

A Novel Preparative Method for Homo- and Heteroannular Conjugated Dienes in Decalin Derivatives by the Palladium-Catalyzed Regioselective Elimination Reaction of Allylic Carbonates under Mild Conditions

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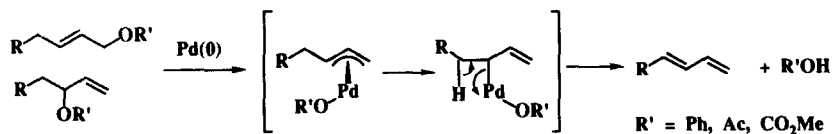
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key words

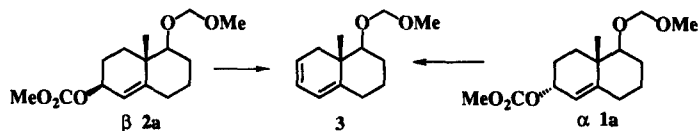
Provitamin D, Allyl carbonates, Palladium phosphine complex catalysts

Abstract; Homoannular conjugated dienes in decalin systems can be prepared by the palladium-catalyzed elimination reaction of α -allylic carbonates, and heteroannular dienes are obtained from β -allylic carbonates.

Both homoannular and heteroannular conjugated dienes in decalin systems are present in a number of natural products, and their regioselective synthesis is an important problem in natural products synthesis. We now wish to report a novel synthetic method for both homo- and heteroannular conjugated dienes at will based on π -allylpalladium chemistry. We found that conjugated dienes are generated by the treatment of allylic compounds with a palladium catalyst via π -allylpalladium complex formation and subsequent elimination of β -hydrogen.¹

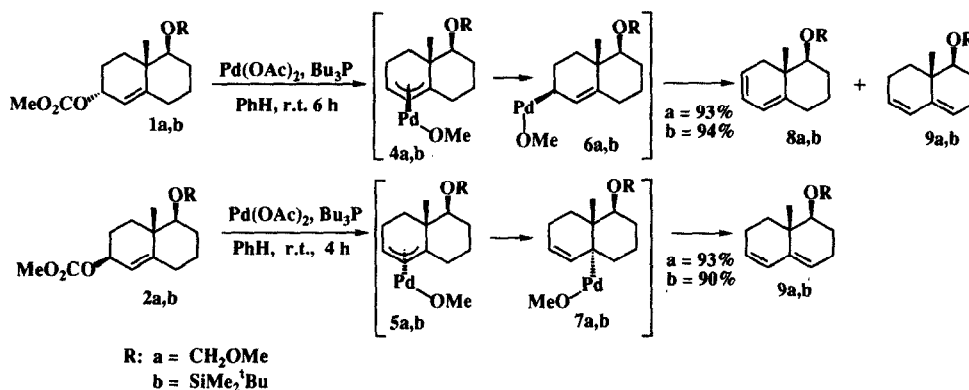


As one useful application of this elimination reaction, we have reported a new synthetic method for homoannular conjugated dienes in decalin derivatives by the palladium-catalyzed elimination reaction of allylic compounds in a previous paper.² The following α - and β -allylic carbonates **1a** and **2a** were converted into the homoannular conjugated dienes **3** with high regioselectivity by the treatment in boiling dioxane with the palladium catalyst prepared from $\text{Pd}_2(\text{dba})_3$ and an excess of *n*-Bu₃P. This method was successfully applied to the synthesis of provitamin D, which has a homoannular conjugated diene in B ring.

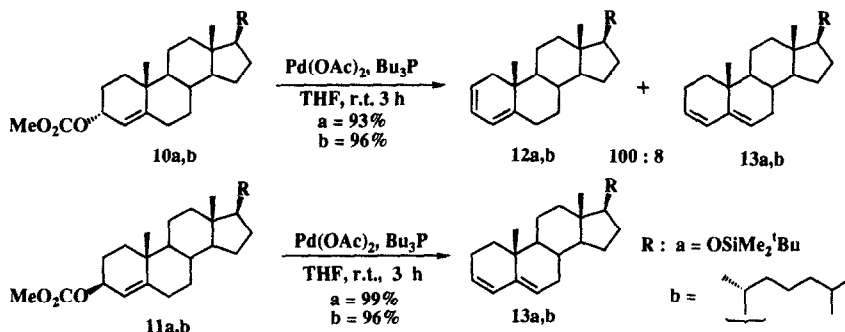


In our continuing studies on various palladium-catalyzed reactions, we have made important observation that preparative methods for palladium catalysts have crucial effects on the catalytic activity and course of catalytic reactions. Typically, we found that the catalyst prepared by mixing Pd(OAc)₂ and pure *n*-Bu₃P in a 1:1 ratio is very active.³ The elimination reaction of the allylic carbonates **1a,b** and **2a,b** proceeded rapidly even at room temperature with this catalyst. More importantly, we found that either the hetero- and homoannular dienes **8a,b** or **9a,b** were obtained regioselectively depending on the stereochemistry of the allylic carbonates. Namely the homoannular dienes **8a,b** were obtained as main products and the heteroannular conjugated dienes **9a,b** as minor products (ca. 5%) when the α -carbonates **1a,b** were treated with the palladium catalyst in THF or benzene at room temperature. When the β -carbonates **2a,b** were subjected to the palladium catalysis, the heteroannular dienes **9a,b** were obtained regioselectively. Stereochemical assignments were made based on NMR spectra.⁴

The initial step is the formation of π -allylpalladium complexes **4** and **5**, which is known to be inversion. The elimination is believed to proceed via the syn elimination of Pd-H from the σ -allylpalladium complexes **6** and **7**. The different σ -allylpalladium complexes **6** (β -Pd complex) and **7** (α -Pd complex) are formed from α - and β -carbonates **1a,b** and **2a,b** by inversion of the stereochemistry and they are responsible for giving the homo- and heteroannular dienes **8a,b** and **9a,b**.

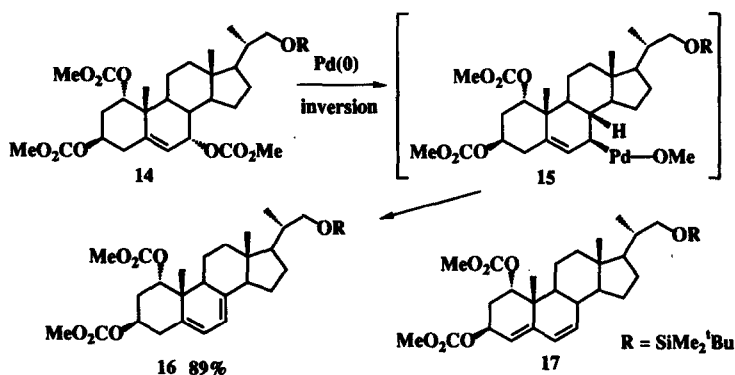


The regioselective elimination reaction was applied to steroids to give the following homo- and heteroannular conjugated dienes **12a,b** and **13a,b** in A ring of steroid depending on the stereochemistry of the allylic carbonates. The 3- α -carbonates **10a,b** afforded the homoannular 2,4-dienes **12a,b** as major products. The heteroannular 3,5-dienes **13a,b** were obtained regioselectively from the 3- β -carbonates **11a,b**.⁴

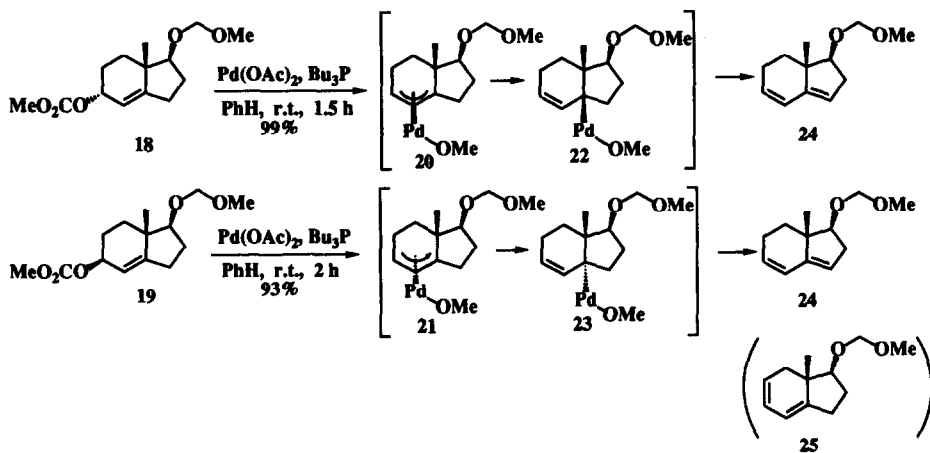


Then the reaction was applied to the synthesis of provitamin D **16**, which has a homoannular conjugated diene in B ring. 7- α -Carbonate **14** was prepared and subjected to the palladium catalysis. The reaction at room temperature was slower than those of **10** and **11**. At 40° C, it completed after 2.5 h. As expected, the regioselective elimination took place to afford the provitamin D **16**, which has the homoannular conjugated diene structure. Corresponding heteroannular diene **17** was not detected. The structure of **16** was confirmed by comparison of its spectral data with those of an authentic sample.⁴

It should be mentioned that, unlike the elimination reaction of the corresponding steroidal allylic trifluoroacetate in boiling dioxane using Pd₂(dba)₃ and excess *n*-Bu₃P in the presence of Et₃N to give only the homoannular diene as reported in the previous paper,² the present reaction of steroidal allylic carbonates **10a,b**, **11a,b** and **14** with the active catalyst proceeds smoothly at room temperature or 40° under neutral conditions to give either homo- or heteroannular conjugated dienes with high regioselectivity depending on the stereochemistry of the allylic carbonates.



The diene formation from the α - and β -carbonates of hydrindene system (**18** and **19**) was tried. In this system, only the heteroannular diene **24** was obtained from both α - and β -allylic carbonates **18** and **19**. The heteroannular diene **24** seems to be the primary product and even a trace of the homoannular diene **25** could not be detected.



The result that only the heteroannular diene **24** was obtained is surprising, and we are planning to explain this result by comparing the stability of the homo- and heteroannular dienes and, if possible, of the intermediate complexes in the hydrindene system by theoretical calculation.

Thus we could establish the novel synthetic method for both homo- and heteroannular dienes in decalin systems at will under mild and neutral conditions by the use of the active palladium catalyst simply by changing the stereochemistry of the allylic carbonates.

References

1. Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.*, 2075 (1978).
2. Takahashi, T.; Nakagawa, N.; Minoshima, T.; Yamada, H.; Tsuji, J. *Tetrahedron Lett.*, 30, 4333 (1990).
3. The purity of n-Bu₃P is crucial for reproducibility of the catalytic reaction. n-Bu₃P in a "Sure-seal" bottle purchased from Aldrich was used.
4. ¹H and ¹³C NMR (400 MHz and 100 MHz, CDCl₃) spectra of the major products.
 - 8a** ¹H, 0.97 (s, 3H, angular CH₃), 5.53-5.60 (m, 1H, C=CH), 5.60-5.69 (m, 1H, C=CH), 5.71-5.79 (m, 1H, C=CH): ¹³C, 118, 123.1, 124.1, 143.6 (olefinic carbons).
 - 9a** ¹H, 1.01 (s, 3H, angular CH₃), 5.29-5.35 (m, 1H, C=CH), 5.57-5.66 (m, 1H, C=CH), 5.90-5.98 (m, 1H, C=CH): ¹³C, 122.2, 125.7, 128.1, 139.6 (olefinic carbons).
 - 12a** ¹H, 0.72 (s, 3H, angular CH₃), 0.92 (s, 3H, angular CH₃), 5.49-5.52 (m, 1H, C=CH), 5.59-5.66 (m, 1H, C=CH), 5.72-5.80 (m, 1H, C=CH): ¹³C, 117.0, 123.0, 123.2, 146.3 (olefinic carbons).
 - 13a** ¹H, 0.75 (s, 3H, angular CH₃), 0.97 (s, 3H, angular CH₃), 5.36-5.41 (m, 1H, C=CH), 5.56-5.62 (m, 1H, C=CH), 5.90-5.97 (m, 1H, C=CH): ¹³C, 122.9, 125.0, 129.0, 141.6 (olefinic carbons).
 - 16** ¹H, 0.62 (s, 3H, angular CH₃), 1.00 (s, 3H, angular CH₃), 3.76 (s, 3H, OCH₃), 3.78 (s, 3H, OCH₃), 4.81-4.94 (m, 2H, CH-O), 5.33-5.39 (m, 1H, C=CH), 5.64-5.70 (m, 1H, C=CH): ¹³C, 115.4, 122.1, 133.8, 141.2 (olefinic carbons), 154.9, 155.0 (C=O carbons)
 - 24** ¹H, 0.96 (s, 3H, angular CH₃), 5.22-5.29 (m, 1H, C=CH), 5.68-5.77 (m, 1H, C=CH), 6.06-6.13 (m, 1H, C=CH): ¹³C, 118.3, 123.1, 129.2, 145.0 (olefinic carbons).

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