Stereochemical Feature of Palladium(II)-Catalyzed Claisen Rearrangement

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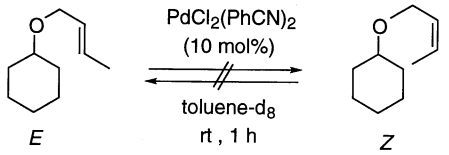
(Received May 9, 1995)

The title rearrangements of the geometrical isomers of crotyl enol ethers are shown to exhibit the identical *anti* diastereoselection, in contrast to the high stereospecificity observed in the thermal rearrangements. These outcomes are discussed on mechanistic grounds.

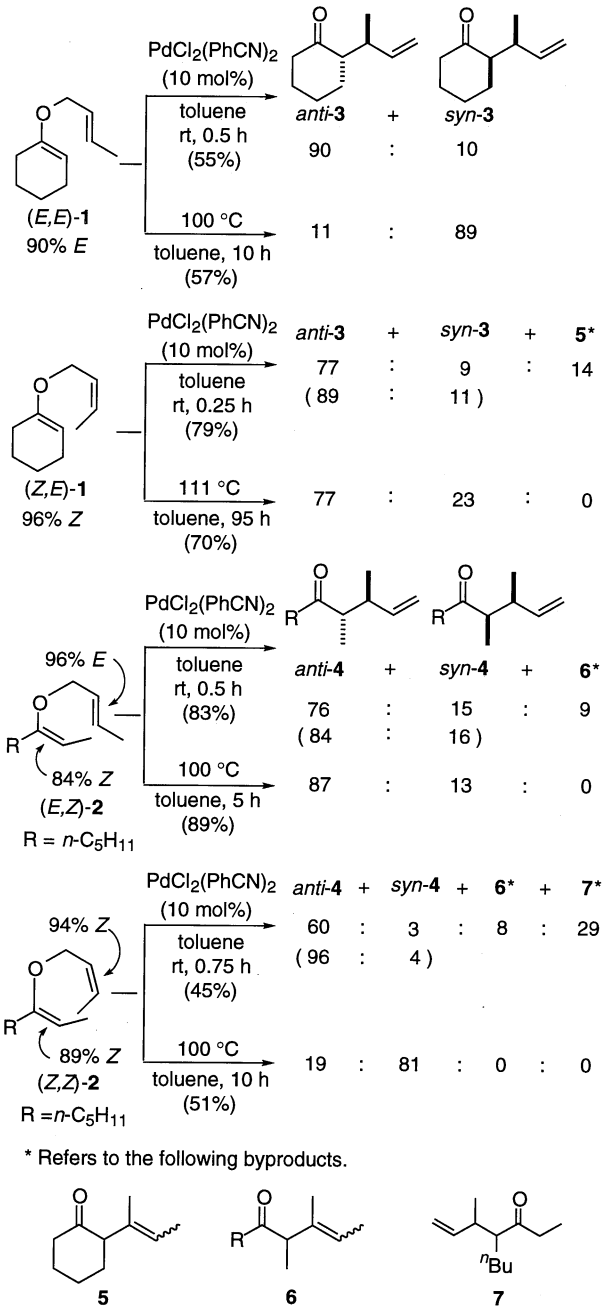
The Claisen rearrangement has found many applications as a powerful tool for stereocontrolled C-C bond formations.[1] Recently we have reported the Pd(II)-catalyzed Claisen variant, in which the Claisen substrate is formed *in situ* from a cyclic enol ether and an allylic alcohol via the Pd(II)- or CF_3CO_2H-catalyzed enol ether exchange.[2] From the standpoint of stereocontrol, the Pd(II)-catalyzed variant is of mechanistic interest and synthetic value, since the Pd(II)-catalyzed reaction of the methyl enol ether of α-tetralone and (*E*)-crotyl alcohol, for instance, affords the *anti* diastereomer of the Claisen product, whereas the thermal reaction gives the *syn* isomer.[2] In order to clarify the stereochemical feature of the Pd(II)-catalyzed Claisen rearrangement, we have now studied the Claisen processes of a full set of the geometric isomers of crotyl enol ethers once isolated, of which the stereochemical outcomes are described in this communication.

Selected as the substrates for study are the two geometrical pairs, crotyl 1-cyclohexenyl ether (**1**) and crotyl (*Z*)-2-octen-3-yl ether (**2**). The former pair was prepared via the Et_2AlI-promoted cleavage of the (*E, E*)- or (*Z, Z*)-biscrotyl ketal,[3,4] whereas the latter pair was obtained via the (*Z*)-selective ethylidenation of the (*E*)- or (*Z*)-crotyl hexanoate using the modified Tebbe reagent developed by Utimoto et al.[4,5] Scheme 1 summarizes the stereochemical outcomes thus observed.[6] Significantly enough, the Pd(II)-catalyzed rearrangements of the four substrates were found to exhibit the identical *anti* diastereoselection, independent of the substrate geometries, while the thermal rearrangements show the high stereospecificity as predicted from the well-known chair transition-state model,[1] namely, (*E, E*) or (*Z, Z*)→*syn* and (*E, Z*) or (*Z, E*)→*anti*. Another notable finding is that in the Pd(II)-catalyzed reactions except for (*E, E*)-**1** the non-Claisen products **5**-**7** were formed as byproducts which apparently arise from the Pd(II)-catalyzed olefin migration of the Claisen product or substrate.[7,8]

Since the occurrence of such olefin migration may complicate the stereochemical analysis of the Pd(II)-catalyzed rearrangement, we made the following control experiments. Eq. 1 shows that neither olefin migration nor geometrical isomerization occur on the crotyl part. Eq. 2 indicates that the Claisen product **3** does

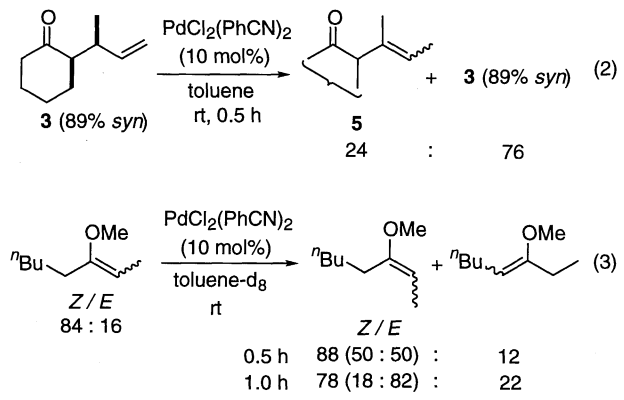


(1)

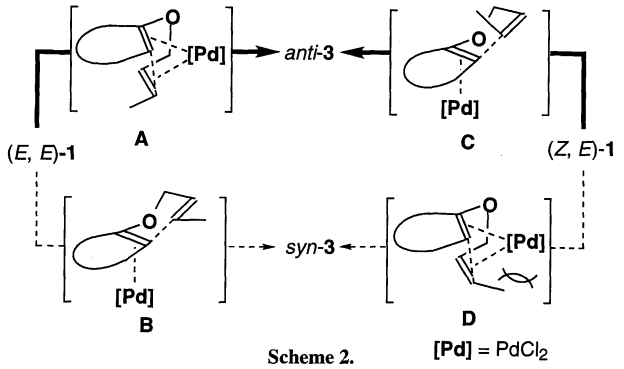


Scheme 1.

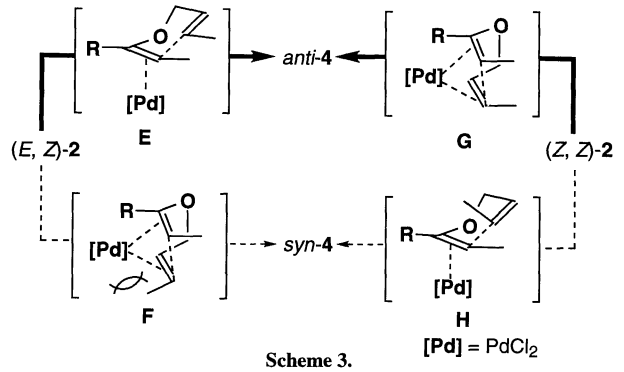
undergo the olefin migration to produce **5** gradually, but not accompanied by any epimerization of *syn*-**3**. Eq. 3 reveals that the acyclic enol ether does undergo both the olefin migration and geometrical isomerization.



With these observations in mind, the *anti* diastereoselection observed uniformly in the Pd(II)-catalyzed rearrangement is rationalized as follows. For the rearrangement of **1** (Scheme 2), the unique (*E, E*)→*anti* selection is best visualized by the boat transition state (TS) **A** as previously proposed,[2] where the Pd(II) coordinates to the two olefinic bond, whereas the (*Z, E*)→*anti* selection reflects the situation that the boat TS **D** is disfavored due to the large steric repulsion of [Pd] and the crotyl-methyl and hence the rearrangement proceeds preferentially through the chair TS **C**, where the Pd(II) monodentately coordinates probably to the electron-rich enol part. Stereochemical analysis of the



Scheme 2.



Scheme 3.

rearrangement of **2**, on the other hand, is more difficult owing to the complexities arising from the geometrical isomerization of the enol ether part mentioned above. Nonetheless, the (*E, Z*)→*anti* selection is best visualized by the chair TS **E** (Scheme 3), similar to TS **C**, since in this case the geometrical isomerization might be minimized as revealed by no formation of byproduct **7**.[9] The *anti* selection observed with (*Z, Z*)-**2**, however, is difficult to analyze because the geometrical isomerization considerably occurs in this case. Thus, the *anti* selection might be considered as the result of the two competing processes, *i. e.* the direct rearrangement of the (*Z, Z*)-**2** through the boat TS **G** or the initial isomerization of (*Z, Z*)-**2** to (*Z, E*)-**2** followed by its rearrangement through the chair TS analogous to TS **C**.

In summary, we have revealed the stereochemical feature of the Pd(II)-catalyzed Claisen rearrangement, which is different in nature from that of the conventional thermal rearrangement. With the unique stereocontrolling ability of the Pd complex in hand, further work is now in progress to develop enantioselective catalysis of the Claisen rearrangement and related reactions.

This work was supported in part by a Grant-in-Aid for Scientific Research in Priority Areas from the Ministry of Education, Science and Culture, Japan.

References and Notes

1 Recent reviews: a) F. E. Ziegler, *Chem. Rev.*, **88**, 1423 (1980); b) S. Blechert, *Synthesis*, **1989**, 71; c) P. Wipe in "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, London (1991), Vol. 5, p 827.

2 a) K. Mikami, K. Takahashi, T. Nakai, *Tetrahedron Lett.*, **28**, 5879 (1987); b) M. Sugiura, M. Yanagisawa, T. Nakai, *Synlett*, **1995**, 447.

3 K. Takai, I. Mori, K. Oshima, H. Nozaki, *Bull. Chem. Soc. Jpn.*, **57**, 446 (1984).

4 The geometrical purities were determined by ^{1}H NMR analyses.

5 T. Okazoe, K. Takai, K. Oshima, K. Utimoto, *J. Org. Chem.*, **52**, 4410 (1987).

6 The diastereomeric products were distinguishable by the ^{1}H NMR spectra ($CDCl_3$); *e. g.*, the signals (ddd) due to the α-hydrogen of the vinyl group are δ 5.64 for *anti*-**3** *vs.* δ 5.79 for *syn*-**3** and δ 5.58 for *anti*-**4** *vs.* δ 5.71 for *syn*-**4**. The isomeric ratios were determined by ^{1}H NMR assays. The ^{1}H and ^{13}C NMR spectra of the byproduct **5**-**7** were in accord with the assigned structures.

7 Pd(II)-catalyzed olefin migrations have been reported: a) P. Golborn, F. Scheinmann, *J. Chem. Soc., Perkin Trans. I*, 2870 (1973); b) J. K. Cha, R. J. Cooke, *Tetrahedron Lett.*, **28**, 5473 (1987). For a Pd(II)-catalyzed geometrical isomerization, see: Y. Wakatsuki, S. Nozakura, S. Murahashi, *Bull. Chem. Soc. Jpn.*, **45**, 3426 (1972).

8 Byproduct **7** is formed apparently from the olefin migration of the substrate followed by the Claisen process.

9 Note that the geometrical isomerization should be accompanied by the olefin migration leading to ketone **7**.