Intermolecular Allene Functionalization by Silver-Nitrene Catalysis

Manuel R. Rodríguez,[a] María Besora,[b,c] Francisco Molina,[a] Feliu Maseras,[b,d,*] M. Mar Díaz-Requejo,[a,*] and Pedro J. Pérez[a,*]

[a]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

[b]Institute of Chemical Research of Catalonia, ICIQ, Av. Països Catalans, 16, Barcelona Institut of Science and Technology, 43007 Tarragona, Spain

[c]Departament de Química Física i Inorgànica, Universitat Rovira i Virgili, 43007 Tarragona, Spain

[d]Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

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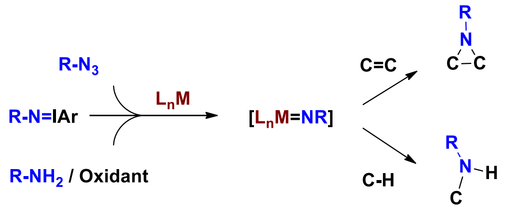
ABSTRACT: Under silver catalysis conditions, using $[Tp^{*,Br}Ag]_2$ as the catalyst precursor, allenes react with PhI=NTs in the first example of efficient metal-mediated intermolecular nitrene transfer to such substrates. The nature of the substituent at the allene seems crucial for the reaction outcome since arylallenes are converted into azetidine derivatives whereas methylene aziridines are the products resulting from alkylallenes. Mechanistic studies allow proposing that azetidines are formed through unstable cyclopropylimine intermediates which further incorporates a second nitrene group, both processes being silver-mediated. Methylene aziridines from alkylallenes derive from catalytic nitrene addition to the allene double bonds. Both routes have resulted productive for further synthetic transformations affording aminocyclopropanes.

INTRODUCTION

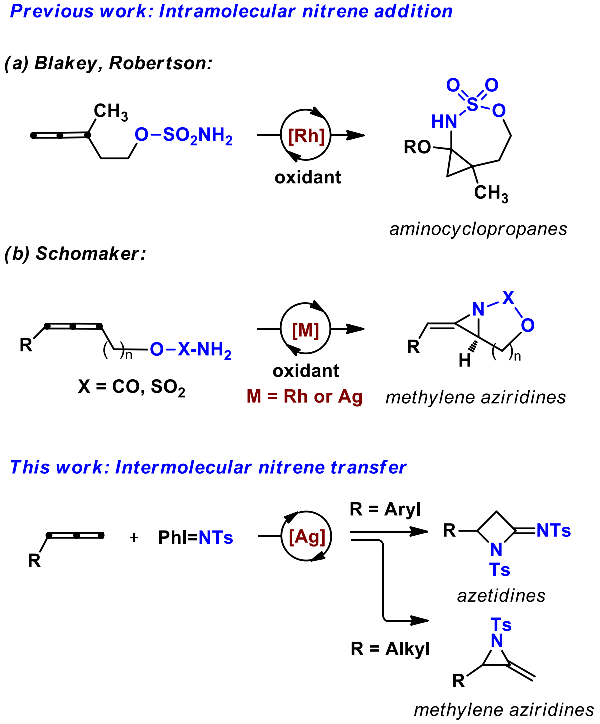
Among the catalytic methods developed in the last decades for the generation of carbon-nitrogen bonds, the metal-induced transfer of nitrene ligands to saturated or unsaturated substrates has emerged as a powerful tool toward that end.[1] The transient metallonitrene intermediates[2] are frequently generated in situ upon reaction of the metal catalyst with azide, iminoiodonane or a mixture of amine and an oxidant. In this manner, a number of compounds such as aziridines or amines, among others, both in inter- or intramolecular transformations, have been prepared (Scheme 1), as a consequence of the addition or insertion of the nitrene unit to C=C or C-H bonds, respectively.

Scheme 1. The metal-catalyzed nitrene transfer reaction.



Allenes have also been studied as substrates in this context, albeit to date metal-catalyzed examples are reduced to intramolecular processes.[3] Intermolecular transformations are only known for free nitrene processes, lacking of any chemo- or regiocontrol.[4] First examples of the former appeared in 2010 when Blakey[5] and Robertson[6] independently reported the rhodium-catalyzed amination of sulfamate-containing allenes leading to aminocyclopropanes (Scheme 2a), using $PhI(OR)_2$ as the oxidant. The use of allenyl carbamates instead of sulfamates provided, under similar reaction conditions and rhodium catalysis, methylene aziridines instead of aminocyclopropanes.[7] From those initial findings, the group of Schomaker[8] has propelled this allene functionalization chemistry, not only with rhodium but also with silver-based catalysts, leading to methylene aziridines *en route* to a number of derivatives (Scheme 2b). Inspired by these precedents, and the lack of intermolecular examples for allene functionalization with the nitrene transfer methodology, we have focused on such goal. Our group has investigated over the years the development of copper- and silver-based catalysts for the incorporation of nitrene units to organic substrates, either the addition to double[9] or triple[10] carbon-carbon bonds or the insertion into C-H bonds,[11] among others.[12] Herein we report the results obtained with allenes as the substrates and PhI=NTs (Ts = p-toluensulfonyl) as the nitrene source (Scheme 2), in the first effective catalytic system for the functionalization of such unsaturated molecules by metal-induced nitrene addition. Interestingly, we have found that the nature of the substituents of the allenes exerts a decisive control in the reaction outcome, leading to azetidines or methylene aziridines from aryl- and alkyl-substituted allenes, respectively. A mechanistic proposal is presented based on experimental data and computational calculations.

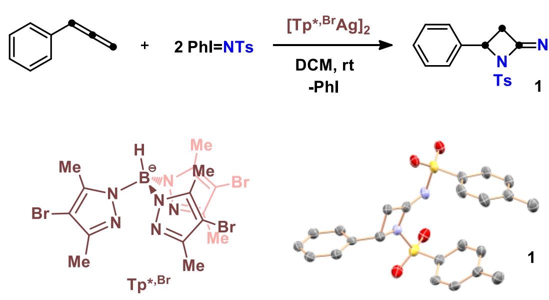
Scheme 2. Allene functionalization by metal-catalyzed nitrene transfer reactions.



RESULTS AND DISCUSSION

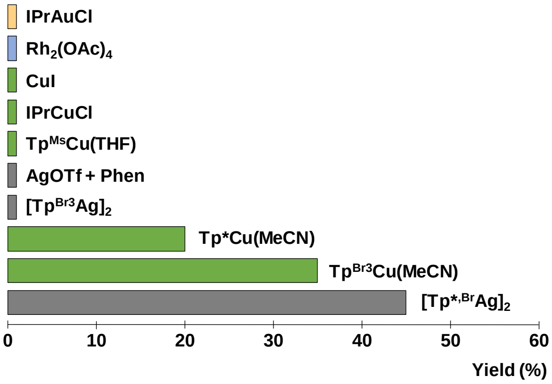
Functionalization of phenylallene: the probe reaction. We first studied the reaction of phenylallene with PhI=NTs in the presence of [Tp^{*,Br}Ag]$_2$ as catalyst, given the already described performance of this silver complex in intermolecular nitrene transfer processes.[9-11] When a 1:40:400 mixture of [Tp^{*,Br}Ag]$_2$:PhI=NTs:phenylallene (0.005 mmol of catalyst employed) was stirred at room temperature for 2 h in CH_2Cl_2, a smooth reaction took place as inferred from the gradual incorporation of insoluble PhI=NTs into the solution. After that time the volatiles were removed and the crude was investigated by NMR, showing deceptively simple spectra. The ^{1}H NMR spectrum contained (see SI), in addition to two inequivalent sets of resonances typical of the tosyl (toluensulfonyl) groups, an ABX spin system, corresponding to a $CH-CH_2$-unit, indicating a substantial modification of the initial 3H pattern in the starting allene substrate. Only when single crystals were grown the structure of this new compound **1** was identified by X-ray studies as that of (*E*)-4-methyl-N-(4-phenyl-1-tosylazetidin-2-ylidene)benzenesulfonamide, derived from the incorporation of two NTs groups to the allene molecule, which has undergone a shift of two H atoms from their initial location (Scheme 3). To our knowledge, there is no precedent of the formation of this type of compounds from allenes in the context of nitrene transfer.

Scheme 3. Azetidine formation from silver-catalyzed nitrene transfer to phenylallene.



After this finding, we performed a study toward catalyst screening, with phenylallene and PhI=NTs, employing several Cu-, Ag- and Au-complexes with Tp^x (hydrotrispyrazolyborate) or NHC (N-heterocyclic carbene) ligands, among others. Additionally, we also selected $Rh_2(OAc)_4$ in view of the previously described catalytic activity in the intramolecular nitrene transfer reactions to allenes.[5-8] The results are shown in Figure 1. Regarding copper-based catalysts, CuI and IPrCuCl revealed essentially no catalytic activity, with product being either not observed or within the detection limit by NMR. Similar behavior was observed with the Tp^{Ms}Cu(THF) catalyst, which was largely surpassed by complexes Tp*Cu(MeCN) and Tp^{Br3}Cu(MeCN), showing the Tp^{Ms} < Tp*< Tp^{Br3} activity trend. Since the order of electronic density at copper for the Tp^{x}Cu cores is Tp* < Tp^{Ms}< Tp^{Br3}, we interpret that (a) the steric pressure of the Tp^{Ms} ligand does not favor this transformation and (b) the more electron deficient metal centers favor the transformation. Also, gold- and rhodium-based catalysts turned out to be practically inactive for this transformation, unlike the excellent results obtained with the latter in the intramolecular transformations mentioned above. Finally, among the silver-based catalysts selected, the [Tp^{*,Br}Ag]$_2$ complex revealed

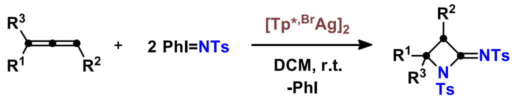
Figure 1. Catalyst screening for the nitrene transfer reaction onto phenylallene.

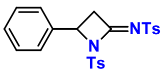
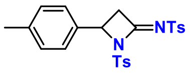
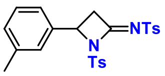
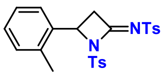
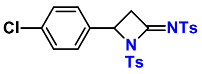
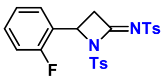
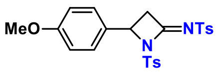
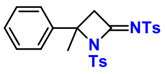
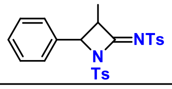


the best activity. The structure of this complex is dinuclear,[13] albeit in solution it equilibrates with mononuclear Tp^{*,Br}Ag units available for catalysis. The perbromo analog $[Tp^{Br3}Ag]_2$ was at variance inactive, in line with the behavior of both complexes in previous studies regarding alkane amidation reactions.[11c]

The use of solvents previously described in rhodium intramolecular allene functionalization such as ^{t}BuCN or isopropylacetate were not useful with our silver catalysts: the nitrile blocked the transformation, very likely due to coordination to the metal center, whereas the acetate only led to 18% yield.

Table 1. Scope of the reaction of PhI=NTs and aromatic allenes using $[Tp^{*,Br}Ag]_2$ as catalyst.[a]



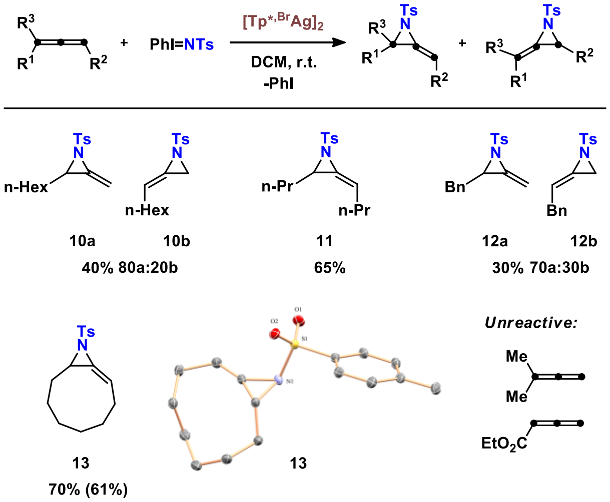
Ent.	R¹	R²	R³	Product		Yield[b]
1	Ph	H	H		1	45%[c]
2	*p*-Tol	H	H		2	55%
3	*m*-Tol	H	H		3	40%
4	*o*-Tol	H	H		4	30%
5	*p*-Cl-C_6H_4	H	H		5	36%[c]
6	*o*-F-C_6H_4	H	H		6	20%
7	*p*-Anisyl	H	H		7	16%
8	Ph	H	Me		8	5%[d]
9	Ph	Me	H		9	6%[d]

[a]Reactions carried out at room temperature with 0.005 mmol of catalyst, 40 equiv of PhI=NTs and 400 equiv of allene in 6 mL of CH_2Cl_2. Reaction time: 2 h. [b]Determined by NMR using 1,3,5-trimethoxybenzene as internal standard. $TsNH_2$ accounted for 100% of initial PhI=NTs not converted in azetidine. [c]Structure confirmed by X-ray studies (see SI). [d]Low yield precluded full characterization.

Scope of the reaction of allenes with PhI=NTs: substrate control of the selectivity. Under the optimized conditions (see SI for all variables studied), the scope of the reaction has been extended to different allenes, a first group bearing an aryl group located at C1. The results are displayed in Table 1. The presence of a Me substituent in the phenyl group led to the corresponding azetidines **2-4** (Table 1, entries 2-4), with yields following the trend *para> meta>ortho*, indicating some steric hindrance of such group in the reaction outcome. In the case of introducing an electron withdrawing substituent in the aryl ring, such as Cl- or F-, the yields in azetidines **5** and **6** were 36% and 20%, respectively (Table 2, entries 5-6). In line with this electronic effect, the OMe derivative was highly reactive, giving rise to a mixture of products where azetidine **7** was present only in 16% yield (Table 1, entry 7). 1,1-Disubstituted allenes were also screened but the expected azetidines were formed in very low yields. In all cases, except for the OMe derivative, the mass balance was completed with $TsNH_2$ formed from initial PhI=NTs.[14]

A second group of allenes investigated contains an alkyl substituent instead an aryl one (Scheme 4). Under the same reaction conditions, hexylallene showed a completely distinct behavior compared with the previous arylallenes. NMR studies of the reaction crude showed two sets of resonances which have been identified as the methylene aziridines **10a** and **10b** in 80:20 ratio respectively, and with a yield of 40% ($TsNH_2$ accounted for 100% initial PhI=NTs). Both compounds **10a** and **10b** result from the respective metal-induced addition of the nitrene unit NTs to the internal or terminal double bond, respectively.

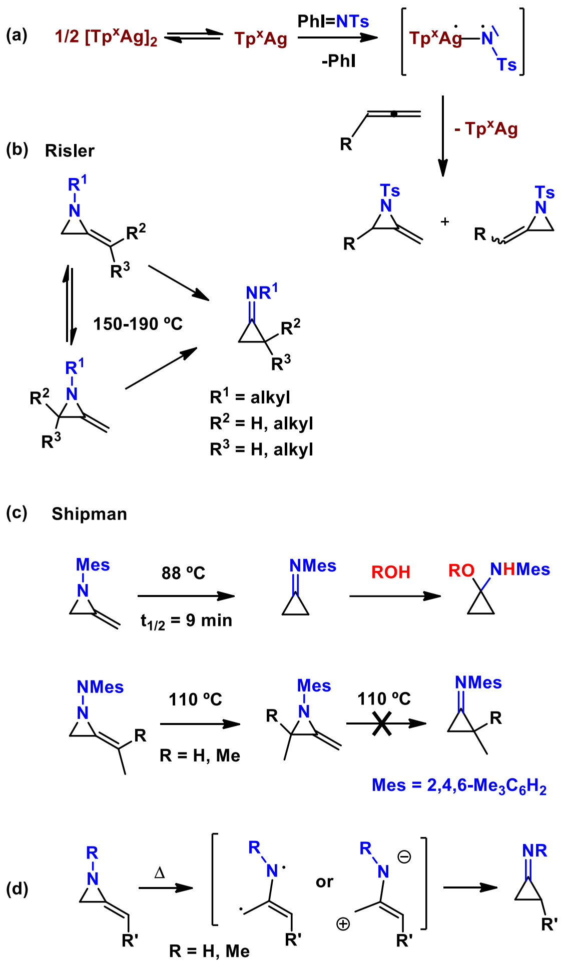
Scheme 4. Scope of the reaction of PhI=NTs and aliphatic allenes using [Tp*,BrAg]2 as catalyst.[a]



[a]Reactions carried out at room temperature with 0.005 mmol of catalyst, 40 equiv of PhI=NTs and 400 equiv of allene in 6 mL of CH2Cl2. Reaction times: 2-4 h. Yields determined by NMR using 1,3,5-trimethoxybenzene as internal standard. TsNH2 accounted for 100% of initial PhI=NTs not converted in methylene aziridine. Isolated yield in brackets.

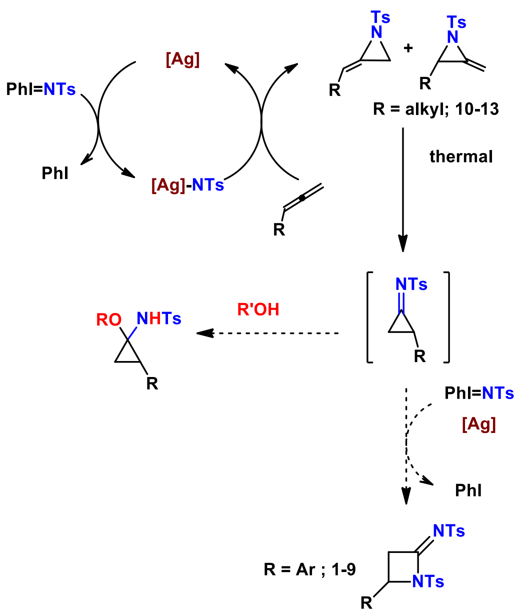
The substrate scope of this latter transformation was next examined with a series of aliphatic allenes (Scheme 4). Moderate to good yields (30-70%) were obtained for the array of substrates selected. Using a symmetric allene ($R^1 = R^2 = {}^n$Pr), the methylene aziridine **11** was obtained with a yield of 65%. The benzyl derivative was less reactive whereas the cyclic symmetrical cyclonone-1,2-diene led to the cyclic methylene aziridine **13**, for which single crystal were grown allowing the determination of the solid-state structure by X-ray studies (Scheme 4). However, disubstitution at C1 or substitution with an electron withdrawing group such as CO_2Et inhibited this transformation. These conversions of allenes into azetidines and methylene aziridines are the first examples of metal-catalyzed routes leading to such compounds in an intermolecular fashion.

Scheme 5. Mechanistic considerations.



Mechanistic precedents and proposal. Previous work from our group[9,15] with the Tp^xAg core (from dinuclear $[Tp^xAg]_2$)[13] in olefin aziridination reactions has shown that the process starts with the formation of a triplet nitrene Tp^xAg-NTs which further interacts with the olefin en route to the formation of the aziridine, in a stereoretentive transformation. In view of these precedents and the related work from the group of Schomaker,[3,8] it seems reasonable proposing the formation of a mixture of methylene aziridines as the result of the Ag-catalyzed transfer of the NTs group to both inequivalent C=C bonds in the allenes (Scheme 5a). These results are in agreement with the reaction outcome for alkyl-substituted allenes, either mono or disubstituted (Scheme 4), but not with that observed for arylallenes (Scheme 3), where azetidines have been generated. However, we must recall independent work by Risler[16] and Shipman[17] on the stability of methylene aziridines. Risler demonstrated that N-alkyl methylene aziridines thermally convert into cyclopropylimines at high temperatures (Scheme 5b). Also, isomerization of methylene aziridines occurs under the reaction conditions. Shipman later demonstrated that N-aryl methylene aziridines undergo such conversion at lower temperatures (Scheme 5c), but the presence of alkyl groups in the alkenyl fragment blocks the formation of the cyclopropylimine. The effect of the N-substituent and the C-substituent can be explained by the stabilization induced by R and R’ in the either diradical or zwiterionic nature of the intermediate (Scheme 5d).

Scheme 6. Plausible mechanistic proposal.



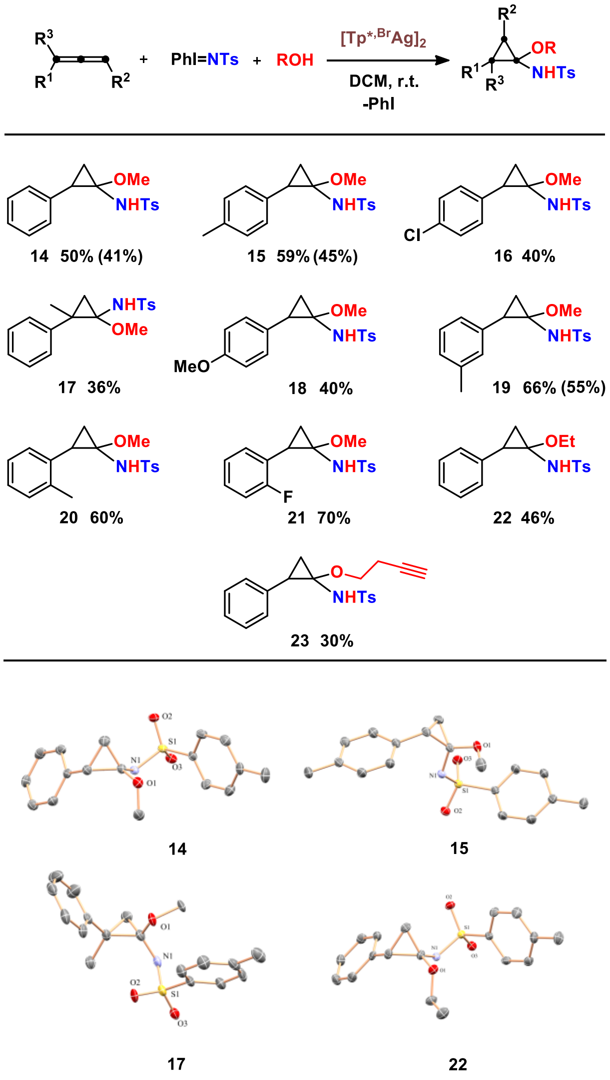
Based on the pieces of information available, we believe that Scheme 6 contains a reasonable initial, yet incomplete explanation of the reaction of allenes and PhI=NTs. In a first step, mixtures of methylene aziridines are formed similarly to already described olefin aziridination with this family of catalysts.[9,15] Those formed from alkylallenes should be stable at room temperature, according with literature precedents. However, the presence of aryl substituents, along with the Ts group located at nitrogen could favor the formation of cyclopropylimines in this case. Thus, such cyclopropylimines should be available at room temperature and trapping with nucleophiles such as alcohols could be observable (vide infra). Finally, the formation of the azetidines from arylallenes should be explained along a pathway involving cyclopropylimine intermediates and another NTs group transferred through the silver center.

Trapping of cyclopropylimines intermediates. Following the previous reasoning, we studied the reaction of 1-arylallenes with PhI=NTs, under the same conditions commented for the generation of azetidines (see Table 1) but using one equiv of an alcohol relative to the allene.

Azetidines were no longer observed, but the series of aminocyclopropanes **14-23** instead (Scheme 7).

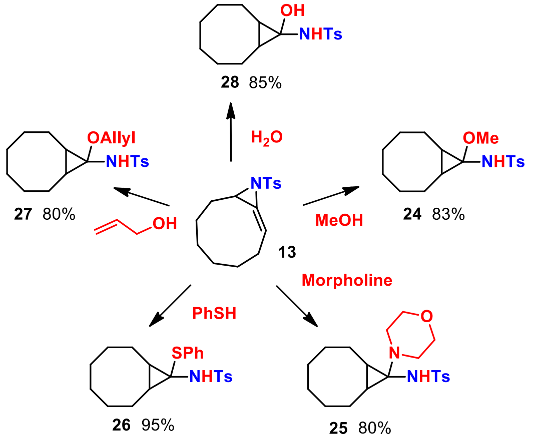
Substitution at aryl group as well as several alcohols such as methanol, ethanol or propargyl alcohol verified this transformation. On the contrary, phenol or 2-bromoethanol did not provide any conversion. The molecular structures of several aminocyclopropanes were determined by X-ray studies (Scheme 7), demonstrating that the aryl and amide groups occupy mutually *cis* positions in all cases except for the tetrasubstituted **17**. ^{1}H NMR data show nearly identical chemical shifts for the methylene protons of the cyclopropane rings, the only distinct pattern being observed for compound **17**.

Scheme 7. Direct Synthesis of Aminocyclopropanes from ArylAllenes.[a]



[a] Reactions carried out at room temperature with 0.005 mmol of catalyst, 40 equiv of PhI=NTs, 400 equiv of allene and 400 equiv the alcohol in 6 mL of CH$_2$Cl$_2$. Reaction times: 2 h. Yields determined by NMR using 1,3,5-trimethoxybenzene as internal standard. TsNH$_2$ accounted for 100% initial PhI=NTs not converted into products. Isolated yields in brackets. ORTEP plots (50% thermal ellipsoids) of the X-ray crystal structures of **14**, **15**, **17** and **22** are shown.

Scheme 8. Aminocyclopropanes from methylene aziridine 13.[a]



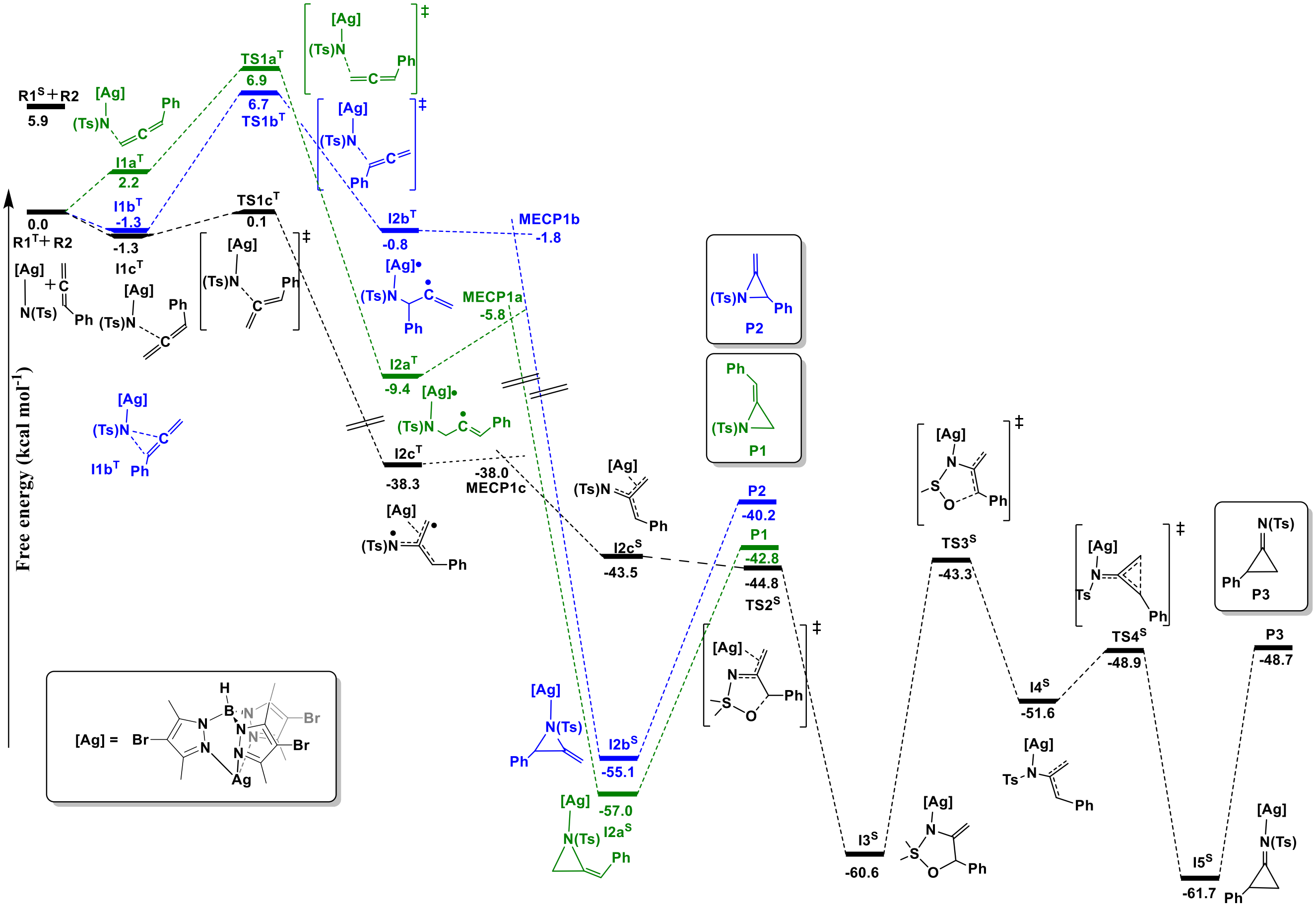
[a] Reactions carried out at 75 °C with 0.2 mmol of **13** and 10 equiv of nucleophile (except morpholine, 1.5 equiv) in 2 mL of MeCN. Reaction time: 2 h. Isolated yields.

When moving to alkylallenes, we first employed 1-hexylallene and cyclonone-1,2-diene as substrates, operating under the same reaction conditions than those leading to methylene aziridines, but in the presence of additional MeOH. NMR studies of the reaction mixtures carried out after PhI=NTs consumption revealed the formation of the methylene aziridines. It seems that at variance with the aryl system, *the methylene aziridines derived from alkylallenes do not suffer isomerization into cyclopropylimines at room temperature*. Taking advantage of the availability of methylene aziridine **13** as an isolated compound, we found that the corresponding aminocyclopropane **20** could be formed upon heating at 75 °C in the presence of methanol. Several nucleophiles (Scheme 8) such as alcohols, water, sulfides and amines could be incorporated into the aminocyclopropanes **24-28** in very good yields (80-95%).

We interpret the formation of aminocyclopropanes **14-28** as an evidence of the formation of cyclopropylimines from the methylene aziridine precursors. Data collected at this stage supports the proposal in Scheme 6 that the methylene aziridines from arylallenes are not stable at room temperature and convert into cyclopropylimines whereas when using alkylallenes the methylene aziridines are stable at room temperature and require heating to induce cyclopropylimine formation.

DFT studies. We first analyze computationally the reaction of arylallene and alkylallene and PhI=NTs induced by the silver catalyst Tp^{*,Br}Ag. Calculations presented in this section are done with the B3LYP-D3 functional including dichloromethane solvent effects through a continuum model. We have previously used a similar methodology with this type of catalysts achieving good results.[18] All reported energies correspond to Gibbs free energies in kcal mol^{-1}. Further data on the method for the calculations are supplied in the Computational Details.

Scheme 9. Computationally postulated early steps for the reaction of phenylallene. Free energies in kcal mol^{-1}.



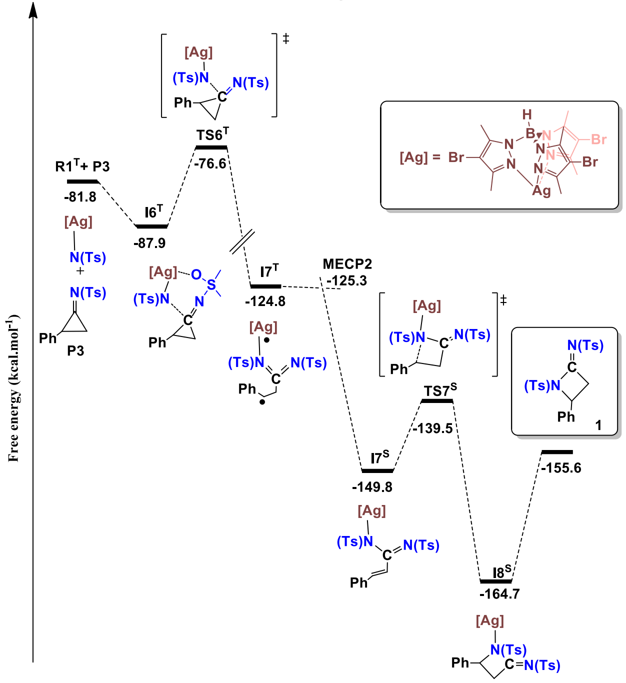
The silver fragment Tp^{*,Br}Ag is known to react with PhI=NTs to form metallonitrenes.[9a,b,19] The ground state of the metallonitrene complex **R1** (Scheme 9) is a triplet, located 5.9 kcal mol^{-1} below the corresponding singlet, and 16.5 kcal mol^{-1} below Tp^{*,Br}Ag and NTs as separate molecules.[9a,b]

The initial reactivity of complex **R1** is outlined in Scheme 9. The nitrene center in **R1** can attack the phenylallene **R2** at three different positions: a) at the less substituted terminal carbon (=CH$_2$), b) at the phenyl substituted terminal carbon (=CHPh), and c) at the phenylallene central carbon (=C=). We have computed the transition states corresponding to each of the attacks: **TS1$_a$**, **TS1$_b$** and **TS1$_c$**, respectively. The barriers corresponding to the attack to terminal carbons are quite low (9.4 and 8.0 kcal mol^{-1} from adduct **I1c^T** to **TS1a^T** and **TS1b^T**) but cannot compete with the attack to the central carbon of the allene, which is clearly the preferred process. Transition state **TS1c^T** has an associated barrier of only 1.4 kcal mol^{-1}.

Transition states **TS1a^T**, **TS1b^T** and **TS1c^T** evolve through multistep processes, see Scheme 9. The triplet intermediates with the new C-N bond formed (**I2a^T**, **I2b^T** and **I2c^T**) will cross to the singlet energy surface through the corresponding MECPs (**MECP1a**, **MECP1b** and **MECP1c**) and form intermediates **I2a^S**, **I2b^S** and **I2c^S**. **I2a^S** and **I2b^S** present already a new C-C bond and correspond to the metal-coordinated forms of products **P1** and **P2**, respectively. For **I2c^S**, located in the lowest barrier favored path, several steps must take place before product **P3** is reached. A very low energy transitions state leads to the **I3^S** intermediate, containing a 5-member ring which involves the three carbons in the starting allene and the Ts group attached to the nitrene center. The cleavage of this ring leads to the formation of a new C-C bond and ultimately to the **P3** product. These are very exergonic processes, thus completely irrerversible. At variance with the proposal shown in Scheme 6 where the cyclopropylimine species would appear because of the thermal rearrangement of the methylene aziridines, calculations show that the presence of the silver catalyst offers a reaction pathway favoring its formation without the intermediacy of the three member rings.

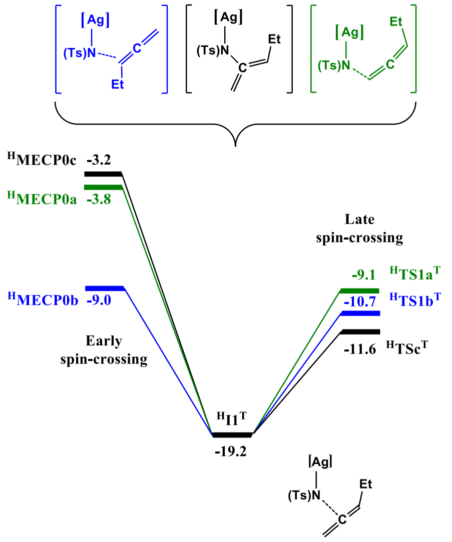
Products **P1**-**P3** are not observed in the reaction mixture of phenylallene and PhI=NTs. However, cyclopropylimine **P3** may evolve to the final product upon reaction with a second metallonitrene complex **R1**, as shown in Scheme 10. A new C-N bond is formed between the nitrogen of the second silver-nitrene and the cyclopropylimine **P3** through **TS6^{T}** with a barrier of only 11.3 kcal mol^{-1}. As the N-C bond is formed, one of the C-C bonds of the cyclopropane is broken, which results in species **I7^{T}**. Through **MECP2** the system crosses to the singlet surface, that is 25 kcal mol^{-1} more stable than the triplet. A second N-C bond is formed through **TS7^{S}**, generating the four membered cycle **I8^{S}**. Product **1**, which is the only one experimentally observed, is delivered after silver decoordination, an energetically disfavored step but easily compensated by ulterior coordination of other species to the silver center.

Scheme 10. Postulated computational mechanism for the formation of compound 1 from cyclopropylimine. Free energies in kcal mol^{-1}.

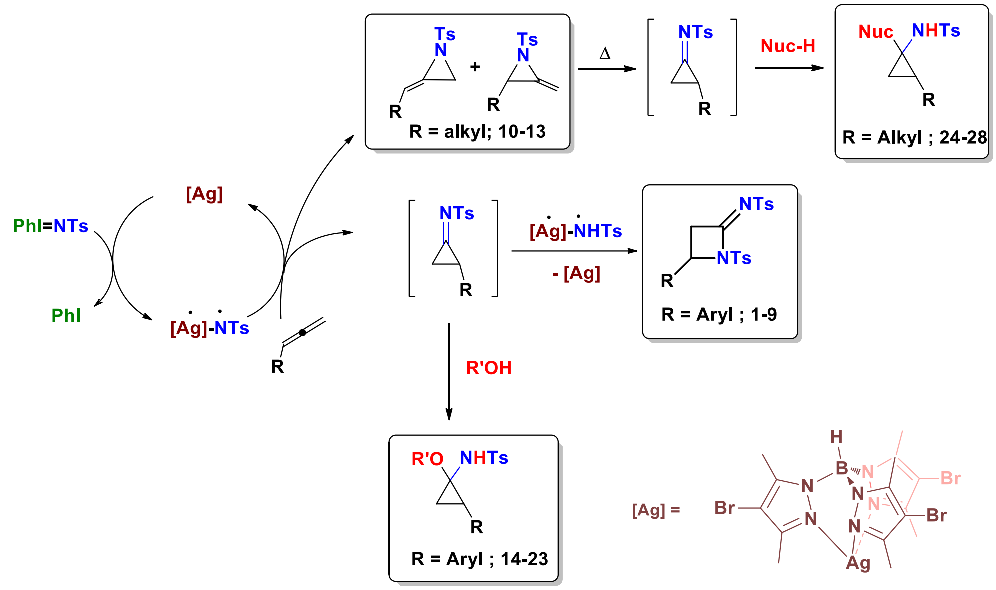


We next shifted our attention to the behavior of alkylallenes, which have been experimentally shown to produce methylene aziridines rather than azetidines. We notice that the mechanism reported above in Scheme 11 may lead to aziridine products **P1** and **P2**, though they are kinetically disfavored with respect to the azetidine emerging from **P3**. We computed a similar mechanism for ethylallene as our model alkylallene system. To our initial disappointment the resulting profile (fully described in the SI, key step in Scheme 11) yielded the same selectivity, which would favor the azetidine. Additional calculations on the ulterior evolution of the azetidine products were also unable to provide a satisfying explanation for the different behavior of alkyl and arylallenes. The problem was finally solved by the characterization of an alternative mechanism where the transition from the triplet to the singlet spin state takes place through an MECP before the formation of the first new nitrogen-carbon bond. We label this alternative mechanism as “early spin-transition”, to differentiate it from the previously reported one where the transition took place after the bonds has been formed and the selectivity has been decided. Both mechanisms could be characterized for ethyl-allene, the corresponding selectivity-determining steps are shown in Scheme 11. The two mechanisms differ in the associated selectivity, the new mechanism reproducing the experimental observation in which the major product is methylene aziridine emerging from the blue pathway. Remarkably, this alternative mechanism is absent in the phenylallene system, which must then react through the “late spin-transition” mechanism reported above, leading to the azetidine through the black pathway in Scheme 9.

Scheme 11. The selectivity-determining step for the two computed mechanisms for alkylallenes. Free energies in kcal mol^{-1}.



Scheme 12. Mechanistic proposal for the different behavior of aryl- and alkylallenes.



We notice there is a minor problem in the computed energetics, as the free energy for ^{H}**MECPob** is still 2.6 kcal mol^{-1} above that of ^{H}**TSc**^{T}. We view this as a minor discrepancy as the reproduction of singlet/triplet energy gaps has been shown to be particularly challenging for DFT methods. More encouragingly, this alternative mechanism provides satisfactory qualitative explanations for the reactivity of alkylallenes. The "early spin-crossing" path was absent in the arylallene system because of the larger triplet/spin gap associated to the stabilization of the triplet state associated to the spin delocalization to the aryl ring. Additionally, the "early spin-crossing" path favors the attack on the terminal substituted carbon since it gives more weight to inductive effects than to the delocalization effects that favor the central carbon in the "late spin-crossing" mechanism. A detailed analysis of spin densities in provided in the SI.

Global mechanistic proposal. From collected experimental and computational data the global mechanistic picture is shown in Scheme 12. A silver-nitrene intermediate is formed from the Tp^{x}Ag core and PhI=NTs, which transfers the nitrene group to the allene C=C bond leading to methylene aziridines for R = alkyl and azetidines for R = aryl. The latter takes place through the formation of a cyclopropylimine intermediate in a silver-catalyzed route, which is kinetically more favorable than the formation of the corresponding methylene aziridines. For alkylallenes, a different selectivity has been calculated due to an earlier transition from the triplet to the singlet spin states.

The presence of the cyclopropylimine intermediate when employing arylallenes explains the formation of aminocyclopropanes when the reaction is carried out in the presence of alcohols, which add to the C=N bond as previously described by Shipman or Blakey, among others.[5,17] In their absence, cyclopropylimine reacts with a second silver-nitrene intermediate en route to the observed azetidine compounds.

At variance with the above, the methylene aziridines generated from alkylallenes are stable under the reaction conditions, and the presence of alcohol does not influence the reaction outcome. Only when they are heated, in the absence of any catalyst and with added nucleophiles, they provide aminocyclopropanes because of the in situ formation of a cyclopropylimine intermediate, which traps the nucleophile.

CONCLUSIONS

We have discovered the catalytic capabilities of a silver complex toward the intermolecular functionalization of allenes toward azetidines or methylene aziridines, depending of the nature (aryl or alkyl) of the substituents in the allene reactant. The azetidines are formed by a sequential process involving silver-mediated cyclopropylimine formation followed by the incorporation of a second, also silver-mediated, nitrene unit. At variance with that, alkylallenes are transformed into methylene aziridines. Aminocyclopropanes can be readily accessed from both alkyl- and arylallenes. This is the first example of efficient modification of allenes by metal-catalyzed nitrene transfer in an intermolecular manner.

EXPERIMENTAL SUMMARY

General Procedure for the reaction of allenes and PhI=NTs. The [Tp^{*,Br}Ag]$_2$ complex[13] (0.005 mmol) was dissolved in deoxygenated DCM (6 mL) and the allene (2 mmol) was added before PhI=NTs (74.4 mg, 0.2 mmol) was incorporated in one portion to the stirred solution. The flask was covered with aluminum foil to protect the reaction mixture from light. After 4h, the solvent was removed under reduced pressure and the crude was analyzed by NMR spectroscopy and/or purified by column chromatography (see SI). For aminocyclopropane synthesis the procedure was identical also adding 2 mmol of the alcohol before addition of PhI=NTs.

Derivatizations of the methylene aziridine 13. (*E*)-10-tosyl-10-azabicyclo[7.1.0]dec-1-ene (58.2 mg, 0.2 mmol) was dissolved in acetonitrile (2 mL) and the corresponding nucleophile was added (2-10 mmol). The reaction mixture was heated at 75 °C for 2 h, and then solvent was removed under reduced pressure. The crude was analyzed by NMR spectroscopy and/or purified by column chromatography.

Computational Details. The presented computational mechanistic study has been performed by optimization of minima and transition states with the B3LYP-D3 functional[20] including the D3 correction developed by Grimme and co-workers[21] and as implemented in Gaussian 09.[22] The 6-31g(d)[23] basis set was used for all atoms except for silver, for which the Stuttgart-Dresden (SDD) basis set with effective core potential (ECP) was used instead. [24] Frequency calculations were carried out at the same level to obtain the free energies and assure the nature of each stationary point. Solvent effects were taken into account by using the SMD[25] solvation model and default options for dichloromethane. For the location of MECPs (Minimum Energy Crossing Points) we used the code provided by Prof. Jeremy Harvey.[26] The geometries of all species relevant for this study are included in a data set collection of computational results available in the ioChem-BD repository.[27]

Supporting Information.

All procedures and characterization data for new compounds, computational data and Cartesian coordinates of the optimized structures. The Supporting Information is available free of charge on the ACS Publications website.

AUTHOR INFORMATION

Corresponding Author

perez@dqcm.uhu.es (PJP), mmdiaz@dqcm.uhu.es (MMDR), fmaseras@iciq.es (FM)

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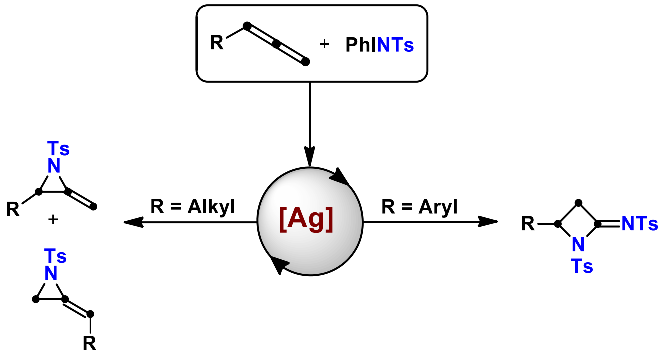
R
+ PhINTs
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R = Alkyl
R = Aryl
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