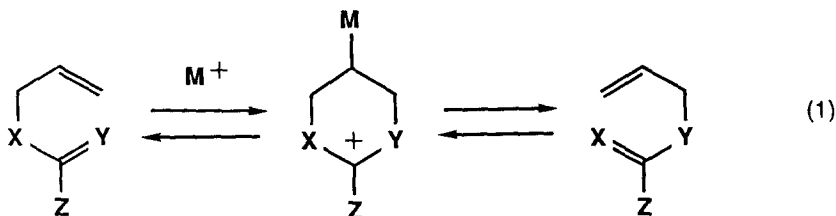# PALLADIUM(II)-CATALYZED CLAISEN REARRANGEMENT

OF ALLYL VINYL ETHERS

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Summary: The Claisen rearrangement of allyl vinyl ethers is catalyzed by $PdCl_2(CH_3CN)_2$, provided that alkyl substituents protect the vinyl ether double bond from coordination by the metal catalyst.

[3,3]Sigmatropic rearrangements are very useful for the formation of C-C, C-O, C-N and C-S bonds. Besides the classical thermal version of the reaction, use is made increasingly of transition metal catalysis, especially by Hg(II)- and Pd(II)-salts, which enable the execution of many of these rearrangements under mild conditions, in high yield, and with high regio- and stereoselectivity. Examples are the Pd(II)-catalyzed Cope rearrangement of 1,5-dienes,[1] and the Hg(II)- or Pd(II)-catalyzed hetero-Cope rearrangements of allylic esters,[2] allyl imidates,[3] and S-allyl thioimidates.[4] These reactions are suggested[1,2] to proceed *via* a "cyclization-induced rearrangement" pathway, which accounts for the action of the metal catalysts (eq. (1)).

$$ \tag{1} $$

In recent reviews,[5,6] however, it has been reported that no examples are known of Hg(II)- or Pd(II)-catalyzed Claisen rearrangements of 3-hetero-1,5-dienes such as allyl vinyl ethers[7] (eq. (1); X = O, Y = CR_2, Z = H, alkyl, phenyl). This exception to the general reaction depicted in eq. (1) was attributed[5] to the (irreversible) binding of the electrophilic metal catalyst at the strongly nucleophilic vinyl ether function[8] instead of at the allylic double bond.

In connection with a mechanistic study on Pd-catalyzed alkylation reactions, we had occasion to prepare a number of allyl 1-cyclohexenyl ethers and to investigate their behaviour towards the action of Pd(II)-salts. In this communication we report for the first time that the Claisen rearrangement of allyl vinyl ethers can be catalyzed by $PdCl_2(CH_3CN)_2$ provided that some stringent structural demands are met.

Treatment of E-2-buten-1-yl 1-cyclohexenyl ether (**1a**)[9] (eq.(2); $R^1=CH_3$; $R^2=R^3=H$) with 0.05 equiv. of $PdCl_2(CH_3CN)_2$[13] in benzene at room temperature for 2 h, produced a ketone in 65% yield. ^{1}H-NMR spectroscopic analysis of the carefully purified product unambiguously identified it as the Claisen product **2a** (eq. (2); Table 1). Significant resonances of the starting material **1a** at δ 6.02 – 5.44 (m, 2H, C-C̱H̱=C-C), 4.62 (br t, 1H, vinylic cyclohexenyl proton), 4.11 (br d, 2H, -CH_2O) and 1.72 ppm (br d, CH_3,superimposed on cyclohexenemethylene protons) had completely disappeared, and instead the characteristic ^{1}H-NMR resonances of the [3,3]sigmatropic rearrangement product **2a** at δ 5.89 – 5.47 (m, 1H, CH=CH$_2$), 5.13 – 4.84 (m, 2H, -CH=CH_2), 2.69 (m, 1H, H-C-CH$_3$) and 1.00 ppm (d, 3H, H-C-CH_3) were found. GLC and ^{1}H-NMR analysis showed that, besides a number of unidentified sideproducts (each less than 2% yield), also a small amount of cyclohexanone (10%) and the carbon-carbon double bond isomerization product 2-(1-methyl-1-propenyl)cyclohexanone **3a** (9%) had been formed.

$$(2)$$
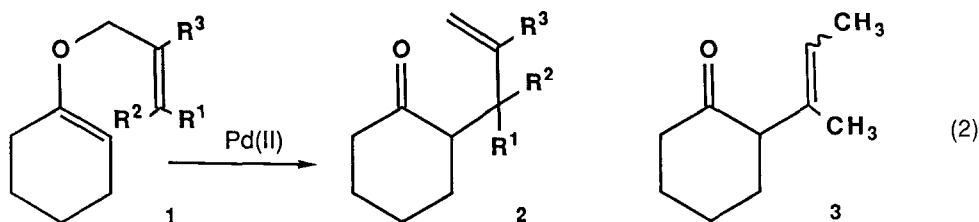
In CH_2Cl_2 as reaction medium (Table 1), the yield of **2a** was somewhat lower (54%) and more cyclohexanone (14%) and **3a** (20%) were found. THF gave the cleanest reaction mixture and the highest yield of **2a** (71%), but the formation of cyclohexanone was most prominent in this solvent (ca. 20%); the double bond isomer **3a** was almost absent. Such solvent effects with respect to the formation of cyclohexanone were even more pronounced in the Pd(II)--catalyzed rearrangement of allyl ether **1b** (Table 1).

No reaction of **1a,b** was observed with $Pd(\phi_3P)_4$, $Pd(OAc)_2$, or $PdCl_2(CH_3CN)_2/Et_3N$.

The related allyl vinyl ethers **1c** and **1d** (Table 1) gave only traces of rearranged products when treated with $PdCl_2(CH_3CN)_2$, probably because bonding of the metal ion to the allylic double bond of these compounds is disfavored (bonding of Pd(II) to a tert carbon in **1c**, and steric hindrance in **1d**). On the other hand, after long reaction times,large amounts of cyclohexanone and the corresponding allylic alcohols were found. The formation of these cleavage products, which apparently competes with the Claisen rearrangement if the latter occurs too slowly or not at all, probably is related to the known Pd(II)-catalyzed ketal hydrolysis[14] and the cleavage of allyl phenyl ether[15] (which, for that matter, proceeds without competing Claisen rearrangement); mechanisms for these two latter reactions are not known.

$$(3)$$
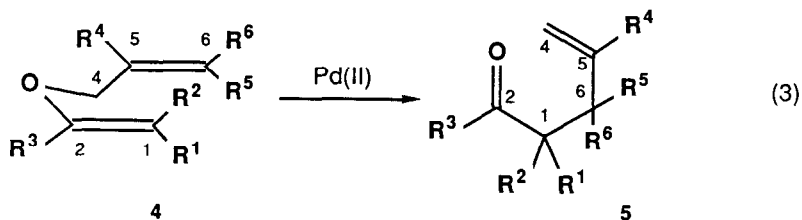
Having established that the Claisen rearrangement can, at least in principle, be pro-
moted by Pd(II), the scope and limitations of the catalyzed reaction was explored in a
range of conformationally flexible, acyclic allyl vinyl ethers[9] of type 4 (eq. (3); Table 1).

Table 1: $PdCl_2(CH_3CN)_2$-catalyzed Claisen rearrangement of allyl vinyl ethers

Rearrangement	Conditions[a] solvent, time	Yield[b] of Claisen product
1 ⟶ **2**		
a : $R^1=CH_3$; $R^2=R^3=H$	C_6H_6 2 h	65%
	CH_2Cl_2, 2 h	54%
	THF , 2 h	71%
b : $R^1=R^2=R^3=H$	C_6H_6 , 2 h	65%
	CH_2Cl_2, 2 h	56%
	THF , 2 h	45%
c : $R^1=R^2=H$; $R^3=Me$	C_6H_6 , 24 h	<2%
d : $R^1=R^2=Me$; $R^3=H$	C_6H_6 , 24 h	<5%
4 ⟶ **5**		
a : $R^1=R^2=R^3=R^4=R^5=H$; $R^6=Me$	C_6H_6 , 24 h	<2%
b : $R^1=R^2=R^3=R^4=H$; $R^5=R^6=Me$	C_6H_6 , 24 h	<5%
c : $R^1=R^2=H$; $R^3=Me$; $R^4=R^5=R^6=H$	C_6H_6 , 24 h	<2%
d : $R^1=R^2=Me$; $R^3=R^4=R^5=R^6=H$	C_6H_6 , 18 h	19%
e : $R^1=H$; $R^2=Me$; $R^3=R^4=R^5=H$; $R^6=Me$	C_6H_6 , 4 h	18%
f : $R^1=H$; $R^2=Me$; $R^3=Et$; $R^4=R^5=R^6=H$	THF , 2 h	71%
g : $R^1=H$; $R^2=Me$; $R^3=Et$; $R^4=R^5=H$; $R^6=Me$	THF , 2 h	93%

[a] All rearrangement were performed by stirring a 0.2 M solution of **1** or **4** in the dry sol-
vent indicated with 0.05 equiv. of $PdCl_2(CH_3CN)_2$ at room temperature. [b] Determined by GLC
analysis.

By reacting **4a-g** under identical conditions with 0.05 equiv. of $PdCl_2(CH_3CN)_2$ in benzene or
THF at room temperature, it became evident why until now no examples of Pd(II)-catalyzed
Claisen rearrangements of allyl vinyl ethers have been reported: Most easily accessible al-
lyl vinyl ethers **4** give only traces of the rearranged product **5**, and the substitution pattern
of the vinyl group determines the outcome of the catalytic reaction to a high degree so that
dramatic effects are observed.
Allyl vinyl ethers **4a,b,c**, in which C-1 (see numbering scheme of eq. (3)) is not substituted
with alkyl groups, gave only a very low yield of the corresponding Claisen products (deter-
mined by IR and ^{1}H-NMR spectroscopy of the concentrated reaction mixture, as well as by
conducting the experiment in benzene-d_6 in a NMR-tube). After 24 h, most of the starting
material had disappeared and had been cleaved to the corresponding (substituted) allyl
alcohol. This is in accordance with the conception that Pd(II) strongly coordinates to the
unsubstituted C-1 of the vinyl ether group and consequently is not available for coordina-

tion to the allyl group. Thus, the essential step, according to the "cyclization-induced rearrangement" mechanism, is blocked, and instead of the Claisen rearrangement, slower side-reactions prevail.

Substitution at C-1 with alkyl groups will retard or even impede coordination to the vinyl group so that metal-catalyzed Claisen rearrangement can proceed. This is the case with the dimethylvinyl compound **4d** which after 18 h at room temperature gives 19% of Claisen product **5d** (the yield is low probably because of steric hindrance) without much competing cleavage to the allyl alcohol. Mono-substituted vinyl ether **4e** also gives some rearrangement to aldehyde **5e** (18% after 4 h) but here, like in **4a-c**, the reaction is seriously diverted by cleavage of the ether bond. Entirely in agreement with this trend, best results were obtained with **4f** and **4g**, in which the alkyl substituents at C-1 and C-2 sufficiently retard coordination of the catalyst to the vinyl group, whereas cyclization to a cyclohexyl cation (eg. (1)) is favored by the donor substituent (Z=Et) present at C-2. In a very clean reaction, more than 90% of Claisen product **5g** was produced from **4g**, and only traces of diethyl ketone and crotyl alcohol were detected.

In view of these results, it is clear that the Pd(II)-catalyzed Claisen rearrangement of allyl vinyl ethers does not have general synthetic utility. It is restricted to those compounds which have a vinyl group protected by alkyl substitution from attack by the metal catalyst. If, however, these requirements are met, the catalyzed reaction may prove to be of value in the rearrangement of heat-sensitive allyl vinyl ethers.

The diastereoselectivity of the catalytic Claisen rearrangement has not yet been investigated thoroughly; preliminary observations indicate a high preference for a chair-like transition state.[1] This aspect is under investigation as part of our further studies into the mechanism of Pd-catalyzed reactions.

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