Diastereoselective Palladium-Mediated Phosphetane Ring Opening and Pd-to-P Phenyl Migration. Synthesis of a New P-Stereogenic C_2-Symmetric Diphosphine Ligand

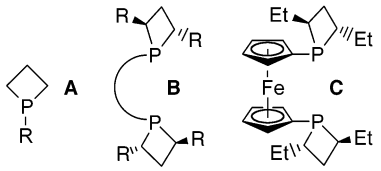
Tim J. Brunker,[†] Jillian R. Moncarz,[†] David S. Glueck,*[,†] Lev N. Zakharov,[‡] James A. Golen,[‡] and Arnold L. Rheingold[‡]

6128 Burke Laboratory, Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755, and Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093

Received March 12, 2004

Summary: Pd[(S,S)-Et-FerroTANE](Ph)(I) undergoes diastereoselective phosphetane ring opening with concomitant Pd-to-P phenyl migration on mild heating. Cleavage of the resulting palladacycle with acid yields Pd[Ferro-CHAIN]I_2, whose reaction with PhMgBr leads to facile opening of the second phosphetane ring and isolation of a complex of a novel C_2-symmetric ligand with P and C stereocenters.

According to a recent review, the most interesting characteristics of the four-membered phosphetane ring system (**A**) are conformational rigidity and moderate strain.[1] The former property makes C_2-symmetric bis-



(phosphetanes) (**B**), such as the commercially available Et-FerroTANE (**C**),[2] valuable ligands in Rh- and Ru-catalyzed asymmetric hydrogenation.[3] The latter property is reflected in the low propensity of phosphetanes to undergo ring-opening reactions, which results in stable metal complexes.[1]

In contrast to this previously reported lack of reactivity, we describe here diastereoselective Pd-mediated phosphetane ring opening, accompanied by Pd-to-P phenyl migration, under mild conditions. Such metal-promoted ring openings have not been observed before but may be an important decomposition pathway for phosphetane ligands in catalysis.[4] Moreover, we have exploited their synthetic potential to synthesize complexes of novel bidentate ligands with both P and C stereocenters.

Pd[(*S*,*S*)-Et-FerroTANE](Ph)(I) (**1**) decomposes slowly at room temperature in solution. Heating a THF solution to 50 °C for 48 h gave three palladacycles (**2a**−**c**) in the approximate ratio 6.3:2.7:1 (Scheme 1).[5] Complex **2c** was easily removed by recrystallization, and samples highly enriched in **2a** were obtained by further recrystallization. NMR data[6] and the crystal structure of **2a** (Figure 1)[7] showed that diastereomers **2** were formed by cleavage of a phosphetane P−C bond and concomitant phenyl migration to P.[8] Formation of **2a** generated a new stereocenter (R_P) and modified one of the phosphetane stereocenters, which is now bound to Pd (S_C).[9]

* To whom correspondence should be addressed. E-mail: glueck@dartmouth.edu.
[†] Dartmouth College.
[‡] University of California, San Diego.

(1) Marinetti, A.; Carmichael, D. *Chem. Rev.* **2002**, *102*, 201−230.
(2) Both **C** and its [Rh(COD)]$^+$ complex are available from Strem Chemicals. The Et-FerroTANE ligand has also been used in Cu- and Pd-catalyzed reactions; see: (a) Lipshutz, B. H.; Noson, K.; Chrisman, W.; Lower, A. *J. Am. Chem. Soc.* **2003**, *125*, 8779−8789. (b) Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14286−14287. (c) Korff, C.; Helmchen, G. *Chem. Commun.* **2004**, 530−531.
(3) (a) Marinetti, A.; Labrue, F.; Pons, B.; Jus, S.; Ricard, L.; Genet, J.-P. *Eur. J. Inorg. Chem.* **2003**, 2583−2590. (b) Marinetti, A.; Genet, J.-P. *C. R. Chim.* **2003**, *6*, 507−514. (c) You, J.; Drexler, H.-J.; Zhang, S.; Fischer, C.; Heller, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 913−916. (d) Berens, U.; Burk, M. J.; Gerlach, A.; Hems, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 1981−1984. (e) Marinetti, A.; Labrue, F.; Genet, J.-P. *Synlett* **1999**, 1975−1977.
(4) Garrou, P. E. *Chem. Rev.* **1985**, *85*, 171−185.

(5) **Preparation and Separation of Palladacycles 2a−c.** Pd[(*S*,*S*)-Et-FerroTANE](Ph)(I) (**1**; 1.481 g, 1.97 mmol) was dissolved in THF (8 mL) and transferred to an ampule under N_2. Some of the solution was placed in an NMR tube; then both the tube and the ampule were placed in an oil bath at 50 °C and the progress of the reaction was monitored periodically by ^{31}P NMR. After 48 h, only peaks corresponding to three new species could be observed (diastereomers **2a**−**c** in a typical ratio 6.3:2.7:1). The combined solution was pumped to dryness in vacuo to give a dark red solid. This was redissolved in CH_2Cl_2 (20 mL) and filtered and then stirred under N_2 while petroleum ether was added slowly. After the addition of ca. 25 mL, a yellow solid precipitated; a further 25 mL was added, and then the solid was isolated by filtration and dried in vacuo to yield 495 mg of product (diastereomer ratio **2a**:**2b** = 6.0:1 by NMR). A further 50 mL of petroleum ether was added to the supernatant in a similar fashion, causing the precipitation of more solid. After drying, 315 mg of product was isolated (diastereomer ratio **2a**:**2b** = 0.9:1 by NMR). The supernatant was then pumped to dryness in vacuo to give a dark red solid. Et_2O (15 mL) was then added, causing most of the residue to dissolve. The solution was filtered off and the residue dried in vacuo to yield 145 mg of product (diastereomer ratio **2a**:**2b**:**2c** = 5.6:3.4:1 by NMR). The Et_2O supernatant was reduced in volume to about 7 mL and placed in the freezer at −20 °C for 3 days to give 150 mg of a brown solid. NMR showed this to be highly enriched in diastereomer **2c** (ratio **2a**:**2b**:**2c** = 1:0.7:6.7). This solid was washed with Et_2O (4 mL) to yield 80 mg of an orange solid shown by NMR to be diastereomerically pure **2c** (5% yield). Recrystallization of this material from CH_2Cl_2/hexane at −30 °C gave a sample suitable for elemental analysis as a CH_2Cl_2 solvate, as shown by ^{1}H NMR spectroscopy. Recrystallization of the first crop from CH_2Cl_2/hexane gave samples of almost diastereomerically pure **2a** (typical ratio **2a**:**2b** = 13:1). Single crystals of **2a** suitable for X-ray diffraction were grown by dissolving samples highly enriched in **2a** in CH_2Cl_2, layering with hexane, and allowing the mixture to stand for several days at −30 °C. Total isolated yield: 1.105 g (1.47 mmol, 75%). The fourth possible diastereomer **2d** (S_P,R_C) was not observed. See the Supporting Information for details of the characterization of **2** and all other new complexes. See ref 6 for ^{31}P{^{1}H} NMR data.

10.1021/om049818+ CCC: $27.50
Publication on Web 04/15/2004

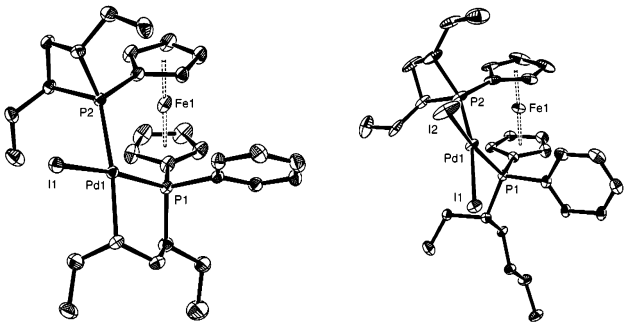
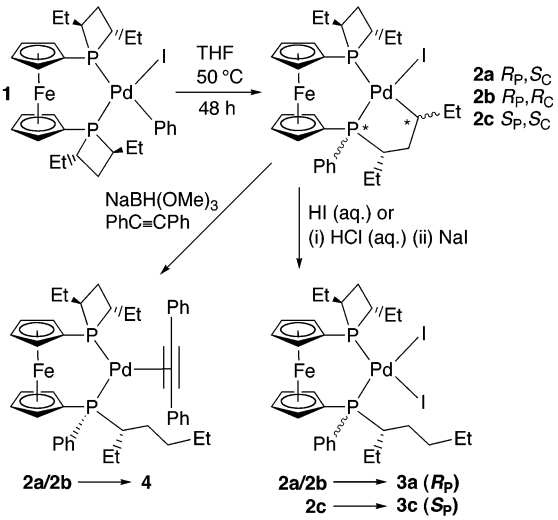


Figure 1. ORTEP diagrams of **2a** (left) and **3a** (right).

Scheme 1



Mixtures enriched in either **2a** or **2b** equilibrate in THF at room temperature to a **2a**:**2b** ratio of 2.8:1, which is similar to that observed in the original synthesis. Since P-epimerization is unlikely, this interconversion suggests that **2a**,**b** differ in configuration at C and the stereochemistry of **2b** must therefore be R_P,R_C.[10] That **2a**,**b** have the same P configuration was confirmed by the Pd−C bond cleavage reactions shown in Scheme 1, which destroy the C stereocenter.

A mixture of **2a** and **2b** reacted with strong acid to yield a *single* diastereomer of Pd[R_P-FerroCHAIN]I_2 (**3a**; Figure 1).[11,12] Similarly, addition of hydride and diphenylacetylene (DPA) to **2a**/**2b** yielded a single diastereomer of the Pd(0) complex Pd[R_P-FerroCHAIN](DPA) (**4**). Complex **2c** must therefore differ from **2a**/**2b** in the configuration at P; as expected, its reaction with acid generated a second diastereomer (S_P) of Pd[FerroCHAIN]I_2 (**3c**). The P−C cleavage that yields **2a**−**c** is therefore highly diastereoselective at P, giving a 9:1 ratio of diastereomers **2a**/**2b**:**2c**.

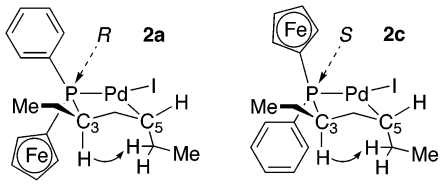


Figure 2. Palladacyclic fragments of **2a**,**c** showing ^{1}H NOEs that establish stereochemistry at the Pd-bound C5.

The C stereochemistry of **2c** (and of **2a**) was determined by ^{1}H NOESY studies. Diagnostic cross-peaks between the PC*H* methine proton and a methylene proton of the palladacycle α-Et group (Figure 2) showed that these groups are cis to each other, which requires Pd-bound C5 to have an *S* configuration (the *S* configuration of C3 is unchanged from the starting ligand). However, we are unable to surmise whether phosphetane ring opening occurs with retention or inversion at C5, since the ready interconversion of **2a** and **2b** in solution indicates that this center is stereochemically labile.

Addition of 1 equiv of PhMgBr to **3a** gave Pd[R_P-FerroCHAIN](Ph)(I) (**5**) as predominantly a single regioisomer, with small amounts of a second regioisomer observed, depending on the reaction conditions. It is unclear whether, in the major regioisomer, the phenyl group lies cis or trans to the phosphetane ring. Nevertheless, heating **5** (as a single regioisomer or a mixture) at 50 °C in THF for 2 h cleanly gave three new species, assigned as diastereomers of the palladacycle obtained by opening of the second phosphetane ring (**6a**−**c** in Scheme 2).[13]

Treatment of this mixture in situ with HCl followed by NaI cleanly yielded two diastereomers of Pd[DiFerroCHAIN]I_2 (**7**),[11] which were readily identified by ^{31}P NMR spectroscopy as C_2-symmetric **7a** (R_P,R_P) and pseudo-meso **7b** (R_P,S_P). The observed ratio of **7b** to **7a** varied between 1.65:1 and 1.25:1, indicating that cleav-

(6) ^{31}P{^{1}H} NMR data: for **1** (in $CDCl_3$), δ 46.4 (d, J = 29 Hz), 32.8 (d, J = 29 Hz); for **2a** (in $CDCl_3$), δ 63.2 (d, J = 48 Hz), 37.2 (d, J = 48 Hz); for **2b** (in $CDCl_3$), δ 64.3 (d, J = 43 Hz), 38.8 (d, J = 43 Hz); for **2c** (in $CDCl_3$), δ 67.3 (d, J = 47 Hz), 47.6 (d, J = 47 Hz); for **3a** (in $CDCl_3$), δ 55.4 (d, J = 12 Hz), 40.2 (d, J = 12 Hz); for **3c** (in $CDCl_3$), δ 59.3 (d, J = 15 Hz), 38.7 (d, J = 15 Hz); for **4** (in C_6D_6), δ 47.4, 28.9; for **5** (in THF), δ 50.0 (d, J = 29 Hz), 21.6 (d, J = 29 Hz) (major); 37.5 (d, J = 30 Hz), 29.9 (d, J = 30 Hz) (minor), ratio major:minor = 4.6:1; for **6** (in THF), δ 75.2 (d, J = 46 Hz), 23.4 (d, J = 46 Hz); 62.9 (d, J = 40 Hz), 25.3 (d, J = 40 Hz); 62.4 (d, J = 45 Hz), 24.7 (d, J = 45 Hz); typical ratio 4.2:1:1.6; for **7a** (in CD_2Cl_2), δ 45.6; for **7b** (in CD_2Cl_2), δ 46.9, 46.6 (AB quartet, J_{AB} = 21 Hz).

(7) For other examples of saturated phosphapalladacycles, see: (a) Portnoy, M.; Ben-David, Y.; Milstein, D. *J. Organomet. Chem.* **1995**, *503*, 149−153. (b) Abdul Malik, K. M.; Newman, P. D. *Dalton* **2003**, 3516−3525.

(8) Such aryl migrations have been previously observed in Pd chemistry. See: (a) Kong, K.-C.; Cheng, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 6313−6315. (b) Goodson, F. E.; Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1997**, *119*, 12441−12453. (c) Alcazar-Roman, L. M.; Hartwig, J. F.; Rheingold, A. L.; Liable-Sands, L. M.; Guzei, I. A. *J. Am. Chem. Soc.* **2000**, *122*, 4618−4630.

(9) The ^{1}H NMR spectrum of the single crystal of **2a** used for X-ray crystallography matched that of the bulk; the C and P stereochemistry in solution was confirmed by ^{1}H NOESY experiments (see the Supporting Information).

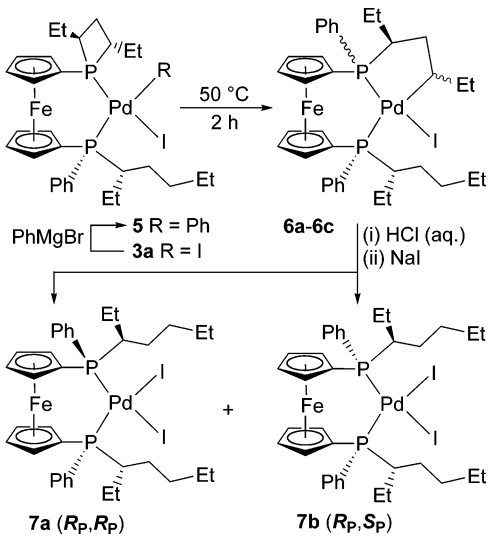
(10) Interconversion of **2a** and **2b** might occur by reversible β-hydride elimination.

(11) We call the new ligands formed by single and double phosphetane ring opening FerroCHAIN and DiFerroCHAIN, respectively.

(12) **Synthesis of 3a**. A mixture of **2a** and **2b** (200 mg, 2.66 × 10^{-4} mol) was dissolved in CH_2Cl_2 (4 mL) and the solution was stirred vigorously. Aqueous HCl (0.25 mL, 37 wt % solution, 3.04 mmol) was added, and the solution became deep red. After 15 min, an aliquot was removed and checked by ^{31}P NMR, which indicated complete conversion of the starting material. The solution was then poured into aqueous $NaHCO_3$ (20 mL) and transferred to a separatory funnel along with CH_2Cl_2 (20 mL). The layers were separated, and the organics were washed with H_2O (20 mL) and dried over $MgSO_4$. The solution was filtered, and all volatiles were removed in vacuo. The residue was redissolved in acetone (5 mL), NaI (230 mg, 1.53 mmol) was added, and the solution was stirred for 1 h. CH_2Cl_2 (20 mL) was added, and the mixture was washed with H_2O (2 × 20 mL). The organics were dried over $MgSO_4$, filtered, and pumped to dryness to yield a red solid that was essentially pure by NMR spectroscopy. Yield: 190 mg (81%, 2.35 × 10^{-4} mol). Single crystals (long needles) suitable for X-ray diffraction were grown by layering a concentrated solution in CH_2Cl_2 with hexane and allowing it to stand at room temperature for 2 days. Complex **3c** was synthesized in a similar fashion.

(13) As for **2**,[5] the fourth possible diastereomer **6d** was not observed.

Scheme 2



age of the second phosphetane ring proceeded with lower diastereoselectivity at P than in the formation of **2**. Diastereomers **7a**,**b** were separated on a small scale by recrystallization from Et_2O or by careful chromatography. The structure of **7a** (Figure 3) confirmed the relative stereochemistry of the two P centers.

In summary, we have demonstrated for the first time that phosphetane rings can undergo facile P−C cleavage when bound to a transition-metal center. This decomposition pathway may prove important in future applications of such ligands in asymmetric catalysis. The doubly ring-opened products **7a**,**b** contain unusual examples of chiral bidentate phosphine ligands with both P and C stereocenters.[14] We are currently testing their utility as catalyst precursors in a range of asymmetric transformations.

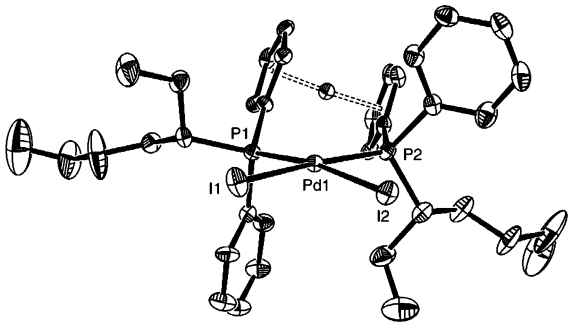


Figure 3. ORTEP diagram of the C_2-symmetric diastereomer **7a**.

Acknowledgment. We thank the National Science Foundation for support.

Supporting Information Available: Text, tables, and figures giving experimental procedures and characterization data for all compounds, including crystallographic data for **2a**, **3a**, and **7a**; X-ray data are also available as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

OM049818+

(14) For some other examples, see: (a) Crepy, K. V. L.; Imamoto, T. *Adv. Synth. Catal.* **2003**, *345*, 79−101. (b) Brauer, D. J.; Machnitzki, P.; Nickel, T.; Stelzer, O. *Eur. J. Inorg. Chem.* **2000**, 65−73.