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Bisguanidinium-Catalyzed Epoxidation of Allylic and Homoallylic Amines Under Phase Transfer Conditions

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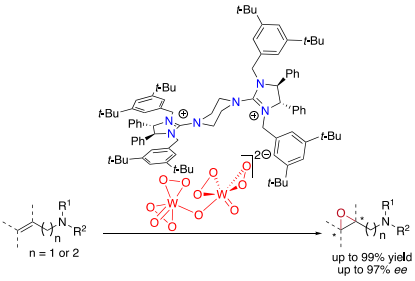
ABSTRACT: A highly enantioselective epoxidation reaction of allylic and homoallylic amines has been disclosed using an ion pair catalyst, which consists of a chiral cationic bisguanidinium [**BG**]$^{2+}$and achiral tetraperoxyditungstate anion $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$. The terminal oxidant is stoichiometric amount of aqueous hydrogen peroxide, an environmentally benign reagent. Up to 96% enantiomeric excess and 99% yields were achieved for 1,1'- disubstituted and 1,2-disubstituted allylic protected amines and 1,2-disubstituted homoallylic protected amines. The identity of the ion pair catalyst was uncovered using *X*-ray crystallography and revealed that the achiral tetraperoxyditungstate anion species $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ is nudged nicely into the central cavity of the chiral dication. The ion pair catalyst was also characterized using IR and Raman spectroscopies. The synthesis of (-)-Venlafaxine was achieved via this reported methodology to demonstrate its usefulness.



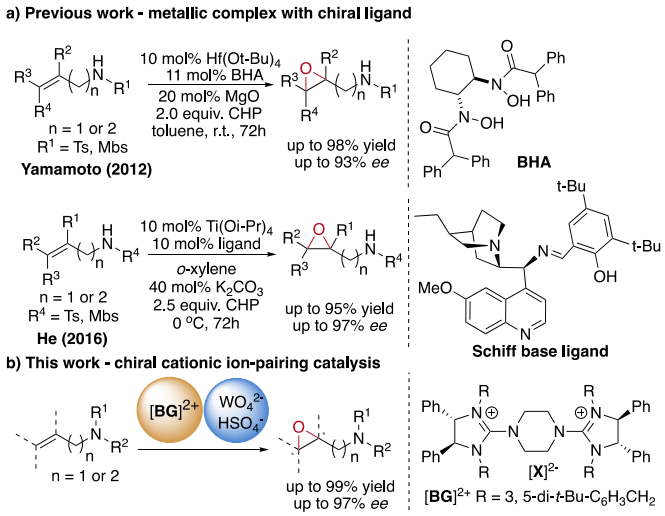
KEYWORDS: asymmetric epoxidation, bisguanidinium, ion pair catalysis, tungstate, venlafaxine

INTRODUCTION

Tungstates are known to be polymeric in aqueous solutions and formation of these polyoxotungstates is highly dependent on the pH and concentration.[1] Peroxotungstates are reported to catalyze oxidation reactions; for example, secondary amines to nitrones,[2] tertiary amines to *N*-oxides,[3] sulfides to sulfoxides,[4] alcohols to aldehydes or ketones[5] and olefins to epoxides.[6] The first catalytic use of tungstate for epoxidation of α,β-unsaturated acids using aqueous H_2O_2 was reported by Payne,[7] and the procedure was later improved by Sharpless.[8] The use of phase transfer catalyst in tungstate-catalyzed oxidations were first reported by Ishii[9-18] and Venturello.[19] It was proposed that tetra(diperoxotungsto)phosphate $[PO_4\{WO(O_2)_2\}_4]^{3-}$ was the catalytically active anion in both oxidation systems. The catalyst was isolated and characterized by Venturello[19-21] using *X*-ray crystallography. Subsequently, Noyori reported a catalytic system consisting of aqueous H_2O_2, sodium tungstate and phase transfer catalyst with $NH_2CH_2PO_3H_2$ as additive. This reaction condition was used to investigate a series of oxidation reactions,[22-26] but the role of (aminomethyl)phosphonic acid and the actual catalytic tungstate species remained unknown. Under similar conditions, Kon reported an efficient tungstate-catalyzed epoxidation of acid-sensitive terpenes and inner olefins with $PhP(O)(OH)_2$ as additive.[27]

Asymmetric epoxidation of allylic amines is one of the most versatile reactions, as the chiral amino-epoxides obtained can be further derivatized to amino alcohol, which are present in the scaffold of many drugs and natural products.[28,29] Due to the competitive *N*-oxidation of amines,[30] there are only few reports on peracid-mediated epoxidations of allylic amines.[31-35] Chemo- and diastereoselective epoxidation of allylic amines have been developed either through *N*-oxide[36-39] or protonated ammonium cation.[40] For similar reasons, there are also few reports on the use of chiral ligand mediated metal-catalyzed asymmetric epoxidation of allylic amines.[41,42] The few examples included Yamamoto's report on the use of Hf(IV)-bishydroxamic acid complex-catalyzed asymmetric epoxidation that was successful for a wide range of substrates including allylic sulfonamides, homoallylic sulfonamides, aldimine and ketimine (Scheme 1a).[41] Separately, He utilized chiral Schiff base/titanium(IV) catalyst for asymmetric epoxidation of the *N*-alkenyl sulfonamides and homoallylic sulfonamides.[42]

We recently demonstrated that ion pair catalyst consisting of a chiral cationic and an inorganic anionic salt can catalyze several reactions with high stereoselectivity.[43-47] We demonstrated that bisguanidinium permanganate can mediate enantioselective dihydroxylation and oxohydroxylation[44] of α,β-unsaturated esters. We have also developed highly efficient and highly enantioselective bisguanidinum-catalyzed sulfoxidation[4,45] of heterocyclic sulfides and alkyl aryl sulfides using aqueous hydrogen peroxide as oxidant. Diphosphatobisperoxotungstate[4] and dinuclear oxodiperoxomolybdosulfate[45] were identified to be the active anionic species respectively. Thus, we like to expand the scope of ion pair catalysis of anionic metal oxides to include asymmetric epoxidation of challenging olefin substrates (Scheme 1b). In this report, we disclose a highly enantioselective epoxidation of allylic and homoallylic amines using a new ion pair catalyst that consists of a chiral cationic bisguanidinium [**BG**]$^{2+}$. According to the *in situ* condition, the active species was isolated and identified successfully by using *X*-ray crystallography, which was shown as a symmetrical achiral tetraperoxyditungstate anion $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ (Figure 1).



Scheme 1. Recent development in asymmetric epoxidation of allylic amines.

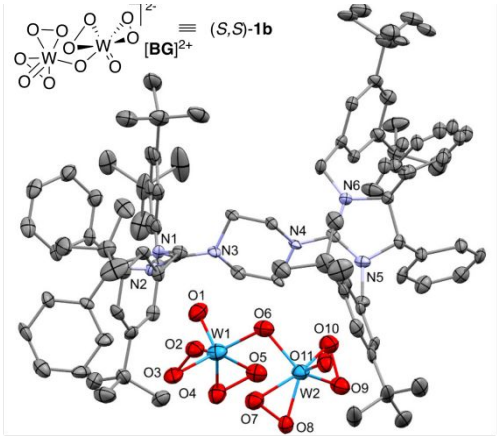


Figure 1. *X*-Ray crystallographic structure of [**BG**]$^{2+}$[$W_2O_2(\mu\text{-}O)(O_2)_4$]$^{2-}$ (*S,S*)-**1b** (ellipsoids at 50% probability).

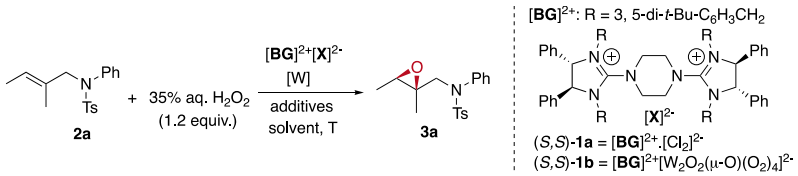
RESULTS AND DISCUSSIONS

Reaction Development. In order to explore the scope of bisguanidinium-catalyzed oxidations, we investigated epoxidation and particularly epoxidation of 1,2-allylic amines and homoallylic amines, which were both inadequately addressed in previous works.[41,42] As amines are more prone to be oxidized than olefins, protecting groups were added to the amines to circumvent the issue of chemoselectivity. During the preliminary study, we tested mono-protected substrates but the reactions were sluggish. When we investigated di-protected substrates, particularly those with a Ts protecting group, results improved (see Supporting Information 3.5).

Using this catalyst, we tested tosyl and phenyl di-protected allylic amine **2a** and found that low yield (5%) of allylic epoxide **3a** was isolated (Table 1, entry 3). We then tested conditions without any additive (entry 1), with acetic acid (entry 2) and with sodium hydrogen sulfate $NaHSO_4$ (entry 4). We found that moderate yield (52%) and good *ee* value (60%) were obtained for allylic epoxide **3a**, when $NaHSO_4$ was used as additive in sub-stoichiometric amount (0.3 equiv.) (entry 4). No side products from the oxidation of nitrogen was observed. When the reaction was carried out at 0 °C, *ee* value of allylic epoxide **3a** improved to 67%; however, the yield decreased to 16% (entry 5). The counterion effect of the tungstate was also examined (entries 5-8) and Ag_2WO_4 was found to give the best results. We propose that the efficient formation of AgCl from Ag_2WO_4 and bisguanidinium chloride allows the complete formation of the ion pair catalyst and this was important to improve the reactivity and selectivity of the reaction (entry 8). Solvent also play a vital role in determining the reactivity and stereoselectivity of this reaction. After screening a large number of solvents (see the Supporting Information 3.2 on detailed optimization table), it was revealed that 4-*tert*-butyltoluene gave the best yield (89%) and best enantioselectivity (94% *ee*) (entry 9).

Identification of ion pair (*S,S*)-1b, [BG]$^{2+}$[$W_2O_2(\mu\text{-}O)(O_2)_4$]$^{2-}$. We were able to prepare the ion pair catalyst (*S,S*)-**1b** as a white powder and $NaHSO_4$ has a crucial role in the formation of the catalyst (Figure 1). If $NaHSO_4$ was not added or replaced with NaH_2PO_4, the preparation of the ion pair catalyst will not be successful. We initially speculated that the structure of the ion pair to be an analogue of dinuclear oxodiperoxomolybdosulfate ion pair, containing a bridging sulfate between two tungsten atoms.[45] After several attempts, we were able to obtain a single crystal suitable for *X*-ray diffraction, grown from DMF at room temperature. While we did indeed obtained a bimetallic anion, there is no sulfate bridge. The achiral tetraperoxyditungstate anion[48] species $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ is found to nudge nicely into the central cavity of the chiral dication. Each tungsten is coordinated to two peroxo-group and a terminal oxo ligand and both tungsten atoms in the anion are linked by a non-linear oxygen bridge [W_1-O_6-W_2: 103.4(4)°]. Thus, the coordination number is 6 on tungsten and in a distorted octahedral arrangement of oxygen atoms. It is interesting to note that the bond length of O_6-W_2 (1.962(10) Å) is slightly longer than O_6-W_1 (1.942(11) Å). Both O_1-W_1 (1.761(10) Å) and O_{11}-W_2 (1.690(10) Å) bonds fall in a typical range for the W=O bond. Influenced by the adjacent metal, the bond lengths of O_5-W_1 (2.003(10) Å) and O_7-W_2 (1.942(10) Å) are longer than the other bond lengths between peroxo-group and tungsten (Figure 1, CCDC 1868566).

Table 1. Optimization table of Asymmetric Epoxidation of Protected 1,2-Allylic Amines.[a]



Entry	$[BG]^{2+}[X]^{2-}$	[W]	Additive	Solvent	T (°C)	yield (%)[b]	*ee* (%)[c]
1	(*S,S*)-**1a**	Na_2WO_4	-	toluene	r.t.	N.R.	N.A.
2	(*S,S*)-**1a**	Na_2WO_4	CH_3CO_2H	toluene	r.t.	<5	10
3	(*S,S*)-**1a**	Na_2WO_4	$NaH_2PO_4.H_2O$	toluene	r.t.	5	-13
4	(*S,S*)-**1a**	Na_2WO_4	$NaHSO_4$	toluene	r.t.	52[d]	60
5	(*S,S*)-**1a**	Na_2WO_4	$NaHSO_4$	toluene	0	16	67
6	(*S,S*)-**1a**	Cs_2WO_4	$NaHSO_4$	toluene	0	50	70
7	(*S,S*)-**1a**	$CaWO_4$	$NaHSO_4$	toluene	0	15	60
8	(*S,S*)-**1a**	Ag_2WO_4	$NaHSO_4$	toluene	0	38	75
9	(*S,S*)-**1a**	Ag_2WO_4	$NaHSO_4$	4-*t*-butyltoluene	0	89	94
10[e]	(*S,S*)-**1b**	-	-	4-*t*-butyltoluene	0	57	92
11[f]	(*S,S*)-**1b**	-	$NaHSO_4$	4-*t*-butyltoluene	0	>99	94

[a]Reaction conditions: **2a** (0.05 mmol), H_2O_2 (0.06 mmol, 1.20 equiv., 35%w/w), $[BG]^{2+}[X]^{2-}$ (0.0025 mmol, 2.5 mol%), $M_x(WO_4)_y$ (0.002 mmol, 2.0 mol%), additive (0.015mmol, 30.0 mol%), 500 µL solvent at 0 °C. [b]Yield of isolated product. [c]Determined with HPLC analysis using a chiral stationary phase. [d]39% of **2a** was recovered. [e]The ion pair catalyst (*S,S*)-**1b** (0.0025 mmol, 2.5 mol%) was synthesized separately then added into the reaction mixture containing the substrate (0.05 mmol) and H_2O_2 (0.06 mmol, 1.20 equiv., 35%w/w) in 500 µL solvent. [f]Using the same condition as entry 10; an additional additive, $NaHSO_4$ (0.005 mol, 10.0 mol%) was added at the beginning of the experiment.

The crystal of ion pair catalyst (*S,S*)-**1b** was added in catalytic amount (2.5 mol%) into a solution containing di-protected allylic amine **2a** and epoxide **3a** was obtained in 92% ee and moderate yield (Table 1, entry 10), demonstrating that the crystal is the active catalyst of the epoxidation. When we repeated the same experiment in the presence of $NaHSO_4$, the yield improved significantly (entry 11). While $NaHSO_4$ is not part of the active catalyst, we speculate that it is important for maintaining the structure of the active catalyst and allowing the catalyst to be re-oxidized by hydrogen peroxide.

Characterization of catalyst using infrared and Raman spectral analysis. Einstein and Penfold identified the hydrated tetraperoxyditungstate $2[K]^+.[W_2O_{11}(H_2O)_2]^{2-}$ using *X*-ray crystallography and shown that each tungstate has a pentagonal bipyramidal arrangement. Each tungstate is 7-coordinated with two peroxy groups, a bridging oxo between the two tungstate and the apical positions are occupied by an oxo group and water.[49] The structure of dehydrated tetraperoxyditungstate $[\{W(=O)(O_2)_2\}_2(\mu\text{-}O)]^{2-}$ or $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ (anion of our ion pair catalyst) was first proposed by Griffith in 1995.[3,50] Without an *X*-ray crystal structure, the catalyst was characterized through IR and Raman analysis. By changing the counterion for $[\{W(=O)(O_2)_2\}_2(\mu\text{-}O)]^{2-}$, several useful sets of data were obtained and characteristic IR and Raman spectroscopic peaks were identified.[50] In this regard, we conducted spectroscopic studies with FT-IR and FT-Raman for our ion pair catalyst, (*S,S*)-**1b** $[BG]^{2+}[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$. This is followed by density functional theory (DFT) calculation to provide qualitative simulated frequencies in a bid to understand the experimental spectra (see the Supporting Information 1.8 on DFT methods). Based on the spectra overlay for (*S,S*)-**1a** $[BG]^{2+}.2[Cl]^-$ and the ion pair catalyst (*S,S*)-**1b** $[BG]^{2+}[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ (Figure 2), the appearance of new peaks could be attributed to the tetraperoxyditungstate, $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$. Frequency analysis of the optimized electronic structure of (*S,S*)-**1b** shows that there are two $\nu_{sym}[W(O_2)]$ (found: 584 and 617 cm^{-1}; calc: 558 and 596 cm^{-1}), one $\nu_{asym}[W(O_2)]$ (found: 642 cm^{-1}; calc: 620 cm^{-1}), one $\nu(W{=}O)$ (found: 816 cm^{-1}; calc: 788 cm^{-1}) and one $\nu_{asym}(W_2O)$ (found: 976 cm^{-1}; calc: 924 cm^{-1}) stretching (Figure 2a). These vibrations were assigned to the new peaks attributed to the tungstate anion for Raman and IR. It should be noted stretching has a strong absorbance peak in IR but is very weak in Raman and vice versa. In general, the experimental and theoretical spectra are overall a good fit, with difference in wavenumber of up to 40 cm^{-1} for IR. The calculated scaled values for Raman spectra are in excellent agreement with the experimentally observed data and is consistent with previously reported tungstate vibrational wavelengths.[50]

Substrate scope of epoxidation. With the optimized condition in hand, we are keen to know how the protecting groups on amine and substitution pattern of olefin affect the reactivity and enantioselectivity of the epoxidation. We used (*S,S*)-**1b** along with $NaHSO_4$ as additive (condition of Table 1, entry 12) to explore the substrates scope of 1,2-allylic amines (Table 2), and the results showed moderate to excellent yields (71 to 99%

yield) and good to excellent enantioselectivities (68 to 97% *ee*). Compared to **3a**, increasing the alkyl chain length at 1-position to two carbons cause a drop in enantioselectivity in epoxide **3b** (89% *ee*). However, when the 1- and 2-position were linked to form cyclic allylic amines, the *ee* values increased to 92% and 97% respectively for epoxides **3c** and **3d**. Next, the effect of the aromatic protected groups on nitrogen was investigated. 1-Napthyl (abbreviated as 1-Np in Table 2) protected cyclic epoxide **3e** and para-methoxyphenyl protected cyclic epoxide **3f** were obtained in excellent enantioselectivities (90-95% *ee*). The effect of other protecting groups was also evaluated; *para*-methoxylbenzyl, 1-napthyl, *para*-methoxyphenyl, and *para*-bromophenyl protected acyclic epoxide **3g-3j** were obtained in 94-96% *ee*. From these results, it was observed that aryl-protecting group on nitrogen does not affect the enantioselectivity of the epoxides significantly. When a phenyl group was added to the terminal position of alkene on 1-position, both yields and *ee* values remained unaffected; but when the length of alkyl chain on 2-position was increased to 3-carbons, the yields are slightly decreased (**3k-3m**). When we lengthen the alkyl chain on position-1 with silyl-protected alcohol group, acyclic epoxide **3n** was obtained in good yield but slightly lower *ee* value.

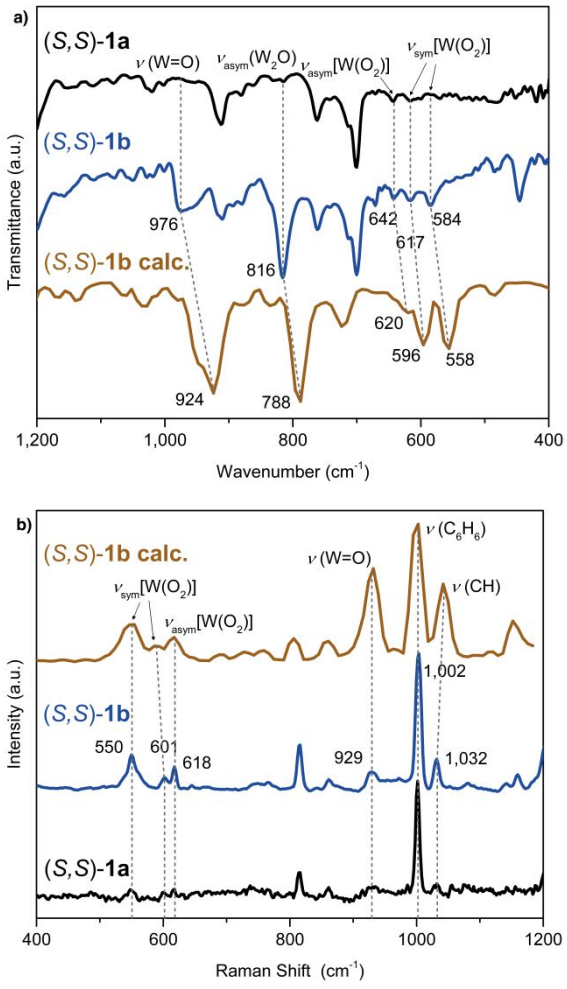
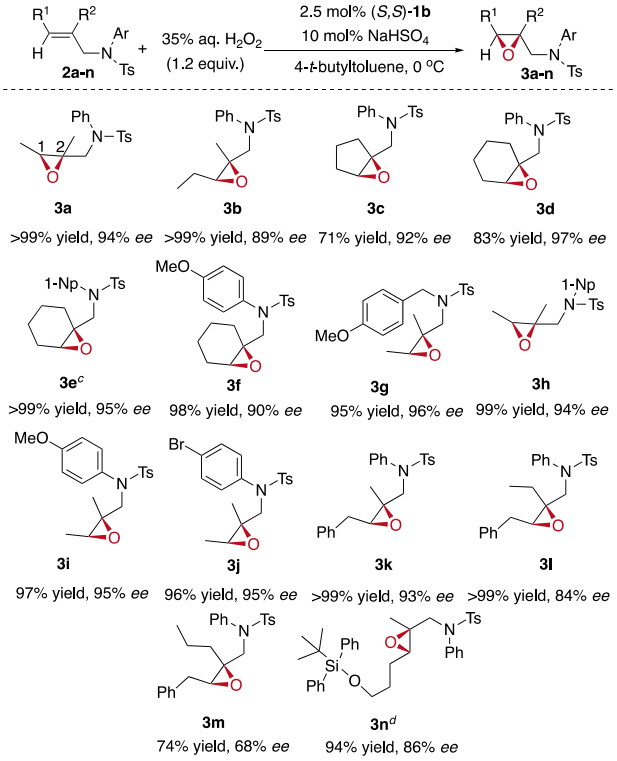


Figure 2. Experimental (in blue) and computational (in khaki) characters of (*S,S*)-**1b**, and (*S,S*)-**1a** was set as blank control (in black). (a) Infrared spectra of (*S,S*)-**1a**, (*S,S*)-**1b** and (*S,S*)-**1b** (calc.). (b) Raman spectra of (*S,S*)-**1b** (calc.), (*S,S*)-**1b** and (*S,S*)-**1a**.

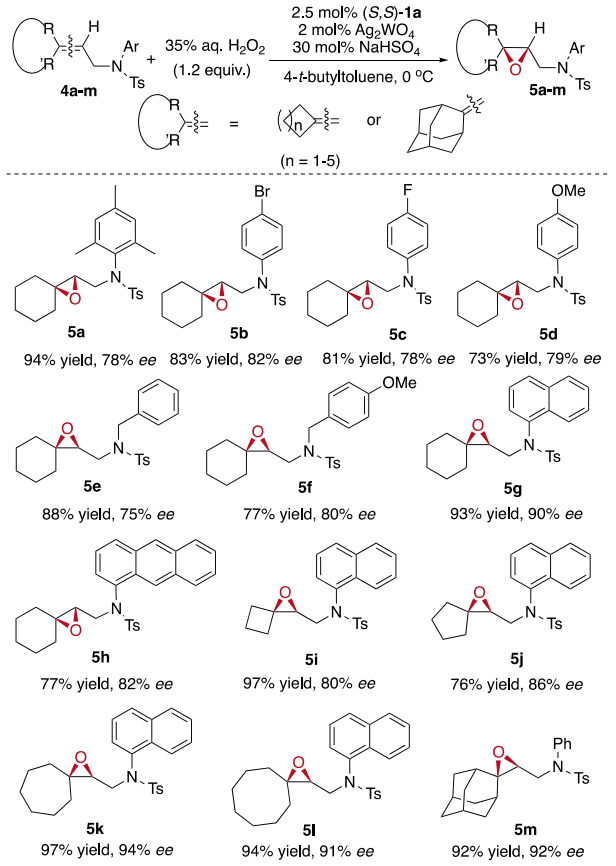
Table 2. Asymmetric Epoxidation of Protected 1,2-Allylic Amine 2[a,b]



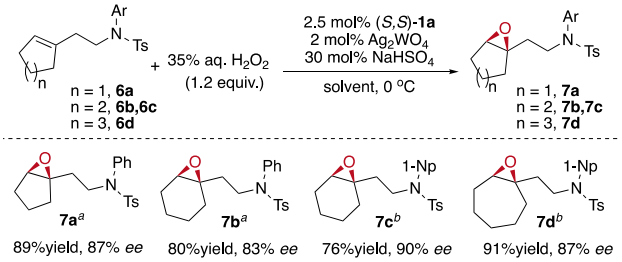
[a]Reaction conditions: **2** (0.1 mmol), H_2O_2 (0.12 mmol, 1.20 equiv, 35%w/w), (*S,S*)-**1b** (0.0025 mmol, 2.5 mol%), $NaHSO_4$ (0.01 mmol, 10.0 mol%), 1.0 mL solvent at 0 °C. [b]Yields were obtained by chromatographic purification. Enantiomeric excess values were determined using chiral HPLC [c]A single crystal of amino-epoxide **3e** (1-Np is 1-napthyl), suitable for *X*-ray structural analysis, was obtained and the absolute stereochemistry was determined to be (*S,S*) (See Figure S1 in the Supporting Information). [d]Reaction was conducted at R.T.

A series of 1,1'-allylic amines were also prepared and investigated for their suitability for this reaction (Table 3). When we use the pre-made catalyst (*S,S*)-**1b** for these experiments with the 1,1'-allylic amines, the reaction rate was slower than the reactions with 1,2-allylic amines (Table 2). After some investigation, we found that if (*S,S*)-**1b** was generated *in situ* from (*S,S*)-**1a**, the reactivity was increased (condition of Table 1, entry 9). For cyclohexyl allylic amines, similar *ee*% (78-82% *ee*) were obtained for both electron donating and withdrawing group on the aryl protecting group of amines (**5a-5d**). When the protecting group was replaced by benzyl, para-methoxylbenzyl(PMB) and 1-anthracenyl, epoxides **5e**, **5f** and **5h** were obtained with similar *ee* respectively. Excellent *ee* value of 90% was achieved when 1-napthyl group was used to protect the amine on cyclohexyl epoxide **5g**. The effect of ring size was also studied and a series of four- to eight-membered cycloalkyl-epoxides were obtained (**5i-5l**). We found that the enantioselectivity was enhanced with the increase in ring size (from 80 to 94% *ee*). With the ring size was larger than or equal to 6 (epoxides **5g, 5k, 5l**), excellent enantioselectivities (up to 94% *ee*) were obtained. 2-Adamantyl substituted epoxide **5m** was also obtained in excellent yield (92%) and *ee*% (92%) under the optimized condition.

Table 3. Asymmetric Epoxidation of Protected 1,1'-Allylic Amines 4.[a,b]



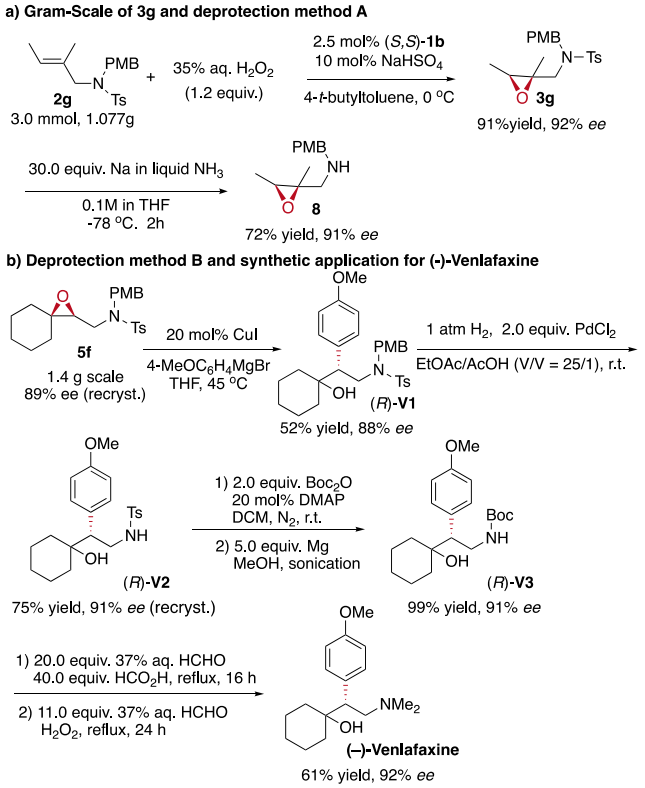
[a]Reaction conditions: **4** (0.1 mmol), H_2O_2 (0.12 mmol, 1.20 equiv, 35%w/w), (*S,S*)-**1a** (0.0025 mmol, 2.5 mol%), Ag_2WO_4 (0.002 mmol, 2.0 mol%), 1.0 mL solvent at 0 °C. [b]Yields were obtained by chromatographic purification. Enantiomeric excess values were determined by chiral HPLC.



Scheme 2. Asymmetric Epoxidation of Protected 1,2-Homoallylic Amines. [a]Reaction conditions: **6** (0.1 mmol), H_2O_2 (0.12 mmol, 1.20 equiv, 35%w/w), (*S,S*)-**1a** (0.0025 mmol, 2.5 mol%), Ag_2WO_4 (0.002 mmol, 2.0 mol%), 1.0 mL 4-*t*-butyltoluene at 0 °C. [b]Reaction conditions: **6** (0.1 mmol), H_2O_2 (0.12 mmol, 4.0 equiv, 35%w/w), (*S,S*)-**1a** (0.0025 mmol, 2.5 mol%), Ag_2WO_4 (0.002 mmol, 2.0 mol%), 2.0 mL mixed solvent (4-*t*-butyltoluene : *i*-Pr_2O = 1:1, v/v) at 0 °C (1-Np is 1-napthyl). [c]Yields were obtained by chromatographic purification. Enantiomeric excess values were determined by chiral HPLC.

Catalytic enantioselective epoxidation of homoallylic amines is highly challenging and there are only two existing examples.[41,42] Moderate to good enantioselectivities were achieved by Yamamoto using Hf(IV)-bishydroxamic acid complex[41] or chiral Schiff base/titanium(IV) as catalyst.[42] With our success with the allylic amines, we extended our investigation towards homoallylic amines with 1,2-substitution and found that epoxidation was able to proceed with excellent enantioselectivity up to 90% and excellent yield up to 91% (Scheme 2).

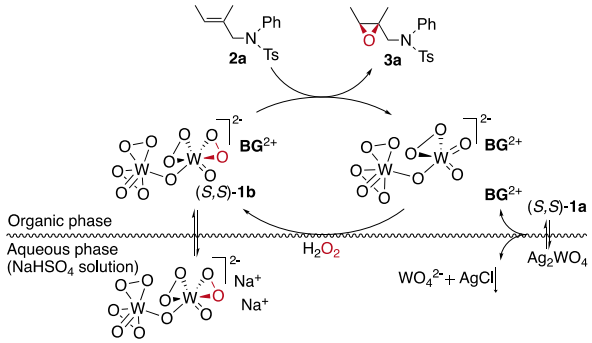
The ability of this methodology to be carried out on a larger scale was demonstrated with the formation of epoxide **3g** on a 3.0 mmol-scale with an *ee* value of 92% and yield of 91% (Scheme 3a). Deprotection of the tosyl-group was achieved using sodium in liquid ammonia, with epoxide **8** obtained without significant decrease in *ee* value. It is interesting to note that the epoxide was retained intact under the basic reaction condition. We have also developed a formal synthesis of enantio-enriched (-)-Venlafaxine from **5f** (Scheme 3b), a serotonin-norepinephrine re-uptake inhibitor used to treat antidepressant. After the ring-opening reaction of **2g** using Grignard reagent, we removed PMB using $PdCl_2/H_2$. A complete removal was achieved when the loading of $PdCl_2$ was increased to 2.0 equivalents. Direct removal of Ts using sodium in liquid ammonia resulted in Birch reduction on PMP (para-methoxyphenyl). If we perform a Boc-protection first, the removal of Ts can be achieved with magnesium. The Boc protecting group can then be smoothly removed under acidic condition (Details are available in Supporting Information 1.9).[51]



Scheme 3. Further transformations of 3 and 5.

Working model. We propose a plausible working model of the reaction in which the tungstate anion was oxidized and dimerized in the presence of $NaHSO_4$ and oxidant (Scheme 4). The solubility of Na_2WO_4 and $NaHSO_4$ were initially poor in water but after the addition of hydrogen peroxide, a clear homogeneous solution was formed. It indicated that the tetraperoxyditungstate $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ anion is highly

soluble and it is then carried into organic phase by bisguanidinium $[\mathbf{BG}]^{2+}$ forming ion pair catalyst, (S,S)-**1b**.[52-54] Substrates are oxidized by (S,S)-**1b** in organic phase and chirality is induced via non-covalent interaction.[55-57] The reduced form of tetraperoxyditungstate is regenerated by hydrogen peroxide.



Scheme 4. Proposed reaction pathway of ion pair phase transfer catalysis.

CONCLUSIONS

In summary, we have found an ion pair strategy for epoxidation of allylic amines and homoallylic amines in high enantioselectivity using bisguanidinium tetraperoxyditungstate as catalyst under phase transfer conditions. Environmentally benign aqueous hydrogen peroxide is used as the terminal oxidant in stoichiometric amount. The catalytic oxidation process provided excellent yields and enantioselectivities for 1,1'- and 1,2-disubstituted allylic protected amines. Low catalyst loading, ease of operation (under air), scalability, and tolerance to functional groups demonstrates the versatility of this method. The structure of the ion pair catalyst $[\mathbf{BG}]^{2+}[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ was elucidated by using *X*-ray crystallography and further characterized with IR and Raman spectroscopies. Furthermore, enantio-enriched (-)-Venlafaxine was produced successfully by our strategy.

ASSOCIATED CONTENT

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Notes

The authors declare no competing interests.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental details, supporting figures, and additional characterizations (PDF).

Crystallographic data for the structure (*S,S*)-**1b** and **3e** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre under deposition number CCDC 1868566 and CCDC 1868567 respectively. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/getstructures (CIF).

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ABBREVIATIONS

PMB, para-methoxybenzyl; Ts, tosyl; 1-Np, 1-napthyl; PMB, para-methoxyphenyl; Boc, *t*-butyloxycarbonyl.

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A highly enantioselective epoxidation reaction of allylic and homoallylic amines has been disclosed using an ion pair catalyst, which consists of a chiral cationic bisguanidinium [**BG**]$^{2+}$and achiral tetraperoxyditungstate anion $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$. The terminal oxidant is stoichiometric amount of aqueous hydrogen peroxide, an environmentally benign reagent. Excellent enantiomeric excess (up to 96%) and yields (up to 99%) were achieved for 1,1'- disubstituted and 1,2-disubstituted allylic protected amines and 1,2-disubstituted homoallylic protected amines. The identity of the ion pair catalyst was uncovered using *X*-ray crystallography and revealed that the achiral tetraperoxyditungstate anion species $[W_2O_2(\mu\text{-}O)(O_2)_4]^{2-}$ is nudged nicely into the central cavity of the chiral dication. The ion pair catalyst was also characterized using IR and Raman spectroscopies. The synthesis of (-)-Venlafaxine was achieved via this new methodology to demonstrate its usefulness.