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# Silver and Platinum-Catalysed Addition of O-H and N-H bonds to allenes

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Transition-metal catalysed nucleophile addition to allenes is a very powerful tool for the synthesis of functionalised molecules containing heteroatoms, heterocycles in the intramolecular version, or allyl derivatives in the intermolecular. The reaction has been explored with a wide variety of metals, being silver one of the most effective. Although platinum has somehow been less explored, different reactivity has been observed with this metal, showing the great potential and versatility of this methodology. This review will highlight the reactions with these two metals, silver and platinum, when oxygen or nitrogen nucleophiles are employed. Although most of the examples describe the intramolecular version, some intermolecular reactions have been described with platinum, and will also be covered.

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## 1. Introduction

The addition of heteroatoms onto an activated C=C bond is a very useful method to gain access to a variety of functionalised molecules in an atom efficient manner. The reaction onto allenic systems has an added value as the regiochemistry can be controlled by using different metals or changing the substituents or the length of the chain between the allene and the heteroatom in the intramolecular case. In particular, the reaction with allenols and amino allenes provides a wide variety of heterocycles, and has been widely used for the synthesis of natural products.

Many metals have been studied in these reactions and some reviews have already covered this reactivity with different type of unsaturated compounds.<sup>1</sup> The purpose of this review is to give a state-of-the-art account of the reaction on allenic systems using silver and platinum complexes with oxygen and nitrogen nucleophiles from the first examples to the latest features of this

useful transformation. The review has been organised first dividing the examples by metal (silver and then platinum), then by nucleophiles (oxygen, then nitrogen), and finally by *intra-versus* intermolecular processes. Some comments comparing reactions covered here with analogous gold-catalysed processes have been included in the discussion to enhance the interest of the manuscript for a general audience.<sup>2</sup>

### 1.1. Silver

Although the focus of this review is on silver-catalysed reactions, the reaction of silver with allenols and amino allenes using stoichiometric amounts of the metal has been known since the 1980's, and therefore examples of those reactions have been included in this review for a wider understanding of this transformation.

There are no formal reported studies on the modification of the reaction conditions needed to turn the silver-mediated process into catalytic. However, by analysing the different described examples, it seems that stoichiometric amounts of silver salts (in general AgNO<sub>3</sub> is the most used) are needed for more challenging transformations, such as synthesis of spirocycles, or bigger rings.

Stoichiometric amounts of silver are also often employed when the intermolecular reaction is applied in the total synthesis of natural products, although some catalytic examples have also been reported.

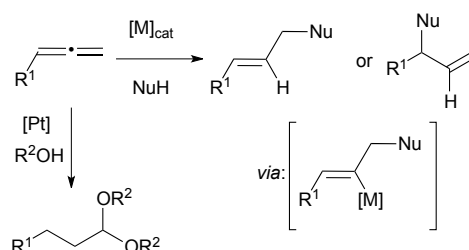
Silver was considered as a Lewis acid more than a transition metal complex in most of the earlier cases. Only more recently  $\eta^2$ -silver complexes, vinyl silver or silver allyl cation intermediates have been proposed to explain the reactivity of these systems.<sup>3</sup> However, not many details about the mechanistic considerations have been reported in the reaction with silver.

All the silver-catalysed examples covered in this review are

intramolecular reactions. No intermolecular addition of nucleophiles to allenes catalysed by silver salts is known to date.

## 1.2. Platinum

Intra- and intermolecular examples of platinum-catalysed addition of nucleophiles to allenes have been reported. Although platinum is supposed to have similar reactivity than gold, the reaction of allenes with nucleophiles catalysed by platinum complexes, has been less explored, especially in the case of nitrogen derivatives.

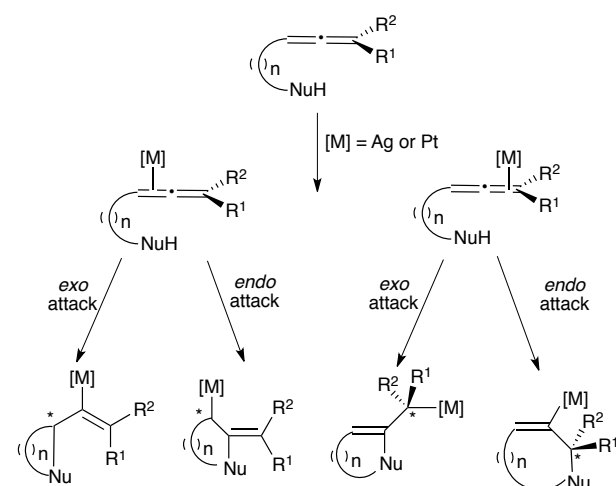


**Scheme 2** General mechanisms for the metal-catalysed reaction of allenes and nucleophiles.

It is very interesting to note that in many of the reported examples of platinum catalysis, divergent reactivity has been encountered, and new reaction modes have been proposed in the intra- and intermolecular version.

## 1.3 General Mechanisms

The general accepted mechanisms for the cyclisation of allenols and amino allenes in the presence of transition metal complexes, including silver and platinum, are summarised in Scheme 1. The metal can coordinate to one or the other double bonds of the allene in a  $\eta^2$ -coordination mode, promoting the *exo*- or *endo*-attack to the terminal or internal carbons to form different size heterocycles. Five- and six-membered rings are often preferred, but bigger rings have been obtained by modulating the substitution in the starting material and the metal employed.



**Scheme 1** Possible mechanisms for the metal-catalysed cyclisation of allenols and amino allenes.

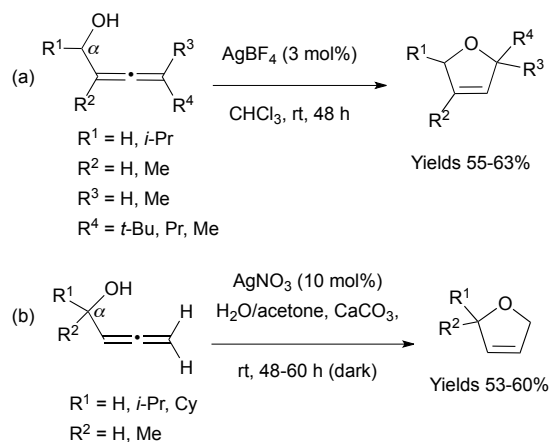
The scheme for the intermolecular reactions is not that general. Traditionally, intermolecular addition of nucleophiles onto transition metal-activated allenes give rise to allyl derivatives by attack of the nucleophile to one of the terminal carbons of the allene. Protonolysis of the vinyl metal intermediate furnishes the allyl derivative (Scheme 2 right).<sup>4</sup> However, more recently, new reactivity has been observed with platinum to give double nucleophilic addition (Scheme 2 down), and will be discussed in the appropriate section.

## 2. Silver-Catalysed Reactions

### 2.1. Intramolecular Addition of O-H

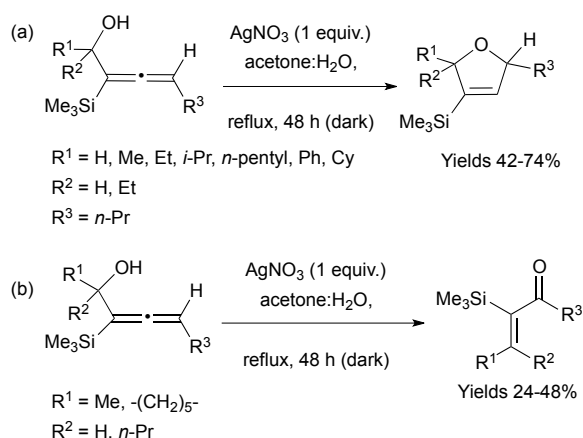
The coinage metal-catalysed addition of O-H to unsaturated bonds has been recently reviewed by Brazier *et al.*<sup>3a</sup> In the present review we will highlight the silver catalysed process involving allenes, and we will include reactions with other oxygen nucleophiles (ketones, acid derivatives) not covered by Brazier's review.

The reaction of  $\alpha$ -allenols in the presence of catalytic amounts of silver salts was first reported by Claesson in 1979.<sup>5</sup>  $\delta$ -Monoalkyl and  $\delta,\delta$ -dialkyl substituted  $\alpha$ -allenols gave 2,5-dihydrofurans by 5-*endo* attack to the distal double bond, when reacted in the presence of 3 mol% of  $\text{AgBF}_4$  in  $\text{CHCl}_3$  (Scheme 3a). However, unsubstituted derivatives needed harsher conditions (10 mol% of silver nitrate in mixtures of water/acetone, in the presence of  $\text{CaCO}_3$ ) to afford the products in moderate yields (Scheme 3b).



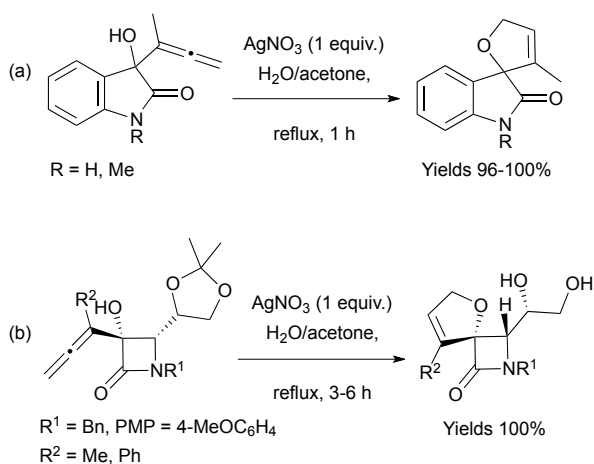
**Scheme 3** First reported silver-catalysed reaction of  $\alpha$ -allenols.

Silver nitrate has been the salt of choice in many transformations of  $\alpha$ -allenols, but stoichiometric amounts have to be used in some challenging cases. For example, Wang *et al.* reported the cyclisation of 3-(trimethylsilyl)-substituted  $\alpha$ -allenols to give 3-(trimethylsilyl)-2,5-dihydrofurans in the presence of 1 equivalent of  $\text{AgNO}_3$  (Scheme 4a).<sup>6</sup> Interestingly, tertiary alcohols gave  $\alpha,\beta$ -unsaturated ketones instead, probably due to formation of a tertiary carbocation (stabilised by the silicon group by hyperconjugation), followed by attack of water to the central carbon of the allene (Scheme 4b).



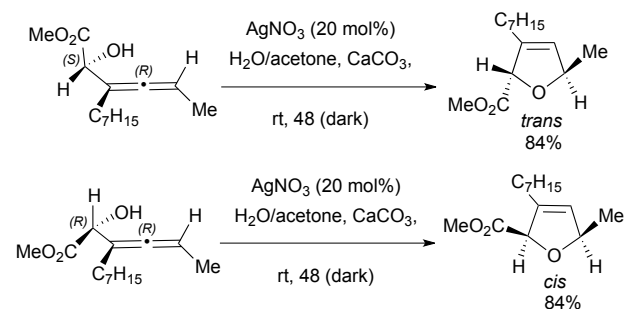
**Scheme 4** Reaction of 3-(trimethylsilyl)-substituted  $\alpha$ -allenols with silver.

Spirocyclic dihydrofuran derivatives have been synthesised using similar conditions with stoichiometric amounts of silver. The reaction has been applied by Alcaide, Almendros *et al.* for the synthesis of spirocyclic oxindoles (Scheme 5a),<sup>7</sup> and spirocyclic 2-azetidinones (Scheme 5b).<sup>8</sup>



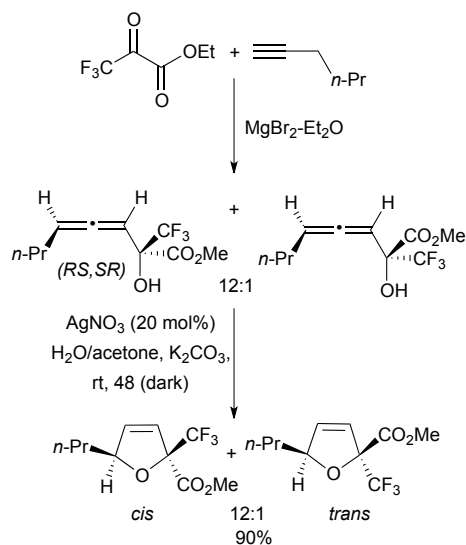
**Scheme 5** Silver-catalysed formation of spirocyclic dihydrofurans.

The catalytic version of this reaction has been widely studied by Marshall *et al.*<sup>9</sup> They reported that the reaction with enantioenriched  $\alpha$ -allenols with catalytic  $\text{AgNO}_3$ , gave stereospecific cyclisation to the corresponding dihydrofurans, and they presumed attack on the allenic double bond *syn* to the side chain containing the OH (Scheme 6).



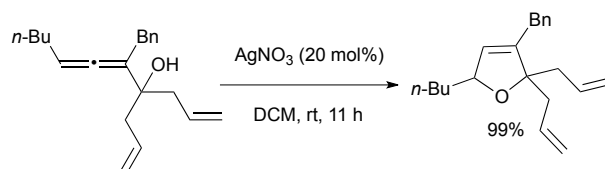
**Scheme 6** Stereospecific cyclisation of  $\alpha$ -allenols.

The stereospecificity of this cyclisation reaction can be used to assign the configuration of diastereometric mixtures of  $\alpha$ -allenols. For example, Burger *et al.*, carried out the silver-catalysed cyclisation of a 12:1 mixture of diastereomeric allenylcarbinols synthesised by  $\text{MgBr}_2\text{-Et}_2\text{O}$  promoted carbonyl-yne reaction of 3,3,3-trifluoropiruvates, and they obtained a 12:1 mixture of 2,5-dihydrofurans in 90% yield.<sup>10</sup>  $^1\text{H}$  and  $^{19}\text{F}$  NMR experiments confirmed the *cis* relationship between the  $\text{CF}_3$  group and the alkyl substituent in the major diastereomer which they related to the (*RS,SR*)-configuration of the major allenol (Scheme 7).



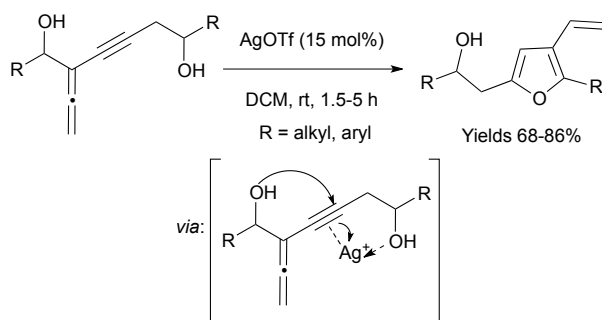
**Scheme 7** Assignment of configuration of  $\alpha$ -allenols based on the silver-catalysed cyclisation.

Interestingly, the reaction seems to be also chemoselective. For example, Ma *et al.* reported that bis-allyl substituted  $\alpha$ -allenols can be converted to the 2,5-dihydrofuran derivatives by attack of the oxygen onto the allene, without involvement of the extra double bonds in the reaction (Scheme 8).<sup>11</sup>



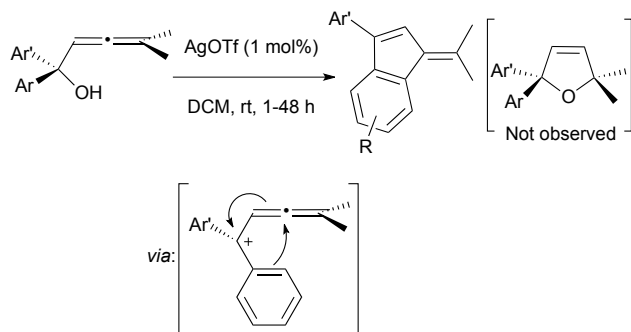
**Scheme 8** Preferred attack of the oxygen onto the allene versus alkene.

However, Lee *et al.* found that when an alkyne is present in the reaction of allenyne-1,6-diols, the silver tends to be more alkyneophilic than allenophilic, and nucleophilic attack of the homoallenyl alcohol occurs onto the activated triple bond to give substituted furans (Scheme 9).<sup>12</sup> In this reaction Ag(I) exhibited the opposite reactivity than Au(III), which has a higher preference in the activation of the allene *versus* the alkyne, and gives dihydrofurans as products. The  $\alpha$ -allenyl hydroxyl group seems to be more nucleophilic due to possible coordination of the other hydroxyl group to the silver salt.



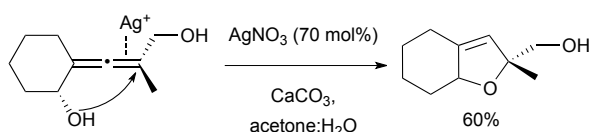
**Scheme 9** Preferred attack of oxygen onto alkyne *versus* allene.

More interestingly,  $\alpha$ -allenols with two aryl groups at the  $\alpha$ -position have been reported by Gandon *et al.* to undergo a silver-catalysed Nazarov-type cyclisation, with no involvement of the hydroxyl group.<sup>13</sup> In this reaction, dihydrofurans are obtained as by-products in a few cases, and the  $4\pi$  electrocyclic cyclisation of the aryl prop-2-ene-1-yl cations involving one of the aromatic rings and the allene takes place to form benzofulvenes (Scheme 10).



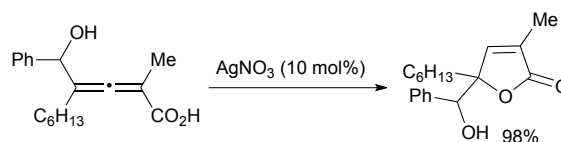
**Scheme 10** Nazarov-type cyclisation of aryl-substituted  $\alpha$ -allenols.

The regioselectivity of the reaction has been studied with  $\alpha,\alpha'$ -allenediols containing primary, secondary and tertiary hydroxyl groups. Marshall *et al.*<sup>14</sup> and Aurrecochea *et al.*<sup>15</sup> reported independently preferential complexation of the  $\text{Ag}^+$  to the less congested end of the allenic system, and therefore cyclisation with the more substituted alcohol was favoured (Scheme 11).



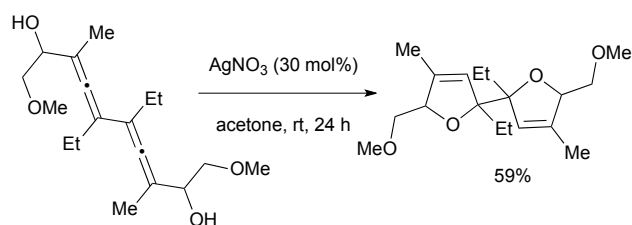
**Scheme 11** Regioselectivity in the reaction of  $\alpha,\alpha'$ -allenediols.

In an example reported by Hammond *et al.*, when a carbinol allenolate is employed, the reaction in the presence of silver occurs preferentially by nucleophilic addition of the acidic oxygen onto the allene and formation of a  $\gamma$ -lactone (Scheme 12).<sup>16</sup>



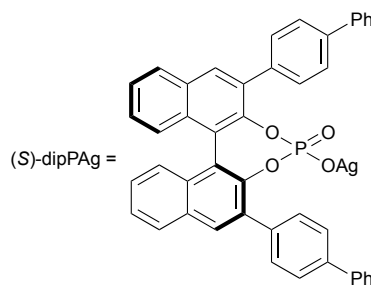
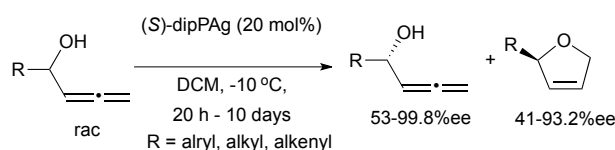
**Scheme 12** Formation of lactone from a carbinol allenolate.

Reaction of bis( $\alpha$ -allenols) has been explored by Krause *et al.* to give mono- or bis-cyclisation with axis-to-centre chirality transfer, depending on the reaction conditions and the substitution in the starting material.<sup>17</sup> In this case, the steric effects have a big influence and bis-cyclisation was achieved effectively for the less substituted derivative with 30 mol% of  $\text{AgNO}_3$  after prolonged reaction times (Scheme 13).



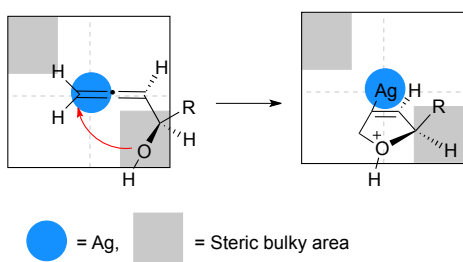
**Scheme 13** Silver-catalysed reaction of bis( $\alpha$ -allenols).

Although there are no examples of enantioselective reaction of  $\alpha$ -allenols in the presence of silver salts, recently Hong *et al.* have reported a chiral silver phosphate-catalysed cycloisomeric kinetic resolution of different substituted  $\alpha$ -allenols to give the 2,5-dihydrofurans and recovered starting materials with high enantioselectivity.<sup>18</sup> The reaction works best with a 3,3-disubstituted Binap-phosphate derivative ((S)-dipPAg), at  $-10^\circ\text{C}$  in DCM with times between 20 h and 10 days, and enantioselectivities from 32 to 99.8% depending on the substrates (Scheme 14).



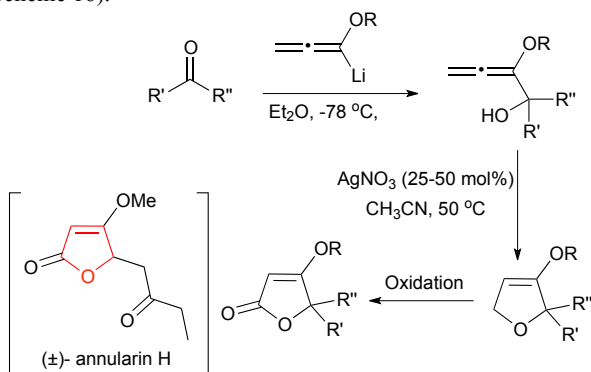
**Scheme 14** Silver phosphate-catalysed cycloisomeric kinetic resolution of  $\alpha$ -allenols.

- 5 The authors proposed coordination of the silver to the allene in a  $\eta^2$ -complexation so when the  $\alpha$ -allenol approaches the metal centre, the *R*-enantiomer coordinates preferentially to the silver since the bulky R-group would lie in the unhindered area, while the *S*-enantiomer remains in the reaction mixture (Scheme 15).  
 10 The bonded *R*-enantiomer suffers cycloisomerisation, and after protodemetalation and ligand exchange with another *R*-enantiomer of the allenol, the enantiomerically enriched 2,5-dihydrofuran is formed.



**Scheme 15** Proposed model for kinetic resolution.

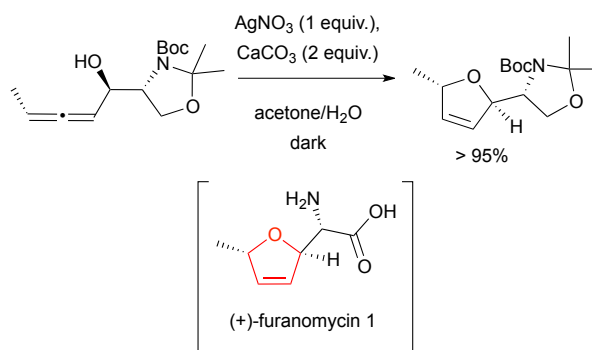
- 15 Cyclisation of  $\alpha$ -allenols in the presence of silver salts has been widely used as key step in many total syntheses of natural products. Reissig *et al.* have prepared 3-alkoxy-2,5-dihydrofurans in two steps using silver-catalysis in the reaction of  $\alpha$ -allenols  
 20 derived from carbonyl compounds and lithiated alkoxyallenes.<sup>19</sup> This transformation needed a higher loading of silver salt (25-50%  $\text{AgNO}_3$  or  $\text{AgBF}_4$ ), and the reaction was cleaner in the absence of the base. However, gold(I) salts seemed to work better in most cases with these substrates, and  $\text{AuCl}$  was the catalyst of  
 25 choice for the preparation of the 3-alkoxy-2,5-dihydrofuran utilised in the synthesis of the natural product annularin H (Scheme 16).



**Scheme 16** Key step in synthesis of annularin H.

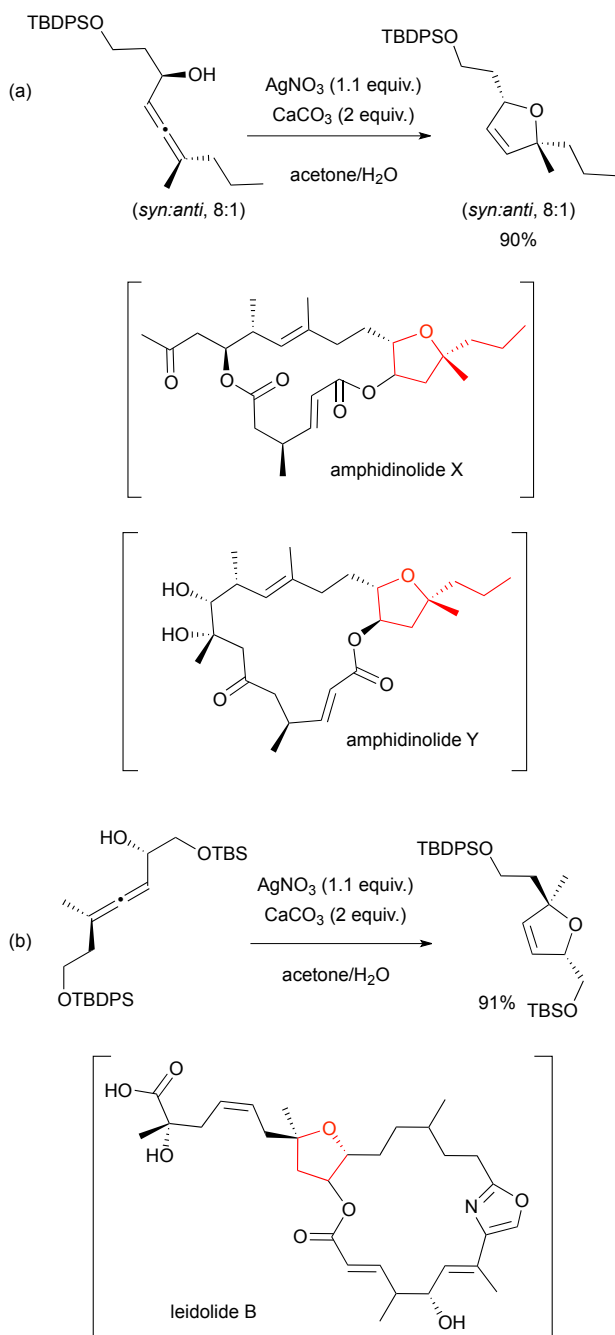
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Standaert *et al.* reported a concise synthesis of (+)-furanomycin 1 in seven steps, where one of the key steps is the silver-catalysed cyclisation of an  $\alpha$ -allenol (Scheme 17).<sup>20</sup>



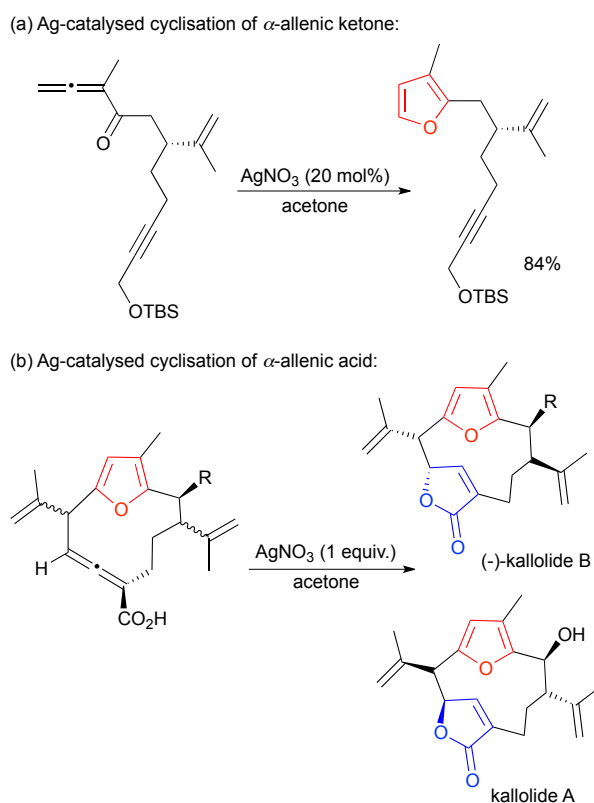
**Scheme 17** Key step in synthesis of (+)-furanomycin 1.

- Fürstner *et al.* have used this methodology in several syntheses of natural products containing furan-derivatives, such as amphidinolide X and Y (Scheme 18a),<sup>21</sup> and more recently  
 40 Leiodolide B (Scheme 18b).<sup>22</sup> In their elegant approach, they use the transfer of chirality from the corresponding allenols as a relay to obtain the desired stereochemistry in the highly substituted tetrahydrofurans in the early stages of the syntheses.



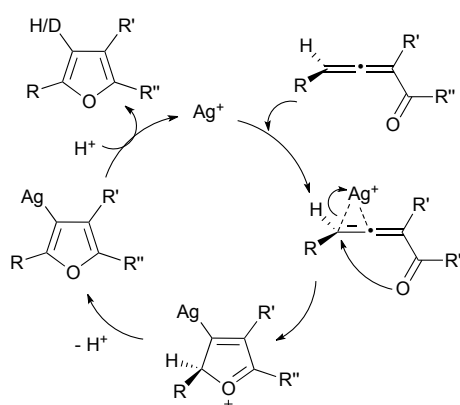
**Scheme 18** Key steps in synthesis of furan-containing natural products.

Similarly to  $\alpha$ -allenyl alcohols,  $\alpha$ -allenyl aldehydes, ketones<sup>23</sup> and acids<sup>24</sup> can react in the presence of silver salts to form furans. Marshall *et al.* developed this reaction during the 1990's, and applied it to the synthesis of 2,5-furano macrocyclic natural products<sup>9c</sup> like kallolide A<sup>25</sup> and kallolide B (Scheme 19).<sup>26</sup>



**Scheme 19** Key step in the synthesis of furan-macrocyclic natural products.

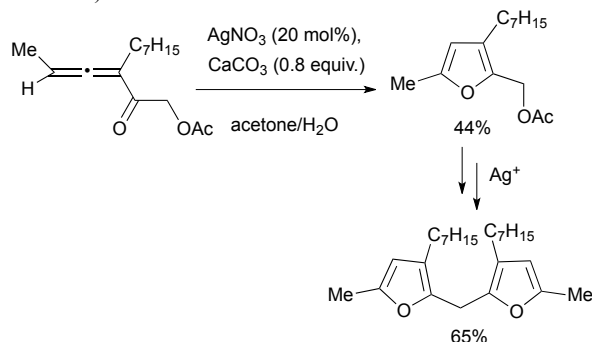
Although the initial conditions for the cyclisation of  $\alpha$ -allenyl ketones were the same used for the  $\alpha$ -allenols, Marshall *et al.* discovered that the reaction worked better in the absence of the base and significant rate acceleration was observed decreasing the water content.<sup>23c</sup> The proposed mechanism consisted in coordination of the silver to the distal double bond of the allene and attack of the carbonyl group in a 5-*endo* fashion, to form a vinyl-silver cation, which after loss of a proton would give a Ag(I)-furan intermediate. Deuteration studies suggested a direct S<sub>E</sub> protonolysis with loss of Ag(I) as the preferred pathway to explain the formation of furan derivatives (Scheme 20).



**Scheme 20** Mechanism of the silver-catalysed cyclisation of  $\alpha$ -allenyl ketones.

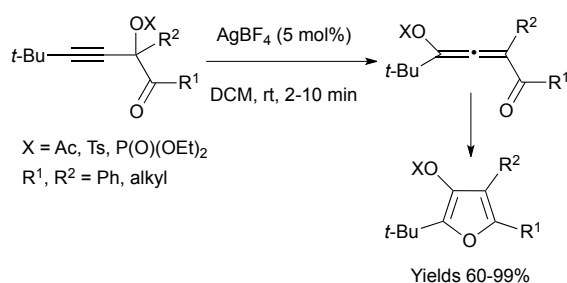
When the reaction was carried out with  $\alpha$ -oxygenated allenones,

2-hydroxy-2,5-dihydrofurans were observed as products, which then suffered dimerization to form bisfuranomethane derivatives (Scheme 21).<sup>23b</sup>



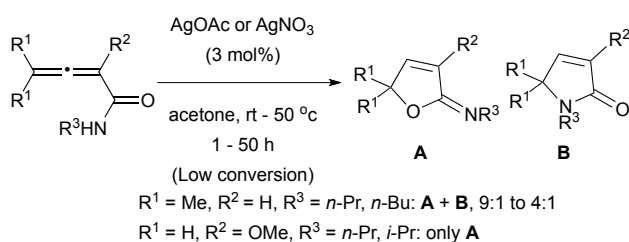
**Scheme 21** Silver-catalysed dimerization of 2-hydroxy-2,5-dihydrofurans.

Gevorgyan *et al.* have reported the synthesis of tri- and tetrasubstituted furans by tandem silver-catalysed formation of allenyl ketones from alkyne derivatives followed by the silver-catalysed cyclisation as described before (Scheme 22).<sup>27</sup>



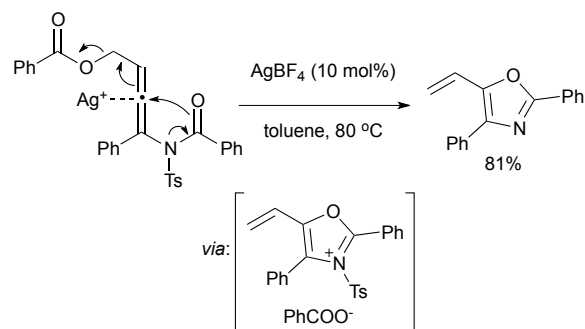
**Scheme 22** Silver-catalysed formation of substituted alkoxyfurans.

As mentioned before, acid derivatives can also be employed in the silver-catalysed cyclisation. Reaction of  $\alpha$ -allenlic carboxamides is interesting as oxygen and nitrogen can act as nucleophile in the cyclisation. Brandsma *et al.* reported that reaction of simple allenlic carboxamide in the presence of silver acetate or silver nitrate gave mixtures of the products from oxygen (2-(5*H*)-furylidenamine, **A**) and nitrogen addition (dihydro-2*H*-pyrrol-2-ones, **B**), being the furylidenamines the major components.<sup>28</sup> However reactions were sluggish and full conversion was not achieved in all the cases. Reaction with derivatives containing a methoxy group in the allenlic system underwent smooth cyclisation under mild conditions to give exclusively the furylidenamines derivatives (**A**, Scheme 23).



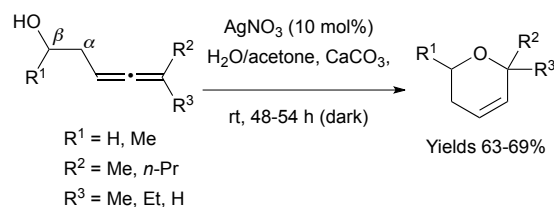
**Scheme 23** Oxygen versus nitrogen attack in  $\alpha$ -allenlic carboxamides.

Very recently, Wan *et al.* have reported the silver-catalysed cyclisation of allenyl-tosylamides containing an acyloxy group for the synthesis of vinyloxazoles (Scheme 24).<sup>29</sup> In this case the nucleophile is in  $\beta$ -position, and instead of the 5-*endo* cyclisation, the 5-*exo* is favoured with attack of the amidic oxygen onto the central carbon of the allene. Although this type of attack to the central carbon is less common, the elimination of both, the sulfonyl and the acyloxy group, favour the formation of the 5-membered ring in this case, to generate the final product.



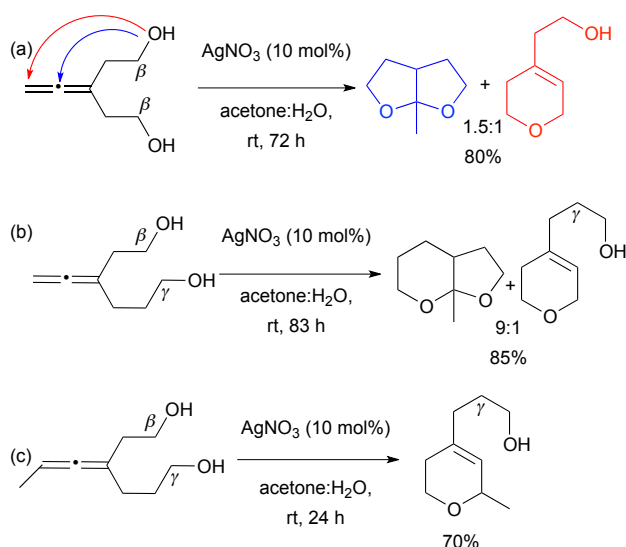
**Scheme 24** Silver-catalysed cyclisation of allenyl-tosylamides.

There are few examples of silver-catalysed reaction of  $\beta$ -allenols. The first example was reported by Claesson in 1979 in the same paper where they report the reaction of  $\alpha$ -allenols.<sup>5</sup> They reported that these substrates needed the more active conditions (10 mol% of silver nitrate in mixtures of water/acetone in the presence of CaCO<sub>3</sub>) to afford 5,6-dihydro-2*H*-pyrans (Scheme 25). Formation of six-membered rings is favoured here by attack of the oxygen to the terminal carbon of the distal double bond of the allene in a 6-*endo* cyclisation.



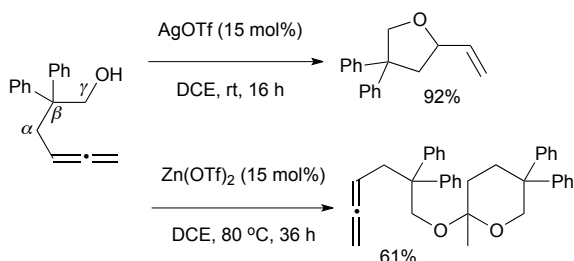
**Scheme 25** Silver-catalysed cyclisation of  $\beta$ -allenols.

A few years later, Gore *et al.* reported the reaction of  $\beta,\beta$ - and  $\beta,\gamma$ -allene-diols and observed favourable reaction of the  $\beta$ -hydroxy group versus the  $\gamma$ -hydroxy group in all cases.<sup>30</sup> Reaction of unsubstituted  $\beta,\beta$ -allenediols under the conditions reported by Claesson, gave preferentially bicyclic acetals by attack to the central carbon of the allene, together with the expected dihydropyran (Scheme 26a). Unsubstituted  $\beta,\gamma$ -allene-diols also gave bicyclic acetals, together with dihydropyran from the attack of the  $\beta$ -hydroxyl group (Scheme 26b). Interestingly, when the  $\beta,\gamma$ -allene-diol had a methyl group in the terminal carbon of the allene, only the dihydropyran from the attack of the  $\beta$ -hydroxy group was observed (Scheme 26c).



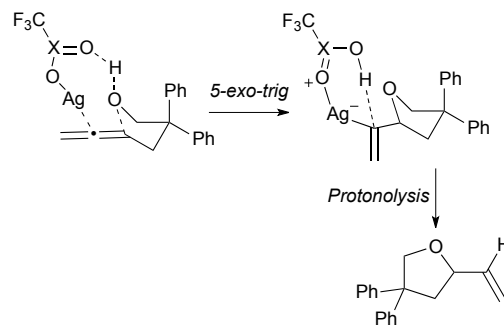
**Scheme 26** Regioselectivity on the silver-catalysed reaction of  $\beta,\beta$ - and  $\beta,\gamma$ -allene-diols.

Silver-catalysed reaction of  $\gamma$ -allenols has been reported by Hii *et al.*<sup>31</sup> The regioselectivity of the reaction was modulated by using different Lewis acids. Silver salts promoted the 5-*exo-trig* cyclisation to give vinyl-substituted tetrahydrofurans, while TfOH, Sn(OTf)<sub>2</sub> or Zn(OTf)<sub>2</sub> favoured the 6-*exo-dig* to give tetrahydropyran rings (Scheme 27).



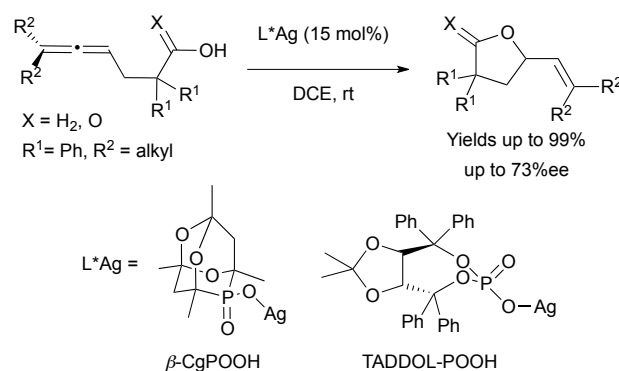
**Scheme 27** Silver-catalysed reaction of  $\gamma$ -allenols.

DFT calculations showed that in the reaction with silver salts, the C-O bond formation occurred with concomitant deprotonation of the hydroxyl group by the counterion on the silver followed by protonolysis of the vinyl-silver intermediate (Scheme 28). Interestingly, modifying the counterion from TfO<sup>-</sup> to TFA reduced the energy barrier by 1.5 kcal mol<sup>-1</sup>. This was in accordance with the experimental results, where reaction with 15 mol% of AgOTf occurred in 16 h, while reaction with Ag(TFA) gave similar yield at room temperature in only 2 h.



**Scheme 28** Cyclisation assisted by silver counterion.

This effect on the silver counterion led to develop the enantioselective version of this reaction by the same group using silver salts of chiral acids.<sup>32</sup> Enantioselectivities up to 73% ee were obtained with oxophosphorous(V) phosphinate ( $\beta$ -CgPOOH) and phosphate (TADDOL-POOH) complexes of silver, by weakly attractive non-covalent interactions between the ligand and the substrate in the transition state structures. The reaction works for  $\gamma$ -allenols and  $\gamma$ -allenic acids to form tetrahydrofurans or lactones respectively (Scheme 29).



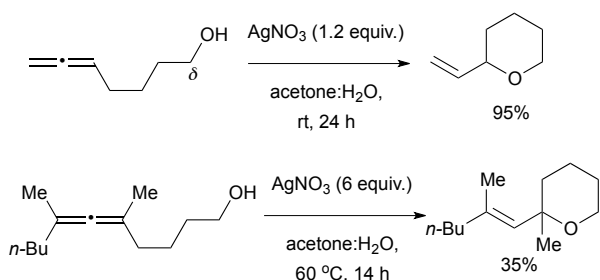
**Scheme 29** Enantioselective silver-catalysed cyclisation of  $\gamma$ -allenols.

This chiral counterion strategy has also been employed in gold chemistry, and high enantioselectivities (up to 99% ee) have been obtained in the intramolecular hydroxylation and hydroamination of allenols.<sup>33</sup> In reported examples, chiral silver salts of Binol-derived phosphates have been employed in combination with gold(I) complexes to induce asymmetry by interaction of the cationic catalyst with the chiral counterion associated with the metal in a ion pair, in reactions where chiral ligands in the gold failed to give good enantioselectivities. X-Ray absorption fine structure spectroscopy (XAFS) and NMR studies suggest that there is a strong bond between the phosphate oxygen and the gold cation during the catalytic cycle, and phosphate assisted proton transfer, similar to the one proposed for the silver-catalysed reaction as shown in Scheme 28, can not be ruled out as the stereochemical determining step in gold catalysis.

Reaction with  $\delta$ -allenols has been reported only with stoichiometric amounts of silver salts to give tetrahydropyrans by 6-*exo* attack. Gore *et al.* reported substitution in the allenic system to have a big influence in the reaction, and up to 6 equivalents of silver were needed in the more challenging



substrates (Scheme 30).<sup>34</sup>



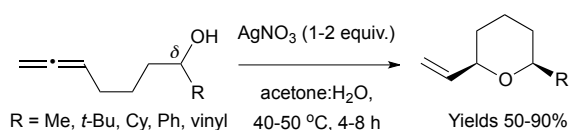
**Scheme 30** Silver-promoted cyclisation of  $\delta$ -allenols.

5

Gallagher *et al.* showed that the reaction is stereoselective and *cis*-2,6-disubstituted tetrahydropyrans are obtained when secondary alcohols are employed in the reaction (Scheme 31).<sup>35</sup>

They proposed a chair like conformation for the reversible

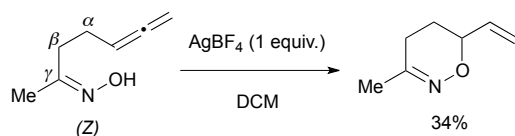
10 cyclisation and irreversible protonation of the *cis*-intermediate.



**Scheme 31** Stereoselective synthesis of tetrahydropyrans.

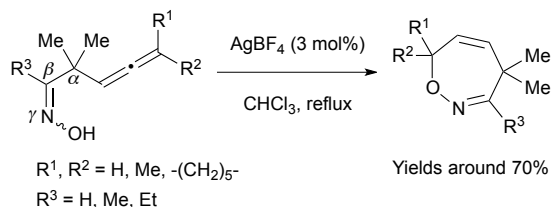
15 (*Z*)- $\gamma$ -Allenyl oximes give also 6-*exo* attack *via* the oxygen, to form oxazines when reacted with 1 equivalent of  $\text{AgBF}_4$  (Scheme 32).<sup>36</sup> In contrast, *E*-isomers give the 5-*exo* attack through the nitrogen to give nitron derivatives with moderate yields (See below, Scheme 48).

20



**Scheme 32** Reaction of (*Z*)- $\gamma$ -Allenyl oximes through the oxygen.

25 Although seven-membered rings are normally more challenging to obtain, silver-promoted 7-*endo* cyclisation of  $\beta$ -allenic oximes through the oxygen, has also been reported to give 4,7-dihydro-1,2-oxazepines (Scheme 33).<sup>37</sup>



30

**Scheme 33** 7-*Endo* cyclisation of  $\beta$ -allenic oximes through the oxygen.

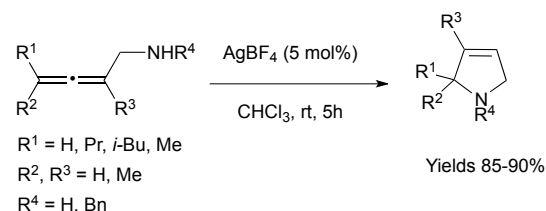
## 2.2. Intramolecular Addition of N-H

35

Reactions with amino allenes have been also described, and in

general follow the same trends as the oxygen derivatives to give preferentially 5- and 6-membered rings. In the presence of silver salts, the *endo* cyclisation with attack to the terminal carbon of the distal double bond is preferred with  $\alpha$ - and  $\beta$ -amino allenes, while  $\gamma$ - and  $\delta$ -amino allenes favour the *exo*-attack to the terminal carbon of the proximal double bond.

45 The first example of silver-catalysed intramolecular addition of  $\alpha$ -N-H nucleophiles to simple allenes was reported by Claesson *et al.*<sup>38</sup> They reported the cyclisation of different substituted primary and secondary  $\alpha$ -amino allenes in the presence of catalytic  $\text{AgBF}_4$ , to give 3-pyrrolines (Scheme 34).

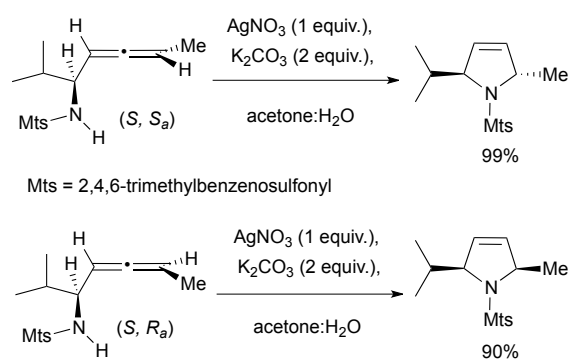


50

**Scheme 34** Silver-catalysed cyclisation of  $\alpha$ -amino allenes.

A few years later, Ibuka *et al.* reported<sup>39</sup> similar 5-*endo* attack to the distal double bond in  $\alpha$ -amino allenes, to form pyrrolidine

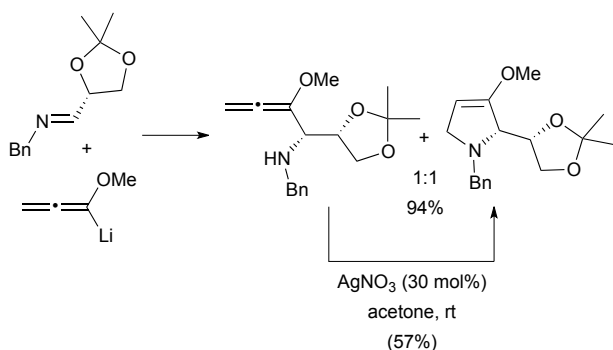
55 derivatives stereoselectively (Scheme 35).



**Scheme 35** Stereoselective synthesis of pyrrolidines.

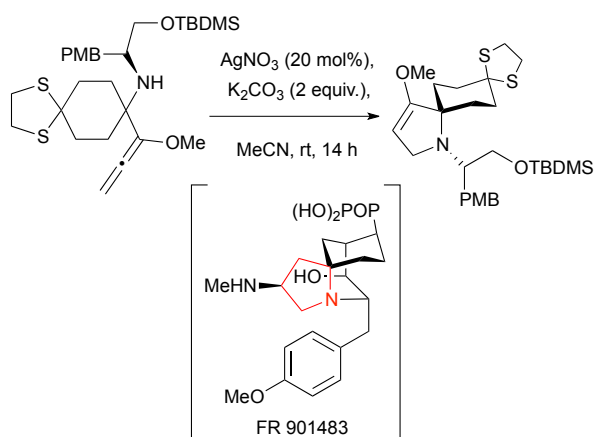
60 In the same year, Reissig *et al.*<sup>40</sup> reported the synthesis of  $\alpha$ -aminoallenes by reaction of methoxyallenes and imines, and then submitted them to reaction with  $\text{AgNO}_3$  in acetone. 2,5-Dihydropyrrole derivatives were obtained in good yields, and when the reaction was performed with an enantiopure derivative

65 from the (*R*)-glyceraldehyde, excellent diastereofacial selectivity was observed (Scheme 36).



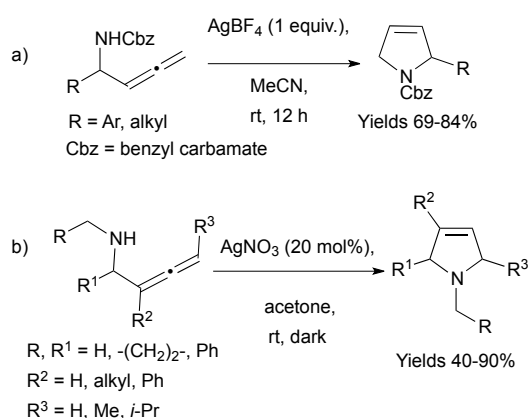
**Scheme 36** Silver-catalysed reaction of methoxy aminoallenes.

They applied this methodology efficiently for the synthesis of the azaspirane core of the tricyclic natural product FR 901483 (Scheme 37).<sup>41</sup>



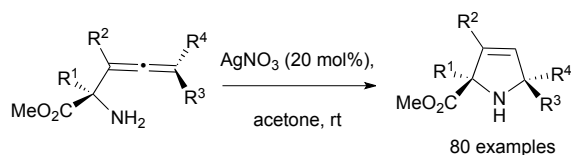
**Scheme 37** Key step in the synthesis of FR 901483.

Synthesis of  $\Delta^3$ -pyrrolines using the silver-catalysed cyclisation of  $\alpha$ -aminoallenes has been consequently reported by several groups, and in some cases, divergent reactivity from other metals has been observed. For example, reaction of Cbz-protected simple  $\alpha$ -aminoallenes with  $\text{AgBF}_4$  (Scheme 38a),<sup>42</sup> or reaction of substituted derivatives with  $\text{AgNO}_3$  gave pyrrolidines in good yields (Scheme 38b),<sup>43,44</sup> while the reaction with  $\text{Pd}(0)$  tends to form arylated pyrrole derivatives instead.<sup>44</sup>



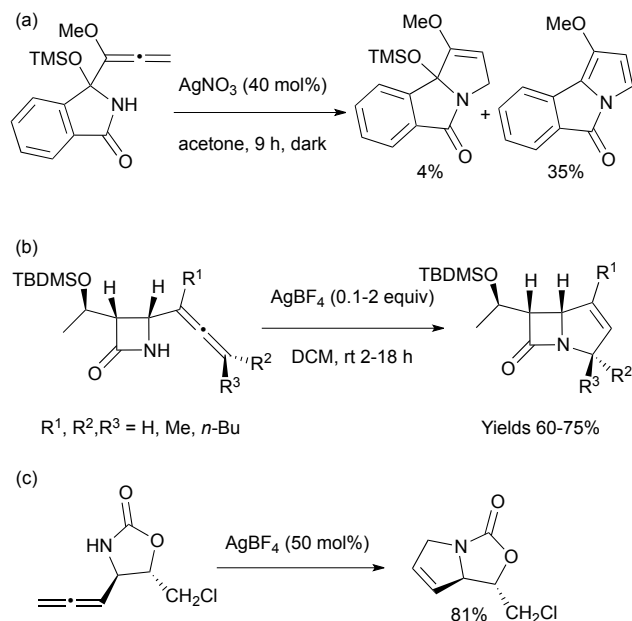
**Scheme 38** Synthesis of substituted pyrrolidines.

Brummond *et al.* have used this methodology to create an 80-member library of 3,4-dehydropyrrolidine amide derivatives for biological evaluation.<sup>45</sup> They used silver-catalysed cyclisation of  $\alpha$ -amino allenes derived from amino acids that proceeded with complete transfer of chirality from the allenes to the pyrrolidines (Scheme 39).



**Scheme 39** Library of 3,4-dehydropyrrolidine amide derivatives.

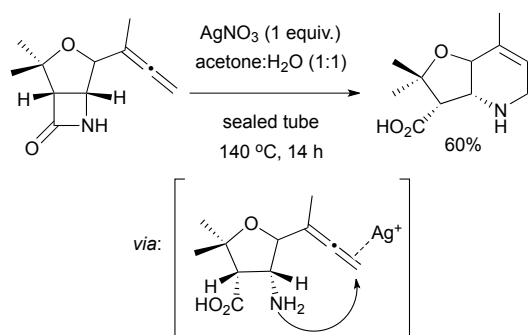
Similarly to the reactions of  $\alpha$ -allenoic acids, nitrogen derivatives such as amides or carbamates are able to participate in the silver-catalysed cyclisation. We have already mentioned the reaction of  $\alpha$ -carboxamides that gave mixtures of the products from oxygen (2-(5*H*)-furylydenamine) and nitrogen addition (dihydro-2*H*-pyrrol-2-ones), being the furylydenamines the major components (see Scheme 23).<sup>28</sup> However, reactions through the nitrogen nucleophile have also been reported. For example pyrroloisindolones and the corresponding pyrroles can be obtained in moderate yields by reaction of allenyl 1-isindolinones with 40 mol% of  $\text{AgNO}_3$  (Scheme 40a),<sup>46</sup>  $\Delta^1$ -carbapenems have been obtained by reaction of 4-allenylazetidones with  $\text{AgBF}_4$  (0.5-2 equivalents) (Scheme 40b),<sup>47</sup> and pyrrolidine azasugar precursors have been synthesised from allenyl carbamates (Scheme 40c).<sup>48</sup>



**Scheme 40** Silver-catalysed or promoted reactions of amino allene derivatives.

The only example in the literature of reaction of  $\beta$ -amino allenes was reported by Alcaide, Almendros *et al.* using an allene- $\beta$ -lactam derivative to form the tetrahydrofuro[3,2-*b*]piperidine core present in several natural products (Scheme 41).<sup>49</sup> The reaction

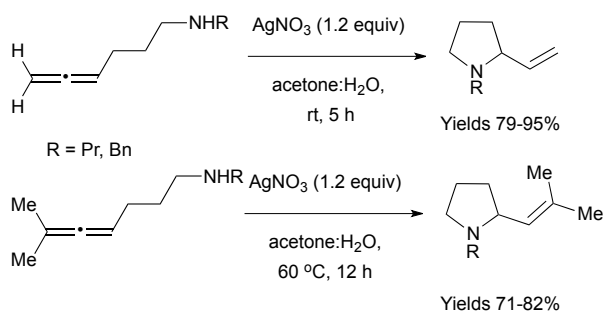
was proposed to proceed by hydrolysis of the lactam ring to give a  $\beta$ -amino ester, which cyclised via a 6-endo attack to the terminal carbon of the allenic system.



**Scheme 41** Silver-promoted reaction of a  $\beta$ -amino allene.

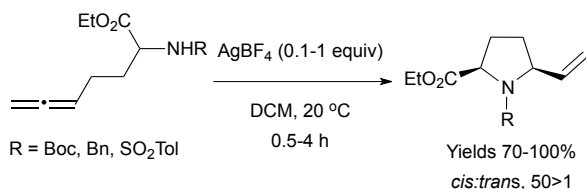
In contrast, several examples of silver-catalysed reaction of  $\gamma$ -amino allenes and  $\gamma$ -amino allene-derivatives have been reported. As in the oxygen analogues, the 5-*exo* cyclisation is the preferred pathway with formation of 2,5-disubstituted vinyl pyrrolidines, by attack of the nitrogen to the terminal carbon of the proximal double bond of the allene.

Gore *et al.* reported the reaction with 1.2 equivalents of  $\text{AgNO}_3$  of different substituted secondary  $\gamma$ -amino allenes, and they showed that while monosubstituted allenes gave the cyclisation at room temperature in 5 h, the more substituted analogous needed 12 h at 60 °C for high conversions (Scheme 42).<sup>50</sup>



**Scheme 42** Silver-promoted reaction of  $\gamma$ -amino allenes.

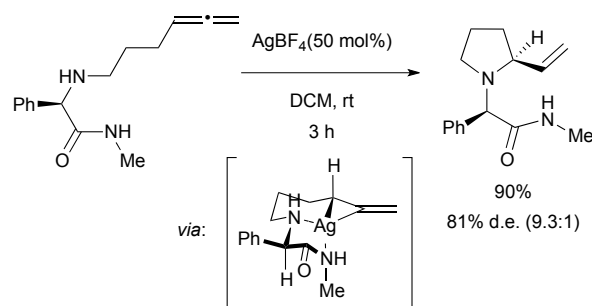
Gallagher *et al.* used 0.1-1 equivalents of  $\text{AgBF}_4$  to give stereoselectively the *cis*-2,5-disubstituted pyrrolidines, when secondary  $\gamma$ -amino allenes were used.<sup>51</sup> The primary amine, however, gave both isomers, suggesting that the physical bulk and not the electronic nature of the substituent in the nitrogen was responsible for the stereoselectivity (Scheme 43).



**Scheme 43** Stereoselective synthesis of *cis*-2,5-disubstituted pyrrolidines.

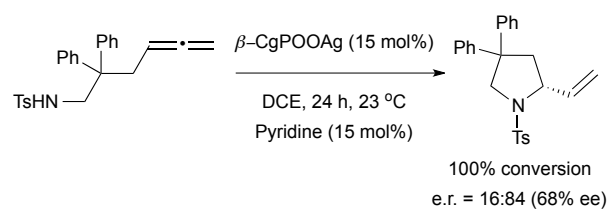
These results led to the same group to investigate the reaction of  $\gamma$ -amino allenes bearing a chiral benzylic residue on the

nitrogen.<sup>52</sup> They found that the concentration of silver salt was more important for the diastereoselectivity than the nature of the counterion ( $\text{BF}_4$  vs  $\text{TfO}$ ). With an optimal 50 mol% of silver salt, they observed that the diastereoselectivity increased with the ability of the coordinating residue on the benzylic substituent to complex the silver. The best result was obtained with amino-derivatives up to 9:1 (80% d.e.), where the major isomer was the one with the phenyl and the vinyl groups on the same side. This was explained by a chair-like conformation intermediate involving addition of silver to the *si*-face of the allene (*pseudoequatorial* conformer preferred), and interaction of the silver with the benzylic residue. Cyclisation at this point should involve a backside attack by the amine to the  $\pi$ -complex, and a second molecule of amino allene might be involved in this step (Scheme 44).



**Scheme 44** Diastereoselective synthesis of pyrrolidines from chiral derivatives.

More recently, Hii *et al.* exploited the enantioselective version of the reaction using complexes of silver with chiral counterions derived from oxophosphorous(V) phosphinate ( $\beta$ -CgPOOH) and phosphate (TADDOL-POOH, see Scheme 29).<sup>32</sup> In comparison with the reaction of the oxygen derivatives,  $\gamma$ -amino allenes gave slower reactions, probably due to slow proton transfer after cyclisation (see Scheme 28). It was found that pyridine speeds up the reaction with the  $\beta$ -CgPOOAg complex, giving the product in 24 h with up to 68% ee (Scheme 45). However, reaction with the TADDOL derivative and pyridine was inhibited.

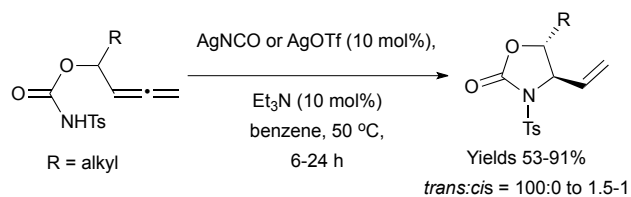


**Scheme 45** Enantioselective silver-catalysed cyclisation of  $\gamma$ -amino allenes.

Several examples have been reported with  $\gamma$ -*N*-allene derivatives such as carbamates, oximes or hydroxylamines. In all these cases, the possibility of oxygen *versus* nitrogen attack exists, and in all the cases attack of the nitrogen in a 5-*exo* mode to the proximal double bond occurs.

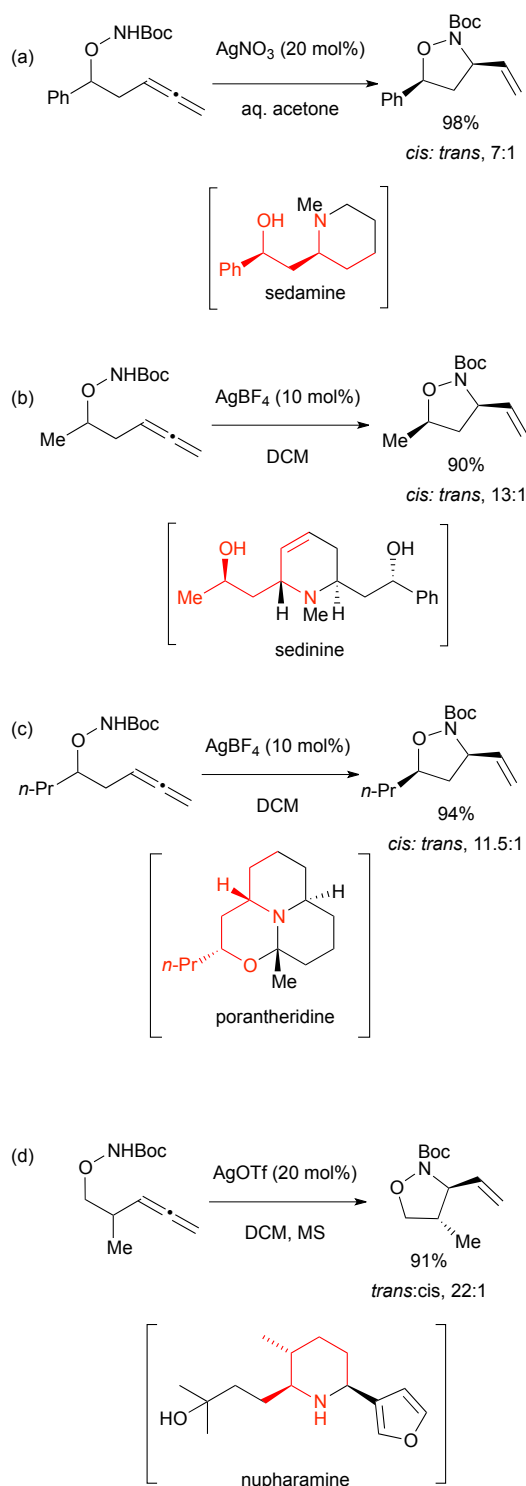
Tamaru *et al.* reported that silver-catalysed reaction of *O*-(2,3-butadienyl) *N*-tosyl carbamates occurs regio- and stereoselectively to give *trans* *N*-tosyl-4-vinyl-2-oxazolidinones as major or only isomer, in the presence of catalytic triethylamine

(Scheme 46).<sup>53</sup>



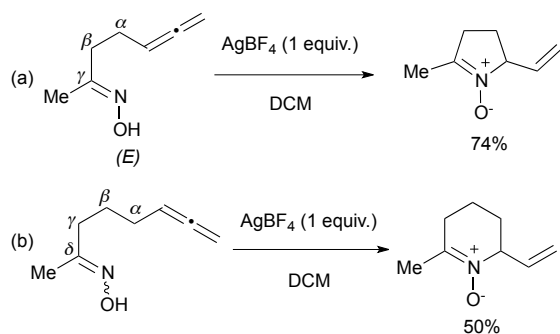
**Scheme 46** Silver-catalysed reaction of *O*-(2,3-butadienyl) *N*-tosyl carbamates.

The group of Bates *et al.* has used extensively the silver-catalysed cyclisation of allenic hydroxylamine derivatives in the total synthesis of piperidine alkaloids, such as sedamine (Scheme 47a),<sup>54</sup> sedinine (Scheme 47b),<sup>55</sup> porantheridine (Scheme 47c),<sup>56</sup> and nupharamine (Scheme 47d).<sup>57</sup> The vinyl pyrrolidine is obtained in all the cases, and then expanded by breaking the N-O bond with the construction of the 6-membered ring present in the natural product by different methods in each case.



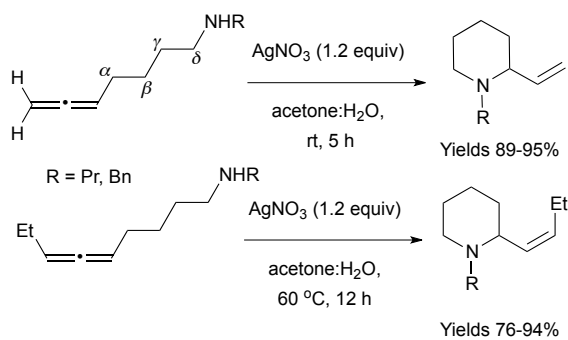
**Scheme 47** Silver-catalysed cyclisation of allenic hydroxylamine derivatives in the total synthesis of piperidine alkaloids.

Similarly, Gallagher *et al.* reported the regioselective synthesis of cyclic nitrones by silver-catalysed cyclisation of (*E*)- $\gamma$ - (Scheme 48a) and  $\delta$ -allenyl oxime derivatives (Scheme 48b).<sup>36,58</sup> In contrast to the  $\beta$ -allenic derivatives (see Scheme 33), and the (*Z*)- $\gamma$ -allenyl oxime (see Scheme 32), in this case 5- or 6-membered rings were obtained with attack of the nitrogen in all cases.



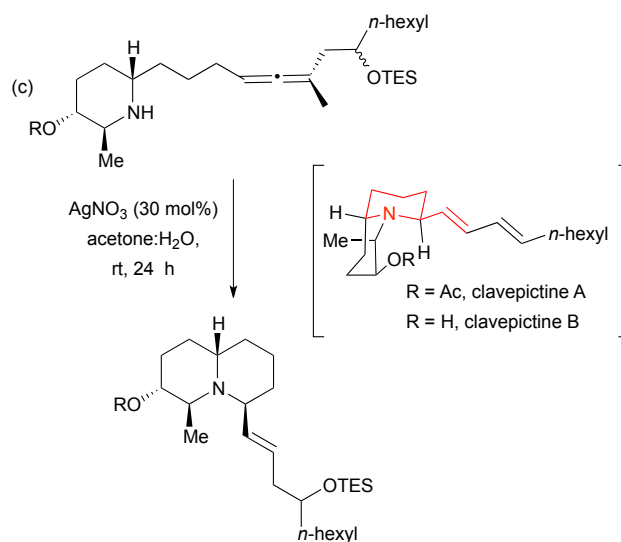
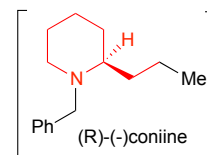
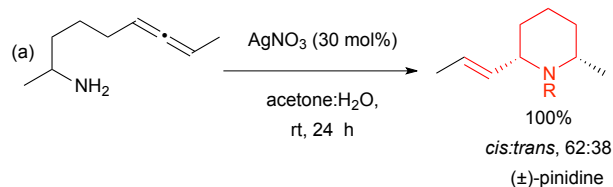
**Scheme 48** Regioselective synthesis of cyclic nitrones.

Reaction with  $\delta$ -amino allenes in the presence of stoichiometric amounts of silver salts has been reported to form piperidines by 6-*exo* attack of the nitrogen.<sup>50</sup> As in the case of the  $\gamma$ -amino allene derivatives (see Scheme 42), monosubstituted allenes gave the cyclisation at room temperature in 5 h, but the more substituted analogous needed 12 h at 60 °C for high conversions (Scheme 49).



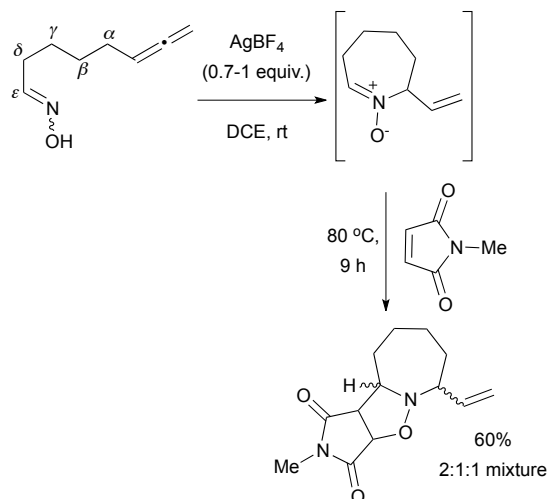
**Scheme 49** Silver-catalysed cyclisation of  $\delta$ -amino allenes.

This methodology has been also efficiently applied to the synthesis of natural products containing the piperidine ring, such as, pinidine (Scheme 50a),<sup>59</sup> coniine (Scheme 50b),<sup>60</sup> or clavепictines A and B (Scheme 50c).<sup>61</sup>



**Scheme 50** Key Steps in the synthesis of piperidine containing products.

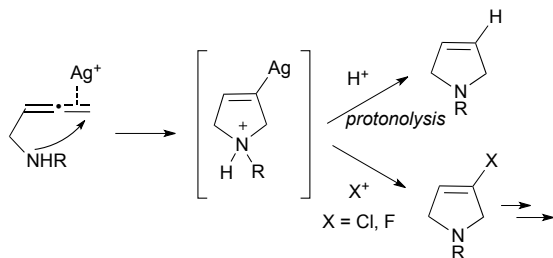
7-Membered rings containing nitrogen are more difficult to obtain than 5- or 6-membered rings. The more challenging cyclisation of  $\epsilon$ -amino allenes with AgOTf has been so far unsuccessful. However, the simple  $\epsilon$ -allenyl oxime derivative gave the 7-*exo* cyclisation to form a cyclic nitron, which, although unstable, could be trapped *in situ* by 1,3-dipolar addition with *N*-methylmaleimide (Scheme 51).<sup>36</sup>



**Scheme 51** Silver-mediated formation of 7-membered ring nitronne trapped *in situ*.

### 2.3. Intramolecular Haloamination

In all the examples described for the intramolecular silver-catalysed hydroamination of allenes, coordination of the silver to one of the double bonds, and attack of the nitrogen to form a vinyl-silver intermediate is proposed. In the hydroamination reaction, protonolysis is the final step to release the product and regenerate the catalysts. However, in recent years, addition of halogenated electrophiles has been employed to break the C-Ag bond and form a C-X (X = halogen), which will give alkenyl halide moieties, as very useful building blocks for further functionalization (Scheme 52).

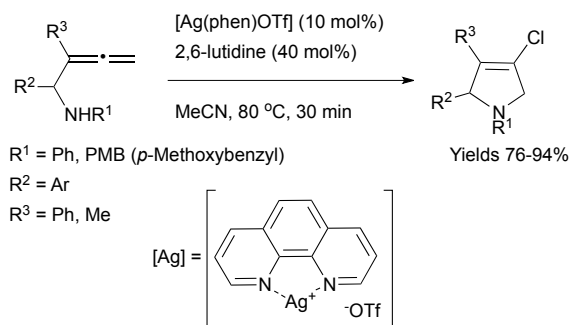


**Scheme 52** Protonolysis versus halogenolysis of vinyl-silver intermediates.

Although this review covers the addition of N-H bonds to allenes, addition of N-X bonds to unsaturated moieties has become increasingly important due to the high potential of the products formed for further functionalization, and therefore, we consider that mention to these reactions is pertinent in this review.

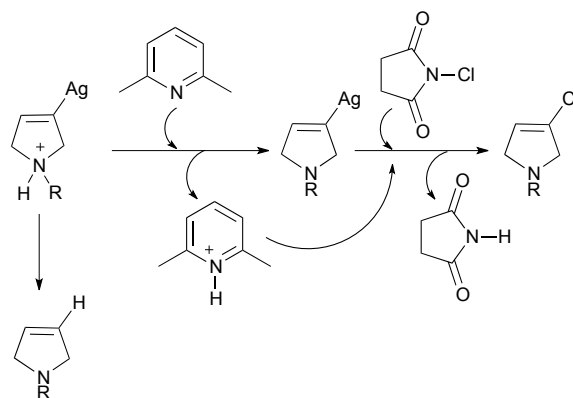
Two examples have been reported for the silver-catalysed aminochlorination and aminofluorination of  $\alpha$ -aminoallenes to give functionalised pyrrolines. The chloroamination reaction was catalysed by [Ag(phen)OTf] in the presence of NCS (*N*-chlorosuccinimide) and 2,6-lutidine as base to prevent formation of the dehalogenated product. The reaction seems general for 1,1-disubstituted  $\alpha$ -aminoallenes, and tolerates a variety of functional

groups (Scheme 53).<sup>62</sup>



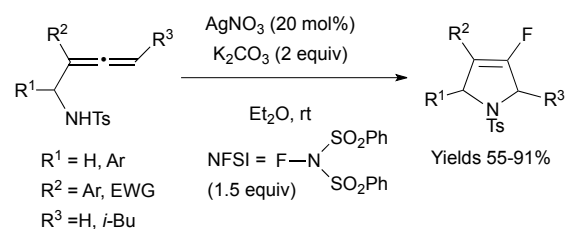
**Scheme 53** Silver-catalysed chloroamination of aminoallenes.

Although chlorination on the nitrogen of the amino allene was observed, mechanistic investigations showed that this was not involved in the reaction either as intermediate or chlorinating agent. The base was proposed to deprotonate the intermediate after cyclisation, to avoid protonolysis and favour the chlorination step (Scheme 54).



**Scheme 54** Role of the base in the silver-catalysed chloroamination of allenes.

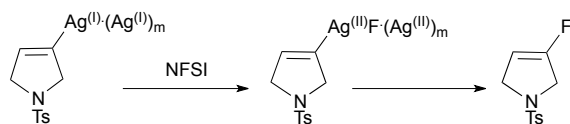
The fluoroamination of  $\alpha$ -amino allenes has been reported to proceed with catalytic  $\text{AgNO}_3$  and NFSI, in the presence of 2 equivalents  $\text{K}_2\text{CO}_3$  as base.<sup>63</sup> The reaction works well for *N*-tosyl derivatives with aromatic or electron-withdrawing substituents in the allene, but alkyl substituted ones gave lower yields. Six-membered rings could also be obtained by reaction with  $\beta$ -amino allenes (Scheme 55).



**Scheme 55** Silver-catalysed fluoroamination of aminoallenes.

Preliminary mechanistic hypothesis involves oxidation of the vinyl-Ag(I) to a vinyl-Ag(II) fluoride, which suffers reductive

elimination. Multinuclear silver complexes might be involved to facilitate the one-electron redox chemistry (Scheme 56).



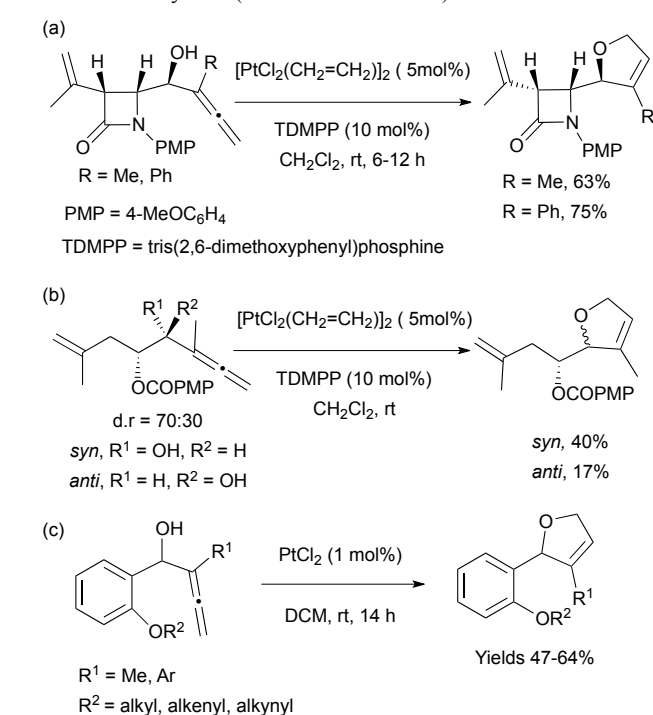
5 **Scheme 56** Multinuclear silver complexes involved in the redox process.

### 3. Platinum-Catalysed Reactions

#### 3.1. Intramolecular Addition of O-H

10 Similarly to the silver process, intramolecular addition of oxygen nucleophiles to allenes catalysed by platinum is a very versatile tool for the construction of oxygen-heterocycles. The advantage of platinum is that only small catalytic amounts are needed, and no stoichiometric quantities have to be employed even in the

15 more challenging cases. Different ring-sizes can be obtained depending on the substitution pattern of the starting material and the platinum complex employed. The reaction of  $\alpha$ -allenols gives preferentially dihydrofurans by 5-endo attack of the oxygen to the distant double bond. 20 Interesting examples have been reported by Alcaide, Almendros *et al.*,<sup>49,64</sup> where the reaction proceeds even with  $\beta$ -lactam based enallenols, possessing an extra double bond in the molecule. They found high chemo-differentiation depending on the metal used, and while platinum and gold tend to activate the allene,



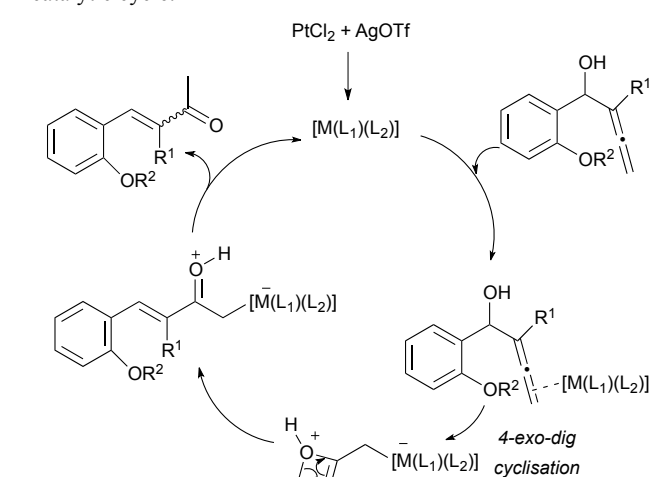
30 **Scheme 57** Platinum-catalysed reaction of  $\alpha$ -allenols.

However, when the catalytic system was changed to  $\text{PtCl}_2/\text{AgOTf}$ , a complete switch in selectivity was observed, and  $\alpha,\beta$ -unsaturated ketones were obtained through a rearrangement



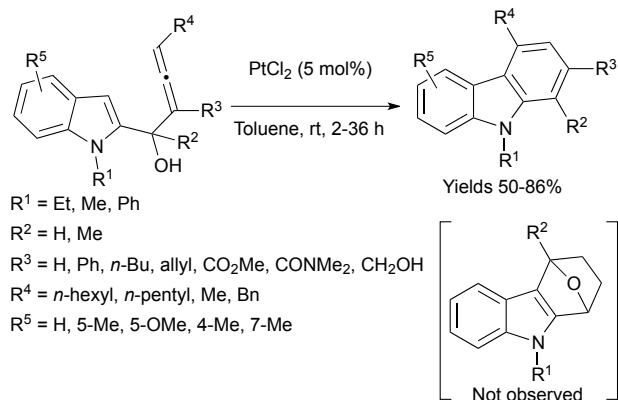
**Scheme 58** Change in selectivity with Pt/Ag systems.

It is very interesting to note that when the reaction was done with 40 a silver free Pt-catalysts, performed by mixing a 1:1 mixture of  $\text{PtCl}_2$  and  $\text{AgOTf}$  and filtering the  $\text{AgCl}$ , the dihydrofuran was obtained and none of the ketone was observed. Although the nature of the active catalytic species remain unknown, silver alone does not catalysed the reaction, pointing to the crucial role



60 **Scheme 59** Mechanistic proposal for the formation of  $\alpha,\beta$ -unsaturated ketones.

*Ma et al* reported the reaction of 1-(indol-2-yl)-2,3-allenols in the presence of  $\text{PtCl}_2$ . However, instead of forming polycyclic 65 products with the attack of the  $\alpha$ -hydroxy group and the indole, they obtained carbazoles as the only product in good yields (Scheme 60).<sup>67</sup>

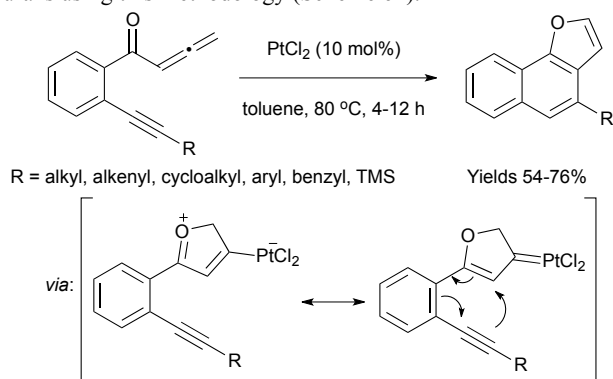


**Scheme 60** Synthesis of carbazoles from 1-(indol-2-yl)-2,3-allenols.

In this reaction only the indole acts as the nucleophile, and the hydroxyl group is lost as water helping to gain aromaticity after cyclisation.

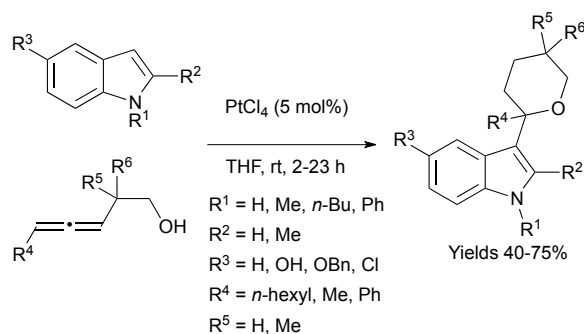
Interestingly, metal-catalysed cyclisation of oxyallenes C3-linked indoles proceeds in different ways depending on the metal and the group on the nitrogen. For example, oxycyclisation to give hydrofurans is observed with gold catalysts when the nitrogen is protected, but with N-H derivatives, benzannulation and Nazarov type chemistry are the preferred pathways with gold and palladium.<sup>68</sup>

Similarly to  $\alpha$ -allenyl alcohols,  $\alpha$ -allenyl ketones can react in the presence of platinum complexes to form furans. The vinyl platinum intermediates proposed in these reactions have some character of platinum carbene, and in the presence of extra unsaturations, can give tandem reactions to form more complex structures. Xu *et al.* described the synthesis of naphtho[1,2-*b*]-furans using this methodology (Scheme 61).<sup>69</sup>



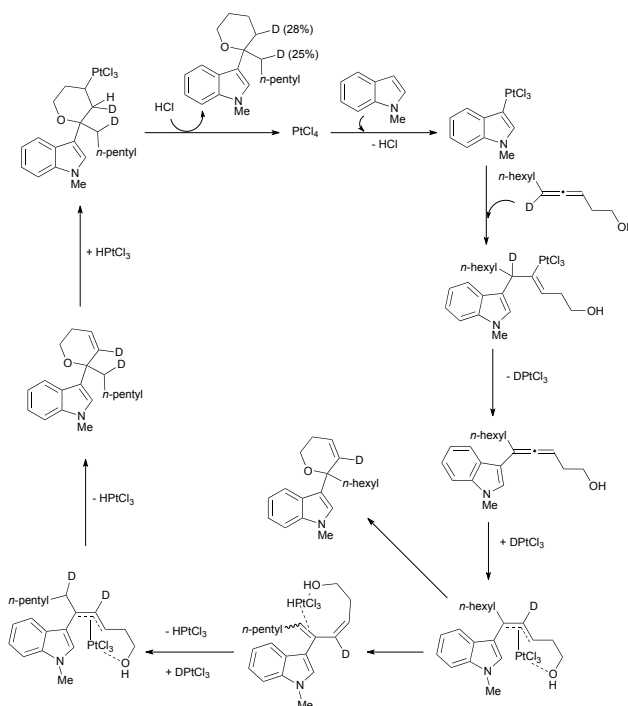
**Scheme 61** Platinum-catalysed reaction of  $\alpha$ -allenyl ketones.

Platinum-catalysed reaction of  $\beta$ -allenols has been less explored. In 2009, Ma *et al.* reported the Pt(IV)-catalysed reaction of indoles with  $\beta$ -allenols. In this reaction indoles containing a six-membered ring ether at the C-3 position were obtained in moderate yields (Scheme 62).<sup>70</sup>



**Scheme 62** Platinum-catalysed reaction of  $\beta$ -allenols.

The proposed mechanism, based in deuterium labelling studies, starts with formation of an indolyl platinum trichloride, which could go carbometallation with the allenol to give a vinyl-platinum intermediate. This intermediate can suffer  $\beta$ -H elimination and generate an indole containing allenol. To explain the observed deuterium incorporation, instead of 6-*endo* direct attack of the oxygen into the allenic system, the authors proposed a series of  $\beta$ -H elimination/hydrometalation steps with H/D-PtCl<sub>3</sub> generated *in situ*, to give a  $\pi$ -allyl platinum complex that can undergo intermolecular allylic substitution with the oxygen nucleophile. The complete saturation in the six-membered ring is explained by hydrometalation of the formed double bond and protonolysis of the dihydropyran intermediate (Scheme 63).

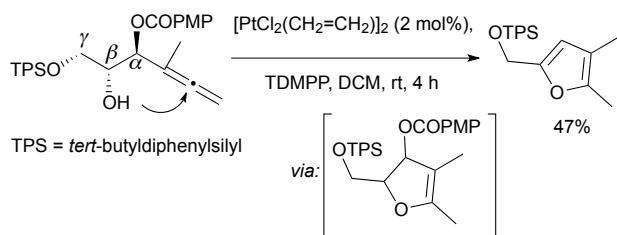


**Scheme 63** Mechanistic proposal for the platinum-catalysed reaction of indoles with  $\beta$ -allenols.

Alcaide, Almendros *et al.* have studied in depth the reaction of  $\beta$ -,  $\beta,\gamma$ - and  $\gamma,\delta$ -allenols derived from *D*-glyceraldehyde in the presence of several metals, finding divergent reactivity depending on the metal, reaction conditions and substitution in the starting allenic system.

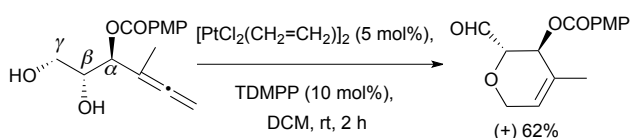


Unexpected 5-*exo* cyclisation to form a furan derivative was observed in the reaction with  $\beta$ -allenols with the complex  $[\text{PtCl}_2(\text{CH}_2=\text{CH}_2)]_2$  and TDMPP (Scheme 64).<sup>71</sup> The reaction seems to proceed by attack of the oxygen into the central carbon of the allene (not a very common reactivity) to give a dihydrofuran that aromatises under the reaction condition.



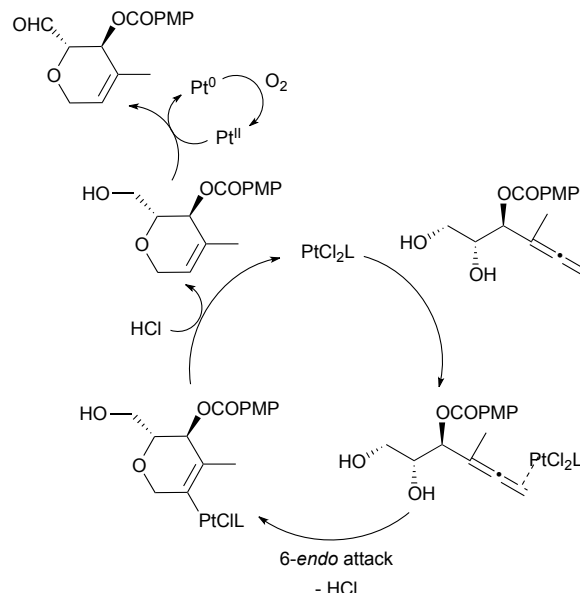
**Scheme 64** Platinum-catalysed reaction of  $\beta$ -allenol derived from *D*-glyceraldehyde.

However, the reaction of the analogous  $\beta,\gamma$ -allenol by removal of the TPS-group, under the similar reaction conditions gave chemo- and regioselective cyclisation of the secondary hydroxyl group ( $\beta$ -OH) at the distal double bond (6-*endo*), with concurrent oxidation to give the dihydropyran-aldehyde derivative (Scheme 65).<sup>72</sup> This aldehyde was not very stable, but could be trapped in situ by a stabilised Wittig reagent.



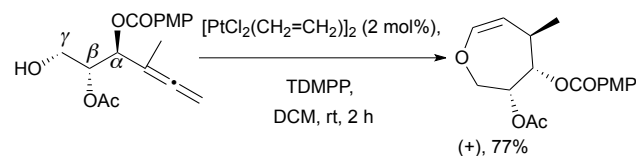
**Scheme 65** Platinum-catalysed reaction of  $\beta,\gamma$ -allenol derived from *D*-glyceraldehyde.

The mechanism proposed for the formation of the oxidised product goes *via* the 6-*endo* oxyplatination of the activated  $\pi$ -complex to form, in the first instance the expected (dihydropyranyl)methanol derivative. This intermediate can be transformed into the aldehyde by aerobic oxidation. When isolated (dihydropyranyl)methanol, which is the product from the gold-catalysed reaction, was reacted in the presence of the platinum catalyst in oxygen atmosphere, the aldehyde was formed in 70% yield (Scheme 66).



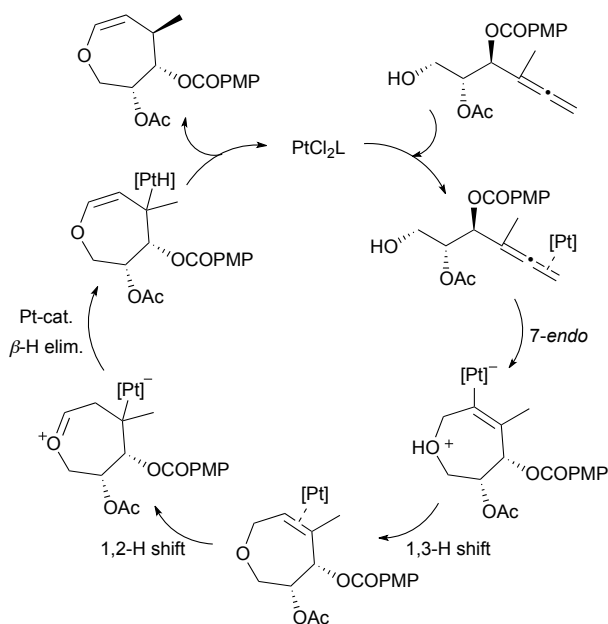
**Scheme 66** Mechanism to explain formation of the oxidised product.

Reaction of the analogous  $\gamma$ -allenol, with the  $\beta$ -hydroxy group protected as an acetate under the same conditions gave the tetrahydrooxepine by activation of the distal double bond and 7-*endo* cyclisation with concomitant isomerisation of the double bond (Scheme 67).<sup>71</sup>



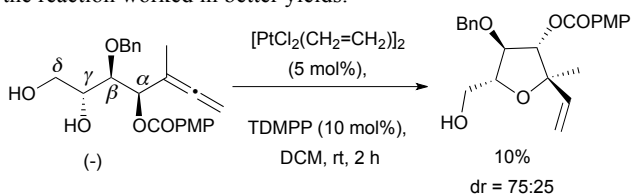
**Scheme 67** Platinum-catalysed reaction of  $\gamma$ -allenol derived from *D*-glyceraldehyde.

DFT calculations support a mechanism where after 7-*endo* cyclisation, a 1,3-H shift will give the  $\pi$ -complexed oxalacycle, which is the regioisomer obtained in the gold-catalysed reaction. This intermediate suffers a 1,2-H migration assisted by a halide ligand, a platinum-catalysed  $\beta$ -H elimination to regenerate the platinumacycle intermediate and final protonolysis to give the isomerised product (Scheme 68). Platinum has a higher tendency to undergo  $\beta$ -H elimination and form platinum-hydrides than gold, which is in accordance with the experimental results obtained by the two metals.



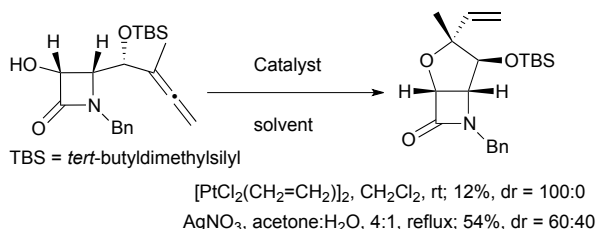
**Scheme 68** Mechanism for the platinum-catalysed 7-endo cyclisation.

Reaction of the  $\gamma,\delta$ -allenic unprotected diol, although reacting through the  $\gamma$ -hydroxy group selectively, didn't give the 7-endo product. In this case, the  $\gamma$ -hydroxy group attack in a 5-*exo*-cyclisation to give the tetrahydrofuran in low yield and diastereoselectivity (Scheme 69). This was also the preferred product in the gold(III)- and lanthanide-catalysed reactions, and the reaction worked in better yields.<sup>72</sup>



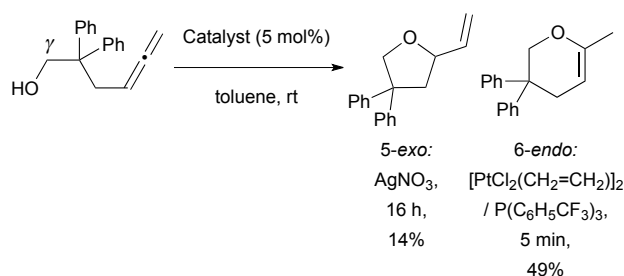
**Scheme 69** Platinum-catalysed reaction of  $\gamma,\delta$ -allenol derived from *D*-glyceraldehyde.

Similarly, reaction of  $\beta$ -lactam based  $\gamma$ -allenols gave low yield and diastereoselectivity towards the 5-*exo* cyclisation in the presence of platinum and silver salts (Scheme 70).<sup>73</sup> These compounds were much better substrates for gold, palladium and even lanthanide-catalysed reactions, to give regioselectively tetrahydrofurans, dihydropyrans or tetrahydrooxepines depending on the metal employed and the substitution pattern in the allene.



**Scheme 70** Platinum-catalysed reaction of  $\beta$ -lactam based  $\gamma$ -allenols.

Widenhofer *et al.* also reported low reactivity of a simple  $\gamma$ -allenols in the presence of platinum and silver catalysts.<sup>74</sup> In their example,  $\text{AgNO}_3$  catalysed the 5-*exo* cyclisation in very low yield and conversion, while the platinum complex gave preferentially the 6-*endo* product in moderate yield (Scheme 71). Again, gold catalysts showed better results with this type of substrates.

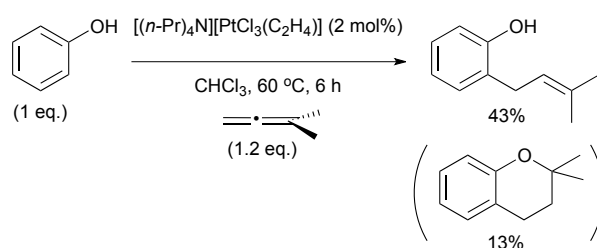


**Scheme 71** Platinum-catalysed reaction of simple  $\gamma$ -allenols.

### 3.2. Intermolecular Addition of O-H

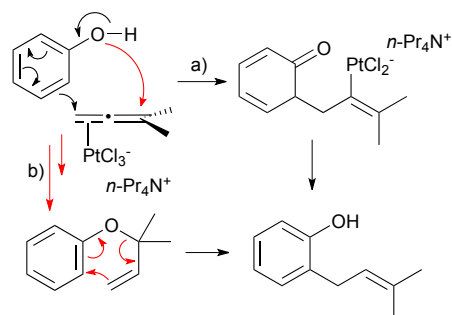
As we have mentioned in the introduction, intermolecular reaction of allenes and nucleophiles have been explored with platinum catalysis, and different reactivity has been encountered depending on the nucleophile and the catalytic system employed.

The first reported example of the intermolecular platinum-catalysed reaction of allenes and alcohols is the work by Panunzi *et al.*<sup>75</sup> In their paper instead of attack of the oxygen at the nucleophile, the authors reported the reaction of 1,1-dimethyl allenes with phenols to give the regioselective *C*-alkenylation of the aromatic ring (Scheme 72). They also isolated chroman derivatives, but they proposed they are formed after the alkenylation by reaction of the phenol with the alkene catalysed by the platinum complex.



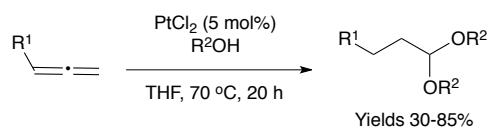
**Scheme 72** Platinum-catalysed reaction of allenes and phenols.

The authors invoke formation of vinyl-platinum intermediates by the attack of the phenol, as the electron-rich aromatic nucleophile, to the less substituted carbon of the allene, activated by the platinum complex (Scheme 73, path a). However, the attack of the oxygen to the more substituted carbon followed by a Claisen rearrangement, would give also the same product (Scheme 73, path b). The corresponding ethers were not detected in the reaction, and therefore the mechanism of *C*-attack to the less substituted terminus of the allene was preferred.



**Scheme 73** Possible mechanisms to obtain C-alkenylation.

More recently our group has discovered a new reactivity in the reaction of allenes and alcohols in the presence of platinum chloride.<sup>76</sup> In our work, instead of mono addition and formation of allyl ethers, as reported with other metals, like gold, addition of two molecules of alcohol to the terminal carbon of the allene with complete saturation of the second double bond was observed, to give aliphatic acetals (Scheme 74).

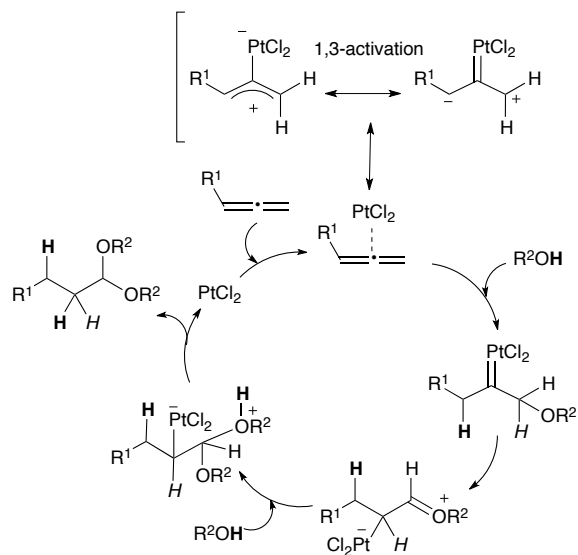


R<sup>1</sup> = Cy, *n*-Hexyl, CH<sub>2</sub>C(CO<sub>2</sub>Me)<sub>2</sub>, CH<sub>2</sub>-phthalimide, Ph, tolyl  
R<sup>2</sup>OH = MeOH, EtOH, BuOH, PhCH<sub>2</sub>OH, OH(CH<sub>2</sub>)<sub>3</sub>OH

**Scheme 74** New reactivity in the platinum-catalysed reaction of allenes and alcohols.

The reaction works only for mono-substituted allenes with different alcohols, including diols to give cyclic acetals. The construction of aldehydes was possible when the reaction was carried out in water.

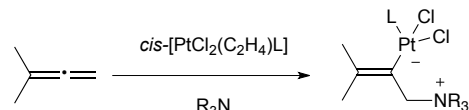
Preliminary mechanistic studies ruled out the involvement of allyl ethers and alkynes as intermediates in this reaction. Deuteration studies showed total incorporation of two deuterium atoms, one on the central carbon and the other one in the internal more substituted carbon of the allene. This suggested a different mechanism involving activation of the allene by the coordination of the platinum to the central carbon, like in a zwitterionic platinum carbene, and 1,3 addition of the alcohol to the allene to form a platinum carbene as the key intermediate. 1,2-H-shift from this intermediate, assisted by the oxygen atom, and attack of the second molecule of alcohol will furnish the intermediate ready for protonolysis to give the acetal and regenerate the platinum complex (Scheme 75).<sup>77</sup>



**Scheme 75** Mechanistic proposal for the platinum-catalysed formation of acetals.

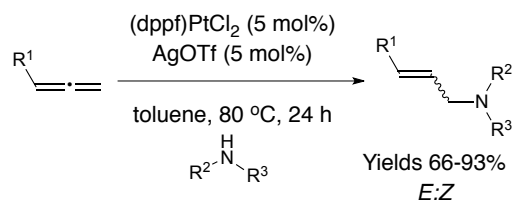
### 3.3. Intermolecular Addition of N-H

In contrast to the example with alcohols as nucleophiles, the reaction of allenes with amines in the presence of platinum seems to follow the normal reactivity pattern to give allyl amines as products. In the stoichiometric reaction of  $\eta^2$ -allene-Pt complexes with amines reported by Panunzi *et al.*,<sup>78</sup> vinyl-platinum complexes from the attack of the amine to the less substituted carbon of the allene were isolated (Scheme 76). Reaction of the vinyl-platinum intermediates with HCl gave the corresponding allyl amines.



**Scheme 76** Stoichiometric reaction of allenes and platinum complex to form isolable vinyl-platinum complexes.

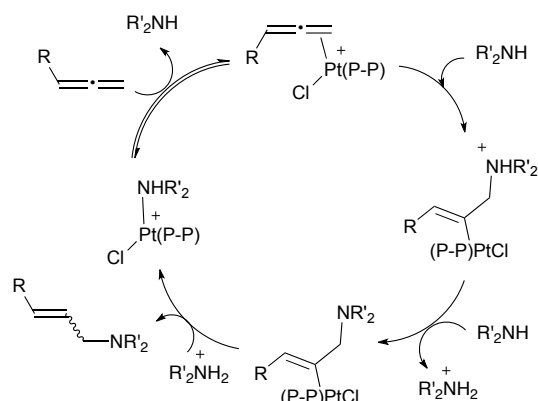
More recently, Widenhoefer *et al.* have developed the catalytic version of this reaction using (dppf)PtCl<sub>2</sub>/AgOTf as catalyst.<sup>79</sup> The reaction works for secondary alkylamines and the best yields and selectivity towards the *E*-allyl amines were obtained using biphosphine ligands, such as dppf in the platinum catalyst. The scope is limited to mono-substituted allenes (Scheme 77).



R<sup>1</sup> = CH<sub>2</sub>C(CO<sub>2</sub>Me)<sub>2</sub>, *n*-octyl, Cy, Bn, Ph, 2-naphthyl  
R<sup>2</sup>, R<sup>3</sup> = Bn, *n*-Bu, Me, Et, morpholine, piperidine, pyrrolidine

**Scheme 77** Platinum-catalysed hydroamination of allenes.

The proposed mechanism involves formation of a cationic platinum complex and  $\eta^2$ -coordination to the less substituted double bond of the allene. Outer-sphere mechanism with attack of the amine to the terminal carbon of the activated double bond would give the vinyl-platinum intermediate similar to the one isolated by Panunzi (Scheme 78).



**Scheme 78** Mechanistic proposal for the platinum-catalysed formation of allyl amines.

#### 4. Conclusions

In this review, the silver and platinum-catalysed reaction of allenes and oxygen and nitrogen nucleophiles have been covered. We have shown that both metals are very useful for the synthesis of functionalised molecules containing oxygen and nitrogen, and the intramolecular version has been applied in the synthesis of many natural products.

The intramolecular silver-catalysed or promoted reaction has been known for a long time, and predictable trends are generally followed: when  $\alpha$ - and  $\beta$ -allenols or amino allenes are used, 5- or 6-*endo* attack of the heteroatom to the terminal carbon of the distal double bond of the allene occur. However, with longer chains, as in  $\gamma$ - and  $\delta$ -derivatives, the 5- or 6-*exo* attack to the terminal carbon on the proximal double bond takes place. These reactions are in most cases stereoselective, but only recently, important advances towards enantiomeric examples using chiral counterions in the silver have been reported. Controlling the stoichiometry of the reaction with silver for the most challenging cases is also a remaining task that will have to be confronted in the near future if we want this reaction to be efficiently applied in the synthesis of natural products.

Platinum catalysis, although follow similar trends than silver, is less predictable, and recent examples have shown new reactivities: in the intramolecular reaction, 4-*exo* cyclisation, 5-*exo* cyclisation with attack to the central carbon, or 7-*endo* cyclisations have been reported; and in the intermolecular versions new interaction allene-metal have been proposed. However, although transfer of chirality has been shown to occur, as in the examples by Alcaide, Almendros *et al.* with derivatives of the *D*-glyceraldehyde, the platinum-catalysed enantiometric version with chiral ligands is still to be uncovered.

While silver and platinum are sometimes neglected in favour to

the more fashionable gold catalysis, they keep showing to be very versatile metals and many new examples have appeared in the past five years as shown in this review. Many avenues remain to be explored and it will be interesting to see the surprises that this too metals, and platinum in particular will bring in the following years.

#### Notes and references

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