

A Highly Effective Cobalt Catalyst for Olefin Aziridination with Azides: Hydrogen Bonding Guided Catalyst Design

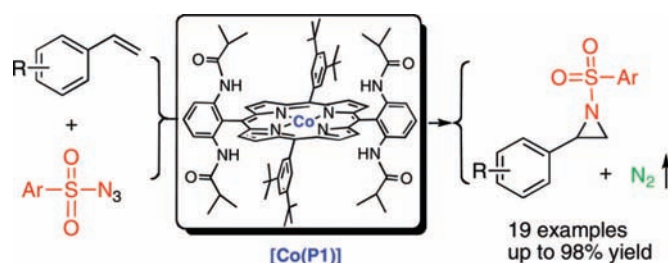
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ABSTRACT



[Co(P1)], which was designed on the basis of potential hydrogen-bonding interactions in the metal–nitrene intermediate, is a highly active aziridination catalyst with azides. [Co(P1)] can effectively aziridinate various aromatic olefins with arylsulfonyl azides under mild conditions, forming sulfonated aziridines in excellent yields. The Co-based system enjoys several attributes associated with the relatively low cost of cobalt and the wide accessibility of arylsulfonyl azides. Furthermore, it generates stable dinitrogen as the only byproduct.

Metal-catalyzed olefin aziridination is a fundamentally and practically important chemical process that has received increasing research attention.¹ The resulting aziridines, the smallest nitrogen-containing heterocyclic compounds, are key elements in many biologically and pharmaceutically interesting compounds and serve as a class of versatile synthons for preparation of functionalized amines.¹ Since the introduction of PhI=NTs as a nitrene source more than three decades ago,² considerable progress has been made in metal-catalyzed olefin aziridination with PhI=NTs and related iminoiodane derivatives,^{1,3} including the notable recent developments with

the use of their in situ variants.^{4,5} Despite these advances, the search for alternative nitrene sources is warranted as the use of PhI=NTs has met with several difficulties. Besides its short shelf life and poor solubility in common solvents, aziridination with PhI=NTs generates a stoichiometric amount of PhI as a byproduct. In view of the similarity to diazo reagents for carbene transfer processes, azides should have the potential to serve as a general class of nitrenesources for metal-mediated nitrene transfer reactions, including aziridination (Scheme 1). In addition to their wide availability and

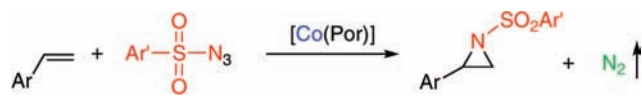
(1) (a) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (b) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701.

(2) Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.

(3) For recent examples with PhI=NTs: (a) Klotz, K. L.; Slominski, L. M.; Hull, A. V.; Gottsacker, V. M.; Que, L., Jr.; Halfen, J. A. *Chem. Commun.* **2007**, 2063. (b) Zdilla, M. J.; Abu-Omar, M. M. *J. Am. Chem. Soc.* **2006**, *128*, 16971. (c) Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202.

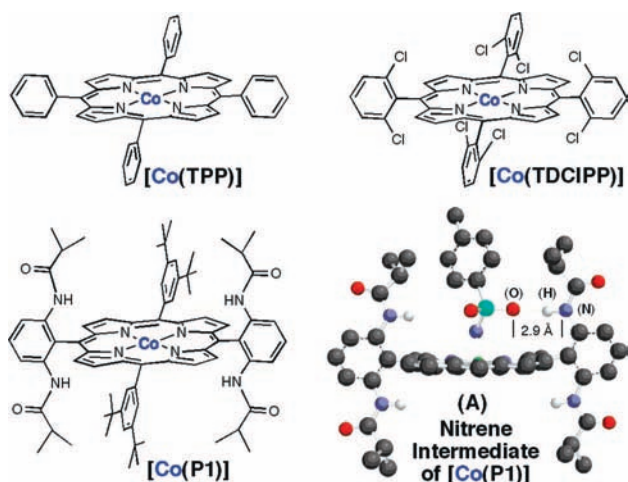
(4) For recent in situ variants, see: (a) Esteoule, A.; Duran, F.; Retailleau, P.; Dodd, R. H.; Dauban, P. *Synthesis* **2007**, 1251. (b) Guthikonda, K.; Wehn, P. M.; Caliendo, B. J.; Du Bois, J. *Tetrahedron* **2006**, *62*, 11331. (c) Li, Z.; Ding, X.; He, C. *J. Org. Chem.* **2006**, *71*, 5876. (d) Xu, Q.; Appella, D. H. *Org. Lett.* **2008**, *10*, 1497.

(5) For other approaches, see: (a) Antilla, J. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 5099. (b) Williams, A. L.; Johnston, J. N. *J. Am. Chem. Soc.* **2004**, *126*, 1612. (c) Vyas, R.; Gao, G.-Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2004**, *6*, 1907. (d) Catino, A. J.; Nichols, J. M.; Forslund, R. E.; Doyle, M. P. *Org. Lett.* **2005**, *7*, 2787.

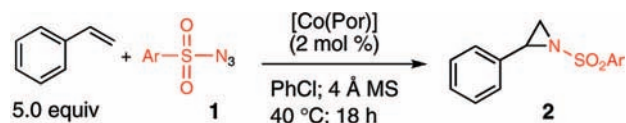
Scheme 1. Cobalt-Catalyzed Olefin Aziridination with Azides

ease of synthesis,⁶ azide-based nitrene transfers would generate chemically stable and environmentally benign nitrogen gas as the only byproduct. Despite these attributes, only a few catalytic systems have been developed that can effectively catalyze the decomposition of azides for aziridination.^{7–11}

We recently reported a Co-based system for catalytic aziridination with azide.^{12a} It was shown that [Co(TPP)] (Figure 1) can catalyze olefin aziridination with commercially

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

available diphenylphosphoryl azide (DPPA) as a convenient new nitrene source, leading to the formation of *N*-phosphorylated aziridines. In an attempt to expand the catalytic process for other azides, it was found that [Co(TPP)] was ineffective for olefin aziridination with sulfonyl azides.¹³ For example, the desired aziridines **2a–c** were obtained only in 11–24% yields from styrene when the common azides **1a–c** were used (Scheme 2).¹⁴ Changing the catalyst to Co(TDCIPP) (Figure 1), which was shown to be effective for

Scheme 2. Synthesis of Chiral Diporphyrin

ArSO ₂ N ₃ (1)	[Co(TPP)]	[Co(TDCIPP)]	[Co(P1)]
4-Me-C ₆ H ₄ SO ₂ N ₃ (1a)	2a : 18%	2a : <5%	2a : 94%
4-MeO-C ₆ H ₄ SO ₂ N ₃ (1b)	2b : 24%	2b : <5%	2b : 88%
4-MeC(O)NH-C ₆ H ₄ SO ₂ N ₃ (1c)	2c : 11%	2c : <5%	2c : 98%

aziridination with bromamine-T,^{12b} produced the desired product in less than 5% yield for each of the cases (Scheme 2).¹⁴ As part of our efforts to develop new porphyrin ligands to enhance Co-based catalytic processes, herein we describe the design and synthesis of a new porphyrin **P1** based on potential hydrogen bonding interaction in the assumed metal–nitrene intermediate (Figure 1). The Co(II) complex of **P1** [Co(**P1**)] was shown to be a highly active catalyst for aziridination of different aromatic olefins with various arylsulfonyl azides, forming the corresponding aziridines in excellent yields under mild conditions (Scheme 2).

Similar to that proposed for other metal-based systems,¹ the Co-catalyzed aziridination can be assumed to proceed via a mechanism involving a key electrophilic Co–nitrene intermediate.¹² Accordingly, elements that can stabilize the formation of and enhance the electrophilicity of the nitrene intermediate should facilitate the catalytic cycle. Due to the existence of the SO₂ group in sulfonyl azides, the *D*_{2h}-symmetric porphyrin **P1**-containing amide functional groups at the ortho positions of *meso*-phenyl groups was designed to invoke a potential hydrogen bonding interaction between the S=O and N–H unit in the supposed nitrene intermediate of [Co(**P1**)] (**A**, Scheme 1).¹⁵ As a result of stabilization and activation of **A** from the hydrogen-bonding interaction,¹⁶ [Co(**P1**)] was expected to be a superior catalyst, in comparison with [Co(TPP)] and [Co(TDCIPP)], for aziridination with sulfonyl azides.

P1 was synthesized from its tetrabrominated precursor via a Pd-mediated quadruple amidation reaction with isobutylamide by following the previously established method (see

(12) (a) Gao, G.-Y.; Jones, J. E.; Vyas, R.; Harden, J. D.; Zhang, X. P. *J. Org. Chem.* **2006**, *71*, 6655. (b) Gao, G.-Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2005**, *7*, 3191. (c) Ruppel, J. V.; Kamble, R. M.; Zhang, X. P. *Org. Lett.* **2007**, *9*, 4889.

(13) Careful control experiments showed that arylsulfonyl azides reported in this work were stable under the conditions used. But it should be noted that some of the azide compounds may be explosive and should be handled with great care.

(14) Except unreacted azides and styrene, no other products were observed.

(15) Simple computer modeling by molecular mechanics with Spartan 04 resulted in a minimized geometry with an O–N–H distance of 2.9 Å, suggesting a possibility of significant hydrogen bonding interaction. It should be noted that there is no experimental evidence for such interactions other than the modeling.

(16) For an example of stabilization and activation of reactive intermediate by hydrogen bonding interactions, see: Lucas, R. L.; Zart, M. K.; Mukerjee, J.; Sorrell, T. N.; Powell, D. R.; Borovik, A. S. *J. Am. Chem. Soc.* **2006**, *128*, 15476.

(6) (a) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297. (b) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188.

(7) (a) Kwart, H.; Khan, A. A. *J. Am. Chem. Soc.* **1967**, *89*, 1951. (b) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.

(8) (a) Cenini, S.; Gallo, E.; Caselli, A.; Ragaini, F.; Fantauzzi, S.; Piangiolino, C. *Coord. Chem. Rev.* **2006**, *250*, 1234. (b) Piangiolino, C.; Gallo, E.; Caselli, A.; Fantauzzi, S.; Ragaini, F.; Cenini, S. *Eur. J. Org. Chem.* **2007**, 743.

(9) (a) Katsuki, T. *Chem. Lett.* **2005**, 1304. (b) Kawabata, H.; Omura, K.; Uchida, T.; Katsuki, T. *Chem. Asian J.* **2007**, *2*, 248.

(10) For a Co-catalyzed hydroazidation of olefins, see: Waser, J.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 8294.

(11) For a Brønsted acid-promoted process, see: Mahoney, J. M.; Smith, C. R.; Johnston, J. N. *J. Am. Chem. Soc.* **2005**, *127*, 1354.

Table 1. [Co(**P1**)]-Catalyzed Aziridination of Styrene with Different Arylsulfonyl Azides^a

entry	azide	aziridine	yield (%) ^b
1			94
2			88
3			98
4			88
5			97
6			96
7			97

^a Reactions were carried out for 18 h in chlorobenzene at 40 °C under N₂ in the presence of 4 Å molecular sieves using 2 mol % of [Co(**P1**)]. Concentration: 0.20 mmol of azide/1 mL of chlorobenzene; Styrene:Azide = 5:1. ^b Isolated yields.

the Supporting Information).¹⁷ [Co(**P1**)] was readily prepared from reaction of **P1** with CoCl₂ in THF in the presence of 2,6-lutidine (see the Supporting Information). Under the same conditions used for the aforementioned reactions by [Co(**T-PP**)] and [Co(**TDCIPP**)], we were delighted to find that employment of [Co(**P1**)] resulted in a dramatic improvement of the catalytic aziridination (Scheme 2). The desired aziridines **2a**, **2b**, and **2c** were obtained in 94%, 88%, and 98% isolated yields, respectively, supporting the hydrogen bonding guided catalyst design.¹⁸

In addition to azides **1a**, **1b**, and **1c** that contain -methyl, -methoxy, and -acetamide groups (entries 1–3), [Co(**P1**)] could effectively activate a wide range of arylsulfonyl azides for aziridination (Table 1). For example, the use of arylsulfonyl azides having *p*-cyano (**1d**), *p*-nitro (**1e**), and *o*-nitro (**1f**) substituents afforded the corresponding aziridination products of styrene **2d–b** in excellent yields (entries 4–6). Naphthalene-1-sulfonyl azide **1g** was found to be an equally active nitrene source (entry 7). The [Co(**P1**)]-based catalytic

Table 2. Aziridination of Aromatic Olefins with Arylsulfonyl Azides by [Co(**P1**)]^a

entry	azide	olefin	aziridine	yield (%) ^b
1				97 (90) ^c
2				89 (83) ^c
3				89
4				88
5				98 (97) ^c
6				94 (83) ^c
7				96
8				95 (90) ^c
9				96
10				75
11				98
12				83 ^d
13				84 ^d
14				93 ^d

^a Reactions were carried out for 18 h in chlorobenzene at 40 °C under N₂ in the presence of 4 Å molecular sieves using 2 mol % [Co(**P1**)]; Olefin:Azide = 5:1; Concentration: 0.20 mmol azide/1 mL chlorobenzene. ^b Isolated yields. ^c Olefin:Azide = 1:1.2. Concentration: 0.20 mmol of azide/1 mL of chlorobenzene. ^d Performed at 60 °C.

aziridination system could be successfully applied to various combinations of arylsulfonyl azides and aromatic olefins (Table 2).¹⁹ For example, using azide **1e** as a nitrene source,

(17) (a) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718. (b) Chen, Y.; Ruppel, J. V.; Zhang, X. P. *J. Am. Chem. Soc.* **2007**, *129*, 12074. (c) Zhu, S.; Ruppel, J. V.; Lu, H.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042.

various styrene derivatives as well as 2-vinylnaphthalene could be aziridinated in high to excellent yields (entries 1–10). Similar results were obtained for azide **1c** (entries 11–14). While most of the reactions were carried out with 5 equiv of olefin, the catalytic process could be operated with olefins as the limiting reagent as demonstrated with some selected examples, albeit in relatively lower yields (entries 1, 2, 5, 6, and 8).

In summary, guided by potential hydrogen-bonding interaction in the proposed intermediate (**A**), we designed and synthesized the new porphyrin **P1** whose Co complex [Co(**P1**)] was shown to be a highly effective catalyst for aziridination of aromatic olefins with arylsulfonyl azides

(18) [Co(**P1**)] could effectively catalyze aziridination of styrene with PhI=NTs, forming the desired aziridine in 84% isolated yield.

(19) The current [Co(**P1**)]-based catalytic system was ineffective for multiple substituted and aliphatic olefins.

under mild conditions. Efforts are underway to expand the substrate scope to include nonaromatic olefins and to develop its asymmetric variants.

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

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