ORGANIC
LETTERS

2005
Vol. 7, No. 15
3191−3193

Cobalt-Catalyzed Efficient Aziridination of Alkenes

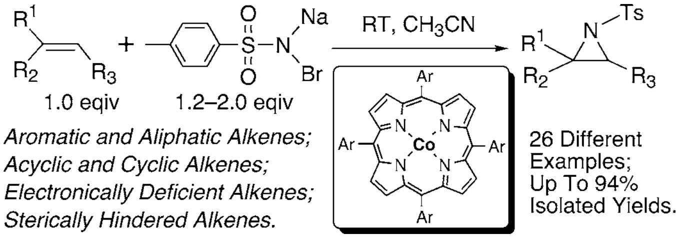
Guang-Yao Gao, Jeremiah D. Harden, and X. Peter Zhang*

Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996-1600

pzhang@utk.edu

Received April 22, 2005

ABSTRACT



Cobalt porphyrins are capable of catalyzing the aziridination of alkenes with bromamine-T as the nitrene source. Among cobalt complexes of different porphyrins, Co(TDClPP) is an effective catalyst that can aziridinate a wide variety of alkenes. The catalytic system can operate at room temperature in a one-pot fashion with alkenes as limiting reagents, forming the desired *N*-sulfonylated aziridine derivatives in high to excellent yields with NaBr as the byproduct.

Aziridines are a class of synthetically and biologically important three-membered heterocyclic compounds that have found many applications.[1] Among synthetic methodologies, transition metal complex mediated aziridination of alkenes with a nitrene source represents a direct and powerful approach for the construction of the aziridine rings.[2] The most widely used nitrene sources for aziridination are the reagent [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (PhI═NTs) and related iminoiodane derivatives.[3] To overcome several limitations associated with the use of PhI═NTs,[4] alternative nitrene sources such as chloramine-T,[5] bromamine-T,[6] and tosyl azide[7] have also been actively pursued. With these nitrene sources, complexes of Mn, Fe, Ru, Rh, and Cu that are supported by different ligands have been identified to catalyze aziridination.[1−9]

The unique ligand environment and metal coordination mode of metalloporphyrins render them a class of attractive catalysts for aziridination and related atom/group transfer reactions.[10] Indeed, the first transition metal complexes that were discovered for aziridination catalytic activity are metalloporphyrins.[11] To date, porphyrin complexes of Fe,

---

(1) (a) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701. (b) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247. (c) Zwanenburg, B.; ten Holte, P. *Top. Curr. Chem.* **2001**, *216*, 93. (d) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347. (e) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.

(2) (a) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (b) Jacobsen, E. N. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 2, p 607. (c) Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693.

(3) (a) Dauban, P.; Dodd, R. H. *Synlett* **2003**, 1571. (b) Koser, G. F. *Top. Curr. Chem.* **2003**, *224*, 137. (c) Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.

(4) For the use of in situ formed iminoiodane, see: (a) Yu, X.-Q.; Huang, J.-S.; Zhou, X.-G.; Che, C.-M. *Org. Lett.* **2000**, *2*, 2233. (b) Dauban, P.; Saniere, L.; Tarrade, A.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7707. (c) Guthikonda, K.; Du Bois, J. *J. Am. Chem. Soc.* **2002**, *124*, 13672.

(5) (a) Simkhovich, L.; Gross, Z. *Tetrahedron Lett.* **2001**, *42*, 8089. (b) Albone, D. P.; Aujla, P. S.; Taylor, P. C.; Challenger, S.; Derrick, A. M. *J. Org. Chem.* **1998**, *63*, 9569. (c) Mairena, M. A.; Diaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Perez, P. J. *Organometallics* **2004**, *23*, 253.

(6) (a) Chanda, B. M.; Vyas, R.; Bedekar, A. V. *J. Org. Chem.* **2001**, *66*, 30. (b) Antunes, A. M. M.; Marto, S. J. M.; Branco, P. S.; Prabhakar, S.; Lobo, A. M. *Chem. Commun.* **2001**, 405.

(7) (a) Omura, K.; Uchida, T.; Irie, R.; Katsuki, T. *Chem. Commun.* **2004**, 2060. (b) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.

(8) For selected examples, see: (a) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326. (b) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742.

(9) A recent addition to the catalyst series is a Ag complex of a substituted terpyridine ligand: Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202.

(10) *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000−2003; Vols. 1−20.

(11) (a) Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073. (b) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161.

10.1021/ol050896i CCC: $30.25

Mn, and Ru have been known to catalyze aziridination.[12] As part of our ongoing efforts in developing metalloporphyrin-based practical atom/group transfer catalytic systems,[13] we reveal herein the first cobalt-based catalytic system that is efficient for the aziridination of different alkenes.[14−16] Cobalt(II) porphyrins (Figure 1) were shown to be effective catalysts for the aziridination of a wide variety of alkenes with bromamine-T (Scheme 1).

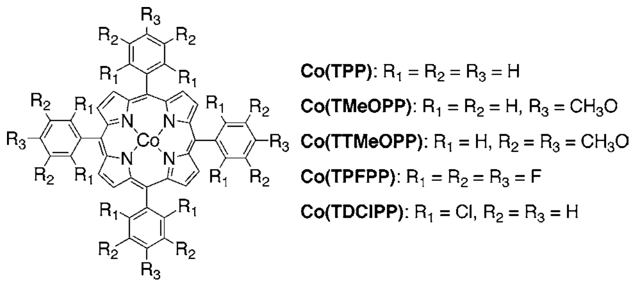
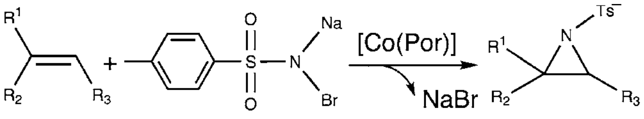


Figure 1. Structures of cobalt(II) porphyrin complexes.

Scheme 1. Aziridination of Alkenes with Bromamine-T Catalyzed by Cobalt(II) Porphyrin Complexes



Using styrene as a model substrate, we first evaluated the catalytic aziridination activities of Co complexes supported by various porphyrins under practical conditions (room temperature, one-pot protocol, and styrene as the limiting reagent). The results are summarized in Table 1. Although the Co complex of the most common porphyrin Co(TPP) could aziridinate styrene in a low yield, the Co complexes of electron-rich porphyrins such as Co(TTMeOPP) and Co(TMeOPP) furnished no or only a trace amount of the desired product (Table 1, entries 1−3). The production of aziridine, however, was tripled when the reaction was catalyzed by the Co complex of an electron-deficient porphyrin Co(TPFPP) (Table 1, entry 4). Significant further improvement was achieved with the Co complex of an electron-deficient and sterically hindered porphyrin Co(TDClPP) as the catalyst, producing the desired aziridine in 83% isolated yield (Table 1, entry 5). Whereas change in the ratio of styrene to bromamine-T from 1:2 to 1:1.2 had no significant influence on the catalytic reaction, an excess of styrene resulted in a relatively lower yield (Table 1, entries 6 and 7). Acetonitrile appeared the solvent of choice for the catalytic reaction, as the uses of other solvents such as tetrahydrofuran, methylene chloride, or toluene gave no or only a trace amount of the desired product (Table 1, entries 8−10). Although a slightly better yield was obtained at 40 °C, further increase in reaction temperature caused a lower yield (Table 1, entries 11 and 12). The room temperature reaction could be effectively carried out at a lower catalyst loading without affecting the yield (Table 1, entry 13). A relatively lower yield was observed when the reaction time was shortened (Table 1, entry 14). The employment of higher catalyst loading, however, could allow the reaction to be finished in a short time without decrease of the yield (Table 1, entry 15).

Table 1. Aziridination of Styrene by Cobalt Porphyrins[a]

entry	S:BT[b]	[Co(Por)][c]	mol (%)	solvent	temp (°C)	time (h)	yield (%)[d]
1	1:2	Co(TPP)	5	CH_3CN	23	18	18
2	1:2	Co(TMeOPP)	5	CH_3CN	23	16	<5
3	1:2	Co(TTMeOPP)	5	CH_3CN	23	20	0
4	1:2	Co(TPFPP)	5	CH_3CN	23	17	53
5	1:2	Co(TDClPP)	5	CH_3CN	23	18	83
6	1:1.2	Co(TDClPP)	5	CH_3CN	23	18	75
7	5:1	Co(TDClPP)	5	CH_3CN	23	17	67
8	1:2	Co(TDClPP)	5	THF	23	20	0
9	1:2	Co(TDClPP)	5	CH_2Cl_2	23	17	<5
10	1:2	Co(TDClPP)	5	$CH_3C_6H_5$	23	19	0
11	1:2	Co(TDClPP)	5	CH_3CN	40	17	84
12	1:2	Co(TDClPP)	5	CH_3CN	82	18	66
13	1:2	Co(TDClPP)	2	CH_3CN	23	17	80
14	1:2	Co(TDClPP)	5	CH_3CN	23	7	71
15	1:2	Co(TDClPP)	10	CH_3CN	23	7	82

[a] Carried out under N_2 in the presence of 5 Å molecular sieves with a concentration of 0.1 mmol styrene/2 mL solvent. [b] The mole ratio of styrene substrate to bromamine-T. [c] See Figure 1. [d] Isolated yields.

Using the above optimized reaction conditions, the new Co(TDClPP)-based catalytic system was found to be suitable for many different types of alkene substrates (Table 2). In addition to styrene, derivatives of styrene with alkyl substituents could be equally aziridinated to afford the desired products in high yields (Table 2, entries 1−4). Functional groups in styrene derivatives could be well tolerated to cleanly generate the corresponding aziridines (Table 2, entries 5−7). Sterically hindered derivatives such as 2,4,6-trimeth-

---

(12) (a) Mahy, J.-P.; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1517. (b) Lai, T.-S.; Kwong, H.-L.; Che, C.-M.; Peng, S.-M. *Chem. Commun*. **1997**, 2373. (c) Simonato, J.-P.; Pecaut, J.; Scheidt, W. R.; Marchon, J.-C. *Chem. Commun*. **1997**, 989. (d) Au, S.-M.; Huang, J.-S.; Yu, W.-Y.; Fung, W.-H.; Che, C.-M. *J. Am. Chem. Soc*. **1999**, *121*, 9120. (e) Liang, J.-L.; Huang, J.-S.; Yu, X.-Q.; Zhu, N.; Che, C.-M. *Chem. Eur. J.* **2002**, *8*, 1563.

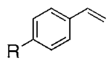
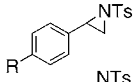
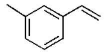
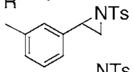
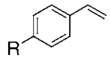
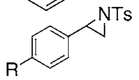
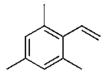
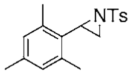
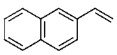
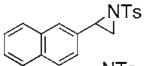
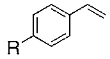
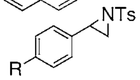
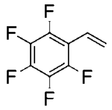
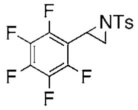
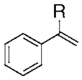
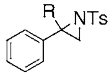
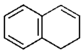
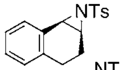
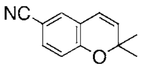
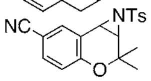
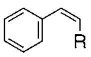
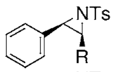
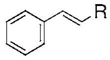
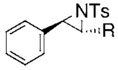
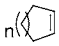
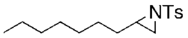
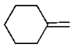
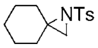
(13) (a) Chen, Y.; Huang, L.; Ranade, M. A.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 3714. (b) Chen, Y.; Huang, L.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 5925. (c) Chen, Y.; Huang, L.; Zhang, X. P. *Org. Lett.* **2003**, *5*, 2493. (d) Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 8179. (e) Lee, M.-Y.; Chen, Y.; Zhang, X. P. *Organometallics* **2003**, *22*, 4905. (f) Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2004**, *69*, 2431 (g) Vyas, R.; Gao, G.-Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2004**, *6*, 1907. (h) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14178.

(14) For cobalt porphyrin-mediated amination with aryl azides, see: Ragaini, F.; Penoni, A.; Gallo, E.; Tollari, S.; Gotti, C. L.; Lapadula, M.; Mangioni, E.; Cenini, S. *Chem. Eur. J.* **2003**, *9*, 249.

(15) Under microwave conditions, $CoCl_2$ was shown to catalyze aziridination of styrene with bromine-T to form the desired aziridine in 56% yield when excess styrene was used (styrene/bromamine-T = 5: 1). See ref 6a.

(16) Co(TPP) was previously found to catalyze aziridination of styrene with bromine-T to form the desired aziridine in 27% yield when excess styrene was used (styrene/bromamine-T = 5: 1). See ref 13a.

Table 2. Aziridination of Different Alkenes by Co(TDClPP)[a]

entry	substrate	product	yield (%)[b]
1 2 3			R = H: 83 R = Me: 76 R = *t*-Bu: 81
4			89
5 6 7			R = ClCH$_2$: 86 R = CF$_3$: 90 R = CH$_3$CO$_2$: 92
8			61
9			53
10 11 12			R = Br: 70 R = Cl: 71 R = F: 86
13			61
14 15			R = Me: 70 R = Ph: 81
16			33
17[c]			66
18 19[d]			R = Me: 94[e] R = Ph: 92[f]
20 21[d]			R = Me: 87[g] R = Ph: 94[h]
22 23 24			n = 1: 61 n = 2: 66 n = 3: 79
25			56
26			67

[a] Carried out at room temperature in CH$_3$CN overnight under N$_2$ with alkenes as limiting reagent (alkene/bromamine-T = 1:2) using 5 mol % Co(TDClPP) in the presence of 5 Å molecular sieves at concentration of 0.2 mmol alkene/4−5 mL CH$_3$CN. [b] Isolated yields. [c] Performed with alkene/bromamine-T = 5:1. [d] Performed with alkene/bromamine-T = 1:3 using 10 mol % Co(TDClPP). [e] *cis*:*trans* = 9:91. [f] *cis*:*trans* = 47:53. [g] *cis*:*trans* = 8:92. [h] *cis*:*trans* = 58:42.

ylstyrene as well as 2-vinylnaphthalene could also be catalytically aziridinated, albeit in lower yields (Table 2, entries 8 and 9). Halogenated styrenes including highly electron-deficient pentafluorostyrene could be successfully converted to the desired aziridines in good to high yields (Table 2, entries 10−13). To the best of our knowledge, this represents the first example of aziridination of pentafluorostyrene. In addition, both α-substituted and β-substituted (cyclic and acyclic) styrenes were suitable substrates for the catalytic process (Table 2, entries 14−21). Whereas a competitive amidation was presumably responsible for the low aziridination yield of 1,2-dihydronaphthalene (Table 2, entry 16), excellent yields were obtained for acyclic β-substituted styrenes in both *cis* and *trans* forms (Table 2, entries 18−21). For the latter substrates, the catalytic reactions by Co(TDClPP) appeared to lack stereospecificity, although high *trans*-stereoselectivity was observed for both *cis*- and *trans*-β-methylstyrenes. In addition to aromatic and conjugated alkenes, acyclic and cyclic aliphatic alkenes with different ring sizes are suitable substrates for the catalytic system (Table 2, entries 22−25). Under similar conditions, *exo*-methylene carbocycles such as methylenecyclohexane could also be successfully aziridinated to afford the desired spirocyclic aziridine in 67% isolated yield (Table 2, entry 26).

In summary, we have developed the first Co-based catalytic system that is efficient for aziridination of various alkenes.[14−16] We demonstrated that the new Co(TDClPP)/bromamine-T catalytic system can be effectively operated under mild and practical conditions with alkenes as limiting reagents and is generally suitable for a wide variety of alkene substrates. Further improvement of the catalytic system including stereospecificity and the development of its asymmetric variant are in progress. The successful demonstration of the catalytic capability of Co(II) porphyrins for aziridination will also likely stimulate future studies to address some interesting mechanistic issues.

Acknowledgment. We are grateful for financial support of this work from the UT Department of Chemistry, the UT Center of Excellence for Structural Biology (CESB), Oak Ridge Associated Universities (ORAU) for a Ralph E. Powe Junior Faculty Enhancement Award, Hereditary Disease Foundation (HDF), and High Q Foundation (HQF).

Supporting Information Available: Analytical data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL050896I