ORGANIC LETTERS

2004
Vol. 6, No. 12
1907−1910

Iron(III) Porphyrin Catalyzed Aziridination of Alkenes with Bromamine-T as Nitrene Source

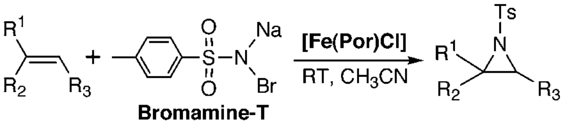
Renu Vyas, Guang-Yao Gao, Jeremiah D. Harden, and X. Peter Zhang*

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

pzhang@utk.edu

Received February 21, 2004 *(Revised Manuscript Received May 6, 2004)*

ABSTRACT



Suitable for Aromatic, Aliphatic, Cyclic and Acyclic
Alkenes as well as α,β-Unsaturated Esters.
Moderate Stereoselectivity for 1,2-Disubstituted Alkenes.

Iron(III) porphyrin complexes Fe(Por)Cl are effective catalysts for aziridination of alkenes using bromamine-T as the nitrene source. The catalytic system can operate under mild conditions with alkenes as limiting reagents. The aziridination reaction is general and suitable for a wide variety of alkenes, including aromatic, aliphatic, cyclic, and acyclic olefins, as well as α,β-unsaturated esters. For 1,2-disubstituted olefins, the reactions proceeded with moderate to low stereospecificity.

Aziridination of alkenes mediated by a transition metal complex is one of the most attractive methods for the efficient and selective construction of synthetically and biologically important aziridines.[1] The reagent [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (PhI═NTs) and related iminoiodane derivatives, aza-analogues of iodosylbenzene, have been extensively used as primary nitrene sources for catalytic aziridination.[2] Although great progress has been made with PhI═NTs in a number of metal-catalyzed systems including asymmetric aziridination,[1,3] the reagent suffers from several drawbacks including its commercial unavailability, high cost, and insolubility along with generation of the heavy PhI byproduct.[4] Consequently, there has been growing interest in developing metal-catalyzed aziridination of alkenes with alternative nitrene sources such as chloramine-T,[5] bromamine-T,[6] and azides.[7]

Metalloporphyrins have played a pivotal role in the development of several important catalytic atom/group

---

(1) (a) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (b) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247. (c) Jacobsen, E. N. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Vol. 2., pp 607−618. (d) Osborn, H. M.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693. (e) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.

(2) (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.

(3) 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. (c) Vedernikov, A.; Caulton, K. G. *Org. Lett.* **2003**, *5*, 2591. (c) Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202.

(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) Minakata, S.; Kano, D.; Fukuoka, R.; Oderaotoshi, Y.; Komatsu, M. *Heterocycles* **2003**, *60*, 289. (b) Jain, S. L.; Sain, B. *J. Mol. Catal. A: Chem.* **2003**, *195*, 283. (c) Gullick, J.; Taylor, S.; McMorn, P.; Bethell, D.; Page, P. B. C.; Hancock, F. E.; King, F.; Hutchings, G. *J. Mol. Catal A: Chem.* **2002**, *180*, 85. (d) Jeong, J. U.; Tao, B.; Sagasser, I.; Henninges, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1998**, *120*, 6844. (e) Albone, D. P.; Aujla, P. S.; Taylor, P. C.; Challenger, S.; Derrick, A. M. *J. Org. Chem.* **1998**, *63*, 9569. (f) Ando, T.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron Lett.* **1998**, *39*, 309. (g) Aujla, P. S.; Baird, C. P.; Taylor, P. C.; Mauger, H.; Vallee, *Tetrahedron Lett.* **1997**, *38*, 7453. (h) Minakata, S.; Kano, D.; Oderaotoshi, Y.; Komatsu, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 79.

(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. (c) Vyas, R.; Chanda, B. M.; Belhekar, A. A.; Patel, D. R.; Ram, R. N.; Bedekar, A. V. *J. Mol. Catal. A: Chem.* **2000**, *160*, 237. (d) Vyas, R.; Chanda, B. M.; Bedekar, A. V. *Tetrahedron Lett.* **1998**, *39*, 4715.

(7) (a) Omura, K.; Murakami, M.; Uchida, T.; Irie, R.; Katsuki, T. *Chem. Lett.* **2003**, 354. (b) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.

10.1021/ol049691k CCC: $27.50

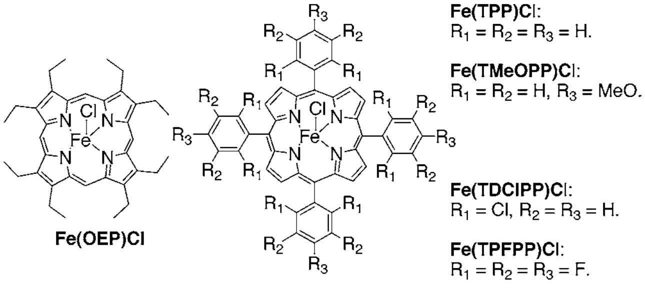


Figure 1. Structures of iron(III) porphyrin complexes.

transfer reactions, including aziridination of alkenes. In fact, metalloporphyrins are the first transition metal complexes that were demonstrated to catalyze aziridination of alkenes.[8] Following this breakthrough, porphyrin complexes of several metal ions such as Fe, Mn, and Ru have been disclosed for aziridination catalytic activity with PhI=NTs.[9] As a part of our program of metalloporphyrin-based atom/group transfer catalysis,[10] we became interested in developing practical catalytic aziridination processes with alternative nitrene sources. We reveal herein that iron(III) porphyrin complexes Fe(Por)Cl (Figure 1) are efficient and general catalysts for aziridination of a wide variety of alkenes using bromamine-T as a nitrene source (Scheme 1).[11] The reactions can be performed under mild conditions with alkenes as limiting reagents and proceed with moderate to low stereospecificity for 1,2-disubstituted alkenes.

Scheme 1. Aziridination of Alkenes Catalyzed by Iron(III) Porphyrin Fe(TPP)Cl

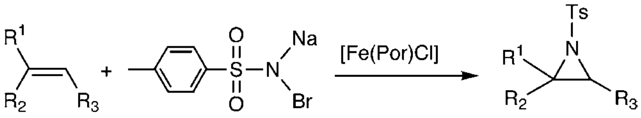
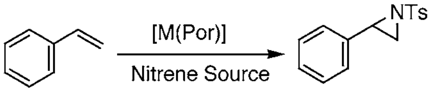


Table 1. Aziridination of Styrene by Metalloporphyrins[a]



entry	nitrene source	metalloporphyrin[b]	yield (%)[c]
1	PhI=NTs	Fe(TPP)Cl	31[d]
2	chloramine-T	Fe(TPP)Cl	5
3	bromamine-T	Fe(TPP)Cl	60
4	bromamine-T	Mn(TPP)Cl	12
5	bromamine-T	Co(TPP)	27
6	bromamine-T	Ru(TPP)(CO)	47
7	bromamine-T	Fe(OEP)Cl	0
8	bromamine-T	Fe(TMeOPP)Cl	25
9	bromamine-T	Fe(TDClPP)Cl	38
10	bromamine-T	Fe(TPFPP)Cl	80

[a] Reactions were carried out for 12 h at room temperature in CH_3CN under N_2 in the presence of 5 Å molecular sieves with a styrene to nitrene source mole ratio of 5:1. [b] Catalyst loading: 5 mol %; see Figure 1 for structures of metalloporphyrins. [c] Yields represent isolated yields of >95% purity as determined by ^1H NMR. [d] From ref 3b.

We first surveyed the catalytic aziridination of styrene by various metalloporphyrins (Figure 1) with different nitrene sources. The reactions were carried out at room temperature in acetonitrile in the presence of 5 Å molecular sieves using 5 mol % catalyst with a styrene to nitrene source mole ratio of 5:1. The results are summarized in Table 1. Although chloramine-T was ineffective for the aziridination by Fe(TPP)Cl (Table 1, entry 2), bromamine-T was found to be a superior nitrene source in comparison with PhI=NTs, affording the desired aziridine in 60% isolated yield (Table 1, entries 1 and 3). Other metal complexes of TPP such as Mn(TPP)Cl, Ru(TPP)(CO), and Co(TPP) could also aziridinate styrene, but with less efficiency (Table 1, entries 4−6). Although porphyrin complexes of Fe, Mn, and Ru have been known to catalyze aziridination,[8,9] to the best of our knowledge, cobalt porphyrins have never been demonstrated for aziridination activity previously. The catalytic activity of Fe(Por)Cl with bromamine-T has a dramatic ligand dependence. Whereas both Fe(MeOPP)Cl and Fe(TDClPP)Cl were less effective than Fe(TPP)Cl (Table 1, entries 8 and 9), no activity was observed with Fe(OEP)Cl (Table 1, entry 7). However, the electron-deficient Fe(TPFPP)Cl improved the isolated yield of the desired aziridine to 80% (Table 1, entry 10).

The substrate scope of the aziridination reactions by Fe(TPP)Cl with bromamine-T was then explored using a variety of alkenes under the same conditions (Table 2, yield A, bromamine-T as the limiting reagent). The catalytic system is suitable for a variety of styrene derivatives with *para*-substituted alkyl and halogen groups, affording the corresponding aziridines in yields similar to or better than that of styrene reaction (Table 2, entries 1−7). Sterically hindered derivatives such as 2,4,6-trimethylstyrene could also be aziridinated, albeit in a lower yield (Table 2, entry 8). Both α- and *β*-substituted styrenes including ethyl *trans*-cinnamate could be successfully converted to the desired aziridines in moderate to good yields (Table 2, entries 9−16). The stereospecificity ranged from moderate to low for the 1,2-disubstituted olefins (Table 2, entries 12−16). Like ethyl *trans*-cinnamate, the α,*β*-unsaturated ester *tert*-butyl acrylate

---

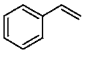
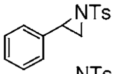
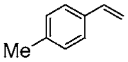
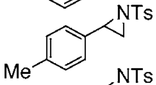
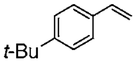
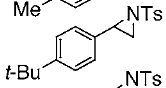
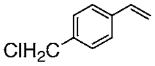
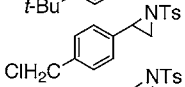
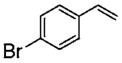
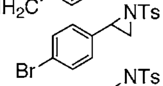
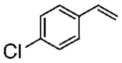
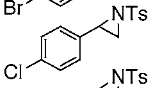
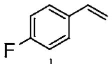
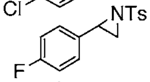
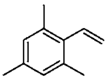
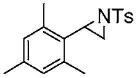
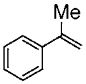
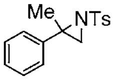
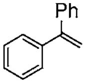
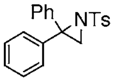
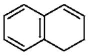
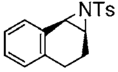
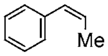
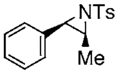
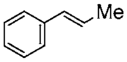
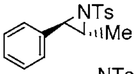
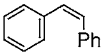
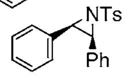
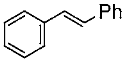
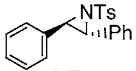
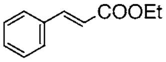
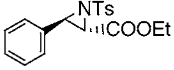
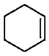
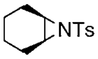
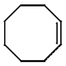
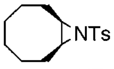
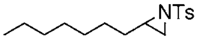
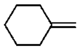
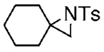
(8) (a) Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073. (b) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161.

(9) (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.

(10) (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.

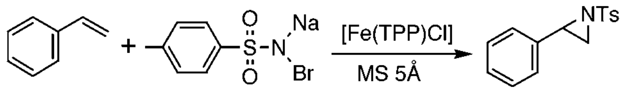
(11) For a iron(IV) corrole/chloramine-T aziridination system, see: Simkhovich, L.; Gross, Z. *Tetrahedron Lett.* **2001**, *42*, 8089.

Table 2. Aziridination of Alkenes with Bromamine-T Catalyzed by Fe(TPP)Cl[a]

entry	substrate	product	yield A (%)[b]	yield B (%)[c]
1			60	77
2			60	75
3			68	--
4			73[g]	--
5			44	--
6			52	80
7			55	--
8			46	--
9			42	--
10			72	--
11			28	48
12			38 (61:39)[d]	54 (56:44)[d]
13			64 (18:82)[d]	75 (18:82)[d]
14			64 (69:31)[d]	68 (60:40)[d]
15			72 (58:42)[d]	70 (50:50)[d]
16			42 (31:69)[d]	--
17			36[e]	--
18			48	47[f]
19			42	45[f]
20			53	60
21			55	60
22			0	50

[a] Carried out at room temperature in CH_3CN for 12 h under N_2 in the presence of 5 Å molecular sieves using 5 mol %. Fe(TPP)Cl. Concentration: 0.1 mmol alkene/2 mL CH_3CN. [b] Isolated yields with Bromamine-T as limiting reagent (alkene/Bromamine-T = 5:1). [c] Isolated yields with alkene as limiting reagent (alkene/Bromamine-T = 1:2). [d] *cis*:*trans* ratios. [e] Performed at 60 °C. [f] Fe(TPFPP)Cl was used. [g] Contaminated with a small amount of side product.

Table 3. Aziridination of Styrene with Bromamine-T Catalyzed by Fe(TPP)Cl under Various Conditions[a]



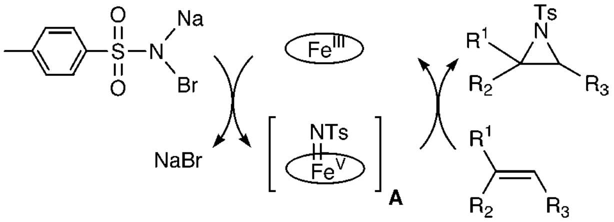
entry	S:BT[b]	[Fe] (mol %)	solvent	temp (°C)	time (h)	yield (%)[c]
1	5:1	5	toluene	23	12	0
2	5:1	5	THF	23	12	0
3	5:1	5	CH_2Cl_2	23	12	5
4	5:1	5	CH_3CN	23	12	60
5	5:1	5	CH_3CN	23	6	64
6	5:1	5	CH_3CN	23	2	42
7	5:1	5	CH_3CN	40	12	65
8	5:1	5	CH_3CN	80	12	80
9	5:1	5	CH_3CN	100	12	39
10	5:1	2	CH_3CN	23	12	10
11	5:1	10	CH_3CN	23	12	70
12	10:1	5	CH_3CN	23	12	55
13	100:1	5	CH_3CN	23	12	45
14	1:1.5	5	CH_3CN	23	12	62
15	1:2	5	CH_3CN	23	12	77
16	1:2	5	CH_3CN	80	12	67
17	1:2	10	CH_3CN	23	12	82
18	1:5	5	CH_3CN	23	12	52

[a] Reactions were 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] S:BT = the mole ratio of styrene substrate to bromamine-T. [c] Yields represent isolated yields of >95% purity as determined by ^1H NMR.

could also be aziridinated in a moderate yield (Table 2, entry 17). Cyclic alkenes with different ring sizes and straight-chain alkenes are also suitable substrates (Table 2, entries 18−21). However, *exo*-methylene carbocycles such as methylenecyclohexane could only be converted to the corresponding spirocyclic aziridine in a trace of amount under the conditions (Table 2, entry 22).

To further improve the Fe(TPP)Cl/bromamine-T aziridination system, detailed optimization of various reaction parameters was carried out using styrene as the model substrate (Table 3). CH_3CN appeared to be the solvent of choice, as other solvents such as toluene, THF, and CH_2Cl_2 gave none or only a trace amount of the desired aziridine (Table 3, entries 1−4). The reaction time could be shortened to 6 h without affecting the yield, but a lower yield was obtained when the reaction was stopped at 2 h (Table 3, entries 5 and 6). Increase in reaction temperature gave better results. For example, the isolated yields were 64% and 80% at 40 and 80 °C, respectively (Table 3, entries 7 and 8). However, further increase of the reaction temperature to 100 °C resulted in dramatic decrease of the desired aziridine due to formation of several unidentified side products (Table 3, entry 9). Decreased yield was observed when a lower catalyst loading was applied (Table 3, entry 10). The aziridine was isolated in 70% yield for a room temperature reaction using a higher catalyst loading (Table 3, entry 11). Whereas increase of styrene to bromamine-T mole ratio worsened the reaction (Table 3, entries 12 and 13), improved results were observed when the reactions were carried out with styrene as the limiting reagent. For example, the isolated yields

Scheme 2. Possible Mechanism for Aziridination of Alkenes Catalyzed by Iron(III) Porphyrin with Bromamine-T



reached 62% and 77% when styrene to bromamine-T mole ratios were 1:1.5 and 1:2, respectively (Table 3, entries 14 and 15), but further increase of bromamine-T equivalence gave a poor result due to the generation of side products (Table 3, entry 18). Side products were also observed when the reaction was done at elevated temperature with styrene to bromamine-T mole ratios of 1:2 (Table 3, entry 16). The best isolated yield (82%) of the desired *N*-(*p*-tolylsulfonyl)-2-phenylaziridine was achieved when a higher catalyst loading was employed at room temperature with the 1:2 ratio (Table 3, entry 17).

On the basis of the above optimization and the consideration of practicality, the aziridination of representative examples of alkenes with bromamine-T was carried out again at room temperature with alkenes as the limiting reagents using 5 mol % Fe(TPP)Cl. As summarized in yield B of Table 2, yields were improved in all of the cases examined. For example, large increases in yields were obtained for styrene derivatives (Table 2, entries 1, 2, and 6). For β-substituted styrenes, good yields were achieved in most cases, but stereospecificities remained almost the same (Table 2, entries 11−15). Similar improvement in yield was also observed for cyclic and straight-chain alkenes (Table 2, entries 20 and 21). Under this new condition, the previous negative reaction of methylenecyclohexane was successfully performed to afford the desired spirocyclic aziridine in 50% yield (Table 2, entry 22).

The catalytic aziridinations by iron(III) porphyrins with bromamine-T are assumed to proceed via a mechanism similar to that proposed for other metalloporphyrin systems with PhI=NTs.[8,9] As shown in Scheme 2, reaction of iron(III) porphyrin with bromamine-T generates the iron-nitrene intermediate **A** with concomitant formation of NaBr. Nitrene transfer from intermediate **A** to alkene substrate produces the aziridine product and regenerates iron(III) porphyrin to turn over the catalytic cycle. However, the low to moderate stereoselectivity observed for 1,2-disubstituted olefins could imply the involvement of a radical intermediate.

In summary, we have revealed for the first time that bromamine-T is an effective nitrene source for aziridination of alkenes by porphyrin complexes of transition metal ions including Mn, Fe, Ru, and Co. We demonstrated that the new Fe(TPP)Cl/bromamine-T catalytic aziridination system can be operated under mild and practical conditions with alkenes as limiting reagents. The catalytic reaction is general and suitable for a wide range of alkene substrates, forming desired aziridines in good yields, although the stereospecificity is only moderate to low for 1,2-disubstituted olefins. Further improvements are expected with iron(III) complexes that are supported by different porphyrin ligands, as we have already demonstrated with Fe(TPFPP)Cl for yield improvement (Table 1, entry 10). The development of an asymmetric version of the catalytic system is in progress.

Acknowledgment. We are grateful for financial support of this work from the UT Department of Chemistry and Oak Ridge Associated Universities (ORAU) for a Ralph E. Powe Junior Faculty Enhancement Award. We wish to acknowledge Dr. Al Tuinman of UT Mass Spectroscopy Center for assistance with high-resolution mass spectroscopy.

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

OL049691K