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Platinum-Catalyzed Divergent Reactivity of α-Hydroxyallenes: Synthesis of Dihydrofurans and α,β-Unsaturated Ketones

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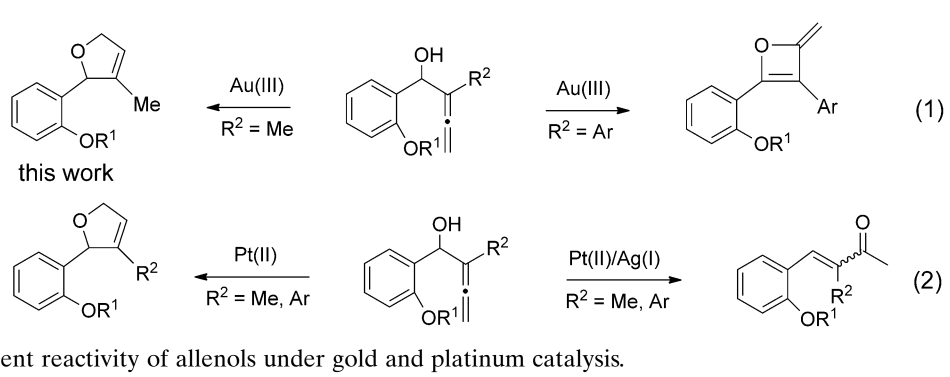
Abstract: α-Allenols were catalytically transformed into dihydrofurans in the presence of platinum dichloride. Notably, using platinum dichloride along with silver triflate as the catalytic system, α,β-unsaturated ketones were obtained. Therefore, the role of the silver salt may not just consist in the activation of the platinum precatalyst.

Keywords: allenes; heterocycles; homogeneous catalysis; platinum; regioselectivity

The use of gold and platinum salts has gained a lot of attention in the recent times because of their powerful soft Lewis acidic nature. The employment of silver additives is a common practice to enhance the activity of the gold catalyst.[1,2] By contrast, it is challenging to develop catalytic systems employing platinum salts and silver additives.

Allenes, a class of compounds with two cumulative carbon-carbon double bonds, are versatile synthetic intermediates in organic synthesis.[3] Following up on our combined interest in the area of metals and allenes,[4] we have recently communicated the gold-catalyzed synthesis of oxetenes through rare 4-*exo*-dig allene cyclization of salicylaldehyde-derived α-allenols [Scheme 1, Eq. (1)].[5]

In contrast to gold catalysis,[6,7] the platinum-catalyzed reactions using allenols as substrates constitute an almost unexplored field of noble metal catalysis. Platinum salts have been used for the oxycyclization of β-allenols and γ-allenols,[8–10] but not for the oxycyclization of α-allenols. The only report on the Pt-catalyzed reaction of α-allenols is the carbocyclization rather than the oxycyclization of 1-(indol-2-yl)-2,3-allenols to provide substituted carbazoles.[11] Taking into account the analogies in the catalytic behavior of



Scheme 1. Divergent reactivity of allenols under gold and platinum catalysis.

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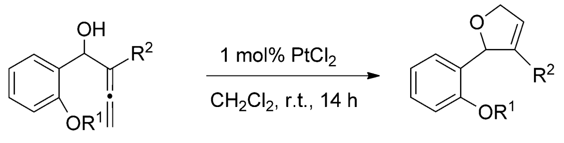
Au and Pt compounds, we decided to study the reactivity of α-hydroxyallenes under platinum catalysis. We wish to report here that the reaction outcome for the platinum-catalyzed reactions of allenols sharply contrasts to that of gold catalysis,[12] because the preparation of both dihydrofurans and α,β-unsaturated ketones *via* platinum catalysis can be efficiently controlled [Scheme 1, Eq. (2)].

Our initial studies concentrated on the platinum-catalyzed cyclization reaction of α-allenol **1a**. Nicely, it was found that $PtCl_2$ or $[PtCl_2(CH_2{=}CH_2)]_2$ were competent catalytic systems for this purpose. Solvent screening demonstrated that dichloromethane was the best choice in the reaction. 1 mol% of $PtCl_2$ provided dihydrofuran **2a** in 64% yield after reacting overnight at room temperature in dichloromethane. Notably, platinum-based catalysis favors a 5-*endo*-trig pathway, while our previous report on gold-based catalysis afforded an oxetene through 4-*exo*-dig cyclization.[5] Thus, complete selectivity can be achieved by using both Au- and Pt-based catalysis. To evaluate the general applicability of this cycloisomerization protocol, a series of aryl- or methyl-substituted allenol derivates **1b–h** was oxycyclized under the same reaction conditions. All of the reactions delivered the substituted dihydrofurans **2b–h** in good yields within acceptable reaction times (Scheme 2). The above results indicate that the Pt-catalyzed reaction shows complementarity with the Au-catalyzed process.

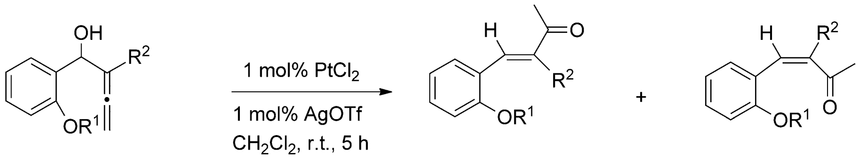


1a R^1 = prop-2-enyl, R^2 = Ph	**2a** (64%)
1b R^1 = 2-methylallyl, R^2 = Ph	**2b** (59%)
1c R^1 = prop-2-ynyl, R^2 = Ph	**2c** (47%)
1d R^1 = methyl, R^2 = Ph	**2d** (55%)
1e R^1 = 2-methylallyl, R^2 = 4-$MeOC_6H_4$	**2e** (53%)
1f R^1 = 2-methylallyl, R^2 = Me	**2f** (51%)
1g R^1 = methyl, R^2 = Me	**2g** (64%)
1h R^1 = but-2-ynyl, R^2 = Me	**2h** (59%)

Scheme 2. Platinum-catalyzed cycloisomerization of allenols **1**.

After identifying an appropriate catalyst for the oxycyclization reaction, we optimized other critical reaction parameters, such as the addition of additives. No benefit occurs across the addition of a phosphine, because the use of $PtCl_2$ in the presence of tris(2,6-dimethoxyphenyl)phosphine gave dihydrofurans **2** in similar yields. In particular, the transformation was strongly influenced by the presence of a silver-based additive. To our surprise, a complete switch of the reactivity was observed when using silver in the process. Gratifyingly, it was found that α-allenol **1a** on exposure to the system $PtCl_2$ (1 mol%)/AgOTf (2 mol%) in dichloromethane at room temperature for 5 h, directly afforded α,β-unsaturated ketone **3a** through a rearrangement process. Changes on the nature of the counterion had little effect in the reaction, because alternate counterions ($AgSbF_6$, $AgBF_4$) showed a minimal effect to improve the yield of the product. We also found that the rearrangement adduct **3a** could be obtained in the presence of 1 mol% $PtCl_2$ and 1 mol% AgOTf (Scheme 3). The above catalytic system was applicable to a variety of allenol derivatives **1b–h**. Thus, starting from **1a–h** the reaction afforded the linear adducts **3a–h** in 41–84% yields with an *E*/*Z* stereoselectivity of 0:100–100:0 as deduced from ^{1}H NMR analysis of the crude reaction mixtures (Scheme 3). Interestingly, adducts **3a**, **3f**, **3g**, and **3h** were exclusively formed as *E*-alkenes, while *Z*-**3e** was achieved as a single isomer. Fortunately, for alkenes **3b–d** the *E*- and *Z*-isomers were chromatographically separable, which allows the isolation of the thermodynamically less stable *Z*-alkenes. Interconversion of the isolated *Z* form of adducts **3c** and **3d** into the *E* configuration spontaneously occurs after several days at room temperature.

Noticeably, despite the above ability (Scheme 2) of platinum-based catalysis for the cycloetherification of



1a R^1 = prop-2-enyl, R^2 = Ph	(*E*)-**3a** (56%)	
1b R^1 = 2-methylallyl, R^2 = Ph	(*E*)-**3b** (47%)	(*Z*)-**3b** (19%)
1c R^1 = prop-2-ynyl, R^2 = Ph	(*E*)-**3c** (17%)	(*Z*)-**3c** (24%)
1d R^1 = methyl, R^2 = Ph	(*E*)-**3d** (41%)	(*Z*)-**3d** (30%)
1e R^1 = 2-methylallyl, R^2 = 4-$MeOC_6H_4$		(*Z*)-**3e** (55%)
1f R^1 = 2-methylallyl, R^2 = Me	(*E*)-**3f** (84%)	
1g R^1 = methyl, R^2 = Me	(*E*)-**3g** (62%)	
1h R^1 = but-2-ynyl, R^2 = Me	(*E*)-**3h** (60%)	

Scheme 3. Platinum-catalyzed rearrangement of allenols **1**.

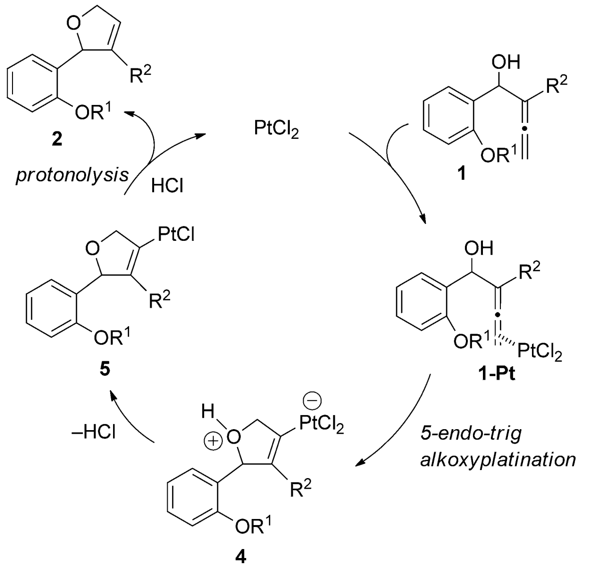
α-allenols **1** to dihydrofurans **2**, no traces of heterocycles were detected using a silver salt as additive (Scheme 3). After control experiments it was demonstrated that the silver salt alone does not catalyze the reaction of interest, and a major part of allenol **1** was recovered unaltered. Thus, it may be safely assumed that the role of the silver salt just consists in the activation of the platinum precatalyst. However, despite proving that the silver activator itself is unreactive, we decided to study how the Ag(I) additive affected the reactivity of the platinum(II)-catalyzed reaction.

A hypothetical Pt-based species free of silver was prepared by premixing for a few minutes $PtCl_2$/AgOTf (1:1) in dichloromethane under Schlenk conditions, followed by filtration through a pack of dry Celite.[13] Thus, a direct comparison of the reactivity with or without the presence of AgCl may be carried out. Worthy of note, the above Pt-based catalyst could not promote the rearrangement reaction of allenol **1f**, giving instead the cycloisomerization adduct **2f**. However, when the mixture of $PtCl_2$ and AgOTf was used directly (without filtration of AgCl), the reaction worked as described in Scheme 3. Interestingly, a mixture of the Pt-based complex obtained from filtration through Celite and AgOTf promoted the rearrangement reaction effectively, which suggested that the combination of platinum and silver made the α,β-unsaturated ketone formation possible. These joined experiments point to the crucial role of silver additives in the platinum-catalyzed reaction of α-allenols. Unfortunately, we were unable to get a crystal structure of the catalyst.

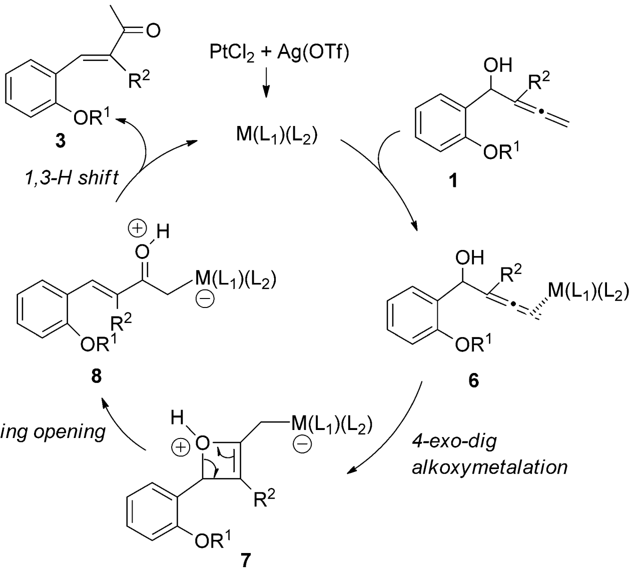
All the successful α,ß-unsaturated ketone formations occurred from 2-alkoxy-substituted α-hydroxyallenes **1**. It is possible that the 2-alkoxy group represents the optimal balance in its ability to both give a good conversion in a reasonable time and coordinate to any metallic species, avoiding the five-membered ring formation.

The achievement of dihydrofurans **2** involving a platinum-based carbophilic π-acid very likely proceeds through a similar reaction mechanism to that reported by us for the gold-catalyzed oxycyclization of allenols.[5] Thus, the initial η-coordination of the metal to the distal double bond of allenols **1** leads to species **1-Pt**, which undergoes a 5-*endo*-trig alkoxyplatination to form zwitterionic dihydrofurans **4**. Loss of HCl in intermediates **4** generates neutral vinylmetal species **5**. Finally, protonolysis of the carbon-platinum bond of **5** liberates dihydrofurans **2** with concomitant regeneration of the Pt(II) catalytic species (Scheme 4).

A mechanistic rationale for the platinum-catalyzed conversion of α-allenols **1** into α,β-unsaturated ketones **3** is more intricate. It is worth noting that the platinum-catalyzed reaction in the presence of the silver additive affords adducts **3** through a rearrangement process instead of oxacycles *via* the usually preferred gold- or platinum-catalyzed cycloetherification reactions. Although speculative at the present moment, the pathway proposed in Scheme 5 could be feasible. It could be presumed that the initially formed metallic complex **6**, through coordination of the metal to the distal allenic double bond of allenols **1**, undergoes a 4-*exo*-dig metala-oxycyclization, giving rise to the oxetene intermediates **7**. Heterocycle ring opening in intermediates **7** through an electrocyclic reaction generates zwitterionic α,β-unsaturated ketones **8**. Subsequent demetalation linked to proton



Scheme 4. Mechanistic explanation for the platinum-catalyzed cycloetherification of allenols **1**.



Scheme 5. Mechanistic explanation for the platinum-catalyzed rearrangement of allenols **1**.

transfer liberates adducts **3**, closing the catalytic cycle and releasing the catalytic species (Scheme 5).

To shed light on the active participation of the allenic alcohol moiety in the transformation from **1** to **3**, an ^{18}O-labeling experiment was initiated. Mass spectrometric analysis of the product of reaction of allenol **1f** under $PtCl_2$-AgOTf catalysis in the presence of 100 mol% $H_2{}^{18}O$, showed that the α,β-unsaturated ketone **3f** (obtained in a diminished yield of 25%) was not ^{18}O-labeled, revealing that the carbonylic oxygen atom was not coming from external H_2O. With the aim of trapping a possible organometallic intermediate in order to understand the mechanism of this reaction, we performed deuterium labeling studies with deuterium oxide as well. Under the same conditions as above but with the addition of one equivalent of D_2O, the rearrangement reaction of allenol **1f** catalyzed by $PtCl_2$-AgOTf in dichloromethane afforded product (*E*)-[D]-**3f** in a low 24% yield with 33% deuterium content, suggesting that deuterolysis of the carbon-metal bond in an intermediate species has occurred (Scheme 6). The mechanism proposed in Scheme 5 is consistent with the above isotope-labeling experiments. We also decided to submit oxetene compounds to the Pt-Ag-catalyzed reaction conditions to demonstrate their intermediacy in this novel reaction. Consequently, oxetene **9** was allowed to react with the catalytic system $PtCl_2$-AgOTf. The reactions did form α,β-unsaturated ketone (*E*)-**3b** in moderate yield (Scheme 6); thus demonstrating the intermediacy of oxetene species. By contrast, when dihydrofuran **2b** was used as the substrate (under otherwise identical conditions) α,β-unsaturated ketone **3b** was not formed.

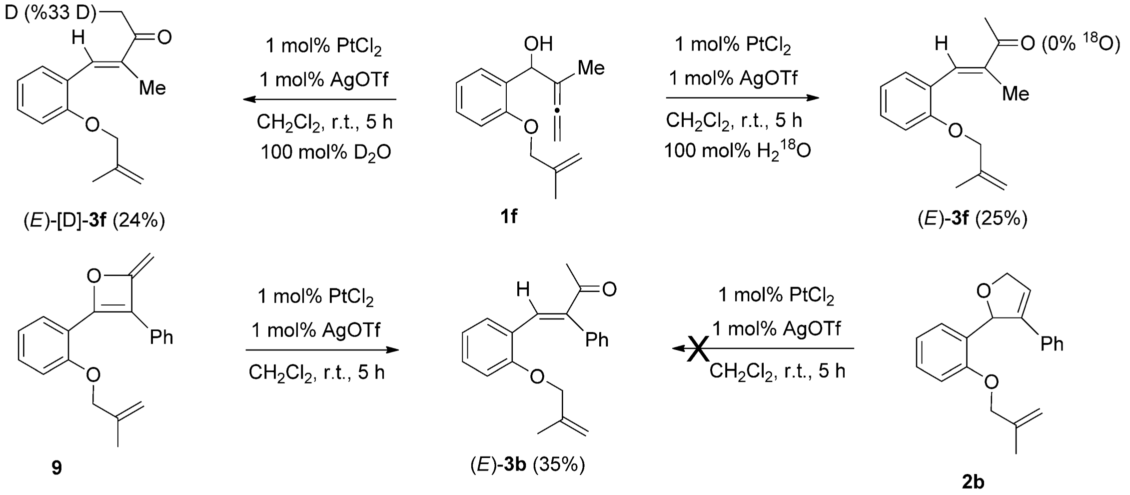
Initially, a mechanistic scenario that involves a direct intramolecular 1,3-shift of the OH group (analogous to the Meyer–Schuster rearrangement) cannot be completely ruled out.[14] However, taking all the experiments into account, in particular the transformation of oxetene **9** into α,β-unsaturated ketone **3b**, the Meyer–Schuster-type rearrangement seems very unlikely.

In conclusion, α-allenols were transformed into dihydrofurans in the presence of $PtCl_2$, while using $PtCl_2$ along with AgOTf as the catalytic system, α,β-unsaturated ketones were obtained. This divergent reactivity points to an important role of the silver salt in the activation of the platinum precatalyst.

Experimental Section

Typical Procedure for the Platinum-Catalyzed Rearrangement Reaction of α-Allenols 1; Synthesis of α,β-Unsaturated Ketone 3a

$PtCl_2$ (0.0108 mmol) and AgOTf (0.0108 mmol) were sequentially added to a stirred solution of the allenol **1a** (300 mg, 1.08 mmol) in dichloromethane (1.08 mL) under argon. The resulting mixture was stirred at room temperature under argon atmosphere until disappearance of the starting material (TLC). The reaction was then quenched with brine (1.0 mL), the mixture was extracted with ethyl acetate (3×5 mL), and the combined extracts were washed twice with brine. The organic phase was dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 7:1) to afford product **3a** as a colorless oil; yield: 168 mg (56%). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.98$ (s, 1 H), 7.26 (m, 3 H), 7.08 (dt, 3 H, $J = 7.8$, 1.7 Hz), 6.77 (d, 1 H, $J = 8.2$ Hz), 6.58 (d, 1 H, $J = 7.8$ Hz), 6.50 (t, 1 H, $J = 7.5$ Hz), 6.03 (m, 1 H), 5.40 (dq, 1 H, $J = 17.3$, 1.3 Hz), 5.26 (dq, 1 H, $J = 10.5$, 1.4 Hz), 4.54 (td, 2 H, $J = 5.0$, 1.5 Hz), 2.33 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 199.8$, 157.6, 141.1, 136.7, 134.5, 133.2, 130.8, 130.5, 130.0 (2 C), 128.8 (2 C), 127.8, 120.3, 117.7, 112.1 (2 C), 69.3, 27.7; HR-MS (ES): $m/z = 278.1314$, calcd. for $C_{19}H_{18}O_2$ $[M]^+$: 278.1307.



Scheme 6. Labeling and control experiments.

Acknowledgements

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6 Platinum-Catalyzed Divergent Reactivity of α-Hydroxyallenes: Synthesis of Dihydrofurans and α,β-Unsaturated Ketones

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