

Rhodium Catalyzed Anti-Markovnikov Addition of Triphenylphosphine to 1,3-Dienes A Novel Method to Separate Pure (Z)-1,3-Alkadienes from Isomeric Mixtures

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Rhodium-catalyzed addition of triphenylphosphine and trifluoromethanesulfonic acid to (*E*)-1,3-dienes gives (*E*)-3-alkenylphosphonium salts in the anti-Markovnikov mode. The addition reactions to (*E*)-1,3-dienes proceed more rapidly than those to (*Z*)-1,3-dienes, which can be utilized to separate pure (*Z*)-1,3-dienes from isomeric mixtures.

We have previously reported that the regioselective addition of triphenylphosphine (**1**) and methanesulfonic acid to alkynes can be catalyzed by transition metal complexes. The Markovnikov adducts are obtained when a palladium complex is employed, and anti-Markovnikov adducts with rhodium complexes.¹ The palladium complex also catalyzes the addition to allenes giving allylphosphonium salts in the Markovnikov mode,² the regioselectivity of which can be explained by the formation of π -allyl complexes. Described here is the addition of **1** and trifluoromethanesulfonic acid **2** to 1,3-dienes **3**. A notable aspect of this reaction is that a rhodium complex gives anti-Markovnikov 1,2-adducts **4** with the phosphine attacking at the 1-carbon atom. In addition, **1** and **2** add to (*E*)-**3** more rapidly than (*Z*)-**3**, which can be utilized to separate pure (*Z*)-**3** from isomeric mixtures.

When (*E*)-6-phenyl-1,3-hexadiene (*E*)-**3a** was treated with equimolar amounts of **1** and **2** in the presence of RhH(PPh₃)₄ (2.5 mol%) in THF at 0 °C for 3 h, (*E*)-(6-phenyl-3-hexenyl)-triphenylphosphonium PF₆ salt (*E*)-**4a** was obtained in 89% yield after anion exchange with LiPF₆ and recrystallization. The addition of phosphine and hydrogen occurs at the 1-carbon and the 2-carbon atom of (*E*)-**3a**, respectively, and no other isomer is detected by ¹H-NMR examination of the crude reaction mixture. The stereochemistry of (*E*)-**4a** was determined by the NOE spectroscopy. The rhodium catalyst is essential for the addition, and no reaction occurs in its absence. Reactions of several (*E*)-**3** are shown in Table 1, which generally give the 1,2-adducts in the anti-Markovnikov mode. The effect of substituents on the aromatic ring is small as indicated by the reactions of 1-aryl-1,3-butadienes (Run 4–6). The addition to isoprene **3g** proceeds at –20 °C more selectively than at 0 °C, and a 1,2-adduct **4g** and a 1,4-adduct, 3-methyl-2-butenylphosphonium salt, are obtained in a ratio of 7 : 1. Pure **4g** is isolated from the mixture by recrystallization in 67% yield.

Next, reactions of (*Z*)-1,3-dienes are examined. Treatment of (*Z*)-**3e** with **1** and **2** at room temperature for 6 h gave 1,2-adduct (*Z*)-**4e** in 45%, which was accompanied by a 1,4-adduct (*E*)-**5e** (15%) (Table 2, Run 3). The stereochemistry of (*Z*)-**4e** was determined by the ¹H-NMR coupling constant (*J* = 10.8 Hz), and the double bond configuration is retained as is in the reactions of (*E*)-**3**. The (*E*)-configuration of (*E*)-**5e** was determined by NOE experiment. The yield of (*Z*)-**4** decreases and that of (*E*)-**5** increases, when aliphatic (*Z*)-**3** is employed (Run 1 and 2).

Table 1. Rhodium-catalyzed addition of PPh₃ and CF₃SO₃H to (*E*)-1,3-diene^a

Run	Substrate	Product	Yield/% ^b
1			89
2			100 ^c
3			74
4			82 ^d
5			68 ^d
6			73 ^d
7			67 ^e

^aConducted in 1 mmol scale. ^bIsolated yield. ^cNMR yield. ^dConducted using 5.0 mol% of RhH(PPh₃)₄. ^eConducted at –20 °C, and **4g** was isolated from a 7 : 1 mixture with 3-methyl-2-butenylphosphonium salt by recrystallization.

Table 2. Rhodium-catalyzed addition of PPh₃ and CF₃SO₃H to (*Z*)-1,3-diene

Run	R	Yield of (<i>Z</i>)- 4 /%	Yield of (<i>E</i>)- 5 /%
1	Ph(CH ₂) ₂ a	29	51
2	<i>n</i> -C ₇ H ₁₅ h	31	56
3	<i>p</i> -Tolyl e	45	15

^aNMR yield.

Notably, (*E*)-**3** reacts considerably faster than (*Z*)-**3**; for example, while the reaction of (*E*)-**3a** takes place at 0 °C, that of (*Z*)-**3a** only at room temperature. The different rate can be utilized to separate (*Z*)-**3** from stereoisomeric mixture of **3**. When **3a** (*E*/*Z* = 50/50) was treated with 0.6 molar amounts of **1** and **2** at 0 °C for 6 h, phosphonium salt (*E*)-**4a** (53% by ¹H-NMR) was

obtained, which was accompanied by the recovered (Z)-**3a** (Table 3, Run 1). The pure (Z)-**3a** can be separated by extraction in 41% yield based on **3a**.³ As judged from the yields of the products, essentially no double bond isomerization appears to take place during the reaction. Several other (Z)-1,3-dienes (**Z-3**) are also efficiently isolated from isomeric mixtures of **3** (Table 3). Although (Z)-1,3-dienes are versatile synthetic intermediates for natural products and functionalized polymers, their preparation is generally not straightforward. (Z)-Selective Wittig reaction was reported by Schlosser using a sophisticated allylphosphonium salt.⁴ Partial *cis*-hydrogenation of enyne⁵ or metal-catalyzed cross-coupling of (Z)-alkenyl halides or (Z)-alkenylmetals⁶ employed stepwise transformations and/or geometrically pure starting materials. The present method may therefore be convenient, since it can isolate pure (Z)-1,3-dienes from isomeric mixtures.

Table 3. Separation of (Z)-1,3-diene from isomeric mixture

$$\begin{array}{c} \text{PPh}_3 \text{ 1} \\ \text{CF}_3\text{SO}_3\text{H 2} \end{array} + \text{R} \begin{array}{c} \diagup \\ \diagdown \end{array} \begin{array}{c} \diagdown \\ \diagup \end{array} \xrightarrow[\text{THF, 0}^\circ\text{C, 6 h}]{\text{RhH(PPh}_3)_4 \text{ (2.5 mol\%)}} \begin{array}{c} \text{R} \begin{array}{c} \diagup \\ \diagdown \end{array} \begin{array}{c} \diagdown \\ \diagup \end{array} \\ \text{(Z)-3} \end{array} + \begin{array}{c} \text{R} \begin{array}{c} \diagup \\ \diagdown \end{array} \begin{array}{c} \diagdown \\ \diagup \end{array} \text{P}^+\text{Ph}_3 \\ \text{CF}_3\text{SO}_3^- \\ \text{(E)-4} \end{array}$$

Run	R ^a	Yield of (Z)- 3 /%		Yield of (E)- 4 /%	
1	Ph(CH ₂) ₂	a	41	53, 21 ^d	
2	<i>n</i> -C ₇ H ₁₅	h	43	47	
3	<i>n</i> -C ₉ H ₁₉	i	49	51	
4	<i>t</i> -BuCH ₂ CHMeCH ₂	j	47	48	

^a**3a**: E/Z = 50/50, **3h**: E/Z = 54/46, **3i**: E/Z = 50/50, **3j**: E/Z = 55/45.
^bIsolated yield based on **3**. ^cNMR yield based on **3**. ^dIsolated yield of PF₆ salt.

In general, transition metal catalyzed addition reactions to 1,3-dienes give 1,4-adducts via π -allyl metal intermediates.⁷ The anti-Markovnikov 1,2-addition in the present reaction is therefore unusual. It is also noted that palladium-catalyzed addition of **1** and **2** to unsaturated compounds studied so far gives the Markovnikov adducts, and rhodium the anti-Markovnikov adducts.^{1,2} The origin and the generalities of these selectivities are now under investigation.

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References and Notes

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- Under an argon atmosphere, a mixture of RhH(PPh₃)₄ (290 mg, 2.5 mol%), **1** (6 mmol, 1.57 g), **3a** (10 mmol, 1.58 g, E/Z = 50/50), and **2** (0.53 mL, 6 mmol) in THF (20 mL) was stirred at 0°C for 6 h. A small amount of activated charcoal was added, and the mixture was stirred for 30 min to adsorb the metal complex. The insoluble materials were removed by filtration, and the solution was concentrated under reduced pressure (53% yield of (E)-**4a** by ¹H-NMR). The residue was washed with ether, and the ether solution was washed with saturated NaHCO₃ and brine. After being dried over MgSO₄ the solution was concentrated, and flash chromatography (hexane) over silica gel gave (Z)-**3a** (650 mg, 41%). The residue obtained by the ether washing was dissolved in ethanol (10 mL), and LiPF₆ (10 mmol, 1.52 g) was added. After being stirred at room temperature for 1 h, the precipitated solid was collected by filtration. To the solid was added CHCl₃, and insoluble CF₃SO₃Li was removed by filtration. The solution was concentrated, and the residue was recrystallized from ethanol giving (E)-**4a** (586 mg, 21%) as colorless solid. Mp. 124.0–125.0°C. ³¹P-NMR (162 MHz, CDCl₃) δ –143.7 (septet, *J* = 435.8 Hz), 22.2.
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