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Room Temperature Activation of Aryloxysulfonyl Azides by [Co(II)(TPP)] for Selective Radical Aziridination of Alkenes via Metalloradical Catalysis

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Abstract

Aryloxysulfonyl azides can be effectively activated by commercially available cobalt(II) complex of *meso*-tetraphenylporphyrin ([Co(TPP)]) at room temperature under neutral and nonoxidative conditions for selective radical aziridination of alkenes via metalloradical catalysis. The [Co(TPP)]-catalyzed radical aziridination system is suitable for different combinations of olefin substrates and aryloxysulfonyl azides, producing various *N*-aryloxysulfonyl aziridine derivatives in good to excellent yields. In addition to generating the environmentally benign N₂ as the only byproduct, this Co(II)-based metalloradical aziridination process features mild reaction conditions and operational simplicity.

Keywords

Metalloradical; Radical; Cobalt; Aziridination; Azide; Porphyrin

1. Introduction

As stable metalloradicals with well-defined open-shell doublet d⁷ electronic structure, cobalt(II) complexes of porphyrins, [Co(Por)], have shown to be effective catalysts for aziridination of a broad spectrum of alkenes with different classes of nitrogen sources via a unique stepwise radical process (Scheme 1).^{1–2} Of various Co(II)-based metalloradical catalysts, Co(II) complexes supported by porphyrin ligands bearing amide functionalities [Co(AmidoPor)] have shown to be particularly effective in activating various organic azides, including phosphoryl azides,³ sulfonyl azides,⁴ and aryl azides,⁵ for radical olefin aziridination, producing the corresponding aziridines in high yields under mild conditions. The high catalytic efficiency of [Co(AmidoPor)] metalloradical catalysts is attributed to the stabilization of the key α-Co(III)-aminyl radical (also known as Co(III)-nitrene radical) intermediate through hydrogen-bonding interaction with the amide group of the porphyrin

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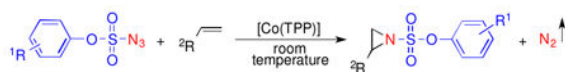
Supplementary Material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/XXXXXX>.

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ligand (Scheme 1: A1).^{1–5} While the effectiveness of [Co(AmidoPor)] have been clearly demonstrated (especially in the case of enantioselective aziridination), it would be practically more desirable if the commercially available Co(II) complex of *meso*-tetraphenylporphyrin ([Co(TPP)]) could be applied effectively as metalloradical catalyst for radical olefin aziridination with azides when the concern of enantioselectivity is unnecessary. This practical desire is translated to the fundamental question of whether [Co(TPP)], which lacks of the hydrogen-bonding capability, can effectively activate azides to generate the corresponding α -Co(III)-aminyl radical (Scheme 1: A2) to serve as active intermediates for the radical aziridination process.

Several different types of organic azides have been previously investigated as nitrogen sources for catalytic olefin aziridination by metalloradical [Co(TPP)], including diphenylphosphoryl azide^{3a} and 4-nitrophenyl azide.^{6–7} In addition to limited substrate scope and low product yields, these existing [Co(TPP)]-based systems typically required the use of high catalyst loading (8–10 mol %) and elevated reaction temperature (75–100 °C).^{3a, 6} Driven by the desire to utilize the commercially available [Co(TPP)] as a practical catalyst for olefin aziridination, we embarked on a project to search for more reactive organic azides that can be activated by [Co(TPP)] to generate the corresponding key α -Co(III)-aminyl radicals under mild conditions. As the outcome of this effort, we herein report our findings that aryloxysulfonyl azides (ArOSO₂N₃) are a new type of organic azides that can be effectively activated by [Co(TPP)] even at room temperature for selective radical aziridination (eq 1). The newly developed Co(II)-catalyzed aziridination can utilize ArOSO₂N₃ with different aryl substituents and is suitable for a wide range of aromatic olefins with diverse electronic and steric properties, affording a series of *N*-aryloxysulfonyl aziridines in good to excellent yields. In addition to generating the environmentally benign N₂ as the only byproduct, the new metalloradical aziridination system enjoys several practical attributes associated with neutral and nonoxidative condition as well as the commercial availability of the catalyst [Co(TPP)].



(1)

2. Results and discussion

After examining different organic azides, we turned our attention to aryloxysulfonyl azides (ArOSO₂N₃), which have not been previously explored as precursors of α -Co(III)-aminyl radicals for Co(II)-based metalloradical catalysis.⁸ In comparison with arylsulfonyl azides (ArSO₂N₃), which has been previously shown to be ineffective for catalytic aziridination by [Co(TPP)],^{4a,9} ArOSO₂N₃ should be more electron-deficient due to the electron-withdrawing effect of the aryloxy groups and might be easier to be activated by [Co(TPP)]. With this assumption in mind, we synthesized a series of aryloxysulfonyl azides from the corresponding phenols in a one-pot procedure by following the literature methods.^{4b,10} For example, azides **2a–e** (Table 1), which contain H, Cl, Br, F, and Ph substituents,

respectively, at the para-position of the aryl ring, were readily prepared from the reactions of the commercially available phenols with SO_2Cl_2 in the presence of pyridine, followed by treatment of the resulting aryloxysulfonyl chlorides with NaN_3 .¹⁰

With 4-phenylphenoxy sulfonyl azide (**2e**) as a model azide reagent, we studied the catalytic aziridination reaction of styrene and found that $[\text{Co}(\text{TPP})]$ was a highly effective metalloradical catalyst to activate the azide even at room temperature for the production of the corresponding aziridine **4ea** (Table 2). Further experiments demonstrated that the effectiveness of the $[\text{Co}(\text{TPP})]$ -catalyzed aziridination reaction could be dramatically impacted by the molar ratio of the azide reagent to styrene substrate. When 10 equivalents of styrene were used, aziridine **4ea** was obtained in 95% yield (Table 2, entry 1). The yield slightly decreased to 82% in the presence of 5 equivalents of styrene (Table 2, entry 2). The aziridination by $[\text{Co}(\text{TPP})]$ became much less effective when a stoichiometric amount of styrene was employed (Table 2, entry 3).¹¹ It was found that the solvent could also influence the outcome of the metalloradical aziridination process by $[\text{Co}(\text{TPP})]$. While chlorobenzene was identified to be an optimal solvent, it was shown that coordinative and more polar solvents such as acetonitrile and THF completely suppressed the catalytic process, leading to no formation of the aziridine product (Table 2, entries 4–5). In stark contrast to the catalytic capability of its $\text{Co}(\text{II})$ metalloradical complex, other transition metal complexes of TPP, such as $\text{Fe}(\text{III})$, $\text{Mn}(\text{III})$, $\text{Zn}(\text{II})$, $\text{V}(\text{IV})$, $\text{Cu}(\text{II})$, $\text{Ni}(\text{II})$ and $\text{Cr}(\text{III})$ complexes (Figure 1), were found to be unable to activate aryloxysulfonyl azide **2e** effectively for aziridination of styrene (Table 2, entries 6–12). It is evident that the metalloradical character of $[\text{Co}(\text{TPP})]$ is key to the success of the catalytic aziridination process with the azide (Scheme 1).

The commercially available metalloradical catalyst $[\text{Co}(\text{TPP})]$ was demonstrated to be effective in activating different aryloxysulfonyl azides at room temperature for radical aziridination. As summarized in Table 3, in addition to 4-phenylphenoxy sulfonyl azide **2e**, phenoxy sulfonyl azide **2a** could be activated by $[\text{Co}(\text{TPP})]$ to aziridinate styrene to give the corresponding aziridine **4aa** in a high yield as well (Table 3, entry 2). Various halogenated phenoxy sulfonyl azides, including chloro-, bromo- and fluoro-substituted azides (**2b–d**), could also be applied for $[\text{Co}(\text{TPP})]$ -catalyzed aziridination of styrene, affording the corresponding aziridine products **4ba**, **4ca** and **4da**, respectively, in excellent yields (Table 3, entries 3–5).

To investigate the substrate scope of the $\text{Co}(\text{II})$ -based catalytic system, 4-phenylphenoxy sulfonyl azide (**2e**) and phenoxy sulfonyl azide (**2a**) were selected as representative nitrogen sources for aziridination reactions of different olefins. As shown in Table 4, the $[\text{Co}(\text{TPP})]$ -catalyzed room-temperature aziridination was demonstrated to be suitable for a wide range of aromatic olefins with various steric and electronic properties. For example, styrene derivatives with electron-donating substituents, including methyl and *tert*-butyl groups, could serve as effective substrates for the metalloradical aziridination, yielding the desired aziridines in high yields (Table 4, entries 1–3 and entries 9–12). As well, fluoro-, chloro- and bromo-substituted styrenes underwent the aziridination reactions smoothly by $[\text{Co}(\text{TPP})]$, affording the corresponding aziridine products effectively (Table 4, entries 4–7 and entries 13–15). Moreover, the electron-deficient 4-trifluoromethylstyrene could also be aziridinated by both azides **2e** and **2a** to produce the aziridines **4eh** and **4ah**,

respectively, in good yields (Table 4, entries 8 and 16). It was noted that the reactivity of the [Co(TPP)]-catalyzed aziridination could be significantly influenced by the steric hindrance of the aromatic olefins. While the aziridination reactions of *para*- and *meta*-substituted styrenes typically gave good to excellent yields of the corresponding aziridines, more sterically hindered *ortho*-substituted styrenes, such as 2-bromo- and 2-methylstyrenes, could be only aziridinated by [Co(TPP)] in moderate yields (Table 4).

3. Conclusions

In summary, we have identified aryloxysulfonyl azides (ArOSO_2N_3) as a new type of nitrogen sources for radical aziridination by Co(II)-based metalloradical catalysis. Due to their high reactivity, we have shown that aryloxysulfonyl azides can be even activated by simple metalloradical catalyst [Co(TPP)] even at room temperature to effect productive aziridination reactions of different aromatic olefins. The [Co(TPP)]/ ArOSO_2N_3 -based aziridination system has several practical attributes associated with metalloradical catalysis. In addition to the neutral and mild reaction conditions, environmentally benign dinitrogen is the only byproduct from the catalytic process. The commercial availability of [Co(TPP)] should further enhance the practicality of this room-temperature aziridination method. The resulting *N*-aryloxysulfonyl aziridines, which can be readily converted to unprotected N–H aziridine derivatives through facile removal of the aryloxysulfonyl groups,¹² may find applications for the synthesis of nitrogen-containing compounds of pharmaceutical importance.^{12b–c,13} More broadly, the demonstrated high reactivity of aryloxysulfonyl azides may stimulate the exploration of their applications for the development of other Co(II)-based metalloradical processes where the α -Co(III)-aminyl radicals serve as the key intermediates (Scheme 1).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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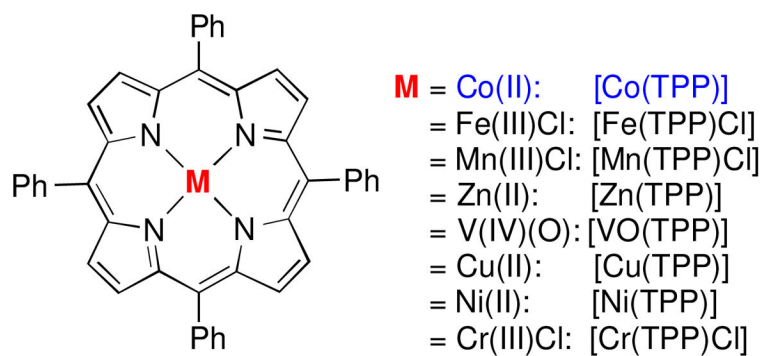
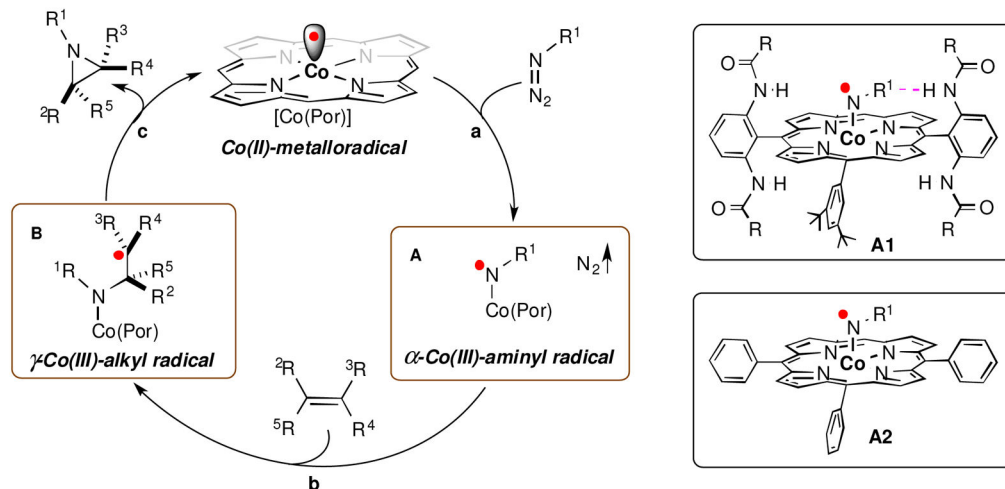
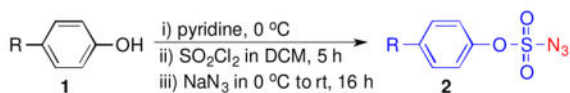


Figure 1.
Structures of porphyrin complexes with metal ions.

**Scheme 1.**

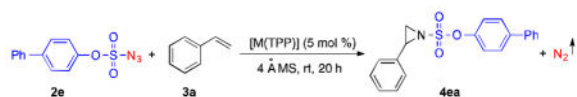
(Left) Pathways of proposed mechanism of radical aziridination via Co(II)-based metalloradical catalysis: a) generation of α -Co(III)-aminyl radical via metalloradical activation of azide by [Co(Por)]; b) formation of γ -Co(III)-alkyl radical through radical addition of α -Co(III)-aminyl radical onto olefin; and c) production of aziridine via 3-exo-tet radical cyclization of γ -Co(III)-alkyl radical. (Right) Structures of postulated α -Co(III)-aminyl radical intermediates supported by amidoporphyrins (**A1**) and TPP (**A2**). For clarity, one 3,5-Di^tBu-Phenyl group on the *meso*-position of the amidoporphyrin (**A1**) and one phenyl group on the *meso*-position of TPP (**A2**) were omitted.

Table 1Preparation of aryloxysulfonyl azides ^[a]

entry	product	yield (%) ^[b]
1	2a	40
2	2b	39
3	2c	40
4	2d	41
5	2e	45

^[a] Reaction conditions: phenols **1** (10 mmol), sulfuryl chloride (22 mmol), NaN₃ (30 mmol).

^[b] Isolated yields.

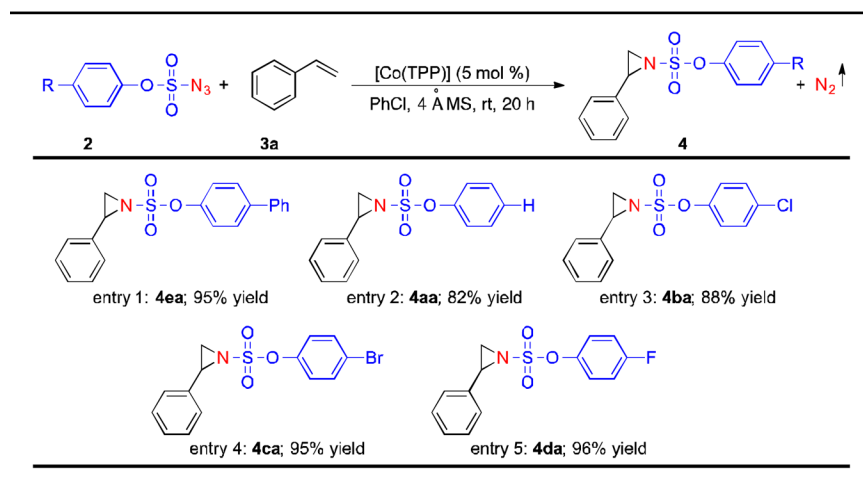
Table 2Catalytic aziridination of styrene with 4-phenylphenoxy sulfonyl azide by metalloporphyrin complexes ^[a]

entry	Azide:Styrene	[M(TPP)]	solvent	yield (%) ^[b]
1	1:10	[Co(TPP)]	PhCl	95
2	1:5	[Co(TPP)]	PhCl	82
3	1:1.2	[Co(TPP)]	PhCl	12
4	1:5	[Co(TPP)]	CH ₃ CN	NR
5	1:5	[Co(TPP)]	THF	NR
6	1:10	[Fe(TPP)Cl]	PhCl	8
7	1:10	[Mn(TPP)Cl]	PhCl	8
8	1:10	[Zn(TPP)]	PhCl	3
9	1:10	[VO(TPP)]	PhCl	6
10	1:10	[Cu(TPP)]	PhCl	8
11	1:10	[Ni(TPP)]	PhCl	4
12	1:10	[Cr(TPP)Cl]	PhCl	4

^[a] Reaction conditions: azide **2e** (0.1 mmol), styrene **3a** (1 mmol) unless otherwise stated, 4 Å MS (100 mg), catalyst (5 mol %) unless otherwise stated, solvent (1 mL), 20 h, rt.

^[b] ¹H-NMR yields.

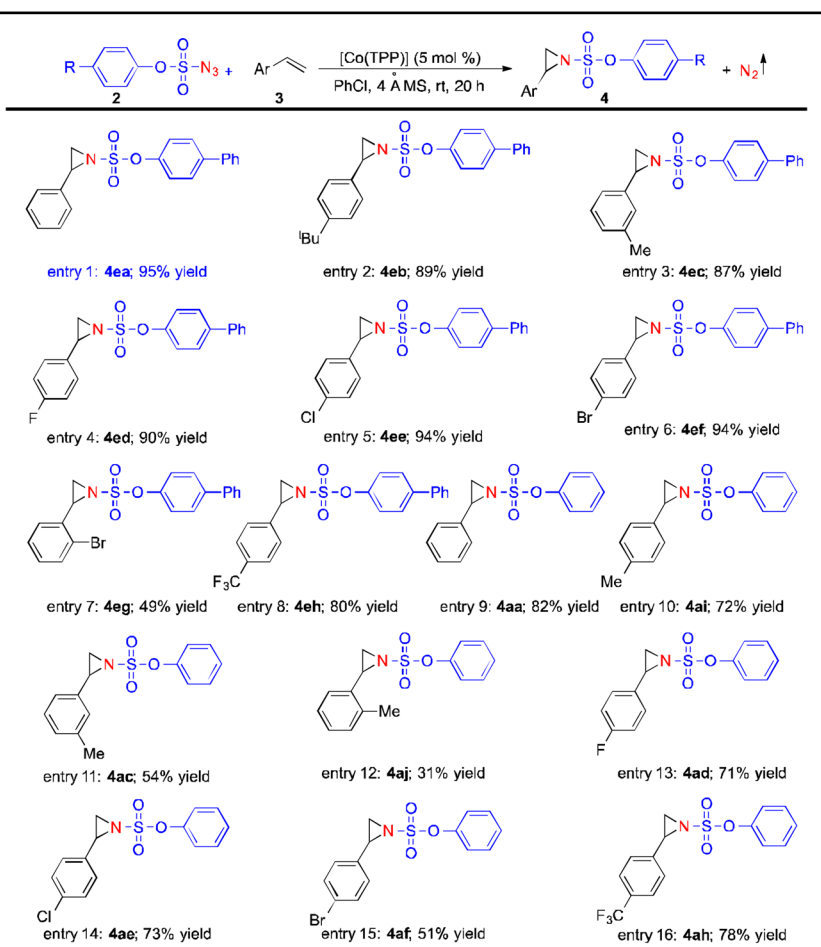
Table 3

Activation of aryloxysulfonyl azides for olefin aziridination by [Co(TPP)] ^[a,b]

[a] Reaction conditions: azide **2** (0.1 mmol), styrene **3a** (0.5 mmol), 4 Å MS (100 mg), [Co(TPP)] (5 mol %), PhCl (1 mL), 20 h, rt.

[b] Isolated yields.

Table 4

[Co(TPP)]-catalyzed aziridination of various styrene derivatives with aryloxysulfonyl azides ^[a,b]

^[a] Reaction conditions: azide **2** (0.1 mmol), olefin **3** (0.5 mmol), 4 Å MS (100 mg), [Co(TPP)] (5 mol %), PhCl (1 mL), 20 h, rt.

^[b] Isolated yields.