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Ionic Hydrogen Bond-Assisted Catalytic Construction of Nitrogen Stereogenic Center via Formal Desymmetrization of Remote Diols

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Abstract: The control of noncarbon stereogenic centers is of profound importance owing to their enormous interest in bioactive compounds and chiral catalyst or ligand design for enantioselective synthesis. Despite various elegant approaches have been achieved for construction of S-, P-, Si- and B-stereocenters over the past decades, the catalyst-controlled strategies to govern the formation of *N*-stereogenic compounds have garnered less attention. Here, we disclose the first organocatalytic approach for efficient access to a wide range of nitrogen-stereogenic compounds through a desymmetrization approach. Intriguingly, the pro-chiral remote diols, which are previously not well addressed with enantiocontrol, are well differentiated by potent chiral carbene-bound acyl azolium intermediates. Preliminary studies shed insights on the critical importance of the ionic hydrogen bond (IHB) formed between the dimer aggregate of diols to afford the chiral N-oxide products that feature a tetrahedral nitrogen as the sole stereogenic element with good yields and excellent enantioselectivities. Notably, the chiral N-oxide products could offer an attractive strategy for chiral ligand design and discovery of potential antibacterial agrochemicals.

The stereoselective preparation of heteroatom-stereogenic frameworks is of pivotal importance owing to their broad applications in pharmaceuticals, materials and enantioselective synthesis as chiral ligands or catalysts.[1] In comparison to the extensive explorations on the construction of the carbon stereocenters,[2] the formation of stereogenic heteroatom centers has also received enormous interest, in particular on the enantioselective control over stereogenic sulfur-,[3a-c] phosphorus-,[3d-f] silicon-[3g-i] and boron-centers[3j-l] over the past decades (Figure 1A). In stark contrast, the stereochemical course of nitrogen, which is the same main group element as phosphorous, has long been overlooked in common tertiary amines due to the rapid interconversion along the nitrogen centers under general conditions,[4] posing notable challenge on the stereocontrol over the *N*-stereogenicity. In addition to placing the N atom in a rigid molecular scaffold to fix the configuration of the nitrogen centers,[5] one alternative strategy is to generate the tetrasubstituted *N*(V) compounds that can provide substantial configurational stability by preventing the fast pyramidal inversion.[6] It is noteworthy that *N*-chiral compounds are a highly important class of scaffolds that can serve as versatile chiral catalysts, reagents, and ligands in asymmetric synthesis.[5f,7] Consequently, the construction of enantiomerically enriched *N*-stereogenic frameworks has garnered considerable attention over

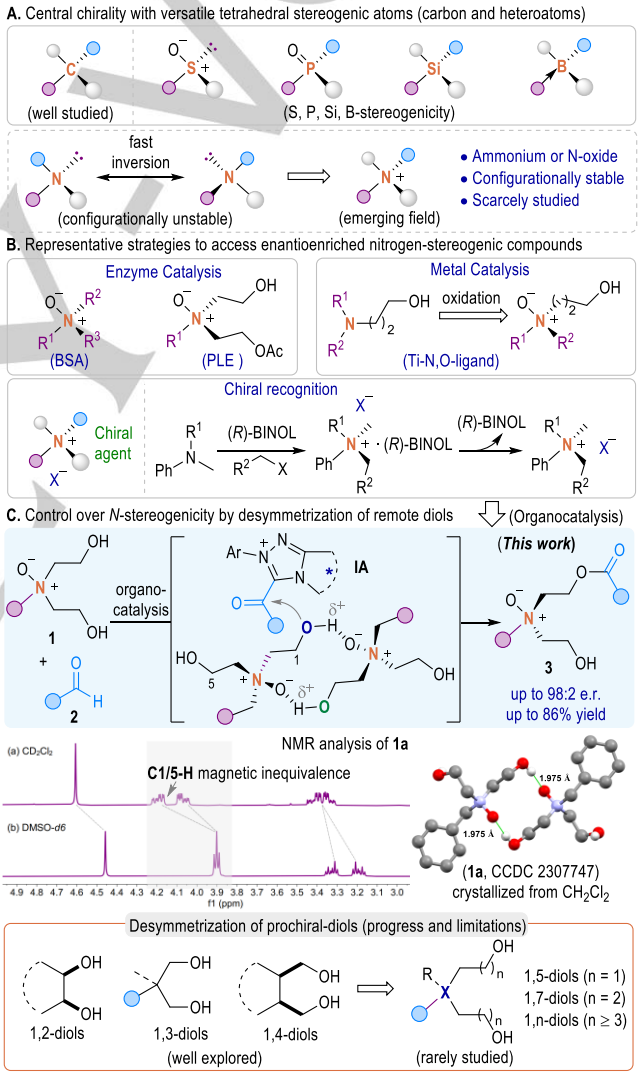

Figure 1. Enantioselective preparation of N-stereogenic frameworks. BSA = Bovine Serum Albumin; PLE = Porcine Liver Esterase.

the past decades. To date, there are still limited approaches on the asymmetric preparation of *N*-chiral functional molecules since the pioneering work on the isolation of enantioenriched *N*(V) stereogenic compounds.[8] For instance, optically pure N-oxides could be accessed by enzyme catalysis, such as Bovine Serum

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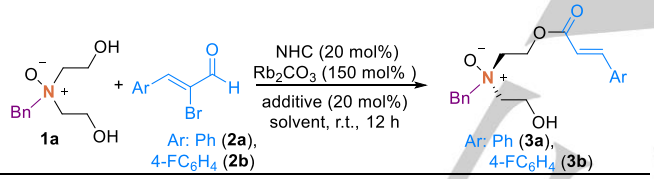
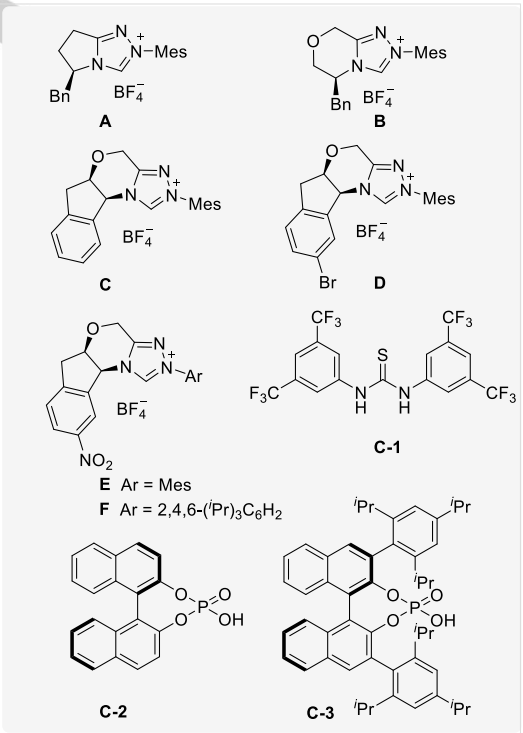
Albumin (BSA)-catalyzed oxidation[9a] or enantioselective hydrolyzation by means of Porcine Liver Esterase (PLE) enzyme catalyst (Figure 1B).[9b] Another catalytic strategy involves the stereoselective oxidation of tertiary amines under the control of a chiral bimetallic titanium catalyst, as reported by Bhadra and Yamamoto.[10] However, these methods often encounter notable challenge on the substrate scope with modest yields or enantioselectivities.[9,10] Strategy by chiral recognition of ammonium centers with enantioenriched resolving agents provides an effective protocol for enantioselective synthesis of ammonium cations.[11] For instance, very recently, Kitching et al. demonstrated an elegant operationally simple stereoselective preparation of chiral quaternary ammonium cations from alkylation of tertiary amines mediated by stoichiometric enantioenriched BINOL.[11a] Aside from these remarkable breakthroughs, a general strategy for highly enantioselective synthesis of *N*-stereogenic compounds continues to be a formidable challenge. In particular, there are few reports with organocatalytic approach to govern the stereocontrol over the stereogenic nitrogen centers with high efficiency, although organocatalysis has been established as the third pillar of asymmetric catalysis.[12]

Here, we document an N-heterocyclic carbene (NHC)[13]-catalyzed desymmetrization approach[14] for efficient access to a wide range of chiral *N*(V)-stereogenic N-oxide products (Figure 1C). The reaction of NHC catalyst with aldehyde moiety initially generates an acyl azolium intermediate **A**.[15] The prochiral diols **1** are well differentiated through esterification with acyl azolium intermediate under the control of NHC catalyst,[14,16] leading to the chiral N-oxides **3** with good yields and excellent enantioselectivities. It is noteworthy that although extensive progress has been achieved for catalyst-controlled enantioselective desymmetrization of prochiral diols, available methods mostly focused on the enantioselective transformations with 1,2-, 1,3- and 1,4-diols.[17] The catalytic desymmetrization of diol substrates with longer length, such as 1,5-, or 1,7-diols, continues to be a formidable challenge,[18] probably owing to the conformational flexibility of the linear alcohol and more remote situation to the key prostereocenter. From studies of diol **1a** with NMR and X-ray analysis (Figure 1C), a dimer aggregate of the diols through a unique ionic hydrogen bond (IHB) is postulated to account for the highly enantioselective formal desymmetrization of 1,5-diols in our study, enabling the practical preparation of highly enantioenriched *N*(V)-stereogenic compounds by means of small-molecule catalysis for the first time. Furthermore, the synthetic utility of the obtained chiral N-oxide products could offer an attractive strategy for chiral ligand design in asymmetric organic synthesis. Last, bioassay examinations reveal that the catalytically prepared products exhibited intriguing antimicrobial activity, which are valuable in the exploration of potent antibacterial agrochemicals for protection of crops.

Table 1. Optimization of the desymmetrization of 1,5-diols.[a]



Entry	NHC	Solvent	Additive	Yield (%)[b]	E.r.[c]
1	**A**	CH_2Cl_2	-	**3a**, 76	55:45
2	**B**	CH_2Cl_2	-	**3a**, 33	60:40
3	**C**	CH_2Cl_2	-	**3a**, 21	64:36
4	**D**	CH_2Cl_2	-	**3a**, 65	74:26
5	**E**	CH_2Cl_2	-	**3a**, 79	85:15
6	**E**	toluene	-	**3a**, 34	76:24
7	**E**	PhCl	-	**3a**, 36	82:18
8	**E**	CH_2Cl_2/PhCl[d]	-	**3a**, 82	87:13
9	**F**	CH_2Cl_2/PhCl[d]	-	**3a**, 83	91:9
10	**F**	CH_2Cl_2/PhCl[d]	**C-1**	**3a**, 64	70:30
11	**F**	CH_2Cl_2/PhCl[d]	**C-2**	**3a**, 83	79:21
12	**F**	CH_2Cl_2/PhCl[d]	**C-3**	**3a**, 86	94:6
13	**F**	CH_2Cl_2/PhCl[d]	(*ent*)-**C-3**	**3a**, 85	83:17
14[e]	**F**	CH_2Cl_2/PhCl[d]	**C-3**	**3b**, 85 (85)	95:5



[a] Reaction conditions (entries 1-13): **1a** (0.03 mmol, 1.0 equiv.), **2a** (0.036 mmol, 1.2 equiv.), NHC **A**-**F** (20 mol%), additive (20 mol%), Rb_2CO_3 (0.045 mmol, 1.5 equiv.), solvent (3.0 mL) at r.t. for 12 h. [b] NMR yield determined by ^{1}H NMR spectroscopy based on **1a**; isolated yield in paratheses. [c] E.r. was determined by chiral HPLC analysis. [d] CH_2Cl_2/PhCl (1:2 v/v, 3.0 mL) was used as solvent. [e] Entry 14: **2b** was used instead of **2a**; Yield and e.r. of product **3b**.

To test our design, we started our study with prochiral N-oxide diol **1a** as the model substrate. Bromoenal **2a** was employed to generate the α,β-unsaturated acyl azolium intermediate as chiral acyl transfer species under the carbene organocatalytic conditions.[19] The effect of various chiral NHC catalysts **A**-**E** was initially explored for their capability to control the *N*-stereocenter of the prochiral diol **1a**. To our delight, NHC **A** catalyst gave the desired product **3a** in 76% yield, albeit in a low 55:45 er value but with a substantial proof of concept on the desymmetrization of 1,5-diols. We next investigated other NHC

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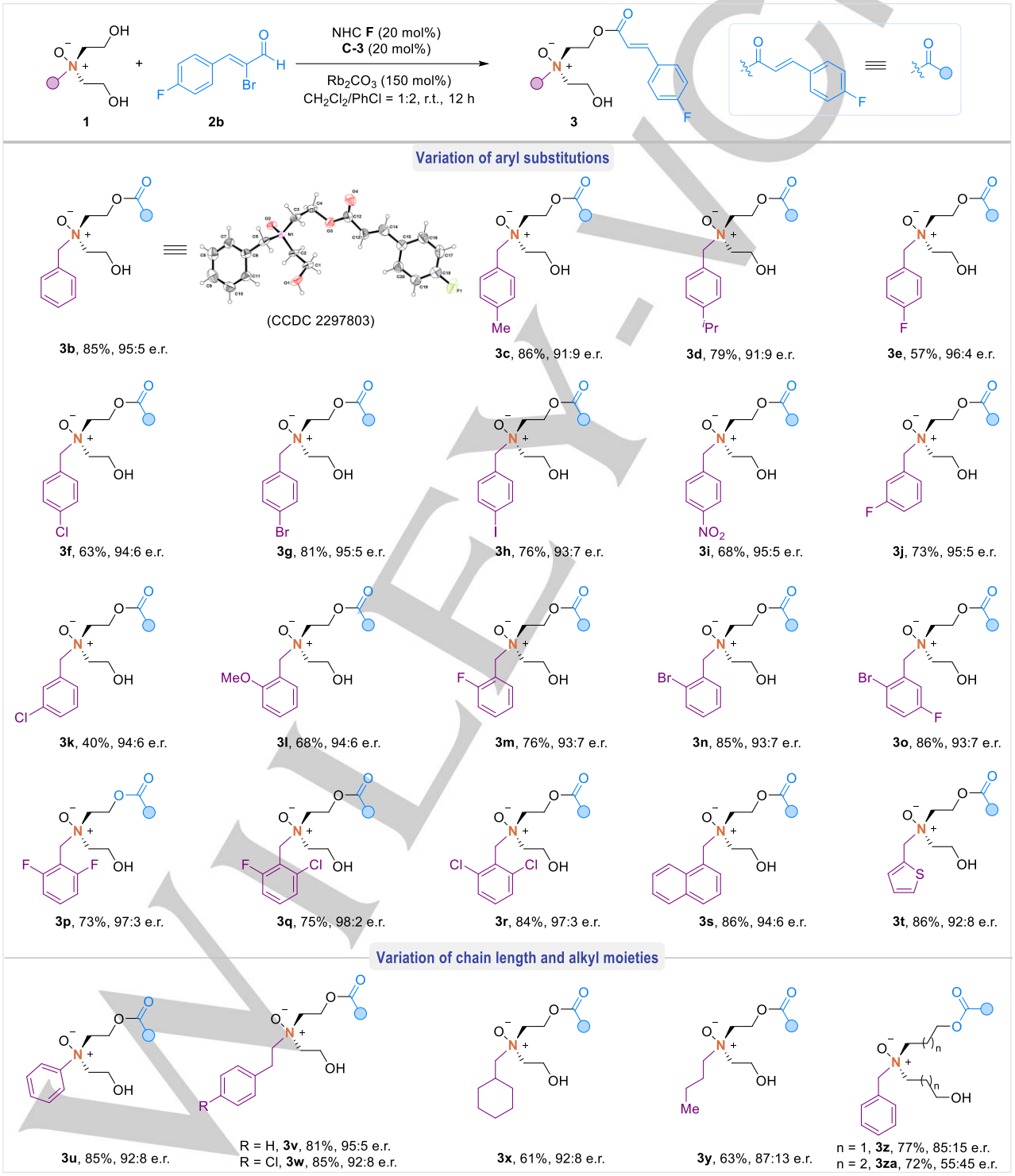
catalysts **B**-**E** and found that indanol-based triazolium carbene catalyst **E** modified with a NO_2 group on the aromatic ring was superior to give the product **3a** in 79% yield and modest enantioselectivity (85:15 er, entry 5). Further screening of the reaction medium revealed a slightly enhanced yield and selectivity (82%, 87:13 er) when the reaction was performed in a CH_2Cl_2-PhCl solvent mixture (entry 8). Moreover, the use of catalyst **F** by switching the Mes (trimethylphenyl) with Trip (triisopropylphenyl) group slightly enhanced the enantioselectivity to 91:9 er (entry 9 vs 8). Prompted by previous elegant examples with the strategy of cooperative NHC and co-catalysts,[14f,20] we then examined various typical hydrogen bond donors and Brønsted acids to tackle a more efficient catalytic system (entries 10-13). We were delighted to find that the chiral phosphoric acid **C-3** was identified as an effective co-catalyst to provide the product **3a** in 86% yield and high optical purity (94:6 er, entry 12). It's worth noting that the configuration of the chiral Brønsted acid **C-3** exerts a pivotal role to influencing the enantioselective control

Table 2. Substrate scope of the chiral N-oxides.[a]



[a] The reactions were conducted with substrate **1** (0.1 mmol, 1.0 equiv.), **2b** (0.12 mmol, 1.2 equiv.), NHC pre-catalyst **F** (20 mol%), **C-3** (20 mol%), and Rb_2CO_3 (0.15 mmol, 1.5 equiv.) in CH_2Cl_2/PhCl (1:2 v/v, 10.0 mL) under nitrogen atmosphere at r.t. for 12 h. Yields of isolated products **3**.

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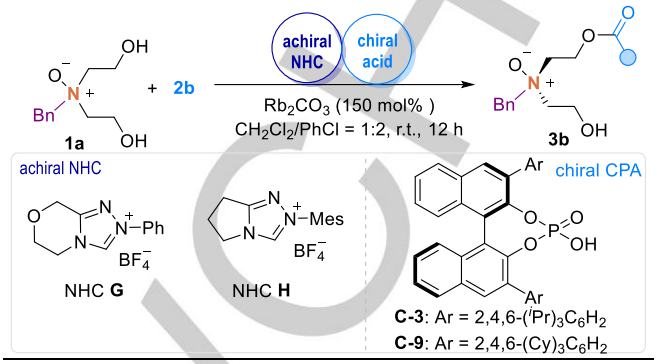
on the product **3a**, as observed by notable decreased er value when with the enantiomer of co-catalyst **C-3** (entry 13). Last, desymmetrization with *para*-F modified bromoenal **2b** smoothly led to the corresponding product **3b** in 85% isolated yield and 95:5 er (entry 14). Importantly, the absolute configuration of the product **3b** was determined to be *S* by X-ray diffraction analysis.

With the optimal catalytic conditions established, we set out to investigate the generality of the carbene-catalyzed synthesis of chiral *N*(V)-stereogenic nitrogen oxides (Table 2). N-oxide **1** possessing various substituents on the *para* sites of the benzyl ring were initially explored. For instance, methyl, as well as *i*Pr group substituted substrates were readily converted, furnishing the corresponding chiral products **3b-d** in 79-86% yields and high enantioselectivities. An array of halogen units (F, Cl, Br, I) were compatible with the catalytic conditions, yielding the products **3e-3h** in 57-81% yields with excellent selectivities of up to 96:4 er. Notably, a substrate with electron-deficient NO_2 group at the benzyl residue also readily proceeded to deliver the product **3i** in 68% yield and 95:5 er. We next examined the variations at *meta*- or *ortho*-positions of the aryl ring for their impact on the stereocontrol over the *N*(V)-stereogenicity. Substrates with F or Cl at the *meta*-position gave rise to the products **3j-3k** smoothly with good er values. Moreover, a diverse range of optical enriched N-oxides with various substituents at *ortho* sites of the aromatic ring, such as OMe, F, Br, 2-Br-5-F, were obtained under the optimal conditions. Noteworthy is that precursor with 2,6-disubstitutions underwent the desymmetrization pathway to give the chiral N-oxides **3p-3r** with improved enantioselectivities. For instance, reaction with **1q** featuring 2-F-6-Cl units gave the desired product **3q** in an excellent 98:2 er value. 2-Naphthyl and heterocyclic thienyl groups were also feasible to furnish the corresponding products **3s-3t** in modest yields and high enantioselectivities.

Next, we turned to examine the length of the N-substitutions and other alkyl substituents. Substrate with a simple N-phenyl ring was readily converted to the corresponding product **3u** in 85% yield and 92:8 er. Extension with two carbons between N atom and aryl ring afforded the products **3v** and **3w** in 81% yield, 95:5 er and 85% yield, 92:8 er, respectively. Notably, the aryl moiety could be replaced with various alkyl units (e.g. cyclohexyl and butyl), furnishing products **3x** and **3y** smoothly under the optimal conditions. Remarkably, substrate with 1,7-diol scaffold was also compatible, giving rise to the corresponding product **3z** in 77% yield and modest enantioselectivity (85:15 e.r.). However, the use of 1,9-diol **1za** gave the corresponding product **3za** in poor selectivity, presumably because of the notably distal distance of 1,9-diols to the nitrogen center.

Encouraged by the successful combination of chiral NHC and phosphoric acid for the highly enantioselective control over the stereogenic nitrogen center, we envisioned an alternative catalytic strategy through chiral phosphoric acid under basic condition as anion binding catalyst while with achiral NHC to access optical enriched N-oxides.[20b, 21i-j] Pleasingly, the reaction with 20 mol% NHC **G** and 20 mol% **C-3** catalyst led to a smooth formation of the desired product **3b** in 64% yield and modest 68:32 er (Table 3, entry 1). Attempts with other combinations of achiral NHC and CPA catalyst also gave comparable enantioselectivities (entries 2-3). Furthermore, the reaction with the enantiomeric **C-3** catalyst under the conditions as in entry 1 afforded the product **3b** in a reversed 32:68 er value (entry 4). The observed results strongly implicate the chiral phosphorate co-catalyst should be involved in the key enantio-determining bond forming step, wherein the chiral phosphate might provide additional interactions with the dimer aggregate of N-oxides that resulted in the enhanced enantiocontrol under the optimal conditions.

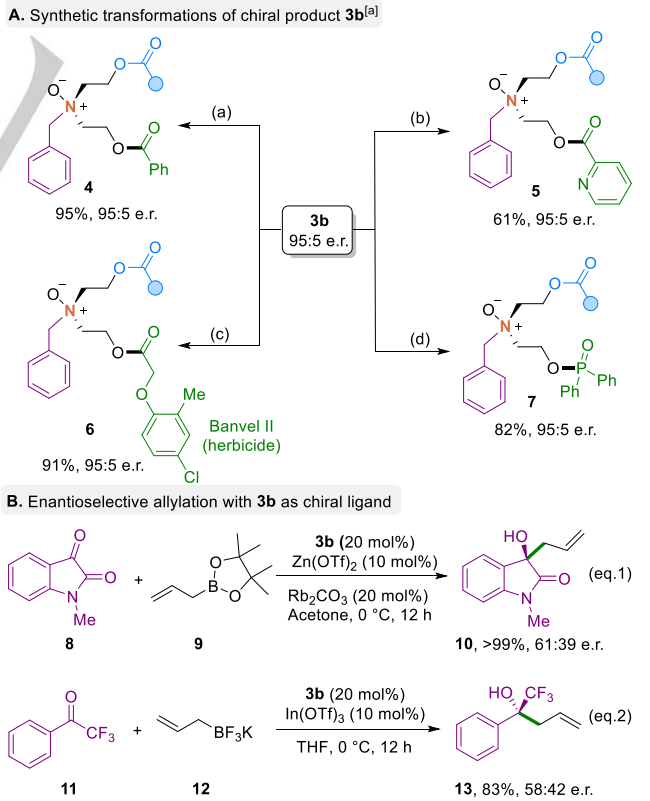
Table 3. Catalysis with chiral acid and achiral azolium.[a]



Entry	NHC	CPA	Yield (%)[b]	E.r.[c]
1	**G**	**C-3**	64	68:32
2	**H**	**C-3**	76	65:35
3	**G**	**C-9**	62	69:31
4	**G**	(*ent*)-**C-3**	53	32:68

[a] Reaction conditions: **1a** (0.03 mmol, 1.0 equiv.), **2b** (0.036 mmol, 1.2 equiv.), NHC **G** (20 mol%), CPA (20 mol%), Rb_2CO_3 (0.045 mmol, 1.5 equiv.), CH_2Cl_2/PhCl (1:2 v/v, 2.0 mL), r.t.,12 h. [b] Yield of **3b** was determined by ^1H NMR spectroscopy, based on **1a**, by using 1,3,5-trimethoxybenzene as an internal standard. [c] E.r. was determined by chiral HPLC analysis.

Scheme 1. Synthetic applications of the obtained chiral N-oxide products.



[a] Conditions: (a) benzoic anhydride, K_2CO_3, **3b**, DMAP, CH_2Cl_2, r.t., 12 h. (b) picolinic acid, **3b**, EDCI, DMAP, CH_2Cl_2, r.t., 12 h. (c) 2-(4-chloro-2-methylphenoxy) acetic acid, **3b**, DCC, DMAP, CH_2Cl_2, r.t., 3 h. (d) diphenylphosphinyl chloride, **3b**, Et_3N, CH_2Cl_2, r.t., 10 min.

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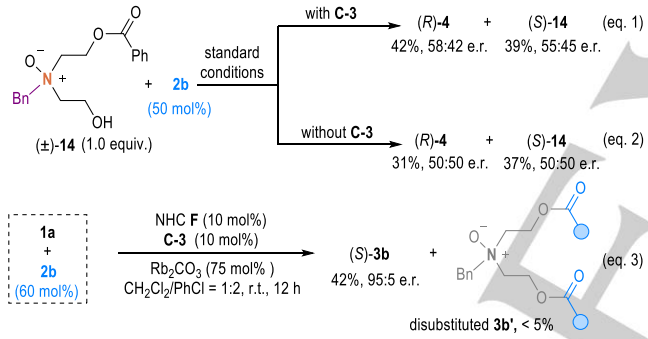
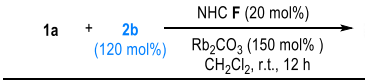
The optically enriched N-oxides prepared in our catalytic approach could readily undergo further synthetic transformations (Scheme 1A). Reaction between **3b** and benzoic acid afforded the chiral N-oxide **4** with 95% yield and 95:5 er. Other functional moieties, such as pyridine that could provide a potential coordination site for ligand design, and commercial herbicide, Banvel II with a carboxylic acid group, were also viable to couple with **3b** to furnish the corresponding products **5** and **6**, that significantly diversify the catalytically obtained N-oxide products. Additionally, phosphorilation with diphenylphosphinyl chloride afforded the product **7** in 82% yield and without erosion of er value. Next, the potential of the prepared chiral N-oxides as a chiral ligand in enantioselective transformations was explored. Using the catalytic approach by Wang/Feng et al.,[21] allylation of isatin **8** with allylborate **9** was performed with Rb_2CO_3 in acetone at 0 °C under the catalysis of $Zn(OTf)_2$ by employment of chiral N-oxide **3b** as the chiral ligand for 12 h. Delightedly, the allylation product **10** could be obtained in excellent yield with a promising enantioselectivity of 61:39 er (Scheme 1B, eq.1). Moreover, asymmetric allylation of CF_3-substituted ketone **11** with allyltrifluoroborate **12** could also be achieved with this strategy to yield the homoallylic tertiary alcohol product **13** (eq.2).[21b] These preliminary findings demonstrate a proof of concept on the development of chiral ligands for enantioselective catalysis with the prepared enantioenriched N-oxides featuring unique *N*-stereogenicity.

Scheme 2. Control experiments and proposed transition state.

(a) Control experiments



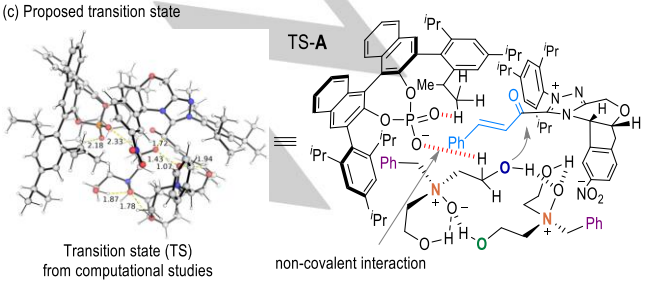
(b) Catalytic reactions with DMSO or H_2O as additives[a]



Entry	Additive	Yield **3b** (%)	E.r. **3b**	Yield **3b'** (%)
1	-	78	87:13	7
2	47 equiv. DMSO	63	70:30	9
3	117 equiv. DMSO	34	67:33	21
4	5 equiv. H_2O	85	73:27	4
5	10 equiv. H_2O	86	66:34	4

[a] See Supporting Information for detailed reaction conditions.

(c) Proposed transition state



A control reaction was performed with the mono-protected substrate (±)-**14** and 0.5 equivalent of **2b** under the standard reaction conditions. The corresponding difunctionalized product (*R*)-**4** was afforded in 42% yield and low enantioselectivity (Scheme 2a, eq. 1). Meanwhile, 39% yield of the substrate (*S*)-**14** was remained in the reaction with a 55:45 er value. However, when without the presence of co-catalyst **C-3**, either **4** or **14** was obtained as a racemate (Scheme 2a, eq. 2). These results imply a pivotal role of the diol functionality for the catalytic stereocontrol. To verify the possibility of enantioenrichment through subsequent kinetic resolution via diacylation process, control experiments (eq. 3 and eq. 4) as illustrated in Scheme 2a were conducted. Product **3b** was obtained in 42% yield and 95:5 e.r. in the presence of **2b** (0.6 equiv.). Meanwhile, reaction between (±)-**3b** and **2b** (0.6 equiv.) afforded the product **3b** in 41% yield and 55:45 er. These results indicate that efficient kinetic resolution via subsequent diacylation is less likely to occur in our reaction. Furthermore, an intriguing dimeric aggregate of substrate **1a** through two intermolecular N^+-O^-···HO ionic hydrogen bonds (IHBs) was observed from the crystallographic analysis (CCDC 2307747, Figure 1C).[22] Noteworthy is that as a special class of hydrogen bonds, IHBs are formed between ions and molecules that result in strong interactions, which could be up to a third of the strength of covalent bonds in some cases.[23a-c] ^{1}H NMR analysis of substrate **1a** in CD_2Cl_2 also revealed significant magnetic inequivalence of C1/5-H, wherein a coalescence peak for these signals were detected in highly polar DMSO or D_2O solvent (Figure 1C, also see Supporting Information for details). We were thereby prompted to carry out control experiments by addition of DMSO or H_2O as good hydrogen bond acceptor that could typically cleave a diverse set of hydrogen bonds.[23d] As illustrated in Scheme 2b, the catalytic reaction with either DMSO or H_2O led to notable decrease of er values (entries 2-5 vs entry 1).

Further density functional theory (DFT) evaluation of the dimeric diol complex stability suggests that the dimeric complex formation is exergonic, with a Gibbs energy of formation of –1.7 kcal/mol in dichloromethane solvent (Section 4.4, Supporting Information). Built upon these studies and additional NMR experiments (Section 2.5, Supporting Information), we proposed that the 1,5-diols substrate **1** most likely adopt a well-organized dimeric structure. Further DFT studies on the enantiodetermining step of the model reaction (entry 5, Table 1) suggests that the transition state (TS) leading to major pathway involves the *Re*-face attack (rather than *Si*-face attack) of the carbonyl carbon of the acyl azolium intermediate by the hydroxyl oxygen atom of the remote diol, whereas the TS leading to the minor pathway involves the *Si*-face attack rather than the *Re*-face attack (Figure S15). Overall, the TS leading to the major product is favored over the TS leading to the minor product by 1.1 kcal/mol, translating to a predicted e.r of 86:14, in agreement with observed experimental er. To discern the role of chiral phosphoric phosphoric anion of **C-3** in augmenting the enantioselectivity, a simplified study of the full system was performed (Section 4.6 of Supporting Information). Analysis of the molecular origins for the enantioselectivity suggests that the TS leading to major pathway (TS-**A**, Scheme 2c) likely benefits from more favorable non-covalent interactions than the TS leading to the minor pathway (Figure S17).

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Table 4. *In vitro* antibacterial activities of the target compounds against *Xoo* and *Xac* at 100 μg/mL.[a]

Compounds	*Xoo* inhibition rate (%)	*Xac* inhibition rate (%)
(*S*)-**3b**	41.51 ± 2.95	22.75 ± 2.86
(*S*)-**3f**	**45.43 ± 2.94**	21.04 ± 1.77
(±)-3f	43.89 ± 1.67	-
(*S*)-**3i**	34.36 ± 2.76	49.81 ± 2.65
(*S*)-**3j**	43.22 ± 1.88	20.51 ± 2.66
(*S*)-**3q**	18.96 ± 1.55	51.86 ± 2.37
(*S*)-**3x**	44.19 ± 3.33	46.85 ± 3.22
(±)-3x	44.01 ± 2.01	38.36 ± 1.77
(*S*)-**4**	11.62 ± 1.22	**52.06 ± 1.18**
(*S*)-**6**	17.09 ± 2.94	**53.03 ± 2.79**
(±)-6	-	47.39 ± 1.21
BT[b] or **TC**[c]	43.23 ± 1.31[b]	49.77 ± 1.18[c]

[a] All data were average data of three replicates. [b] Commercial bactericide, BT = Bismerthiazol was used as the positive control. [c] Commercial bactericide, TC = Thiodiazole copper was used as the positive control.

Motivated by the diverse biological activities of N-oxides,[24] we evaluated the antibacterial activity of the prepared chiral N-oxide products to search for novel leads of potential agrochemicals in crop protection. To this end, in vitro bioassay study on the inhibition activity against *Xanthomonas oryzae* pv. *oryzae* (*Xoo*) and *Xanthomonas axonopodis.* pv. *citri* (*Xac*) were performed by the turbidimeter test (Table 4).[25] Intriguingly, **3f** displayed a comparable inhibition efficiency against *Xoo,* a pathogen that could lead to bacterial leaf blight disease (BLB) of rice plant, at a concentration of 100 μg/mL with the commercially available pesticide, bismerthiazol (**BT**). Meanwhile, the obtained N-oxide derivatives showed promising inhibitive activities against *Xac*, which could cause yellow to brown canker lesion on leaves, fruits or branches of citrus trees. Compounds **4** and **6** demonstrated inhibition rates of 52.06% and 53.03%, respectively, which slightly surpassed the inhibitory efficacy of bactericide, thiodiazole copper (**TC**) as the positive control. Furthermore, the configuration of the products does not show significant impact on their bioactivity, wherein the racemic products (±)-**3x**, and (±)-**6** show slightly lower inhibition activity against *Xoo* or *Xoc* than their (*S*)-isomeric products **3x** and **6**.

In summary, we have developed an organocatalytic approach to govern the stereocontrol over the stereogenic nitrogen centers by means of NHC catalysis. A wide range of N-oxide products with chiral tetrahedral *N*(V) scaffolds were obtained with high yields and excellent enantioselectivities by a formal desymmetrization of remote diols through the potent NHC-bound acyl azolium intermediates. A unique ionic hydrogen bond (IHB) leading to the formation of a dimer aggregate of substrates was pivotal to the efficient differentiation of remote diols. Furthermore, the importance of the prepared chiral N-oxide products was demonstrated by the chiral ligand design for asymmetric allylation reaction and *in vivo* antibacterial studies for further exploration of potent antibacterial agrochemicals in crop protection. Notably, our study represents the first success on the control over nitrogen centers by means of small-molecule catalysts, and we hope it could inspire further exploration of new catalytic systems to access this long term-overlooked *N*-stereogenic frameworks for vast potential applications in asymmetric catalysis as chiral catalysts or ligands and new agrochemical discovery.

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[22] Deposition Number(s) 2307747 (for **1a**), 2297803 [for (*S*)-**3b**], and 2313383 [for (*S*)-**3g**] contain(s) the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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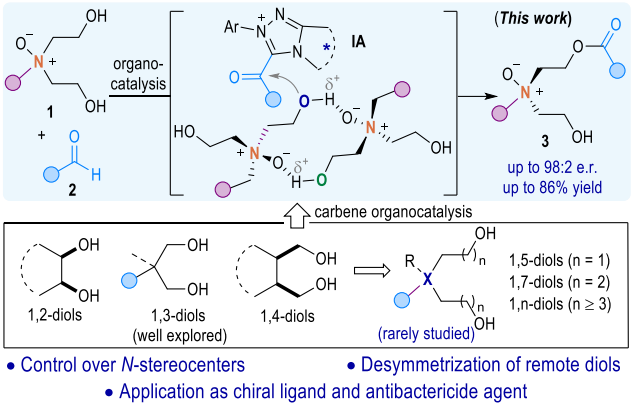

An ionic hydrogen bond-assisted carbene organocatalytic approach to afford a wide range of chiral *N*(V)-stereogenic N-oxide products is disclosed by formal desymmetrization of remote diols.