DOI 10.5012/bkcs.2009.30.12.3075

Iminophosphoranylferrocenes as New Nucleophilic Organocatalysts for Regioselective Ring-opening of Epoxides

Nasiruzzaman Sk, Md., Vo Do Minh Hoang, and Tae-Jeong Kim*

*Department of Applied Chemistry, Kyungpook National University, Taegu 702-701, Korea. *E-mail: tjkim@knu.ac.kr*
Received September 12, 2009, Accepted October 6, 2009

Key Words: Iminophosphoranylferrocene, Organocatalyst, Ring-opening, Epoxides, Regioselective

The Lewis base-catalyzed ring opening of epoxides with TMSCl (or $SiCl_4$) has been of intense research interest.[1-3] A wide variety of chiral Lewis bases such as N-oxides and phosphine oxides are proven to be highly efficient in catalyzing the formation of chlorohydrins mediated by $SiCl_4$. In particular, Fu has recently established that a phosphaferrocene catalyzes the ring opening of epoxides with TMSCl, and more recently the same author reported very high yield for the enantioselective ring opening of *meso*-epoxides catalyzed by a series of ferrocene-fused planar-chiral N-oxides.[4,5] Denmark had earlier accomplished a regioisomeric ratio up to 1:18 for the same reaction by employing a HMPA as a nucleophilic catalyst.[6]

We have recently reported the serendipitous formation of 1,2-ferrocenediylazaphosphinines (**1a**) and 1'-diphenylphosphino-1,2-ferrocenediylazaphosphinines (**1b**) (Chart 1), *via* an unusual cyclization, from the reaction of glyoxal with 1-(α-aminoethyl)-2-diphenylphosphinoferrocene (PPFA-NH_2) and [1-(α-aminoethyl)-1',2-bis(diphenylphosphino)]ferrocene (BPPFA-NH_2), respectively.[7,8] These compounds constitute a new class of planar chiral ferrocenes that are of intense current research interest in the field of asymmetric catalysis.[9] We have further demonstrated that they are not only versatile ligands in a Cu-catalyzed cyclopropanation of styrene and Pd-/Mo-catalyzed allylic alkylation of allyl acetates to achieve a complete diastereoselectivity but also nucleophilic catalysts for highly regioselective ring-opening of epoxides.[10,11]

Intrigued by these observations, we have further investigated the preparation of ferrocene-based iminophosphoranes such as **2** (Chart 1) and demonstrated that they can serve as a new class of practical ligands for Pd-catalyzed allylic alkylation of allyl acetates[12] and Rh-/Ir- catalyzed asymmetric hydrogenation of various olefins.[13,14] More recently, Ru-catalyzed asymmetric cyclopropanation of various olefins has also been carried out successfully to achieve high diastereoselectivity (up to 95/5 *dr* in favor of the *cis*-isomer).[15] One may anticipate that **2** should act as tightly binding chelates and thus would be capable of stabilizing metal centers involved in catalytic cycles, even in rather low oxidation states.[16,17] Furthermore, very high stereoselectivity observed with **2** in the reactions cited above may be somehow related with the presence of the sterically demanding iminophosphoranes.

It is thus strongly recommended to design and synthesize 1,2-ferrocenediylazaphosphinines substituted by iminophosphoranes such as **3** for use as a ligand or a nucleophilic catalyst in various organic transformations. As the first step to benchmark the potentiality of **3**, we wish to report their synthesis and application as nucleophilic catalysts to the ring-opening of a series of epoxides with TMSCl. We have reasoned that our compounds **2** and **3**, carrying in principle donor sites of sp^2-nitrogen and one carbonyl oxygen (**3**), would put an entry into a new family of nucleophilic catalysts.

Results and Discussion

Synthesis and characterization. Scheme 1 shows the preparative method leading to the formation of a series of 1'-iminophosphoranyl-1,2-ferrocenediylazaphosphinines (**3a-c**). The method requires initially the reaction of [1-(α-aminoethyl)-2-(diphenylphosphino)]ferrocene (PPFA-NH_2) with glyoxal to form *via* heterocyclization 1,2-ferrocenediylazaphosphinine (**1a**).[7] Simple extension of the same method by replacing PPFA-NH_2 with [1-(α-aminoethyl)-1',2-bis(diphenylphosphino)]ferrocene (BPPFA-NH_2) led to the formation of a phosphine analogue, 1'-diphenylphosphino-1,2-ferrocenediylazaphosphinine (**1b**).[8] Subsequent employment of the conventional Staudinger reaction that involves the reaction of **1b** with arylazides led eventually to the formation of their iminophosphorane analogues of 1,2-ferrocenediylazaphosphinines (**3a-c**).

Catalysis. In an effort to benchmark the potential of our compounds **2a-c** and **3a-c** as Lewis base catalysts, we also per-

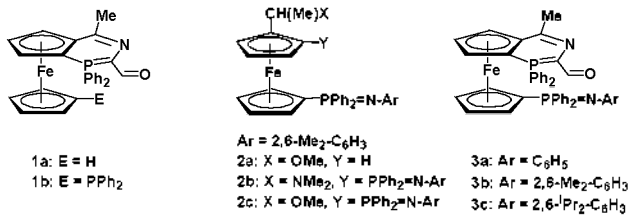
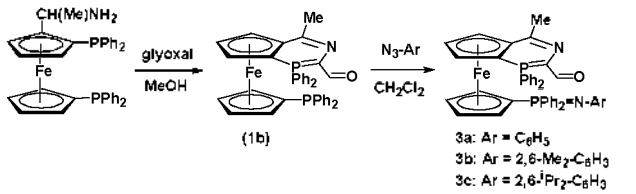
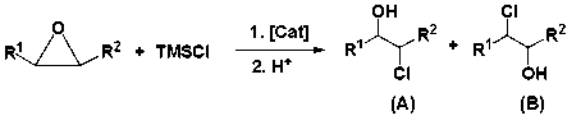


Chart 1



Scheme 1

Table 1. Regioselective Ring-Opening of Epoxides with TMSCl Catalyzed by **2** and **3**



Entry	Epoxide	Catalyst	Time (h)	Yield (%)[a]	A:B[b]
1		**2a**	1	99	-
2		**2b**	1	99	-
3		**2c**	1	99	-
4		**3a**	0.25	99	-
5		**3b**	0.25	99	-
6		**3c**	0.25	99	-
7		**2a**	2	99	9:90
8		**2b**	2	98	2:98
9		**2c**	2	98	5:95
10	Ph	**3a**	2	99	3:97
11		**3b**	2	99	8:92
12		**3c**	2	99	4:96
13		**2a**	2	99	94:6
14		**2b**	2	98	63:37
15		**2c**	2	98	87:13
16	Ph Me	**3a**	2	99	100:0
17		**3b**	2	98	100:0
18		**3c**	2	99	100:0
19		**2a**	2	99	100:0
20		**2b**	2	99	25:75
21		**2c**	2	98	100:0
22	Bu	**3a**	2	99	100:0
23		**3b**	2	99	100:0
24		**3c**	2	99	100:0
25		**2a**	2	99	82:18
26		**2b**	2	99	73:27
27		**2c**	2	99	81:19
28	$ClCH_2$	**3a**	2	99	94:6
29		**3b**	2	99	91:9
30		**3c**	2	99	93:7
31		**2a**	2	99	99:1
32		**2b**	2	98	99:1
33		**2c**	2	98	99:1
34	$PhOCH_2$	**3a**	2	99	100:0
35		**3b**	2	99	100:0
36		**3c**	2	99	100:0

[a]Determined by GC. [b]Determined by GC.

formed the catalytic ring opening of some epoxides with TMSCl. Typical experimental procedure involves treatment of an epoxide with 1.2 equiv of TMSCl and 5 mol% of **2** or **3** in CH_2Cl_2 at room temperature, followed by deprotection of the resulting TMS ether with acid to afford cleanly a chlorohydrin as a product. The results are illustrated in Table 1.

The table shows that regardless of the types of catalysts, all reactions, except cyclohexene oxide, go to completion within 2 h with inversion of configuration at the carbon undergoing substitution as verified by comparison with the known chlorohydrins. The reactivity of **3** both in terms of reaction time and the chemical yield compares well with that of **1a** or **1b** in spite of the presence of sterically demanding iminophosphoranes. Yet, no ring opening is observed in the absence of the catalysts under otherwise identical conditions.

Cis-cyclohexene oxide reacts at the highest rate than any of the substrates employed (runs 1-6). Slower reaction rates with other unsymmetrical epoxides carrying bulkier functional groups may be explained in terms of hindered approach to the TMS-nucleophile intermediate. The regioselectivity in the reaction of these unsymmetrical epoxides is governed by both steric and electronic effects. This is illustrated in the high level but opposite sense of regioselectivity in the opening of styrene oxide (runs 7-12) and other terminal epoxides (runs 13-36). For example, in the case of alkene oxides (R^1 = CH_2Cl, Bu, CH_2OPh) and 2-methyl styrene oxide (R^1 = Ph; R^2 = Me), displacement occurs preferentially at the less hindered carbon (runs 13-36), barring an overriding electronic effect observed with styrene oxide (runs 7-12). It is worth noting that parallel observations have already been made by us and others. However, little effect on the regioselectivity is observed by a structural change in the catalyst. In fact, in some cases, introduction of the sterically demanding iminophosporane as in **2** or **3** even enhances not only catalytic performance but also regioselectivity when compared with **1a** or **1b**.

Although detailed mechanistic studies have yet to be carried out, our working hypothesis for the catalytic cycle may be the same as that proposed by others.[6] As such, the first step in the catalytic cycle is expected to be the formation of a cationic complex **I** or **II** and **III** or **IV** between TMSCl and **2** or **3** (Chart 2). Donor-stabilized silyl cations are ubiquitous, and the structure and reactivity of resulting pentacoordinate silicon compounds are now well documented.[18] The presence of the neighboring phosphoranylimine may provide a better platform for the stabilization of the silyl complex, leading to higher efficiency. Subsequent complexation of the epoxide to the silicon cation followed by nucleophilic attack with the chloride ion in an S_N2 fashion will eventually lead to ring-opening.

Experimental Section

Materials and methods. All manipulations were carried out under an atmosphere of nitrogen using Schlenk techniques. Solvents were purified by standard methods and were freshly distilled prior to use. All commercial reagents were used as received unless otherwise stated. ^1H and ^{31}P NMR spectra were recorded on a Varian Unity Plus spectrometer operating at 300 and 121.5 MHz, respectively. ^1H shifts are reported relative to internal TMS and ^{31}P shifts relative to 85% H_3PO_4. Coupling constants are in Hz. Mass spectra were obtained with Micromass QUATTRA II GC8000 series model with electron energy of 20 or 70 eV. Microanalyses were performed by the Center for Instrumental Analysis, KNU. GC-Mass spectra were obtained by using a Micromass high resolution Quatro II GC8000 series model with an electronic energy of 20 or 70 eV. Starting compounds and BPPFA-NH_2 were prepared according to the literature methods.

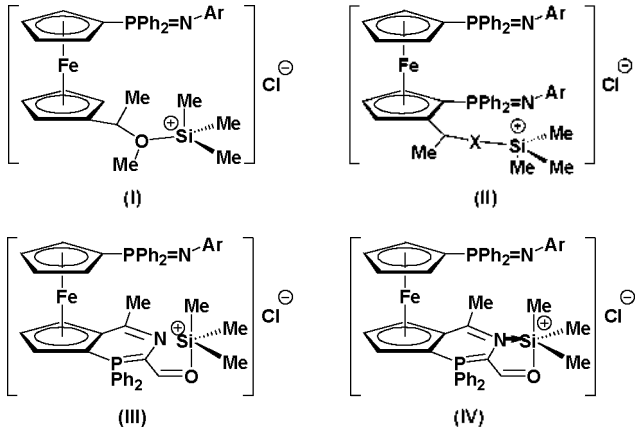


Chart 2

Synthesis of 3a. To a solution of **1b** (0.50 g, 0.78 mmol) in dichloromethane (20 mL) was added drop wise an equimolar amount of azidobenzene (0.090 g, 0.78 mmol) under an inert atmosphere. After stirring for 4 h at RT, the solvent was removed under vacuum and the remaining solid washed with ether (20 mL). The solid was taken up in a small amount of dichloromethane for chromatographic separation on silica gel. A single orange band was eluted with mixture of hexane and ethyl acetate (8:2) to give orange solids after removal of solvents. Recrystallization from a mixture of dichloromethane and hexane (1:4) yielded 0.17 g of **3a** (29.8%). ^{1}H NMR ($CDCl_3$) δ 9.56 (d, J = 25, 1H, CHO), 7.75-7.20 (m, 20H, PPh_2 & = PPh_2), 7.18-6.82 (m, 5H, N-C_6H_5), 4.77-4.34 (m, 3H, C_5H_3), 4.10/3.40 (br, 4H, C_5H_4), 2.21 (s, 3H, CH_3). ^{31}P NMR ($CDCl_3$) δ 0.44 (s), -5.71 (s). HRMS: 727.3396 [M^+ + H]. Anal. Calc. for $C_{44}H_{36}N_2OP_2Fe$: C, 72.74; H, 4.99; N, 3.86. Found: C, 72.06; H, 4.56; N, 3.66.

Synthesis of 3b. The title compound was prepared in the same manner as described above for **3a** by simply replacing azidobenzene with azido-2,6-dimethylbenzene. The product was obtained as a brown solid. Yield: 25%. ^{1}H NMR ($CDCl_3$) δ 9.54 (d, J = 25, 1H, C*H*O), 7.75-7.20 (m, 20H, PPh_2, = PPh_2), 6.88-6.62 (m, 3H, N-C_6H_3), 4.77-4.34 (m, 3H, C_5H_3), 4.10/3.40 (br, 4H, C_5H_4), 2.21 (s, 3H, CH_3), 1.97 (s, 6H, *C*H_3-C_6H_3). ^{31}P NMR ($CDCl_3$) δ -5.67 (s), -8.86 (s). HRMS: 755.0282 [M^+ + H]. Anal. Calc. for $C_{46}H_{40}N_2OP_2Fe$: C, 73.22; H, 5.34; N, 3.71. Found: C, 72.96; H, 5.23; N, 3.66.

Synthesis of 3c. The title compound was prepared in the same manner as described above for **3a** by simply replacing azidobenzene with azido-2,6-diisopropylbenzene. The product was obtained as a brown solid. Yield: 21%. ^{1}H NMR ($CDCl_3$) δ 9.54 (d, J = 25, 1H, CHO), 7.75-7.20 (m, 20H, PPh_2 & = PPh_2), 6.93-6.76 (m, 3H, N-C_6H_3), 4.73-4.34 (3H, C_5H_3), 4.40/3.40 (br, 4H, C_5H_4), 3.30 (sept, J = 6.6, 2H, *CH*Me_2), 2.21 (s, 3H, CH_3), 0.95 (d, J = 6.9, 6H, CH*Me*$_2$), 0.84 (d, J = 6.9, 6H, CH*Me*$_2$). ^{31}P NMR ($CDCl_3$) δ -5.64 (s), -9.72 (s). HRMS: 811.1200 [M^+ + H]. Anal. Calc. for $C_{50}H_{48}N_2OP_2Fe$: C, 74.07; H, 5.97; N, 3.46. Found: C, 73.87; H, 5.46; N, 2.95.

General procedure for the ring-opening reaction. Representative procedure for Table 1, including monitoring the background reaction: a solution was prepared of hex-1-ene oxide (0.148 g, 1.48 mmol) and TMSCl (0.230 mL, 1.81 mmol) in CH_2Cl_2 (4.52 mL) in a Schlenk tube. After degassing the solution by the freeze-and-thaw method three times, a portion of this stock solution was transferred to a 5 mL screw-capped vial (background reaction), and 1.69 mL of the stock solution (0.49 mmol of epoxide, 0.60 mmol of TMSCl) was transferred to a Schlenk tube containing catalyst **3** (0.025 mmol). The two reactions were allowed to proceed at room temperature and monitored by GC equipped with CBP-20 on a Shimadzu GC-17A. After 15 min, the catalyzed reaction was complete and 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 room temperature. The resulting chlorohydrins were purified by flash chromatography on silica gel (hexane:ethylacetate 8:2), and their NMR identifications were made by comparison with literature data.

Conclusion

In summary, we put into entry iminophoranyl-1,1`-bis(diphenylphosphino)-2-[(dimethylamino)ethyl]ferrocene (**2a-c**) and 1`-iminophosphoranyl-1,2-ferrocenediylazaphosphinines (**3a-c**) as a new class of Lewis base catalysts for ring-opening of some epoxides. Their catalytic performances in terms of both reactivity and regioselectivity compares well with not only their parent 1,2-ferrocenediylazaphosphinines (**1a** & **1b**) but also well-documented catalysts such as phosphaferrocene and HMPA, although asymmetric version of this reaction has yet to be carried out.

Acknowledgments. This work was supported by the Ministry for Health, Welfare & Family Affairs through the Korea Healthcare Technology R&D Project (grant No.A090193). Spectral measurements were performed by the KBSI.

References

1. Erden, I. In *Comprehensive Heterocyclic Chemistry*, 2nd ed.; Padwa, A., Ed.; Pergamon Press: Oxford, 1996; Vol. 1A, Chapter 1.03. (b) Bartok, M.; Lang, K. L. In *The Chemistry of Heterocyclic Compounds*; Weissberger, A.; Taylor, E. C., Eds.; Wiley: New York, 1985; Vol. 42, Part 3, p. 1. (c) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323. (d) Denmark, S. E.; Barsanti, P. A.; Beutner, G. L.; Wilson, T. W. *Adv. Synth. Catal.* **2007**, *349*, 567.
2. (a) Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*, Vol. 7, Oxidation; Ley, S. V., Ed.; Pergamon Press: Oxford, 1991; Chapter 3.2. (b) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: Weinheim, 1993; Chapter 4.1. (c) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: Weinheim, 1993; Chapter 4.2.
3. For leading references of enantioselective ring opening of epoxides, see: (a) Nugent, W. A. *J. Am. Chem. Soc.* **1992**, *114*, 2768. (b) Martínez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (d) Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1668. (e) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron*

1996, *52*, 14361. (f) Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 2252.
4. Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 4534.
5. Tao, B.; Lo, M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 353.
6. Denmark, S. E.; Barsanti, P. A.; Wong, K.-T.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 2428.
7. Hwang, G.-H.; Ryu, E.-S.; Park, D.-K.; Shim, S. C.; Cho, C. S.; Kim, T.-J.; Jeong, J. H.; Cheong, M. *Organometallics* **2001**, *20*, 5784.
8. Paek, S. H.; Co, T. T.; Lee, D. H.; Park, Y. C.; Kim, T.-J. *Bull. Korean Chem. Soc.* **2002**, *23*, 1702.
9. For recent reviews on planar chiral ferrocenes, see: (a) Richards, C. J.; Locke, A. J.; *Tetrahedron: Asymmetry* **1998**, *9*, 2377. (b) Kagan, H. B.; Riant, O. *Advances in Asymmetric Synthesis*; Hassner, A., Ed.; JAI Press Inc.: Greenwich, CT, 1997; vol. 2, p. 189. (c) Arrayás, R. G.; Adrio, J.; Carretero, J. C.; *Angew. Chem. Int. Ed.* **2006**, *45*, 7674.
10. Co, T. T.; Paek, S. H.; Shim, S. C.; Cho, C. S.; Kim, T.-J.; Choi, D. W.; Kang, S. O.; Jeong, J. H. *Organometallics* **2003**, *22*, 1475.
11. Paek, S. H.; Shim, S. C.; Cho, C. S.; Kim, T.-J. *Synlett.* **2003**, *6*, 849.
12. Co, T. T.; Shim, S. C.; Cho, C. S.; Kim, D. U.; Kim, T.-J. *Bull. Korean Chem. Soc.* **2005**, *26*, 1359.
13. Co, T. T.; Paek, S. H.; Shim, S. C.; Cho, C. S.; Kim, T.-J.; *Organometallics* **2005**, *24*, 4824.
14. Co, T. T.; Kim, T.-J. *Chem. Commun.* **2006**, 3537.
15. Hoang, Vo D. M.; Reddy, P. A. N.; Kim, T.-J. *Tetrahedron Lett.* **2007**, *48*, 8014.
16. (a) Boubekeur, L.; Ricard, L.; Mézailles, N.; Floch, P. L. *Organometallics* **2005**, *24*, 1065. (b) Boubekeur, L.; Ricard, L.; Mézailles, N.; Demange, M.; Auffrant, A.; Floch, P. L. *Organometallics* **2006**, *25*, 3091.
17. (a) Kubo, K.; Nakazawa, H.; Inagaki, H.; Miyoshi, K. *Organometallics* **2002**, *21*, 1942. (b) Vicente, J.; Abad, J.-A.; Clemente, R.; López-Serrano, J.; de Arellano, M. C. R.; Jones, P. G.; Bautista, D. *Organometallics* **2003**, *22*, 4248. (c) Leeson, M. A.; Nicholson, B. K.; Olsen, M. R. *J. Organomet. Chem.* **1999**, *579*, 243. (d) Avis, M. W.; van der Boom, M. E.; Elsevier, C. J.; Smeets, W. J.; Spek, A. L. *J. Organomet. Chem.* **1997**, *527*, 263. (e) Avis, M. W.; Goosen, M.; Elsevier, C. J.; Veldman, N.; Kooijman, H.; Spek, A. L. *Inorg. Chim. Acta* **1997**, *264*, 43. (f) Boubekeur, L.; Ulmer, S.; Ricard, L.; Mézailles, N.; Floch, P. L. *Organometallics* **2006**, *25*, 315.
18. (a) Holmes, R. R. *Chem. Rev.* **1996**, *96*, 927. (b) Chuit, C.; Corriu, R. J. P.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. (c) Haaland, A. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 992.