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ARTICLE

Synthesis of a new series of Ni(II), Cu(II), Co(II) and Pd(II) complexes with an ONS donor Schiff base: Crystal Structure, DFT study and catalytic investigation of Palladium and Nickel complexes towards deacylative sulfenylation of active methylenes and regioselective 3-sulfenylation of indoles via thiouronium salt formation

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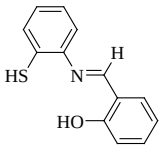
A series of Ni(II), Cu(II), Co(II), and Pd(II) complexes have been synthesized with a chelating Schiff base ligand coordinated to metal center with ONS donor atoms. The ligand and complexes are characterized with elemental analysis and spectroscopic techniques like FT-IR, ^{1}H-NMR, UV–Visible spectroscopy. The single crystal structure of Pd(II) complex is obtained by X-ray diffraction analysis and exhibits slightly distorted square planar geometry. The structure is optimized by DFT; TD-DFT calculation to elaborate the electronic structure and NBO for charge distribution analysis of the Pd(II) complex. The synthesized Pd(II) and Ni(II) complexes as catalyst have been investigated in C-S cross coupling of indoles and active methylenes. The metal propelled regioselective transformation afforded 3-sulfenylated indoles while, β-diketones favored deacylated monosulfenyl ketones in excellent yield via thiouronium salt formation. Pd(II) complex displays slightly better reactivity whereas Ni(II) complex is cost-efficient. The method is fast, easy to handle and cost effective in terms of high reactivity of catalyst, use of non-toxic solvent, and cheaper aryl halides and thiourea replace conventional sulfur sources, providing a practical access to organic transformations.

Introduction

The Schiff base ligands and their metal complexes enfold a fascinating background in clinical, biological, industrial and analytical field.[1] They inspire chemists all over the world due to opportunities for inducing substrate chirality, tuning the metal-centered electronic factor and enhancing stability of either homogeneous or heterogeneous catalyst. The N,S donor Schiff base complexes are important, because they have mimic characteristics of biologically significant metalloenzymes.[2] Complexes of ONS-chelating ligands display interesting physico-chemical properties, pronounced biological activities and act as models of metalloenzyme active sites.[3] Schiff bases from salicylaldehyde and ortho-substituted amine meet the requirements of forming chelate complexes (**Fig. 1**). This type of ligands form salen complexes with various transition metals, especially with Cu metal salts.[4]

Chelated transition metal complexes are valued because of their wide applications in various fields.[5] The ONS-donor ligand stabilizes synthesis of both Cu(II) and Cu(I) complexes owing to weak π-accepting nature and varied softness of donor atoms.[6] Ni(II) complexes incorporating thioether and imine donors have relevant properties of metalloproteins and applicable in redox protein design.[7] The Ni(II) complex of 2-acetylpyridine Schiff base of S-methyl dithiocarbazat is applicable in P388 Lymphocytic Leukaemia test system.[8]



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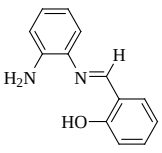
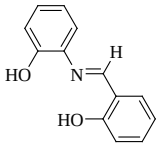


N-salicylidene-1,2-diaminobenzene



N-salicylidene-2-aminophenol

Fig. 1 Examples of chelate ligands

Transition metal Schiff base complexes find applications in cross-coupling reactions[9] especially in thiolation reactions. The Cu complexes of O,N donor Schiff bases deal with thiolation and selenation of aryl/alkenyl halides.[6e,10] Nickel in presence of phosphine ligand, catalyzes Csp^2-S bond formation.[11]

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Sometimes as precatalyst, Ni(II) also replaces palladium complexes.

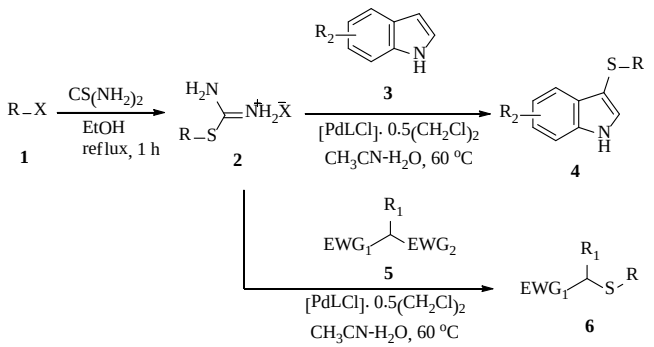
Metal complexes of palladium with ONS-donor Schiff bases display marked catalytic reactivity in organic transformations such as polymerization of ethylene, oxidation, epoxidation, allylic alkylation, Heck reaction and Suzuki–Miyaura coupling reactions etc.[9b,12] Palladium also catalyzes thiolation of aryl and heteroaryl C-H bonds due to its stereo-specific nature, functional group tolerance and ability towards rapid conversion and high yield.[13]

Many synthetic procedures have been developed till date for direct C–H bond sulfenylation of indole rings. The significant metal catalyzed procedures include either salts or complexes of vanadium,[9c] palladium,[14] indium,[15] copper,[16] Iron[17] ruthenium,[18] magnesium[19] and cerium[20] etc. Despite the significance, these metal assisted transformations are less popular, often due to high catalyst load, use of additives and high heat conditions. Transition metal Schiff base complexes help limit these drawbacks with its excellent catalytic nature. High thermal and moisture stability of these complexes attribute applications in temperature sensitive reactions (>100°C).[1g] The metal Schiff base complexes involve simplified reaction techniques, cheaper solvents, and reduce side reactions by reducing high temperature. The Pd(II) Schiff base complexes make a worthy contribution over metal salt to inhibit palladium black formation under basic condition,[21] also use of copper or silver as additives[14,22] in a reaction are often restricted.

Despite of being well liked, these transition metal Schiff base complexes are never explored in indole sulfenylation reactions. Just like indoles, sulfenylation of diketones are also important as they are intermediates in alkylation,[23] epoxidation,[24] ring cleavage reactions[25] etc.[26] However, little information is available on metal assisted C-H thiolation of active methylene compounds.[27]

Sulfenylation reactions mostly require conventional sulfur sources e.g. thiols,[9c] disulfides, sulfenyl halides[14b,27a] and arylsulfonyl chlorides[16a] etc.[14a] An alternative to these sulfur sources are highly anticipated to avoid shortcomings of unstable and pricey reagents, excess reagent load and toxicity, awful-smell, long reaction time, and requirement of an inert atmosphere. Aryl halides and thiourea together can be an excellent replacement; however, the single report of using aryl halide in indole sulfenylation required cu-metal and DMAP as a ligand, along with chlorinated additives, strong base and high heat condition.[16c] To overcome these limitations, metal Schiff base complexes can be used along with thiouronium salt as a sulfur precursor.

In this report, we have investigated synthesis and characterization of a novel ONS-donor Schiff base from 3-bromo-5-chloro-2-hydroxybenzaldehyde and 2-(benzylthio) aniline, and a series of stable metal complexes from the ligand with Cu(II), Ni(II), Co(II), and Pd(II) ions. The geometry of the Pd(II) complex is confirmed by single crystal X-ray study and electronic structure is supported by DFT calculation. TD-DFT is used to simulate the experimental electronic spectra of the complex. The catalytic excellency of Pd(II) and Ni(II) complexes have been witnessed in regioselective 3-sulfenylation of indoles and deacylative C-S cross coupling of active methylenes via thiouronium salt as an intermediate, synthesized from aryl halides and thiourea (**Scheme 1**).



Scheme 1. General scheme for synthesis of 3-sulfenyl indoles and monosulfenyl ketones.

Experimental

Materials and methods

All chemicals were used without further purification. Nickel chloride hexahydrate, copper nitrate trihydrate, cobalt acetate tetrahydrate were purchased from Merck India and 3-bromo-5-chloro-2-hydroxybenzaldehyde and sodium tetrachloropalladate were purchased from Alfa Aesar. Substituted Indoles and active methylenes were purchased from Alfa Aesar, Sigma-Aldrich and E. Merck; solvents used were extra pure grade purchased from Merck India and dried by the reported procedure.[28] 2-(Benzylthio) aniline was prepared according to a literature method.[29]

Physical measurements

Elemental analyses were recorded on a Perkin-Elmer Model 240C elemental analyser. Electronic spectra were measured on a Cary 100 Bio UV–Visible spectrophotometer. Magnetic susceptibilities were measured on a conventional Gouy balance using freshly prepared $Hg[Co(NCS)_4]$ as the calibrant with a Magway MSB MK1 magnetic susceptibility balance, Sherwood Scientific, Cambridge, UK. Infrared spectra of the ligand and complexes were recorded on a Bruker 3000, Hyperion Microscope with Vertex 80 FTIR System with KBr pellets. Melting points were recorded on a Veego melting point apparatus and were uncorrected. The ^1H & ^{13}C NMR spectra were recorded on a Varian, Mercury Plus 400 MHz & Bruker 500 MHz Nuclear Magnetic Resonance (NMR) Spectrometer in $CDCl_3$ solution, using TMS as the internal standard.

Synthesis

Synthesis of Ligand HL. To an ethanol dissolved solution of 2-(Benzylthio) aniline (0.215 g, 1 mmol), another ethanolic solution of 3-bromo-5-chloro-2-hydroxybenzaldehyde (0.235 g, 1 mmol) was added dropwise with continuous stirring. The resulting solution was refluxed at 60 °C for 1 h and completion of the reaction was monitored through TLC. The solution was kept overnight at 0 °C to provide a brown amorphous powder; the precipitate was filtered off, washed with 25% ethanol-water and dried in vacuum (10^{-2} torr). Yield was almost quantitative. M.P: 198 °C. IR (KBr, cm^{-1}) 3425 (m),

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1610 (s), 1441 (s), 1164 (s), 762 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.95 (1H, s, OH), 8.93 (1H, s, CH=N), 7.21-7.63 (11H, m, Ar-H) and 4.11 (2H, s, CH_2). ^{13}C NMR ($CDCl_3$, 500 MHz): δ 40.66, 115.54, 117.23, 122.28, 125.85, 127.13, 127.40, 127.79 (2C), 128.75 (2C), 129.29, 129.68, 133.46, 136.25, 137.12, 137.70, 155.65, 159.44, 160.25. UV-Vis [DMF, λ_{max}, nm (ε_{max}, $Lmol^{-1}cm^{-1}$)]: 220 (12250), 317 (8670), 390 (10370), 466 (3580). Anal. Calc. for $C_{20}H_{15}BrClNOS$ C, 55.51; H, 3.49; N, 3.24; S, 7.41; O, 3.70. Found: C, 54.95; H, 3.31; N, 3.02; S, 7.19; O, 4.10.

Synthesis of complexes

[NiL_2] complex. To a basic solution (NaOH 0.08 g, 2 mmol) of ligand HL (0.864 g, 2 mmol) in hot methanol, another methanolic $NiCl_2.6H_2O$ solution (0.237 g, 1 mmol) was added dropwise with continuous stirring. The mixture was stirred for 1 h and color of the solution changed to dark brown. The solution was concentrated to half of its volume. A brown precipitate was formed, washed several times with 25% methanol-water to remove impurities and dried under vacuum at 10^{-2} torr (Purity was checked by TLC). Yield 69%; MP: > 300 °C. IR (KBr, cm^{-1}): 1605 (s), 1440 (s), 1137 (s), 756 (s). UV-Vis [DMF, λ_{max}, nm (ε_{max}, $Lmol^{-1}cm^{-1}$)]: 234 (18260), 278 (15395), 334 (9600), 470 (5420). Anal. Calc. for $C_{40}H_{28}Br_2Cl_2N_2NiO_2S_2$: C, 52.10; H, 3.06; N, 3.04; S, 6.95; O, 3.47. Found: C, 51.89; H, 3.10; N, 2.88; S, 6.72; O, 3.15.

[CuL_2] complex. [CuL_2] complex was prepared by the same procedure as [NiL_2] complex with $Cu(NO_3)_2.3H_2O$ (0.199 g, 1 mmol). The dark-green solution obtained after completion of the reaction was kept undisturbed for 2 days and a green precipitate could be derived. The precipitate was washed with 25% methanol-water and dried under vacuum at 10^{-2} torr (Purity was checked by TLC). Yield 70%; MP: > 300 °C. IR (KBr, cm^{-1}): 1600 (s), 1440 (s), 1156 (s), 745 (s). UV-Vis [DMF, λ_{max}, nm (ε_{max}, $Lmol^{-1}cm^{-1}$)]: 228 (11250), 282 (4725), 338 (2645). Anal. Calc. for $C_{40}H_{28}Br_2Cl_2CuN_2O_2S_2$: C, 51.82; H, 3.04; N, 3.02; S, 6.92; O, 3.45. Found: C, 51.72; H, 2.85; N, 2.75; S, 6.64; O, 3.34.

[CoL_2] complex. [CoL_2] Complex was prepared by the same procedure as [NiL_2] complex with $Co(CH_3COO)_2.4H_2O$ (0.249 g, 1 mmol). The red colored solution obtained after completion of the reaction was kept undisturbed for 2 days. The black precipitate formed was washed several times with 25% methanol-water and dried under vacuum at 10^{-2} torr (Purity was checked by TLC). Yield 65%; MP: > 300 °C. IR (KBr, cm^{-1}): 1598 (s), 1424 (s), 1153 (s), 747 (s). UV-Vis [DMF, λ_{max}, nm (ε_{max}, $Lmol^{-1}cm^{-1}$)]: 228 (11250), 282 (4725), 338 (2645). Anal. Calc. for $C_{40}H_{28}Br_2Cl_2CoN_2O_2S_2$: C, 51.82; H, 3.04; N, 3.02; S, 6.92; O, 3.45. Found: C, 51.68; H, 3.12; N, 2.94; S, 6.71; O, 3.18.

[PdLCl]. 0.5(CH_2Cl_2) complex. In a typical procedure, a $Na_2[PdCl_4]$ solution (0.147 g, 0.5 mmol) in ethanol medium (20 mL) was added dropwise to another warm ethanol solution (25 mL) of ligand, HL (0.194 g, 0.45 mmol). The solution quickly turned red; it was continuously stirred for 1 h at 60 °C over water bath and further allowed to cool. The crystalline solid formed was filtered, washed several times with 25% ethanol-water to remove impurities and dried under vacuum (10^{-2} torr) (Purity was checked by TLC). The orange red needle like crystals of Pd(II) complex, suitable for single crystal XRD analysis were obtained by recrystallization from DCM-hexane solvent system (10:1) after slow evaporation (2 days). Yield 68%; MP: > 300 °C. IR (KBr, cm^{-1}): 1595 (s), 1425 (s), 1150 (s), 745 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.36 (1H, s, CH=N), 6.74-7.34 (11 H, m, Ar-H) and 4.35 (2H, s, CH_2). ^{13}C NMR ($CDCl_3$, 500 MHz): δ41.95, 118.15, 125.94, 126.27, 127.59, 127.91, 128.37 (2C), 128.83, 129.23 (2C), 132.94, 133.86, 134.35, 136.92, 137.53, 138.01, 155.92, 160.26, 164.01. UV-Vis [DMF, λ_{max}, nm (ε_{max}, $Lmol^{-1}cm^{-1}$)]: 282 (8150), 348 (3265), 358 (3045), 446 (2620), 490 (2470). Anal. Calc. for $[C_{20}H_{15}BrCl_2NOPdS].0.5(CH_2Cl_2)$ C, 39.96; H, 2.45; N, 2.27; S, 5.20; O, 2.60. Found: 39.69; H, 2.37; N, 2.09; S, 4.87; O, 2.39.

Crystallographic measurements

X-ray diffraction experiment was carried out with a Bruker APEX-II CCD diffractometer for Pd(II) complex using graphite monochromated Mo-Kalpha radiation (l¼ 0.71073_A, u-scans) at 296 K temperature. Structure was determined by using SHELXS-97 program.[30] Cell measurement and data reduction were done by Bruker SAINT.[31] Multi-scan method (SADABS) was used for absorption corrections.[31a] Full matrix least-squares on F^2 were performed using the SHELXS-97 program. All non-H atoms were refined in anisotropic approximation using reflector with I>2σ (I).

Computational details

The calculations were carried out using Gaussian 09W program package.[32] The molecular structure of the synthesized palladium complex was optimized in the ground state by Density Functional Theory (DFT)[33] using Becke's three parameter hybrid method[34] with the Lee, Yang and Parr correlation functional methods (B3LYP)[35] invoking gradient geometry optimization.[36] LanL2DZ effective core potential (ECP) basis sets were employed for palladium metal and 6-31G* for the remaining atoms (ligand).[37]

Catalytic Activity study

General procedure for [PdLCl]. 0.5(CH_2Cl_2) catalysed sulfenylation of indoles and active methylenes. In a RB flask, a solution of aryl halide (2 mmol) and thiourea (2 mmol) in ethanol medium (5-10 mL) was refluxed for 1 h and after cooling, the solution was evaporated to dryness. The corresponding product S-alkyl isothiourea salt was obtained as a white solid or sticky oil. The product was washed with Et_2O (3 x 5 mL) to remove any dissolved organic impurities. The yield obtained was almost quantitative. The isothiourea salt without purification, further dissolved in minimum water (1-2 mL) and an acetonitrile solution of pd(II) complex (3 mol%) was added to it and continuously stirred for 5 minutes at 60 °C. The respective indole/active methylene solution (0.85 mmol, in acetonitrile) then added to the above mixture and stirring continued. The progress of the reaction was monitored through TLC. The reaction was very fast and it took almost 0.5-2.0 h for completion providing excellent yield of products. The organic layer was extracted with ethyl acetate and dried over anhydrous Na_2SO_4. The solvent then removed under vacuum and the residue was purified by chromatography (eluting with 10:1 hexane/ EtOAc).

Results and discussion

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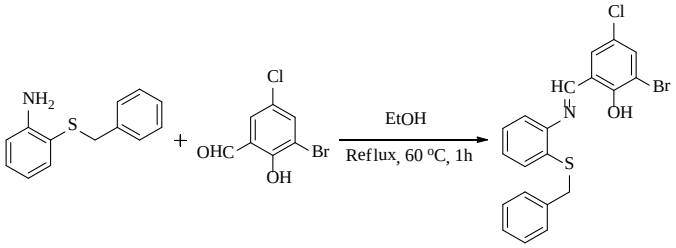
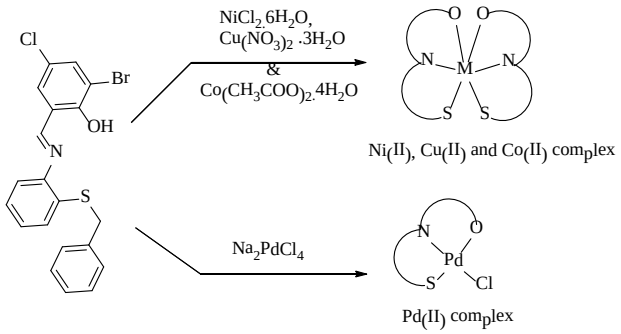
Synthesis

The novel ONS donor Schiff base ligand, HL was synthesized from condensation of 3-bromo-5-chloro-2-hydroxybenzaldehyde and 2-(benzylthio) aniline in absolute ethanol (**Scheme 2**). The ligand, HL is a brown solid, stable in air and soluble in most organic solvents.



Scheme 2 Synthesis of ligand, HL.

The synthesized ligand formed a series of new metal complexes by coordinating with Ni, Cu, Co, and Pd metal centers (**Scheme 3**). A 2:1 molar ratio of Ligand, HL and metal (Ni, Cu and Co) provided complexes of octahedral geometry; whereas Pd(II) complex showed distorted square planar geometry.



Scheme 3 Synthesis of Ni, Cu, Co, Pd complexes with ligand, HL.

The ligand and complexes formed are air stable and non-hygroscopic. They are soluble in common solvents like ethanol, methanol, acetonitrile and DMF. All synthesized compounds are characterized by UV-Vis, FT-IR, and elemental analysis. Moreover, the ligand and Pd(II) complex have been characterized by ^{1}H & ^{13}C-NMR spectroscopy. Molecular structure of the Pd(II) complex is established by the single crystal X-ray diffraction technique. The analytical data shows that, experimental and calculated percentage of elements are in good agreement.

^{1}H & ^{13}C NMR spectra of ligand, HL and Pd(II) complex

In ^{1}H NMR spectra, the signals at 7.21–7.63 and 6.74–7.34 ppm are assigned to aromatic protons of the ligand and Pd(II) complex respectively. For ligand HL, the singlet signal at 13.95 ppm can be assigned to –OH group and disappearance of the signal in spectra of the complex indicates engagement of oxygen atom on complexation.[38] Meanwhile, the singlet peak at 8.93 ppm of the ligand is assigned to -N=CH- group, while for the complex, the chemical shift is slightly up field in 8.36 ppm indicating coordination through nitrogen atom of imine group.[39] The benzylic (-CH_2-) protons are found around 4.11 ppm in case of ligand, although in the Pd(II) complex, the peak has been shifted slightly down field at 4.35 ppm due to bulkier environment on complexation. The ^{13}C NMR spectra for both ligand, HL and Pd(II) complex display 18 different peaks. The signals at 160.25 ppm and 40.66 ppm in ligand, HL can be assigned to imine (-CH=N-) and benzylic (-CH_2-) carbon centers. On complexation, the respective signals shifted slightly downfield to 164.01 and 41.95 ppm.

Magnetic measurement

The magnetic moment (μ_{eff}) of Ni(II) complex is 2.74 BM, close to the spin-only value of 2.83 BM expected for a d^8 system in O_h symmetry. The value obtained for Cu(II) complex is in the expected range (1.84 BM) of a d^9 octahedral configuration.[40] The Co(II) complex shows magnetic value 4.70 BM for high spin octahedral symmetry and Pd(II) complex is diamagnetic.

Electronic Spectra

The electronic spectra of ligand at concentration 10^{-4} M and complexes at concentration $2x10^{-4}$ M in DMF are shown in **Fig. 2**. The electronic spectrum of the ligand shows four peaks at 220, 317, 390 and 466 nm which may be assigned to π-π* transition of the phenyl ring and n-π* transition of imine moiety.[41] However, electronic transitions of complexes are grouped in different spectral zones: 228-282 nm due to π-π* transition of phenyl ring, 278-390 nm appears due to n-π* transition and 421-490 nm may be assigned to MLCT. Complexes show a relatively weak absorption band in the region of 601-652 nm due to ligand field transitions, except Pd(II) complex. However, the expected d-d transitions in complexes are masked by CT absorptions.[42] All electronic spectral data of compounds are listed in **Table 1**.

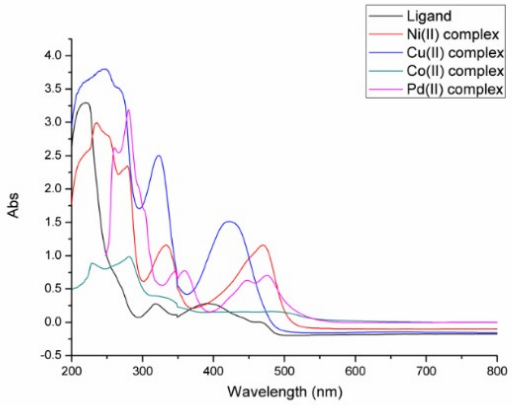


Fig. 2 Electronic spectra of ligand (10^{-4} M), Ni(II) complex ($2x10^{-4}$ M), Cu(II) complex($2x10^{-4}$ M), Co(II) complex($2x10^{-4}$ M), and Pd(II) complex($2x10^{-4}$ M) in DMF.

Table 1 Electronic spectral data of ligand and complexes

Compound	λ nm (ε_{max} $Lmol^{-1}cm^{-1}$)
Ligand	220 (12250), 317 (8670), 390 (10370), 466 (3580)
Ni(II) complex	234 (18260), 278 (15395), 334 (9600), 470(5420)
Cu(II) complex	247 (17450), 320 (13655), 421 (9340)
Co(II) complex	228 (11250), 282 (4725), 338 (2645), 514 (1450)
Pd(II) complex	282 (8150), 348 (3265), 358 (3045), 446 (2620), 490 (2470)

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Table 2 Characteristics infrared spectral bands of all synthesized compounds

Compd.	ν(O-H) (cm^{-1})	ν(C=N) (cm^{-1})	ν(C=C) (cm^{-1})	ν(C-O) (cm^{-1})	ν(C-S) (cm^{-1})
Ligand	3425	1610	1441	1164	762
Ni(II) complex	-	1605	1440	1137	756
Cu(II) complex	-	1600	1440	1156	745
Co(II) complex	-	1598	1424	1153	747
Pd(II) complex	-	1595	1425	1150	745

Table 3 Crystal structure and structure refinement details of the Pd(II) complex

Compound	Pd(II) complex
CCDC entry no.	1521756
Empirical formula	$C_{41}H_{30}Br_2Cl_6N_2O_2Pd_2S_2$
Formula weight	1232.11
T (K)	296(2)
λ (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	
a (Å)	10.6104(7)
b (Å)	19.4262(12)
c (Å)	21.1694(14)
α (°)	90.00
β (°)	98.098(4)
γ (°)	90.00
V ($Å^3$)	4319.9(5)
Z	4
D_{calc} (Mg/m^3)	1.894
μ (mm^{-1})	3.190
F (0 0 0)	2408.0
Crystal size (mm^3)	0.33 x 0.27 x 0.21
θ(°)	3.61-16.93
Index ranges	-14 ≤ h ≤ 14
	-26 ≤ k ≤ 19
	-28 ≤ l ≤ 28
Reflections collected	31336
Independent reflections (R_{int})	11068(0.1153)
Completeness (%)	98.5
Absorption correction	multi-scan(SADABS)
Max and min transmission	0.4192 and 0.5540
Refinement method	Full matrix least-squares on
Data/restraints/parameters	F^2
Goodness-of-fit on F^2	11068/0/514
Final R indices [I>2σ(I)]	0.929
R indices (all data)	R1=0.0656, wR2=0.1178
Largest difference in peak and hole($eÅ^{-3}$)	R1=0.1564, wR2=0.1527
	0.687/-1.147

Infrared Spectra

In the IR spectrum of ligand, HL the band at 1610 cm^{-1} confirms the presence of an azomethine group (>C=N-). The ligand shows a broad peak at 3425 cm^{-1} for phenolic O-H bond and strong peaks at 1441 cm^{-1} and 1164 cm^{-1} are attributed to C=C and C-O bonds respectively. Band at 762 cm^{-1} can be assigned to thioether stretch. In the IR spectra of Ni(II), Cu(II), Co(II) and Pd(II) complexes, the bands in the range of 1598-1605 cm^{-1} are associated with υ(>C=N-) vibration. Shifting of frequency of υ(>C=N-) by 6-7 cm^{-1} compared to corresponding band of the ligand indicates coordination via oxygen atom and deprotonation upon complexation. Moreover, phenolic C-O and C-S band in complexes also shifted from 1164 cm^{-1} and 762 cm^{-1} compared to ligand, indicating coordination via sulfur and oxygen atoms.[43] Some specific assigned bands for the ligand and complexes are summarized in **Table 2** (Spectra provided in SI).

X-ray crystallography

In quest of molecular structure of Pd(II) complex, the binding pattern and crystal arrangements have been investigated by single crystal X-ray diffraction studies. Crystal data and structure refinements of Pd(II) complex are given in **Table 3**. The crystals of Pd(II) complex was obtained through slow diffusion of hexane into DCM solution. Prospective view of molecular structure of the complex is shown in **Fig. 3**. The Pd(II) Complex crystallizes in monoclinic space group P2(1)/c, contains two molecules in the asymmetric unit. Also, one DCM molecule observed in asymmetric unit of the crystal lattice, it may attach during recrystallization from DCM. The Pd(II) atom is tetracoordinated in a distorted square planner geometry by one Schiff base anion ligand and one chlorine atom. The Schiff base ligand, HL coordinates to the metal ion through thioether sulfur, imine N and phenolic O atom; in this process the ligand loses one hydrogen atom from phenolic –OH group. All important bond lengths and bond angles of Pd(II) complex are listed in **Table 4**. The imine double bond is in trans-geometry, which allows nitrogen to donate to the Pd metal atom. The C=N bond length is in expected range of typical coordinated C=N bond. The Pd–S and Pd–O bond lengths show good trend with regular Pd–S and Pd–O bond lengths.[44]

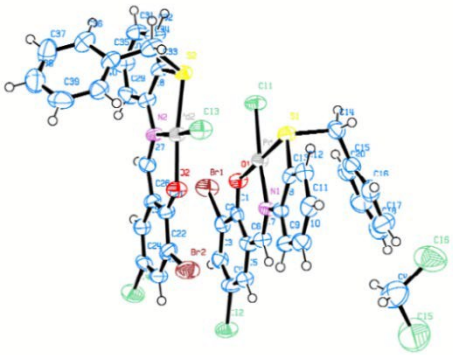

Fig. 3 Molecular structure of Pd(II) complex, shown with 50 % probability ellipsoids.

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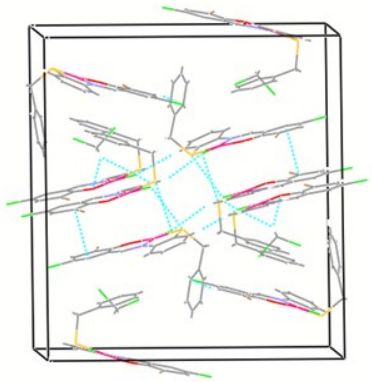

Fig. 4 Crystal packing of Pd(II) complex with non-covalent bonds.

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Table 4 Selected bond lengths (Å) and angles (°) for Pd(II) complex, from the optimized and crystallographic data.

Bond lengths	Expt	Calcd	Bond angles	Expt	Calcd
Pd(1)—O(1)	2.007(4)	2.033	O(1)—Pd(1)—N(1)	94.4(2)	93.144
Pd(1)—N(1)	2.001(5)	2.039	O(1)—Pd(1)—S(1)	177.47(14)	178.904
Pd(1)—S(1)	2.2354(19)	2.317	N(1)—Pd(1)—S(1)	87.07(17)	86.246
Pd(1)—Cl(1)	2.3039(18)	2.369	O(1)—Pd(1)—Cl(1)	88.75(14)	91.353
Pd(2)—O(2)	1.999(5)	2.034	N(1)—Pd(1)—Cl(1)	175.67(17)	174.276
Pd(2)—N(2)	2.000(5)	2.039	S(1)—Pd(1)—Cl(1)	89.66(7)	89.198
Pd(2)—S(2)	2.2326(19)	2.315	O(2)—Pd(2)—N(2)	94.5(2)	93.361
Pd(2)—Cl(3)	2.3021(19)	2.371	O(2)—Pd(2)—S(2)	174.49(15)	179.567
S(1)—C(13)	1.779(7)	1.793	N(2)—Pd(2)—S(2)	86.82(16)	86.338
S(1)—C(14)	1.839(7)	1.880	O(2)—Pd(2)—Cl(3)	89.24(14)	91.186
S(2)—C(33)	1.775(7)	1.792	N(2)—Pd(2)—Cl(3)	174.89(17)	173.971
S(2)—C(34)	1.848(7)	1.879	S(2)—Pd(2)—Cl(3)	89.80(7)	89.091
O(1)—C(1)	1.303(7)	1.286			
O(2)—C(21)	1.828(9)	1.286			
N(1)—C(8)	1.424(8)	1.420			
N(1)—C(7)	1.285(8)	1.305			
N(2)—C(28)	1.422(8)	1.422			
N(2)—C(27)	1.303(8)	1.305			

Table 5 Electronic transitions calculated by the TD-DFT/B3LYP method and experimental absorption bands of Pd(II) complex

The most important orbital excitations	λ(nm)	E (eV)	f	Character	Experimental λ (nm)
HOMO-2→LUMO	497	2.4916	0.0037	Ligand/Pd→Ligand (ILCT, MLCT)	490
HOMO-2→LUMO+1	494	2.5096	0.0142	Ligand/Pd →Ligand/Solvent (ILCT/MLCT)	
HOMO→LUMO+2	441	2.8062	0.0170	Ligand /Solvent→Ligand (ILCT)	446
HOMO→LUMO+3	437	2.8329	0.0685	Ligand/Solvent→Ligand (ILCT)	
HOMO-4→LUMO	359	3.4480	0.0004	Ligand→Ligand/Solvent (ILCT)	358
HOMO-4→LUMO+1	355	3.4875	0.0007	Ligand→Ligand (ILCT)	
HOMO-7→LUMO	349	3.5455	0.0142	Ligand→Ligand/Solvent (ILCT)	348
HOMO-7→LUMO+1	348	3.5853	0.0072	Ligand→Ligand (ILCT)	
HOMO-5→LUMO	345	3.5853	0.0072	Ligand→Ligand/Solvent (ILCT)	
HOMO-12→LUMO+3	290.84	4.2630	0.0427	Ligand/Pd→Ligand (ILCT/MLCT)	285
HOMO-1→LUMO+5	290.71	4.2649	0.0055	Ligand→Ligand/Cl (ILCT, LLCT)	
HOMO-15→LUMO	289.88	4.2770	0.0109	Ligand/Pd→Ligand/Solvent (ILCT/MLCT)	
HOMO-15→LUMO+1	288.21	4.3018	0.0379	Ligand/Pd→Ligand (ILCT/MLCT)	
HOMO-16→LUMO	285.98	4.3354	0.0139	Ligand→Ligand/Solvent (ILCT)	
HOMO-16→LUMO+1	284.90	4.3518	0.0140	Ligand→Ligand (ILCT)	
HOMO-13→LUMO+2	282.34	4.3913	0.0033	Ligand/Pd→Ligand (ILCT/MLCT)	
HOMO-14→LUMO+2	281.60	4.4028	0.0147	Ligand→Ligand (ILCT)	

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The bite angles O(1)–Pd(1)–N(1), N(1)–Pd(1)–S(1), O(1)–Pd(1)–Cl(1) and S(1)–Pd(1)–Cl(1) are 94.4(2), 87.07(17), 88.75(14) and 89.66(7) respectively. Again, angles O(1)–Pd(1)–S(1) and N(1)–Pd(1)–Cl(1) at 177.47(14) and 175.67(17) confirm slightly distorted square planar geometry of the Pd(II) complex. The bond length and bond angles of both the asymmetric unit i.e. Pd(1) and Pd(2) center are not exactly same, this may be due to its position and interaction with the solvent molecule (CH_2Cl_2) present in the crystal. The crystal packing structure is shown in **Fig. 4**.

Computational Study

The geometry of the Pd(II) complex have been optimized using the Density functional theory (DFT) based on B3LYP method in conjugation with 6-31+G* and LANL2DZ basis sets. A TD-DFT calculation is also employed in order to have a better understanding of electronic spectra of the complexes. The calculated bond distances and bond angles are listed in **Table 4**. As shown in **Table 4**, the theoretically calculated bond distances and bond angles are in well agreement with the results obtained from the X-ray diffraction studies, except for a slight discrepancy in O(2)—Pd(2)—S(2) bond angle. The Pd-S bond of the complex shows maximum deviation of 0.081 Å compared to other metal-atom bonds. The HOMO-LUMO diagram of the complex is shown in **Fig. 7**.

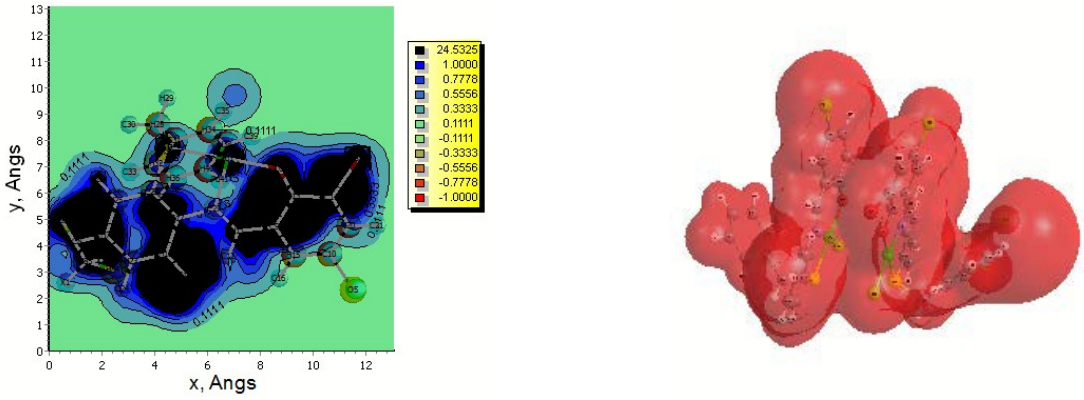

Fig. 5 Charge distribution 2D and 3D diagram of the Pd(II) complex.

The electronic absorption spectra were calculated using the TD-DFT method in acetonitrile solvent employing Polarizable Continuum Model (PCM). The calculated and experimental absorption data, HOMO–LUMO energy gaps, and the character of electronic transitions are given in **Table 5**. In order to have a clear picture and better understanding, we have listed (**Table 5**) all the theoretically calculated transitions that fall within the experimental range. Our TD-DFT calculation predicts two transitions at 497 and 494 nm, which majorly possess MLCT character (along with the least dominant ILCT character) which can be assigned to dπ(M)→pπ(L) transitions**.** These transitions are in excellent agreement with the experimentally calculated transition at 490 nm. On the other hand, the experimental peak at 348 nm, 358 nm, and 446 nm are characterized by set of theoretically calculated bands around 345-349 nm, 355-359 nm, and 437-441 nm respectively. All these transitions possesses ILCT character and can be assigned for pπ(L)→pπ(L) transitions. The experimental peak at 285 nm is explained by set of peak in the range of 281-290 nm, these bands are assigned to a mixture of LLCT, ILCT and MLCT character. The LLCT may be assigned to pπ(L)→pπ(Cl), also some transition to solvent molecule (CH_2Cl_2) occurs. All these results are found to be in good agreement with the experimental electronic spectra.

Charge distribution

The charge distribution analysis is an important tool to elucidate the pattern of electron delocalization from ligand to metal in a complex. In the ligand HL, the charges on N and S are obtained as -0.462 e and 0.271 e respectively. However, on complexation, the negative charge on N reduces to -0.451 e and the positive charge on S increases to 0.429 e. The charge on Pd is found to be 0.379 e which is much lower than its formal charge of +2. All these results confirm that, the ligand transfers its negative charge to the Pd metal on complex formation. In free Pd(II) state, the population of $4d_{xy}$, $4d_{xz}$, $4d_{yz}$, $4d_{x^2-y^2}$ and $4d_{z^2}$ orbitals are 1.999, 1.999, 1.999, 1.4986 and 0.499 e respectively. But on complex formation, the population on $4d_{xy}$, $4d_{xz}$, $4d_{yz}$, $4d_{x^2-y^2}$ and $4d_{z^2}$ orbitals change and attain a value of 1.591, 1.920, 1.652, 1.952 and 1.815 e respectively. It is clearly visible that population is reduced in $4d_{xy}$ and $4d_{yz}$ orbitals and increased in $4d_{x^2-y^2}$ and $4d_{z^2}$ orbitals on complexation. The population of the remaining three orbitals are less affected on

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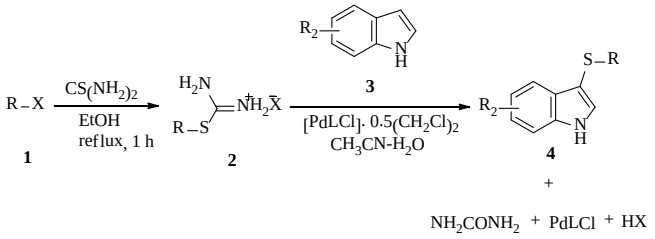
interaction with the metal (Pd). Charge distribution 2D and 3D diagram of the Pd(II) complex are shown in **Fig. 5**.

Catalytic Activity

Pd(II) complex, [PdLCl]. 0.5(CH_2Cl_2) catalyzed regioselective 3-sulfenylation of indoles and deacylative C-S coupling of active methylene compounds. The acclaimed reactivity of Pd(II) complex as a potent catalyst in organic cross-coupling reactions can also be noticed in our report on regioselective synthesis of 3-sulfenylated indoles and sulfenylated carbonyls. Unlike our reported works,[26a,45] we have used readily accessible aryl halide and thiourea as a replacement of aryl thiol or disulfide, to introduce arylthio- groups to the investigated heterocycles. The reaction proceeds through S-aryl isothiouronium chloride salt **2** formation and its coupling with substituted indole derivatives, **3** provided desired 3-sulfenylated products, **4** (**Scheme 4**).

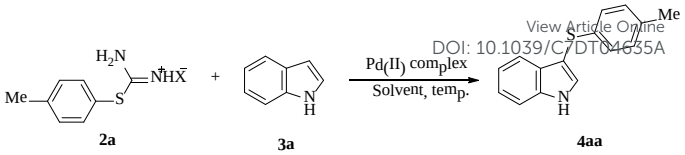


Scheme 4 Palladium complex assisted sulfenylation of indoles

The reaction optimization started with treatment of S-(4-methylphenyl) isothiouronium chloride **2a** and indole **3a** as model substrates. The isothiourea salt **2a** found insoluble in most of the non-polar organic solvents; it was prepared by refluxing 1:1 ratio of 4-methylphenyl chloride and thiourea in ethanol medium. Without purification, the salt **2a** was dissolved in minimum water (1-2 mL) and a solution of indole (**3a**) and Pd(II) complex (3 mol%) in acetonitrile (10-12 mL) was added to it with continuous stirring maintained at 60 °C. The salt **2a** did not completely dissolve in water. A 1:1:0.85 was the required molar amount of aryl halide: thiourea: indole, providing excellent yield of **4aa** (95%, entry 3, **Table 6**). The reaction was monitored through TLC and it took almost 0.5 h for completion. The slight excess of undissolved **2a** could be obtained along with the product **4aa**. The increased molar ratio of indole (1:1:1) could not enhance the product yield and unreacted indole observed on TLC monitoring (entry 2, Table 6), whereas decreased molar ratio (1:1:0.5) provided decreased product yield (70%, entry 6, **Table 6**).

At room temperature, the reaction was slow and provided low yield of **4aa** (65%, entry 1, **Table 6**). Even so, increasing temperature from 60° to 100 °C, the conditions remained unaffected (entry 4, **Table 6**). Maximum yield of this reaction could be obtained when thiouronium salt, **2a** was prepared from 1:1 ratio of aryl halide (2mmol) and thiourea (2 mmol) and treated directly to indole (1.7 mmol) at 60 °C and effectively catalysed by 3 mol% of Pd(II) complex under continuous stirring (**entry 3**, **Table 6**). The entry **3** is considered as the optimum reaction condition.

Table 6 Optimization of reaction conditions[a]



entry	**1a**:$CS(NH_2)_2$: **3a**	Temp (°C)	Solvent	Yield[b] (%)
1	1:1:1	r.t.	CH_3CN-H_2O	65
2	1:1:1	60	CH_3CN-H_2O	94
3	**1:1:0.85**	**60**	**CH_3CN-H_2O**	**95**
4	1:1:0.85	100	CH_3CN-H_2O	96
5	1:1:0.85	60	CH_3CN	Trace
6	1:1:0.5	60	CH_3CN-H_2O	70
7	1:1:0.85	80	PEG-H_2O	88
8	1:1:0.85	60	Toluene-H_2O	-
9	1:1:0.85	100	DMSO-H_2O	55
10	1:1:0.85	60	MeOH-H_2O	40
11	1:1:0.85	60	DCM-H_2O	40
12	1:1:0.85	60	DMC-H_2O	-

[a] 4-methylchlorobenzene (2.0 mmol), thiourea (2.0 mmol), water (2 mL), acetonitrile (10-12 mL), palladium complex (3 mol%), indole (1.7 mmol), 60 °C. [b] isolated yield.

Table 7 Catalyst load[a]

entry	Catalyst	Catalyst load (mol%)	Yield[b] (%)
1	Pd(II) complex	1	64
2	Pd(II) complex	2.0	80
3	Pd(II) complex	**3.0**	**95**
4	Pd(II) complex	5.0	96
5	-	-	0
6	$PdCl_2$	3.0	40
7	$Pd(OAc)_2$	3.0	50
8	$Pd(OAc)_2$	20.0	75
9[c]	Complex 8	3.0	88
10[d]	Complex 9	3.0	75
11	NiL_2	3.0	86
12	NiL_2	5.0	90

[a] 4-methylchlorobenzene (2.0 mmol), thiourea (2.0 mmol), water (2 mL), acetonitrile (10-12 mL), palladium complex (3 mol%), indole (1.7 mmol), 60 °C. [b] isolated yield. [c] nearly 1 h. [d] 1.5-2 h

Further increase in catalyst load (5 mol%) merely had any impact on the reaction (entry 4, **Table 7**), whereas decreasing the catalyst amount, had adverse effect on its yield (entry 1 & 2, **Table 7**). The reaction stopped in the absence of palladium center (entry 5, **Table 7**) indicating its importance. Compared to the metal salts of palladium (entry 6, 7 & 8, **Table 7**), the synthesized Pd(II) complex, **7** found more reactive. The electron cloud around Pd-center from S, N and O-atom of the ligand enhances catalytic efficiency of the complex.

The catalytic behavior of complex **7** was further compared with our previously reported palladium complexes **8** and **9** (**Fig. 6**). We performed our optimized sulfenylation reaction with complexes **8** & **9** (entry 9 & 10, **Table 7**) maintaining other parameters as constant. The complexes were found catalytically active in regioselective 3-

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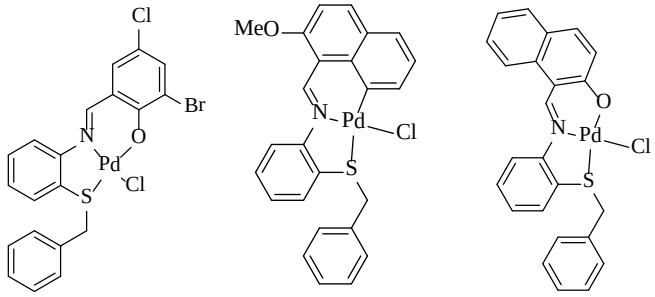
sulfenylation, although less productive than complex **7** and took longer time for completion of the reaction.



7 **8** **9**

Fig. 6 Structure of three Pd catalyst, **7** [PdLCl]. $0.5(CH_2Cl_2)$, **8** (Ref. 5a) and **9** (Ref. 47a).

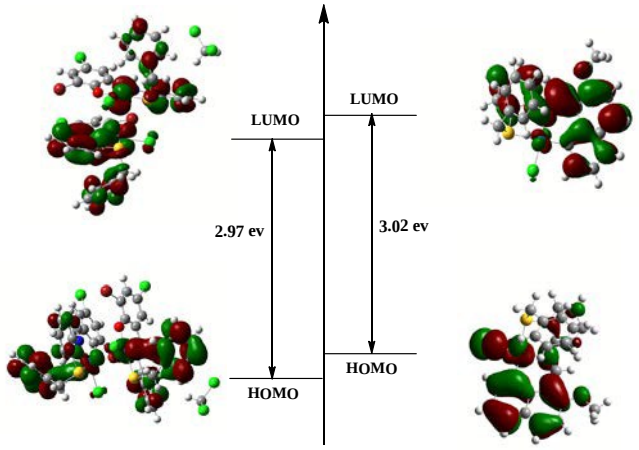


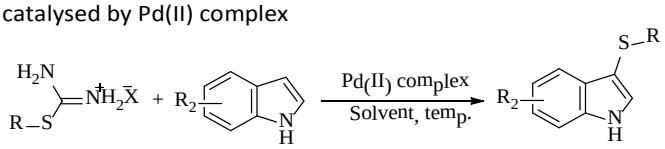
Fig. 7 HOMO-LUMO energy gap comparison of [PdLCl]. 0.5 (CH_2Cl_2), **7** and complex **8**.

The anomaly in reactivity of these complexes can be justified by HOMO-LUMO energy gap as well. It has been established in numerous literature[46] that the HOMO-LUMO gap is a good measure of chemical reactivity and kinetic stability of a molecule. Molecules with a lower energy gap undergo easy excitation leading to kinetic instability and enhanced reactivity. A broad energy gap leads to kinetic stability but less reactivity. The dependence of reactivity on energy gap is justified in our earlier report,[5a] where high reactivity of palladacycle **8** over complex **9** is validated from both theoretical and experimental observation. Thus, in this report palladacycle **8** is taken as a model for computation investigation (**Fig. 7**). The energy gap of complexes **7**, **8** and **9** are 2.97 eV, 3.02 eV and 3.23 eV respectively, which predicts complex **7** as the kinetically least stable and the most reactive complex among all (**Fig.7**).

We also tried our synthesized NiL_2 complex as a catalyst to replace Pd(II) complex, **7** in the optimized reaction. As expected, Ni(II) complex had a very good reactivity and 5 mol% of catalyst load provided 90% of sulfenylated indoles (entry 12, **Table 7**). From **Table 7** we can say that Pd(II) complex, **7** behaves as a highly efficient catalyst providing 95% of yield with only 3 mol% of catalyst load. While, considering its cost effect, we can also use synthesized NiL_2 complex with 5 mol% catalyst load giving 90% of product **4aa**.

The solvent optimization showed that, water in minimum content is essential to dissolve the thiouronium salt, **2a**; whereas, indole and Pd(II) complex were dissolved in respective organic solvents to proceed the reaction. It was found that, water miscible solvents like acetonitrile, PEG, DMSO (entry 3, 7 & 9) etc. are convenient compared to MeOH and THF. DCM (entry 11) and DMC (entry 12) found unsuited for this C-S coupling reaction. The excellent reactivity in acetonitrile medium (entry 3, Table 8) is probably due to its great solubilizing property and suitability of complex mediated transformations in acetonitrile solvent.[39,47]

Table 8 Substrate scope of regioselective 3-sulfenylation catalysed by Pd(II) complex



2 **3** **4**

Sl no	**2**	R	**3**	R_2	**4**	Yield[b] (%)
1	**2a**	4-MePh-	**3a**	-	**4aa**	95
2	**2b**	4-ClPh-	**3a**	-	**4ba**	91
3	**2c**	2-Npth-	**3a**	-	**4ca**	95
4	**2d**	Ph-	**3a**	-	**4da**	93
5	**2e**	1-Npth-	**3a**	-	**4ea**	91
6	**2f**	4-NO_2	**3a**	-	**4fa**	87
7	**2g**	2-NO_2	**3a**	-	**4ga**	83
8	**2h**	4-BrPh-	**3a**	-	**4ha**	92
9	**2b**	4-ClPh-	**3b**	5-Br	**4bb**	86
10	**2i**	4-MeOPh-	**3b**	5-Br	**4ib**	88
11	**2a**	4-MePh-	**3c**	2-Me	**4ac**	90
12	**2d**	Ph-	**3d**	5-Me	**4da**	94
13	**2a**	4-MePh-	**3e**	6-Me	**4ae**	97
14	**2d**	Ph-	**3f**	5-NO_2	**4df**	84
15	**2h**	4-Br	**3g**	5-Cl	**4hg**	86

[a] alkyl halide (2.0 mmol), thiourea (2.0 mmol), water (2 mL), acetonitrile (10-12 mL), palladium complex (3 mol%), indole (1.7 mmol), 60 °C. [b] isolated yield.

To get highly pure product, the vacuum dried mixture was diluted with 10 mL of water and further added diethyl ether to the reaction vessel. The sulfenylated product and the metal complex could be extracted immediately to the ethereal phase leaving **2a** as a suspension in water along with by-products. The organic portion was dried in vacuum and simply passed through a silica column to get product of high purity.

A series of reactions were performed between substituted thiouronium salts **2** and various indoles **3** (**Table 8**) under optimized reaction condition (**Table 6**, **entry 3**). The substrates reacted well and respective products were obtained effortlessly. The electronic effect of the substituents displayed visible impact in terms of reactivity and yield. Electron releasing groups provided better yield of thiolated indoles than deactivating groups. The methyl substituted indoles afforded maximum yield of 97%. Again, halogen (-Cl, -Br) and nitro (ortho and para) substituted indoles afforded desired products without any difficulties.

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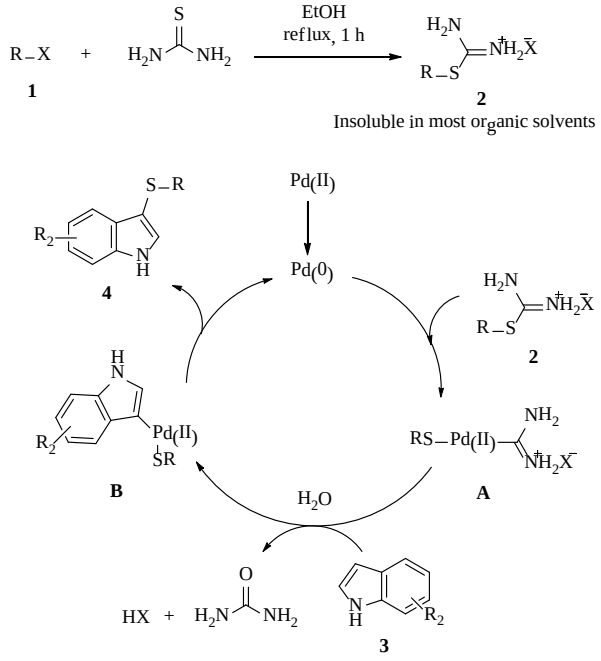
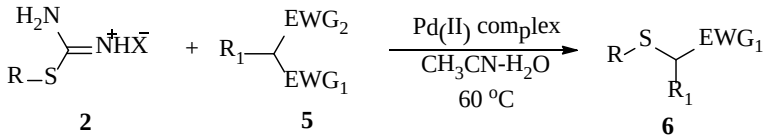


Scheme 5 Plausible reaction mechanism for Pd(II) complex catalysed C-S coupling

A probable mechanism for catalytic sulfenylation of indole is shown in **scheme 5**. The reaction is expected to follow the typical catalytic pathway of palladium catalyzed cross-coupling reactions[13a,48] where a Pd zerovalent species is formed *in situ* from Pd divalent catalyst precursors and Pd(0) corresponds to active starting catalyst in the catalytic cycle.[48] The oxidative addition of isothiourea salt to Pd(0) species probably generates intermediate **A**, which in presence of electron rich indole, **3** in acetonitrile-water medium provides intermediate **B**, releasing urea to the solution. Finally, reductive elimination provides the coupling product, **4** and regenerates the Pd zerovalent species.

Under optimized reaction condition, we have also investigated reaction of diketone compounds, **5** with thiouronium salt **2**. Compared to indoles, reactions with active methylene compounds are bit slower and took almost 1.5-3 h for completion. The reactions undergo deacylative C-S cross-coupling to give α-sulfenyl monoketones as desired product, avoiding thiol or disulfide unlike earlier reports.[45a,e] Reaction of different diketones and substituted thiouronium salts under optimized condition provided excellent yield of products **6** without any hazard. The extension of substrate scope is depicted in **Table 9**. It shows selective elimination of acyl groups upon sulfenylation, clearly visible in case of ethyl acetoacetate and

Table 9 Substrate scope of regioselective 3-sulfenylation catalysed by Pd(II) complex



Sl. No	2	5	R	R_1	EWG_1	EWG_2	6	Yield[b] (%)
1	**2a**	**5a**	4-MePh-	H	MeCO-	MeCO-	**6aa**	96
2	**2b**	**5a**	4-ClPh-	H	MeCO-	MeCO-	**6ba**	92
3	**2d**	**5a**	Ph-	H	MeCO-	MeCO-	**6da**	93
4	**2f**	**5a**	4-NO_2Ph-	H	MeCO-	MeCO-	**6fa**	87
5	**2a**	**5b**	4-MePh-	Me	MeCO-	MeCO-	**6ab**	93
6	**2d**	**5b**	Ph-	Me	MeCO-	MeCO-	**6db**	88
7	**2f**	**5b**	4-NO_2Ph-	Me	MeCO-	MeCO-	**6fb**	85
8	**2g**	**5b**	2-NO_2Ph-	Me	MeCO-	MeCO-	**6gb**	82
9	**2g**	**5c**	2- NO_2Ph-	H	MeCOO-	MeCO-	**6gc**	80
10	**2d**	**5d**	Ph	H	EtCOO-	EtCOO-	**6dd**	85
11	**2g**	**5d**	2-NO_2Ph-	H	EtCOO-	EtCOO-	**6gd**	80
12	**2g**	**5e**	2-NO_2Ph-	H	EtCOO-	MeCO-	**6ge**	83

[a] 4-methylchlorobenzene (2.0 mmol), thiourea (2.0 mmol), water (2 mL), acetonitrile (10-12 mL), palladium complex (3 mol%), active methylene (1.7 mmol), 60°C. [b] isolated yield.

methyl acetoacetate. In absence of acyl group, e.g. in diethylmalonate, EtCOO- (ester) is eliminated. The presence of two flanking groups in active methylene compounds probably inhibit its approach to intermediate **A**, and hence deacylation occurs, also justifying long time required compared to the investigated heterocycles.

Conclusions

Thus, we have synthesized a novel tridentate ONS donor ligand from 2-(Benzylthio) aniline and 3-bromo-5-chloro-2-hydroxybenzaldehyde. The ligand is characterized by spectroscopic study and elemental analysis. Four stable complexes have been synthesized from Ni, Cu, Co, and Pd metal salts. The synthesized complexes are characterized by different analytical methods, viz. UV-Visible, FT-IR, and magnetic measurement. Pd(II) complex formed quality crystals that are suitable for structural (single crystal XRD) analysis and geometry found to be slightly distorted square planar. The geometry of the Pd(II) complex is optimized with DFT method, and the structural parameters are found to be in good agreement with the experimental one. TD-DFT calculation has been used to elaborate the electronic spectra of the Pd(II) complex

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whereas NBO calculation is used for pictorial depiction of charge distribution. Out of the four complexes, Pd(II) and Ni(II) complexes have been investigated in C-S cross coupling reactions. The Pd(II) complex proved to be an excellent catalyst in regioselective 3-sulfenylation of various indoles and synthesis of monosulfenyl ketones from alkyl halides and thiourea. In acetonitrile-water medium, synthesized NiL_2 can also be used as a replacement of Pd(II) to give desired products with slightly less reactivity.

Conflicts of interest

There are no conflicts to declare.

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Supplementary data

CCDC 1521756 contains the supplementary crystallographic data for palladium complex. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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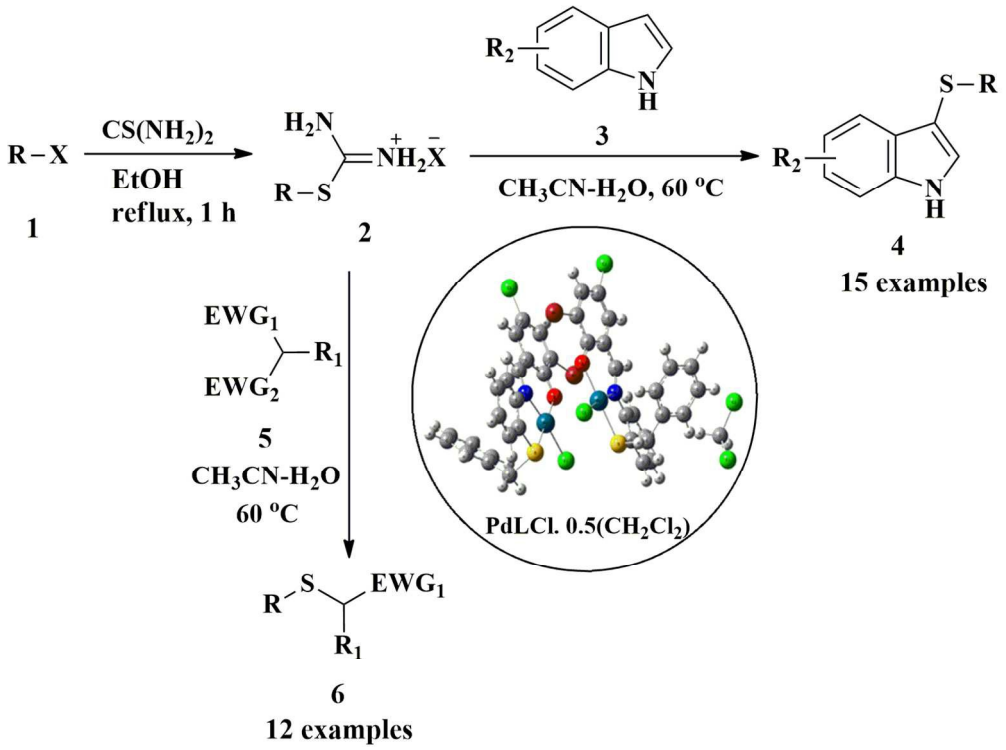

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