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Conformational change in a urea catalyst induced by sodium cation and its effect on enantioselectivity of a Friedel–Crafts reaction

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ABSTRACT

While developing bis-camphorsulfonyl urea as a hydrogen-bonding catalysts, we discovered that the native conformation of the catalyst is unsuitable for inducing enantioselectivity. By complexing the catalyst with weakly Lewis acidic sodium cations, we were able to change the conformation of the catalyst and attain a significant improvement in the selectivity. We provide structural information from X-ray crystallography to show that the uncomplexed catalyst is indeed in an unfavorable conformation. Infrared and Raman spectroscopic studies show that sodium binds the catalyst through the carbonyl and sulfonyl groups. Simulated IR and Raman spectra match well with the experimentally recorded spectra, thereby corroborating the proposed conformational change. This result shows that weak Lewis acids can be used to tune the conformation of hydrogen-bonding catalysts and enhance the selectivity of reaction catalyzed by these systems.

1. Introduction

The conformation of a hydrogen-bonding catalyst is an important determinant of the selectivity in the reactions catalyzed by them.[1–6] Modulating the conformational equilibrium will have a significant impact on the outcome of reactions catalyzed by these systems. This is usually accomplished by structural modifications to the catalyst that will engender the required conformational biasing.[7–11] An alternative to this approach is the use of an additive that will enforce conformational rigidity. During the development of a bis-sulfonyl urea catalyst, we discovered that the weakly Lewis acidic sodium cation can bind to Lewis basic sites on the urea. This results in a change in the conformation of the catalyst and an enhancement in the selectivity of the reactions catalyzed by this system. Conformational change upon sodium binding is supported by structural studies and theoretical calculations. In nature, a similar approach is seen in zinc finger proteins, wherein a zinc cation is used to stabilize protein conformation.[12] Metal coordination that provides rigid scaffolding to ligands is also seen in the case of ferrocenyl phosphine ligands.[13–15]

Hydrogen-bond-promoted catalysis has been developed over the last 15 years by several research groups.[16–22] Studies from the Sigman group[23,24] and the Luo and Cheng groups[25] have shown that the acidity of the hydrogen bond donor can be directly correlated to reactivity as well as selectivity. More recently, work from the Schreiner group has shown that the acidity of the donor can be correlated to the turnover frequency.[26] Similarly, the Ellman group has developed acidic sulfinamide based catalysts for hydrogen-bond-promoted reactions.[27–31] Inspired by these examples, we decided to explore the use of a C_2 symmetric sulfonyl urea (**3**, Scheme 1) as a potential catalyst for hydrogen-bond-promoted reactions. The pK_as of *N*-acyl sulfonamides have been reported to be around two.[32–34] Therefore, we expected the sulfonyl urea **3** to be a selective hydrogen-bonding catalyst. In order to realize the potential of **3**, we had to first overcome the inherent conformational bias that prevented good selectivity. We achieved this by using a weakly Lewis acidic sodium cation. Structural studies based on IR and Raman spectroscopy reveal that the sodium cation binds to the oxygen atoms of the carbonyl group and sulfonyl group. The IR and Raman spectra were simulated from the proposed structure and this correlated with the experimentally obtained spectra. Lewis acid coordination to achiral ureas has been explored previously by the Smith and Mattson groups. This lead to enhanced acidity and turnover frequency.[35–41] To the best of our knowledge, our work is the first example where a Lewis acid has been used to enhance the enantioselectivity of a chiral urea catalyzed reaction. Controlling the conformation of catalysts in this manner should be a broadly applicable strategy.

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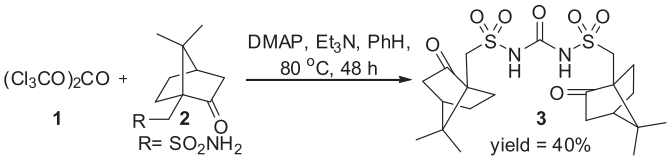
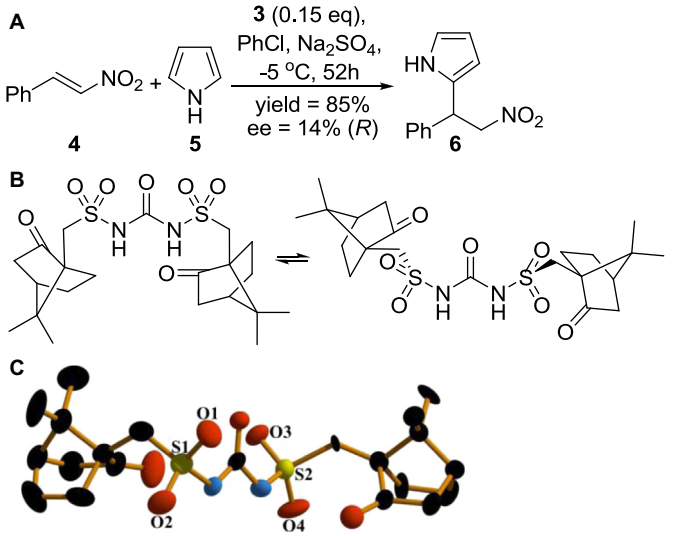


Scheme 1. Synthesis of bis-camphorsulfonyl urea.

2. Results and discussion

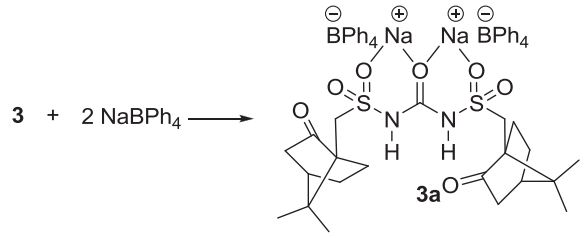
Our studies began with the synthesis of bis-camphorsulfonyl urea (**3**) in a single step from camphor sulfonamide and triphosgene (Scheme 1). The urea **3** was isolated after a simple extractive work up followed by recrystallization and the reactions could be performed on a 1 g scale. To evaluate our catalyst, we decided to pursue the previously described enantioselective Friedel–Crafts reaction of nitrostyrene with pyrrole.[42,43] Under the conditions described in Scheme 2 (panel A), we obtained the product with low selectivity. A control reaction in the absence of catalyst showed very little background reaction. We hypothesized that the lack of selectivity may be due to an unfavorable conformation in which the chiral elements in the catalyst are away from the incipient chiral center (Scheme 2, panel B). The oxygens on the carbonyl and sulfonyl groups bear partial negative charges and the dipole–dipole repulsion between these groups is expected to push them away from each other. This would put the chiral camphor groups away from the hydrogen bond donors. When nitrostyrene binds the urea **3** in this conformation, the camphor groups will be away from the incipient chiral center. Therefore, the camphor groups are not able to induce bias in the approach of pyrrole toward either face of the nitrostyrene, thereby resulting in poor selectivity. To verify this, we grew single crystals of the catalyst and determined the solid state structure using X-ray diffraction (Scheme 2, panel C).



Scheme 2. (A) Initial result for Friedel–Crafts reaction catalyzed by **3**. (B) Proposed conformational equilibrium. (C) Crystal structure of urea **3**.

The crystal structure revealed that one of the sulfonyl oxygens (O2 and O4) in each of the sulfonyl groups is in an anti-periplanar orientation (177.5° and 174.3°) with respect to the urea carbonyl group. The other oxygen (O1 and O3) is in a *gauche*-like orientation in each case (49.2° and 47.2°, respectively). Notably, each of the camphor groups is also in a *gauche*-like conformation with respect to the urea carbonyl (56.3° and 59.3°). This suggests that when nitrostyrene binds the urea **3**, the bias-inducing camphor groups will be away from the incipient chiral center, thereby supporting our hypothesis.

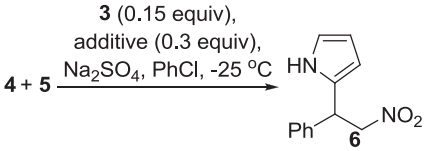
Conformational locking due to dipole–dipole repulsion has been invoked as the driving force for face selection in the Evans aldol reaction.[44] Alternatively, the dipoles can be brought into a *syn*-periplanar orientation by coordination to the Lewis acidic center that holds the enolate and the aldehyde as seen in the Crimmins aldol reaction.[45–47] As a result, there is a reversal of face selection. Inspired by this precedent, we hypothesized that a weak Lewis acid like Na^+ would be able to coordinate the oxygen atoms on the carbonyl and sulfonyl via a six-membered chelate (Scheme 3). The formation of a chelate should in turn push the camphor groups toward the hydrogen bond donors. Binding of nitrostyrene in this conformation would ensure that the bias-inducing camphor groups are closer to the incipient chiral center.



Scheme 3. Proposed change in conformation due to sodium binding.

To test this hypothesis we added 2 equiv of sodium tetraphenylborate with respect to urea **3** to the Friedel–Crafts reaction. A reversal in face selection was observed along with a slight improvement in the enantioselectivity (Table 1, entry 1). Encouraged by this initial result, we screened tetraphenylborate salts of other alkali metals along with magnesium bromide etherate (Table 1). However, the reactions with other alkali metal ions were very slow and the selectivity did not improve. In the case of magnesium bromide the reactions were completed immediately with little selectivity. Control reactions showed that magnesium bromide etherate can catalyze the rapid reaction of nitrostyrene and pyrrole. On the other hand, there was very little background reaction in the presence of $NaBPh_4$. This implied that only weak Lewis acids should be used for the successful implementation of our idea, as strong Lewis acids may catalyze rapid background reaction. Addition of 1 equiv of $NaBPh_4$ (with respect to urea **3**), did not lead to substantial improvements in the selectivity.[48] This shows that 2 equiv of sodium cation are required.

Table 1
Screen of metal salts

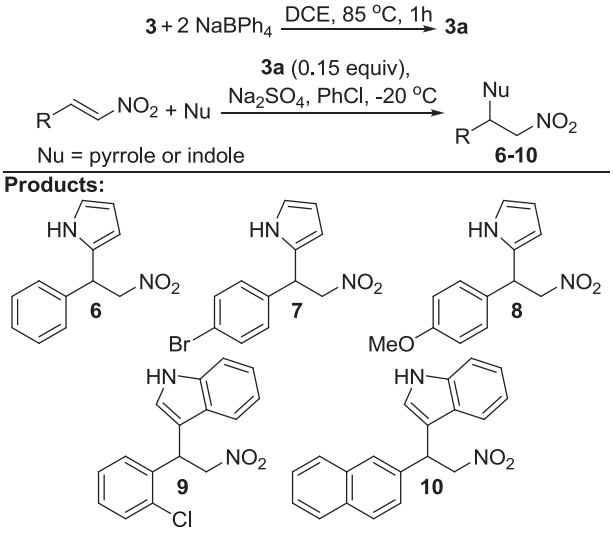


Entry	Additive	Time (*h*)	% Yield	% ee
1	$NaBPh_4$	36	69	16 (*S*)
2	$LiBPh_4$	72	60	3 (*S*)
3	$KBPh_4$	90	77	15 (*R*)
4	$RbBPh_4$	102	76	15 (*R*)
5	$CsBPh_4$	102	66	15 (*R*)
6	$MgBr_2 \cdot Et_2O$	0.5	62	2 (*R*)

Based on these results, we decided to further optimize the reaction that used 2 equiv of $NaBPh_4$ (with respect to urea **3**) as the additive. $NaBPh_4$ is poorly soluble in chlorobenzene. We

hypothesized that this might lead to incomplete complexation and optimized the conditions for dissolution and complexation of $NaBPh_4$. Under our optimized conditions, we were able to obtain the product **6** in 64% ee (*S*-isomer). In the absence of $NaBPh_4$ under otherwise identical conditions, we obtained 15% ee (*R*-isomer) from our reaction. This clearly showed that the addition of $NaBPh_4$ had a beneficial effect on the selectivity of the reaction. To show that this is indeed generally the case for this catalyst system, we evaluated the reaction of other nitrostyrenes with pyrrole and indole[49–54] as the nucleophiles (Table 2) and obtained products **7**–**10**. In each of the cases, there was a clear enhancement of selectivity in the presence of $NaBPh_4$ along with a reversal of face selection.

Table 2
Comparison of reactions with and without $NaBPh_4$

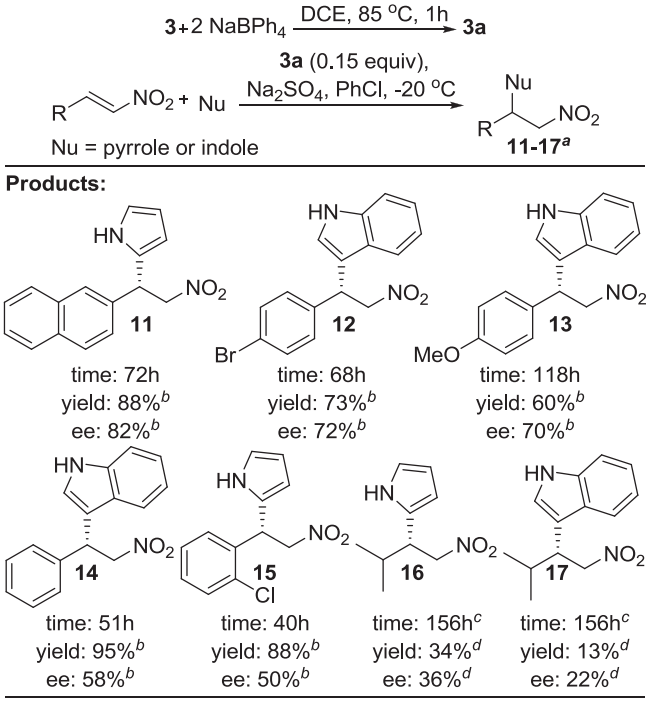


Product	Time[a] *h*	% Yield[a,b]	% ee without $NaBPh_4$[c]	% ee with $NaBPh_4$[b,c]
6	36 (60)	89 (87)	15 (*R*)	64 (*S*)
7	78 (96)	86 (78)	10 (*R*)	72 (*S*)
8	65 (138)	89 (78)	11 (*R*)	56 (*S*)
9	25 (55)	93 (97)	7 (*S*)	66 (*R*)
10	58 (114)	60 (93)	4 (*S*)	66 (*R*)

Conditions for reactions with and without $NaBPh_4$: pyrrole or indole (3 equiv), Na_2SO_4 (2.5 equiv), nitroalkene (0.56 M). Enantiomeric excess (ee) was measured by HPLC using a chiral stationary phase. See Supplementary data for details.
[a] Values in the parentheses corresponds to results without $NaBPh_4$.
[b] Average of three runs.
[c] Configuration of major isomer was assigned by comparing values from literature.[55,56]

We evaluated the substrate scope of this reaction with various nitroalkenes (Table 3). Aryl groups with electron donating and electron withdrawing moieties worked well in this reaction. However, nitroalkenes with alkyl substituents performed poorly in the reaction (Table 3, **16** and **17**). Next, we sought to clarify the role of $NaBPh_4$ in enhancing the selectivity of the test reaction. The sodium complex turned out to be poorly soluble and attempts at obtaining single crystals suitable for X-ray diffraction studies failed. The poor solubility also hindered our efforts to obtain NMR spectra of the complex. Therefore, we sought to study the structure of the sodium complex using IR and Raman spectroscopy. Vibrational spectroscopy is a highly sensitive tool for studying complexation. Subtle changes in the structure, coordination, bond lengths, and bond angles can cause small to large changes in vibrational spectra (IR and Raman spectra). These techniques are used commonly for assessing such changes. A shift of few wavenumbers in the

Table 3
Scope of Friedel–Crafts reaction



Conditions: Pyrrole or indole (3 equiv), Na_2SO_4 (2.5 equiv), nitroalkene (0.56 M). Enantiomeric excess (ee) was measured by HPLC using a chiral stationary phase. See Supplementary data for details. [a]Configuration of major isomer was assigned by comparing values from literature.[55,56] [b]Average of three runs. [c]Reaction did not go to completion. [d]Average of two runs.

frequency is detectable and is a significant indicator for structural changes. Binding of sodium cations with the Lewis basic sites on the catalyst is expected to change the stretching frequency of the bonds associated with the Lewis basic atoms. The infrared and Raman spectrum of urea **3** is shown in Fig. 1 (panel A and panel B). A detailed assignment of the IR and Raman spectra is included in the Supplementary data. Here, we will focus our discussion on the carbonyl and sulfonyl group frequencies for elucidation of the conformation. Based on our density functional theory (DFT) calculations[57] and the previously reported spectrum of a similar compound,[58] we assigned the mode at 1747 cm^{-1} to the keto carbonyl of camphor and the shoulder at 1706 cm^{-1} to the urea carbonyl. The calculated values of these modes appear at 1760 and 1712 cm^{-1}, respectively. We then recorded the IR spectrum of the urea–$NaBPh_4$ complex (**3a**). In this spectrum the shoulder at 1706 cm^{-1} disappeared. Instead, a peak around 1620 cm^{-1} was observed along with two shoulders. Curve fitting analysis with Lorentzian functions reveals the appearance of a peak at 1602 cm^{-1}, which we assigned to the urea carbonyl complexed with sodium. This overlaps with the O–H bending region of water. To confirm our assignment, we used DFT to calculate the IR spectrum of our putative complex.[57] Here the sodium bound carbonyl mode appears at 1610 cm^{-1}, thereby confirming our assignment of the experimental spectrum. Thus the shift of around 100 cm^{-1}, observed in IR spectrum, is well reproduced in the theoretical calculations, which predicted a shift of 102 cm^{-1} (Fig. 1, panel C).[57] In the Raman spectra of urea **3** (Fig. 1, panel B), the stretching frequencies of the urea carbonyl and the keto carbonyl are seen at 1708 cm^{-1} and 1755 cm^{-1}, respectively. In the complex **3a**, the 1708 cm^{-1} mode disappears. The expected mode around 1600 cm^{-1} is masked by the

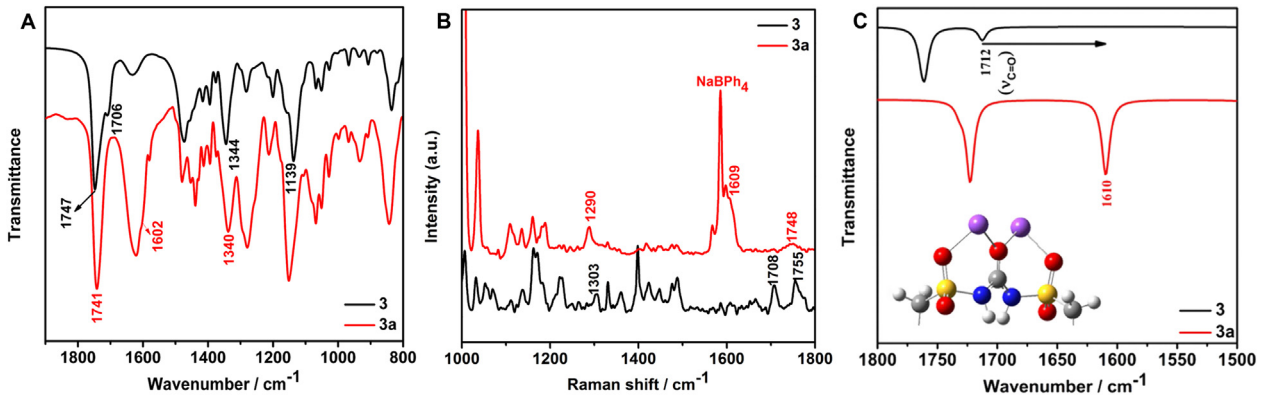


Fig. 1. (A) Infrared spectra of **3** and **3a**. (B) Raman spectra of **3** and **3a**. (C) Calculated infrared spectra for **3** and **3a** in the C=O stretching region. Inset shows a part of the optimized structure of **3a**. Color representation: white—hydrogen, gray—carbon, blue—nitrogen, red—oxygen, yellow—sulfur, and violet—sodium.

phenyl ring modes of $NaBPh_4$. This clearly showed that the urea carbonyl is bound to the sodium cation. The sulfonyl stretching modes in the IR spectrum of urea **3** are seen at 1344 cm^{-1} (antisymmetric) and 1139 cm^{-1} (symmetric).[59,60] Upon complexation, we observed a sulfonyl mode at 1340 cm^{-1}, which we assigned to the sodium bound sulfonyl oxygen. Since the symmetric stretching mode of sulfonyl group in the complex overlaps with tetraphenylborate modes, we were unable to make a clear assignment. In our DFT calculation, the sulfonyl modes in urea **3** appear at 1303 cm^{-1} and 1079 cm^{-1}, which shifts upon complexation to 1294 and 1069 cm^{-1}, respectively. Correlation between experimental and theoretical spectra supports the coordination of sodium to the sulfonyl oxygen. In the Raman spectrum, the sulfonyl antisymmetric stretch of urea **3** is seen at 1303 cm^{-1}, which shifts to 1290 cm^{-1} upon complexation, whereas calculations show a shift of 5 cm^{-1}. Disagreement between the theory and experimental value could most probably be due to the fact that in the calculation we considered a single molecule in gas phase. This ignores the intermolecular interactions present in real system. The calculations could be possibly improved by the inclusion of the counter anions (tetraphenylborate), whose relative position with the catalyst is not known experimentally. As a control, we have simulated the infrared spectra for other possible conformations using a lower level theory (B3LYP/6-31G(d), see Supplementary data, Table S3). The simulated and experimental spectra did not match well for these conformations. We have also simulated the structure of a single sodium complexed to urea (B3LYP/6-31G(d,p), Supplementary data, Table S4). Again a poor correlation was observed with experimentally recorded spectrum. Overall the best match was seen between the experimental and simulated spectra for the conformation shown in Fig. 1 (panel C) wherein two sodium cations are bound to the urea carbonyl.[61–64] This substantiates our hypothesis that the sodium cation forms a complex through coordination of the oxygens on the urea carbonyl and sulfonyl groups. As a result, the camphor groups should be closer to the hydrogen bond donors as shown in Scheme 3. When nitroalkenes bind the catalyst in this conformation, the incipient stereocenter is closer to the bias-inducing camphorsulfonyl groups, thereby resulting in greater enantioselection.

3. Conclusions

In conclusion, we have synthesized a novel bis-sulfonyl urea as a catalyst for enantioselective reactions. The simplicity of the synthesis should allow the wide application of this urea for a variety of hydrogen-bond-promoted reactions. Currently, we are examining the use of this catalyst for other reactions. The conformational flexibility of hydrogen-bonding catalysts leads to smaller free energy differences between diastereomeric transition states, which results in lower enantioselectivity. Reducing the conformational mobility is therefore a key principle in the design of novel hydrogen-bonding catalysts. This is often accomplished by increasing the structural complexity of the catalyst. As shown here, conformational freedom can also be restricted by using weak Lewis acids to bind Lewis basic sites on the catalyst. Based on our initial study of a Friedel–Crafts reaction, we conjectured that the urea was locked in an unfavorable conformation. By complexing with $NaBPh_4$, we were able to enhance the enantioselectivity of the reaction. Infrared and Raman studies showed that the urea binds the sodium cation through the carbonyl and sulfonyl oxygens. Calculation of the expected IR and Raman spectra from our optimized structure yielded spectra that closely match with the experimentally obtained one. This further supports the idea that complexation with sodium locks the catalyst in a more favorable conformation for enantioselection. The generality of this approach is currently under evaluation.

4. Experimental section

4.1. General

All glassware was dried overnight in an oven prior to use. Reactions were carried out under argon atmosphere using standard Schlenk techniques. Reactions were monitored by thin layer chromatography (TLC) using TLC silica gel plates. Flash chromatography was performed using silica gel 230–400 mesh. Unless otherwise noted all reagents were used as received from commercial suppliers without further purification. Anhydrous dichloroethane and chlorobenzene were purchased and used directly for reactions. DMAP was recrystallized from toluene. Triethylamine and benzene were distilled from CaH_2 prior to use. Analytical grade Na_2SO_4 was crushed and dried at 600 °C for 6–7 h under inert atmosphere and used in the reactions. Analytical grade cyclohexane, dichloromethane, and toluene were used for recrystallization. Grease free solvents were obtained by distillation and used for chromatography. Infrared spectra were recorded using an FTIR spectrometer. Sample pellets for IR spectroscopic studies were prepared by mixing a few milligrams of compound with dry KBr. ^1H and ^{13}C NMRs were recorded on a 400 MHz Fourier transform NMR spectrometer. Chemical shifts are reported in parts per million (ppm) with respect to the residual undeuterated solvent in $CDCl_3$ (δ=7.27 ppm) at room temperature. ^{13}C NMRs were recorded at 100 MHz using proton decoupling. Chemical shifts are reported with respect to the deuterated solvent in $CDCl_3$ (δ=77.16 ppm) or $(CD_3)_2CO$ (δ=29.84 ppm) at room temperature. HRMS was recorded using Q-TOF spectrometer. Melting points were recorded using an electrothermal capillary melting point apparatus and are uncorrected. Camphor sulfonamide[65] and nitro olefins[66] were

synthesized using previously reported procedures. Compounds **6**–**8**,[67] **9**–**10**,[56] **11**,[67] **12**–**14**,[68] **15**–**16**,[67] and **17**[68] have been reported previously in the literature. Crystallographic data for the structure of **3** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 943949).

4.2. Synthesis of urea catalyst (3)

Camphor sulfonamide (2.35 g, 10.2 mmol) and DMAP (1.24 g, 10.2 mmol) were weighed into a 100 mL 2-neck flask and the flask was flushed with argon. To this, benzene (25 mL) and triethylamine (1.42 mL, 10.2 mmol) were added. In a separate flask, triphosgene (502 mg, 1.7 mmol, equivalent to 5.1 mmol of phosgene) was dissolved in benzene (25 mL) under argon and cannulated dropwise in to the flask containing camphor sulfonamide at 0 °C. After completion of addition, the reaction mixture was slowly warmed to 40 °C and stirred for 2 h (reaction mixture was a milky white suspension). The temperature was then raised to 80 °C and the contents were stirred for 48 h (precipitation of a white solid was observed as the reaction progressed). It was then cooled to 0 °C and quenched by dropwise addition of 4 M HCl in dioxane (7 mL) followed by stirring for 12 h. The contents were then diluted with ethyl acetate (~75 mL) and washed with 1 M HCl (3×75 mL). The organic layer was extracted with saturated $NaHCO_3$ until all of the catalyst was extracted in to the aqueous layer (checked by TLC). The aqueous layer was separated and washed with ethyl acetate. After acidification with 1 M HCl, it was extracted with dichloromethane (3×100 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated. The residue (1.58 g) was dissolved in a mixture of toluene (17.8 mL) and dichloromethane (5.4 mL). After transferring to a Schlenk tube, the solution was layered with cyclohexane (30 mL) and crystals of **3** (1.08 g) were collected by filtration after 10 days (Yield: 44%, Average yield: 40% over three runs). Mp 149–152 °C (dec); R_f: 0.5 in 10% MeOH/CH_2Cl_2. $[\alpha]_D^{24}$ +42.0 (*c* 1, CH_2Cl_2). Crystallographic data for the structure of **3** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 943949). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (br s, 2H, NH), 3.97 (d, *J*=15.1 Hz, 2H, C$H_aH_bSO_2$), 3.39 (d, *J*=15.1 Hz, 2H, C$H_aH_bSO_2$), 2.43 (ddd, *J*=18.7, 4.4, 3.3 Hz, 2H, CH_2*exo*CO), 2.29 (ddd, *J*=14.7, 11.7, 3.7 Hz, 2H, CH_2CH_2*exo*CH), 2.15 (dd, *J*=4.4, 4.4 Hz, 2H, CH), 2.11–2.02 (m, 2H, CH_2*exo*$C_{quaternary}$), 1.97 (d, *J*=18.7 Hz, 2H, CH_2*endo*CO), 1.89 (ddd, *J*=14.0, 9.3, 4.6 Hz, 2H, CH_2CH_2*endo*CH), 1.49 (ddd, *J*=12.8, 9.3, 3.8 Hz, 2H, CH_2*endo*$C_{quaternary}$), 1.07 (s, 6H, Me_2C), 0.94 (s, 6H, Me_2C); ^{13}C NMR {^{1}H} (100 MHz, $CDCl_3$) δ 216.3, 148.1, 59.2, 52.3, 49.0, 43.1, 42.9, 27.1, 26.3, 20.0, 19.6; ν_{max} (KBr) 1747, 1734, 1706, 1482, 1470, 1344, 1162, 1139, 1131 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{21}H_{33}N_2O_7S_2$ 489.1724; Found 489.1726.

4.3. Sample procedure for the catalytic enantioselective Friedel–Crafts reaction

*4.3.1. 2-(2-Nitro-1-phenylethyl)-1H-pyrrole (**6**).*[67] Sodium tetraphenylborate (253 mg) was weighed in to a 10 mL flask and dried at 80 °C for 1 h under high vacuum. To this, catalyst **3** (180 mg) was added under argon atmosphere followed by 1,2-dichloroethane (8.8 mL). The flask was fitted with a condenser and the contents were refluxed for 1 h at 85 °C with vigorous stirring. It was then cooled to 45 °C and the solvent was removed by sparging with argon. The residue was dried under high vacuum for an hour (the solvent can also be removed using a rotary evaporator. In this case the vacuum is released using argon). The obtained complex **3a** was used immediately to setup three reactions with different nitro olefins.

A dried Schlenk tube was charged with 118 mg of complex **3a** (0.1 mmol), 100 mg of (*E*)-1-(2-nitrovinyl)benzene (0.67 mmol), and 245 mg of Na_2SO_4. The tube was flushed with argon and 820 μL of chlorobenzene was added. The contents were stirred at room temperature for 45 min (NOTE: a slow stir rate was used to avoid deposition of solids above the solvent level). The tube was cooled to −20 °C, stirred for 45 min, and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) was added. After completion of reaction (by TLC), the product was purified by column chromatography on silica gel to yield 127 mg of **6** as a pale yellow solid (Yield: 88%, Average yield: 89% over three runs). R_f: 0.50 in 20% EtOAc/hexanes. Enantiomeric excess (ee)=65% (Average ee=64% over three runs). $[\alpha]_D^{25}$ −36.8 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1H, NH), 7.39–7.30 (m, 3H, H_{arom}), 7.26–7.24 (m, 2H, H_{arom}), 6.70 (ddd, *J*=2.7, 2.7, 1.5 Hz, 1H, $H_{pyrrole}$), 6.19–6.17 (m, 1H, $H_{pyrrole}$), 6.11–6.09 (m, 1H, $H_{pyrrole}$), 5.00 (dd, *J*=12.0, 7.3 Hz, 1H, $O_2NCH_aH_bCH$), 4.91 (dd, *J*=7.4, 7.4 Hz, 1H, $CHCH_aH_bNO_2$), 4.82 (dd, *J*=12.0, 7.6 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR {^{1}H} (100 MHz, $CDCl_3$) δ 138.1, 129.4, 129.1, 128.3, 128.1, 118.3, 108.8, 106.0, 79.4, 43.1; ν_{max} (liquid film) 3426, 1550, 1430, 1378, 704 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{12}H_{13}N_2O_2$ 217.0972; Found 217.0973.

*4.3.2. 2-(1-(4-Bromophenyl)-2-nitroethyl)-1H-pyrrole (**7**).*[67] Prepared according to sample procedure using (*E*)-1-bromo-4-(2-nitrovinyl)benzene (153 mg, 0.67 mmol) and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) to yield 174 mg of **7** as a white solid (Yield: 88%, Average yield: 86% over three runs). R_f: 0.40 in 20% EtOAc/hexanes. Enantiomeric excess=76% (Average ee=72% over three runs). $[\alpha]_D^{25}$ −44.7 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1H, NH), 7.49 (dt, *J*=8.9, 2.2 Hz, 2H, H_{arom}), 7.12 (dt, *J*=8.8, 2.1 Hz, 2H, H_{arom}), 6.72 (ddd, *J*=2.6, 2.6, 1.5 Hz, 1H, $H_{pyrrole}$), 6.19–6.17 (m, 1H, $H_{pyrrole}$), 6.09–6.07 (m, 1H, $H_{pyrrole}$), 4.98 (dd, *J*=12.2, 7.0 Hz, 1H, $O_2NCH_aH_bCH$), 4.88 (dd, *J*=7.5, 7.5 Hz, 1H, $CHCH_aH_bNO_2$), 4.79 (dd, *J*=12.2, 8.0 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR {^{1}H} (100 MHz, $CDCl_3$) δ 137.2, 132.4, 129.7, 128.4, 122.3, 118.6, 108.9, 106.1, 79.0, 42.5; ν_{max} (liquid film) 3433, 1550, 1488, 1378, 727 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{12}H_{12}BrN_2O_2$ 295.0077; Found 295.0073.

*4.3.3. 2-(1-(4-Methoxyphenyl)-2-nitroethyl)-1H-pyrrole (**8**).*[67] Prepared according to sample procedure using (*E*)-1-methoxy-4-(2-nitrovinyl)benzene (120 mg, 0.67 mmol) and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) to yield 151 mg of **8** as a yellow oil (Yield: 92%, Average yield: 89% over three runs). R_f: 0.36 in 20% EtOAc/hexanes. Enantiomeric excess=61% (Average ee=56% over three runs). $[\alpha]_D^{25}$ −54.0 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1H, NH), 7.16 (dt, *J*=8.7, 2.6 Hz, 2H, H_{arom}), 6.89 (dt, *J*=8.8, 2.6 Hz, 2H, H_{arom}), 6.70 (ddd, *J*=2.7, 2.7, 1.6 Hz, 1H, $H_{pyrrole}$), 6.19–6.16 (m, 1H, $H_{pyrrole}$), 6.08–6.06 (m, 1H, $H_{pyrrole}$), 4.98 (dd, *J*=11.9, 7.0 Hz, 1H, $O_2NCH_aH_bCH$), 4.86 (dd, *J*=7.5, 7.5 Hz, 1H, $CHCH_aH_bNO_2$), 4.78 (dd, *J*=12.0, 8.1 Hz, 1H, $O_2NCH_aH_bCH$), 3.80 (s, 3H, OMe); ^{13}C NMR {^{1}H} (100 MHz, $CDCl_3$) δ 159.5, 130.0, 129.4, 129.2, 118.2, 114.7, 108.8, 105.7, 79.6, 55.5, 42.4; ν_{max} (liquid film) 3418, 2919, 1550, 1511, 1249, 1030, 722 cm^{-1}; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{13}H_{15}N_2O_3$ 247.1077; Found 247.1068.

*4.3.4. 3-[1-(2-Chlorophenyl)-2-nitroethyl]-1H-indole (**9**).*[56] Prepared according to sample procedure using (*E*)-1-chloro-2-(2-nitrovinyl)benzene (123 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 186 mg of **9** as a white viscous oil (Yield: 92%, Average yield: 93% over three runs). R_f: 0.27 in 20% EtOAc/hexanes. Enantiomeric excess=67% (Average ee=66% over three runs). $[\alpha]_D^{25}$ −22.9 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (br s, 1H, NH), 7.46–7.44 (m, 2H, H_{arom}), 7.39–7.37 (m, 1H, H_{arom}), 7.25–7.16 (m, 4H, H_{arom}), 7.15–7.14 (m, 1H, H_{arom}), 7.09 (ddd, *J*=8.0, 7.1, 1.0 Hz, 1H, H_{arom}), 5.76 (dd, *J*=7.8, 7.8 Hz, 1H, $CHCH_aH_bNO_2$), 5.03 (dd, *J*=12.9, 8.6 Hz, 1H, $O_2NCH_aH_bCH$), 4.98 (dd, *J*=12.8, 7.1 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR {^{1}H} (100 MHz, $CDCl_3$) δ 136.6, 136.5, 133.9,

130.2, 129.1, 128.9, 127.4, 126.3, 122.8, 122.1, 120.1, 119.0, 113.2, 111.5, 77.8, 38.0; ν_{max} (liquid film) 3420, 3060, 1551, 1378, 744 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{14}ClN_2O_2$ 301.0738; Found 301.0731.

4.3.5. 3-[1-Naphth-2-yl-2-nitroethyl]-1H-indole (***10***).[56] Prepared according to sample procedure using (*E*)-2-(2-nitrovinyl)naphthalene (134 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 132 mg of **10** as a gray solid (Yield: 62%, Average yield: 60% over three runs). *Rf*: 0.23 in 20% EtOAc/hexanes. Enantiomeric excess=68% (Average ee=66% over three runs). $[\alpha]_D^{25}$ −3.3 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (br s, 1H, NH), 7.82–7.80 (m, 4H, H_{arom}), 7.51–7.43 (m, 4H, H_{arom}), 7.39–7.37 (m, 1H, H_{arom}), 7.21 (ddd, *J*=8.1, 7.1, 1.0 Hz, 1H, H_{arom}), 7.09–7.05 (m, 2H, H_{arom}), 5.38 (dd, *J*=8.0, 8.0 Hz, 1H, $CHCH_aH_bNO_2$), 5.17 (dd, *J*=12.6, 7.5 Hz, 1H, $O_2NCH_aH_bCH$), 5.07 (dd, *J*=12.6, 8.5 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 136.8, 136.7, 133.6, 132.9, 128.9, 128.0, 127.8, 126.54, 126.48, 126.3, 126.2, 125.9, 122.9, 121.9, 120.2, 119.1, 114.5, 111.5, 79.5, 41.8; ν_{max} (liquid film) 3426, 3055, 1550, 1378, 744 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{17}N_2O_2$ 317.1285; Found 317.1286.

4.3.6. 2-(1-(Naphthalen-2-yl)-2-nitroethyl)-1H-pyrrole (***11***).[67] Prepared according to sample procedure using (*E*)-2-(2-nitrovinyl)naphthalene (134 mg, 0.67 mmol) and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) to yield 155 mg of **11** as a gray solid (Yield: 87%, Average yield: 88% over three runs). *Rf*: 0.40 in 20% EtOAc/hexanes. Enantiomeric excess 83% (Average ee=82% over three runs). $[\alpha]_D^{25}$ −85.3 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.86–7.81 (m, 4H, H_{arom}), 7.72 (br s, 1H, NH), 7.55–7.49 (m, 2H, H_{arom}), 7.33 (dd, *J*=8.5, 1.8 Hz, 1H, H_{arom}), 6.71–6.69 (m, 1H, $H_{pyrrole}$), 6.22–6.19 (m, 1H, $H_{pyrrole}$), 6.15 (m, 1H, $H_{pyrrole}$), 5.12–5.06 (m, 2H, $O_2NCH_aH_bCH$, $CHCH_aH_bNO_2$), 4.94 (dd, *J*=15.2, 10.8 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 135.4, 133.5, 133.1, 129.4, 129.0, 128.0, 127.9, 127.1, 126.8, 126.6, 125.5, 118.5, 108.9, 106.0, 79.2, 43.2; ν_{max} (liquid film) 3430, 1550, 1377, 749, 726 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{15}N_2O_2$ 267.1128; Found 267.1124.

4.3.7. 3-[1-(4-Bromophenyl)-2-nitroethyl]-1H-indole (***12***).[68] Prepared according to sample procedure using (*E*)-1-bromo-4-(2-nitrovinyl)benzene (153 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 132 mg of **12** as a white solid (Yield: 75%, Average yield: 73% over three runs). *Rf*: 0.27 in 20% EtOAc/hexanes. Enantiomeric excess=76% (Average ee=72% over three runs). $[\alpha]_D^{25}$ −1.3 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (br s, 1H, NH), 7.46 (dt, *J*=8.9, 2.2 Hz, 2H, H_{arom}), 7.42–7.37 (m, 2H, H_{arom}), 7.24–7.20 (m, 3H, H_{arom}), 7.10 (ddd, *J*=8.0, 7.1, 1.0 Hz, 1H, H_{arom}), 7.04 (dd, *J*=2.5, 0.6 Hz, 1H, H_{arom}), 5.17 (dd, *J*=7.9, 7.9 Hz, 1H, $CHCH_aH_bNO_2$), 5.07 (dd, *J*=12.5, 7.3 Hz, 1H, $O_2NCH_aH_bCH$), 4.92 (dd, *J*=12.5, 8.6 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 138.4, 136.7, 132.2, 129.6, 128.5, 126.0, 123.0, 121.7, 120.3, 118.9, 114.1, 111.6, 79.3, 41.2; ν_{max} (liquid film) 3423, 1550, 1488, 1378, 1011, 744 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{14}BrN_2O_2$ 345.0233; Found 345.0231.

4.3.8. 3-[1-(4-Methoxyphenyl)-2-nitroethyl]-1H-indole (***13***).[68] Prepared according to sample procedure using (*E*)-1-methoxy-4-(2-nitrovinyl)benzene (120 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 126 mg of **13** as a white solid (Yield: 63%, Average yield: 60% over three runs). *Rf*: 0.23 in 20% EtOAc/hexanes. Enantiomeric excess=73% (Average ee=70% over three runs). $[\alpha]_D^{24}$ −24.8 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (br s, 1H, NH), 7.46–7.44 (m, 1H, H_{arom}), 7.37 (dt, *J*=8.1, 0.8 Hz, 1H, H_{arom}), 7.26 (dt, *J*=9.5, 2.5 Hz, 2H, H_{arom}), 7.21 (ddd, *J*=8.2, 7.1, 1.1 Hz, 1H, H_{arom}), 7.09 (ddd, *J*=8.0, 7.1, 1.0 Hz, 1H, H_{arom}), 7.04 (dd, *J*=2.5, 0.7 Hz, 1H, H_{arom}), 6.86 (dt, *J*=9.4, 2.6 Hz, 2H, H_{arom}), 5.15 (dd, *J*=8.0, 8.0 Hz, 1H, $CHCH_aH_bNO_2$), 5.06 (dd, *J*=12.3, 7.5 Hz, 1H, $O_2NCH_aH_bCH$), 4.91 (dd, *J*=12.3, 8.4 Hz, 1H, $O_2NCH_aH_bCH$), 3.79 (s, 3H, OMe); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 159.0, 136.6, 131.3, 128.9, 126.2, 122.8, 121.6, 120.0, 119.1, 114.9, 114.4, 111.5, 79.9, 55.4, 41.0; ν_{max} (liquid film) 3414, 1550, 1512, 1249, 746 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{17}H_{17}N_2O_3$ 297.1234; Found 297.1230.

4.3.9. 3-(2-Nitro-1-phenylethyl)-1H-indole (***14***).[68] Prepared according to sample procedure using (*E*)-1-(2-nitrovinyl)benzene (100 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 172 mg of **14** as a light yellow oil (Yield: 96%, Average yield: 95% over three runs). *Rf*: 0.27 in 20% EtOAc/hexanes. Enantiomeric excess=60% (Average ee=58% over three runs). $[\alpha]_D^{24}$ −18.9 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H, NH), 7.46 (dd, *J*=8.0, 0.8 Hz, 1H, H_{arom}), 7.39–7.31 (m, 5H, H_{arom}), 7.30–7.25 (m, 1H), 7.21 (ddd, *J*=8.2, 7.2, 1.1 Hz, 1H, H_{arom}), 7.08 (ddd, *J*=8.0, 7.1, 1.0 Hz, 1H, H_{arom}), 7.06 (dd, *J*=2.5, 0.6 Hz, 1H, H_{arom}), 5.21 (dd, *J*=8.0, 8.0 Hz, 1H, $CHCH_aH_bNO_2$), 5.09 (dd, *J*=12.5, 7.6 Hz, 1H, $O_2NCH_aH_bCH$), 4.96 (dd, *J*=12.5, 8.4 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 139.3, 136.6, 129.0, 127.9, 127.7, 126.2, 122.8, 121.7, 120.1, 119.1, 114.6, 111.5, 79.7, 41.7; ν_{max} (liquid film) 3423, 1550, 1456, 1379, 744, 703 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{15}N_2O_2$ 267.1128; Found 267.1129.

4.3.10. 2-(1-(2-Chlorophenyl)-2-nitroethyl)-1H-pyrrole (***15***).[67] Prepared according to sample procedure using (*E*)-1-chloro-2-(2-nitrovinyl)benzene (123 mg, 0.67 mmol) and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) to yield 152 mg of **15** as a white solid (Yield: 91%, Average yield: 88% over three runs). *Rf*: 0.30 in 10% EtOAc/hexanes. Enantiomeric excess=52% (Average ee=50% over three runs). $[\alpha]_D^{24}$ −51.4 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (br s, 1H, NH), 7.46–7.41 (m, 1H, H_{arom}), 7.26–7.23 (m, 2H, H_{arom}), 7.17–7.12 (m, 1H, H_{arom}), 6.73 (ddd, *J*=2.7, 2.7, 1.5 Hz, 1H, $H_{pyrrole}$), 6.20–6.18 (m, 1H, $H_{pyrrole}$), 6.15–6.13 (m, 1H, $H_{pyrrole}$), 5.47 (dd, *J*=8.8, 6.7 Hz, 1H, $CHCH_aH_bNO_2$), 4.95 (dd, *J*=13.3, 8.9 Hz, 1H, $O_2NCH_aH_bCH$), 4.88 (dd, *J*=13.3, 6.6 Hz, 1H, $O_2NCH_aH_bCH$); ^{13}C NMR $\{^1H\}$ (100 MHz, $(CD_3)_2CO$) δ 137.7, 134.2, 130.7, 130.1, 129.8, 128.7, 128.4, 119.1, 108.7, 107.2, 78.0, 40.2; ν_{max} (liquid film) 3433, 1552, 1377, 1036, 758, 731 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{12}ClN_2O_2$ 251.0582; Found 251.0582.

4.3.11. 2-(3-Methyl-1-nitrobutan-2-yl)-1H-pyrrole (***16***).[67] Prepared according to sample procedure using (*E*)-3-methyl-1-nitrobut-1-ene (77 mg, 0.67 mmol) and a solution of pyrrole in chlorobenzene (4.03 M, 500 μL, 2 mmol) to yield 51 mg of **16** as a colorless oil (Yield: 42%, Average yield: 34% over two runs). *Rf*: 0.50 in 20% EtOAc/hexanes. Enantiomeric excess=44% (Average ee=36% over two runs). $[\alpha]_D^{25}$ +10.6 (*c* 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (br s, 1H, NH), 6.69 (ddd, *J*=2.7, 2.7, 1.5 Hz, 1H, $H_{pyrrole}$), 6.18–6.15 (m, 1H, $H_{pyrrole}$), 6.00–5.98 (m, 1H, $H_{pyrrole}$), 4.68 (dd, *J*=12.6, 6.1 Hz, 1H, $O_2NCH_aH_bCH$), 4.59 (dd, *J*=12.6, 9.0 Hz, 1H, $O_2NCH_aH_bCH$), 3.36 (ddd, *J*=9.0, 6.3, 6.3 Hz, 1H, $CHCH_aH_bNO_2$), 2.03–1.91 (m, 1H, $CHMe_2$), 0.98 (d, *J*=6.8 Hz, 3H, Me_2CH), 0.91 (d, *J*=6.7 Hz, 3H, Me_2CH); ^{13}C NMR $\{^1H\}$ (100 MHz, $CDCl_3$) δ 128.7, 117.2, 108.8, 106.2, 78.4, 44.3, 30.9, 20.8, 19.6; ν_{max} (liquid film) 3422, 2964, 1551, 1381, 721 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_9H_{15}N_2O_2$ 183.1128; Found 183.1122.

4.3.12. 3-(3-Methyl-1-nitrobutan-2-yl)-1H-indole (***17***).[68] Prepared according to sample procedure using (*E*)-3-methyl-1-nitrobut-1-ene (77 mg, 0.67 mmol) and indole (235 mg, 2 mmol) to yield 20 mg of **17** as a light yellow oil (Yield: 13%, Average yield: 13% over two runs). *Rf*: 0.30 in 20% EtOAc/hexanes. Enantiomeric excess=24% (Average ee=22% over two runs). $[\alpha]_D^{25}$ +11.5 (*c* 0.1, CH_2Cl_2). ^1H NMR

(400 MHz, $CDCl_3$) δ 8.08 (br s, 1H, NH), 7.63–7.61 (m, 1H, H_{indole}), 7.39–7.36 (m, 1H, H_{indole}), 7.21 (ddd, J=8.1, 7.1, 1.1 Hz, 1H, H_{indole}), 7.14 (ddd, J=8.0, 7.2, 1.1 Hz, 1H, H_{indole}), 7.03 (d, J=2.4 Hz, 1H, H_{indole}), 4.81 (dd, J=12.0, 6.3 Hz, 1H, $O_2NCH_aH_bCH$), 4.73 (dd, J=12.0, 9.1 Hz, 1H, $O_2NCH_aH_bCH$), 3.69 (ddd, J=9.1, 6.7, 6.7 Hz, 1H, $CHCH_aH_bNO_2$), 2.25–2.13 (m, 1H, $CHMe_2$), 1.02 (d, J=6.8 Hz, 3H, Me_2CH), 0.94 (d, J=6.7 Hz, 3H, Me_2CH); ^{13}C NMR {^1H} (100 MHz, $CDCl_3$) δ 136.4, 127.0, 122.4, 122.2, 119.8, 119.2, 113.4, 111.5, 78.8, 42.7, 30.8, 20.8, 20.2; ν_{max} (liquid film) 3420, 2962, 1550, 1383, 743 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{17}N_2O_2$ 233.1285; Found 233.1284.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.03.068.

References and notes

1. Lippert, K. M.; Hof, K.; Gerbig, D.; Ley, D.; Hausmann, H.; Guenther, S.; Schreiner, P. R. *Eur. J. Org. Chem.* **2012**, 5919–5927.
2. Knowles, R. R.; Jacobsen, E. N. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20678–20685.
3. Wittkopp, A.; Schreiner, P. R. *Chem.—Eur. J.* **2003**, *9*, 407–414 For examples of conformational effects in other organocatalysts see Refs. 4–6.
4. Tárkányi, G.; Király, P.; Soós, T.; Varga, S. *Chem.—Eur. J.* **2012**, *18*, 1918–1922.
5. Zimmer, L. E.; Sparr, C.; Gilmour, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11860–11871.
6. Bürgi, T.; Baiker, A. *J. Am. Chem. Soc.* **1998**, *120*, 12920–12926.
7. Miller, S. J. *Acc. Chem. Res.* **2004**, *37*, 601–610.
8. Greenfield, S. J.; Agarkov, A.; Gilbertson, S. R. *Org. Lett.* **2003**, *5*, 3069–3072.
9. Jarvo, E. R.; Miller, S. J. *Tetrahedron* **2002**, *58*, 2481–2495.
10. Gilbertson, S. R.; Collibee, S. E.; Agarkov, A. *J. Am. Chem. Soc.* **2000**, *122*, 6522–6523.
11. Imperiali, B.; Kapoor, T. M. *Tetrahedron* **1993**, *49*, 3501–3510.
12. Branden, C.; Tooze, J. *Specific Transcription Factors Belong to a Few Families. Introduction to Protein Structure*, 2nd ed.; Garland Publishing, Taylor & Francis Group: New York, 1998; pp 175–203.
13. Hierso, J.-C.; Beaupérin, M.; Meunier, P. *Eur. J. Inorg. Chem.* **2007**, 3767–3780.
14. Barbaro, P.; Bianchini, C.; Giambastiani, G.; Parisel, S. L. *Coord. Chem. Rev.* **2004**, *248*, 2131–2150.
15. Colacot, T. J. *Chem. Rev.* **2003**, *103*, 3101–3118.
16. Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713–5743.
17. Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543.
18. Connon, S. J. *Chem.—Eur. J.* **2006**, *12*, 5418–5427.
19. Pihko, P. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2062–2064.
20. Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289–296 For pioneering earlier work see Refs. 21–22.
21. Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901–4902.
22. Schreiner, P. R.; Wittkopp, A. *Org. Lett.* **2002**, *4*, 217–220.
23. Jensen, K. H.; Sigman, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 4748–4750.
24. Jensen, K. H.; Sigman, M. S. *J. Org. Chem.* **2010**, *75*, 7194–7201.
25. Li, X.; Deng, H.; Zhang, B.; Li, J.; Zhang, L.; Luo, S.; Cheng, J.-P. *Chem.—Eur. J.* **2010**, *16*, 450–455.
26. Jakab, G.; Tancon, C.; Zhang, Z.; Lippert, K. M.; Schreiner, P. R. *Org. Lett.* **2012**, *14*, 1724–1727.
27. Kimmel, K. L.; Weaver, J. D.; Lee, M.; Ellman, J. A. *J. Am. Chem. Soc.* **2012**, *134*, 9058–9061.
28. Kimmel, K. L.; Robak, M. T.; Thomas, S.; Lee, M.; Ellman, J. A. *Tetrahedron* **2012**, *68*, 2704–2712.
29. Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Tetrahedron* **2011**, *67*, 4412–4416.
30. Kimmel, K. L.; Robak, M. T.; Ellman, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 8754–8755.
31. Robak, M. T.; Trincado, M.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 15110–15111.
32. Yates, M. H.; Kallman, N. J.; Ley, C. P.; Wei, J. N. *Org. Process Res. Dev.* **2009**, *13*, 255–262.
33. Lobb, K. L.; Hipskind, P. A.; Aikins, J. A.; Alvarez, E.; Cheung, Y.-Y.; Considine, E. L.; De Dios, A.; Durst, G. L.; Ferrito, R.; Grossman, C. S.; Giera, D. D.; Hollister, B. A.; Huang, Z.; Iversen, P. W.; Law, K. L.; Li, T.; Lin, H.-S.; Lopez, B.; Lopez, J. E.; Cabrejas, L. M. M.; McCann, D. J.; Molero, V.; Reilly, J. E.; Richett, M. E.; Shih, C.; Tiecher, B.; Wikel, J. H.; White, W. T.; Mader, M. M. *J. Med. Chem.* **2004**, *47*, 5367–5380.
34. Wright, J. B.; Willitte, R. E. *J. Med. Chem.* **1962**, *5*, 815–822.
35. Nickerson, D. M.; Angeles, V. V.; Auvil, T. J.; So, S. S.; Mattson, A. E. *Chem. Commun.* **2013**, 4289–4291.
36. So, S. S.; Mattson, A. E. *J. Am. Chem. Soc.* **2012**, *134*, 8798–8801.
37. Nickerson, D. M.; Mattson, A. E. *Chem.—Eur. J.* **2012**, *18*, 8310–8314.
38. So, S. S.; Auvil, T. J.; Garza, V. J.; Mattson, A. E. *Org. Lett.* **2012**, *14*, 444–447.
39. So, S. S.; Burkett, J. A.; Mattson, A. E. *Org. Lett.* **2011**, *13*, 716–719.
40. Hughes, M. P.; Smith, B. D. *J. Org. Chem.* **1997**, *62*, 4492–4499.
41. Hughes, M. P.; Shang, M. Y.; Smith, B. D. *J. Org. Chem.* **1996**, *61*, 4510–4511.
42. Sheng, Y.-F.; Gu, Q.; Zhang, A.-J.; You, S.-L. *J. Org. Chem.* **2009**, *74*, 6899–6901.
43. Liu, H.; Lu, S.-F.; Xu, J.; Du, D.-M. *Chem.—Asian J.* **2008**, *3*, 1111–1121.
44. Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129.
45. Crimmins, M. T.; King, B. W.; Tabet, E. A.; Chaudhary, K. *J. Org. Chem.* **2001**, *66*, 894–902 For other examples of dipole–dipole repulsion in selective reaction see Refs. 46–47.
46. Clayden, J.; McCarthy, C.; Westlund, N.; Frampton, C. S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1363–1378.
47. Giese, B.; Damm, W.; Wetterich, F.; Zeitz, H.-G. *Tetrahedron Lett.* **1993**, *34*, 5885–5888.
48. The obtained selectivity with 1 equiv of $NaBPh_4$ with respect to catalyst is 0% ee.
49. Schafer, A. G.; Wieting, J. M.; Mattson, A. E. *Org. Lett.* **2011**, *13*, 5228–5231.
50. Ganesh, M.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 16464–16465.
51. Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 4016–4018.
52. Fleming, E. M.; McCabe, T.; Connon, S. J. *Tetrahedron Lett.* **2006**, *47*, 7037–7042.
53. Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576–6579.
54. Zhuang, W.; Hazell, R. G.; Jørgensen, K. A. *Org. Biomol. Chem.* **2005**, *3*, 2566–2571.
55. Trost, B. M.; Müller, C. *J. Am. Chem. Soc.* **2008**, *130*, 2438–2439.
56. Lu, S.-F.; Du, D.-M.; Xu, J. *Org. Lett.* **2006**, *8*, 2115–2118.
57. Kundu, P. P. Experimental and Quantum Calculation Studies of Molecular Systems of Biological and Chemical Importance by Raman, Infrared, and SERS. Ph.D. Thesis, Jawaharlal Nehru Centre for Advanced Scientific Research, 2014.
58. Meganathan, C.; Sebastian, S.; Sivanesan, I.; Lee, K. W.; Jeong, B. R.; Oturak, H.; Sudha, S.; Sundaraganesan, N. *Spectrochim. Acta, Part A* **2012**, *95*, 331–340.
59. Chandran, A.; Mary, Y. S.; Varghese, H. T.; Panicker, C. Y.; Pazdera, P.; Rajendran, G.; Babu, N. *J. Mol. Struct.* **2011**, *992*, 77–83.
60. Chohan, Z. H.; Youssoufi, M. H.; Jarrahpour, A.; Hadda, T. B. *Eur. J. Med. Chem.* **2010**, *45*, 1189–1199.
61. For an example of a urea carbonyl bound to two sodium cations see: Armentano, D.; De Munno, G.; Rossi, R. *New J. Chem.* **2006**, *30*, 13–17 For other examples see Refs. 62–64.
62. Al-Harbi, A.; Sattler, W.; Sattler, A.; Parkin, G. *Chem. Commun.* **2011**, 3123–3125.
63. Geier, J.; Harmer, J.; Grützmacher, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 4093–4097.
64. Gilroy, J. B.; Lemaire, M. T.; Patrick, B. O.; Hicks, R. G. *CrystEngComm* **2009**, *11*, 2180–2184.
65. Davis, F. A.; Jenkins, R. H.; Awad, S. B.; Stringer, O. D.; Watson, W. H.; Galloy, J. *J. Am. Chem. Soc.* **1982**, *104*, 5412–5418.
66. Kumaran, G.; Kulkarni, G. H. *Tetrahedron Lett.* **1994**, *35*, 9099–9100.
67. Guo, F.; Chang, D.; Lai, G.; Zhu, T.; Xiong, S.; Wang, S.; Wang, Z. *Chem.—Eur. J.* **2011**, *17*, 11127–11130.
68. Lin, S.-Z.; You, T.-P. *Tetrahedron* **2009**, *65*, 1010–1016.