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A Well-Defined (POCOP)Rh Catalyst for the Coupling of Aryl Halides with Thiols

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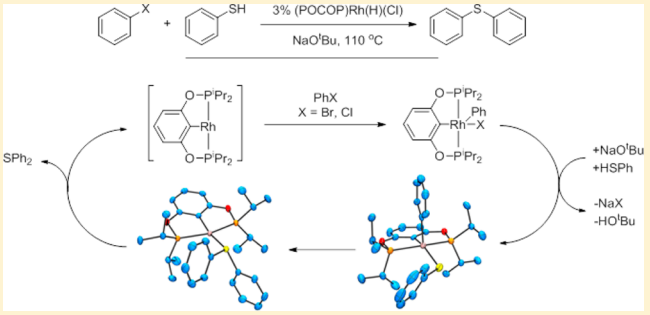
Supporting Information

ABSTRACT: This article describes a well-defined pincer-Rh catalyst for C−S cross-coupling reactions. (POCOP)Rh(H)(Cl) serves as an active precatalyst for the coupling of aryl chlorides and bromides with aryl and alkyl thiols under reasonable conditions (3% mol cat., 110 °C, 2−24 h, >90% yield). For select substrates, >90% yields were obtained with catalyst loading as low as 0.1%. Key mechanistic intermediates have been isolated and fully characterized, including (POCOP)Rh(Ph)(SPh) (**6a**) and (POCOP)Rh(SPh_2) (**6b**). The aryl/bis(phosphinite) (POCOP)Rh system has been shown to favor aryl thiolate reductive elimination at elevated temperatures and in some cases at room temperature, compared with the analogous diarylamido/bis(phosphine) (PNP)Rh pincer system. Concerted reductive elimination has been studied with **6a** directly and in the presence of aryl bromide and aryl chloride traps. This investigation demonstrates a clear rate dependence on aryl chloride concentration during catalysis, a dependence that is absent when using aryl bromides. The rate of catalysis is dramatically reduced or brought to zero for *ortho*-tolyl halides, which can be traced to slower C−S coupling and slower carbon−halogen oxidative addition for *ortho*-substituted aryls. The influence of the sterics in the thiol component is less straightforward. The S−H oxidative addition product (POCOP)Rh(H)(SPh) (**16**) has been fully characterized and its reactivity has been examined, resulting in the isolation of the sodium-thiolate adduct (POCOP)Rh(NaSPh) (**19**). The solid-state structure of **19** shows Na interactions not only with sulfur, but also with a neighboring Rh and the chelating aryl carbon of the pincer framework. The reactivity of **16** and **19** indicates that these potential side products should not hinder catalysis.



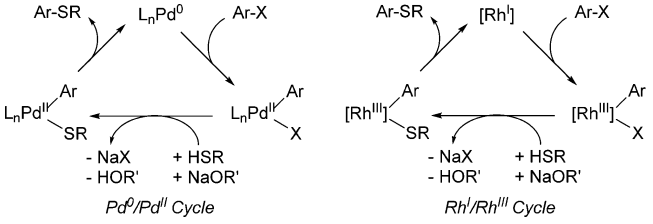
INTRODUCTION

The prevalence of aryl sulfides in biologically and pharmaceutically active compounds has sparked an increased interest toward improving methodologies to form these groups.[1] Aryl-sulfur bonds can be formed by the direct reaction of thiolates with aryl halides under harsh conditions (>200 °C).[2] The development of transition metal catalysts for C−S coupling of aryl halides with thiols is complicated by the poisoning of a number of catalysts by thiols, as noted by Hartwig.[3] The Cu-catalyzed Ullman reaction[4] allowed progress in selectivity and more reasonable reaction conditions. More recently, other transition metals, including Ni[5] and Co,[6] have also been used to catalyze the coupling of aryl halides with thiols to form diaryl thioethers. However, they are characterized by modest turnover numbers and difficulty in engaging aryl chlorides.

Pd catalysts are ubiquitous in carbon−carbon and carbon−heteroatom coupling,[7,8] and they have also been used for C−S coupling.[3,9−11] The utility of Pd catalysis with aryl chlorides hinges on the use on bulky designer NHC ligands[10] or "fourth-generation" bidentate phosphines.[3] Arguably the most successful system was developed by Hartwig et al., with the Pd center supported by the Josiphos-type "CyPF-^{t}Bu" ligand.[3,11] The CyPF-^{t}Bu/Pd system was capable of impressive 10^2−10^4 turnovers over 5−50 h with aryl chlorides and bromides. It still required a relatively high temperature for operation (>100 °C) and the cost of the CyPF-^{t}Bu ligand is quite high (hundreds of dollars per g).

The wide-scale success in using Pd to effectively perform coupling reactions owes to its capacity to undergo two-electron oxidative addition (OA) and reductive elimination (RE) events, alternating between Pd^0 and Pd^{II} oxidation states. The mechanism of CyPF-^{t}Bu/Pd-catalyzed C−S cross-coupling reactions was extensively examined by Hartwig and co-workers.[12] Scheme 1 shows the three steps that in broad

Scheme 1. General Pd^0/Pd^{II} and Rh^I/Rh^{III} Cycles for the Coupling of Aryl Halides with Thiols To Form Sulfides



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strokes are typical[7,8] for Pd-catalyzed aryl halide coupling reactions in general: OA of aryl halide to Pd^0, transmetalation at Pd^{II}, and RE of the coupled product from Pd^{II} to regenerate Pd^0.

We have recently reported[13,14] on the ability of Rh complexes supported by PNP and POCOP pincer[15] ligands to mimic the chemistry typical for L_nPd-based catalysts. This mimicry is somewhat suprpising given that the Rh^I/Rh^{III} couple (d^8/d^6) and Pd^0/Pd^{II} (d^{10}/d^8) possess different numbers of d-electrons and different geometries about the metal center. Our investigations have shown that (pincer)Rh^I fragments easily undergo OA with aryl halides to give (pincer)Rh^{III}(Ar)(Hal) complexes, and clean carbon−carbon RE from (pincer)-Rh^{III}(Ar)(Ar′).[13] Besides stoichiometric reactions, we were able to demonstrate the catalytic proficiency of (POCOP)Rh in Kumada coupling of aryl iodides,[14a] and modest activity in C−N coupling of aryl bromides and chlorides.[14b] Non-pincer complexes of Rh have also been used for select aryl halide coupling reactions.[16,17] They likely make use of the Rh^I/Rh^{III} cycle, as well, but mechanistic information about these processes is scarce, with the exception of the Bergman−Ellman arylation of heterocycles.[17] Previous reports of aryl−sulfur coupling with Rh involved thiolation of electron deficient aryl fluorides[18] or reaction of aryl fluorides with a R_2S_2/R'_3P combination of reagents,[19] but not the coupling of unactivated aryl chlorides with thiols.

Against this backdrop, we sought to explore whether a well-defined (pincer)Rh catalyst can be effective for C−S coupling according to the envisioned Rh^I/Rh^{III} mechanism shown in Scheme 1. This inquiry has been successful, and here we describe the efficacy of the (POCOP)Rh pincer system in catalyzing the coupling of aryl chlorides and bromides with aryl and alkyl thiols, and report preliminary mechanistic findings.

RESULTS AND DISCUSSION

Catalyst Screening. We set out to evaluate (POCOP)Rh-(H)(Cl) (**1**), (PNP)Rh(H)(Cl) (**2**), (POCOP^{tBu})Rh(H)(Cl) (**3**), and (^{Napt}POCOP)Rh(H)(Cl) (**4**) as a representative group of precatalysts (Scheme 2). The synthesis of **1**−**4** and their respective ligands has been described elsewhere.[14,20,21]

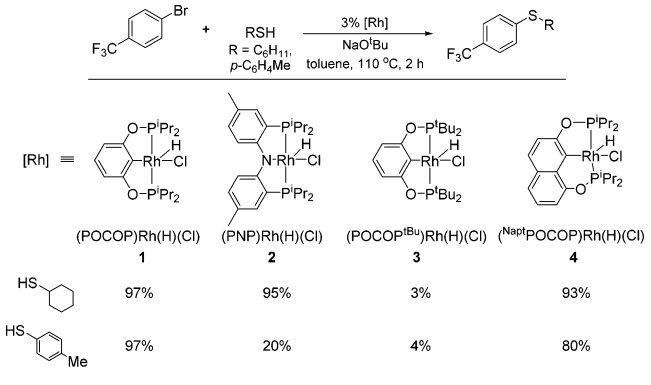
Complexes **1**−**4** are similar in that the Rh center in each is supported by a monoanionic pincer ligand with opposing phosphine/phosphinite arms. Complex **2** provides for a different central donor atom: amido in **2** vs aryl in others. Complex **3** possesses much greater steric bulk in the P^tBu_2 "arms". Complex **4** presents a five- and a six-membered ring fused about Rh, resulting in a different P−Rh−P pincer bite angle. Using Fryzuk's notation for pincer ligands,[22] **4** can be described as a {[5,6]-PCP} ligand in contrast to {[5,5]-PCP} for **1** and **3** and {[5,5]-PNP} for **2**.

Each compound **1**−**4** was tested as a catalyst under the same conditions (3% loading, 2 h, 110 °C) for the coupling of *p*-MeC_6H_4SH or *c*-$C_6H_{11}SH$ with *p*-$BrC_6H_4CF_3$ using NaO^tBu as a base (Scheme 2). Dehydrochlorination of (pincer)Rh(H)(Cl) with NaO^tBu is expected[13,14] to provide access to the catalytically relevant three-coordinate (pincer)Rh intermediate.[23] The use of the CF_3-substituted aryl halide allowed for the reactions to be conveniently monitored by ^{19}F NMR spectroscopy.

The reactions using the bulkiest complex **3** produced only a near-stoichiometric amount of the expected C−S coupling products, but the use of complexes that contained smaller P^iPr_2 side arms (**1**, **2**, and **4**) clearly led to catalytic diorganosulfide production. **1** displayed the greatest activity yielding 97% of the C−S coupled products with both thiol substrates. The diarylamido-based **2** worked well with *c*-$C_6H_{11}SH$ producing 95% of the coupled product, but gave only 20% conversion for the reaction with *p*-MeC_6H_4SH. The naphthalenediol-based **4** worked almost as well as **1** for both coupling test reactions. We selected **1** for more in-depth studies.

Scope. The results of a survey of the catalytic activity of **1** in the coupling of aryl chlorides and bromides with alkyl or aryl thiols are shown in Figure 1. Several general observations can

Scheme 2. Catalyst Screening for the Coupling of *p*-$BrC_6H_4CF_3$ with *c*-$C_6H_{11}SH$ and *p*-MeC_6H_4SH



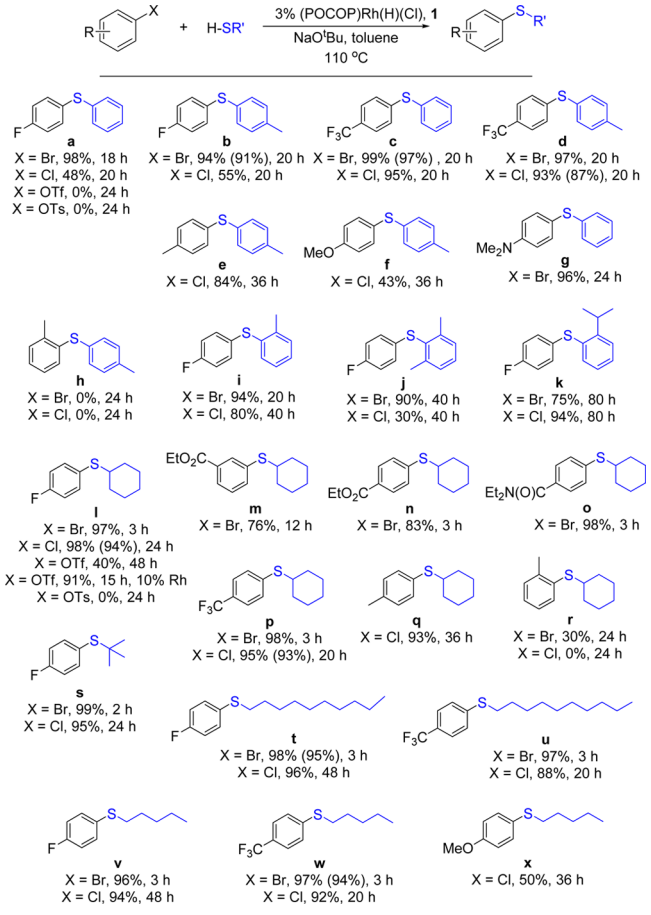


Figure 1. Scope of (POCOP)Rh(H)(Cl) (**1**) catalyzed coupling of aryl halides with aryl and alkyl thiols. NMR yields are given; isolated yields in parentheses.

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be made that dovetail related trends in Pd catalysis.[7] Aryl bromides were more reactive than aryl chlorides across the board. More electron-poor aryl halides also reacted faster. This can be exemplified by the ca. 50% yield of **a**/**b** starting from *p*-ClC_6H_4F vs >90% yield of **c**/**d** starting from *p*-$ClC_6H_4CF_3$ after the same period of time. Primary and secondary (*c*-$C_6H_{11}SH$) alkyl thiols reacted faster than aromatic thiols (e.g., **l**/**v** vs **a**/**b**), as they do with Pd catalysts.[11] Most reactions between alkyl thiols and *para*-substituted aryl bromides were complete after 3 h at 110 °C, with NMR yields of 96% or greater. The analogous reactions with aryl chlorides were slower to reach completion, 20 −48 h, but product yields were still high (88−98%, except **x**). The formation of **q** with the more electron rich *p*-MeC_6H_4Cl was also successful, yielding 93% after 36 h. However, the use of *p*-$MeOC_6H_4Cl$ gave only 50% of **x** after 36 h. The ester-substituted aryl bromides (**m**, **n**) gave diminished yields of the corresponding thioethers (the balance being the hydrodehalogenation products). The $-CONEt_2$ (**o**) and $-NMe_2$ (**g**) substituted aryl bromides worked well, however.

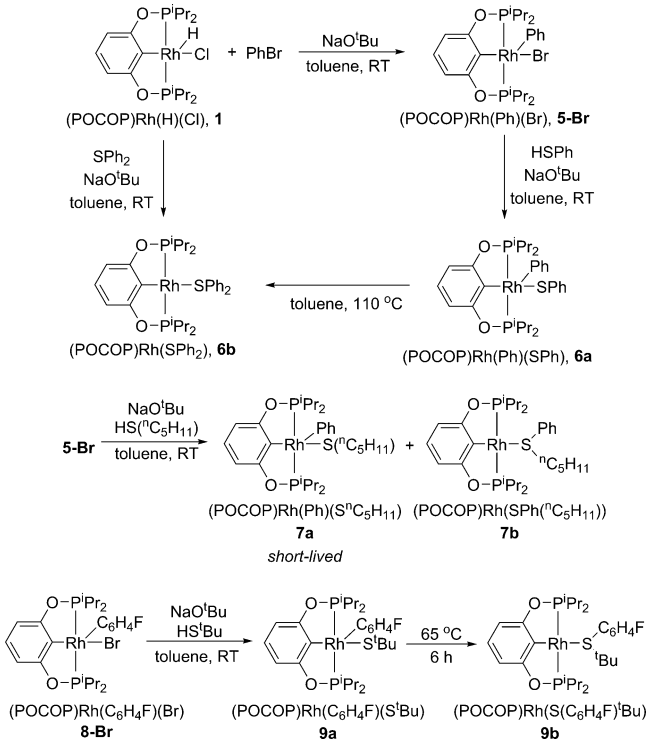
c-$C_6H_{11}SH$ gave a modest 30% yield of the coupling product when paired with *o*-MeC_6H_4Br and none with *o*-MeC_6H_4Cl (**r**). The attempted coupling of *o*-MeC_6H_4Cl or *o*-MeC_6H_4Br was entirely unsuccessful with an unencumbered aryl thiol (*p*-MeC_6H_4SH, **h**). However, *ortho*-substituted diaryl sulfide products were synthesized in moderate to good yields via the coupling of *ortho*-substituted aryl thiols with *p*-ClC_6H_4F or *p*-BrC_6H_4F (**i**−**k**). As the steric bulk was increased from **i** to **j** and **k**, the reaction times required for high conversion also increased to 40 and 80 h, respectively. Increased steric bulk of the reagents appears to be inhibitive of the catalysis, but it affects the thiol to a different degree than the aryl halide coupling partner (vide infra). We did not observe catalytic formation of thioethers in reactions with *p*-fluorophenyl tosylate (**a**, **l**). *p*-Fluorophenyl triflate reacted only sluggishly with cyclohexanethiol (**l**) and not at all with thiophenol (**a**).

Many of the reactions also produced a minor quantity (≤5%, except esters **m** and **n**, which gave 24% and 17%, respectively) of the corresponding Ar−H (Tables S4 and S5 in the Supporting Information). Its origin remains unclear but we have been able to establish that traces of moisture are not responsible. We tested this by examining formation of PhF in the synthesis of **b** and **v** with ArBr using reagents either simply degassed or rigorously dried by distillation from CaH_2. However, all reactions produced an equal amount of ca. 3% PhF. The formation of Ar−H is not detrimental to product isolation when aryl halides of relatively low molecular weight are used.

In order to examine the longevity of the catalyst, we conducted a series of coupling reactions with decreased catalyst loadings (Tables S6 and S7 in the Supporting Information) using *p*-MeC_6H_4SH and *p*-$F_3CC_6H_4X$ (X = Br or Cl) as substrates in one set of experiments, and *c*-$C_6H_{11}SH$ and *p*-FC_6H_4X (X = Br or Cl) in another. We were able to observe TON of up to 2500 with ArBr and 350 with ArCl but at low conversions. The lowest practical catalyst loading (>90% conversion in <3 d) is probably 0.1% for aryl bromides and 1% for aryl chlorides.

Synthesis of Intermediates. We previously described the synthesis of various (POCOP)Rh(Ar)(X) (X = Cl, Br, I) analogues.[14,16] (POCOP)Rh(Ph)(Br) (**5-Br**) was formed by treatment of **1** with NaO^tBu in the presence of PhBr (Scheme 3). The reaction occurred upon mixing at room temperature as indicated by a distinct color change from orange to red.

Scheme 3. Synthesis of Complexes 5−9



Treatment of **5-Br** with an additional equivalent of NaO^tBu in the presence of HSPh resulted in immediate formation of (POCOP)Rh(Ph)(SPh) (**6a**) (Scheme 3). Inspection of the ^1H and $^{31}P\{^1H\}$ NMR spectra of a C_6D_6 solution of **6a** after 1 wk at ambient temperature indicated approximately 3% conversion to (POCOP)Rh(SPh_2) (**6b**). **6b** was synthesized directly from **1** by treatment with NaO^tBu in the presence of SPh_2 at ambient temperature (Scheme 3). Independent thermolysis of **6a** or **6b** at 65 °C produced an equilibrium mixture of **6b**:**6a** in a 48:1 ratio.

The alkylthiolate analogues, (POCOP)Rh(Ph)($S^nC_5H_{11}$) (**7a**) and (POCOP)Rh(C_6H_4F)(S^tBu) (**9a**), were synthesized using the same method as for **6a** (Scheme 3). **7a** could only be observed in solution in a mixture and underwent 60% conversion to the reductive coupling product (POCOP)Rh-($SPh(^nC_5H_{11})$) (**7b**) after 15 min at room temperature, while **9a** produced no observable quantity of its reductive coupling product (POCOP)Rh($S(C_6H_4F)^tBu$) (**9b**) after 24 h at room temperature. However, thermolysis of **9a** (9 h at 65 °C) resulted in quantitative conversion to **9b**.

Molecular structures of **6a** and **6b** in the solid state were determined by single-crystal X-ray diffractometry (Figure 2). X-ray-quality crystals of **6a** were obtained from a saturated pentane solution at −35 °C. The solid-state structure presented a distorted square pyramidal coordination environment about the d^6 Rh^{III} metal center.[24] The geometry about Rh is quite similar to the structure of (POCOP)Rh(Ph)(I) we reported previously.[14] The phenyl group in **6a** minimizes the steric clash with the ^{i}Pr substituents on the phosphorus atoms by adopting a conformation where the plane of the phenyl ring is approximately perpendicular to the P−Rh−P vector. X-ray-quality crystals of **6b** were grown from a saturated toluene solution layered with pentane at −35 °C. **6b** adopts a distorted square planar geometry about Rh, as would be expected for a four-coordinate Rh^I complex.

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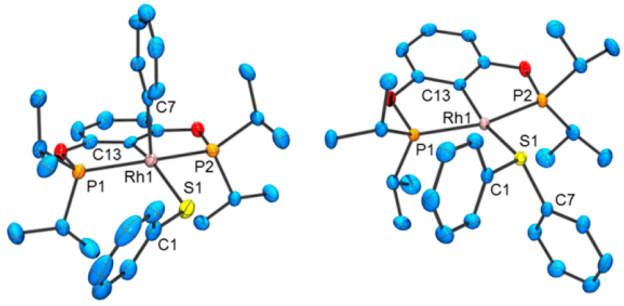
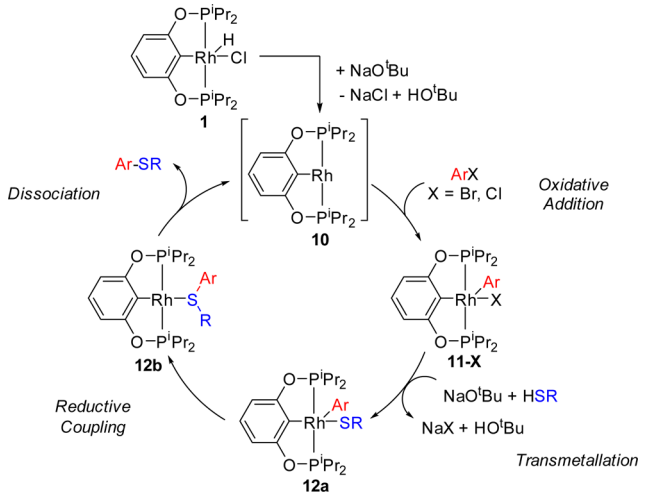


Figure 2. ORTEP drawings (50% probability ellipsoids) of (POCOP)-Rh(Ph)(SPh) (**6a**) (left) and (POCOP)Rh(SPh_2) (**6b**) (right) showing selected atom labeling. Hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg) for **6a**: Rh1−S1, 2.366(1); S1−C1, 1.774(5); Rh1−C7, 2.3852(8), Rh1−S1−C1, 114.7(2); C13−Rh1−S1, 154.6(1); C13−Rh−C7, 87.7(1); C7−Rh1−S1, 116.2(1). Selected bond distances (Å) and angles (deg) for **6b**: Rh1−S1, 2.3266(6); S1−C1, 1.786(2); S1−C7, 1.797(2); Rh1−S1−C1, 116.93(8); Rh1−S1−C7, 118.00(7); C13−Rh1−S1, 166.90(6); C1−S1−C7, 99.8(1).

Mechanism. The proposed mechanism for catalytic C−S coupling with **1** is shown in Scheme 4. NaO^{t}Bu serves to

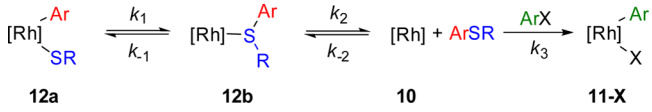
Scheme 4. Proposed Catalytic Cycle for the Coupling of Aryl Halides with Thiols Using 1 as the Catalyst



dehydrochlorinate **1** and produce the unobserved, unsaturated (POCOP)Rh^I fragment (**10**). We have previously demonstrated the importance of three-coordinate (pincer)Rh^I fragments in concerted OA reactions.[13,14] OA of an aryl halide to **10** would then produce (POCOP)Rh(Ar)(X) (**11-X**). This species would undergo transmetalation with NaSR[25] to produce (POCOP)Rh(Ar)(SR) (**12a**). The aryl/thiolato complex **12a** can undergo reductive coupling to form the thioether adduct (POCOP)Rh(ArSR) (**12b**), followed by thioether dissociation to re-form the unsaturated (POCOP)Rh^I fragment.

Isolation of compounds **5**/**6** allowed for closer study of each of the elementary reactions making up the proposed catalytic cycle. We were especially interested in elucidating parameters affecting the overall rate of catalysis. The transmetalation step can be confidently dismissed from this consideration given that it is rapid and irreversible even at room temperature. Thus, we focused on the remaining three steps with potential to be rate-limiting: reductive coupling (**12a** → **12b**), product dissociation (**12b** → **10**), and OA (**10** → **11-X**). Scheme 5 illustrates these three steps and highlights the rate constants relevant to the

Scheme 5. Elementary Steps of the Catalytic Cycle with Notations for Rate Constants

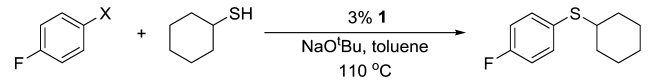


following discussion. The OA step is clearly irreversible in all cases, and we need only concern ourselves with the forward reaction (k_3). On the other hand, the reductive coupling step (k_1/k_{-1}) and the product dissociation step (k_2/k_{-2}) deserved closer attention.

As was mentioned above, the equilibria between **6a** and **6b** or **7a** and **7b** strongly favor the C−S coupled Rh^I products. This means that the $k_1 \gg k_{-1}$ and that the oxidative cleavage reaction (corresponding to k_{-1}) is not relevant to considerations of the rate-limiting step. Interestingly, we previously described an equilibrium observed for the (PNP)Rh analogues of **6a** and **6b** with a 1:1 ratio of (PNP)Rh(Ph)(SPh) and (PNP)Rh(SPh_2).[26] The increased preference for the Rh^I isomer may be attributed to the less electron rich nature of the (POCOP)Rh system vs (PNP)Rh;[27] which likely contributes to the enhanced catalytic performance with **1** compared to **2**.

Next, we explored the influence of the aryl halide substrate (Br vs Cl) on the reaction rates. In general (Figure 1), the use of ArBr led to faster catalysis than the use of analogous ArCl. In a specific comparison, we examined the apparent rate of the coupling of *p*-FC_6H_4X (X = Br, Cl) with *c*-$C_6H_{11}SH$ using either 1.1 or 10 equiv of *p*-FC_6H_4X (Table 1). The apparent

Table 1. Effects of Aryl Halide and Thioether Concentrations



			yield (%)	
X	equiv Ar−X	equiv thioether	1 h	3 h
Br	1.1	0	80	97
Br	1.1	1	88	96
Br	10	0	81	97
Cl	1.1	0	17	40
Cl	1.1	1	6	17
Cl	10	0	50	90

rate of catalysis was faster with *p*-FC_6H_4Br than with *p*-FC_6H_4Cl. It was the same with 1.1 and 10 equiv of *p*-FC_6H_4Br, while the analogous reactions with FC_6H_4Cl exhibited enhanced conversion with 10 equiv of FC_6H_4Cl.[28] In addition, we found (Table 1) that excess thioether inhibits the coupling of cyclohexanethiol with *p*-FC_6H_4Cl but not with *p*-FC_6H_4Br.

In a related pair of experiments, we examined the thermolysis of **6a** in the presence of PhBr or PhCl. In either reaction, 40% consumption of **6a** was observed after 4 h at 65 °C. But, whereas in the reaction with PhBr, the only product detected was **5-Br** in 40% yield, the reaction with PhCl at the same point in time produced 30% **6b** and 10% (POCOP)Rh(Ph)(Cl) (**5-Cl**). Additional thermolysis at 100 °C resulted in complete conversion to the respective (POCOP)Rh(Ph)(X) products (**5-Br** or **5-Cl**) in both reactions. Related observations were

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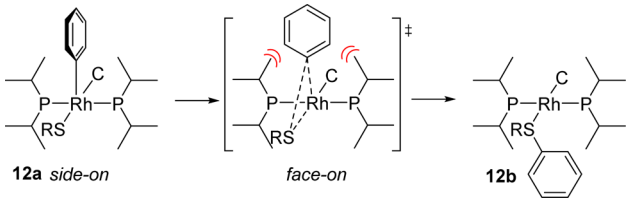
made in analyzing catalytic mixtures at intermediate conversion for the apparent resting state of the catalyst. In the case of PhCl/HSPh coupling we detected both **6a** and **6b**, while in the PhBr/HSPh coupling, only **6a** was detected.

These results indicate several things about the kinetics and mechanism for the coupling of simple aryl halides with PhSH. The rate of reductive coupling is independent of the identity of ArX, which is consistent with concerted, monomolecular C−S reductive coupling. The reductive coupling (k_1) is the rate-limiting step in catalysis involving ArBr. Dissociation of ArSAr′ is much faster ($k_2 \gg k_1$) and k_{-1} is of no concern given that $k_1 \gg k_{-1}$. Both the non-observation of **8** and the lack of apparent dependence on [ArBr] in catalysis suggest that once generated, the (POCOP)Rh intermediate is always trapped by ArBr to irreversibly form the OA product (POCOP)Rh(Ar)(Br) and the reverse trapping of (POCOP)Rh by the thioether product is not competitive (k_3[ArBr] $\gg$ k_{-2}[ArSAr′] in the relevant concentration ranges). In contrast, the trapping of (POCOP)Rh with the thioether product is competitive with ArCl: k_3[ArCl] is comparable to k_{-2}[ArSAr′], and so the rate of catalysis is sensitive to [PhCl].

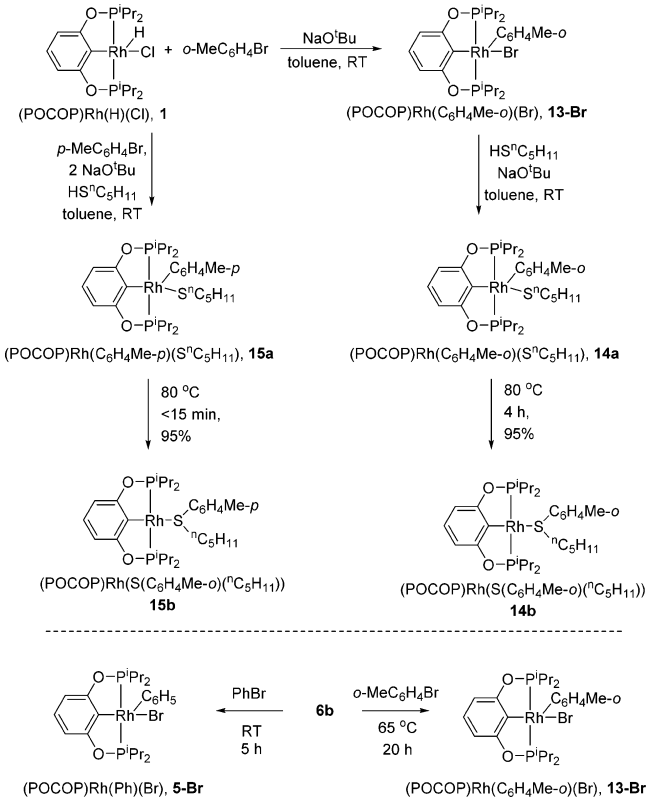
Changes in the steric bulk of the substrates have the potential to affect various steps along the catalytic cycle. Bulkier aryl halides or organothiols would result in sterically more imposing thioether products, which may accelerate catalysis by virtue of increasing k_2 and decreasing k_{-2} (Scheme 5). This may be especially in play in the catalytic synthesis of S^{t}Bu-derived **s** (Figure 1), one the bulkiest thoethers in our study. The catalysis proceeded quite well compared to other thiols (cf. **a**, **l**, **t**), considering that the rate of reductive coupling (**9a** → **9b**) was rather slow. On the other hand, increased steric bulk can adversely affect k_1 and k_3. Goldman, Krogh-Jespersen, et al. previously showed that, for Ar−X (X = Me, Ph, $CHCH_2$, CCH) RE from five-coordinate (PCP)Ir(Ar)(X), the aryl group must be oriented "face-on" toward X in the transition state.[29] The steric influence of the phosphines in the ground state of (PCP)Ir(Ar)(X) favors the "side-on" orientation of the aryl group with respect to X, and the necessary rotation of the aryl can be a considerable component of the activation barrier. This situation can be contrasted with the typical $(R_3P)_nPd(Ar)(X)$ (n = 1, 2) intermediates, where the steric bulk of the phosphines favors "face-on" orientation of the aryl with respect to X in the ground state and encourages faster RE.[30] The (POCOP)Rh(Ar)(X) system is sterically and electronically analogous to Goldman's (PCP)Ir(Ar)(X) system. From this vantage point (Scheme 6), the rotation of the aryl group in (POCOP)Rh(Ar)(SR) should be expected to be greatly inhibited by the *ortho*-substituent. *Ortho*-substitution also has the potential to inhibit OA of the aryl halide to (POCOP)Rh since it presumably proceeds via a transition state with similar spatial requirements.

Scheme 6. Schematic Illustration of the Rotation of the Aryl Group Necessary for Attaining the Transition-State Geometry for C−S Reductive Coupling



Scheme 7 contains a series of reactions shedding light on the influence of the *ortho*-substituent in the aryl halide. Compound

Scheme 7. Reactions Arising from *o*-Tolyl Halides



13-Br was synthesized in the manner analogous to **5-Br**. It was found to exist as a mixture of two rotamers. Variable-temperature NMR observations in the 20−110 °C range showed no change in the width of the signals of **13-Br** and no change in the ratio of rotamers, indicating slow rotation on the NMR time scale even at 110 °C. In contrast, examination of NMR spectra of **5-Br** showed coalescence of the Rh−Ph ^{1}H NMR resonances above 100 °C, consistent with a faster rotation about the Rh−C_{aryl} bond in the absence of the *ortho*-substituent.

Transmetalation gave access to *o*- and *p*-tolyl isomers **14a** and **15a**. Their thermolyses demonstrated that C−S reductive coupling is indeed slower for the *o*-tolyl: 33% conversion to the reductively coupled product **14b** was recorded for **14a** after 15 min at 80 °C (4 h to 95%), while the conversion of **15a** to **15b** was complete[31] by that point (12% conversion observed in several min at room temperature during preparation). Oxidative addition was examined using reactions of *o*-MeC_6H_4Br and PhBr with **8**. With PhBr, 40% conversion was observed after 10 min at room temperature (5 h at room temperature to complete conversion), while for *o*-MeC_6H_4Br, reaching 40% conversion required 1 h at 65 °C (20 h at 65 °C to complete conversion). Looking at the OA comparison, we found that the reaction of **6b** proceeded much faster with PhBr than with *o*-MeC_6H_4Br (Scheme 7). Thus, while RE and OA reactions stemming from *o*-tolyl halides are in principle accessible, they are both much slower. Whether that alone accounts for the very poor reactivity of *o*-tolyl halides in (POCOP)Rh catalysis is not fully clear. The reduced rate of the reactions in the desired cycle

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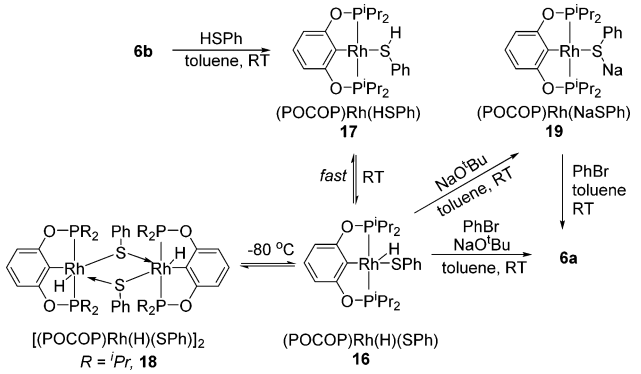
potentially opens the door to catalyst-killing side reactions, although we have not observed any direct evidence of them.

The Hartwig group carried out extensive studies on the influence of steric and electronic parameters on the rate of C−S RE from square-planar Pd(II) compounds.[32] In contrast to our findings here, they found that introduction of a single *o*-methyl group into the Pd-bound aryl slightly accelerates RE from (DPPE)Pd(Ar)(S^{t}Bu), although further buildup of steric pressure in the aryl is deactivating.

Steric bulk would only impact the rate of catalysis if the RLS is accelerated or decelerated. The observed effect of the sterics of the thiolate group on the rate of catalysis and RE is less straightforward. It is clear from the relative stability of **9a** vs that of **7a** that increased steric bulk on the thiolate ligand ultimately increases the barrier for reductive coupling. However, the catalytic reaction to form **l** from the secondary alkyl thiol (*c*-$C_6H_{11}SH$) and *p*-FC_6H_4Cl was faster (98%, 24 h) than the reaction to form **v** from the primary alkyl thiol (*n*-$C_5H_{11}SH$) and *p*-FC_6H_4Cl (94%, 48 h). Examination of the catalytic coupling reactions with *ortho*-substituted aryl thiols (Figure 1, **i**−**k**) shows an eventual decrease in the productivity of catalysis as the steric bulk of the substituent is increased from **i** to **j** and **k**. Compared to **i**, the reaction time increased by a factor of 2 for the formation of **j** and increased by a factor of 4 for **k**, consistent with an increased barrier for reductive coupling with bulky thiolate groups. Interestingly, the rate of formation of **i** is similar or even greater to that of the *para*-substituted **b** and non-substituted **a**. *Ortho*-substitution in the aryl thiol does not appear to have as dramatic of an inhibiting effect as *ortho*-substitution in the aryl halide, likely because it is farther removed from the Rh center and has less impact on the ease of achieving the orientation necessary for the C−S bond-forming transition state. At the same time, *ortho*-substitution in the diaryl thioether may have a positive effect on k_2 (Scheme 5). All of these results indicate that there is a delicate balance between the sterics of the thiolate group and its effect on the rate of catalysis. The 1998 Hartwig study[30] of C−S RE from Pd(II) found that increasing steric bulk in *alkyl*thiolates was beneficial, while increasing steric bulk in *aryl*thiolates was detrimental to the rate of RE.

Additional Reactivity. Hartwig and co-workers previously identified $L_nPd(H)(SR)$ as the catalyst resting state for C−S coupling reactions catalyzed by $L_nPd(Ar)(X)$.[12] We were interested to see if the (POCOP)Rh system would react with thiols in a similar fashion, as well as the potential for a hydrido/thiolato complex of this nature to impede catalysis. Treatment of **6b** with HSPh resulted in formation of (POCOP)Rh(H)(SPh) (**16**) upon mixing (Scheme 8). The ^{1}H NMR spectrum of **16** displayed a hydride resonance at −23.00 ppm and slightly broadened POCOP signals. The spectrum displayed 1 methine resonance and 2 resonances for the methyl protons of the isopropyl groups, which is the pattern for a C_{2v}-symmetric complex. However, **16** should be C_s-symmetric (by analogy with **1**, for example) and should display two distinct methine resonances and four different resonances for the methyl protons. The apparent C_{2v} symmetry could be the result of fast reversible S−H reductive coupling on the metal, which would create a rapid exchange between two degenerate forms of **16** and the unobserved C_{2v}-symmetric thiol adduct (POCOP)Rh(HSPh) (**17**). **19** was examined by NMR spectroscopy in the −80 °C to +20 °C range (Figure S15−S17 in the Supporting Information). As a solution of **16** in d_8-toluene was cooled to −60 °C, two distinct methine resonances

Scheme 8. Formation of 16 and 19



and four distinct methyl resonances were visible in the ^{1}H NMR spectrum, consistent with the expected C_s-symmetric structure for **16**. As the solution reached −80 °C, a new set of resonances appeared, corresponding to an additional C_s-symmetric compound. The new resonances included a new hydride resonance at −16.9 ppm, consistent with a hydride that is not *trans* to an open coordination site. These data led us to tentatively assign the new complex as [(POCOP)Rh(H)(SPh)]$_2$ (**18**), the dimer of **16**. A rapid equilibrium between **16** and **18** would not explain the C_{2v} symmetry observed for **16** at room temperature. Moreover, the observed hydride chemical shift at −23.00 ppm at room temperature is consistent with a hydride *trans* to an empty site and is similar to the chemical shift of the hydride in **16** observed at −80 °C. Thus, the dimeric **18** is not present in solutions of **16** at room temperature in a significant amount.

Treatment of **16** with 1 equiv NaO^{t}Bu resulted in an immediate color change to yellow-brown (Scheme 8). Analysis of the reaction by ^{1}H NMR spectroscopy showed conversion to a new compound accompanied by the disappearance of the hydride resonance and the appearance of HO^{t}Bu. The identity of the new compound was determined to be (POCOP)Rh(NaSPh) (**19**) by X-ray crystallography (Figure 3), and is consistent with the formal deprotonation of the coordinated thiol by NaO^{t}Bu. The extended solid-state structure of **16** shows a chain structure where sodium has close interactions in one (POCOP)Rh(SPh) unit with sulfur (Na−S, 2.751(2) Å), and in another with the rhodium center (Na···Rh, 2.8958(13) Å) and the Rh-bound carbon (Na···C, 2.881(3) Å).[33]

16 and **19** both convert to the product-forming **6a** under the conditions of catalysis (Scheme 8). **16** converted to **6a** when treated with NaO^{t}Bu (to yield **19**) and then PhBr after 1 h at room temperature (cf. **6b** requiring 5 h for complete reaction with PhBr). Complex **6b** showed no reaction with NaSPh at room temperature or after thermolysis at 110 °C. These reactions illustrate that neither **16** nor **19** should form in an appreciable concentration under the conditions of catalysis (and we have not observed them in analyzing catalytic mixtures, *vide supra*). These findings pertain to the reactions involving NaSPh, PhBr, and SPh_2, but it is possible that other combinations of substituents may favor sodium thiolate complexes to a greater degree.

■ CONCLUSION

In summary, we have presented a well-defined (POCOP)Rh system for the catalytic coupling of aryl bromides and chlorides with aryl and alkyl thiols. Our preliminary mechanistic studies

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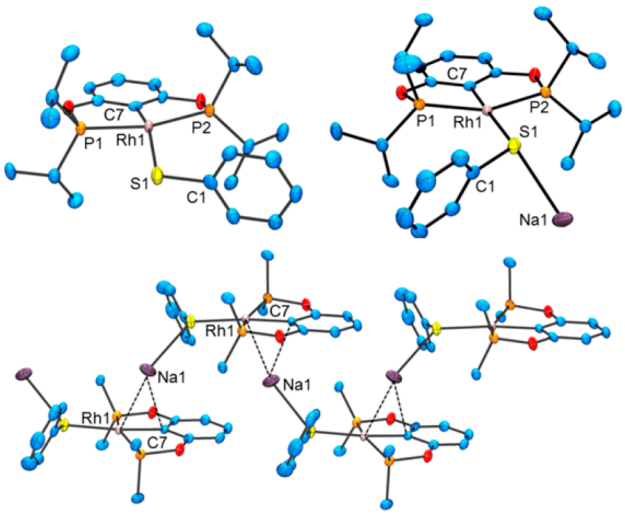

Figure 3. ORTEP drawings (50% probability ellipsoids) of (POCOP)-Rh(H)(Ph)(SPh) (**16**) (top left) and (POCOP)Rh(NaSPh) (**19**) (top right). Hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg) for **16**: Rh1−S1, 2.323(3); S1−C1, 1.78(1); Rh1−S1−C1, 113.8(8), C7−Rh1−S1, 157.7(3). Selected bond distances (Å) and angles (deg) for **16**: Rh1−S1, 2.3852(8); S1−C1, 1.790(3); S1−Na1, 2.751(2); Rh1−S1−C1, 112.60(8); Rh1−S1−Na1, 132.70(4); Na1−S1−C1, 87.59(8); C7−Rh1−S1, 174.45(7)(3). The extended crystal packing of **19** (bottom) showing selected atom labeling. Hydrogen atoms and isopropyl methyl groups are omitted for clarity. The extended crystal packing structure of **19** shows sodium interactions with sulfur (Na−S, 2.751(2) Å), neighboring rhodium centers (Na···Rh, 2.8958(13) Å), and the chelating aryl carbon of the pincer framework (Na···C, 2.881(3) Å).

showed increased favorability toward aryl−sulfur RE with (POCOP)Rh relative to the analogous (PNP)Rh system. They also exposed the apparent dependence of the rate of catalysis on aryl chloride but not aryl bromide concentration. The analysis of steric effects in the aryl halide and in the thiol component reveals a rather complex picture, where the influence of the sterics depends on the nature of the rate-limiting step for various substrate couples. Reactions of PhSH and PhSNa with the catalytically active species were examined and deemed not to be detrimental under catalytic conditions. These results support the proposed Rh^{I}/Rh^{III} mechanism for aryl halide thiol cross-coupling reactions with Rh.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of experimental procedures and characterization; crystallographic information in the form of CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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