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Catalytic Asymmetric Intramolecular Aminopalladation: Improved Palladium(II) Catalysts

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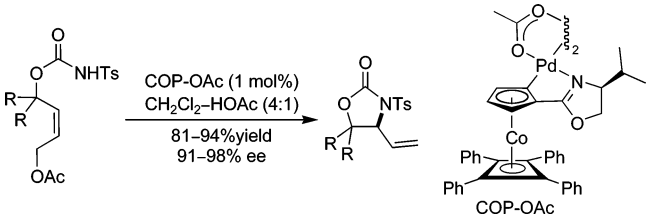

Cobalt oxazoline palladacyclic (COP) complex **4** containing acetate as a bridging ligand is an excellent catalyst for asymmetric intramolecular aminopalladation to synthesize 4-vinyloxazolidin-2-ones in 91−98% ee. In contrast to previously reported Pd(II) catalysts, COP-OAc (**4**) promotes the asymmetric cyclization of (*Z*)-allylic *N*-tosylcarbamates without prior activation by silver salts.

Significant development of the catalytic asymmetric chemistry of palladium(II) has occurred only in the past decade.[1−3] In 2002, we reported the asymmetric construction of enantioenriched 4-vinyloxazolidin-2-ones from derivatives of (*Z*)-butene-1,4-diol using the ferrocene oxazoline palladacyclic (FOP) catalyst **1b**.[4,5] For example, cyclization of (*Z*)-allylic *N*-tosylcarbamate **5** with 0.5−5 mol % of FOP trifluoroacetate catalyst **1b** in 1:1 CH_2Cl_2−$MeNO_2$ at room temperature produced the vinyloxazolidinone **6** in good yield (91−98%) and enantioselectivity (90−93% ee) (eq 1). Unfortunately, the iodine-bridged precatalyst **1a** was inactive, thus requiring **1a** to be preactivated by reaction with 4 equiv of silver(I) trifluoroacetate. We disclose herein a better palladium(II) catalyst for this reaction, di-μ-acetatobis[(η^5-(*S*)−(p*R*)-2-(2′-(4′-methylethyl)oxazolinyl)cyclopentadienyl,1-C,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium (COP-OAc, **4**),[6] which does not require preactivation with a silver salt.

TABLE 1. Enantioselective Conversion of 5 to (*S*)-6[a]

entry	catalyst (mol %)	solvent (% HOAc)	time (h)	yield[b] (%)	ee[c] (%)
1[d]	**2** (5.0)	CH_2Cl_2 (0)	48	51	77
2[d]	**3** (5.0)	CH_2Cl_2 (0)	48	87	94
3	**4** (1.0)	CH_2Cl_2 (0)	6	>99	71
4	**4** (1.0)	CH_2Cl_2 (5)	7	87	87
5	**4** (5.0)	CH_2Cl_2 (15)	4.5	>99	90
6	**4** (1.0)	CH_2Cl_2 (20)	10	94	92
7	**4** (1.0)	HOAc (100)	16	75	90
8	**4** (0.1)	CH_2Cl_2 (20)	4.5	4[e]	
9[f]	**4** (1.0)	CH_2Cl_2 (20)	29	87	95

[a] Conditions: 23 °C, [substrate] = 0.6 M. [b] Yield after column chromatography. [c] Determined by HPLC analysis using a Chiracel OD-H column (±2%). [d] 23 °C, [substrate] = 1.5 M. [e] Conversion (%, by NMR analysis). [f] Reaction conducted at 0 °C.

Recently, we reported that the cobalt oxazoline palladacyclic catalysts **2** (COP-Cl) and **3** (COP-hfacac) promote the asymmetric rearrangement of prochiral allylic imidates to form enantioenriched chiral allylic amides without activation by silver salts[7] and that COP complex **4** (COP-OAc) catalyzes the asymmetric reaction of these precursors with carboxylic acids to form chiral allylic esters.[8] Thus, we examined initially the asymmetric cyclization of allylic *N*-tosylcarbamate **5** to 2-oxazolidinone **6** using these three COP catalysts. As summarized in Table 1, COP-Cl (**2**) displayed low reactivity, producing vinyloxazolidinone **6** in modest enantiopurity (entry 1). Monomeric COP catalyst **3** was more effective, giving oxazolidinone (*S*)-**6** in 87% yield and 94% ee after 48 h at room temperature (entry 2).[9] Catalyst **4** containing acetate as a bridging ligand showed enhanced reactivity.

(1) For the first examples, see: (a) Hosokawa, T.; Miyagi, S.; Murahashi, D.-I.; Sonoda, A. *J. Chem. Soc., Chem. Commun.* **1978**, 687−688. (b) Hosokawa, T.; Uno, T.; Inui, S.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1981**, *103*, 2318−2323. (c) Hosokawa, T.; Murahashi, S.-I. *Acc. Chem. Res.* **1990**, *23*, 49−54.

(2) Tsuji, J. *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*; Wiley: Chichester, England, 2004.

(3) Allylic imidate rearrangements: (a) Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 1449−1456. (b) Hollis, T. K.; Overman, L. E. *Tetrahedron Lett.* **1997**, *38*, 8837−8840. (c) Uozumi, Y.; Kato, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1065−1072. (d) Cohen, F.; Overman, L. E. *Tetrahedron: Asymmetry* **1998**, *9*, 3213−3222. (e) Jiang, Y.; Longmire, J. M.; Zhang, X. *Tetrahedron Lett.* **1999**, *40*, 1449−1450. (f) Leung, P.-H.; Ng, K.-H.; Li, Y.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1999**, 2435−2436. (g) Donde, Y.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 2933−2934. (h) Kang, J.; Hyung, K. Y.; Choi, D. H. *Tetrahedron Lett.* **2002**, *43*, 9509−9512. (i) Kang, J.; Kim, T. H.; Yew, K. H.; Lee, W. K. *Tetrahedron: Asymmetry* **2003**, *14*, 415−418. Synthesis of heterocycles: (j) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Am. Chem. Soc.* **1997**, *119*, 5063−5064. (k) Uozumi, Y.; Kyota, H.; Kato, K.; Ogasawara, M.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 1620−1625. (l) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604−7605. (m) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *J. Am. Chem. Soc.* **2001**, *123*, 2907−2908. (n) Tietze, L. F.; Sommer, K. M.; Zinngrebe, J.; Stecker, F. *Angew. Chem., Int. Ed.* **2005**, *44*, 257−259. Other reactions: (o) Sodeoka, M.; Ohrai, K.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 2648−2649. (p) Sugiura, M.; Nakai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2366−2368. (q) Hagiwara, E.; Fujii, A.; Sodeoka, M. *J. Am. Chem. Soc.* **1998**, *120*, 2474−2475. (r) El-Qisairi, A.; Hamed, O.; Henry, P. M. *J. Org. Chem.* **1998**, *63*, 2790−2791. (s) Mikami, K.; Hatano, M.; Terada, M. *Chem. Lett.* **1999**, 55−56. (t) Perch, N. S.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 6960−6961. (u) Stark, M. A.; Jones, G.; Richards, C. J. *Organometallics* **2000**, *19*, 1282−1291.

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(5) For a non-asymmetric variant of this reaction, see: Lei, A.; Liu, G.; Lu, X. *J. Org. Chem.* **2002**, *67*, 974−980.

(6) (a) Anderson, C. E.; Kirsch, S. F.; Overman, L. E.; Richards, C. J.; Watson, M. P. *Org. Synth.*, submitted for publication; available from the senior author upon request. (b) Stevens, A. M.; Richards, C. J. *Organometallics* **1999**, *18*, 1346−1348. (c) COP-OAc can be generated from COP-Cl[6a,b] by reaction in CH_2Cl_2 at room temperature with 2.5 equiv of AgOAc, followed by filtration through silica gel. (*S*)-COP-Cl is available currently from Aldrich Chemical Co. (64663-6); both (*S*)- and (*R*)-COP-OAc will be available commercially shortly.

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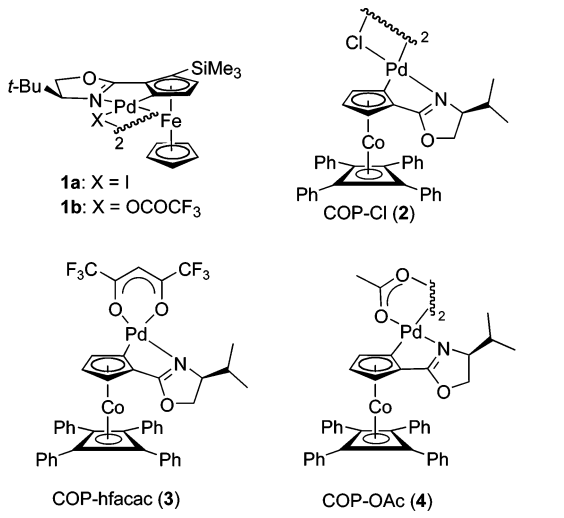
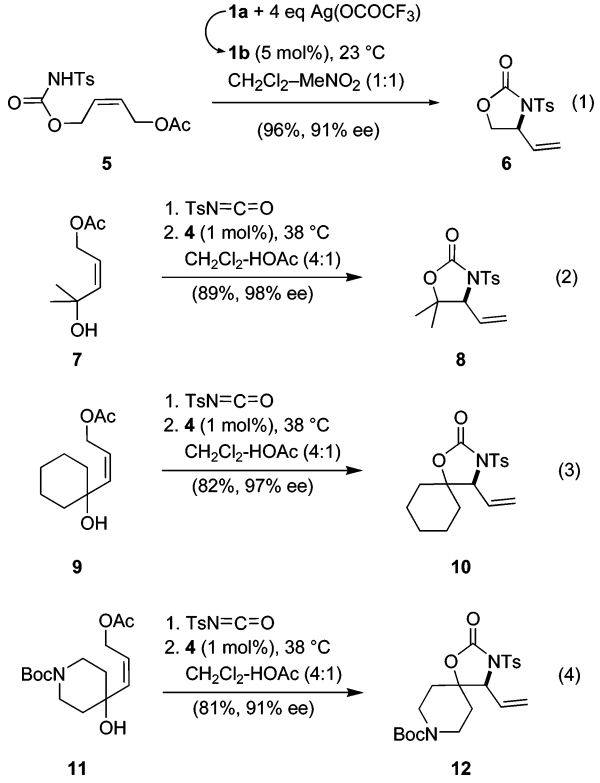
Thus, oxazolidinone (*S*)-**6** was obtained in excellent yield after 6 h in CH_2Cl_2 at room temperature in the presence of 1 mol % of COP-OAc (**4**), although enantiopurity was modest (entry 3). To our surprise, adding acetic acid as a cosolvent significantly improved enantioselection in forming oxazolidinone (*S*)-**6**, although the catalysis rate was slowed somewhat (entries 4−7).[10] The best compromise between reaction rate and enantioselectivity was realized using a 4:1 mixture of CH_2Cl_2−HOAc, in which case oxazolidinone (*S*)-**6** was produced in in 94% yield and 92% ee after 10 h using 1 mol % of catalyst **4** (entry 6). Performing the cyclization of carbamate **5** at 38 °C slightly increased the reaction rate with little erosion in enantioselectivity. Reducing the catalyst concentration to 0.1 mol % led to only 4% conversion after 4.5 h at room temperature (entry 8). Enantiomeric purity of (*S*)-**6** was improved to 95% ee at 0 °C, however a reaction time of 29 h was required to obtain a satisfactory yield (entry 9). As the use of an excess of a silver salt is not required for the COP-OAc catalyzed cyclization of **5** to (*S*)-**6**, this method is more practical than the one we reported previously.[4]

It is also possible to conduct the COP-OAc-catalyzed cyclization with crude allylic *N*-tosylcarbamates prepared in situ from the reaction an allylic alcohol with an *N*-sulfonylisocyanate, a modification that is particularly advantageous with tertiary allylic alcohols whose sulfonylcarbamate derivatives are quite labile. Three examples of this sequence are shown in eqs 2−4. In each case, the 5,5-disubstituted 2-vinyloxazolidin-2-one product was produced in high enantiomeric purity (91−98% ee) and in good overall yield (81−89%) when the cyclization was carried out at 38 °C in 4:1 CH_2Cl_2−HOAc using 1 mol % of COP-OAc (**4**). As observed with FOP catalyst **1b**, the intramolecular aminopalladation method reported herein is limited to (*Z*)-allylic acetates; *E* stereoisomers were not transformed at room temperature or at 38 °C.

In conclusion, we have described an improved method for the palladium(II)-catalyzed asymmetric cyclization of prochiral (Z)-4-acetoxy-3-alkenyl *N*-tosylcarbamates to give chiral 2-vinyloxazolidin-2-ones. As preactivation of the catalyst by reaction with silver salts is not required, the COP-OAc (**4**) catalyzed reaction has distinct advantage over the FOP-catalyzed procedure described earlier from our laboratories.[4]





Experimental Section.

Prochiral (*Z*)-4-acetoxybut-2-enyl tosylcarbamate (**5**) and (*Z*)-acetoxybutenols **7**, **9**, and **11** were prepared by literature procedures.[4,5]

Representative Procedure for COP-OAc-Catalyzed Cyclization of Tosylcarbamates. COP-OAc (**4**; 1 mol %, 3.0×10^{-3} mmol, 4.5 mg) was added to a solution of tosylcarbamate **5** (98 mg, 0.30 mmol) in CH_2Cl_2−HOAc (4:1, v/v; 0.5 mL), and the reaction vial was sealed, protected from light, and maintained at room temperature. After 10 h, the orange solution was concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel with 8:2 hexanes−EtOAc as eluent gave 3-*p*-toluenesulfonyl-4-vinyloxazolidin-2-one [(*S*)-**6**][4,5] as a colorless solid (75 mg, 0.28 mmol; 94%): mp 75−77 °C (lit.[4] mp 69−72 °C); $[\alpha]^{25}_{589} = -30.5$ ($c = 2.1$, $CHCl_3$) [lit.[4] $[\alpha]^{25}_{589} = -29.0$ ($c = 1.1$, $CHCl_3$)]; HPLC analysis indicated an enantiomeric excess of 92% [Chiralcel OD-H column; flow: 1.0 mL/min; hexanes/*i*-PrOH, 90:10; 230 nm; minor enantiomer (+)-**6**, $t_R = 25.95$ min; major enantiomer (−)-**6**, $t_R = 27.93$ min]; other characterization data were identical to those reported.[4]

Representative Procedure for COP-OAc-Catalyzed Cyclization of Crude Tosylcarbamates Prepared in Situ. *p*-Toluenesulfonyl isocyanate (0.64 mmol, 130 mg, 0.097 mL) was added dropwise to an ice-cold solution of alcohol **9** (0.50 mmol, 99 mg) in CH_2Cl_2 (0.5 mL). The ice bath was removed, and the solution was allowed to warm to room temperature. After 3 h, the mixture was concentrated under reduced pressure. To this residue were added CH_2Cl_2−HOAc (4:1, v/v; 0.5 mL) and COP-OAc (**4**; 1 mol %, 5.0×10^{-3} mmol, 7.6 mg), and the reaction vial was sealed, protected from light and maintained at room temperature for 5 h, and then warmed to 38 °C for 15 h. The orange solution was concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel

(9) COP-hfacac (**3**) was also used in solvents other than CH_2Cl_2. In CH_3CN, acetone and THF under identical conditions, catalyst **3** showed lower reactivity with enantioselectivities ≤60% ee.

(10) The origin of this effect remains unclear.

with 85:15 hexanes−EtOAc as eluent gave vinyl-substituted 2-oxazolidinone (*S*)-**10**[4] as a colorless solid (137 mg, 0.41 mmol; 82%): mp 106−108 °C; $[\alpha]^{25}_{589} = -37.1$ ($c = 2.8$, $CHCl_3$) [lit.[4] $[\alpha]^{25}_{589} = -35.9$ ($c = 1.0$, $CHCl_3$)]; HPLC analysis indicated an enantiomeric excess of 97% [Chiralcel OD-H column; flow: 1.0 mL/min; hexanes/*i*-PrOH, 90:10; 230 nm; minor enantiomer (+)-**10**, $t_R = 10.11$ min; major enantiomer (−)-**10**, $t_R = 12.36$ min]; other characterization data were identical to those reported.[4]

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Supporting Information Available: Copies of HPLC traces used to determine enantiopurity of cyclization products; copies of ^1H and ^{13}C NMR spectra for 2-oxazolidinone products. This material is available free of charge via the Internet at http://pubs.acs.org.

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