Communications to the Editor

The First Observation of Syn–Anti Dichotomy in the Formation of (π-Allyl)palladium Complexes

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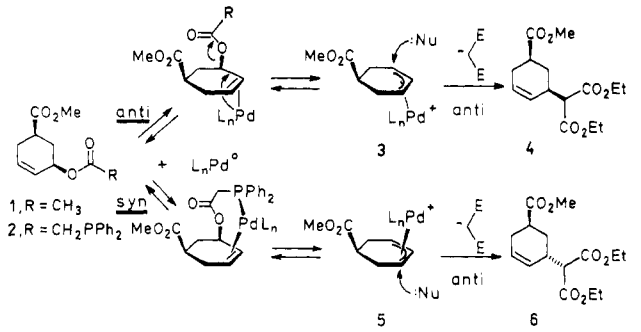
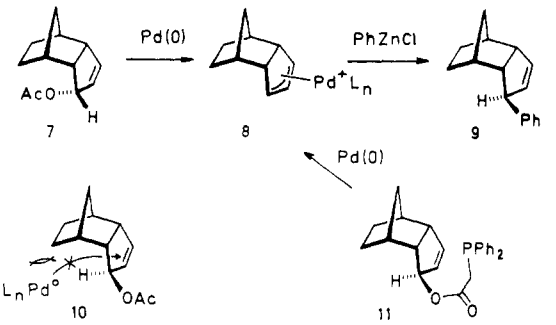
Previous studies carried out in the last two decades[1] demonstrated that formation of the (π-allyl)palladium complexes from allylic esters uniformly proceeds via an anti mechanism (**1** → **3**).[2] The following reaction with stabilized C-nucleophiles leads to **4**, again via an anti mechanism[1] (Scheme I). In contrast, reaction of the complexes with organometallics,[3] such as aryl- and vinylzinc halides,[4,5] gives syn products in the second step.

However, a syn mechanism for the complex formation should also be stereoelectronically allowed, in spite of being apparently higher in energy. This raises the question of whether or not the syn route could be boosted, e.g., by a precoordination of the Pd(0) reagent to the allylic leaving group.[6] We prepared phosphinoacetate[9] **2** (Scheme I) and treated it with $LiCH(CO_2Et)_2$ and a catalytic-(5 mol %)to-stoichiometric amount of Pd(0) in various solvents and temperature range. We found that with this substrate we could achieve up to a 3:2 ratio[11] of the products **4** and **6**. Since blank experiments showed that no epimerization of **2** occurred prior to the reaction, this result suggests that the minor product

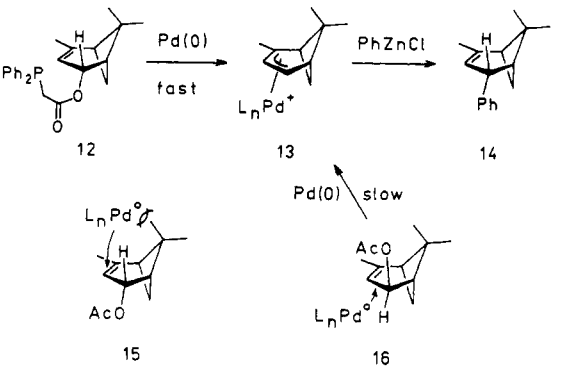
Scheme I



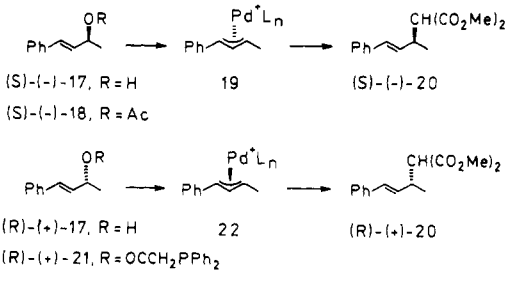
Scheme II



Scheme III



Scheme IV



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(9) Prepared by esterification of the corresponding alcohol with $Ph_2PCH_2CO_2H$[10] using the DCC/DMAP method.

(10) Jarolim, T.; Podlahová, J. *J. Inorg. Nucl. Chem.* **1976**, *38*, 125.

(11) $(Ph_3P)_4Pd$ (25 mol %), THF, 45 °C, 15 min.

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6 might really arise by the mechanism we looked for, involving precomplexation of the palladium reagent to the Ph_2P- group and formation of the complex **5**. But still, the competing anti mechanism in the first step remains the dominant reaction pathway giving finally the epimer **4** as the major product.

Although the stereoselectivity we achieved was not good,[12] this result was encouraging, and we turned our attention to sterically biased substrates **7**, **10**, and **11** (Scheme II). The acetate **7** is known[5] to form the intermediate Pd complex **8** via an ordinary anti mechanism and produce phenyl derivative **9** on the subsequent syn reaction with PhZnCl. In contrast, the epimeric acetate **10** is inert for the severe steric hindrance.[5] It turned out, to our delight, that the ester **11** of the same configuration as the inert acetate **10** readily reacted with PhZnCl/Pd(0), giving **9** as the sole product, identical with the compound obtained from the acetate **7** (Scheme II). Since the second step is known[4,5] to proceed stereospecifically in a syn fashion, the intermediate complex **8** formed from **11** should be the same as that arising from **7**. This is, again, consistent with the syn mechanism of the first step. Similarly, the phosphino ester **12** derived from (−)-*trans*-verbenol readily affords the corresponding phenyl derivative **14** as the result of the syn,syn two-step pathway (Scheme III). In contrast, the acetate **15** is inert under the same reaction conditions, while its epimer **16** reacts sluggishly, producing finally **14** via the ordinary anti,syn mechanism involving the complex **13**.

Since we have observed a clean syn mechanism of the complex formation with our sterically biased allylic esters, it was of interest to explore the reaction with a substrate free of any steric hindrance. (−)-Acetate **18** (58% ee) is known to produce (−)-**20** (58% ee) via the anti,anti sequence (Scheme IV) on a Pd(0)-catalyzed reaction with dimethyl sodiomalonate.[2c] We have prepared (diphenylphosphino)acetate (+)-**21** from the enantiomeric alcohol (+)-**17** of >99% ee[13] and carried out the Pd(0)-catalyzed reaction under the standard conditions. To our surprise, the reaction furnished a dextrorotatory product, which is consistent with the anti,anti pathway. Optical rotation of the product (+)-**20** indicated about 84% optical purity,[17] while ^1H NMR spectrum taken in the presence of $Eu(tfc)_3$ implied 74% ee.[18] It is obvious that in this case the precoordination of the Pd(0) reagent largely failed. However, the lower enantiomeric purity of the product suggests that **21** reacts via a mixture of two mechanisms, the classical anti,anti fashion (87%) accompanied by ca. 13% of the syn,anti pathway in contrast to the acetate **18** where the former clearly dominates. Hence, the anti,anti mechanism is apparently lower in energy even for the phosphinoacetate **21**.

In conclusion, these experiments bring, for the first time, an evidence that syn mechanism of the formation of palladium η^3-complex from allylic substrates may be enforced by precoordination of the Pd(0) reagent to a specially designed leaving group.[19] This finding broadens the applicability of the transition-metal-catalyzed allylic substitution, since it shows that in substrates where the classical anti route of the complex formation is impaired by steric congestion, our new leaving group enables the reaction to occur.

Acknowledgment. We thank Drs. M. Buděšinský and J. Zajíček for taking NMR spectra and Dr. A. Jegorov for a generous gift of (diphenylphosphino)acetic acid.

Supplementary Material Available: IR and NMR characterization of **2**, **11**, **12**, **14**, and **21** (2 pages). Ordering information is given on any current masthead page.

(12) In contrast to the cuprates, no substantial syn pathway could be detected in the Pd-catalyzed reaction of carbamates (**1**, R = $NHCH_2Ph$, NHPh, and $N(CH_3)_2$). We have always isolated **4** in good yields and with high diastereoisomeric excess (>10:1), while **1**, R = NH_2, remained unreacted.

(13) We were unable to reproduce the asymmetric reduction of benzylidene acetone described in the literature.[14] On the other hand, we have achieved an excellent kinetic resolution of the racemic alcohol **17** via the stoichiometric Sharpless epoxidation using (+)-diisopropyl tartrate.[15] This procedure gave us (+)-**17** whose $[\alpha]_D$ +24.5° (*c* 2.8, $CHCl_3$) indicates >99% ee[16] in agreement with the ^1H NMR spectra taken in the presence of $Eu(tfc)_3$.

(14) Terashima, S.; Takano, N.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1980**, 1026.

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(16) Partridge, S. M.; Phillips, H. *J. Chem. Soc.* **1936**, 85.

(17) According to ref 2c, the maximum specific rotation of (+)-**20** is $[\alpha]_D$ +68.9° (*c* 1.0, $CHCl_3$). Our product had $[\alpha]_D$ +58° (*c* 3.9, $CHCl_3$).

(18) In addition to **20**, 5% of allylic isomer was formed as revealed by ^1H NMR spectrum of the crude product.

(19) For a recent report of syn substitution of aliphatic allylic acetate catalyzed by Mo(0), see: Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670.

A Model Reaction for Mo(VI) Reduction by Molybdopterin

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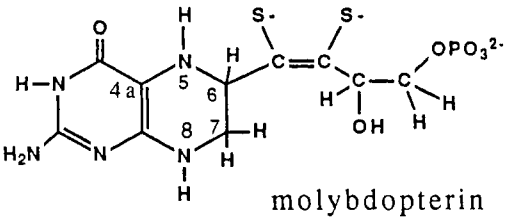
The molybdenum cofactor, Mo-co, is a dissociable cofactor common to xanthine oxidase, sulfite oxidase, nitrate reductase, and other enzymes involved in oxygen atom transfer.[1] Mo-co possesses one molybdenum atom and a pterin component known as molybdopterin.[2] The proposed structure for molybdopterin is supported by spectroscopic and chemical data.[2-4]



molybdopterin

The function of molybdopterin in Mo-co has not been determined. Molybdopterin may be present to coordinate the molybdenum atom through the dithiolene sulfur atoms.[4] On the basis of the known redox roles played by tetrahydropterin cofactors in other metalloenzymes,[5] we propose a different, perhaps additional, role for molybdopterin. We show that a tetrahydropterin is capable of reducing molybdenum(VI) in a sulfur coordination environment.

$MoO_2(detc)_2$ [detc = diethyldithiocarbamate] has been intensely studied because it mimics certain aspects of the Mo site in Mo-co-containing enzymes.[6-8] The reaction chemistry of $MoO_2(detc)_2$ includes the oxo-transferase activity characteristic of molybdoenzyme substrate reactions.[9-12] We have found that 6,7-dimethyl-5,6,7,8-tetrahydropterin (H_4dmp) is able to reduce

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