Communication

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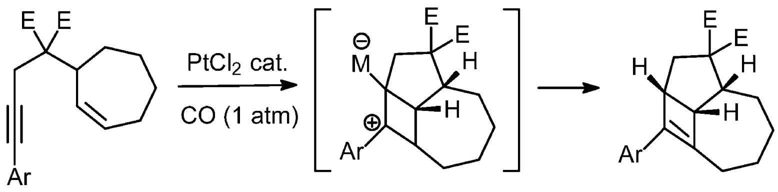

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Cyclobutenes by Platinum-Catalyzed Cycloisomerization Reactions of Enynes

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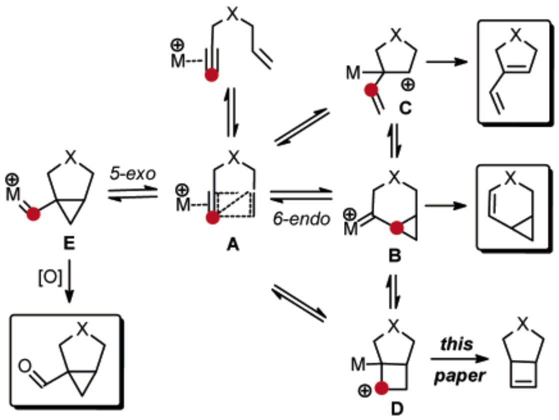
Although the ability of $PtCl_2$ to induce a host of selective rearrangements of polyunsaturated compounds was recognized only recently,[1] this branch of catalysis research is now rapidly expanding. Driven by the high affinity of Pt(+2) or other noble metal cations to the π-systems of the substrates, such transformations engender a significant increase in molecular complexity, while being operationally simple, safe, and convenient to perform.[2,3]

It is generally accepted that nonstabilized platinum carbenes constitute the actual intermediates in these reactions.[2,4] Because such species are best viewed as latent "non-classical" cations **A** that evolve along different pathways,[5] the diversity of product structures accessible by this methodology is easy to explain (Scheme 1). Specifically, the canonical form **B** representing a complexed cyclopropyl methyl cation leads to vinylcyclopropanes which are well documented reaction products, especially for substrates with heteroatoms in the tether (X = NTs, O);[6] another conceivable cyclopropyl methyl cation form **E** (5-*exo* cyclization mode) has also been experimentally verified.[7] The corresponding representation of the reactive intermediate as "homoallylic cation" **C** visualizes the enyne metathesis pathway to 1,3-diene products, which has been studied in great detail.[2] In contrast to these established "outlets", the remaining canonical form **D** representing the putative cyclobutenyl cation has been repeatedly invoked but hardly confirmed experimentally.[8,9] This paper shows how simple structural modifications in the substrates allow one to substantiate this immanent reactive intermediate and thereby give access to polycyclic skeletons that are difficult to obtain otherwise. Moreover, a convenient way to accelerate these novel Pt(+2)-catalyzed skeletal rearrangements is outlined.

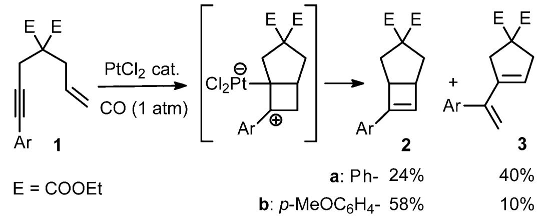
For the canonical form **D** to gain weight in the equilibrium shown in Scheme 1, it may suffice to substitute the color-coded position with an appropriate cation-stabilizing group. The most expedient way to do so uses enynes with aromatic residues on their alkyne unit (Scheme 2).

In fact, small amounts of cyclobutene **2a** were obtained in addition to the regular "metathesis product" **3a**[1] when compound **1a** was exposed to catalytic amounts of $PtCl_2$ in toluene at 80 °C. Gratifyingly, substrate **1b**, bearing a *p*-methoxyphenyl ring able to stabilize a putative benzylic cation of type **D** more effectively, clearly favors **2b** over **3b**. The reaction, however, was fairly slow and required >16 h to go to completion. In an attempt to accelerate this transformation, the mixture was stirred under an atmosphere of CO. By virtue of its strongly π-acidic character, this ligand should increase the electrophilicity of the metal center and, hence, the cationic character of the reactive intermediate while being sufficiently labile on the Pt(+2) template not to block the necessary coordination sites for the reaction to proceed.[10] In line with this rationale, only 2 h reaction time was necessary to effect the rearrangement of **1b** when performed under CO (1 atm), providing the desired cyclobutene **2b** in 58% yield.[11] The diagnostic pink color of the mixture fades away when the conversion is complete, thus allowing one to conveniently monitor the course of this reaction.[12]

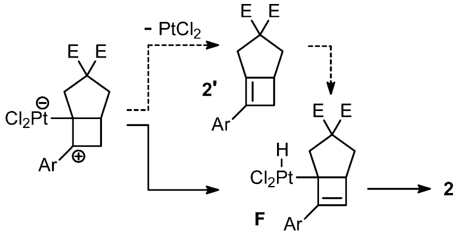
Scheme 1



Scheme 2



Scheme 3



Extensive NMR studies provide unambiguous proof for the constitution of **2** (and all other cyclobutenes described below; cf. Supporting Information). Although a detailed mechanistic picture requires further studies, the site of unsaturation in **2** suggests that the cation of type **D** favors loss of a proton over simple elimination of $PtCl_2$ to avoid positioning the alkene in the highly unfavorable bridgehead position of the "anti-Bredt" isomer **2′** (Scheme 3).[13−16] The formally resulting allylplatinum hydride species **F** then undergoes reductive elimination to give the observed product **2**. No indications whatsoever are available that **2** is derived from the isomeric compound **2′** by shift of the double bond. Therefore, it is also unlikely that the $PtCl_2$-catalyzed reactions described herein proceed via metallacyclopentenes,[17] as such intermediates would necessarily lead to **2′** rather than **2** as the primary product.

As shown by the examples compiled in Scheme 4, the $PtCl_2$-catalyzed cyclobutene formation is fairly general for carbocyclic skeletons. It is interesting to note that substrate **4** bearing the ether substituent in the *ortho*- rather than the *para*-position of the phenyl ring affords product **5** in 84% isolated yield, with virtually no metathesis product being detected in the crude mixture. Likewise,

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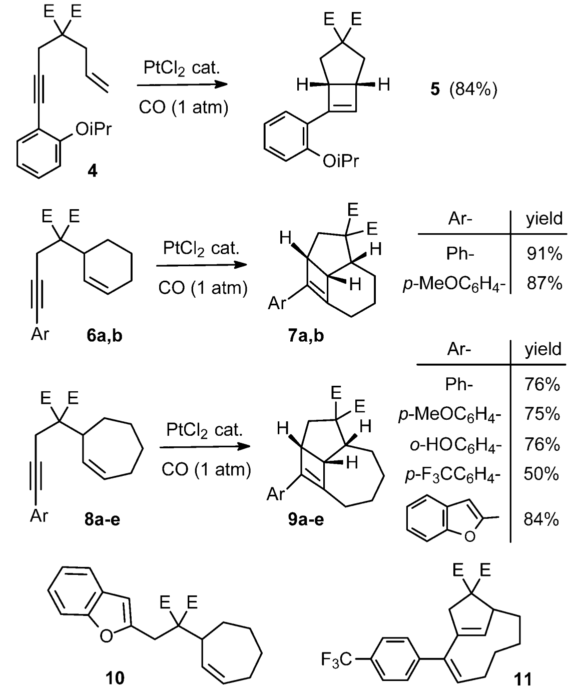
Scheme 4



Ar-	yield
Ph-	91%
p-MeOC$_6$H$_4$-	87%

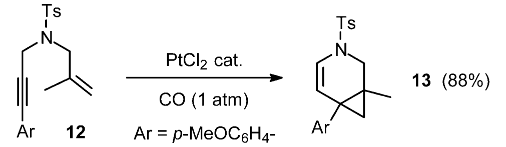
Ar-	yield
Ph-	76%
p-MeOC$_6$H$_4$-	75%
o-HOC$_6$H$_4$-	76%
p-F$_3$CC$_6$H$_4$-	50%
(2-methylbenzofuran-yl)	84%

enynes of type **6** and **8** perform remarkably well despite the high stain of the resulting tricyclic skeletons. As expected, variations of the substituent on the phenyl ring affect the product distribution, most likely by modulating the stability of the presumed benzylic cation **D**. Thus, substrates **8a**,**b** provide the cyclobutenes **9a**,**b** in high yields; likewise, **8c** gives compound **9c** in 76% yield together with 11% of **10** derived from direct attack of its phenolic −OH group onto the initial alkyne−Pt(+2) π-complex. In contrast, compound **8d** (Ar = *p*-F$_3$CC$_6$H$_4$) affords a mixture of cyclobutene **9d** and the metathesis product **11** (1.5:1, 84%). Replacement of the electron-deficient arene by the electron-rich benzofuran in **8e** re-establishes the formation of the cyclobutene product. It should be emphasized that all examples depicted in Scheme 4 show a particularly pronounced effect of CO on the reaction rates.[11] Only very poor conversions are reached under argon, even if the mixtures are stirred for several days at 80 °C, whereas all rearrangements proceed smoothly when performed under CO (1 atm) as described.

As mentioned above, enynes with heteroelements in the tether tend to form vinylcyclopropanes as products supposedly via the canonical form **B**, which is stabilized by orbital overlap between the metal carbene moiety and the adjacent C−X (X = O, NTs) bond. To see whether substrates of this type might be forced to deviate from this preferred pathway, enyne **12** was reacted with PtCl$_2$ catalyst in toluene under CO atmosphere (Scheme 5). The only product isolated, however, was cyclopropane **13**, thus showing that the resonance stabilization in **B** is more effective than the stabilization of the benzylic cation in **D** by the attached electron-rich arene ring.

In summary, evidence is provided for an essential component of the cationic manifold by which the diverse array of rearrangement reactions catalyzed by PtCl$_2$ is explained. Furthermore, access is gained to various target structures of significant complexity from readily available starting materials.

Scheme 5



Acknowledgment. Financial support by the MPG and the Fonds der Chemischen Industrie is gratefully acknowledged. We thank Umicore AG, Hanau, for a gift of noble metal salts.

Supporting Information Available: Experimental part including spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Kinetic experiments show that in our case the presence of CO *decelerates* the “enyne metathesis” pathway but accelerates cyclobutene formation. This result contrasts a report of Murai et al. in which enyne metathesis catalyzed by [RuCl$_2$(CO)$_3$]$_2$ is accelerated when performed under a CO atmosphere: Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049.

(12) Only enynes with ether substituents on their phenyl rings show this characteristic coloration of the reaction mixture.

(13) In addition, coordination of Pt(+2) in intermediate **F** to CO reduces its electron density and, hence, its ability to eliminate directly, thus rendering proton loss a competitive process.

(14) A similar argument pertains to products **7** and **9**, which are significantly more stable than their positional isomers.

(15) Cyclobutenes with the double bond in the same location are extremely scarce; two examples are described as products of palladol-catalyzed processes: (a) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636. (b) Trost, B. M.; Trost, M. K. *Tetrahedron Lett.* **1991**, *32*, 3647.

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