PtCl$_2$-Catalyzed Cycloisomerizations of Allenynes

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The PtCl$_2$-catalyzed cycloisomerization of enyne systems has recently witnessed tremendous developments, including the use of very diverse precursors as well as applications in the total synthesis of natural products.[1] Because these reactions have appeared as highly substrate-dependent,[2] a general mechanistic view has so far remained elusive.[3] Thus, the reactivity of novel unsaturated systems should have an important impact in terms of synthetic applications and mechanistic findings. In that context, allenyne substrates are highly appealing candidates that, to the best of our knowledge, have never been examined.
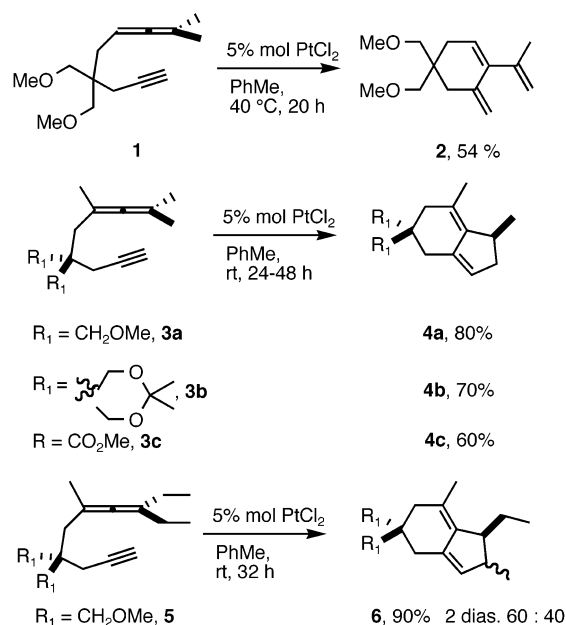
Besides intramolecular Pauson–Khand reactions,[4] allenynes have been much less involved in transition metal-mediated cyclizations than their enyne analogues.[5] These substrates exhibit different modes of cyclization when the metallic catalyst is varied. For instance, six-membered ring carbocycles were obtained from 1,7-allenynes by using cobalt[6] and iridium[7] catalysts, whereas palladium[8] and rhodium[7–9] catalysts allow the formation of either six-[7–9] or five-membered[8] rings. Titanium(II) complexes lead also to cyclopentane derivatives.[10] Herein, we describe new modes of cycloisomerization reaction of differently substituted allenynes upon treatment with a catalytic amount of PtCl$_2$.

Our initial findings showed that the reactivity of allenyne systems of type **1** was highly dependent upon the substitution of the allene moiety. Upon exposure to a catalytic amount of PtCl$_2$, precursor **1** provided the Alder-ene adduct **2** (Scheme 1), while precursors **3**, bearing an additional methyl group, provided bicyclic products **4** in good yields. It is worthy of note that the formation of bicyclic adducts has no precedent in the field of allenyne cycloisomerizations. In the same reaction conditions, diethyl substrate **5** also underwent a smooth transformation into the analogous **6** as a mixture of diastereomers. These intriguing findings led to the following mechanism proposal (Scheme 2).

Regioselective formation of platinacyclopentene intermediate **a** is followed by β-elimination to give platinahydride **b**. For R$_2$ = H, reductive elimination provides Alder-ene adduct **2**. However, for R$_2$ = Me, the β-elimination generates an unconjugated diene because of a strong 1,3-allylic strain between the two methyl groups. This would set the resulting methallyl group in good position for an unprecedented 5-*endo-trig* carboplatination step leading to intermediate **c**.[11] Final reductive elimination would then deliver products **4**.

Altering the substitution on the alkyne partner furnished additional mechanistic elements. Precursors **7**, **9**, or **11** bearing a methyl or an ethyl group on the alkyne underwent a clean conversion into vinylallene substrates **8**, **10**, and **12** (Scheme 3). Once again, an unprecedented reactivity has taken place in this

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Scheme 1

series, and the behavior of **7** has to be directly compared with the work of Brummond,[7] in which a cyclohexyltriene is exclusively formed from the corresponding malonate precursor with [Rh-(CO)$_2$Cl]$_2$.

Deuterium labeling with precursor **9D** is still consistent with the formation of platinacyclopentene intermediate **a**. This one would now evolve by β-elimination to **d**, followed by reductive elimination to **10D** (Scheme 4). In contrast with Brummond's case,[7] the elimination involves the allylic hydrogen atoms and not the one of the gem-dimethyl group. Such a distinct pathway between rhodium and platinum might be attributed to distinct geometries between the intermediate cyclopentene complexes.[12,13] Interestingly, cyclic 1,2,4-triene derivatives are versatile precursors of hydrindenones[14] and of retinoic acid analogues.[15]
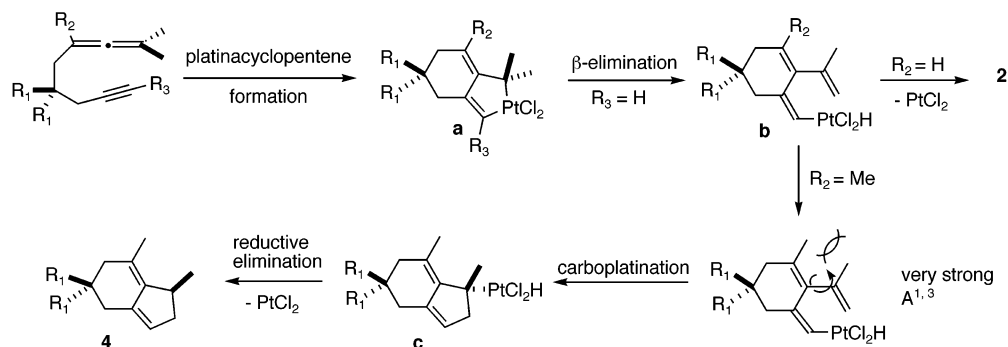
Finally, we could extend this reactivity to diyne systems such as **13**. Initial 1,3-migration of the acetate group gives birth to intermediate allenylester **15**,[16] that undergoes cycloisomerization to provide dienyl acetate **16** (Scheme 5). This adduct showed some instability, and it was perfectly characterized as the bicyclic enone **14**.[17]

In conclusion, we have shown that the unprecedented PtCl$_2$-catalyzed cycloisomerization of allenyne systems is a highly versatile tool for obtaining products that cannot be attainable with other metals. Simple adjustment of the allene or alkyne substitution can direct the reactivity in a completely selective manner and give
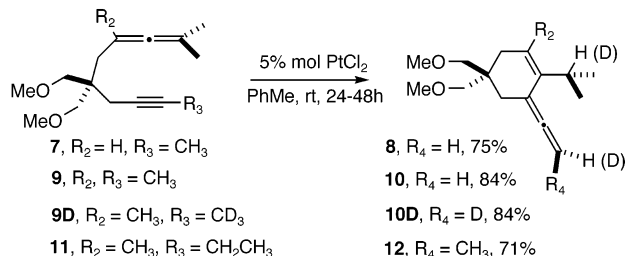
Scheme 2

Scheme 3

7, R₂ = H, R₃ = CH₃
9, R₂, R₃ = CH₃
9D, R₂ = CH₃, R₃ = CD₃
11, R₂ = CH₃, R₃ = CH₂CH₃

5% mol PtCl₂
PhMe, rt, 24-48h

8, R₄ = H, 75%
10, R₄ = H, 84%
10D, R₄ = D, 84%
12, R₄ = CH₃, 71%

Scheme 4

Scheme 5

1. PtCl₂, PhMe, 90°C, 6h
2. K₂CO₃, MeOH, rt, 1.5 h
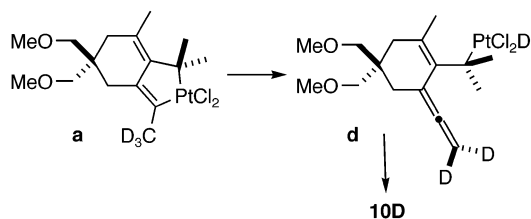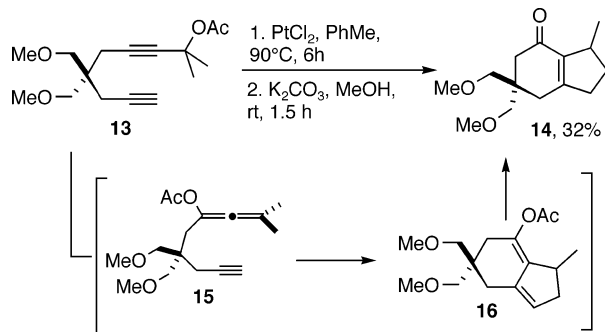
14, 32%

birth to important carbocyclic platforms (hydrindenes, cyclic vinylallenes, and trienes). Further work to apply these findings to total synthesis is underway.

Supporting Information Available: Experimental procedures and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Adduct **14** is contaminated by 5−10% of the hydrolyzed Alder-ene adduct.

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