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Microwave-Assisted C–C and C–S Couplings Catalysed by Organometallic Pd-SCS or Coordination Ni-SNS Pincer Complexes

CLUSTER ISSUE

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A family of SCS and SNS pincer compounds of the type $[PdCl\{C_6H_3\text{-}2,6\text{-}(CH_2SR)_2\}]$ {R = *t*Bu (**3a**), *s*Bu (**3b**), *i*Bu (**3c**)} and $[NiCl_2\{C_5H_3N\text{-}2,6\text{-}(CH_2SR)_2\}]$ {R = *t*Bu (**4a**), *s*Bu (**4b**)} have been prepared. Among these, complexes **3b**, **3c**, **4a**–**4c** are reported for the first time. Dimeric compounds such as $[NiCl\{C_5H_3N\text{-}2,6\text{-}(CH_2S\mathit{i}Bu)_2\}\mu\text{-}Cl]_2$ (**4c**) were found in the solid state for the nickel complexes with lower steric hindrance exhibiting octahedral metal centers, whereas other nickel structures such as $[NiCl_2\{C_5H_3N\text{-}2,6\text{-}(CH_2S\mathit{t}Bu)_2\}(\mathit{i}PrOH)]$ (**4d**) could also expand their coordination number by coordinating to solvents. The single crystal X-ray diffraction results for **4a**, **4c** and **4d** are presented. The catalytic activity of the six compounds was studied in C–C and C–S cross-coupling reactions under conventional heating and under microwave irradiation conditions. The palladium catalysts enabled good to excellent conversions in Suzuki–Miyaura couplings of *p*-substituted halobenzenes with phenylboronic acid. Comparable yields resulted from application of the nickel complexes in the thioetherification of iodobenzene with different disulfides. The fast increase in reaction temperature associated with microwave irradiation, in combination with the robust pincer catalysts, allowed for quantitative conversions in only minutes.

Introduction

Transition metal-assisted cross-coupling reactions are widely used catalytic tools in synthetic chemistry. The Suzuki–Miyaura C–C coupling reaction has been used for a wide range of applications such as the preparation of pharmaceuticals, sensors and polymers.[1] Alongside, carbon–hetero atom couplings, C–S thioetherifications also represent essential processes for the synthesis of biomolecules, etc.[2] Along with the application of these synthetic technologies, the combining of catalyst design with modern instrumentation and alternative energy sources constitutes an expected next step. One approach has involved the use of microwave irradiation resulting in superb reduction of reaction times.[3] The most advantageous utilization of this rapid heating method involves its combination with high temperature-tolerant catalysts so that the latter can be used in very low concentrations.

Along these lines, ECE pincer complexes are well-known robust species that have proven to be good catalytic performers in a myriad of transformations.[4] Their stability at ambient conditions and ability to tolerate the presence of both oxygen and moisture implicates, however, a common requirement for heat for their catalytic activation. As a result, these complexes represent good candidates for microwave-assisted catalysis. Palladium SCS pincer catalysts,[5] are among the most robust species,[5a] and have been studied under microwave irradiation conditions for the Heck reaction where they could be recycled.[6] Previous experiments with phosphine ligands resulted in decomposition under these reaction conditions.[7] Other sulfur containing ligands are the SNS pincer counterparts where straightforward complexation can be achieved with nickel as the metallic center.[8]

The aim of this work was to synthesize a series of alkyl-substituted SCS-Pd^{II} and SNS-Ni^{II} pincer precatalysts and to evaluate their catalytic performance in Suzuki–Miyaura and thioetherification cross-couplings under both conventional and microwave-dependent heating conditions.

Results and Discussion

Palladium catalysts **3a**–**3c** were readily prepared from direct C–H activation of pincer proligands **1a**–**1c** of the type $C_6H_4\text{-}1,3\text{-}(CH_2SR)_2$, R = *t*Bu, *s*Bu, *i*Bu substituents. In a similar manner, nickel catalysts were prepared by direct complexation with pyridine-based ligand analogs **2a**–**2c**

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C_5H_3N-2,6-$(CH_2SR)_2$ bearing the same SR mercaptan motifs (Scheme 1). All metallation reactions proceeded in good to excellent yields resulting in microcrystalline powders for **3a**–**3b**, **4a**–**4c and 4b**. Nickel complex **4a**, with the most sterically demanding environment around the nickel center suffered changes in colour when dissolved in coordinating solvents such as acetonitrile, methanol and the like. This phenomenon was observed to proceed at a very slow rate for **4b** but did not occur at all with **4c**. With the less sterically demanding environment around the nickel center, the latter complex displayed dimerism in the solid state as further discussed below.

Slow concentration of organic solvent solutions of complexes **3a**, **4a** and **4c** in CH_2Cl_2 afforded crystals suitable for X-ray diffraction analyses. The solid-state structures of **3a** showed a square-planar geometry in structural agreement with previously reported crystallographic data.[9] The crystal structure of nickel complex **4a**, with *tert*-butyl substituents, showed a slightly distorted trigonal bipyramidal geometry. Moreover, when such species were concentrated

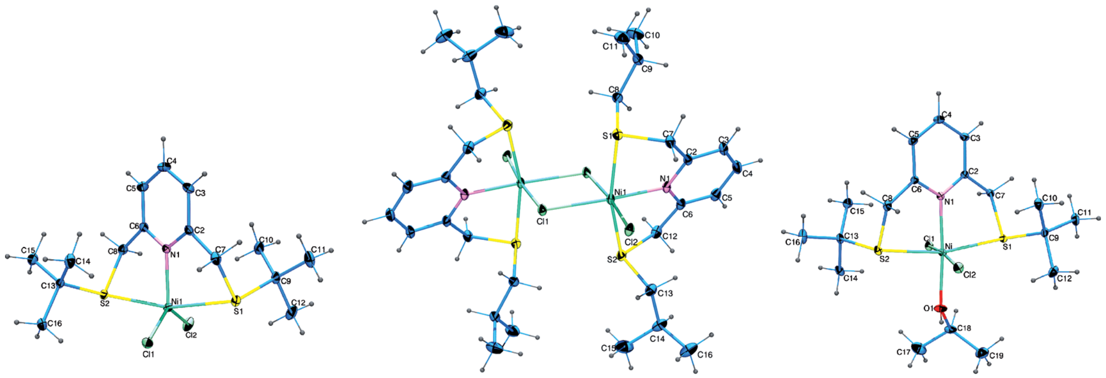
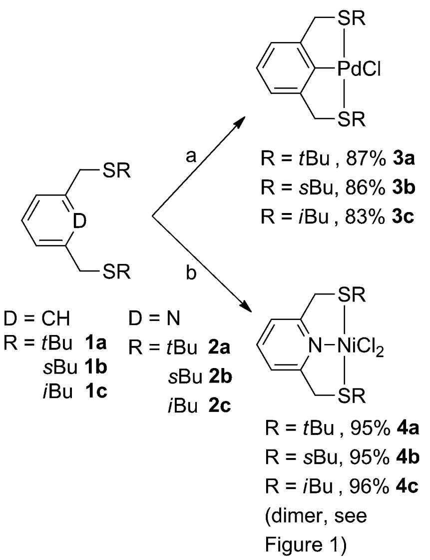


Figure 1. X-ray diffraction ORTEP diagram (50% probability) of species [$NiCl_2\{C_5H_3N$-2,6-$(CH_2S\mathit{t}Bu)_2\}$] (**4a**), [$NiCl\{C_5H_3N$-2,6-$(CH_2S\mathit{i}Bu)_2\}\mu$-$Cl]_2$ (**4c**) and [$NiCl_2\{C_5H_3N$-2,6-$(CH_2S\mathit{t}Bu)_2\}(\mathit{i}PrOH)$] (**4d**).

Table 1. Crystal data and structure parameters for **4a**, **4c** and **4d**.

	4a	**4d**	**4c**
Empirical formula	$C_{15}H_{25}Cl_2NNiS_2$	$C_{18}H_{33}Cl_2NNiOS_2$	$C_{32}H_{54}Cl_8N_2Ni_2S_4$
Formula weight	413.09	479.18	996.03
Temperature [K]	298(2)	298(2)	298(2)
Wavelength [Å]	0.71073	0.71073	0.71073
Crystal system	monoclinic	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$	$C2/c$
Unit cell dimensions			
a [Å]	9.116(1)	13.6865(19)	26.106(3)
b [Å]	25.494(3)	11.6090(16)	13.5860(15)
c [Å]	17.256(2)	15.346(2)	16.7959(19)
α [°]	90	90	90
β [°]	98.800(2)	107.108(2)	130.330(2)
γ [°]	90	90	90
Volume [Å^3]	3963.1(8)	2330.3(6)	4541.3(9)
Z	8	4	4
Density (calcd.) [Mg/m^3]	1.385	1.349	1.457
Absorption coefficient [mm^{-1}]	1.453	1.248	1.509
F(000)	1728	1000	2064
Crystal size [mm]	0.32 × 0.08 × 0.04	0.30 × 0.10 × 0.06	0.40 × 0.10 × 0.08
θ range for data correction [°]	1.60–25.36	1.75–25.38	1.81–25.32
Index ranges	$-10 \le h \le 10$, $-30 \le k \le 30$, $-20 \le l \le 20$	$-16 \le h \le 16$, $-13 \le k \le 14$, $-18 \le l \le 18$	$-31 \le h \le 31$, $-16 \le k \le 16$, $-20 \le l \le 20$
Reflexions collected	32656	18850	18478
Independent reflexions [R_{int}]	7240 [0.1058]	4272 [0.0695]	4153 [0.0856]
Absorption correction	semi-empirical from equivalents	empirical	empirical
Maximum and minimum transmission	0.9436 and 0.7497	0.9355 and 0.7518	0.8917 and 0.5335
Refinement method		full-matrix least-squares on F^2	
Data/restraints/parameters	7240/0/391	4272/1/240	4153/25/233
Goodness-of-fit on F^2	1.000	0.810	0.951
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0625, wR_2 = 0.1133	R_1 = 0.0348, wR_2 = 0.0517	R_1 = 0.0454, wR_2 = 0.0956
R indices (all data)	R_1 = 0.1174, wR_2 = 0.1334	R_1 = 0.0618, wR_2 = 0.560	R_1 = 0.0742, wR_2 = 0.1025
Largest difference peak and hole [e Å^{-3}]	0.416 and –0.331	0.405 and –0.258	0.582 and –0.519

$R_1 = |F_o - F_c|/|F_o|$, $wR_2 = [w(F_o)^2 - (F_c)^2 - w(F_o)^2]^{1/2}$



Scheme 1. Synthesis of catalysts **3** and **4**. Reagents and conditions: a) $PdCl_2$, toluene, reflux, 2 h; b) $NiCl_2·6H_2O$, acetone, 25 °C, 0.5 h.

from 2-propanol, coordination of the solvent occurred resulting in octahedral species **4d** as shown in Figure 1. On the other hand, the analogue species with isobutyl substituents formed a dimer presenting two distorted octahedral nickel centers bridged by two chloride substituents resulting in the formula $[NiCl\{C_5H_3N\text{-}2,6\text{-}(CH_2SR)_2(\mu\text{-}Cl)\}]_2$; R = *i*Bu. Halogen-bridged dimeric pincer species have been observed before.[8a,8b,10] In our experiments, we propose that the bulkiness of the butyl isomers is responsible for the different coordination behaviour of the three species, with *tert*-butyl substituents generating enough steric hindrance so as to prevent association of two monomers. Conversely, dimerism can occur slowly with *sec*-butyl groups and more quickly (and to our observations, irreversibly) with isobutyl groups. Crystallographic data is presented in Table 1 and relevant bond lengths and angles are shown in Table 2.

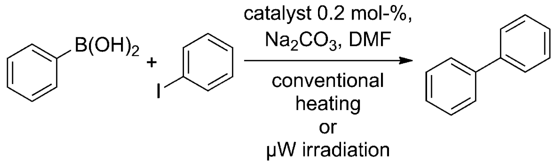
Table 2. Selected bond lengths and angles from SNS Ni complexes **4a**, **4c** and **4d**.

	Bond	Length [Å]	Bond	Angle [°]
4a	Ni–N1	1.996(4)	Cl1–Ni–Cl2	134.77(7)
	Ni–Cl2	2.2460(17)	N–Ni1–Cl2	115.29(13)
	Ni–S1	2.5087(16)	S1–Ni–S2	164.60(6)
	Ni–S2	2.5043(16)	Cl2–Ni–S2	87.47(6)
	Ni–Cl1	2.2685(16)	N–Ni–S2	82.51(13)
4c	Ni–N	2.066(3)	N–Ni–Cl1	174.08(9)
	Ni–S1	2.4670(12)	S1–Ni–S2	163.95(4)
	Ni–S2	2.4411(12)	N–Ni–Cl2	93.86(9)
	Ni–Cl2	2.3928(11)	Cl1–Ni–S1	98.24(4)
	Ni–Cl1	2.4083(11)	Cl2–Ni–S1	86.67(4)
			Cl2–Ni–Cl1	92.06(4)
4d	Ni–N	2.044(2)	S2–Ni–S1	166.25(3)
	Ni–S2	2.4854(8)	N–Ni–O	176.19(9)
	Ni–S1	2.4677(8)	Cl1–Ni–Cl2	172.70(3)
	Ni–Cl1	2.4098(8)	S2–Ni–N	83.24(7)
	Ni–Cl2	2.3811(8)	Cl1–Ni–N	92.70(6)
	Ni–O2	2.075(2)	S2–Ni–Cl1	100.97(3)

Suzuki–Miyaura C–C Couplings

The evaluation of catalytic activity for compounds **3** and **4** was performed on the C–C coupling reaction between an aryl halide and phenylboronic acid. Reactions were conducted in DMF with Na_2CO_3 as the base and with a catalyst loading of 0.2 mol-%. In the first instance, iodobenzene was utilized to screen the activity of catalysts under different heating methods; the results are presented in Table 3. Whereas nickel complexes were not active in the Suzuki–Miyaura reaction (Table 3, Entry 4), good to excellent yields of biphenyl adduct were obtained with palladium catalysts according to the heating method employed, classic or microwave-assisted, respectively (Table 3, Entries 1–3).

Table 3. Trial C–C Suzuki–Miyaura couplings. Evaluation of catalysts **3** and **4** under conventional heating and microwave irradiation conditions for transformation of iodobenzene.

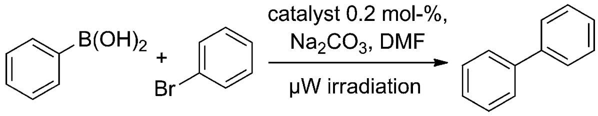


Entry	Catalyst	% Conversion[a]		
		Conventional heat (110 °C, 10 h)	Microwave irradiation[b] (75 W, 5 min)	(75 W, 10 min)
1	**3a**	34.4	67.4	> 99
2	**3b**	35.0	64.3	> 99
3	**3c**	36.1	69.3	> 99
4	**4a–4c**	< 1	< 1	< 1

[a] The mol-% of iodobenzene converted to biphenyl was determined by GC–MS analysis. [b] Ceiling temperature was 200 °C.

Successively, using bromobenzene as a substrate that is more difficult to activate, the palladium catalysts showed important activity achieving up to 84% conversion in 10 min of microwave irradiation (Table 4). Here, the difference in Pd ligands was found to have little to no impact on the conversions.

Table 4. C–C Suzuki–Miyaura couplings. Catalytic evaluation of SCS Pd^{II} catalysts **3a–3c** under microwave irradiation for the transformation of bromobenzene.

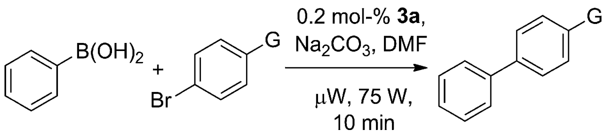


Entry	Catalyst	% Conversion[a]	
		(75 W, 5 min)	(75 W, 10 min)
1	**3a**	76.6	84.3
2	**3b**	76.4	84.1
3	**3c**	73.7	83.6

[a] In all cases, the ceiling temperature was 200 °C. The mol-% of iodobenzene converted to biphenyl was determined by GC-MS analysis.

Later, when bromobenzenes with *para* substituents were used as substrates for **3a** as the selected catalyst, remarkable conversions were found for those substrates with increasingly electron-withdrawing substituents (Table 5, Entries 1–4). Below those cases where maximum conversion was reached, we found a correlation between the efficiency of conversion and the Hammet parameter (σ)[11] of the *para* substituents (Figure 2). This implies higher rates for more electron-withdrawing substituents in the substrate. Inspired, in part, by this realization, we postulate that the use of irradiation as the heating method does not interfere with the oxidative addition as the rate-determining step.[12]

Table 5. C–C Suzuki–Miyaura couplings. Catalytic evaluation of **3a** under microwave irradiation conditions for the transformation of *p*-substituted bromobenzenes.



Entry	G substituent	% Conversion[a]
1	CN	98.8
2	NO_2	> 99
3	COMe	95.7
4	CHO	96.1
5	H	76.8
6	Me	64.1
7	OMe	57.8

[a] The ceiling temperature was 200 °C. The mol-% of each *p*-bromobenzene converted into desired biphenyl product was determined by GC-MS analysis.

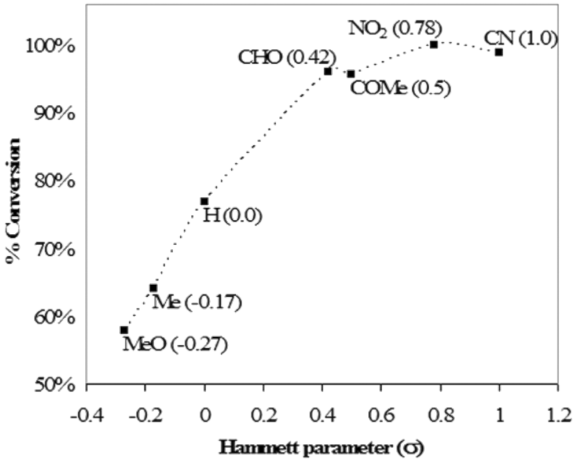
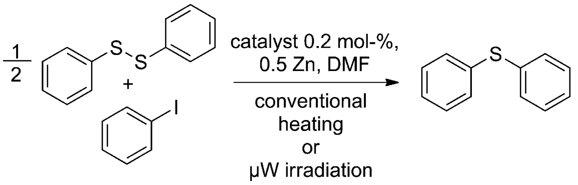


Figure 2. The % conversion for the Suzuki–Miyaura couplings catalysed by **3a** using different *p*-substituted bromobenzenes vs. Hammett parameter.[11]

Thioetherification C–S Couplings

Following similar conditions (i.e. 0.2 mol-% of catalyst loading under irradiation or classical heating), we studied the arylation of diphenyldithioether. The C–S coupling toward diphenylthioether required metallic zinc for disulfide bond reduction. Table 6 presents the results of all reactions employing **3** and **4** catalysts using iodobenzene as the arylating substrate.

Table 6. C–S diarylthioetherification couplings. Catalytic evaluation of **3** and **4** under conventional heating and microwave irradiation conditions for the transformation of iodobenzene.



Entry	Catalyst	% Conversion[a]	
		Conventional heat (110 °C, 10 h)	Microwave irradiation (100 W, 5 min)[b]
1	**3a**	24.2	13.6
2	**3b**	n.d.	8.4
3	**3c**	14.4	7.1
4	**4a**	64.7	> 99
5	**4b**	40.9	> 99
6	**4c**	38.8	> 99

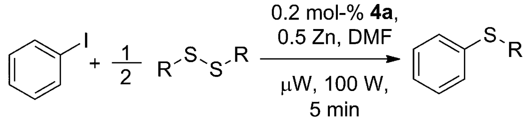
[a] The mol-% of iodobenzene converted to diphenylthioether determined by GC-MS analysis. [b] Ceiling temperature was 200 °C.

The results of Table 6 reveal excellent efficiencies of conversion when nickel catalysts were used with microwave irradiation conditions. Such reactions proceeded in only minutes and with excellent yields (Table 6, Entries 4–6). Conventional heating, on the other hand, resulted in an interesting trend of activities, **4a** > **4b** ≈ **4c**. This trend appears to be dictated by the steric demands of the sulfur substituents as indicated by the *Front Strain Parameters*[13] which are *t*Bu 3.82, *s*Bu 2.51, *i*Bu 1.86. Consistent with the bulkiness of the ligands in question, we propose that the interaction between the catalysts and substrates is greater when the former is in the monomeric form (see above).

In contrast to the Suzuki–Miyaura coupling experiments discussed above, Ni^{II} compounds were found to exert better activity for C–S couplings under both classical and microwave heating conditions. This is likely due to the required intermediates suggested by previously proposed mechanisms for this transformation, wherein metallic intermediates follow a M^{I}-M^{III}-M^{I} cycle,[14] best achieved with nickel species.

Additional experiments were carried out using microwave irradiation conditions and with different dithioethers as the substrate; complex **4a** was chosen as the catalyst in these cases. The results in Table 7 reveal diminished conversion efficiencies as steric demands of the starting aliphatic dithioethers increase (Table 7, Entries 1–5). This observation likely results from the increasingly limited accessibility of the S–S bond as the R group size increases.

Table 7. C–S diarylthioetherification couplings. Catalytic activity evaluation of **4a** under microwave irradiation conditions for the transformation of dithioethers.



Entry	R	% Conversion[a]
1	Me	> 99
2	*n*Bu	> 99
3	*i*Bu	43.8
4	*s*Bu	16.3
5	But	< 1
6	Ph	> 99

[a] Ceiling temperature was 200 °C. The mol-% of each dithioether converted into the desired thioether was determined by GC-MS analysis.

Conclusions

We have provided a facile and high yielding procedure for the production of both organometallic and coordination SCS and SNS pincer compounds. In a manner more dramatic for the Ni-SNS pincer species, subtle changes in steric hindrance provoked both structural and reactivity differences. As expected, the organometallic Pd-SCS pincer compounds were more efficient catalysts in Suzuki–Miyaura couplings whereas the coordination Ni-SNS complexes proved to be excellent catalysts for the thioetherification of iodobenzene, requiring, in this case, the presence of metallic Zn as a necessary reducing agent. Notably, in both cases the use of microwave irradiation dramatically reduced reaction times for both catalytic C–C and C–S couplings thus proving highly beneficial. The use of these complexes for other Pd- and Ni-catalysed reactions is currently under study in our research group.

Experimental Section

General Procedures: Unless otherwise stated, all organic and organometallic reactions were conducted under a dry nitrogen atmosphere using standard Schlenk techniques. Organic solvents were dried with appropriate materials and distilled prior to use. All reagents were obtained commercially and used without further purification. ^{1}H and ^{13}C spectra were recorded with a JEOL GX300 spectrometer. Chemical shifts are reported in ppm downfield of TMS using the solvent $CDCl_3$ (δ = 7.26 ppm) as an internal standard. Positive-ion FAB mass spectra were recorded with a JEOL JMS-SX102A mass spectrometer operated at an accelerating voltage of 10 kV. Samples were desorbed from a nitrobenzyl alcohol (NOBA) matrix using 3 keV xenon atoms. Mass measurements in FAB^{+} are performed at a resolution of 3000 using magnetic field scans and the matrix ions as the reference material or, alternatively, by electric field scans with the sample peak bracketed by two (polyethyleneglycol or cesium iodide) reference ions. GC-MS analysis were performed with an Agilent 6890N GC with a 30.0 m DB-1MS capillary column coupled to an Agilent 5973 Inert Mass Selective detector. Percent of conversion (% Conversion) is determined from the residual aryl halide, the product obtained and the corresponding standard solutions. Magnetic dipole moments of the metallic centres are reported in Bohr Magnetons (μ_B) as a result of the addition of diamagnetic contributions of the each atom in its corresponding molecule (and the contribution of pyridine) and the experimental paramagnetic measurement of the solid powder of each sample on a Magway MSB Mk1, Sherwood Scientific LTD Magnetic Susceptibility Balance. Microwave driven reactions were carried out using a CEM Discover reactor coupled to a CEM Explorer robotic system. Palladium dichloride was purchased from Pressure Chemical Co.; Nickel dichloride hexahydrated, α,α-dichlorometaxylene [in this article mentioned as 1,3-bis(chloromethyl)benzene], 2,6-bis(chloromethyl)pyridine, sodium hydride and *tert*-, iso- and sec-butylthiol were commercially obtained from Aldrich Chemical Co. All compounds were used as received without further purification.

Representative Synthesis of α,α′-Bis(butylthio)metaxylene Ligands [C_6H_4-1,3-($CH_2SR)_2$] {R = *t*Bu (1a), *s*Bu (1b), *i*Bu (1c)} and [C_5H_3N-2,6-($CH_2SR)_2$] {R = *t*Bu (2a), *s*Bu (2b), *i*Bu (2c)}:[15] For the synthesis of ligand **1a**: *tert*-butylmercaptan (2.8 mL, 2.24 g, 25 mmol) was added dropwise to a stirred suspension of sodium hydride (897 mg, 37.5 mmol) in freshly distilled THF (100 mL) at room temperature. After vigorous stirring for 10 min, a solution of α,α′-dichlorometaxylene (2.1792 g, 12.5 mmol) in THF (30 mL) was slowly added. The resulting mixture was stirred for 5 h and then the solids were filtered off. Volatiles were removed under vacuum to give the desired product as a colorless crystalline powder (Yield: 97%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 18 H, CH_3), 3.74 (s, 4 H, CH_2), 7.19, 7.20, 7.32 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.8 (CH_3), 33.2 (CH_2), 42.8 (Me_3C), 127.4 (Ar_{C4}), 128.5 (Ar_{C2}), 129.5 (Ar_{C3}), 138.7 (Ar_{C1}) ppm.

For the Synthesis of 1b and 1c: This series of ligands was synthesized in a similar manner as for ligand **1a** but in these cases using *sec*-butylmercaptan (**1b**) or isobutylmercaptan (**1c**) in equimolar amounts, yield of **1b**, 97%, colorless viscous oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 [t, ^{3}J(H,H) = 7.41 Hz, 6 H, *n*-CH_3], 1.23 [d, ^{3}J(H,H) = 6.84 Hz, 6 H, *s*-CH_3], 1.54 [m, ^{3}J(H,H) = 31.59 Hz, 4 H, $MeCH_2$], 2.57 (m, 2 H, CH), 3.71 (s, 4 H, $ArCH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3 (*n*-CH_3), 20.7 (*s*-CH_3), 29.5 ($MeCH_2$), 34.91 ($ArCH_2$), 41.1 (CH), 127.4 (Ar_{C4}), 128.6 (Ar_{C5}), 129.3 (Ar_{C2}), 139.1 (Ar_{C1}) ppm, yield of **1c**, 94%, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 [d, ^{3}J(H,H) = 6.6 Hz, 12 H, CH_3], 1.77 (m, 2 H, CH), 2.29 [d, ^{3}J(H,H) = 6.87 Hz, 4 H, *i*PrCH_2], 3.67 (s, 4 H, $ArCH_2$), 7.18, 7.19, 7.24 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1 (CH_3), 28.3 (CH), 36.7 ($ArCH_2$), 40.6 (*i*PrCH_2), 127.5 (Ar_{C4}), 128.6 (Ar_{C5}), 129.5 (Ar_{C2}), 139.0 (Ar_{C1}) ppm.

For the Synthesis of 2a–2c: These ligands were obtained using the same synthetic procedure used to obtain ligands **1a**–**c**. However, in these cases reactions made use of 2,6-bis(chloromethyl)pyridine as the aromatic backbone in equimolar amounts, yield of **2a**, 95%, crystalline powder; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 18 H, CH_3), 3.89 (s, 4 H, CH_2), 7.28 [d, ^{3}J(H,H) = 7.71 Hz, 2 H, Ar-3-H], 7.57 (t, 1 H, Ar-4-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.1 (CH_3), 35.6 (CH_2), 43.2 (Me_3C), 121.4 (Ar_{C3}), 137.2 (Ar_{C4}), 158.6 (Ar_{C2}) ppm, yield of **2b**, 98%, light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 [t, ^{3}J(H,H) = 7.41 Hz, 6 H, *n*-CH_3], 1.2 [d, ^{3}J(H,H) = 6.57 Hz, 6 H, *s*-CH_3], 1.51 [m, ^{3}J(H,H) = 31.86 Hz, 4 H, $MeCH_2$], 2.64 (c, 2 H, CH), 3.79 (s, 4 H, $ArCH_2$), 7.22 [d, ^{3}J(H,H) = 7.68 Hz, 2 H, Ar-3-H], 7.56 (t, ^{1} H, Ar-4-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3 (*n*-CH_3), 20.6 (*s*-CH_3), 29.4 ($MeCH_2$), 36.9 (CH), 41.4 ($ArCH_2$), 121.0 (Ar_{C3}), 137.2 (Ar_{C4}), 158.7 (Ar_{C2}) ppm. **2c**, 98%, light yellow oil; ^{1}H NMR

(300 MHz, $CDCl_3$): δ = 0.92 [d, ^3J(H,H) = 6.6 Hz, 12 H, CH_3], 1.76 (sept, 2 H, CH), 2.36 [d, ^3J(H,H) = 6.6 Hz, 4 H, *i*PrCH_2], 3.77 (s, 4 H, ArCH_2), 7.23 [d, ^3J(H,H) = 7.71 Hz, 2 H, Ar-3-H], 7.59 (t, 1 H, Ar-4-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1 (CH_3), 28.3 (CH), 38.6 (ArCH_2), 40.9 (*i*PrCH_2), 121.1 (Ar_{C3}), 137.3 (Ar_{C4}) ppm.

Representative Synthesis of Pd^{II}-SCS Pincer Compounds of the Type [PdCl{C_6H_3-2,6-($CH_2SR)_2$}] {R = *t*Bu (3a), *s*Bu (3b), *i*Bu (3c)}: For the synthesis of compound **3a** a variation of the method described by B. L. Shaw and co-workers[9] was followed: a freshly made solution of ligand **1a** (1.4156 g, 5.02 mmol) in toluene (25 mL) was slowly added to a stirred suspension of $PdCl_2$ (0.8866 g, 5 mmol) in toluene (35 mL); the resulting mixture was stirred at reflux temperature for 2 h under nitrogen atmosphere and then it was allowed to reach room temperature. Solids were filtered off and volatiles evaporated under vacuum to give a dark brownish solid which was completely redissolved in CH_2Cl_2 (7 mL) and precipitated with hexane (40 mL). After vigorous stirring for 15 min in an open flask, the solution was filtered to give a dark orange powder (Yield 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 18 H, CH_3), 4.17 (s, 4 H, CH_2), 6.90–6.92 (m, 3 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.6 (CH_3), 42.6 (CH_2), 51.9 (Me_3C), 121.5, (Ar_{C3}), 124.5 (Ar_{C4}), 149.9 (Ar_{C1}), 159.0 (Ar_{C2}) ppm. MS-FAB$^+$ $[M]^+$ = 424 (5%) *m*/*z*, $[M - Cl]^+$ = 387 (100%) *m*/*z*.

For the synthesis of isobutyl- and *sec*-butyl-derived compounds **3b** and **3c**, respectively, the same synthetic procedure as that used to achieve compound **3a** was followed. However, in these cases reactions used the corresponding ligands of the type [C_6H_4-1,3-($CH_2SR)_2$] (**1b** and **1c**), for which synthesis has been described above. Compound **3b** (Yield 86%) yellow viscous oil. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.33 (*n*-CH_3), 20.56 (*s*-CH_3), 29.22 ($MeCH_2$), 41.5 (CH), 48.84 (ArCH_2), 122.12 (Ar_{C3}), 124.6 (Ar_{C4}), 149.84 (Ar_{C2}), 159.23 (Ar_{C1}) ppm. MS-FAB$^+$ $[M]^+$ = 424 (3%) *m*/*z*, $[M - Cl]^+$ = 387 (100%) *m*/*z*. Compound **3c** (Yield 83%) yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.1 [d, ^3J(H,H) = 6.6 Hz, 12 H, CH_3], 2.11 (m, 2 H, CH), 3.16 (b, 4 H, *i*PrCH_2), 4.22 (s, 4 H, ArCH_2), 6.94 (m, 2 H, Ar-3-H), 6.95 (m, 1 H, Ar-4-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (CH_3), 28.2 (CH), 47.5 (*i*PrCH_2), 48.2 (ArCH_2), 122.3 (Ar_{C3}), 124.6 (Ar_{C4}), 148.9 (Ar_{C2}), 159.7 (Ar_{C1}) ppm. MS-FAB$^+$ $[M]^+$ = 424 (3%) *m*/*z*, $[M - Cl]^+$ = 387 (100%) *m*/*z*.

Representative Synthesis of Ni^{II}-SNS Pincer Compounds of the Type [$NiCl_2${C_5H_3N-2,6-($CH_2SR)_2$}] {R = *t*Bu (4a), *s*Bu (4b), *i*Bu (4c)}: For the synthesis of **4a** a suspension of ligand **2a** (1.4175 g, 5 mmol) in acetone (25 mL) was added dropwise to a stirring suspension of [$NiCl_2(H_2O)_6$] (1.188 g, 5.02 mmol) in acetone (35 mL) at room temperature. After 30 min, the resulting green suspension was filtered and the solids dissolved in CH_2Cl_2 (50 mL) to give a dark red solution. The combined fractions were concentrated in vacuo, redissolved in CH_2Cl_2 (12 mL) and precipitated after 30 min of vigorous stirring with hexanes (60 mL) in an open flask. The suspension was filtered to give a dark pink powder (Yield 95%). Solutions in alcohols and ethers were found to be green whereas solutions in CH_2Cl_2 (from pre-dried compound) were found to assume a red colour. Paramagnetic (magnetic dipole moment of Ni^{II}: 2.87 μ_B). MS-FAB$^+$ $[M + H_2O]^+$ = 430 (2%) *m*/*z*, $[M - 2Cl - 2t\mathrm{Bu}]^+$ = 228 (100%) *m*/*z*, $[M - 2Cl - \mathrm{But}]^+$ = 284 (85%) *m*/*z*, $[M - Cl]^+$ = 376 (56%) *m*/*z*, $[M - 2Cl]^+$ = 341 (42%) *m*/*z*.

For the synthesis of *sec*-butyl- and isobutyl-derived compounds **3b** and **3c**, respectively, the same synthetic procedure used to generate **4a** was followed. However, in these cases, reactions used corresponding ligands of the type [C_5H_4N-2,6-($CH_2SR)_2$] (**2b** and **2c**), for which synthesis was described above. Compound **4b** (Yield 95%) green powder; solutions in alcohols and ethers were found to be green and solutions in CH_2Cl_2 (from pre-dried compound) also assumed a green colour; paramagnetic (magnetic dipole moment of Ni^{II}: 2.92 μ_B). MS-FAB+ $[M]^+$ = 413 (3%) *m*/*z*, $[M - Cl]^+$ = 376 (100%) *m*/*z*, $[M–2Cl]^+$ = 341 (33%) *m*/*z*, $[2M - Cl]^+$ = 789 (2%) *m*/*z*; elemental analysis (% calculated for $C_{15}H_{25}Cl_2NNiS_2$: C, 43.61; H, 6.1) found: C, 43.27, H, 5.94. Compound **4c** (Yield 96%) powder and solutions in alcohols, ethers, and CH_2Cl_2 were found to be light green; paramagnetic (magnetic dipole moment of Ni^{II}: 2.82 μ_B). MS-FAB+ $[M]^+$ = 413 (2%) *m*/*z*, $[M - Cl]^+$ = 376 (100%) *m*/*z*, $[M - 2Cl]^+$ = 341 (27%) *m*/*z*, $[2M - Cl]^+$ = 789 (3%) *m*/*z*.

Alternative Synthesis of Compounds 4a–4c: For the synthesis of **4a**, a solution of *tert*-butylmercaptan (0.46 g, 0.58 mL, 5.1 mmol) in THF (20 mL) was added dropwise to a stirring suspension of sodium hydride (180 mg, 7.5 mmol) in THF (70 mL). After 10 min, a solution of 2,6-bis(chloromethyl)pyridine (880.2 mg, 5 mmol) in THF (20 mL) was slowly added. After 5 h whilst stirring, the solids were filtered off and the light yellow solution was added to a suspension of [$NiCl_2(H_2O)_6$] (1.2118 g, 5.1 mmol) in THF (50 mL). After 1 h, the solids were filtered off and the green solution was concentrated by rotavapor and then dried overnight in vacuo at 40 °C to give the desired product as a dark pink powder (yield 92%). Distillation of the removed volatiles gave THF with 95% purity.

The method described above was followed as the alternative synthesis of compounds **4b** and **4c** with the corresponding *sec*-butyl and isobutyl mercaptans in equimolar quantities, yields: **4b**, 91%; **4c**, 93%.

Representative Procedure for the Catalytic Evaluation of C–C Suzuki–Miyaura Couplings: A glass tube was equipped with a stirring bar and sodium carbonate (0.318 g, 3 mmol), phenylboronic acid (0.3654 g, 3 mmol), benzene halide (iodobenzene: 0.28 mL, 2.5 mmol; bromobenzene: 0.26 mL, 2.5 mmol; or the corresponding *p*-substituted bromobenzene in equimolar quantities), DMF (4.5 mL) and the catalyst (2.1 mg, 5 µmol), then the tube was sealed. For the reactions under conventional heating, the tube was immersed in a heat transfer oil bath with magnetic stirring at 110 °C. After 10 h, the tube was removed from the oil bath and allowed to reach room temperature. For the reactions under microwave irradiation conditions, the tube was deposited in a white Teflon® isolator container which is part of the microwave reactor device. A tube pressure monitoring sensor was also configured, time counting started and a continuous pulse of microwaves at a constant power of 75 W was irradiated until the reaction mixture reached 200 °C at which point the pulse was paused. The pulse was continued when the temperature had fallen to 197 °C; these cycles were stopped when the desired time of reactions had been accomplished from the start of the very first pulse and then the tube was cooled with a flow of air to 50 °C; this complete irradiation procedure was automated. For both conventional and microwave heating conditions, once the reaction mixture was at room temperature, solids were filtered off and a sample was diluted with CH_2Cl_2 (0.5:1.5 mL). Experiments were performed in duplicate and 1 µL of each sample was analyzed by GC–MS.

Representative Procedure for the Catalytic Evaluation of C–S Thioetherification Couplings: A glass tube was equipped with a stirring bar and powdered zinc (0.1962 g, 3 mmol), iodobenzene (0.28 mL, 2.5 mmol), DMF (4.5 mL), catalyst (2.1 mg, 5 µmol) and diphenyldisulfide (0.327 g, 2.5 mmol) or, for the latter, the corresponding disulfide in equimolar quantities. The tube was then sealed. For the reactions under conventional heating, the tube was immersed in a heat transfer oil bath with magnetic stirring at 110 °C. After 10 h the tube was removed from the oil bath and allowed to cool to room temperature. For reactions under microwave irradiation conditions, the tube was deposited in a white Teflon® isolator which is part of the microwave reactor device. A tube pressure monitoring sensor was also suited; then time counting started and a continuous pulse of microwaves at a constant power of 100 W was irradiated until the mixture of reaction reached 200 °C at which point the pulse was paused. The pulse was continued when the temperature had fallen to 197 °C; these cycles were stopped when the desired time of reactions had been accomplished from the start of the very first pulse and then the tube was cooled with a flow of air to 50 °C. This complete irradiation procedure was automated. For both conventional and microwave heating conditions, once the reaction mixture was at room temperature, solids were filtered off and a sample was diluted with CH_2Cl_2 (0.5:1.5 mL). Experiments were performed in duplicate and 1 µL of each sample was analyzed by GC–MS.

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