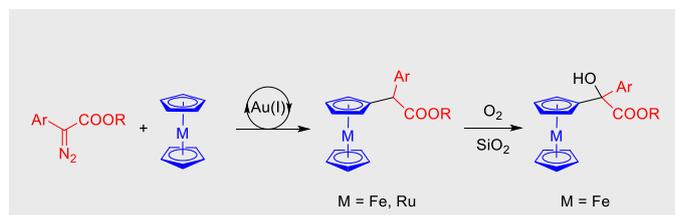
Keywords: metallocenes • gold • diazo compounds • oxidation • C-H activation

- [1] M. R. Fructos, T. R. Belderrain, P. de Fremont, N. M. Scott, S. P. Nolan, M. M. Díaz-Requejo, P. J. Pérez, *Angew. Chem.* **2005**, *117*, 5418; *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 5284.
- [2] For recent reviews: a) M. R. Fructos, M. M. Díaz-Requejo, P. J. Pérez, *Chem. Commun.* **2016**, *52*, 7326; b) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506; c) F. Wei, C. Song, Y. Ma, L. Zhou, C.-H. Tung, Z. Xu, *Sci. Bull.* **2015**, *60*, 1479; d) D. B. Huple, S. Ghorpade, R.-S. Liu, *Adv. Synth. Catal.* **2016**, *358*, 1348. For a recent contribution, see: e) S. B. Wagh, Y.-C. Hsu, R.-S. Liu, *ACS Catal.* **2016**, *6*, 7160.
- [3] I. Rivilla, P. Gómez-Emeterio, M. R. Fructos, M. M. Díaz-Requejo, P. J. Pérez, *Organometallics*, **2011**, *30*, 2855.

- [4] Z. Yu, B. Ma, M. Chen, H.-H. Wu, L. Liu, J. Zhang, *J. Am. Chem. Soc.* **2014**, *136*, 6904.
- [5] Y. Xi, Y. Su, Z. Yu, B. Dong, E. J. McClain, Y. Lan, X. Shi, *Angew. Chem.* **2014**, *126*, 9975; *Angew. Chem. Int. Ed.* **2014**, *53*, 9817.
- [6] For recent mechanistic studies on gold-catalyzed arene C-H bond functionalization involving formal carbene insertion, see: a) Y. Liu, Z. Yu, J. Z. Zhang, L. Liu, F. Xia, J. Zhang, *Chem. Sci.* **2016**, *7*, 1988; b) M. R. Fructos, M. Besora, A. A. C. Braga, M. M. Díaz-Requejo, F. Maseras, P. J. Pérez, *Organometallics*, **2017**, *36*, 172.
- [7] Selected revisions on properties and applications of ferrocene derivatives: a) S. S. Braga, A. M. S. Silva, *Organometallics*, **2013**, *32*, 5626; b) *Ferrocenes: Ligands, Materials and Biomolecules* (Ed.: P. Štěpnička) Wiley: Chichester, U.K., **2008**; c) *Ferrocenes*, (Eds.: A. Togni, T. Hayashi), VCH, Weinheim, **1995**; d) D. R. Van Staveren, N. Metzler-Nolte, *Chem. Rev.* **2004**, *104*, 5931; e) R. G. Arrayás, J. Adrio, J. C. Carretero, *Angew. Chem.* **2006**, *118*, 7836; *Angew. Chem. Int. Ed.* **2006**, *45*, 7674; f) *Chiral Ferrocenes in Asymmetric Catalysis*, (Eds.: L.-X. Dai, X.-L. Hou), Wiley-VCH, Weinheim, **2009**.
- [8] S. Siegel, H.-G. Schmalz, *Angew. Chem.* **1997**, *109*, 2569; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2456.
- [9] E. López, G. Lonzi, L. A. López, *Organometallics*, **2014**, *33*, 5924.
- [10] This regioselectivity pattern has been found in most gold-catalyzed transformations involving vinyl diazo compounds. For selected examples, see: a) V. V. Pagar, A. M. Jadhav, R.-S. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 20728; b) J. Barluenga, G. Lonzi, M. Tomás, L. A. López, *Chem. Eur. J.* **2013**, *19*, 1573; c) G. Lonzi, L. A. López, *Adv. Synth. Catal.* **2013**, *355*, 1948; d) J. F. Briones, H. M. L. Davies, *J. Am. Chem. Soc.* **2013**, *135*, 13314.
- [11] Very recently we have reported the gold-catalyzed reaction of ferrocene with propargylic esters leading functionalized ferrocene derivatives: E. López, T. Suárez, A. Ballesteros, L. A. López, *Eur. J. Inorg. Chem.* **2017**, DOI: 10.1002/ejic.201600836.
- [12] In most cases mixtures of ethyl fumarate and maleate were the only reaction products identified.
- [13] The copper-catalyzed reaction resulted in the formation of the alkene derivative resulting from the dimerization of the carbene ligand.
- [14] For related aerobic oxidations, see references [8] and [9].
- [15] CCDC numbers 1513625 (**3b**), 1513626 (**4b**) and 1513627 (**6b**), contain the supplementary crystallographic data for these structures. These data are provided free of charge by the Cambridge Crystallographic Data Centre.
- [16] For recent solid-state NMR studies on the behavior of adsorbed metallocenes on silica gel, see: a) K. J. Cluff, N. Bhuvanesh, J. Blümel, *Organometallics* **2014**, *33*, 2671; b) K. J. Cluff, M. Schnellbach, C. R. Hilliard, J. Blümel, *J. Organomet. Chem.* **2013**, *744*, 119.
- [17] K. J. Cluff, J. Blümel, *Chem. Eur. J.* **2016**, *22*, 16562. For previous Mössbauer spectroscopic studies of ferrocene adsorbed on silica gel reporting the formation of ferrocenium ions, see: H. Sato, *Hyperfine Interact.* **1990**, *57*, 2089.
- [18] This electron transfer/deprotonation sequence has been proposed for the C-H activation of benzylic C-H bonds in complexes of structure CpFe(arene) upon contact with air: D. Astruc, J.-R. Hamon, E. Román, P. Michaud, *J. Am. Chem. Soc.* **1981**, *103*, 7502.
- [19] Although at this stage the actual role of silica gel remains unclear, it could also stabilize some of the intermediates participating in the oxidation process. In this regard, the stabilization of the oxygen anion radical intermediate by coordination with an acid has been proposed to account for the dramatic acceleration effect of imidazolium ionic liquids on electron transfer reactions. D. S. Choi, D. H. Kim, U. S. Shin, R. R. Deshmukh, S. Lee, C. E. Song, *Chem. Commun.* **2007**, 3467.
- [20] For the oxidation behaviour of ruthenocene derivatives, see: a) M. G. Hill, W. M. Lamana, K. R. Mann, *Inorg. Chem.* **1991**, *30*, 4687; b) S. Trupia, A. Nafady, W. E. Geiger, *Inorg. Chem.* **2003**, *42*, 5480.

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FULL PAPER



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Gold-Catalyzed Intermolecular Formal Insertion of Aryldiazo Esters into Cp-H Bonds of Cp_2M ($\text{M} = \text{Fe, Ru}$)

The gold-catalyzed reaction of ferrocene and ruthenocene with aryldiazo compounds yielded functionalized metallocene derivatives resulting from a formal insertion of a gold carbene intermediate into the Cp-H bond. Whereas the ruthenium derivatives are quite stable, the iron analogues undergo an aerobic oxidation when adsorbed on silica gel and exposed to dioxygen. This Cp-H functionalization/aerobic oxidation sequence can be performed in a one-pot procedure.