Palladium-Catalyzed Elimination Reaction of Acyclic (*E*)-Allylic Acetates: The Stereochemistry Elucidated by "*Syn*-Effect"

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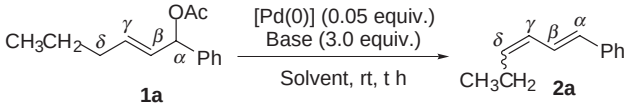
The stereochemistry of the elimination reaction of acyclic (*E*)-allylic acetates into the corresponding 1,3-dienes catalyzed by palladium in the presence of a base was investigated. The *Z*/*E* ratios of the resulting 1,3-dienes varied with the δ-substituents of the starting allylic acetates. This phenomenon was discussed based on the concept of a "*syn*-effect," which is most primarily rationalized by a $\sigma \rightarrow \pi^*$ interaction.

The palladium-catalyzed elimination reaction of allylic compounds is a useful method for the preparation of 1,3-dienes as versatile synthetic intermediates.[1] In the case of allylic acetate, it is generally thought that allylpalladium complexes are initially formed by oxidative addition of Pd(0) followed by β-elimination of HPdOAc from the π-allylpalladium complexes to regenerate Pd(0) with liberation of HOAc. The elimination is often carried out in the presence of a suitable base to capture HOAc. The pathway of the elimination is reported to be varied depending on the employed conditions.[2]

Previously we investigated the stereochemistry of the desulfonylation reaction of α,α-dialkylated (*E*)-allylic sulfones with a base and found that the sterically unfavorable (*Z*)-dienes were predominantly formed.[3] The result was rationalized by "conformational acidity" that essentially implies a "*syn*-effect."[4,5] We proposed that the "*syn*-effect" is primarily caused by a $\sigma \rightarrow \pi^*$ interaction.[3,5b–e] Herein, we described that the sterically unfavorable (*Z*)-dienes were also produced in the elimination reaction of acyclic (*E*)-allylic acetates catalyzed by palladium under the specific conditions utilizing a base, and the stereochemistry was elucidated by the concept of the "*syn*-effect."

First the palladium-catalyzed elimination reaction of δ-ethyl substituted (*E*)-allylic acetates **1a** was examined under various conditions, and the results are summarized in Table 1. When $[Pd(PPh_3)_4]$ was used as a catalyst in the presence of DBU in THF at rt, the elimination proceeded to give the 1,3-diene **2a** in the preference of (*E*)-isomer[6] (Entry 1). By the use of bidentate ligands, *Z*-selectivities were increased (Entries 2–4). Among the bidentate ligands, dppe, whose bite angle 86° is smaller than others,[7] showed *Z*-preference (*Z*/*E* = 57/43) (Entry 4). It was confirmed that in the absence of a palladium catalyst, no elimination proceeds even in refluxing THF. Among the bases examined, DBU realized higher *Z*-selectivity (Entries 4–7). In less polar solvents, Et_2O and toluene, *Z*-selectivity was decreased (Entries 8, 9).

A regioisomeric (*E*)-allylic acetate **3** was also subjected to the elimination reaction under the same conditions as those in Entry 4. The corresponding 1,3-diene **2a** was obtained with almost the same *Z*/*E* ratio of 54/46. This result suggested that the reaction proceeded via the same π-allylpalladium intermediate (**B**, Scheme 1, R = CH_3CH_2).

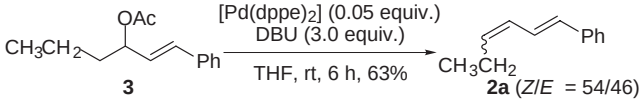


1a **2a**

Table 1. Elimination reaction of (*E*)-allylic acetate **1a** into **2a**

Entry	[Pd(0)]	Base	Solvent	t/h	Yield/%	*Z*/*E*[a]
1	$[Pd(PPh_3)_4]$	DBU	THF	90	42	11/89
2	$[Pd(dppb)_2]$	DBU	THF	8	61	23/77
3	$[Pd(dppp)_2]$	DBU	THF	22	79	38/62
4	$[Pd(dppe)_2]$	DBU	THF	6	87	57/43
5	$[Pd(dppe)_2]$	Et_3N	THF	20	71	46/54
6	$[Pd(dppe)_2]$	$^iPr_2NEt$	THF	20	77	48/52
7	$[Pd(dppe)_2]$	TMEDA	THF	68	52	27/73
8	$[Pd(dppe)_2]$	DBU	Et_2O	19	71	42/58
9	$[Pd(dppe)_2]$	DBU	toluene	68	26	18/82

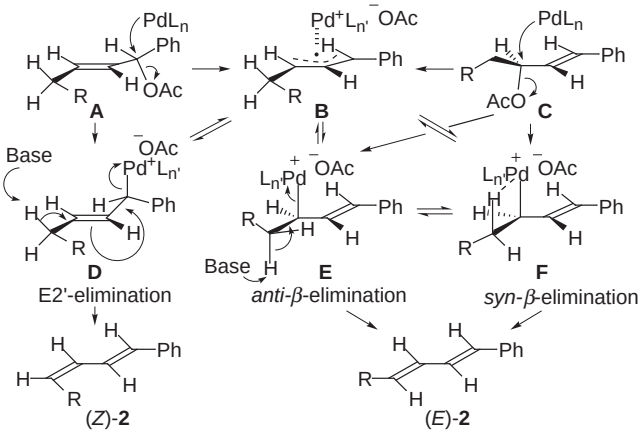
[a]The ratios were determined by 400 MHz ^1H NMR spectra. Only the stereochemistry of C_γ–C_δ double bond is shown.[6]



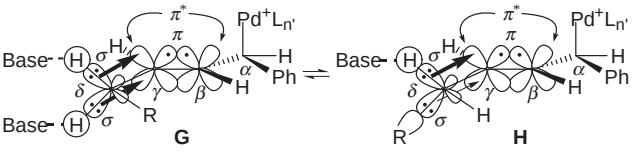
3 **2a** (*Z*/*E* = 54/46)

The reaction pathway of the present elimination could be elucidated as follows (Scheme 1). When the reaction was carried out using palladium complex with monodentate ligand PPh_3 (Entry 1) or in less polar, namely less coordinatable, solvents (Entries 8, 9), *syn*-β-elimination via σ-allylpalladium complex **F** might proceed predominantly without participation of the base to give (*E*)-diene selectively, because of facile generation of a vacant coordination site on the Pd(II) center. Such an agostic interaction might be difficult for the palladium species coordinated by a bidentate ligand with small bite angle to avoid *syn*-β-hydride elimination (Entries 2–4).[8] The influence of the base on the proton elimination would contrast with the *syn*-β-elimination (Entries 4–7). Unprecedented *Z*-preference using DBU (Entry 4) might be ascribed to the participation of the base in the transition state such as **D**.[9]

As mentioned above, we previously found that the sterically unfavorable (*Z*)-dienes were predominantly formed in the desulfonylation reaction of (*E*)-allylic sulfones with the base and the result was rationalized by the "conformational acidity" that essentially implies the "*syn*-effect."[3] In the present elimination, *Z*-preference might be also explained based on the concept of the "*syn*-effect" in E2′-elimination from σ-complex **D**. That is, at the transition state of deprotonation, the eclipsed conformations **G** and **H** might be predominant due to hyperconjugation of the developing anion generated by the interaction of H_δ(s) with base(s), in both of which the developing anion is aligned with the π^*-orbital and other conformations could be neglected. Between the conformations **G** and **H**, the CC eclipsed *syn*-conformation



Scheme 1.



G might be preferred to CH eclipsed form **H**, because hyperconjugative electron donation by C–H_δ bond is more effective than that by C–C bond.[10] If this is the case of the present elimination, the degree of the "*syn*-effect," which depends on the δ-substituents R of (*E*)-allylic acetates **1**, might be similar to that of the previous desulfonylation reaction of allylic sulfones. Then the elimination reaction of various (*E*)-allylic acetates was examined by the use of [Pd(dppe)$_2$] in the presence of DBU in THF and the results are summarized in Table 2.

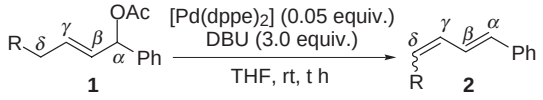


Table 2. Elimination reaction of (*E*)-allylic acetates **1** into **2**

Entry	R	**1**	t/h	Yield/%	Z/E[a]
1	CH_3CH_2	**a**	6	87	57/43
2	CH_3	**b**	5	80	64/36
3	$(CH_3)_2CH$	**c**	7	77	17/83
4	$(CH_3)_3C$	**d**	10	60	<1/99
5	Ph	**e**	4	98	6/94
6	BnO	**f**	5	71	95/5
7	BnS	**g**	3	89	80/20

[a]The ratios were determined by 400 MHz ^{1}H NMR spectra. Only the stereochemistry of C_γ–C_δ double bond is shown.[6]

As expected, *Z*-selectivity with respect to the δ-alkyl substituents decreased along with their bulkiness; CH_3– > CH_3CH_2– > $(CH_3)_2CH$– > $(CH_3)_3C$– (Entries 1–4). In the case of δ-Ph substituent, high *E*-selectivity was observed (Entry 5). δ-BnO group showed the highest *Z*-selectivity (Entry 6), while δ-BnS substituted acetate **1g** afforded rather high *Z*-preference of diene **2g** (Entry 7). The relative degree of the "*syn*-effect" depending on the δ-substituents R of (*E*)-allylic acetates **1** for elimination reaction was similar to our previous observation on the desulfonylation reaction of allylic sulfones[3] as follows;

$$\text{BnO–} > \text{BnS–} > \text{CH}_3\text{–} > \text{CH}_3\text{CH}_2\text{–} > (\text{CH}_3)_2\text{CH–} > \text{Ph–} > (\text{CH}_3)_3\text{C–}$$

In the case of δ-benzyloxy substituted (*E*)-allylic acetate **1f** (R = BnO), CH eclipsed form **H** is unfavorable due to low donor ability of C–O bond.[11] Thus exclusive formation of (*Z*)-**2f** via conformation **G** might have been observed. The bulkiness of Ph and $(CH_3)_3C$ groups might exclude the conformation **G** to give (*E*)-dienes **2d**, **2e** selectively.[12,13]

In conclusion, the stereochemical outcome in the elimination reaction of acyclic (*E*)-allylic acetates to the corresponding dienes by the use of [Pd(dppe)$_2$] as a catalyst in the presence of DBU was elucidated by E2′-elimination, and unprecedented *Z*-preference could be well rationalized by the "*syn*-effect" in the transition state of deprotonation, which arose from a $\sigma \rightarrow \pi^*$ interaction. It is noteworthy that the highest *Z*-selectivity was observed for the benzyloxy substituent among the examined substrates.

References and Notes

1 a) J. Tsuji, "Palladium Reagents and Catalysts," John Wiley & Sons, Ltd., Chichester (1995), pp 356–363. b) I. Shimizu, "Handbook of Organopalladium Chemistry for Organic Synthesis," ed. by E. Negishi, John Wiley & Sons, Inc., New York (2002), Vol. 2, Chap. V. 2.5.1.

2 The reaction pathway of elimination reaction of cyclic allylic compounds to the corresponding 1,3-dienes has been discussed, and not only *syn*-β-elimination but also *anti*-elimination was proposed to be taken place, especially in the presence of a base. a) E. Keinan, S. Kumar, V. Dangur, and J. Vaya, *J. Am. Chem. Soc.*, **116**, 11151 (1994). b) P. G. Andersson and S. Schab, *Organometallics*, **14**, 1 (1995). c) J. M. Takacs, E. C. Lawson, and F. Clement, *J. Am. Chem. Soc.*, **119**, 5956 (1997).

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4 The "*syn*-effect" is herein defined as an effect which stabilizes the *syn*-conformation against the steric hindrance.

5 Related studies on the "*syn*-effect"; a) T. Hirata, Y. Sasada, T. Ohtani, T. Asada, H. Kinoshita, H. Senda, and K. Inomata, *Bull. Chem. Soc. Jpn.*, **65**, 75 (1992). b) T. Nakamura, S. K. Guha, Y. Ohta, D. Abe, Y. Ukaji, and K. Inomata, *Bull. Chem. Soc. Jpn.*, **75**, 2031 (2002). c) S. K. Guha, A. Shibayama, D. Abe, Y. Ukaji, and K. Inomata, *Chem. Lett.*, **32**, 778 (2003). d) S. K. Guha, Y. Ukaji, and K. Inomata, *Chem. Lett.*, **32**, 1158 (2003). e) S. K. Guha, A. Shibayama, D. Abe, M. Sakaguchi, Y. Ukaji, and K. Inomata, *Bull. Chem. Soc. Jpn.*, **77**, 2147 (2004). See also references cited therein.

6 In the present reaction, stereochemistry of C_α–C_β double bond was *E* in all cases. Herein, only the stereochemistry of C_γ–C_δ double bond was discussed.

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8 The angles {Cl–Pd–Cl, P–Pd–P} in the complexes [$PdCl_2$(dppe)] {94°, 86°},[7] [$PdCl_2$(dppp)] {91°, 91°},[7] and [$PdCl_2$(dppb)] {90°, 94°}[14] might correlate with the *syn*-β-elimination; that is, the phosphine ligand that forms the complex having larger Cl–Pd–Cl and smaller P–Pd–P angles decelerates *syn*-β-elimination because β-agostic interaction would occur in the geometry in which the angle H–Pd–C is small, ca. 63° based on calculation.[15]

9 The *anti*-β-elimination via **E** could be ruled out because (*E*)-diene is anticipated to be produced selectively due to steric repulsion between substituents.

10 a) T. Laube and H. U. Stilz, *J. Am. Chem. Soc.*, **109**, 5876 (1987). b) T. Laube and T.-K. Ha, *J. Am. Chem. Soc.*, **110**, 5511 (1988). c) P. R. Rablen, R. W. Hoffmann, D. A. Hrovat, and W. T. Borden, *J. Chem. Soc., Perkin Trans. 2*, **1999**, 1719.

11 Y. Apeloig, P. v. R. Schleyer, and J. A. Pople, *J. Am. Chem. Soc.*, **99**, 5901 (1977).

12 In the cases of **1a**, **1b**, **1f**, **1g**, it is also possible to stabilize the *syn*-conformation at the transition state of E2′-elimination by 6π-electron homoaromaticity involving the developing charge at the δ-position and a pseudo *p*-orbital of the neighboring CH_2 (R = CH_2R′), or a lone pair of electrons in a *p*-orbital of the neighboring hetero atom X (R = XR′), respectively.[3,5]

13 The order of BnS group varied depending on the reactions.[3,5] This might be related to the energy level of π^* in the substrates, because $\sigma_{C\text{-}S} \rightarrow \pi^*$ interaction could also work in the transition state; see Ref. 5e and references cited therein. When the energy level of π^* is not close enough to that of $\sigma_{C\text{-}S}$, 6π-electron homoaromaticity[12] might relatively more contribute to the "*syn*-effect" of the BnS group.

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