π-Bound Phosphorus Heterocycles as Catalysts: Ring Opening of Epoxides with TMSCl in the Presence of a Phosphaferrocene

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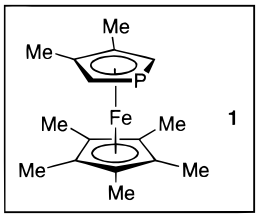
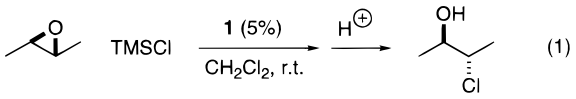
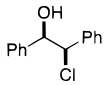
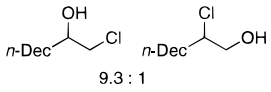
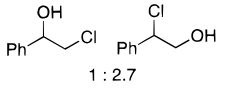
We have recently begun to explore the reactivity of heterocycles that are π-bound to transition metals, with the goal of developing new families of chiral nucleophilic catalysts and new classes of chiral ligands. To date, we have focused our attention primarily on *nitrogen* heterocycles, and we have demonstrated that π-bound pyrrole and pyridine derivatives do indeed serve as effective catalysts for a number of processes, including the acylation of alcohols and the addition of $ZnEt_2$ to aldehydes.[1] In this report, we establish that π-bound *phosphorus* heterocycles can also function as catalysts, specifically, that phosphaferrocene **1**[2] catalyzes the ring opening of epoxides with TMSCl (eq 1).[3]





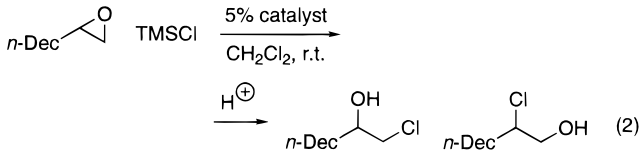
Phosphines serve as nucleophilic catalysts for a wide array of reactions.[4] We have determined that, like PPh_3,[5] phosphaferrocene **1** catalyzes the cleavage of epoxides by TMSCl. Thus, treatment of an epoxide with 1.2 equiv of TMSCl and 5 mol % of **1** in CH_2Cl_2 at room temperature, followed by deprotection of the resulting TMS ether with acid, cleanly affords a chlorohydrin (eq 1; Table 1). The reaction proceeds with inversion of configuration at the carbon undergoing substitution (Table 1, entries 1−3). In the case of an unsymmetrical epoxide, displacement occurs preferentially at the less hindered carbon (Table 1, entry 4), barring an overriding electronic effect

Table 1. Ring Opening of Epoxides with TMSCl in the Presence of Catalyst 1 (Eq 1)

Entry	Substrate	Product(s)	Yield (%)
1			96
2			80
3			94
4		 9.3 : 1	100
5		 1 : 2.7	88

(Table 1, entry 5). For each substrate depicted in Table 1, no ring opening (<5% conversion) is observed in the absence of catalyst **1** under otherwise identical conditions.

On the basis of the differing ratios of regioisomers produced in the phosphaferrocene-, PPh_3-, and Bu_4NCl-catalyzed reactions of 1-dodecene oxide (eq 2), we speculate that a pentacoordinate **1**·TMSCl adduct[6,7] may be a reactive intermediate in the ring-opening process catalyzed by the phosphaferrocene. We are pursuing studies designed to test this hypothesis.



Phosphaferrocene **1**	9.3 : 1
PPh_3	3.6 : 1
Bu_4NCl	4.9 : 1

In conclusion, we have presented the first examples of a π-bound phosphorus heterocycle serving as a catalyst. Future work will focus on the development of chiral complexes for asymmetric catalysis.

Experimental Section

General Methods. ^{31}P NMR chemical shifts are reported in ppm downfield from H_3PO_4 (δ scale).

$FeCl_2$ (Aldrich) was ground to a fine powder prior to use. *n*-BuLi (1.6 M in hexanes; Strem), 2-chloroacetophenone (Aldrich), $MgBr_2$·Et_2O (Aldrich), $NaBH_4$ (Aldrich), naphthalene (Aldrich), 1,2,3,4,5-pentamethylcyclopentadiene (Strem), PPh_3 (Aldrich), and sodium (Aldrich) were used without further purification. Chlorotrimethylsilane (Aldrich), cyclohexene oxide (Aldrich), cyclopentene oxide (Aldrich), 1-dodecene oxide (Aldrich), and styrene oxide (Aldrich) were distilled prior to use. *cis*-Stilbene oxide (Aldrich) was purified by flash chromatography.

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THF was distilled from sodium/benzophenone, CH_2Cl_2 was distilled from CaH_2, and CD_2Cl_2 was dried over alumina.

All reactions were carried out in oven-dried glassware with magnetic stirring under an atmosphere of nitrogen or argon using standard Schlenk or glovebox techniques.

Preparation of Catalyst 1. This procedure is nearly identical to that of Mathey.[8] A solution of naphthalene (4.12 g, 32.1 mmol) in THF (15 mL) was added to a flask containing sodium (0.781 g, 34.0 mmol) and 3,4-dimethyl-1-phenylphosphole[9] (3.00 g, 16.0 mmol), resulting in a dark-red solution, which was stirred at ~30 °C for 3 h. The excess sodium was then removed, and $MgBr_2 \cdot Et_2O$ (4.15 g, 16.1 mmol) was added. The resulting yellow-brown slurry was stirred at ~30 °C for 2 h.

Cp*Li was prepared by treating a solution of 1,2,3,4,5-pentamethylcyclopentadiene (2.5 mL, 16 mmol) in THF (20 mL) with *n*-BuLi (1.6 M in hexanes; 10.0 mL, 16 mmol), resulting in a yellow solution and a large quantity of precipitate. This mixture was added to a stirred slurry of $FeCl_2$ (2.02 g, 16.0 mmol) in THF (5 mL). After completion of the addition, the reaction was stirred for 1 h at ~30 °C, resulting in a forest-green solution containing a very fine precipitate. The 3,4-dimethylphospholyl anion slurry (previous paragraph) was then added, immediately providing a dark-brown mixture. The reaction was stirred at ~30 °C for 13.5 h and then refluxed for 1.5 h. After the mixture was cooled to room temperature, the solvents were removed in vacuo, and the resulting brown residue was extracted repeatedly with hexane. The washings were filtered, and the solvent was removed in vacuo. The resulting orange solid was sublimed (40 °C, 100 mTorr) and then chromatographed (adsorption alumina), affording an orange-yellow solid that was identical by ^{1}H, ^{13}C, and ^{31}P NMR with literature data for complex **1**.[2]

Independent Preparation of Reaction Products. All authentic products were prepared by the PPh_3-catalyzed ring opening of epoxides with TMSCl.[5] The resulting TMS ethers were cleaved by treatment with HCl (1 M in Et_2O), and the product alcohols were purified by flash chromatography and characterized by ^{1}H and ^{13}C NMR.

Representative Procedure for Table 1, Including Monitoring the Background Reaction: Ring Opening of 1-Dodecene Oxide. A solution was prepared of 1-dodecene oxide (0.273 g, 1.48 mmol) and TMSCl (0.230 mL, 1.81 mmol) in CD_2Cl_2 (4.52 mL). A portion of this stock solution was transferred to a sealable NMR tube (background reaction), and 1.69 mL of the stock solution (0.49 mmol of epoxide, 0.60 mmol of TMSCl) was transferred to a flask containing catalyst **1** (7.5 mg, 0.025 mmol). The resulting homogeneous orange solution was then transferred to a sealable NMR tube. The two reactions were followed by ^{1}H NMR.

After 6 h, ^{1}H NMR showed that the catalyzed reaction was complete and that the background reaction had not proceeded (<5% conversion). For the catalyzed reaction, the solvent was removed in vacuo, and the TMS ether was treated with HCl (1 M in Et_2O) for 1 h at rt. The resulting chlorohydrins were purified by flash chromatography (20% Et_2O/pentane), yielding 110 mg (101%) of a 9.3:1 mixture of secondary:primary alcohols.

Note: A control experiment (no catalyst **1**) was conducted for each substrate illustrated in Table 1.

Ring opening of *cis*-stilbene oxide (Table 1, entry 1): run on 99 mg (0.50 mmol) of substrate; isolated 112 mg (96%) of product; reaction time: 100 h.

(R*,R*)-2-Chloro-1,2-diphenylethan-1-ol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.27 (br s, 1H), 4.98 (d, J = 8.2 Hz, 1H), 5.05 (d, J = 8.2 Hz, 1H), 7.10−7.30 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.5, 78.7, 127.0, 128.0, 128.1, 128.3, 128.5, 137.7, 138.8; TLC (10% Et_2O/pentane; phosphomolybdic acid) R_f = 0.20. Treatment of the chlorohydrin with pyridine regenerated *cis*-stilbene oxide (95% isomeric purity).

Ring opening of cyclopentene oxide (Table 1, entry 2): run on 44 mg (0.52 mmol) of substrate; isolated 50 mg (80%) of product; reaction time: 2 h.

***trans*-2-Chlorocyclopentanol:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50−1.65 (m, 1H), 1.75−1.85 (m, 3H), 2.10−2.35 (m, 2H), 2.37 (s, 1H), 3.95−4.25 (m, 1H), 4.20−4.30 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 31.2, 33.2, 65.6, 80.2; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.20. Treatment of the chlorohydrin with KOH regenerated cyclopentene oxide.

Ring opening of cyclohexene oxide (Table 1, entry 3): run on 48 mg (0.50 mmol) of substrate; isolated 63 mg (94%) of product; reaction time: 2 h.

***trans*-2-Chlorocyclohexanol:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15−1.35 (m, 3H), 1.50−1.75 (m, 3H), 2.00−2.10 (m, 1H), 2.10−2.20 (m, 1H), 3.00 (br s, 1H), 3.40−3.50 (m, 1H), 3.65−3.75 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 25.4, 33.1, 35.0, 67.1, 75.0; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.30. Treatment of the chlorohydrin with pyridine regenerated cyclohexene oxide.

Ring opening of 1-dodecene oxide (Table 1, entry 4): run on 91 mg (0.49 mmol) of substrate; isolated 110 mg (101%) of product; reaction time: 6 h. ^{1}H NMR revealed a 9.3:1.0 mixture of secondary:primary alcohols.

1-Chlorododecan-2-ol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 7.0 Hz, 3H), 1.20−1.60 (m, 18H), 2.42 (br s, 1H), 3.47 (dd, J = 7.0, 11.0 Hz, 1H), 3.61 (dd, J = 3.3, 11.0 Hz, 1H), 3.78 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 25.6, 29.4, 29.5, 29.6, 31.9, 34.3, 50.5, 71.5; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.35.

2-Chlorododecan-1-ol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.5 Hz, 3H), 1.20−1.60 (m, 16H), 1.70−1.80 (m, 2H), 2.29 (br s, 1H), 3.60−3.70 (m, 1H), 3.75−3.85 (m, 1H), 3.95−4.05 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 26.4, 29.1, 29.3, 29.5, 29.6, 31.9, 34.3, 65.4, 67.1; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.25.

Ring opening of styrene oxide (Table 1, entry 5): run on 60 mg (0.50 mmol) of substrate; isolated 69 mg (88%) of product; reaction time:0.1 h. ^{1}H NMR revealed a 1.0:2.7 mixture of secondary:primary alcohols. The identity of the secondary alcohol was confirmed by comparison with 2-chloro-1-phenylethan-1-ol prepared by reduction of 2-chloroacetophenone with $NaBH_4$.

2-Chloro-1-phenylethanol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (br s, 1H), 3.66 (dd, J = 8.7, 11.2 Hz, 1H), 3.76 (dd, J = 3.6, 11.4 Hz, 1H), 4.91 (dd, J = 3.5, 8.6 Hz, 1H), 7.30−7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.0, 74.2, 126.2, 128.6, 128.8, 140.0; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.40.

2-Chloro-2-phenylethanol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (br s, 1H), 3.85−3.95 (m, 2H), 4.99 (t, J = 6.6, 1H), 7.35−7.45 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.8, 67.9, 127.5, 128.8, 128.9, 137.9; TLC (20% Et_2O/pentane; phosphomolybdic acid) R_f = 0.30.

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Supporting Information Available: ^{13}C NMR spectra of the reaction products (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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