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Small Molecule Regulation of Self-Association and Catalytic Activity in a Supramolecular Coordination Complex

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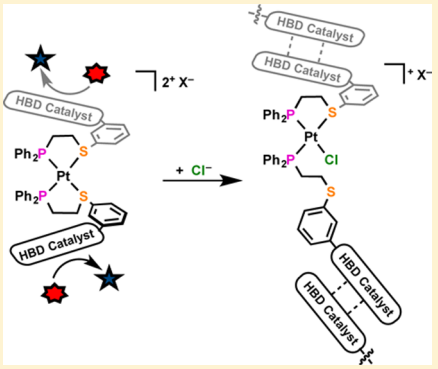
Supporting Information

ABSTRACT: Herein, we report the synthesis and characterization of the first weak-link approach (WLA) supramolecular construct that employs the small molecule regulation of intermolecular hydrogen bonding interactions for the in situ control of catalytic activity. A biaryl urea group, prone to self-aggregation, was functionalized with a phosphinoalkyl thioether (P,S) hemilabile moiety and incorporated into a homoligated Pt(II) tweezer WLA complex. This urea-containing construct, which has been characterized by a single crystal X-ray diffraction study, can be switched in situ from a rigid fully closed state to a flexible semiopen state via Cl^- induced changes in the coordination mode at the Pt(II) structural node. FT-IR and ^1H NMR spectroscopy studies were used to demonstrate that while extensive urea self-association persists in the flexible semiopen complex, these interactions are deterred in the rigid, fully closed complex because of geometric and steric restraints. Consequently, the urea moieties in the fully closed complex are able to catalyze a Diels-Alder reaction between cyclopentadiene and methyl vinyl ketone to generate 2-acetyl-5-norbornene. The free urea ligand and the semiopen complex show no such activity. The successful incorporation and regulation of a hydrogen bond donating catalyst in a WLA construct open the doors to a vast and rapidly growing catalogue of allosteric catalysts for applications in the detection and amplification of organic analytes.



INTRODUCTION

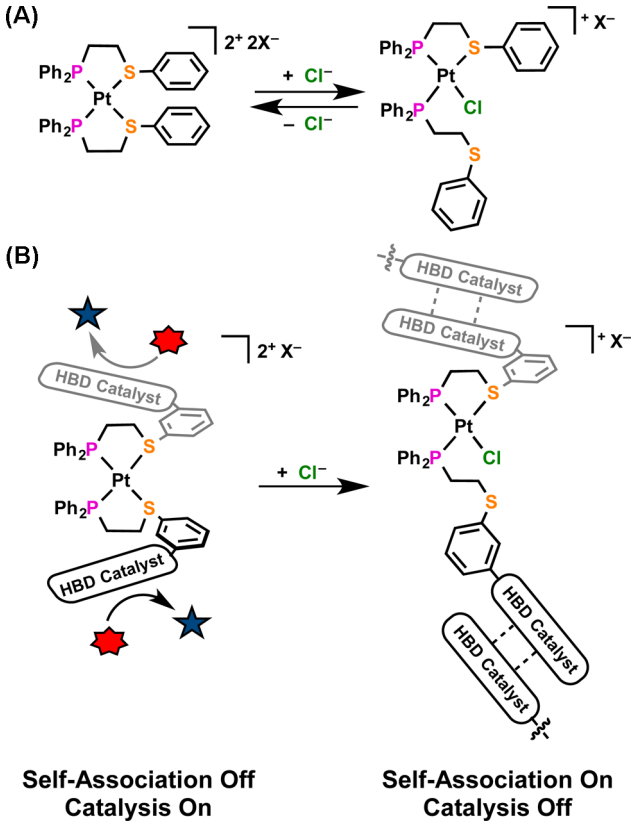
Supramolecular coordination chemistry has been used to assemble a wide variety of catalytically interesting structures.[1−12] In particular, the weak-link approach (WLA) to supramolecular coordination chemistry is a powerful tool for the convergent and modular synthesis of catalytically active structures that can be toggled between multiple configurations in response to chemical effectors.[13−17] This structural switching is reminiscent of allosteric enzymes in which the activity of a catalytic site is regulated by recognition events at a chemically orthogonal regulatory site.[18−22] In the case of the WLA, structural regulation is achieved through the reversible coordination of small molecule "effectors" (e.g., Cl^-, CO) to structural metal sites (e.g., Rh(I), Pt(II)) typically[23] bound to phosphine−heteratom (P,X; X = S, O, Se, N) hemilabile ligands. Thus, tweezer-like,[17,19,24,25] macrocyclic,[13,14,17,26] and triple-decker WLA structures[22,27] can be toggled reversibly between open, flexible, and closed, rigid constructs (Scheme 1A). Through the synthetic incorporation of metallocatalysts (i.e., porphyrins and salens) into WLA architectures, we have demonstrated several examples of in situ regulation of catalytic activity via changes in coordination chemistry.[14,19−22,28] Previously, we have shown that the catalytic activity of binuclear metalloporphyrin and salen catalysts incorporated into a WLA macrocycle can be reversibly regulated via precise control of macrocycle pore size, thus catalyst proximity and substrate access to the catalytic site, leading to applications in signal sensing[29] and amplification.[30] Additionally, the allosteric regulation of a mononuclear Al(III)-salen catalyst for living lactone polymerization has been demonstrated using a triple-decker architecture in which coordination chemistry at the structural nodes controls the ability of sterically bulky blocking groups to occlude substrates from the catalyst.[22] To further broaden the scope of catalysts amenable to regulation in functional WLA systems beyond bi- and mononuclear metallocatalysts, we have begun investigating the incorporation and regulation of hydrogen bond donating (HBD) catalysts. In contrast to controlling activity via catalyst proximity or steric occlusion of substrates, the activity of HBD catalysts can potentially be regulated by controlling competing intra- and intermolecular hydrogen bonding interactions via configurational changes imposed by the coordination mode of ligands at the structural regulatory site. The incorporation of HBD catalysts in WLA architectures would allow for the in situ regulation of a broad and rapidly growing range of reactions, such as Michael-type conjugate additions,[31−33] multicomponent cascade reactions,[34,35] and ring-opening copolymerizations of cyclic esters,[36,37] for applications such as PCR-like detection and amplification of organic molecules.

Of the many potential incorporable HBD catalysts,[38−41] we chose to initially investigate the utility of diaryl urea derivatives

Received: January 8, 2014
Published: March 14, 2014

   dx.doi.org/10.1021/ja500214r | J. Am. Chem. Soc. 2014, 136, 4689−4696

Scheme 1. (A, Top) Toggling between the Rigid, Fully Closed (Left) And the Flexible, Semiopen (Right) State in a Model Tweezer WLA Complex and (B, Bottom) Proposed WLA Complex Architecture for the Regulation of Diphenyl Urea Self-Association and Thus Catalytic Activity

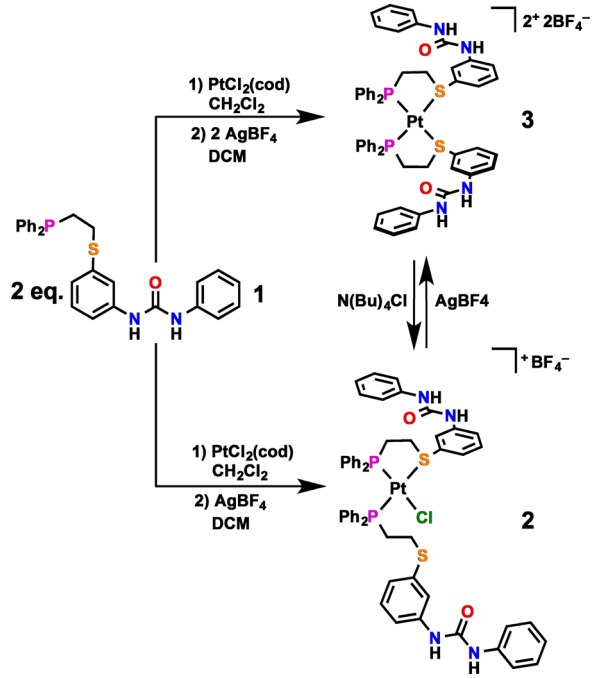


because of their synthetic accessibility,[42−44] thermodynamic stability,[45] and predicted orthogonality to the Pt(II) WLA structural metal sites. Diaryl urea derivatives contain two proximal N−H bonds capable of cooperative hydrogen bond donation to a single basic hydrogen bond acceptor.[39,46−48] These HBD groups are bound to an electron rich carbonyl moiety, a common hydrogen bond acceptor (HBA). In solution, the intermolecular hydrogen binding of these HBD and HBA moieties causes extensive "chainlike" aggregation,[49−54] which prevents substrate recognition and drastically reduces the catalytic utility of diphenyl urea derivatives.[39,48] Therefore, it was reasoned that through sequestration of the HBD and HBA moieties from one another in solution, aggregation could be deterred, substrate recognition enhanced, and catalytic activity increased. Consequently, it was hypothesized that controlling the self-association of a diphenyl urea moiety could be used as a platform for the regulation of catalytic activity in a WLA construct. In particular, in the catalytically "on" state, geometric and steric constraints and electrostatic interactions with the charged regulatory site deter urea self-association, thus allowing for substrate recognition and promoting catalytic activity (Scheme 1B), whereas in the "off" state, these structural constraints are alleviated, aggregation occurs, and activity is diminished. The structural addressability of the WLA structure would allow for in situ control of the catalytic activity of a diphenyl urea moiety by regulating its ability to self-associate. To test our hypothesis, urea functionalized hemilabile ligands were incorporated into a homoligated Pt(II) WLA tweezer-like construct. The urea self-association and substrate recognition properties of the complex's multiple structural configurations were determined via ^{1}H NMR and FT-IR spectroscopy. Finally, via ^{1}H NMR spectroscopy, the ability of the WLA construct to regulate the catalytic activity of the incorporated urea moiety was determined.

RESULTS AND DISCUSSION

Synthesis and Characterization. Studies have shown that biaryl monourea derivatives self-associate predominantly through a "chainlike" mode, in which the HBD urea protons cooperatively bind the HBA carbonyl oxygen of a second urea moiety in an ideally coplanar fashion.[51−54] With this in mind, we set out to synthesize a homoligated WLA complex that in the rigid, fully closed state would deter the formation of these highly oriented hydrogen bonding events via the effective isolation of the HBA moiety while simultaneously promoting the ability of the HBD N−H bonds to recognize substrates in solution. Thus, we designed meta-substituted urea-containing ligand **1**, which we hypothesized would "wrap around" the Pt(II) center upon chelation of the P,S moiety, thus sequestering the HBA carbonyl while simultaneously exposing the HBD moiety (Scheme 2). In the rigid fully closed state (**3**),

Scheme 2. Synthesis of Semiopen Complex 2 and Fully Closed Complex 3



the chelating urea-containing ligands would be geometrically and sterically constrained, effectively isolating the HBD and HBA moieties, thus deterring intermolecular self-association and enhancing substrate recognition. In contrast, in the flexible semiopen state (**2**), these constraints would be alleviated, allowing aggregation to occur and diminishing substrate binding.

The meta-substituted P,S-diphenyl urea ligand **1** was obtained by the nucleophilic addition of the precursor 3-(2-diphenylphosphanylethylthio)phenylamine (3-P,S-phenylamine) to phenyl isocyanate. Recrystallization afforded **1** as an analytically pure white powder, as confirmed by ^{1}H and

dx.doi.org/10.1021/ja500214r | J. Am. Chem. Soc. 2014, 136, 4689−4696

$^{31}P\{^{1}H\}$ NMR spectroscopy ($^{31}P\{^{1}H\}$ NMR signal: δ −18.04) and ESI/MS.

The desired homoligated Pt(II) complexes **2** and **3** were synthesized by the addition of 2 equiv of ligand **1** to 1 equiv of $PtCl_2$(cod) in CH_2Cl_2. Semiopen complex **2** was isolated by the abstraction of the outer-sphere Cl^- with 1 equiv of $AgBF_4$. $^{31}P\{^{1}H\}$ NMR spectroscopy of **2** shows two resonances, one at 8.84 ppm (J_{P-Pt} = 3203 Hz) and the other at 44.63 ppm (J_{P-Pt} = 3557 Hz), correlating to the phosphorus-bound ligand and the fully chelating ligand, respectively.[17,55] Upon the addition of 2 equiv of **1** to $PtCl_2$(cod), fully closed complex **3** was obtained via the abstraction of both the inner- and outer-sphere Cl^- anions with 2 equiv of $AgBF_4$. The $^{31}P\{^{1}H\}$ NMR spectrum of **3** shows a single, sharp resonance at 47.05 ppm (J_{P-Pt} = 3110 Hz), consistent with equivalent, chelated ligands.[17] The relatively large P−Pt coupling constants in both complexes **2** and **3** are consistent with the predicted cis configurations of the ligands.[17,56] Fully closed complex **3** can be converted to semiopen complex **2** by the addition of 1 equiv of tetrabutylammonium chloride, demonstrating the ability to toggle between two coordination states in solution. Single crystals of **3** suitable for X-ray diffraction analysis were grown by the slow diffusion of hexanes into a dichloroethane solution of **3** (Figure 1).

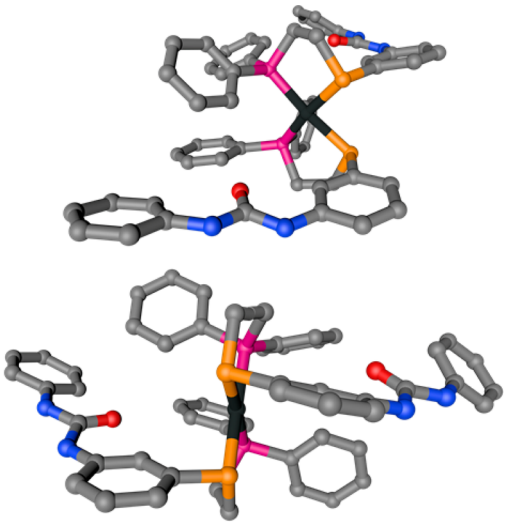


Figure 1. Solid-state X-ray structure of **3** viewed front-on and side-on with outer-sphere anions, hydrogens, and solvent omitted for clarity: C, gray; P, magenta; S, orange; O, red; N, blue; Pt, black.

The solid-state structure of **3** agrees with the solution phase assignment described above. Furthermore, the solid-state structure is consistent with the predicted ligand orientation, showing approximately parallel planar urea moieties wrapped around the Pt(II) center. In this orientation, the ability of the urea-containing ligands to aggregate in a "chainlike" manner is significantly diminished. Essential to the promotion of substrate binding and catalytic activity over self-association, the HBA carbonyl moiety is oriented toward the Pt(II) center, whereas the HBD N−H bonds are exposed. Although the urea moiety does possess some innate flexibility, the solid state structure suggests that its observed orientation is stabilized by through-space electrostatic interactions between the partially anionic carbonyl[57,58] and the Pt(II) center.[59,60] Treating the oxygen and platinum atoms as point charges and using the observed Pt−O distance of 4.55 ± 0.095 Å, a simple calculation using Coulomb's law gave an electrostatic interaction of approximately 10.1 ± 0.21 kcal/mol. Even though the structure of fully closed **3** in solution may deviate from the observed solid-state configuration, the orientation of the urea-containing ligands in **3** suggests that electrostatic interactions may act cooperatively with geometric considerations to create an architecture in which the self-association of the urea moiety is suppressed.

Characterization of Urea Self-Association. In order to determine if the observed solid-state structure is consistent with the solution phase configuration, it was necessary to examine urea self-association in situ. Because of the widespread use of urea derivatives in polymer and material self-assembly, intermolecular self-association of urea derivatives has been extensively characterized.[51,53,61,62] Specifically, FT-IR spectroscopy is used to study the N−H bond vibrations in urea derivatives. The stretching of free, non-hydrogen bound N−H bonds displays a sharp band at approximately 3450−3400 cm^{-1}, whereas the stretching of N−H bonds participating in hydrogen bonding appears as a characteristically broad band around 3400−3250 cm^{-1}.[51,53,61,63] Therefore, the self-association properties of ligand **1**, semiopen complex **2**, and fully closed **3** were studied by FT-IR spectroscopy. FT-IR spectra of **1**, **2**, and **3** were taken in the relatively nonassociative solvent CH_2Cl_2 at concentrations of 0.03, 0.015, and 0.015 M, respectively. At these concentrations, both free ligand **1** and semiopen complex **2** exhibit extensive self-association, manifested as broad bands in the N−H stretching region (Figure 2A,B). Unlike ligand **1** and semiopen complex **2**, the FT-IR spectrum of fully closed complex **3** shows no observable

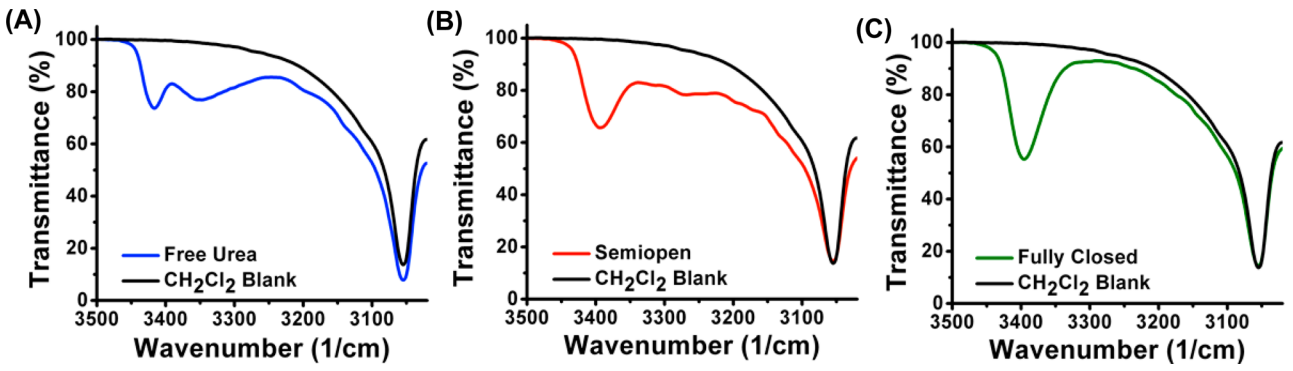


Figure 2. FT-IR spectra of the N−H stretching region (3500−3020 cm^{-1}) for (A) **1** (0.03 M), (B) **2** (0.015 M), and (C) **3** (0.015 M). **1** and **2** show urea self-association as a broad stretch from 3400 to 3200 cm^{-1}. **3** only shows free N−H stretching.

dx.doi.org/10.1021/ja500214r | J. Am. Chem. Soc. 2014, 136, 4689−4696

hydrogen bonding, only exhibiting a sharp band in the free N−H stretching region (Figure 2C), suggesting that at the above concentration the supramolecular architecture imposed by fully closed complex **3** prevents self-association of the urea moieties.

Because of the fact that urea aggregation is highly concentration dependent, it was important to examine the ability of **3** to suppress aggregation over a wide concentration range. Therefore, the relative intensity of the free N−H vibration band as a function of concentration for ligand **1**, semiopen complex **2**, and fully closed complex **3** was compared. If aggregation of the urea-containing ligand is possible in the system, the intensity of the free N−H stretching bands would decrease with increasing concentration. At sufficiently low concentrations (6.0×10^{-3} M urea-containing ligand), the FT-IR spectra of **1**, **2**, and **3** display negligible hydrogen bound N−H stretching bands. By use of these spectra as references, it is possible to determine the relative intensity of the free N−H stretching bands in solutions of higher concentration.[53] Figure 3 shows that with increasing concentrations from 0.006 to 0.15 M, ligand **1** and semiopen complex **2** display a sharp reduction in the free N−H stretching bands. In contrast, over the observed concentration range, fully closed complex **3** displays negligible reduction of free N−H groups. From this study, it can be inferred that over the examined concentration range, semiopen complex **2** permits aggregation analogous to ligand **1**, whereas fully closed complex **3** inhibits the formation of detectable urea self-association.

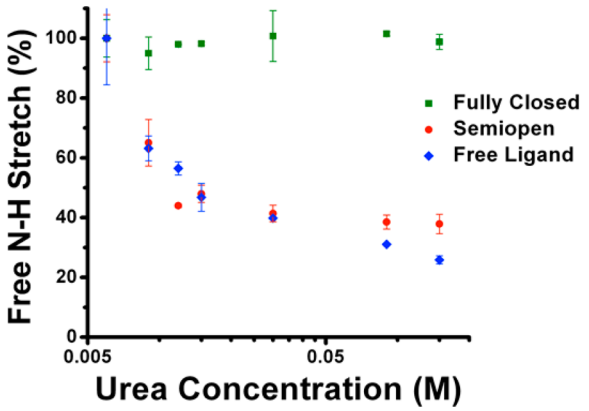


Figure 3. FT-IR spectroscopy concentration gradient study of the non-hydrogen bound N−H stretch of **1** (blue), **2** (red), and **3** (green) from 0.006 to 0.15 M. Concentration of complexes accounts for two urea ligands per complex. **1** maintains free N−H stretching over the studied concentration range.

To further our understanding of the aggregation of the urea moiety, self-association constants for **1**, **2**, and **3** were calculated. By use of ^{1}H NMR spectroscopy, the K_a for self-association was calculated by fitting plots of the chemical shift of the urea moiety N−H proton resonance as a function of concentration in CD_2Cl_2.[64] Ligand **1** and semiopen complex **2** possess K_a values of 3.2 ± 1.0 and 1.7 ± 0.6 M^{-1} (Figure 4A,B)), respectively, which are similar to previously reported monourea derivatives.[51] In the case of fully closed complex **3**, however, there is no observable change in chemical shift with increasing concentration from 0.01 to 0.05 M (Figure 4C), giving a negligible K_a value, and quantitatively enforcing the observation that the structure of fully closed complex **3** prevents self-association of the urea moiety. The FT-IR and ^{1}H NMR spectroscopy data have demonstrated that whereas **2** permits self-association, in **3** the HBD and HBA moieties of the urea-containing ligands are isolated from each other in solution, thus preventing aggregation from occurring. Of note, self-association was also studied by dynamic light scattering (DLS), but aggregation is not sufficient to elicit a DLS response.

Substrate Association Studies. In addition to prohibiting urea self-aggregation, for fully closed complex **3** to improve the catalytic activity of a diphenyl urea derivative, the HBD N−H pairs must be able to recognize and bind HBA substrates. To evaluate the ability of **3** to promote substrate recognition over self-association, the association constants of ligand **1**, semiopen complex **2**, and fully closed complex **3** with furanone were determined via ^{1}H NMR spectroscopy. K_a values were calculated by fitting plots of the changing chemical shift of the urea moiety N−H proton resonance as a function of furanone equivalents per urea (Figure 5). The furanone association constants for ligand **1** and semiopen **2** were calculated to be 3.92 ± 0.79 and 11.63 ± 4.78 M^{-1}, respectively. In comparison, fully closed complex **3** exhibits a significantly higher K_a of 78.39 ± 10.24 M^{-1}, 7-fold greater than the K_a value of the semiopen complex. From the elevated association constant of **3** two points can be inferred: First, in the fully closed state, the HBD moieties are oriented outward from the Pt(II) structural center, thus exposing them to substrates in solution. Second, by prevention of the competitive urea derivative self-association pathway, the HBD moieties become more available to binding other HBA substrates.

A job plot was constructed to further characterize the substrate binding event and determine the stoichiometry of furanone binding to **3**.[30,65] When plotted as a function of the

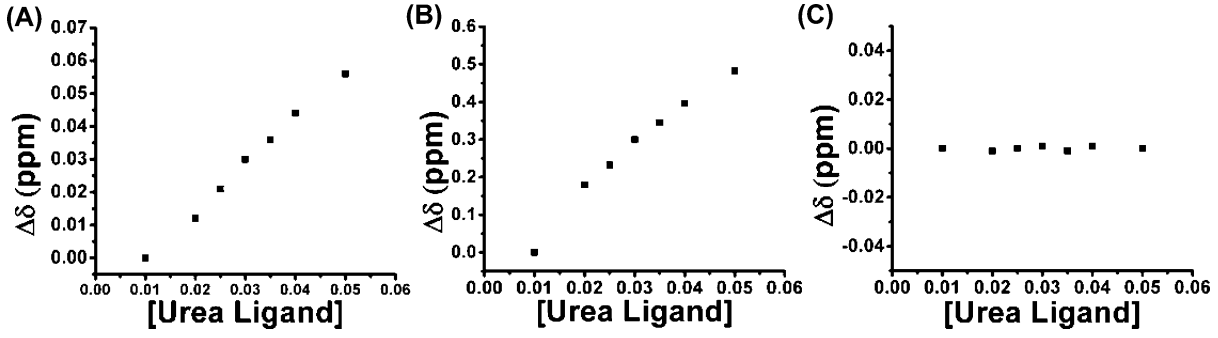


Figure 4. Δδ(ppm) of urea protons vs urea concentration in CD_2Cl_2 for (A) **1**, (B) **2**, and (C) **3**. **1**: K_a = 3.2 ± 1.0 M^{-1}. **2**: K_a = 1.7 ± 0.6 M^{-1}. **3**: K_{as}= neglible. **2** and **3** have $BArF^-$ counteranion(s).

dx.doi.org/10.1021/ja500214r | J. Am. Chem. Soc. 2014, 136, 4689−4696

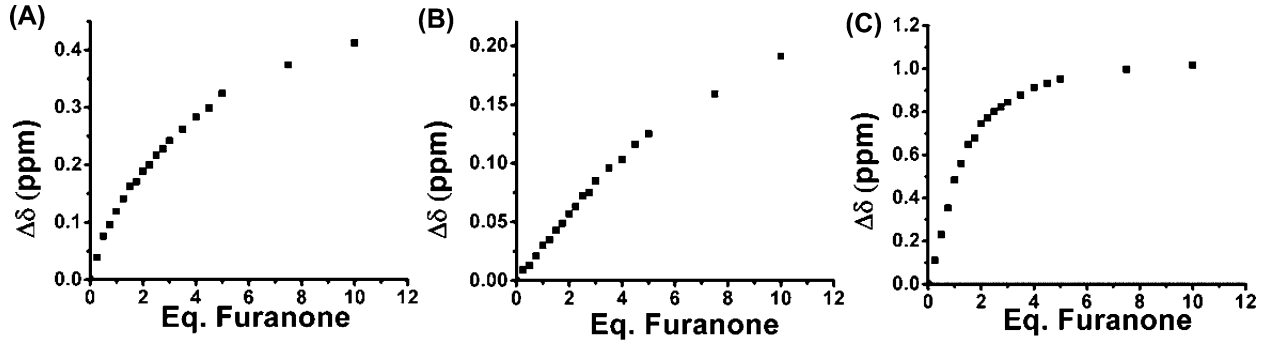


Figure 5. $\Delta\delta$(ppm) of urea protons vs equivalents of furanone (per urea) in CD_2Cl_2 for (A) **1**, (B) **2**, and (C) **3**. **1**: K_a = 3.92 ± 0.79 M^{-1}. **2**: K_a = 11.63 ± 4.78 M^{-1}. **3**: K_a = 78.39 ± 10.24 M^{-1}. **2** and **3** have $BArF^-$ counteranion(s).

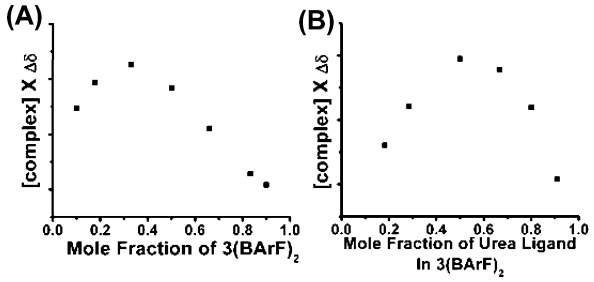


Figure 6. Job plot for binding event between **3** and furanone: (A) plotted as a function of the mole fraction of **3**, giving 2:1 furanone/**3** binding stoichiometry; (B) plotted as a function of the mole fraction of urea in **3**, giving 1:1 furanone/urea binding stoichiometry.

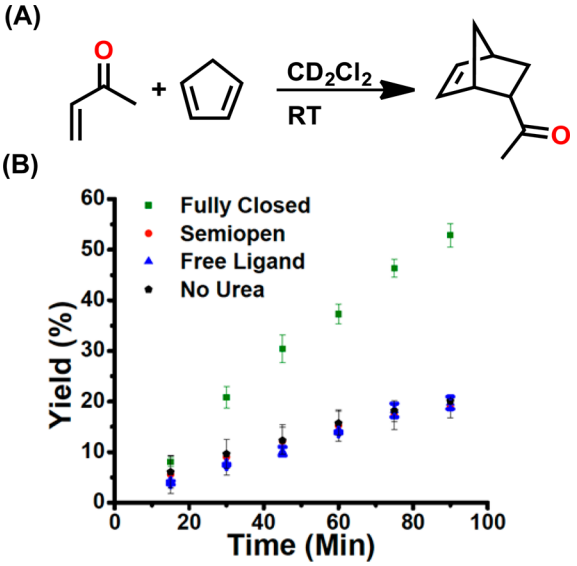


Figure 7. (A) Diels-Alder reaction between methyl vinyl ketone (MVK) and cyclopentadiene (CPD). (B) **3** (green) shows catalysis of a Diels-Alder reaction between MVK and CPD, whereas **2** (red) and **1** (blue) show no catalysis. Reaction progress was monitored by ^1H NMR spectroscopy. Conditions were the following: 1:1 MVK/CPD, rt, CD_2Cl_2, 10 mol % urea ligand.

mole fraction of the complex, the plot maximum occurs at 0.33 mole fraction **3** (Figure 6A), which is interpreted as 2:1 furanone/**3** binding stoichiometry. By use of the same data, plotted as a function of urea ligand, we see a maximum at 0.5 mole fraction (Figure 6B), corresponding to 1:1 furanone/urea ligand stoichiometry. This strongly suggests that within the context of fully closed complex **3**, the urea-containing ligands bind substrate independent of one another.

Catalytic Activity and Regulation. Through extensive FT-IR and ^1H NMR spectroscopy studies, we have demonstrated that changes in coordination chemistry can be used to regulate the self-association and substrate binding of a diphenyl urea-containing ligand. The semiopen state (**2**) exhibits aggregation and substrate binding similar to **1**, whereas the fully closed state (**3**) deters aggregation, making the HBD moiety available for substrate recognition. Therefore, to test our hypothesis that controlling self-association can be used as a platform for regulating catalytic activity, we compared the ability of ligand **1**, semiopen complex **2**, and fully closed complex **3** to catalyze a Diels-Alder reaction between methyl vinyl ketone (MVK) and cyclopentadiene (CPD) to generate 2-acetyl-5-norbornene (Figure 7A).[7,66] Each reaction was carried out with a 1:1 MVK/CPD stoichiometric ratio in CD_2Cl_2 at room temperature. **1**, **2**, and **3** were loaded at 10 mol % with respect to the urea moieties. As seen in Figure 7B, neither ligand **1** nor semiopen complex **2** shows any acceleration of the reaction in comparison to the urea-free control. Unlike **1** and **2**, fully closed complex **3** demonstrates both rate acceleration and catalytic turnover, with a turnover frequency of 6.48 × 10^{-4} s^{-1}. Thus, the simultaneous prevention of self-association and promotion of substrate recognition, as affected by the coordination mode of the WLA center, can increase the catalytic activity of diphenyl urea derivative.

Finally, we investigated the potential to exploit the hemilabile nature of the ligands in the WLA system to regulate the catalytic activity of the diphenyl urea ligand in situ. By use of the conditions described above, fully closed complex **3** was used to catalyze the reaction for 35 min, followed by the addition of 1 equiv of NBu_4Cl to the reaction solution. As seen in Figure 8, the reaction rate is immediately and drastically reduced because of the immediate formation of the semiopen complex. Through affecting the coordination mode of the hemilabile ligands, the ability of the urea moiety to self-associate is increased; thus, substrate recognition and catalytic activity is diminished. Therefore, controlling self-association of a urea derivative via incorporation into an appropriately designed WLA architecture not only can increase the catalytic activity of the HBD catalyst but also allows for regulation of urea's catalytic activity in situ.

CONCLUSIONS

In using self-association as a regulatory tool for catalytic activity, we have transformed a critical weakness of urea HBD catalysts

dx.doi.org/10.1021/ja500214r | J. Am. Chem. Soc. 2014, 136, 4689−4696

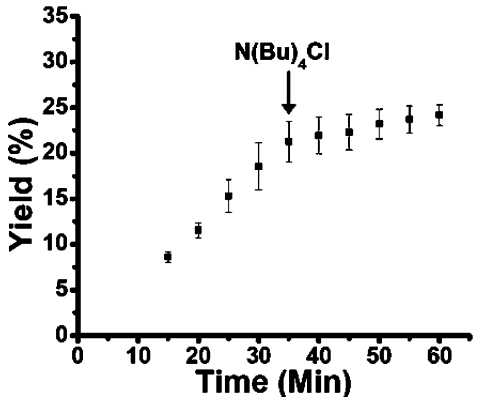


Figure 8. In situ addition of NBu_4Cl after 35 min to a solution of **3** catalyzing the Diels-Alder reaction between MVK and cyclopentadiene shows immediate turn-off of catalysis, due to formation of **2**.

into a valuable asset. Through the use of this novel regulatory methodology, we have demonstrated the ability to "turn on" a catalytically dormant diphenyl urea moiety by the inhibition of detrimental self-association, subsequently promoting substrate recognition and catalysis. In employing the weak-link approach to metal-directed assembly to synthesize our supramolecular construct, we have incorporated the capacity to switch between rigid and flexible configurations via changes in coordination, allowing for in situ regulation of catalytic activity. The ability to regulate catalytic activity by controlling the self-association properties of the urea moiety precludes the synthesis of and dependence on the large, convoluted blocking ligands previously used to sterically regulate catalytic moieties in WLA constructs. By this first demonstration of the ability to regulate a HBD catalyst via control of competing hydrogen bonding pathways in a WLA architecture, the door has been opened for the incorporation and regulation of other HBD catalysts, such as squaramides[40,67] and guanidinium[68−70] derivatives, which in general have considerably greater catalytic activity and a broader range of potential substrates. Moving forward, challenges include achieving complete allosteric control of HBD catalytic activity through reversible in situ interconversion between rigid and flexible coordination modes in the presence of substrates. This work sets the stage for the integration and regulation of various HBD catalysts in WLA constructs, which will allow for the harnessing of the rich and rapidly growing diversity of HBD catalyzed reactions for applications such as allosteric control of living copolymerizations and PCR-like detection and amplification of organic molecules.

EXPERIMENTAL SECTION

General Methods. Phosphine−thioether ligand **1** and precursors were prepared and stored using standard Schlenk techniques under an inert nitrogen atmosphere unless noted otherwise. The synthesis of Pt(II) complexes, **2** and **3**, and their manipulations and characterization were performed under ambient conditions. All solvents used for ligand and complex synthesis were anhydrous grade, purchased from Sigma-Aldrich. Deuterated solvents were purchased from Cambridge Isotope Laboratories and used as received. Ligand precursor, 1-chloro-2-(diphenylphosphino)ethane, was prepared as previously reported.[22] Dicyclopentadiene from Aldrich Chemical Co. was thermally cracked (160−170 °C) and freshly distilled to isolate cylcopentadiene for use in catalytic experiments. All other chemicals were purchased from Aldrich Chemical Co. and used as received. ^{1}H NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer. ^{1}H NMR spectra were referenced internally to residual protons in the deuterated solvents (dichloromethane-d_2 = δ 5.32 ppm). $^{31}P\{^1H\}$ NMR spectra were referenced to an external 85% H_3PO_4 standard (δ 0 ppm). Electrospray ionization (ESI) mass spectra were recorded on an Agilent 6120 LC−TOF instrument in positive ion mode.

Synthesis. *3-(2-Diphenylphosphanylethylthio)phenylamine.* 1-Chloro-2-(diphenylphosphino)ethane (4.00 g, 16.08 mmol) and 3-aminothiophenol (2.01 g, 16.08 mmol) were dissolved in degassed anhydrous acetonitrile (20 mL) in an oven-dried Schlenk flask. With stirring, cesium carbonate (5.24 g, 16.08 mmol) was added, and the reaction mixture was heated to reflux for 12 h under nitrogen. The mixture was filtered through a glass frit, and the retentate was washed with acetonitrile. The solvent was removed from the filtrate under reduced pressure. Silica gel column chromatography (dichloromethane) afforded the product as an off-white solid (4.07 g, 75% yield). ^{1}H NMR (400.16 MHz, 25 °C, CD_2Cl_2): δ 7.45−7.42 (m, 4H), 7.35 (m, 6H), 7.02 (t, J_{H-H} = 8 Hz, 1H), 6.62−6.60 (m, 1H), 6.51 (m, 1H), 6.48−6.46 (m, 1H), 3.66 (br s, 2H), 3.00−2.94 (m, 2H), 2.42−2.38 (m, 2H). $^{31}P\{^1H\}$ NMR (161.98 MHz, 25 °C, CD_2Cl_2): δ −17.08 (s). ESIMS (*m/z*): 337 $[M]^+$. Found 337.

*N-Phenyl-N′-3-(2-Diphenylphosphanylethylthio)phenylurea (**1**).* 3-(2−Diphenylphosphanylethylthio)phenylamine (2.0 g, 5.92 mmol) and phenyl isocyanate (0.78 g, 6.51 mmol) were dissolved in degassed anhydrous tetrahydrofuran and stirred at reflux for 12 h under nitrogen. The solvent was removed under reduced pressure. Minimal degassed ethanol (10 mL) was added to solubilize the mixture. Degassed hexanes (100 mL) were added, and the mixture was sonicated for 20 min, giving an oily precipitate. The supernatant was decanted, and the oily product was washed with hexanes (3 × 20 mL). The oil was dried under vacuum to give a white, fluffy solid (2.43 g, 90% yield). ^{1}H NMR (400.16 MHz, 25 °C, DMSO-d_6): δ 8.72 (s, 1H), 8.69 (s, 1H), 7.51 (s, 1H), 7.45 (d, J_{H-H} = 8 Hz, 2H), 7.41−7.36 (m, 10H), 7.28 (t, J_{H-H} = 8 Hz, 2H), 7.18 (d, J_{H-H} = 8 Hz, 2H), 6.97 (t, J_{H-H} = 8 Hz, 1H), 6.80 (m, 1H), 2.93 (m, 2H), 2.40 (m, 2H). $^{31}P\{^1H\}$ NMR (161.98 MHz, 25 °C, DMSO-d_6): δ −17.31 (s). ESIMS (*m/z*): 456 $[M]^+$. Found 456.

*Semiopen Complex (BF_4^-) (**2**).* A solution of $PtCl_2$(cod) (300 mg, 0.80 mmol) in dichloromethane (10 mL) was added dropwise to a solution of **1** (732 mg, 1.60 mmol) in dichloromethane (10 mL) in a 50 mL oven-dried Schlenk flask. The solution was stirred vigorously for 3 h. The mixture was then added dropwise to a slurry of silver tetrafluoroborate (155 mg, 0.80 mmol) in dichloromethane (5 mL). The solution was stirred in the dark for 1 h. The resulting mixture was filtered through a Celite pad in a fritted funnel. The Celite was washed with dichloromethane (3 × 10 mL). The filtrate was collected and concentrated (2 mL) under reduced pressure. Hexanes (30 mL) were added, and the resulting mixture was stored at −20 °C for 1 h. The suspension was filtered using a glass frit, and the resulting white product was washed with hexanes (3 × 10 mL). The product was dried in vacuo (925 mg, 94% yield). ^{1}H NMR (400.16 MHz, 25 °C, CD_2Cl_2): 8.70 (s, 2H), 8.40−8.33 (m, 2H), 7.92 (m, 2H), 7.71−7.12 (br m, 32H), 7.02 (t, J_{H-H} = 4 Hz, 2H), 6.84 (m, 2H), 3.03−2.67 (br m, 8H). $^{31}P\{^1H\}$ NMR (161.98 MHz, 25 °C, DMSO-d_6): δ 44.63 (br s, J_{P-Pt} = 3557 Hz, 1P), 8.84 (br s, J_{P-Pt} = 3203 Hz, 1P). Observed broadening of $^{31}P\{^1H\}$ spectrum occurs due to "windshield wiping" of ligands.[55] ESI/MS (*m/z*): 1142 $[M - BF_4]^+$. Found 1142.

*Fully Closed Complex ($BF_4^-)_2$ (**3**).* **3** was synthesized via two methods: (a) direct synthesis from **1** and $PtCl_2$(cod) and (b) isolation of **2** and subsequent abstraction of the inner-sphere chloride.

(a) A solution of $PtCl_2$(cod) (300 mg, 0.80 mmol) in dichloromethane (10 mL) was added dropwise to a solution of **1** (732 mg, 1.60 mmol) in dichloromethane (10 mL) in a 50 mL oven-dried Schlenk flask. The solution was stirred vigorously for 3 h. The mixture was then added dropwise to a slurry of silver tetrafluoroborate (310 mg, 1.60 mmol) in dichloromethane (10 mL). The solution was stirred in the dark for 1 h. The resulting mixture was filtered through a Celite pad in a fritted funnel. The Celite was washed with dichloromethane (3 × 10 mL). The filtrate was collected and concentrated (2 mL) under reduced pressure. Hexanes (30 mL) were added, and the resulting

mixture was stored at −20 °C for 1 h. The suspension was filtered using a glass frit, and the resulting white product was washed with hexanes (3 × 10 mL). The product was dried in vacuo (984 mg, 96% yield).

(b) A solution of **2** (200 mg, 0.17 mmol) in dichloromethane (10 mL) was added dropwise to a slurry of silver tetrafluoroborate (32.7 mg, 0.17 mmol) in dichloromethane (10 mL). The solution was stirred in the dark for 1 h. The resulting mixture was filtered through a Celite pad in a fritted funnel. The Celite was washed with dichloromethane (3 × 10 mL). The filtrate was collected and the solvent removed under vacuum to give a white powder (197 mg, 95% yield). ^{1}H NMR (400.16 MHz, 25 °C, CD_2Cl_2): 8.15 (s, 2H), 7.88−7.30 (m, 36 H), 7.05 (t, J_{H-H} = 4 Hz, 2H), 6.80 (m, 2H), 3.57−2.43 (br m, 8H). ^{31}P{^{1}H} NMR (161.98 MHz, 25 °C, DMSO-d_6): δ 47.05 (s, J_{P-Pt} = 3110 Hz, 2P). ESIMS (*m/z*): 1107 $[M - 2BF_4]^{2+}$. Found 1107.

Fully Closed Complex (BArF$^-$)$_2$. A solution of sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BArF$^-$) (75 mg, 0.085 mmol) in diethyl ether (5 mL) was added to a slurry of **3** (54 mg, 0.042 mmol) in diethyl ether (5 mL). The mixture was stirred for 12 h at room temperature and then filtered using a glass frit. The filtrate was collected, and the solvent was removed under vacuum to yield a brown solid (109 mg, 90% yield). ^{1}H NMR (400.16 MHz, 25 °C, CD_2Cl_2): δ 7.70 (s, 16H), 7.54 (s, 8H), 7.48−7.32 (m, 36H), 7.05 (t, J_{H-H} = 4 Hz, 4H), 6.89 (s, 2H), 3.10−2.89 (m, 8H). ^{31}P{^{1}H} NMR (161.98 MHz, 25 °C, DMSO-d_6): δ 45.11 (s, J_{P-Pt} = 3119 Hz, 2P).

Semiopen Complex (BArF$^-$). **2**(BArF$^-$) was formed in situ by the addition of one equivalent of $N(Bu)_4Cl$ (10 mg, 0.036 mmol) to **3**(BArF$^-$)$_2$ (102.0 mg, 0.036 mmol) in CH_2Cl_2, giving the immediate quantitative formation of the semiopen complex (99% yield). ^{1}H NMR (400.16 MHz, 25 °C, CD_2Cl_2): δ 9.03 (s, 2H), 8.73 (s, 2H), 7.72 (s, 16H), 7.55 (s, 8H), 7.49 (d, J_{H-H} = 4 Hz, 4H), 7.40−7.33 (m, 24H), 7.26 (t, J_{H-H} = 4 Hz, 4H), 7.05 (m, 4H), 6.95 (m, 2H), 3.04 (m, 8H), 1.62−1.54 (m, 16H, $N(CH_2CH_2CH_2CH_3)_4^+$), 1.44−1.36 (m, 8H, $N(CH_2CH_2CH_2CH_3)_4^+$), 0.99 (t, J_{H-H} = 4 Hz, 12H, $N(CH_2CH_2CH_2CH_3)_4^+$). ^{31}P{^{1}H} NMR (161.98 MHz, 25 °C, DMSO-d_6): δ 44.45 (br s, J_{P-Pt} = 3551 Hz, 1P), 8.42 (br s, J_{P-Pt} = 3208 Hz, 1P).

Single Crystal X-ray Diffraction. Crystallographic data (Table S1) and ORTEP diagram (Figure S1) are displayed in the Supporting Information. A single crystal was mounted using oil (Infineum V8512) on a glass fiber. All measurements were made on a CCD area detector with graphite monochromated Mo Kα radiation. Data were collected using Bruker APEXII detector and processed using APEX2 from Bruker. All structures were solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in idealized positions but not refined. Their positions were constrained relative to their parent atom.

■ ASSOCIATED CONTENT

Supporting Information

Details of FT-IR and ^{1}H NMR spectroscopy studies of urea self-association and substrate association, Job plot, catalytic studies, crystal structure ORTEP diagram and structure details (including CIF file), ^{31}P{^{1}H} and ^{1}H NMR spectra of **1**, **2**, and **3**, and ^{1}H NMR spectra of **2**(BArF$^-$) and **3**(BArF$^-$)$_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This material is based upon work supported by the U.S. Army under Contract/Grant W911NF-11-1-0229, the Office of the Assistant Secretary of Defense for Research and Engineering, DoD/NSSEFF Program/Naval Postgraduate School under Awards N00244-09-1-0012 and N00244-09-1-0071, and the National Science Foundation under Grant CHE-1149314.

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