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Reaction Diversity of the S–S Bond Promoted by Metal Coordination: From Discovery to Controllable Reactions

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Promoted by $NiCl_2$ coordination in the mixed solvent MeOH/CH_2Cl_2, diverse in situ S–S bond reactions, such as *S*-oxidation and S–S and C–S bond scission, occurred in the disulfide ligand of 2-ppds {bis[4-(pyridin-2-yl)pyrimidin-2-yl]disulfane} to yield three new components identified as 2-mpp [2-methoxy-4-(pyridin-2-yl)pyrimidine], 2-ppst {*S*-[4-(pyridin-2-yl)pyrimidin-2-yl] 4-(pyridin-2-yl)pyrimidine-2-sulfonothioate} and 2-pps {bis[4-(pyridin-2-yl)pyrimidin-2-yl]sulfane}. More importantly, such in situ reactions could be efficaciously controlled so that they proceed in a highly selective manner. Thus, $NiCl_2$-mediated in situ reaction of 2-ppds with the aid of continuous air bubbling through the reaction mixture exclusively led to 2-pps, whereas replacement of $NiCl_2$ by $Cu(OAc)_2$ afforded 2-mpp alone. A confirmatory experiment proved that 2-ppst served as a decisive intermediate in these in situ reactions.

Introduction

In recent years, increasing research interest has been concerned with in situ metal/heterocyclic disulfide reactions under hydro(solvo)thermal conditions. On the one hand, in situ hydro(solvo)thermal metal/ligand reactions show great advantages in obtaining coordination architectures that are structurally novel, especially those that are unattainable by direct methods.[1] On the other hand, it is particularly noteworthy that heterocyclic disulfide compounds often exhibit diverse reactions under different hydro(solvo)thermal conditions. For example, 4-dpds (or 2-dpds) may undergo either in situ S–S bond cleavage to produce pyridinethionate or pyridinethione[2] or both in situ S–S and C–S bond scission to give 4-dps[2c,3] or even concurrent C–S cleavage and rearrangement[3] (4-dpds = dipyridin-4-yl disulfide; 2-dpds = dipyridin-2-yl disulfide; 4-dps = dipyridin-4-yl sulfide). Moreover, in situ C–S and S–S bond scission may partly occur in 4-dpds to yield attractive supramolecular architectures with mixed ligands of 4-dpds and 4-dps.[4] In contrast, most in situ metal/heterocyclic disulfide reactions under ambient conditions are confined to the oxidative addition of the disulfide to low-valent metal centres.[5] A more recent example is the observation of insertion or the extrusion of one sulfur atom from the disulfide mediated by metal coordination under mild conditions.[6] Nevertheless, the control of in situ metal/ligand reactions is still a great challenge for chemists largely because of the intricate mechanisms involved in these reactions.[1d,1e] Over the past few years, we have focused our attention on the coordination chemistry of organic ligands containing the HPPT*n* unit [HPPT*n* = 4-(pyridin-*n*-yl)pyrimidine-2-thiol (*n* = 2–4)].[7] We have reported a unique Cu_4S_4 cluster bearing the HPPT2 unit obtained through in situ C–S cleavage[7e] and also described a fascinating example of the anion-modulated reversible conversion of molecular assembly between a macrocycle and a linear chain.[7c] Herein we would like to unveil the reaction diversity of the S–S bond in 2-ppds {2-ppds = bis[4-(pyridin-2-yl)pyrimidin-2-yl]disulfane} promoted by metal coordination and in particular to demonstrate how such in situ metal/disulfide reactions can be controlled.

Results and Discussion

A mixture of a CH_2Cl_2 solution containing 2-ppds and an MeOH solution of 1 equiv. of $NiCl_2$ was allowed to stand at room temperature for 1 d to generate dark-green block crystals. Single-crystal X-ray diffraction analysis revealed that an unexpected mononuclear Ni^{II} compound [$NiCl_2$(2-pps)] was obtained with the newly generated ligand 2-pps {2-pps = bis[4-(pyridin-2-yl)pyrimidin-2-yl]-sulfane; Scheme 1}. As depicted in Figure 1, compound [$NiCl_2$(2-pps)] crystallizes in the space group *C*2/*c*, and the Ni^{II} ion is situated on a two-fold axis that passes through both the Ni and S atoms. The six-coordinate Ni^{II} ion adopts a distorted octahedral coordination geometry with four N atoms in equatorial positions and two chlorine atoms in axial positions. Both the least-squares planes defined by Ni1N1C5C6N2 and Ni1N1AC5AC6AN2A are slightly inclined to each other with a small dihedral angle of 9.33°.

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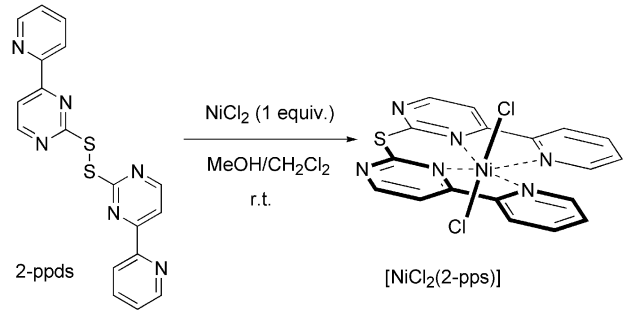


Scheme 1. Formation of $[NiCl_2(2\text{-pps})]$ by the in situ reaction of 2-ppds with $NiCl_2$.

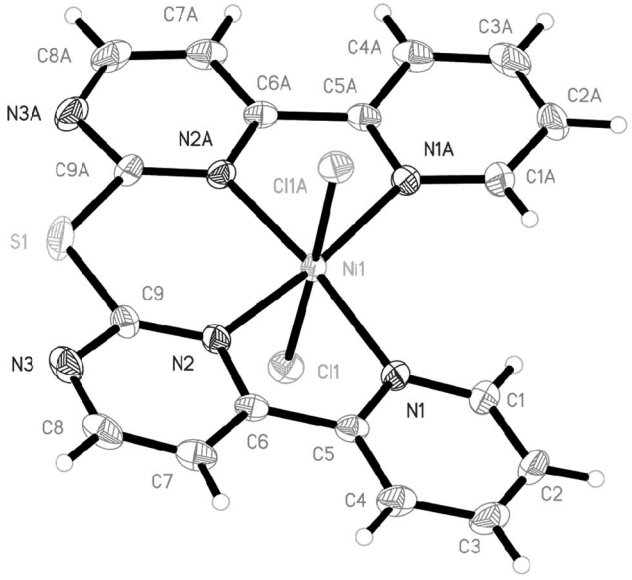
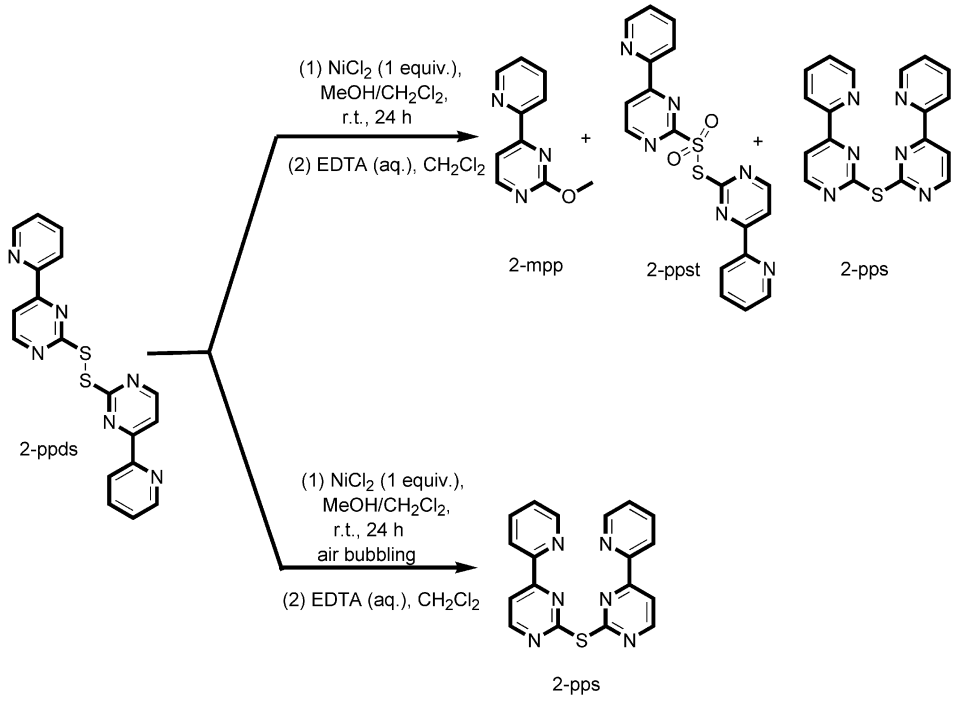


Figure 1. ORTEP diagram of $[NiCl_2(2\text{-pps})]$ with thermal ellipsoids at the 30% probability level.

Unambiguously, 2-ppds underwent in situ S–S and C–S bond scission to form 2-pps, which was simultaneously coordinated to an Ni^{2+} ion. Tong and co-workers reported an example in which 4-dpds was converted into 4-dps under solvothermal conditions by a disproportionation reaction, which was corroborated by the formation of elementary sulfur crystals.[3] However, in our case the formation of sulfur was not observed, which implies that the conversion from 2-ppds to 2-pps may take place in a different manner. To our surprise, treatment of the reaction mixture with excess EDTA (EDTA = ethylenediaminetetraacetic acid disodium salt) followed by extraction with CH_2Cl_2 released three new components in addition to 2-ppds. The microanalysis data revealed four components in the extract (in order of decreasing R_f values in TLC): 2-mpp [2-methoxy-4-(pyridin-2-yl)pyrimidine], 2-ppst {*S*-[4-(pyridin-2-yl)pyrimidin-2-yl] 4-(pyridin-2-yl)pyrimidine-2-sulfonothioate}, 2-ppds and 2-pps. As far as we know, this is the first example of diverse in situ reactions of the S–S function in one pot under ambient conditions. Apparently, in situ S–S bond reactions are triggered by Ni^{2+} ion coordination given the fact that there is no change in 2-ppds in the absence of $NiCl_2$. Because the reaction was conducted under aerobic conditions, the formation of 2-ppst should be the consequence of metal-mediated oxidation, with oxygen from air serving as the oxidant. Moreover, 2-ppst may serve as a key intermediate in the formation of 2-pps on the basis of the reactivity of the thiosulfonate.[8] In addition, it can also be noticed that the filtrate obtained from the preparation of $[NiCl_2(2\text{-pps})]$ crystals slowly continues to generate another crop of $[NiCl_2(2\text{-pps})]$ crystals if it is left to stand in air. With this in mind, we conceived that continuously bubbling air through the reaction mixture would be expected to accelerate the transformation of 2-ppds into 2-ppst, which could be further converted into 2-pps. In fact, 2-ppds can almost completely be converted into 2-pps as anticipated if there is a continuous flow of air (Scheme 2).

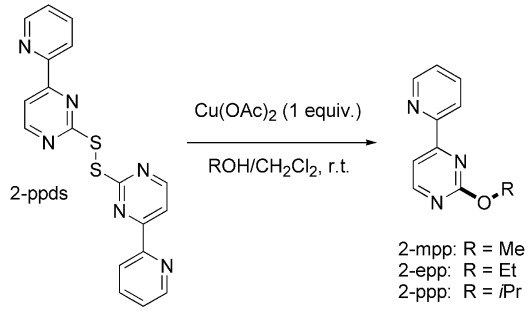
The initial success stimulated us to study how such in situ reactions can be controlled to selectively produce 2-mpp, which is a minor product in the reaction with $NiCl_2$. The screening of various divalent transition-metal chlorides (MCl_2; M = Mn^{2+}, Fe^{2+}, Co^{2+}, Cu^{2+}, Zn^{2+}) gave different results. It was observed that 2-ppds was barely affected by $MnCl_2$ and $FeCl_2$, whereas the other metal chlorides might induce similar in situ reactions, but these were not as efficient as with $NiCl_2$. However, it was discovered that the use of $Cu(OAc)_2$ and $Co(OAc)_2$ exclusively led to 2-mpp, with $Cu(OAc)_2$ being superior to $Co(OAc)_2$ in terms of reaction rate. In the above reaction, EtOH and *i*PrOH were also used to test the generality of this $Cu(OAc)_2$-mediated reaction (Scheme 3). The use of EtOH also selectively afforded the expected 2-epp [2-epp = 2-ethoxy-4-(pyridin-2-yl)pyrimidine]. The reaction was sluggish with *i*PrOH, but the desired product, 2-ppp [2-isopropyloxy-4-(pyridin-2-yl)-pyrimidine], was smoothly obtained but in a longer reaction time. Although the $Cu(OAc)_2$-mediated desulfurization of 2-ppds to give new alkyloxy-substituted products is very facile, this reaction is limited to 2-ppds and is not effective with other aromatic disulfides. This unique reaction for 2-ppds has been ascribed to its extraordinary structure. We assume that the two bipyridine-like units in 2-ppds play a pivotal role in this reaction as their ready chelation to metal ions would promote the oxidation of the disulfide bond and trigger a cascade of reactions. In addition, it is also worth noting that this unique reaction may be the consequence of the synergistic action of the two metal cations and their counterions. By simple substitution of anions from chloride to acetate, the choice of $Ni(OAc)_2$ markedly changed the reaction outcome, affording 2-mpp as the main product despite the fact that the efficiency of $Ni(OAc)_2$-mediated reactions is very poor. It seems that the AcO^- anion is capable of guiding this reaction towards 2-mpp over other in situ reactions. More strikingly, the replacement of Ni^{2+} with Cu^{2+} significantly accelerated the reaction. The formation of 2-mpp shows that methanol participates in the reaction; it is presumed that methanol binds to the metal ions prior to further reaction because no 2-mpp is found to be formed by simply mixing methanol with 2-ppds, 2-ppst or 2-pps in



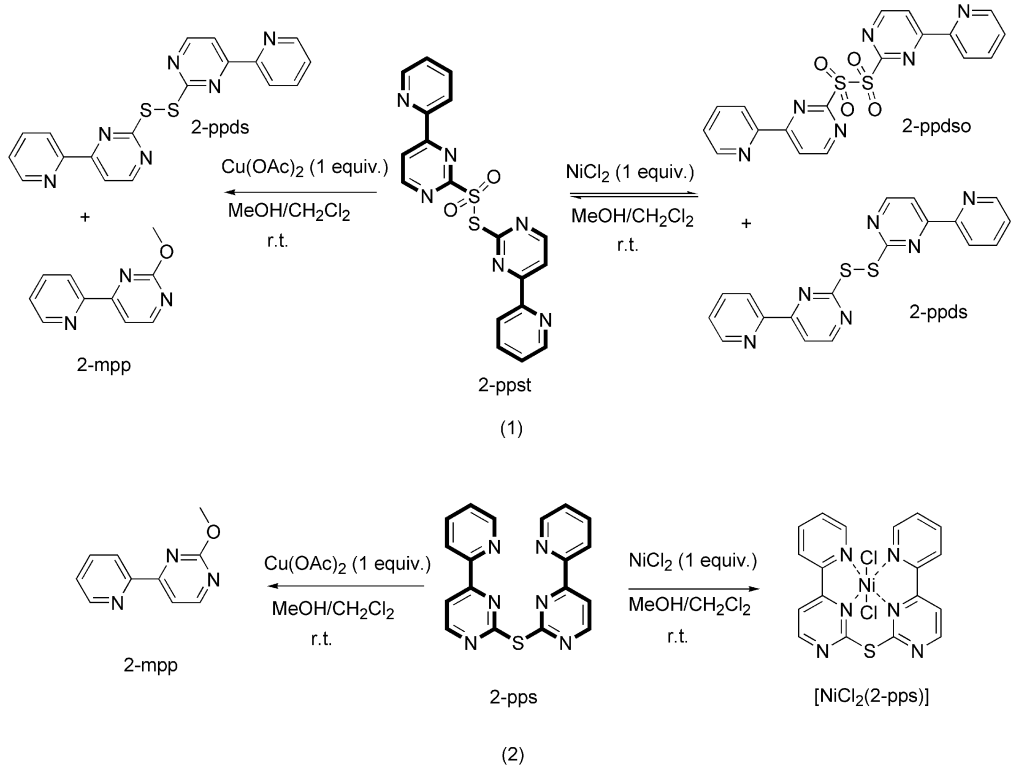
Scheme 2. Reaction diversity (1) and controllable selectivity (2) of the in situ $NiCl_2$-mediated reaction of 2-ppds.

the absence of $Cu(OAc)_2$. This suggests that the reaction outcome is closely related to the solvent-coordination ability of the metal ions, which is influenced by the intrinsic coordination number of the metal ion as well as their counterions. With $NiCl_2$, Ni^{2+}, with a preference for square-planar coordination geometry, is coordinated by one bipyridine-like unit and two firmly bound chloride anions, which limits the ligation of the methanol molecule. The acetate anions are weakly coordinating and therefore allow methanol coordination. The Cu^{2+}-induced acceleration may result from its normal penta/hexacoordination, which would allow more methanol molecules to be coordinated compared with Ni^{2+} ions. The difference in solvent-coordination ability may also be used to explain the different reaction rates for methanol, ethanol and isopropyl alcohol as the more bulky the solvent donor, the poorer the coordination ability. However, it should be stressed that the exact roles of AcO^- and Cu^{2+} need more supporting evidence.

The formation of 2-pps and 2-mpp undoubtedly results from in situ S–S and C–S bond scission in 2-ppds. However, elucidation of the reaction mechanism is not an easy task. In fact, the mechanism of S–S bond scission is quite complicated and may occur by several pathways.[9] In the $NiCl_2$-promoted reaction, 2-ppst is postulated as a decisive intermediate in the formation of 2-pps, as has been stated above. Notably, 2-ppst has also been detected in the $Cu(OAc)_2$-mediated in situ reaction. To further disclose the role of 2-ppst in both $NiCl_2$- and $Cu(OAc)_2$-mediated reactions, confirmatory experiments were carried out in which 2-ppst was treated with 1 equiv. of $NiCl_2$ or $Cu(OAc)_2$ in MeOH/CH_2Cl_2. In the case of $Cu(OAc)_2$, 2-ppst was completely converted into 2-mpp and 2-ppds, which indicates that 2-ppst is critical for the formation of 2-mpp. In contrast, in the case of $NiCl_2$, it was found that 2-ppst is in equilibrium with 2-ppds and a new species 2-ppdso {2-ppdso = bis[4-(pyridin-2-yl)pyrimidin-2-yl]disulfone} and that no 2-pps was generated from this reaction. But the reaction could subsequently be propelled to produce 2-pps with the aid of air bubbling. It seems that the conversion from 2-ppst to 2-pps is driven not only by Ni^{2+} coordination, but also by other factors. Furthermore, the coexistence of 2-ppds, 2-ppst and 2-ppdso suggests that a homolytic reaction takes place at the S–S bond of 2-ppst. Interestingly, the reactions of 2-pps with $NiCl_2$ or $Cu(OAc)_2$ also displayed disparate results. Treatment of 2-pps with $NiCl_2$ rapidly gave the insoluble [$NiCl_2$(2-pps)]. In contrast, 2-pps was expediently transformed into 2-mpp on treatment with $Cu(OAc)_2$ under the same conditions (Scheme 4).



Scheme 3. Controllable synthesis of 2-RO-4-(pyridin-2-yl)pyrimidine by the in situ $Cu(OAc)_2$-mediated reaction of 2-ppds (R = Me, Et, *i*Pr).



Scheme 4. In situ reactions of 2-ppst (1) and 2-pps (2) promoted by $NiCl_2$ and $Cu(OAc)_2$.

Conclusions

We have demonstrated the in situ reaction diversity of the S–S bond promoted by metal coordination and specifically elucidated how such in situ reactions can be controlled to selectively produce the desired product. A cascade of reactions, such as oxidation and S–S and C–S bond scission, in 2-ppds has proved the crucial role of metal coordination. The strikingly different reaction results for $NiCl_2$ and $Cu(OAc)_2$ are presumed to emanate from the cooperative effect of the metal cations and their counterions. Future effort will be needed to clarify the detailed mechanism involved in these in situ reactions.

Experimental Section

General: All reagents were used as received without further purification. HPPT2 [HPPT2 = 4-(pyridin-2-yl)pyrimidine-2-thiol] was prepared according to our previously reported method.[7e] Disulfide 2-ppds was obtained according to a modified literature method.[10] All manipulations were undertaken in air unless stated otherwise. Flash chromatography was performed by using silica gel (300–400 mesh). Elemental analyses were conducted with a Perkin–Elmer 1400C analyser. ^1H and ^{13}C NMR spectra were recorded with a Bruker AVANCE-300 spectrometer. Infrared spectra were performed with a Bruker Vector 22 spectrophotometer in KBr pellets in the 400–4000 cm^{-1} region. Electrospray ionization (ESI) mass spectra were performed with a Finnigan MAT SSQ 710 mass spectrometer in the scan range 100–1200 a.m.u.

Preparation of 2-ppds: Over a period of 20 min, a solution of SO_2Cl_2 (0.5 mL) in CH_2Cl_2 (20 mL) was added dropwise to the suspension of HPPT2 (1.89 g, 10.0 mmol) in CH_2Cl_2 (30 mL). After the addition, the mixture was stirred at room temperature for 30 min. The solid was collected by filtration and dissolved in H_2O (30 mL). With a 5% NaOH aqueous solution, the solution pH was adjusted to 8–9 at which a white precipitate was obtained. Yield: 87%. IR (KBr): $\tilde{\nu}$ = 3050 (w), 2993 (w), 1565 (s), 1531 (s), 1419 (s), 1329 (s), 1202 (s), 1178 (m), 1156 (m), 993 (m), 868 (w), 826 (m), 868 (m), 795 (s), 763 (s), 737 (m), 712 (m), 642 (m), 617 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.69–8.67 (d, J = 5.1 Hz, 2 H, $H_{pyrimidinyl}$), 8.65–8.64 (m, 2 H, $H_{pyridyl}$), 8.37–8.34 (d, J = 8.0 Hz, 2 H, $H_{pyridyl}$), 8.11–8.09 (d, J = 5.1 Hz, 2 H, $H_{pyrimidinyl}$), 7.76–7.70 (m, 2 H, $H_{pyridyl}$), 7.36–7.32 (m, 2 H, $H_{pyridyl}$) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 27 °C): δ = 169.3, 163.5, 158.8, 153.0, 149.4, 137.0, 125.5, 121.9, 113.9 ppm. MS (ESI): m/z (%) = 399 (100) $[2\text{-ppds} + Na]^+$. $C_{18}H_{12}N_6S_2$ (376.46): calcd. C 57.43, H 3.21, N 22.32; found C 57.55, H 3.30, N 22.18.

Preparation of $[NiCl_2(2\text{-pps})]$: A CH_2Cl_2 (10 mL) solution of 2-ppds (0.2 mmol, 75.4 mg) was mixed with an MeOH (20 mL) solution of $NiCl_2 \cdot 6H_2O$ (0.2 mmol, 47.7 mg). The mixture was left to stand for 1 d to generate dark-green crystals. The resulting crystals were filtered and dried in vacuo. One of the crystals was chosen for X-ray diffraction analysis.

$[NiCl_2(2\text{-pps})]$: Yield: 32.0 mg (33.8%, based on 2-ppds). IR (KBr): $\tilde{\nu}$ = 3062 (w), 3019 (w), 1581 (s), 1543 (s), 1478 (w), 1412 (m), 1352 (s), 1187 (s), 1115 (w), 1018 (m), 867 (w) 831(w), 797 (m), 757 (m), 732 (m), 657 (w), 637 (w) cm^{-1}. $C_{18}H_{12}Cl_2N_6NiS$ (473.99): calcd. C 45.61, H 2.55, N 17.73; found C 45.37, H 2.72, N 17.58.

Reaction Diversity of the In Situ $NiCl_2$-Mediated Reaction of 2-ppds: A CH_2Cl_2 (60 mL) solution of 2-ppds ligand (940.0 mg, 2.5 mmol) was added to a solution of $NiCl_2$ (596.2 mg, 2.5 mmol) in methanol (120 mL). The mixture was stirred at room temperature for 24 h and then quenched with excess EDTA solution, followed by extrac-

tion with CH_2Cl_2. The CH_2Cl_2 extract was dried with anhydrous $MgSO_4$ and then subjected to flash chromatography (eluting solvent: EtOAc/petroleum ether, 1:4).

2-mpp: Isolated yield: 73.8 mg (7.9%, based on sulfur). R_f = 0.57 (EtOAc/petroleum ether, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.73–8.72 (d, J = 4.4 Hz, 1 H, $H_{pyridyl}$), 8.68–8.66 (d, J = 5.1 Hz, 1 H, $H_{pyrimidinyl}$), 8.52–8.49 (d, J = 8.0 Hz, 1 H, $H_{pyridyl}$), 8.03–8.01 (d, J = 5.1 Hz, 1 H, $H_{pyrimidinyl}$), 7.90–7.85 (m, 1 H, $H_{pyridyl}$), 7.44–7.40 (m, 1 H, $H_{pyridyl}$), 4.12 (s, 3 H, CH_3) ppm. MS (ESI): m/z (%) = 210 (100) [2-mpp + Na]$^+$. $C_{10}H_9N_3O$ (187.20): calcd. C 64.16, H 4.85, N 22.45; found C 64.30, H 4.72, N 22.48.

2-ppst: Isolated yield: 272.4 mg (26.7%, based on sulfur). R_f = 0.50 (EtOAc/petroleum ether, 1:2). IR (KBr): $\tilde{\nu}$ = 3053 (w), 2926 (w), 1559 (s), 1534 (s), 1473 (w), 1419 (s), 1344 (s), 1183 (s), 1081 (w), 993 (w), 858 (w) 826(w), 795 (w), 764 (m), 743 (w), 713 (w), 640 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.78–8.76 (d, J = 5.2 Hz, 2 H, $H_{pyrimidinyl}$), 8.74–8.72 (d, J = 4.8 Hz, 2 H, $H_{pyridyl}$), 8.64–8.62 (d, J = 7.9 Hz, 2 H, $H_{pyridyl}$), 8.20–8.18 (d, J = 5.2 Hz, 2 H, $H_{pyrimidinyl}$), 7.93–7.88 (m, 2 H, $H_{pyridyl}$), 7.46–7.42 (m, 2 H, $H_{pyridyl}$) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 27 °C): δ = 169.8, 164.0, 159.0, 153.2, 149.6, 137.2, 125.8, 122.3, 114.5 ppm. MS (ESI): m/z (%) = 431 (100) [2-ppst + Na]$^+$. $C_{18}H_{12}N_6O_2S_2$ (408.46): calcd. C 52.93, H 2.96, N 20.58; found C 52.97, H 2.92, N 20.55.

2-ppds: Isolated yield: 232.3 mg (24.7%, based on sulfur). R_f = 0.37 (EtOAc/petroleum ether, 1:2).

2-pps: Isolated yield: 288.3 mg (33.5%, based on sulfur). R_f = 0.20 (EtOAc/petroleum ether, 1:2). IR (KBr): $\tilde{\nu}$ = 3055 (w), 2930 (w), 1560 (s), 1535 (s), 1473 (w), 1411 (m), 1338 (s), 1176 (s), 1080 (w), 995 (m), 855 (w) 828 (w), 795 (m), 761 (m), 741 (m), 714 (w), 642 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.82–8.80 (d, J = 5.2 Hz, 2 H, $H_{pyrimidinyl}$), 8.72–8.70 (m, 2 H, $H_{pyridyl}$), 8.33–8.31 (m, 2 H, $H_{pyridyl}$), 8.25–8.23 (d, J = 5.2 Hz, 2 H, $H_{pyrimidinyl}$), 7.77–7.72 (m, 2 H, $H_{pyridyl}$), 7.40–7.36 (m, 2 H, $H_{pyridyl}$) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 27 °C): δ = 168.6, 164.0, 159.0, 153.3, 149.5, 137.0, 125.6, 122.0, 114.8 ppm. MS (ESI): m/z (%) = 367 (100) [2-pps + Na]$^+$. $C_{18}H_{12}N_6S$ (344.39): calcd. C 62.77, H 3.51, N 24.40; found C 62.73, H 3.49, N 24.38.

Controllable Syntheses of 2-pps: A CH_2Cl_2 (20 mL) solution of 2-ppds ligand (0.4 mmol) was added to a solution of $NiCl_2$ (0.4 mmol) in methanol (40 mL). The mixture was stirred and bubbled with air continuously. After 24 h, the reaction mixture was quenched with excess EDTA solution and then extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried with anhydrous $MgSO_4$ and then subjected to flash chromatography (eluting solvent: EtOAc/petroleum ether, 1:2) to yield 2-pps and 2-mpp in 83 and 6% yields, respectively.

Controllable Syntheses of 2-RO-4-(pyridin-2-yl)pyrimidine [R = Me (2-mpp), Et (2-epp), *i*Pr (2-ppp)]: A CH_2Cl_2 (20 mL) solution of 2-ppds ligand (0.4 mmol) was added to a solution of $Cu(OAc)_2$ (0.4 mmol) in methanol (40 mL). After stirring for 12 h, the reaction mixture was quenched with excess EDTA solution and then extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried with anhydrous $MgSO_4$ and then subjected to column chromatography (eluting solvent: EtOAc/petroleum ether, 1:2) to yield 2-mpp in 91% yield. According to the same procedure, substitution of EtOH for MeOH afforded 2-epp in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.72–8.70 (d, J = 3.9 Hz, 1 H, $H_{pyridyl}$), 8.65–8.63 (d, J = 5.0 Hz, 1 H, $H_{pyrimidinyl}$), 8.51–8.49 (d, J = 8.0 Hz, 1 H, $H_{pyridyl}$), 8.00–7.98 (d, J = 5.0 Hz, 1 H, $H_{pyrimidinyl}$), 7.88–7.82 (m, 1 H, $H_{pyridyl}$), 7.42–7.38 (m, 1 H, $H_{pyridyl}$), 4.57–4.50 (q, J = 7.1 Hz, 2 H, OCH_2), 1.52–1.47 (t, J = 7.1 Hz, 3 H, CH_3) ppm. MS (ESI): m/z (%) = 224 (100) [2-epp + Na]$^+$. $C_{11}H_{11}N_3O$ (201.22): calcd. C 65.66, H 5.51, N 20.88; found C 65.70, H 5.62, N 20.68. Replacement of MeOH by *i*PrOH produced 2-ppp in 83% yield after 3 d. ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.71–8.70 (d, J = 3.8 Hz, 1 H, $H_{pyridyl}$), 8.64–8.63 (d, J = 5.0 Hz, 1 H, $H_{pyrimidinyl}$), 8.50–8.47 (d, J = 8.0 Hz, 1 H, $H_{pyridyl}$), 7.97–7.96 (d, J = 5.0 Hz, 1 H, $H_{pyrimidinyl}$), 7.87–7.81 (m, 1 H, $H_{pyridyl}$), 7.42–7.37 (m, 1 H, $H_{pyridyl}$), 5.44–5.37 (m, 1 H, CH), 1.47–1.45 (d, J = 6.2 Hz, 6 H, CH_3) ppm. MS (ESI): m/z (%) = 238 (100) [2-ppp + Na]$^+$. $C_{12}H_{13}N_3O$ (215.25): calcd. C 66.96, H 6.09, N 19.52; found C 66.79, H 6.12, N 19.58.

Confirmatory Experiments

In Situ Reaction of 2-ppst with $NiCl_2$: A CH_2Cl_2 (10 mL) solution of 2-ppst (0.2 mmol, 81.9 mg) was mixed with an MeOH (20 mL) solution of $NiCl_2{\cdot}6H_2O$ (0.2 mmol, 47.7 mg). The mixture was stirred overnight, quenched with a saturated EDTA solution and extracted with CH_2Cl_2. The extract was dried with anhydrous $MgSO_4$ and subjected to flash chromatography (eluting solvent: EtOAc/petroleum ether, 1:3). The two major products 2-ppds and 2-ppdso were isolated in 33 and 37% yields (based on 2-ppst), respectively.

2-ppdso: Isolated yield: 37%. R_f = 0.27 (EtOAc/petroleum ether, 1:2). IR (KBr): $\tilde{\nu}$ = 3055 (w), 1559 (s), 1533 (s), 1473 (w), 1420 (s), 1344 (s), 1187 (s), 1147 (w), 1085 (w), 993 (w), 854 (w), 827(w), 794 (w), 763 (m), 741 (w), 714 (w), 640 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.62–8.60 (m, 2 H), 8.49–8.46 (m, 4 H), 7.97–7.96 (d, J = 5.1 Hz, 2 H), 7.83–7.77 (m, 2 H), 7.38–7.34 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 27 °C): δ = 169.5, 163.4, 158.4, 152.7, 149.3, 137.0, 125.7, 122.2, 113.9 ppm. MS (ESI): m/z (%) = 463 (100) [2-ppdso + Na]$^+$. $C_{18}H_{12}N_6O_4S_2$ (440.46): calcd. C 49.08, H 2.75, N 19.08; found C 49.12, H 2.72, N 19.38.

In Situ Reaction of 2-ppst with $Cu(OAc)_2$: The in situ reaction between 2-ppst and 1 equiv. of $Cu(OAc)_2$ was performed in the same manner as the above. The resulting dark-brown solution was quenched with a saturated EDTA solution and then extracted with CH_2Cl_2. The two major products 2-ppds and 2-mpp were separated by flash chromatography in 45 and 36% yields, respectively.

In Situ Reaction of 2-pps with $NiCl_2$: A CH_2Cl_2 (10 mL) solution of 2-pps (68.8 mg, 0.2 mmol) was mixed with an MeOH (20 mL) solution of $NiCl_2{\cdot}6H_2O$ (47.7 mg, 0.2 mmol). The mixture was stirred overnight to give a green suspension. The precipitated solid of [$NiCl_2$(2-pps)] was collected by filtration and dried in vacuo. Yield: 93%.

In Situ Reaction of 2-pps with $Cu(OAc)_2$: In situ reaction of 2-pps with $Cu(OAc)_2$ was carried out in the same way as that with $NiCl_2$. The resulting dark-brown solution was quenched with a saturated EDTA solution. The CH_2Cl_2 extract was subjected to flash chromatography to give the main product of 2-mpp in 62% yield.

X-ray Crystallographic Study: Diffraction intensities for [$NiCl_2$(2-pps)] were collected at 298(2) K with a Bruker SMART CCD-4K diffractometer by employing graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). The data were collected by using SMART[11] and reduced by the SAINT program.[12] All the structures were solved by direct methods and refined by full-matrix least-squares methods on F_{obs}^2 using the SHELXTL software package.[13] All the non-hydrogen atoms were refined anisotropically, whereas all the hydrogen atoms were calculated by geometrical methods and refined as a riding model. CCDC-725564 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[$NiCl_2$(2-pps)]: $C_{18}H_{12}Cl_2N_6NiS$, M = 474.00, monoclinic, space group $C2/c$ (no. 15), a = 14.622(2), b = 10.311(1), c = 13.351(1) Å, β = 112.681(1)°, V = 1857.1(3) Å^3, Z = 4, T = 298(2) K, $F(000)$ = 960, D_c = 1.695 g cm^{-3}, μ(Mo-K_α) = 1.463 mm^{-1}, R_1 = 0.0272, wR_2 = 0.0721 [$I > 2\sigma(I)$], GOF = 1.08.

Supporting Information (see also the footnote on the first page of this article): MS (ESI) and NMR spectra for the organic compounds reported in this paper.

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