

(NHC)M Cores as Catalysts for the Olefin Aziridination Reaction (M= Cu, Ag, Au): Evidencing a Concerted Mechanism for the Nitrene Transfer Process

Jorge Pérez-Ruíz, Pedro J. Pérez,* M. Mar Díaz-Requejo*

†Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química, Universidad de Huelva, 21007 Huelva, Spain.

KEYWORDS : N-Heterocyclic carbene, nitrene transfer, olefin aziridination, coinage metals

ABSTRACT: Complexes [(NHC)MCl] (M = coinage metal) have been evaluated as catalyst for the olefin aziridination reaction using PhI=NTs as nitrene source, with moderate to high activity being found depending of the metal and the olefin. At variance with frequently employed copper catalysts with bi-, tri- or tetradentate, N-donor ligands, these monodentate, C-donor ligand infer a remarkable effect in the reaction mechanism. Experimental evidences support the proposal of a concerted mechanism and the absence of radical intermediates, which are the commonly proposed species involved in these nitrene transfer reactions.

INTRODUCTION

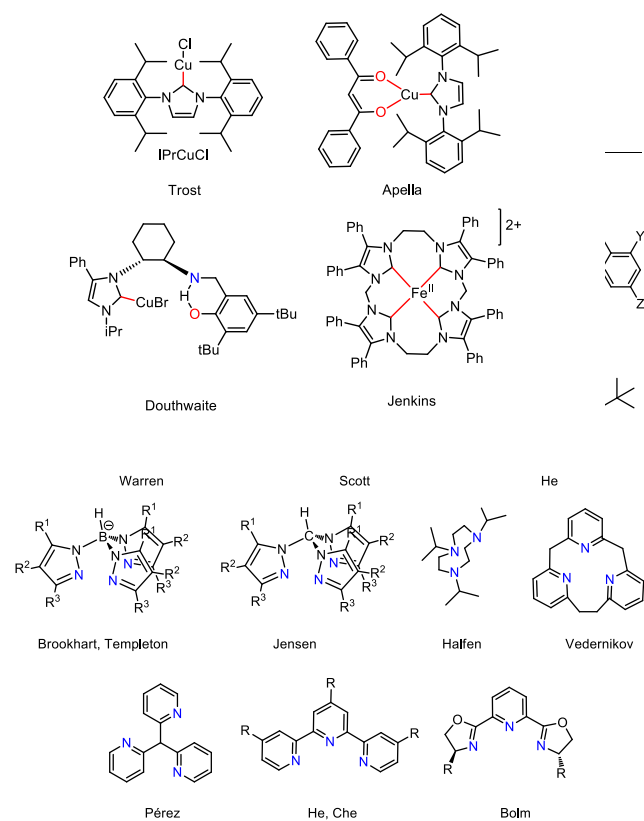
Since the seminal work by Kwart and Khan for a nitrogen atom transfer process using powdered copper and phenylsulfonyl azide,¹ the nitrene transfer reaction has become a fundamental tool for the construction of molecules with new C-N bonds.² A considerable number of catalytic systems based on transition metals from groups 7 to 11 have been described for the transfer of nitrenes to saturated and unsaturated substrates using azides or iminiodonanes, as nitrene sources. The most studied reaction is the olefin aziridination,³ and N-donor ligands are very frequently the ligand of choice. Groves described the first example with such N-containing ligands (Scheme 1), a porphyrin bound to manganese (TPP-Mn^V).⁴ Shortly after, Mansuy expanded such finding to Mn(III) and Fe(III),⁵ and later Zhang adapted the porphyrine ligand to cobalt.⁶

At the beginning of the 90s of the last century Evans introduced bisoxazoline-type ligands for the asymmetric aziridination of olefins (Scheme 1), thus opening the use of bidentate, N donor-based ligands in this chemistry.⁷ Other systems employing N-N ligands have been reported by Che,⁸ Jiao,⁹ Jacobsen,¹⁰ Warren,¹¹ Scott¹² or He.¹³

In 1993, Brookhart and Templeton introduced the use of hydrotrispyrazolylborate ligands (Tp^x), bonded to copper, as catalyst (Scheme 1) for the olefin aziridination reaction.¹⁴ After that finding, our group has developed several catalytic systems employing these N-donor tridentate ligands for nitrene transfer reactions.¹⁵ Other catalytic systems based on tridentate, N-based ligands have been described by Jensen,¹⁶ Pérez,¹⁷ Halfen,¹⁸ Verdenikov,¹⁹ He,²⁰ Che²¹ or Bolm.²²

At variance with the above polydentate, N-based ligands, the use of catalysts containing N-heterocyclic carbene ligands for the nitrene transfer reaction is quite limited (Scheme 2). Trost described the use of IPrCuCl for a step in

Scheme 2. Catalytic Systems for the Nitrene Transfer Reaction containing N-Heterocyclic Carbene Ligands

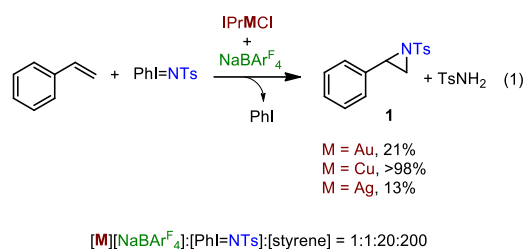


the total synthesis of agelastatin A.²³ Later, Apella reported²⁴ the catalytic activity of the tridentate complex IPrCu(DMB) for the aziridination of aliphatic olefins using

PhIO as oxidant. Douthwaite described the preparation of unstable copper complexes with NHC–phenoxyimine / amine ligands.²⁵ One last example has been reported by Jenkins with a macrocyclic tetracarbene iron complex [(TC)Fe(NCMe)₂](PF₆) using aryl azides as a nitrene source.²⁶ In view of this yet reduced knowledge about the use of [(NHC)M] cores for nitrene transfer and our previous experience with such catalysts for carbene transfer reactions,²⁷ we decided to study the catalytic behavior of a series of coinage metal (NHC)MCl complexes toward that end. We have not only found that the copper-containing complex displays a good catalytic activity for this transformation; in addition, we have collected evidence which allows proposing that this transformation takes place in a concerted manner, without the participation of relevant radical intermediates, at variance with many examples in the literature which are based on such intermediates.

RESULTS AND DISCUSSION

Study of the catalytic activity of the (NHC)MCl system. In 2005, our group discovered the catalytic potential of the IPrAuCl complex for the transfer of carbene groups to unsaturated substrates using ethyl diazoacetate as the carbene source. The catalytically active species is a cationic metallocarbene [IPrAu=C(H)CO₂Et]⁺.²⁸ Given the lack of



nitrene transfer reactions using [(NHC)Au] cores as catalysts, we decided to start our study using the IPrAuCl complex in the presence of NaBARF₄ as halide scavenger. We selected styrene as the model substrate and PhI=NTs as a nitrene source for this reaction (eq 1). Following standard procedures (see Experimental), aziridine **1** was detected in 21% yield at the end of the reaction. We then moved onto the copper analog, IPrCuCl, previously employed by Trost²³ albeit under large excess of oxidant. Under the same conditions shown in eq 1, quantitative yield (based on PhI=NTs) into **1** was measured. To complete the triad, the experiment carried out employing the silver IPrAgCl led to 13% yield of the aziridine, showing the better performance of copper for this transformation.

The role of the counterion derived from the halide scavenger was found relevant in our previous studies²⁹ with carbene transfer reactions, as the result of the effect of the ionic pair in the electrophilicity of the intermediates. Therefore, we run a series of experiments employing AgOTf, AgBF₄, AgSbF₆ and the already checked NaBARF₄. Yields varied from 80 to >98% (Figure 1). Interestingly, the experiment carried out in the absence of halide scavenger led to 90% yield into **1**, evidencing chloride decoordination equilibrium in solution.²⁷

To investigate further in this regard, we run several experiments with and without added halide scavenger with the more reactive copper-based catalyst. Figure 2 shows the results obtained, which are significantly different for both situations. In the absence of NaBARF₄, moving from 20 to 50 and 100 equiv of styrene led to yield values of aziridine **1** of 49, 68 and 84%. On the other hand, experiments carried out with one equiv of NaBARF₄ relative to copper and 20 or 100 equiv of styrene gave very similar outcomes (78 and 82%).

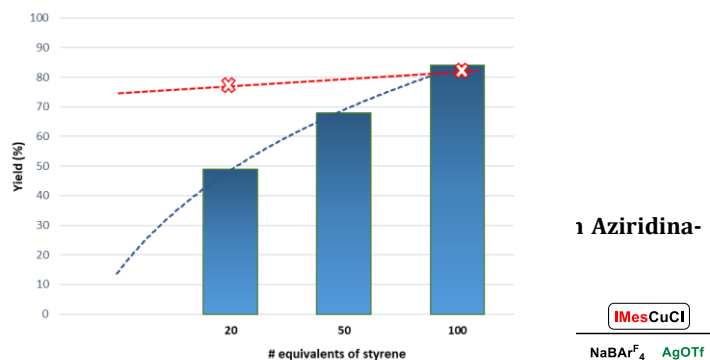


Figure 2. Effect of olefin concentration in styrene aziridination catalyzed by IPrCuCl in the absence of halide scavenger (bars) and in the presence (cross).

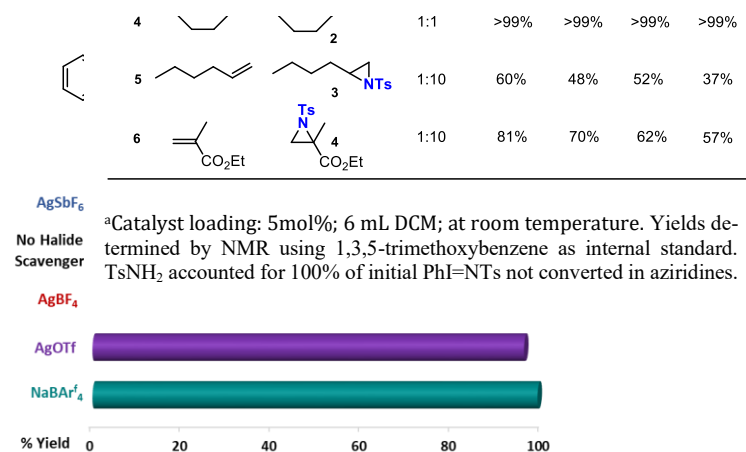


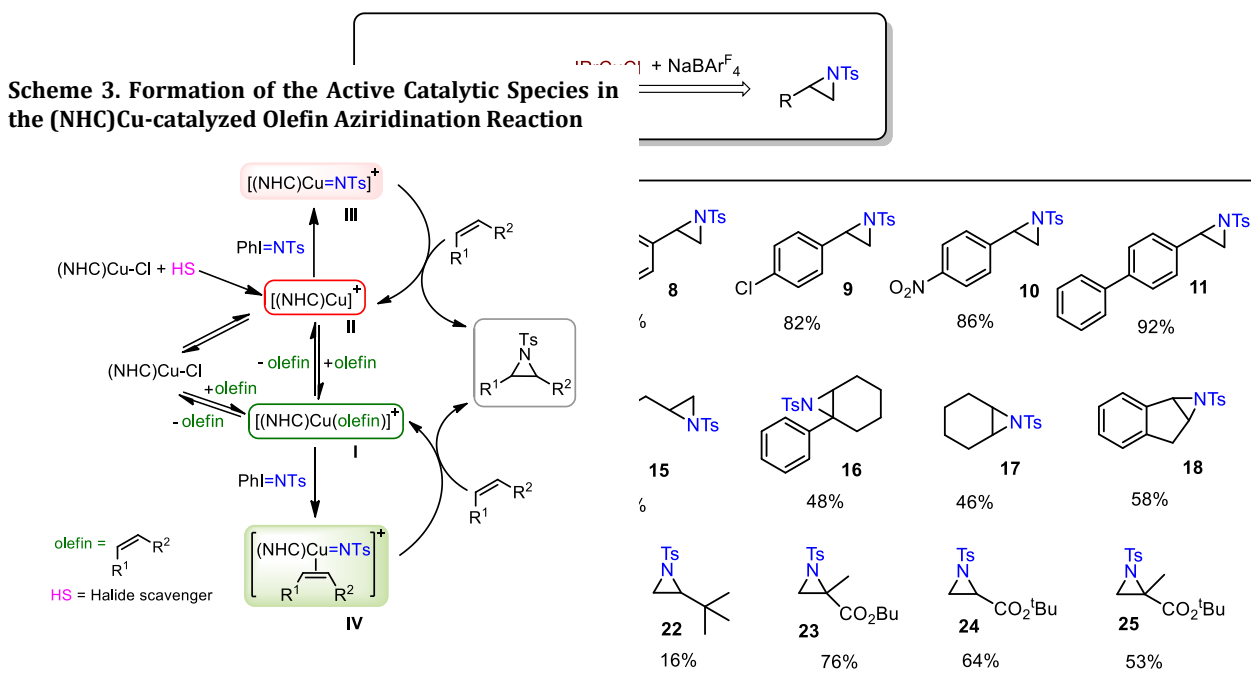
Figure 1. Halide scavenger screening for the nitrene transfer reaction to styrene using IPrCuCl as precatalyst.

Scheme 3 shows a mechanistic view accounting for these observations. With no halide scavenger added, a chloride decoordination / olefin coordination equilibrium takes place. The nitrene precursor may interact either with the olefin adduct **I** or with a coordinatively unsaturated species **II** generating copper-nitrenes intermediates **III** and/or **IV**, from which aziridine is formed via inner or outer sphere steps. It is worth mentioning that PhI=NTs decomposes with time giving TsNH₂, and therefore the lower the amount of active copper in solution, the higher the amount of TsNH₂.

The NHC ligand coordinated to the metal center is another variable that may affect the catalytic process. Table 1

than those found with cyclopentene (**19**). An activated cyclopentene led to higher yield (**18**).

Scheme 4. Scope of the aziridination reaction using [IPrCuCl/NaBAR^F₄] as catalyst.^a



^aReaction conditions: [Cat]/[PhI=NTs]/[olefin] = 1:20:200, r.t., DCM, 3h. Yields determined by NMR using 1,3,5-trimethoxybenzene as internal standard. TsNH₂ accounted for 100% of initial PhI=NTs not converted in aziridine.

shows the results employing IMesCuCl and IPrCuCl, using NaBAR^F₄ and AgOTf as halide scavenger, and with a set of representative olefins. The IPrCuCl/NaBAR^F₄ couple displays the best results with the four olefins with yields ranging from quantitative to the moderate 60% observed with n-hexane as the substrate. It is noteworthy that copper-based catalyst provides very high yields of aziridines **1** and **2** employing stoichiometric mixture of the olefin and PhI=NTs avoiding the need of excess of the former. The use of the silver- and gold-based catalysts with these olefins provided very low yield in all cases (5-22%).

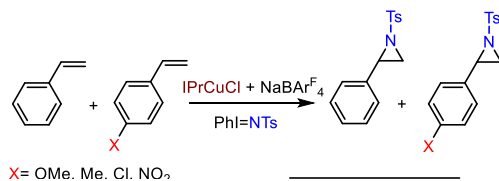
Scope of the aziridination reaction with IPrCuCl as pre-catalyst. Given the high activity of the copper-based system with the representative olefins shown above, we decided to extend the scope of the reaction to wider set of olefins. The results are shown in Scheme 4, with yields being from moderate to high. In a first group bearing an aryl group bonded directly to the double bond, the yields are very high regardless of the nature of the substituent on the ring, or the position on it (**5-12**). In the case of 1,1-disubstituted olefins, the activity is also very high (**13, 14**). With allylbenzene as the substrate, yield reached 42% (**15**). No allylic C-H functionalization was observed,³⁰ TsNH₂ accounting for 100% of initial PhI=NTs not converted into aziridine.

For the cyclic olefins aziridine yields were moderate, except in the case of *cis*-cyclooctene where the aziridine **2** is obtained quantitatively. In the case of two C₆ cyclic olefin (**16** and **17**), the yields were quite similar (46-48%) and higher

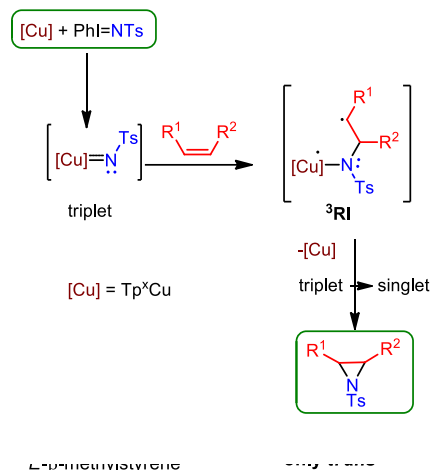
Next, we chose linear dienes leading to yields around 70% (**20, 21**). The use of excess of olefin precludes the double aziridination, in order to compare the results with the other olefins. In the case of the 3,3-dimethylbut-1-ene, only 16% of aziridine **22** was obtained. Although steric factors could be argued to explain for that, we cannot provide evidences toward that end.

Olefins with carboxylate substituents have also been evaluated. Despite the deactivated nature of these olefins, yields between 53%-81% were obtained depending on the substituent on the carboxylate group (**4, 23-25**), as evidence of the high activity of this catalytic system.

Scheme 6. Competition Experiments with *p*-substituted Styrenes



Scheme 5. Previous Mechanistic Pathways Proposed for Copper Catalysts with Polydentate N-donor Ligands



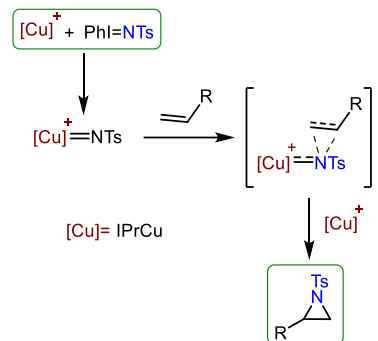
Mechanistic Considerations. Recently, our group has carried out an extensive study on the mechanism that governs the aziridination reaction of olefins catalyzed by Tp^xM complexes (M = Cu, Ag), based on experimental data and theoretical calculations.³¹ For the copper catalysts, the metallo-nitrene intermediates formed upon reaction with PhI=NTs (in the triplet state) reacts with the olefin leading to a radical intermediate ³RI (Scheme 5) before ring closing takes place, in a step-wise mechanism. The proposal was sustained by several experimental evidence: (a) data from competition experiments with *p*-substituted styrenes required a dual Hammett equation possessing both polar and radical factors; (b) the aziridination reaction of olefins with a defined stereochemistry (*Z* or *E*) took place in a non-stereospecific manner; and (c) the addition of radical traps such as BHT led to inhibition of the catalytic reaction, due to the interception of the radical intermediates. On these bases, we have now performed a series of experiments with the IPrCuCl/NaBARF₄ system to collect information toward a mechanistic explanation.

*Competition Experiments with *p*-Substituted Styrenes.* The relative rates of catalytic aziridination of a series of *p*-substituted styrenes using IPrCuCl/NaBARF₄ with PhINTs were determined through competition experiments. As shown in Scheme 6, the relative reactivity values can be adjusted with the general Hammett equation, with a $\rho = -0.45$ value. Two comments arise this finding. First, the negative value suggests an electrophilic intermediate accessed through a transition state which develops a certain positive charge, as in the olefin cyclopropanation reaction.^{14b} Second, the lack of radical contribution to the Hammett equation, which was

observed for copper with polydentate ligands,^{31,32} constitutes a significant difference for this catalyst containing a C-donor, monodentate ligand.

Use of olefins with well-defined stereochemistry. We have carried out experiments employing *Z*-2-pentene and *E*- β -methylstyrene, leading to the corresponding aziridines **26** and **27**, with complete retention of the initial stereochemistry. Albeit this result cannot rule out the formation of intermediate ³RI in Scheme 5, it is also in agreement with a plausible

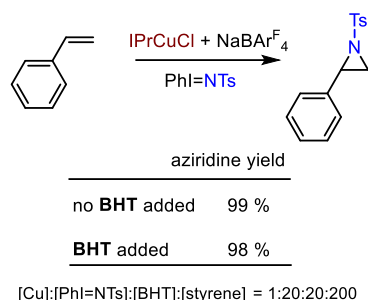
Scheme 9. Simplified mechanistic picture for the IPrCu-catalyzed nitrene transfer reaction.



concerted mechanism (see below).

Effect of the Presence of BHT as the Radical Inhibitor. To conclude, two experiments have been carried out for the aziridination of styrene catalyzed by IPrCuCl/NaBARF₄ that only differ in the presence or absence of *t*-butylhydroxytoluene (BHT) as a radical inhibitor. As seen in Scheme 8 the yields are almost identical with or without BHT. This is at variance with all previous work with Cu- or Ag-based catalysts bearing polydentate ligands, for which the addition of BHT substantially inhibited the reaction yields. This finding unambiguously indicates that no carboradical intermediates exist, at least with a life-time relevant to consider a stepwise mechanism.

Scheme 8. Effect of the Presence of BHT as the Radical Inhibitor.



Mechanistic picture. Based on the above evidences, it seems clear that this NHC-based copper catalytic system considerably differs from other copper-based systems with polydentate N-donor ligands.^{31,32} As shown in Scheme 9 the reaction of the IPrCu⁺ core with PhI=NTs would lead to a copper nitrene intermediate (very likely in its singlet state) which further reacts with the olefin similarly to an olefin cyclopropanation reaction, in a concerted but asynchronous manner, following early examples from Brookhart lab with iron carbenes.³³ This is consistent with the use of the general Hammett equation, and with the lack of changes in stereochemistry or effect of radical inhibitor in the reaction outcome.

CONCLUSIONS

We have explored the catalytic capabilities of (NHC)MCl complexes toward the olefin aziridination reaction using PhI=NTs as nitrene source. The catalytic activity is noteworthy for the copper derivative, and less efficient for silver and gold counterparts. Styrenes are efficiently converted into aziridines whereas alkyl-olefins or olefins with electron-withdrawing substituents led to moderate conversions. A mechanistic relevant conclusion is that this transformation occurs in a different manner to catalyst containing polydentate N-donor substituents. Instead of the radical-involving, stepwise mechanism, a concerted route, similar to that proposed for olefin cyclopropanation reactions is proposed based on experimental evidences. This significant change obtained when C-donor monodentate NHC ligand is employed opens a window in the field of the nitrene transfer reaction which will be expanded in the incoming years.

EXPERIMENTAL SECTION

General Methods. All air -and moisture- sensitive manipulations were carried out with standard Schlenk techniques under nitrogen atmosphere. Solvents were purchased from commercial sources, dried by distillation under nitrogen atmosphere using the suitable drying agent and deoxygenated immediately before their use. Reagents and the halide scavengers (except NaBARF₄) were acquired from commercial sources. The complexes (NHC)MCl (M= Cu, Ag, Au),³⁴ NaBARF₄,³⁵ and the nitrene precursor (PhI=NTs)³⁶ were prepared according to literature methods.

NMR spectra were recorded on the Agilent 400MR spectrometer as solutions at 298 K and Bruker Avance III HD 400 MHz spectrometer at ambient temperature. Chemical

shifts (δ) were referenced to internal solvent resonances and reported relative to TMS (tetramethylsilane) for ¹H and ¹³C NMR.

General catalytic experiment. In a Schlenk tube, under inert atmosphere, the complex (NHC)MCl (0.01 mmol) and the halide scavenger (0.01 mmol) were dissolved in deoxygenated DCM (6 mL) before the olefin was added (2 mmol). Then PhI=NTs (0.2 mmol) was added in one portion, and the mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the reaction crude was filtered using celite. The residue was analyzed by NMR spectroscopy, and products were identified by comparison with the values reported in the literature.³⁷ Yields were determined by NMR using 1,3,5-trimethoxybenzene as internal standard. TsNH₂ accounted for 100% of initial PhI=NTs not converted in aziridine.

Aziridination Competition Experiments. These experiments were carried out by following the above procedure, using an equimolar mixture of styrene and the corresponding *para*-substituted styrene. The relative ratio of aziridines was obtained by ¹H NMR spectroscopy of the reaction crude in CDCl₃.

Effect of radical inhibitor. This catalytic reaction was carried out in an identical manner to that described above, with the addition of 20 equiv. (with respect to the catalyst) of *t*-butylhydroxytoluene (BHT) to the reaction mixture, and using IPrCuCl/NaBARF₄ as the precatalyst.

ASSOCIATED CONTENT

Supporting Information.

Experimental details and spectroscopic data showing identifications and quantification of products. This material is available free of charge via the Internet at <http://pubs.acs.org>

AUTHOR INFORMATION

Corresponding Author

M. Mar Díaz-Requejo

Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química, Universidad de Huelva, 21007 Huelva, Spain.

E-mail: mmdiaz@dqcm.uhu.es

Orcid: 0000-0001-8295-4059

Pedro J. Pérez

Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química, Universidad de Huelva, 21007 Huelva, Spain.

E-mail: perez@dqcm.uhu.es

Orcid: 0000-0002-6899-4641

Author

Jorge Pérez-Ruíz

Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química, Universidad de Huelva, 21007 Huelva, Spain.

SI

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank to Ministerio de Ciencia e Innovación for Grant PID2020-113797RB-C21, also financed by FEDER “Una manera de hacer Europa”. We also thank Junta de Andalucía (P20-00348) and Universidad de Huelva (P.O.Feder UHU-202016). JPR thanks Fondo de Garantía Juvenil for a research contract.

REFERENCES

- (1) Kwart, H.; Khan, A. A. Copper-Catalyzed Decomposition of Benzenesulfonyl Azide in Cyclohexene Solution. *J. Am. Chem. Soc.* **1967**, *89*, 1950-1951.
- (2) (a) Dequirez, G.; Pons, V.; Dauban, P. Nitrene Chemistry in Organic Synthesis: Still in Its Infancy?. *Angew. Chem Int. Ed.* **2012**, *51*, 7384-7395. (b) Chang, J. W. W.; Ton, T. M. U.; Chan, P. W. H. Transition-metal-catalyzed aminations and aziridinations of C-H and C=C bonds with iminoiodinanes. *Chem. Rev.* **2011**, *11*, 331-357. (c) Díaz-Requejo, M. M.; Caballero A.; Fructos, M. R.; Pérez, P. J. Alkane C-H Activation by Single-Site Metal Catalysis, Springer, Amsterdam, **2012**, Chap. 6. (d) Zalatan, D. N.; Du Bois, J. Metal-catalyzed oxidations of C-H to C-N bonds. *Top. Curr. Chem.* **2010**, *292*, 347-378.
- (3) (a) Sweeney, J. B. Aziridines: epoxides' ugly cousins? *Chem. Soc. Rev.* **2002**, *31*, 247-258. (b) Padwa, A.; Murphee, S. S.; Gribble, G.W., Gilchrist, T. L. Progress in Heterocyclic Chemistry. *Elsevier Science: Oxford*, U.K., **2000**; Vol. 12, p 57. (c) Pearson, W. H.; Lian, B. W.; Bergmeier, S. C.; Padwa, A. Comprehensive Heterocyclic Chemistry II. *Ed.; Pergamon Press: Oxford*, U.K., **1996**; Vol. 1A, p 1. (d) Rai, K. M. L.; Hassner, A.; Padwa, A. Comprehensive Heterocyclic Chemistry II. *Ed.; Pergamon Press: Oxford*, U.K., **1996**; Vol. 1A, p 61. (e) Tanner, D. Chiral Aziridines-Their Synthesis and Use in Stereoselective Transformations. *Angew. Chem., Int. Ed.* **1994**, *35*, 599-619. (f) Degennaro, L.; Trinchera, P.; Luisi, R. Recent Advances in the Stereoselective Synthesis of Aziridines. *Recent Chem. Rev.* **2014**, *114*, 7881-7929.
- (4) Groves, J. T.; Takahashi, T. Aliphatic hydroxylation catalyzed by iron porphyrin complexes. *J. Am. Chem. Soc.* **1983**, *105*, 6243-6248.
- (5) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. Iron- and manganese-porphyrin catalyzed aziridination of alkenes by tosyl- and acyl-iminoiodobenzene. *J. Chem. Soc., Chem. Commun.* **1984**, 1161-1163.
- (6) (a) Gao, G. Y.; Harden, J. D.; Zhang, X. P. Cobalt-Catalyzed Efficient Aziridination of Alkenes. *Org. Lett.* **2005**, *7*, 3191-3193. (b) Riart-Ferrer, X.; Sang, P.; Tao, J. R.; Xu, H.; Jin, L. M.; Lu, H. J.; Cui, X.; Wojtas, L.; Zhang, X. P. Metalloradical activation of carbonyl azides for enantioselective radical aziridination. *Chem* **2021**, *7*, 1120-1134.
- (7) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. A method for rhodium(II)-catalyzed aziridination of olefins. *J. Am. Chem. Soc.* **1993**, *115*, 5326-5327.
- (8) Kwong, H. L.; Liu, D.; Chan, K. Y.; Lee, C. S.; Huang, K. H.; Che, C. M. Copper(I)-catalyzed asymmetric alkene aziridination mediated by PhI(OAc)₂: A facile one-pot procedure. *Tetrahedron Lett.* **2004**, *45*, 3965-3968.
- (9) Xu, J.; Ma, L.; Jiao, P. Asymmetric aziridination of chalcones catalyzed by a novel backbone 1,8-bisoxazolinylanthracene (AnBOX)-copper complex. *Chem. Commun.* **2004**, 1616-1617.
- (10) Li, Z.; Conser, K. R.; Jacobsen, E. N. Iron(II)-Catalyzed Inter-molecular Amino-Oxygenation of Olefins through the N-O Bond Cleavage of Functionalized Hydroxylamines. *J. Am. Chem. Soc.* **1993**, *115*, 5326-5327.
- (11) Amisial, L. D.; Dai, X.; Kinney, R. A.; Krishnaswamy, A.; Warren, T. H. Cu(I) beta-diketiminates for alkene aziridination: reversible Cu-arene binding and catalytic nitrene transfer from PhI=NTs. *Inorg. Chem.* **2004**, *43*, 6537-6539.
- (12) Gillespie, K. M.; Sanders, C. J.; O'Shaughnessy, P.; Westmoreland, I.; Thickitt, C. P.; Scott, P. Enantioselective Aziridination Using Copper Complexes of Biaryl Schiff Bases. *J. Org. Chem.* **2002**, *67*, 3450-3458.
- (13) Li, Z.; Ding, X.; He, C. Nitrene Transfer Reactions Catalyzed by Gold Complexes. *J. Org. Chem.* **2006**, *71*, 5876-5880.
- (14) (a) Pérez, P. J.; Brookhart, M.; Templeton, J. L. A copper(I) catalyst for carbene and nitrene transfer to form cyclopropanes, cyclopropenes, and aziridines. *Organometallics* **1993**, *12*, 261-262. (b) Díaz-Requejo, M. M.; Pérez, P. J.; Brookhart, M.; Templeton, J. L. Substituent Effects on the Reaction Rates of Copper-Catalyzed Cyclopropanation and Aziridination of para-Substituent Styrenes. *Organometallics* **1997**, *16*, 4399-4402.
- (15) (a) Mairena, M. A.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. Copper-Homoscorpionate Complexes as Very Active Catalyst for the Olefin Aziridination Reaction. *Organometallics* **2004**, *23*, 253-256 (b) Llaveria, J.; Beltrán, A.; Díaz-Requejo, M. M.; Matheu, M. I.; Castellón, S.; Pérez, P. J. Efficient Silver-Catalyzed Regio- and Stereospecific Aziridination of Dienes. *Angew. Chem. Int. Ed.* **2010**, *49*, 7092-7095. (c) Beltrán, Á.; Llaveria, J.; Locati, A.; Matheu, M. I.; Sameera, W. M. C.; Maseras, F.; Díaz-Requejo, M. M.; Castellón, S.; Pérez, P. J. Chemo-, Regio-, and Stereoselective Silver-Catalyzed Aziridination of Dienes: Scope, Mechanistic Studies, and Ring-Opening Reactions. *J. Am. Chem. Soc.* **2014**, *136*, 5342-5350. (d) Rodríguez, M. R.; Beltrán, Á.; Mudarra, A. L.; Álvarez, E.; Maseras, F.; Díaz-Requejo, M. M.; Pérez, P. J. Catalytic Nitrene Transfer to Alkynes: A Novel and Versatile Route for the Synthesis of Sulfinamides and Isothiazoles. *Angew. Chem. Int. Ed.* **2017**, *56*, 12842-12847.
- (16) Liang, S.; Jensen, M. P. Half-Sandwich Scorpionates as Nitrene Transfer Catalysts. *Organometallics* **2012**, *31*, 8055-8058.

- (17) Pérez, J.; Morales, D.; García-Escudero, L. A.; Martínez-García, H.; Miguel, D.; Bernard, P. Synthesis of new copper(I) complexes with tris(2-pyridyl) ligands. Applications to carbene and nitrene transfer reactions. *Dalton Trans* **2009**, 375-382.
- (18) (a) Halfen, J. A.; Hallman, J. K.; Schultz, J. A.; Emerson, J. P. Remarkably efficient olefin aziridination mediated by a new copper (II) complex. *Organometallics* **1999**, *18*, 5435-5437. (b) Halfen, J. A.; Fox, D. C.; Mehn, M. P.; Que, L. Enhanced reactivity of copper catalyst for olefin aziridination by manipulation of ligand denticity. *J. Inorg. Chem.* **2001**, *40*, 5060-5061.
- (19) Vedernikov, A. N.; Caulton, K. G. Facile Alkane Functionalization in Copper-[2.1.1]-(2,6)-pyridinophane-PhINTs Systems. *Org. Lett.* **2003**, *5*, 2591-2594.
- (20) Cui, Y.; He, C. Efficient Aziridination of Olefins Catalyzed by a Unique Didilver(I) Compound. *J. Am. Chem. Soc.* **2003**, *125*, 16202-16203.
- (21) Liu, P.; Wong, E. L. M.; Yuen, A. W. H.; Che, C. M. Highly efficient alkene epoxidation and aziridination catalyzed by iron (II) salt + 4,4',4''-trichloro-2,2':6',2''-terpyridine/4,4''-dichloro-4'-O-PEG-OCH₃-2,2':6',2''-terpyridine. *Org. Lett.* **2008**, *10*, 3275-3278.
- (22) Nakanishi, M.; Salit, A. F.; Bolm, C. Iron-catalyzed aziridination reactions. *Adv. Synth. Catal.* **200**, *8*, 350, 1835-1840.
- (23) Trost, B. M.; Dong, G. B. Total Synthesis of Agelastin A. *J. Am. Chem. Soc.* **2006**, *128*, 6054-6055.
- (24) Xu, Q.; Apella, D. H. Aziridination of Aliphatic Alkenes Catalyzed by N-Heterocyclic Carbene Copper Complexes. *Org. Lett.* **2008**, *10*, 7,1497-1500.
- (25) Simonovic, S.; Whitwood, A. C.; Clegg, W.; Harrington, R. W.; Hursthouse, M. B.; Male, L.; Douthwaite, R. E. Investigation of the Role of Electrogenerated N-Heterocyclic Carbene in the Staudinger Synthesis in Ionic Liquid. *Eur. J. Inorg. Chem.* **2009**, 1786-1795.
- (26) (a) Cramer, S. A.; Jenkins, D. M. Synthesis of aziridines from alkenes and aryl azides with reusable macrocyclic tetracarbene iron catalyst. *J. Am. Chem. Soc.* **2011**, *133*, 19342-19345. (b) Isbill, S. B.; Chandrachud, P. mP.; Kern, J. L.; Jenkins, D. M.; Roy, S. Elucidation of the Reaction Mechanism of C2 + N1 Aziridination from Tetracarbene Iron Catalysts. *ACS Catal.* **2019**, *9*, 6223-6233.
- (27) Fructos, M. R.; Belderrain, T. R.; de Fremont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. A Gold Catalyst for Carbene-Transfer Reactions from Ethyl Diazoacetate. *Angew. Chem., Int. Ed.* **2005**, *44*, 5284-5288.
- (28) Fructos, M. R.; Besora, M.; Braga, A. A. C.; Díaz-Requejo, M. M.; Maseras, F.; Pérez, P. J. Mechanistic Studies on Gold-Catalyzed Direct Arene C-H Bond Functionalization by Carbene Insertion: The Coinage-Metal Effect. *Organometallics* **2017**, *36*, 172-179.
- (29) Fructos, M. R.; de Fremont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. Alkane Carbon-Hydrogen Bond Functionalization with (NHC)MCl Precatalysts (M = Cu, Au; NHC = N-Heterocyclic Carbene). *Organometallics* **2006**, *25*, 2237-2241.
- (30) (a) Fructos, M. R.; Trofimenko, S.; Díaz-Requejo, M. M.; Pérez, P. J. Facile Amine Formation by Intermolecular Catalytic Amidation of Carbon-Hydrogen Bonds. *J. Am. Chem. Soc.* **2006**, *128*, 11784-11791. (b) Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. Cyclohexane and Benzene Amidation by Catalytic Nitrene Insertion into C-H Bonds with the Copper-Homoscorpionate Catalyst Tp^{Br}3Cu(NCMe). *J. Am. Chem. Soc.* **2003**, *125*, 12078-12079.
- (31) Maestre, L.; Sameera, W. M. C.; Díaz-Requejo, M. M.; Maseras, F.; Pérez, P. J. A General Mechanism for the Copper and Silver-Catalyzed Olefin Aziridination Reactions: Concomitant Involvement of the Singlet and Triplet Pathways. *J. Am. Chem. Soc.* **2013**, *135*, 1338-1348.
- (32) Bagchi, V.; Paraskevopoulou, P.; Das, P.; Chi, L.; Wang, Q.; Choudhury, A.; Mathieson, J. S.; Cronin, L.; Pardue, D. B.; Cundari, T. R.; Mitrikas, G.; Sanakis, Y.; Stavropoulos, P. A Versatile Tripodal Cu(I) Reagent for C-N Bond Construction Via Nitrene-Transfer Chemistry: Catalytic Perspectives and Mechanistic Insights on C-H Aminations/Amidations and Olefin Aziridinations. *J. Am. Chem. Soc.* **2014**, *136*, 11362-11381.
- (33) Brookhart, M.; Studabaker, W. B. Cyclopropanes from Reactions of Transition-Metal-Carbene Complexes with Olefins. *Chem. Rev.* **1987**, *87*, 411-432.
- (34) Fructos, M. R.; Belderrain, T. R.; Nicasio, M. C.; Nolan, S. P.; Kaur, H.; Díaz-Requejo, M. M.; Pérez, P. J. Complete Control of the Chemoselectivity in Catalytic Carbene Transfer Reactions from Ethyl Diazoacetate: An N-Heterocyclic Carbene-Cu System That Suppresses Diazo Coupling. *J. Am. Soc. Chem.* **2004**, *126*, 10846-10847.
- (35) Brookhart, M.; Grant, B.; Volpe, Jr. A. F. [(3,5-(CF₃)₂C₆H₃)₄B]-[H(OEt₂)₂]⁺: a convenient reagent for generation and stabilization of cationic, highly electrophilic organometallic complexes. *Organometallics* **1992**, *11*, 3920-3922.
- (36) Yamada, Y.; Yamamoto, T.; Okawara, M. Synthesis and Reaction of New Type I-N Ylide, N-Tosyliminoiodinane. *Chem. Lett.* **1975**, 361-362.
- (37) See SI for a complete list of references for each aziridine.

FOR THE TABLE OF CONTENT ONLY

