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Synthesis of aminoalcohols from substituted alkenes *via* tungstenooxaziridine catalysis†

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Herein we report the $\text{WO}_2\text{Dipic}(\text{H}_2\text{O})$ promoted oxyamination of alkenes using sulfonamides as the quantitative source of *N*. The reaction works for activated and unactivated alkenes in high yields, diastereoselectivities, and stereospecificity. A catalytic cycle involving the formation of tungstenooxaziridine complex **1** as the active catalyst and hydrolysis of tungstenooxazolidine intermediate **A** as the rate-determining-step has been proposed. Initial kinetic and competition experiments provide evidence for the proposed mechanism.

Introduction

The stereoselective oxyamination of alkenes for the synthesis of aminoalcohols and derivatives remains as one of the most fundamental transformations in organic chemistry to this date.¹ Much progress has been achieved towards the stereoselective difunctionalization of alkenes, however there are very few methods that are able to achieve direct oxyamination with high chemo-, regio-, and stereoselectivities.² This structural motif is prevalent in natural products and commercially available drugs with very important pharmacological profiles³ but also across a large array of chiral ligands, auxiliaries and organocatalysts.⁴ Therefore, the continuous development of novel methods for the systematic synthesis of aminoalcohols has great significance.⁵ Since the pioneering work by Sharpless in asymmetric aminohydroxylation,^{2b} multiple strategies have been developed to access aminoalcohols.⁶ Unfortunately, most suffer from poor regioselectivity or rely on intramolecular methods that require further functional group manipulations. Thus, direct stereoselective oxyamination methods continue to receive much attention in the field of organic chemistry (Fig. 1). Ground-breaking work by Yoon discovered that *N*-EWG oxaziridines can trigger oxyamination pathways by careful exposure to very specific transition-metal environments.⁷ Terminal alkenes, when using a copper catalyst, undergo oxyamination with high regioselectivity for

oxygen on the least substituted carbon and when using an iron catalyst, oxyamination occurs with high regioselectivity for oxygen on the more substituted carbon.⁸

Other efforts have found other transition metals also achieve oxyamination outcomes with general success (Mn, Pd, Ir, Cu, and Se).⁹ Moreover, efforts in visible-light photocatalysis have also demonstrated synthetically useful efficiencies and generality.¹⁰ This new generation of methods offers a large array of catalysts with unique properties, but regioselectivity

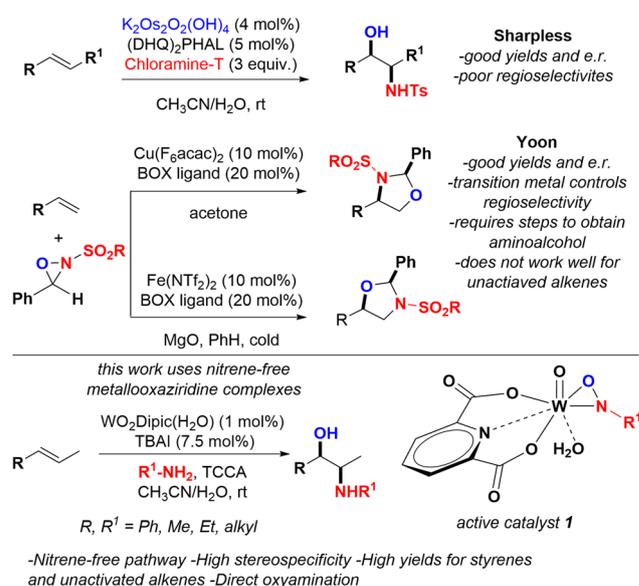


Fig. 1 Advances in stereoselective oxyamination.

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and poor reactivity across unactivated alkenes remains a problem.

Metallooxaziridines can be obtained from reacting metal-oxides and *amino*-containing reagents.¹¹ Their chemical properties are analogous to peroxy-complexes that transfer *O* atoms across alkenes and are comparable to metal oxide complexes known to achieve oxyamination reactions.¹² The chemistry of these metallooxaziridines has not been fully exploited; however, we recently reported that zirconooxaziridines are suitable catalysts for the highly stereoselective and stereospecific aziridination of unactivated alkenes.¹³ Early work by Sharpless provided some insights into the unique properties of these complexes as he found that *Mo* and *W* oxaziridines were able to activate π -systems.¹⁴

The Moura-Letts laboratory is focused on developing novel methods for the synthesis of complex nitrogen-containing molecules.¹⁵ Thus, we envisioned creating a well-defined catalytic system for the oxyamination of alkenes *via* the formation of metallooxaziridines as the active catalyst for the reaction. To the best of our knowledge, this would be the first report for such a catalytic process.

Results and discussion

Since the discovery of zirconooxaziridine catalysis for the aziridination of alkenes, some results indicated that other chemical pathways could be optimized upon changing the transition-metal in the metallooxaziridine centre. The high chemoselectivity observed for LZrON-Ts was in part due to the group IV transition-metal nature of *Zr* and the geometry of the

respective LUMO across the *Zr*-*N* bond. Thus, analogous to Cu^{II} and Fe^{III} -promoted chemo- and regioselective diversity in oxyaminations,⁸ it was hypothesized that high-oxidation state group VI transition metal complexes (LMO₂NTs) would provide LUMO's leading to different chemo- and regioselective outcomes. Fortunately, it was discovered that while LWO₂NTs provided aziridine in very low yield, it provided aminoalcohol **3a** with high selectivity. As observed for Fe^{III} oxyaminations, the reaction chemoselectivity allows the transformation to occur across the *N*-*O* bond and, regioselective addition of *N*-Ts to the least substituted side of the alkene.¹⁶

The basic premise behind this study was to develop a simple and efficient oxyamination process with high stereoselectivity and stereospecificity for unactivated and activated alkenes (Table 1). Although our efforts for the aziridination of alkenes relied on chloramine T as the source of *N*, we discovered that further diversification could be introduced with sulfonamides and trichloroisocyanuric acid (TCCA) as an activator/oxidant to provide *in situ* RSO₂NHCl (RSO₂-chloramine).¹⁷ Initial results using 1-hexene, indicated that metal oxides at 5 mol%, phase-transfer catalyst (PTC) at 7.5 mol%, and excess *p*-toluenesulfonamide/TCCA in CH₃CN/H₂O (10/1) promoted oxyamination in low yields, with a clear indication that *W* was able to provide the expected product with synthetically useful selectivities (entry 3). It was anticipated that dipicolinic acid (Dipic) would provide a more stable complex and it was found that WO₂Dipic(H₂O) improved the reaction yield to 48% and 10 : 1 : 1 **3a** : **4a** : **5a** product ratio (entry 5); *V* or *Mo* were not as successful at improving the reaction yield (entries 6 and 7). The nature of the PTC was tested, and it was found that TBAI provided a small increase in reaction performance (62% yield,

Table 1 Reaction optimization

Entry ^{a,b}	Metal catalyst	PTC	Solvent	Temp	Yield (%)	3a : 4a : 5a
1	MoO ₃ ^c	CTAB	CH ₃ CN/H ₂ O	rt	5	1 : 1 : 1
2	V ₂ O ₅ ^c	CTAB	CH ₃ CN/H ₂ O	rt	4	1 : 1 : 0
3	WO ₃ ^c	CTAB	CH ₃ CN/H ₂ O	rt	24	4 : 1 : 0
4	ZrO ₂ ^c	CTAB	CH ₃ CN/H ₂ O	rt	6	1 : 0 : 5
5	WO ₂ Dipic ^{c,d}	CTAB	CH ₃ CN/H ₂ O	rt	48	10 : 1 : 1
6	V ₂ O ₃ Dipic ^{c,d}	CTAB	CH ₃ CN/H ₂ O	rt	10	2 : 1 : 1
7	MoO ₂ Dipic ^{c,d}	CTAB	CH ₃ CN/H ₂ O	rt	8	2 : 1 : 0
8	WO ₂ Dipic ^{c,d}	TBAB	CH ₃ CN/H ₂ O	rt	38	10 : 1 : 0.5
9	WO ₂ Dipic ^{c,d}	TBAI	CH ₃ CN/H ₂ O	rt	62	12 : 1 : 0.5
10	WO ₂ Dipic ^{c,d}	TBACl	CH ₃ CN/H ₂ O	rt	44	10 : 1 : 1
11	WO ₂ Dipic ^{c,d}	CTAI	CH ₃ CN/H ₂ O	rt	39	10 : 1 : 1
12	WO ₂ Dipic ^d (10 mol%)	TBAI ^e	CH ₃ CN/H ₂ O	rt	58	10 : 2 : 3
13	WO ₂ Dipic ^d (1 mol%)	TBAI	CH ₃ CN/H ₂ O	rt	88	16 : 0.5 : 1
14	WO ₂ Dipic ^d (1 mol%)	TBAI	DCE/H ₂ O	rt	73	16 : 1 : 1
15	WO ₂ Dipic ^d (1 mol%)	TBAI	CH ₂ Cl ₂ /H ₂ O	rt	35	16 : 1 : 1
16	WO ₂ Dipic ^d (1 mol%)	TBAI	DMF/H ₂ O	rt	53	15 : 1 : 2
17	WO ₂ Dipic ^d (1 mol%)	TBAI	CH ₃ CN/H ₂ O	0 °C	48	16 : 1 : 1
18	WO ₂ Dipic ^d (1 mol%)	TBAI	CH ₃ CN/H ₂ O	60 °C	32	8 : 1 : 2

^a Isolated yields. ^b TsNH₂ (1.5 equiv.) is mixed with TCCA (0.5 equiv.) in CH₂Cl₂ at 0 °C for 30 min then solvent removed and CH₃CN/H₂O 0.125M (10 : 1), metal oxide, additive and alkene are added. ^c 5 mol% of metal and 7.5 mol% of PTC. ^d WO₂Dipic(H₂O), Dipic = dipicolinic acid. ^e 15 mol%. CTA = cetrimonium, TBA = tetrabutyl n-butylammonium.



entry 9). The different catalytic steps in this reaction take place in different phases in the reaction mixture. Thus, efficient PTCs are crucial to achieve conversion due to poorly soluble $\text{WO}_2\text{Dipic}(\text{H}_2\text{O})$ and *in situ* formed chloramine. Other catalysts failed to improve the reaction yield beyond the efficiency obtained with TBAI (entries 8, 10 and 11).

To further improve the reaction performance, catalyst loading was increased to 10 mol% but a complex mixture and lowered chemo- and regioselectivity due to catalyst decomposition was observed (entry 12); however, when loading was reduced to 1 mol% the yield and product ratio increased to 88% and 16 : 0.5 : 1 respectively (entry 13). The reaction solvent was also examined, and $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ remained to be optimal. Coordinating solvents (CH_3CN) are known to accelerate *N*-Ts transfer reactions and the role of H_2O as a ligand in the proposed process was anticipated. The reaction at different temperatures also failed to provide similarly high yields and selectivities (entries 17 and 18).

Given the results observed for the oxyamination of 1-hexene, this study focused on addressing the generality across different types of unactivated alkenes (Table 2).¹⁸ 1-Octene provided the corresponding aminoalcohol in equally high yield and similar observable rate (91% and 16 h, entry 2). Activation of alkenes, depending upon the nature of the *N*-transfer reagent, often suffers from poor diastereospecificity due to the formation of nitrene reactive intermediates that lead to stereochemical erosion.¹⁹ Analogous to the aziridination reaction, high stereospecificity was expected due to the fast formation of metalloheterocyclic intermediates (intermediate **A**) through a biradical transition state.

Thus, we tested 1,2-disubstituted alkenes and we found that (*E*)-2-octene, and symmetric (*E*)-4-octene reacted to produce the corresponding aminoalcohols in high yields and diastereoselectivities without visible stereochemical erosion (entries 3 and 4). Correspondingly, (*Z*)-4-octene provided the product in good yield, high diastereoselectivity and a comparable observable rate (88% and 18 h, entry 5). These results provide indication of a highly stereospecific delivery of both groups across the alkene, the high *syn*-selectivity correlates well with a tungstenoxaziridine *syn*-addition across the *N*-O bond. Further exploration of the scope revealed that cyclohexene, 1-methylcyclohexene, cyclooctene, and indene provided the corresponding aminoalcohols in high yields and slightly slower rates despite the increased substitution (18–22 h, entries 6–9).²⁰ The reaction proved to be successful across a variety of unactivated alkenes with high stereoselectivity and stereospecificity. The focus then turned towards addressing the generality across styrenes with activating and deactivating substituents (Table 3).

Styrene (entry 1) and styrenes with various alkyl electron-donating-groups (EDGs) were successful at providing the expected aminoalcohols in high yields and at faster observable rates (4–8 h, entries 2–6). Moreover, 4-methoxy styrene worked in similarly high yield and faster observable rate (3 h, entry 7). Other substitution patterns (biphenyl and naphthyl, entries 8 and 9) were also very productive for this transformation. The

Table 2 Reaction scope

2		Reaction conditions		3	
		Ts-NH ₂ (1.5 equiv), TCCA (0.5 equiv) WO ₂ Dipic(H ₂ O) (1 mol%), TBAI (7.5 mol%) CH ₃ CN/H ₂ O, rt			
Entry	Alkene	Product ^c	Yield ^{a,b} (%)	d.r	
1	2a	3a	88	—	
2	2b	3b	91	—	
3	2c	3c	82 ^d	18 : 1	
4	2d	3d	84	20 : 1	
5	2e	3e	88	20 : 1	
6	2f	3f	93	20 : 1	
7	2g	3g	91	18 : 1	
8	2h	3h	95	20 : 1	
9	2i	3i	92	19 : 1	

^a Conditions: TsNH₂ (1.5 equiv.) is mixed with TCCA (0.5 equiv.) in CH_2Cl_2 at 0 °C for 30 min then solvent removed and $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ 0.125M (10 : 1), metal oxide, additive and alkene are added, and reaction stirred at rt for 16 h or until full conversion by TLC. ^b Isolated yields. ^c Reaction was purified by standard silica gel chromatography. ^d 6 : 1 mixture of 3e and 4c.

electronic properties around the ring were then changed; and 4-fluoro, 4-chloro, and 4-iodo provided aminoalcohol **3** in similar yields without apparent loss in observable reaction rates (4–8 h, entries 10–12). Moreover, 3-chloro, 2-chloro, 2,6-dichloro, and 4-trifluoromethyl worked in similar high yields but slower rates (12–14 h, entries 13–16). Surprisingly, 4-cyano and 4-nitro worked in slightly lower yields but there was no noticeable decrease in reaction rates (5 and 6 h, entries 17 and 18). The small differences in reaction efficiencies across styrenes with different substitution patterns support a concerted mechanism. We were also interested in addressing the reaction selectivity across disubstituted styrenes. It was discovered that α -methyl-styrene, α -methyl-toluene, and β -methyl-styrene provided aminoalcohol **3** in high yields and without activation of the allylic methyl group (entries 19–21).

Scope of sulfonamides would allow the introduction of more complex functionality across aminoalcohol **3** (Table 4). It was found that sulfonamides with different nitro groups around the ring reacted to form the respective *N*-transfer



Table 3 Reaction scope

Entry	Alkene	Product ^c	Yield ^{a,b} (%)
1	2j 	3j 	91
2	2k R = 4-methyl	3k R = 4-methyl	88
3	2l R = 3-methyl	3l R = 3-methyl	89
4	2m R = 2-methyl	3m R = 2-methyl	86
5	2n R = 4- <i>t</i> -butyl	3n R = 4- <i>t</i> -butyl	90
6	2o R = 2,4,6-trimethyl	3o R = 2,4,6-trimethyl	86
7	2p R = 4-methoxy	3p R = 4-methoxy	88
8	2q R = 4-phenyl	3q R = 4-phenyl	84
9	2r R = 2-naphthyl	3r R = 2-naphthyl	80
10	2s R = 4-fluoro	3s R = 4-fluoro	82
11	2t R = 4-chloro	3t R = 4-chloro	80
12	2u R = 4-iodo	3u R = 4-iodo	86
13	2v R = 3-chloro	3v R = 3-chloro	89
14	2w R = 2-chloro	3w R = 2-chloro	84
15	2x R = 2,6-dichloro	3x R = 2,6-dichloro	91
16	2y R = 4-trifluoromethyl	3y R = 4-trifluoromethyl	86
17	2z R = 4-cyano	2z R = 4-cyano	80
18	2aa R = 4-nitro	3aa R = 4-nitro	82
19	2ab 	3ab 	91
20	2ac 	3ac 	88
21	2ad 	3ad 	84 ^d

^a Conditions: TsNH₂ (1.5 equiv.) is mixed with TCCA (0.5 equiv.) in CH₂Cl₂ at 0 °C for 30 min then solvent removed and CH₃CN/H₂O 0.125M (10 : 1), metal oxide, additive and alkene are added, and reaction stirred at rt for 16 h or until full conversion by TLC. ^b Isolated yields. ^c Reaction was purified by standard silica gel chromatography. ^d 10 : 1 mixture of 3ad (22 : 1 d.r.) and 4ad.

reagent and then provided **3** in great yields (entries 1–3). Moreover, substituted heterocyclic sulfonamides reacted well and the respective aminoalcohols were also obtained in high yields (entries 4–6). Substituted benzenesulfonamides (4-Br, 4-F, 2-Me) and methylsulfonamide also provided **3** in great yields and optimal stereoselectivities (entries 7–10).

The foundational knowledge discovered for the zirconooxaziridine-mediated aziridination of alkenes along with the available studies on metal-oxide promoted alkene difunctionalization helped design the mechanistic studies for this reaction. The main questions to be addressed were the mode of *N*-Ts group transfer, competing pathways and the mode of OH transfer across the alkene and metal-centre.

Based on the observed chemoselectivity and high stereoselectivity, we anticipated a potentially fast tungstenooxaziridine addition across the alkene with formation of short-lived biradical species through homolytic cleavage of the *N*-O bond in the transition state.²¹ Experiments with deuterated sub-

Table 4 Reaction scope

Entry	Sulfonamide	Product ^c	Yield ^{a,b} (%)
1		3ae 	93
2		3af 	89
3		3ag 	84
4		3ah 	82
5		3ai 	86
6		3aj 	88
7		3ak 	80
8		3al 	84
9		3am 	91
10		3an 	84

^a Conditions: RNH₂ (1.5 equiv.) is mixed with TCCA (0.5 equiv.) in CH₂Cl₂ at 0 °C for 30 min then solvent removed and CH₃CN/H₂O 0.125M (10 : 1), metal oxide, additive and *t*-butylstyrene are added and reaction stirred at rt for 16 h or until full conversion by TLC. ^b Isolated yields. ^c Reaction was purified by standard silica gel chromatography.

strates showed that **2j1-d** and **2p1-d** reacted to provide **3j1-d** and **3p1-d** without any deuterium scrambling, thus both experiments confirming that a highly concerted *syn*-addition is likely to be the predominant pathway. We also wanted to address if **3** formed through hydrolysis of aziridine **5** under the reaction conditions, and we found that **5j** does not provide **3j** under the reaction conditions. Other control experiments showed that WO₂Dipic(H₂O) is crucial for reaction conversion, thus no halogen-mediated activation pathway is taking place, and that the reaction can also work under stoichiometric amounts of **1** (low conversion, details on ESI†).

Thus, we propose a catalytic cycle in which **1** forms within minutes from reacting WO₂Dipic(H₂O) with Ts-chloramine, obtained *in-situ* from reacting *p*-toluenesulfonamide and TCCA (Fig. 2). Complex **1** can also be efficiently isolated by reacting WO₂Dipic(H₂O) and *p*-toluenesulfonamide/TCCA or chlora-



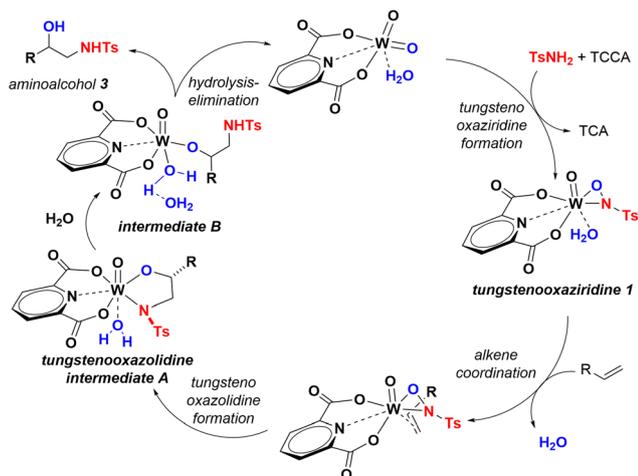


Fig. 2 Proposed catalytic cycle.

mine T in CHCl_3 or MeOH, and its presence can be detected in the catalytic reaction mixture spectroscopically.²² Ligand exchange allows for alkene coordination in such a way, so the HOMO of styrene is aligned with the $N\text{-O}$ bond α^* (LUMO) of complex 1. This is then followed by fast *syn*-addition across the alkene to provide tungstenoxazolidine intermediate A. The intermediate then undergoes slow, rate-determining-step hydrolysis followed by incorporation of a second water molecule to provide intermediate B. The water molecule in A exchanges across the weakly coordinating $N\text{-Ts}$ group and the resulting intermediate B is then poised to trigger fast proton transfer to release 3 and regenerate precatalyst $\text{WO}_2\text{Dipic}(\text{H}_2\text{O})$.²³

Further analysis of the reaction kinetics revealed that hydrolysis of intermediate A is irreversible with a secondary kinetic solvent isotope effect (KSIE, $K_{\text{H}_2\text{O}}/K_{\text{D}_2\text{O}} = 0.83$, details in ESI[†]). The inverse KSIE obtained through pseudo-first-order kinetics validates a slow, rate-determining hydrolytic step. Experimental verification was obtained by further deuterium-labeling competition studies (Fig. 3). The results showed no secondary KIE when reacting a 1 : 1 mixture of **2j**/**2j2-d**₂ ($k_{\text{H}}/k_{\text{D}} = 1.02$) and **2l**/**2j1-d** ($k_{\text{H}}/k_{\text{D}} = 1.01$). These results are in agreement with a fast, highly concerted tungstenoxaziridine addition across the alkene step and a slow hydrolytic rate-determining-step. The proposed catalytic cycle is in further agreement with a Hammett correlation study employing sub-

stituted styrenes (**2j**,**k**,**n**,**p**,**s**,**u**), which shows ρ -values of -1.87 for EDG-styrenes and 0.75 for EWG-styrenes. Concave Hammett plots are often observed on highly concerted cycloadditions with developing biradical characters in their transition-states, thus confirming the proposed catalytic cycle.

Conclusions

In summary, this work managed the discovery of a stereoselective tungstenoxaziridine-mediated catalytic oxyamination of alkenes. The reaction works with high efficiency and stereoselectivity for alkenes with diverse substitution patterns and for styrenes with a variety of functional groups. The proposed catalytic cycle involves the formation of active catalyst tungstenoxaziridine 1 that then delivers the $N\text{-Ts}$ and O groups through the formation of tungstenoxazolidine intermediate A, followed by rate-determining-step hydrolysis to provide aminoalcohol 3. Further experiments to better understand and fully characterize all mechanism intermediates are ongoing and a follow up manuscript is in preparation.

Author contributions

R. M. and B. D. contributed equally for most of the experiments ($\sim 60\%$). E. L. D. (20%) and J. M. D. (10%) performed significant parts of the experiments as well. A. A. P and T. T made significant contributions at the discovery stage. D. A. R., A. M. H., J. L. S., D. A. M., S. J. F., A. N. S., and M. E. R. participated in compound characterization, and SI preparation. G. M. L. wrote the draft and supervised the research. All authors discussed the results and prepared the manuscript.

Conflicts of interest

There are no conflicts to declare.

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References

- (a) C. Wata and T. Hashimoto, Organoiodine-Catalyzed Enantioselective Intermolecular Oxyamination of Alkenes, *J. Am. Chem. Soc.*, 2021, **143**, 1745–1751; (b) H. Lei, J. H. Conway, C. C. Cook and T. Rovis, Ligand Controlled Ir-Catalyzed Regiodivergent Oxyamination of Unactivated Alkenes, *J. Am. Chem. Soc.*, 2019, **141**, 11864–11869; (c) I. Cho, C. K. Prier, Z.-J. Jia, E. K. Zhang, T. Goerbe and F. H. Arnold, Enantioselective Aminohydroxylation of

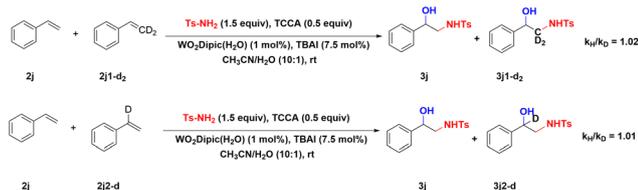


Fig. 3 Deuterium-labeling competition studies.



- Styrenyl Olefins Catalyzed by an Engineered Hemoprotein, *Angew. Chem., Int. Ed.*, 2019, **58**, 3138–3142; (d) H.-C. Shen, Y.-F. Wu, Y. Zhang, L.-F. Fan, Z.-Y. Han and L.-Z. Gong, Palladium-Catalyzed Asymmetric Aminohydroxylation of 1,3-Dienes, *Angew. Chem., Int. Ed.*, 2018, **57**, 2372–2376; (e) M. M. Heravi, T. B. Lashaki, B. Fattahi and V. Zadsirjan, Application of Asymmetric Sharpless Aminohydroxylation in Total Synthesis of Natural Products and Some Synthetic Complex Bioactive Molecules, *RSC Adv.*, 2018, **8**, 6634–6659.
- 2 (a) A. Gontala, H. Huh and S. K. Woo, Photoredox-Catalyzed Synthesis of Beta-Amino Alcohols: Hydroxymethylation of Imines with alpha-Silyl Ether as Hydroxymethyl Radical Precursor, *Org. Lett.*, 2023, **25**, 21–23; (b) K. B. Sharpless, A. O. Chong and K. Oshima, Osmium-Catalyzed Vicinal Oxyamination of Olefins by Chloramine-T, *J. Org. Chem.*, 1976, **41**, 177–179; (c) G. Li, H.-T. Chang and K. B. Sharpless, Catalytic Asymmetric Aminohydroxylation (AA) of Olefins, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 451–454; (d) T. J. Donohoe, P. D. Johnson, M. Helliwell and M. Keenan, The Regioselective Aminohydroxylation of Allylic Carbamates, *Chem. Commun.*, 2001, 2078–2079; (e) T. J. Donohoe, P. D. Johnson, A. Cowley and M. Keenan, The Tethered Aminohydroxylation (TA) of Cyclic Allylic Carbamates, *J. Am. Chem. Soc.*, 2002, **124**, 12934–12935; (f) P. H. Fuller, J.-W. Kim and S. R. Chemler, Copper Catalyzed Enantioselective Intramolecular Aminohydroxylation of Alkenes, *J. Am. Chem. Soc.*, 2008, **130**, 17638–17639.
- 3 (a) N. U. Sata and N. Fusetani, Amininols A and B, New Bicyclic Aminoalcohols from an Unidentified Tunicate of the Family Polyclinidae, *Tetrahedron Lett.*, 2000, **41**, 489–492; (b) E. Abraham, S. G. Davies, N. L. Millican, R. L. Nicholson, P. M. Roberts and A. D. Smith, Asymmetric Synthesis of Vicinal Aminoalcohols: Xestoaminol C, Sphinganine and Sphingosine, *Org. Biomol. Chem.*, 2008, **6**, 1655; (c) E. D. Calder, A. M. Zaed and A. Sutherland, Preparation of anti-Vicinal Aminoalcohols: Asymmetric Synthesis of D-Erythro-Sphinganine, (+)-Spisulosine, and D-Ribo-Phytosphingosine, *J. Org. Chem.*, 2013, **78**, 7223–7233; (d) J. N. Park, S. Y. Ko and H. Y. Koh, Synthetic Applications of the Cyclic Iminocarbonate Rearrangement: Enantioselective Synthesis of Chloramphenicol and 4_epi-Cytoxazone, *Tetrahedron Lett.*, 2000, **41**, 5553–5556.
- 4 (a) A. V. Malkov, M. A. Kabeshov, M. Bella, O. Kysilka, D. A. Malyshev, K. Pluháčková and P. Kočovský, Vicinal Aminoalcohols as Organocatalysts in Asymmetric Cross-Aldol Reaction of Ketones: Application in the Synthesis of Convolutamydine A., *Org. Lett.*, 2007, **9**, 5473–5476; (b) M. M. Heravi, V. Zadsirjan and B. Farajpour, Applications of Oxazolidinones as Chiral Auxiliaries in the Asymmetric Alkylation Reaction Applied to Total Synthesis, *RSC Adv.*, 2016, **6**, 30498–30551; (c) G. Desimoni, G. Faita and K. A. Jørgensen, C2-Symmetrical Chiral Bis(Oxazoline) Ligands in Asymmetric Catalysis, *Chem. Rev.*, 2006, **106**, 3561–3651.
- 5 (a) K. S. Williamson, D. J. Michaelis and T. P. Yoon, Advances in the Chemistry of Oxaziridines, *Chem. Rev.*, 2014, **114**, 8016–8036; (b) C.-Y. Huang and A. G. Doyle, The Chemistry of Transition Metals with Three-Membered Ring Heterocycles, *Chem. Rev.*, 2014, **114**, 8153–8198.
- 6 (a) E. M. Mumford, B. N. Hemric and S. E. Denmark, Catalytic, Enantioselective Syn-Oxyamination of Alkenes, *J. Am. Chem. Soc.*, 2021, **143**, 13408–13417; (b) G. Yin, X. Mu and G. Liu, Palladium(II)-Catalyzed Oxidative Difunctionalization of Alkenes: Bond Forming at a High-Valent Palladium Center, *Acc. Chem. Res.*, 2016, **49**, 2413–2423; (c) S. Dong, X. Liu, Y. Zhu, P. He, L. Lin and X. Feng, Organocatalytic Oxyamination of Azlactones: Kinetic Resolution of Oxaziridines and Asymmetric Synthesis of Oxazolin-4-ones, *J. Am. Chem. Soc.*, 2013, **135**, 10026–10029; (d) M. C. Paderes, J. B. Keister and S. R. Chemler, Mechanistic Analysis and Optimization of the Copper-Catalyzed Enantioselective Intramolecular Alkene Aminooxygenation, *J. Org. Chem.*, 2013, **78**, 506–515; (e) D. J. Michaelis, C. J. Shaffer and T. P. Yoon, Copper(II)-Catalyzed Aminohydroxylation of Olefins, *J. Am. Chem. Soc.*, 2007, **129**, 1866–1867.
- 7 (a) K. S. Williamson and T. P. Yoon, Iron Catalyzed Asymmetric Oxyamination of Olefins, *J. Am. Chem. Soc.*, 2012, **134**, 12370–12373; (b) D. J. Michaelis, M. A. Ischay and T. P. Yoon, Activation of N-Sulfonyl Oxaziridines Using Copper(II) Catalysis: Aminohydroxylation of Styrenes and 1,3-Dienes, *J. Am. Chem. Soc.*, 2008, **130**, 6610–6615; (c) K. M. Partridge, M. E. Anzovino and T. P. Yoon, Cycloadditions, of N-Sulfonyl Nitrones Generated by Lewis Acid Catalyzed Rearrangement of Oxaziridines, *J. Am. Chem. Soc.*, 2008, **130**, 2920–2921.
- 8 K. S. Williamson and T. P. Yoon, Iron-Catalyzed Aminohydroxylation of Olefins, *J. Am. Chem. Soc.*, 2010, **132**, 4570–4571.
- 9 (a) M. Nishimura, S. Minakata, T. Takahashi, Y. Oderaotoshi and M. Komatsu, Asymmetric N1 Unit Transfer to Olefins with a Chiral Nitridomanganese Complex: Novel Stereoselective Pathways to Aziridines and Oxazolines, *J. Org. Chem.*, 2002, **67**, 2101–2110; (b) S. Hajra, S. M. S. Akhtar and S. M. Aziz, Catalytic Asymmetric Aminolactonization of 1,2-Disubstituted Alkenoic Acid Esters, *Chem. Commun.*, 2014, **50**, 6913–6916; (c) R. Zhu and S. L. Buchwald, Copper-Catalyzed Oxytrifluoromethylation of Unactivated Alkenes, *J. Am. Chem. Soc.*, 2015, **137**, 8069–8077; (d) H.-C. Shen, Y.-F. Wu, Y. Zhang, L.-F. Fan, Z.-Y. Han and L.-Z. Gong, Palladium-Catalyzed Asymmetric Aminohydroxylation of 1,3-Dienes, *Angew. Chem., Int. Ed.*, 2018, **57**, 2372–2376; (e) S. Kim, D. Kim, S. Y. Hong and S. Chang, Tuning Orbital Symmetry of Iridium Nitrenoid Enables Catalytic Diastereo- and Enantioselective Alkene Difunctionalization, *J. Am. Chem. Soc.*, 2021, **143**, 3993–4004.
- 10 N. L. Reed, M. I. Herman, V. P. Miltchev and T. P. Yoon, Photocatalytic Oxyamination of Alkenes: Copper(II) Salts as Terminal Oxidants in Photoredox Catalysis, *Org. Lett.*, 2018, **20**, 7345–7350.



- 11 D. A. Muccigrosso, S. E. Jacobson, P. A. Apgar and F. Mares, Group 6 Metallooxaziridines: Preparation, Characterization, and Reaction with Cyclohexanone, *J. Am. Chem. Soc.*, 1978, **100**, 7063–7065.
- 12 J. A. Connor and E. A. V. Ebsworth, Peroxy Compounds of Transition Metals, *Adv. Inorg. Chem. Radiochem.*, 1964, **6**, 279–381.
- 13 A. Pinarci, N. Daniecki, T. M. TenHoeve, B. Delosso, R. Madiu, L. Mejia, S. E. Bektas and G. Moura-Letts, Synthesis of N-Tosylaziridines from Substituted Alkenes via Zirconooxaziridine Catalysis, *Chem. Commun.*, 2022, **58**, 4909–4912.
- 14 (a) L. S. Liebeskind, K. B. Sharpless, R. D. Wilson and J. A. Ibers, The First d0 Metallooxaziridines. Amination of Olefins, *J. Am. Chem. Soc.*, 1978, **100**, 7061–7063; (b) S. K. Dutta, D. B. McConville, W. J. Younfs and M. Chaudhury, Reactivity of Mo-Ot Terminal Bonds toward Substrates having Simultaneous Proton- and Electron-Donor Properties, *Inorg. Chem.*, 1997, **36**, 2517–2522.
- 15 (a) P. Das, D. W. Almond, L. N. Tumbelty, B. E. Austin and G. Moura-Letts, From Heterocycles to Carbocycles: Synthesis of Carbocyclic Nucleoside Analogues from Enals and Hydroxylamines, *Org. Lett.*, 2020, **22**, 5491; (b) G. J. Haun, A. N. Paneque, D. Almond, B. E. Austin and G. Moura-Letts, Synthesis of Chromenoisoxazolidines from Substituted Salicylic Nitrones via Visible-Light Photocatalysis, *Org. Lett.*, 2019, **21**(5), 1388; (c) D. J. Quinn, L. N. Tumbelty, E. M. Moscarello, A. N. Paneque, A. H. Zinsky, M. Russ, G. J. Haun and G. M. Moura-Letts, One-Pot Synthesis of Vinylisoxazolidines from Simple Hydroxylamines and Conjugated Carbonyls, *Tetrahedron Lett.*, 2017, **58**(50), 4682–4686; (d) P. Trieu, W. H. Filkin, A. Pinarci, E. M. Tobias, R. Madiu, B. Delosso, J. Roldan, P. Das, B. E. Austimn and G. Moura-Letts, Synthesis, of Isoxazolidines from Substituted Vinylnitrones and Conjugated Carbonyls via Visible-Light Photocatalysis, *ChemPhotoChem*, 2023, **3**, e202200277.
- 16 D. J. Michaelis, K. S. Williamson and T. P. Yoon, Oxaziridine-Mediated Enantioselective Aminohydroxylation of Styrenes Catalyzed by Copper(II) Bis(oxazoline) Complexes, *Tetrahedron*, 2009, **65**, 5118–5124.
- 17 D. A. Rogers, A. T. Bensalah, A. T. Espinosa, J. L. Hoerr, F. H. Refai, A. K. Pitzel, J. J. Alvarado and A. A. Lamar, Amplification of Trichloroisocyanuric Acid (TCCA) Reactivity for Chlorination of Arenes and Heteroarenes via Catalytic Organic Dye Activation, *Org. Lett.*, 2019, **21**, 4229–4233. Sulfonamides and TCCA (trichloroisocyanuric acid) produce Ts-chloramines with full conversion at 0 °C.
- 18 *General protocol for synthesis of aminoalcohol 3*: In a 16 mL vial packed with a magnetic stirrer, sulfonamide (0.75 mmol, 1.5 equiv.) and of TTCA (0.25 mmol, 0.5 equiv.) were mixed in CH₂Cl₂ (4 mL) at 0 °C for 30 min. The solvent was then removed under vacuum and the residue was reconstituted with CH₃CN/H₂O (4 mL, 10 : 1) and then WO₂Dipic(H₂O) (0.005 mmol, 1 mol%), TBAI (0.0375 mmol, 7.5 mol%) and alkene (0.5 mmol, 1 equiv.) were added and the resulting mixture was allowed to stir for 16 h or until disappearance of alkene by TLC. The crude was then filtered by a 1 : 1 silica gel/celite pad and the resulting crude was then purified by silica gel chromatography to provide the corresponding aminoalcohol.
- 19 P. Muller and C. Fruit, Enantioselective Catalytic Aziridination and Asymmetric Nitrene Insertions into CH Bonds, *Chem. Rev.*, 2003, **103**, 2905–2920.
- 20 The relative stereochemistry for aminoalcohols **3c–3i** was determined by NMR analysis of the coupling constants between the newly formed stereocenters.
- 21 K. Yamaguchi, H. Isober, M. Shoji, T. Kawakami and K. Miyagawa, The Nature of the Chemical Bonds of High-Valent Transition-Metal Oxo (M=O) and Peroxo (MOO) Compounds: A Historical Perspective of the Metal Oxy-Radical Character by the Classical to Quantum Computations, *Molecules*, 2023, 7119. Review on stereospecificity of biradical forming reactions.
- 22 Efforts to duplicate the reaction efficiencies under stoichiometric conditions provided lower yields, but reactions in CDCl₃ at one equiv. of **1** displayed the characteristic resonances for the Ts group in **1**.
- 23 H. Sugimoto, A. Mikami, K. Kai, P. K. Sajith, Y. Shiota, K. Yoshizawa, K. Asano, T. Suzuki and S. Itoh, Cis-1,2-Aminohydroxylation of Alkenes Involving a Catalytic Cycle of Osmium(III) and Osmium(V) Centers: Os(O)(NHTs) Active Oxidant with a Macrocyclic Tetradentate Ligand, *Inorg. Chem.*, 2015, **54**, 7073–7082. Intermediate **A** was measured by MS and 1H-NMR in a stoichiometric reaction in the absence of water.

