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Nickelation of PCP- and POCOP-Type Pincer Ligands: Kinetics and **Mechanism**[†]

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Supporting Information



ABSTRACT: This report describes the results of a combined experimental and computational investigation on the kinetics and mechanism of the C-H metalation step involved in the formation of PCP- and POCOP-type complexes of nickel. The kinetics of the C-H nickelation reaction was probed through competition studies involving two ligands reacting with a substoicheometric quantity of {(*i*-PrCN)NiBr₂}_n. These experiments have confirmed that metalation is more facile for aromatic ligands 1,3-(*i*- $Pr_2PE)_2C_6H_4$ vs their aliphatic counterparts 1,3-(*i*-Pr_2PECH_2)_2CH_2 (sp² C-H > sp³ C-H; E = O, CH₂), ligands bearing phosphine moieties vs those with phosphinite moieties (PCP > POCOP), ligands bearing P substituents i-Pr₂P vs t-Bu₂P and Ph₂P, and POC_{sp}²OP ligands 1,3-(*i*-Pr₂PO)₂C₆R_nH_{4-n} bearing electron-donating vs electron-withdrawing substituents (*p*-OMe \approx m-OMe > p-Me > m-CO₂Me > p-CO₂Me > m,m-Cl₂). Among the latter, there is a 6-fold difference in C–H metalation rate between ligands bearing p-OMe and p-COOMe, whereas the most readily metalating ligand, $1,3-(i-Pr_2PCH_2)_2C_6H_4$, is metalated ca. 270 times more readily relative to the least reactive ligand, 1,3-(i-Pr₂POCH₂)₂CH₂. Density functional calculations indicate that PCP- or POCOP-type pincer ligands react with NiBr₂ to generate nonmetalated intermediates that form the corresponding pincer complexes via a two-step mechanism involving an ionic dissociation of the bromide to give a tight ion pair intermediate, followed by bromide-assisted deprotonation of the C-H bond. The type of structure adopted by the nonmetalated intermediates (mono- or dinuclear; tetrahedral, cis or trans square planar) and the energy barriers for the metalation transition states depend on the steric properties of the PR₂ moiety. The presence of a base that can neutralize the HBr generated in the metalation step is crucial for rendering the metalation process exergonic. One rationale for the more facile metalation of PCP ligands in comparison to their POCOP counterparts is the greater donor character of phosphine moieties, which allows a more effective stabilization of the coordination and metalation transition states wherein the strongly donor halide ligand is displaced by a much weaker C-H bond donor. The aromatic ligands metalate more readily than their aliphatic analogues for multiple reasons, including the higher ground state energy of the nonmetalated intermediates formed with aromatic ligands, the stronger C_{sp²}-Ni bond formed via metalation, and the more stabilized anionic charge on the C atom being metalated.

■ INTRODUCTION

Historically, the bulk of the experimental efforts dedicated to promoting transition-metal-mediated C-H activation reactions has involved complexes of 4d and 5d transition metals.^{1,2} Their strong M-H and M-C bonds have contributed to our perception of these metals as being much more adept at promoting C-H activation reactions relative to their lighter counterparts. Nevertheless, many reports of C-H activation/ metalation by 3d metals have appeared over the past decades and lately are appearing more frequently.³ Indeed, Kleiman and Dubeck reported an early instance of chelate-assisted C-H nickelation nearly 50 years ago,⁴ while pincer-type complexes of nickel were among the first such complexes reported. Thus, Shaw showed that heating $[Ni(H_2O)_6]Cl_2$ and 1,3-(t $Bu_2PCH_2)_2-C_6H_4$ in EtOH at 80 °C for 5 min gave the corresponding PCP-type complex A, shown in Chart 1.⁵

Shaw's early reports have inspired many other groups to use a C-H nickelation strategy for preparing a variety of nickel complexes featuring pincer ligands based on both aromatic and aliphatic skeletons (Chart 1);⁶ there is also increasing reliance on direct C-H metalation reactions for preparation of pincer complexes of other 3d metals.^{7,8} While formation of a pincer complex is an overall intermolecular metalation process, the C-H metalation step involved in this process is considered to be intramolecular in nature, because it is thought to occur in the intermediate generated following the initial binding of the

Received: May 5, 2012 Published: August 23, 2012 Chart 1



ligand moieties (double chelate-assisted activation). In some instances, intermediates en route to a pincer complex featuring a C–H moiety "poised" for metalation have been detected or isolated.⁹

A broad survey of the literature on pincer complexes of nickel reveals that they can be prepared via C-H nickelation in the case of bis(phosphine) (PCP),^{6,10} bis(phosphinite) (POCOP),^{11,12} and amino(phosphinite) (POCN)¹³ ligands, whereas virtually all reported cases of complexes featuring bis(amino) moieties (NCN) are prepared via alternative synthetic routes, ^{14,15} C–H nickelation being generally inaccessible for this family of ligands.¹⁶ Indeed, the success of the C-H nickelation step depends not only on the nature of ligand donor moieties but also on the hybridization of the C atom being nickelated $(sp^2 vs sp^3)$, the type of nickel precursor used, and the reaction conditions (temperature, solvent, etc.). The importance of the "linker" moiety is evident from the observation that aromatic ligands of the type $1,3-Q_2-C_6H_4$ $(Q_2 = (R_2PCH_2)_{2J} (R_2PO)_{2J} R_2PO/R_2NCH_2)$ nickelate much more readily in most cases without detectable intermediates,¹⁷ whereas the analogous ligands based on aliphatic backbones generate mixtures of nickelated and non-nickelated products, some of which are illustrated in Scheme 1.^{10a,b,18,19}

In an effort to understand the different aptitudes of pincer ligands for C–H nickelation, we have undertaken a combined

Scheme 1

experimental and computational study to probe the rates and mechanisms of these reactions. The experimental work has sought to quantify the relative nickelation rates for PCP- and POCOP-type pincer ligands as a function of donor moiety (i.e., P substituents), hybridization of the central carbon atom ($sp^2 vs$ sp³), and ring substituents R' in $1,3-(R_2PO)_2C_6H_nR'_{4-n}$. The computational studies, on the other hand, have focused on identifying the reaction pathways and structures of intermediates and/or transition states, with the goal of identifying the factors governing C-H nickelation reactions and shedding light on their mechanisms.²⁰ The overall objective is to determine whether the C-H nickelation reactions involved in the synthesis of PCP- and POCOP-type pincer nickel complexes are best viewed as proceeding by oxidative addition/reductive elimination steps, being electrophilic or nucleophilic in nature, or otherwise belonging to other reaction schemes under consideration by the community of researchers.²¹

RESULTS AND DISCUSSION

Experimental Studies. The ligands required for the kinetic studies are shown in Chart 2. Ligands 1–4 were selected to quantify how nickelation rates are influenced by the type of donor moiety (PCP vs POCOP) and linker skeleton (aromatic vs aliphatic), while 1a–j were selected to evaluate the impact of ring substituents on the nickelation of this family of ligands. The experimental work began by synthesizing the PCP and POCOP using modified versions of previously reported procedures.²² In general, the POCOP ligands can be prepared by reacting the requisite diol preligands with ClPR₂ in the presence of base.²³ This methodology is much more straightforward and often gives better yields in comparison to the synthesis of PCP ligands, which are obtained from the reaction of suitable dihalides with $[R_2P]^-$ or $R_2PH/base.^{24,25}$

Previous reports have indicated that the choice of Ni precursor and presence of a suitable base are important factors for success in the synthesis of PCP- and POCOP-type pincer complexes.^{10,11b,c,13a,18} In our experience, the best precursors for C–H nickelation of pincer ligands are (MeCN)_nNiBr₂²⁶





and {(*i*-PrCN)NiBr₂}_{*m*}²⁷ the latter being more suitable for conducting kinetic studies owing to its well-defined molar mass.²⁸ The importance of base for the nickelation of PCP ligands has been demonstrated by the low yields of (PCP)NiBr (<50%) and recovery of the protonated (unmetalated) ligand as a precipitate.^{10a} Similarly, the complexes (POCN)NiBr can be prepared in 80–90% yields when NEt₃ is added to the reaction mixture, whereas much lower yields are obtained (~35%) in the absence of added base.^{13a,b} On the other hand, Morales-Morales's group has reported that refluxing PO-C^HOP^{Ph} and NiCl₂ in toluene in the absence of any added base gives (POCOP^{Ph})NiCl with 80% yield.^{11a}

To further probe the importance of base for nickelation of POCOP ligands, we used ³¹P NMR to monitor the reaction of ligand 1a with $\{(i\text{-PrCN})\text{NiBr}_2\}_n$ in the absence of an added base. The signal for 1a (148.1 ppm) disappeared over time, and we observed a singlet resonance at 188.6 ppm due to the pincer complex (POCOP)NiBr (1a'), in addition to a new peak at 134.7 ppm. Addition of NEt₃ to the reaction mixture led to the formation of a white precipitate and caused the suppression of the latter peak and the reappearance of the original signal for ligand 1a. An independent test established that reaction of 1a with excess HX generates the diprotic species shown in Scheme 2 (no hydrolysis back to resorcinol); we conclude, therefore,



that the HX generated during the formation of our pincer complexes must be quenched to prevent protonation of unreacted ligands. Thus, the competition nickelation reactions were conducted in the presence of NEt_3 to ensure that these reactions are driven to completion.

Kinetic Studies. Initial tests showed that UV–vis spectroscopy could not be used for monitoring the metalation reactions, due to significant overlap in the absorption energies of some ligands and their respective complexes; in contrast, the ${}^{31}P{}^{1}H$ NMR chemical shifts of various ligands and complexes were free of overlap for the most part, making this the most suitable method for kinetic studies. Preliminary measurements showed that, under the pseudo-first-order conditions, nickelation of the aromatic ligands 1 and 2 is too rapid for monitoring by NMR: most reactions were essentially finished in the time of mixing. Employing low reaction temperatures or very dilute samples slowed down these reactions somewhat (2-5 min), but not sufficiently to allow convenient rate measurements.²⁹ As a result, we have opted to measure *relative* rates of nickelation via competition experiments, as described below.

Relative Nickelation Rates. The competition experiments were conducted as follows. Mixtures of 1.0-1.1 equiv of each of the two ligands under study were prepared and analyzed by ³¹P NMR to register the initial molar ratio. THF was used as solvent for mixtures of aromatic ligands 1 and 2, whereas toluene was used in the case of aliphatic ligands 3 and 4. Each mixture was then added to a homogeneous solution containing $\{(i-PrCN)NiBr_2\}_n$ and NEt₃ with stirring at room temperature; the initial Ni:L:L':NEt₃ molar ratio was approximately 0.75:1.0:1.0:2.0 (eq 1). Stirring the resulting mixture at room temperature for a few minutes was sufficient to nickelate the aromatic ligands 1 and 2, as signaled by the nearly instantaneous color change from blue to brown and then vellow, followed by the gradual precipitation of a white solid (HNEt₃Br). It is worth noting that these mixtures remain homogeneous throughout the reaction, except for the precipitation of the ammonium salt at the end.

Nickelation of the aliphatic ligands 3 and 4 followed a different path: stirring the mixture at room temperature caused a color change from blue to deep purple, which changed to yellow only after the reaction mixture was heated to ca. 70–90 °C for 2–3 days. The ³¹P NMR spectra of these mixtures have established that the yellow color corresponds to the target pincer complexes, whereas the sparingly soluble deep purple species is an NMR-silent nonmetalated species described previously.^{10a,b,18}

Integration of the ³¹P signals due to the pincer complexes present in the final reaction mixtures allowed us to establish the relative nickelation aptitudes of the ligands studied. That the nickelation rates can be considered invariable under the conditions of these kinetic studies was confirmed by the

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Table 1. Relative Nickelation Rates for Various POCOP and PCP Ligands^a





^{*a*} For details of the procedure used for conducting these competition studies, see the main text or the Experimental Section. Footnotes in the body of the table are as follows. (†) The relative rates of nickelation for these ligands could not be determined directly, because the ³¹P NMR signals of their complexes overlapped. We integrated, instead, the signals for free ligands remaining after the nickelation and used their ratio for deducing the relative rates of nickelation. (‡) In this case, addition of $\{(i-PrCN)NiBr_2\}_n$ caused the reaction mixture to turn green initially and the nickelation was fairly slow: the mixture was analyzed 1 h later after the anticipated white precipitate (HNEt₃Br) and yellow color appeared.

Scheme 3



observation that no reaction occurs after stirring for 24 h mixtures of complex 1e' and the free ligand 1a (1 day at 55 °C) or complex 3' and ligand 4 (70 °C).³⁰ Most experiments were carried out in triplicate and showed fairly reproducible results, the relative rates varying by ca. 10% on average. The results of these competition experiments are presented in Table 1 and discussed below.

The first two entries of Table 1 show the results of competition experiments that served to quantify our previous

observations that nickelation is much more facile for the aromatic ligands. Monitoring these experiments by ³¹P NMR also revealed important insights about how the nickelation proceeds. For instance, holding the reaction mixture containing $1a/3/{(i-PrCN)NiBr_2}_n/NEt_3$ at room temperature over several hours led to none of the anticipated nickelated product, 1a': the ³¹P NMR spectra of this mixture showed only the signals for 1a (major) and 3 (trace), but none for 1a', which was unexpected because nickelation of 1a to 1a' normally

occurs in less than 2 min at room temperature in the absence of 3. On the basis of our previous observation that 3 reacts with $Br_2Ni(NCMe)_n$ to give a nonmetalated, NMR-silent species that does not undergo metalation at ambient temperature,³¹ we infer that at room temperature the nickel precursor is ligated by the aliphatic ligand 3 and remains trapped in the form of a nonmetalated (and NMR-silent) species. Heating the mixture for several hours at 70 °C in the presence of 3 led to the appearance of the pincer complex 1a' and free ligand 3, presumably because heating releases the nickel precursor and allows it to react with 1a. These observations can be rationalized by invoking a reaction scheme under Curtin-Hammett control: the nonmetalated intermediates interconvert rapidly via a binding equilibrium that favors ligation of Ni(II) by 3, and the subsequent nickelation steps are slower and irreversible (Scheme 3).

Next, we probed the question of which donor moiety, phosphine or phosphinite, would be more adept at facilitating the nickelation of pincer ligands. The results shown in entries 3 and 4 establish that nickelation is more than 5 times faster for the PCP ligands 2 and 4 vs their POCOP analogues 1 and 3. These observations, combined with the fact that NCN-type ligands $1,3-(CH_2NR_2)_2-C_6H_4$ do not undergo nickelation, $^{14-16,18}$ demonstrate the importance of the donor moiety character (PCP > POCOP \gg NCN). P substituents were also found to have a major influence on the nickelation rates of POC_{sp}²OP ligands (entries 5 and 6: *i*-Pr₂P \gg *t*-Bu₂P, Ph₂P); previous studies have also shown that nickelation proceeds more readily with the PCP ligand 4 in comparison to its *t*-Bu₂P analogue.^{10a,b}

The impact of ring substituents on the nickelation rates was studied next. Among the variously substituted POC_{sp}²OP ligands, those bearing the electron-donating substituents Me and OMe accelerated the nickelation rates relative to the unsubstituted ligand 1a (entries 7-9), while ligands bearing electron-withdrawing substituents showed significantly slower nickelation rates (entries 10-12; see the Supporting Information for a plot of the Hammett parameters). It appears, therefore, that nickelation of these aromatic POCOP ligands is akin to an electrophilic aromatic substitution,³² whereas the opposite has been observed for direct palladation of aromatic C-H bonds. For instance, the groups of Maseras and Echavaren have demonstrated a Pd-catalyzed C-H activation/cyclization reaction that proceeds preferentially on aromatic rings bearing electron-withdrawing groups,³³ and Fagnou's group has reported extensively on the much more facile palladation of electron-poor aromatic rings.³⁴

In the case of MeO-substituted ligands, the substitution pattern (meta vs para) seems to have little or no effect on metalation (entry 13), which is very different than in the case of MeO₂C-substituted ligands: a *p*-COOMe group appears to be more effective in hindering the nickelation than a *m*-COOMe group (entry 4).³⁵ Finally, comparison of the results shown in entry 15 vs entries 3 and 4 demonstrates that judicious choice of ring substituents can induce as significant an impact on the nickelation rate as induced by the character of the donor moiety. Chart 3 shows the relative rates of metalation for all the pincer ligands studied here, normalized to the POC_{sp}³OP ligand 3.

Density Functional Investigation. Nickelation of the PCP and POCOP pincer ligands has been investigated by quantum mechanical calculations to shed light on reaction mechanisms and interpret the observed relative rates of





nickelation. Our efforts have focused on identifying possible ground-state structures for the nonmetalated (LH)NiBr₂ complexes and the corresponding pincer species LNiBr (L = PCP- and POCOP-type pincer ligands), in addition to any plausible intermediates and transition states involved in the metalation pathway. All stationary point structures presented were verified as minima or saddle points with full calculation of the Hessian using Gaussian 09^{36} with the $M06^{37}$ density functional method using an ultrafine integration grid. The choice of M06, which is a hybrid meta functional that was designed for broad applicability including transition metals,³ was based on several recent computational benchmark and experimental comparative studies showing that M06 is the most accurate functional currently available for organometallic systems.³⁹ In addition, the M06 functional is known to accurately reproduce Ni-P type bond energies, whereas many other common density functionals fail.⁴⁰ Nevertheless, comparison is also made throughout the present study to results obtained from computations based on B3LYP, BP86, and MPWPW91 functionals.

All optimizations were carried out in implicit THF solvent using the CPCM model combined with UAKS radii. The basis set employed consisted of LANL2TZ(f) with the polarizing f exponent set to 3.130 for Ni, LANL2DZdp for Br, and 6-311G(2d,p) for all other atoms. Unless otherwise noted, all reported energy values are free energies in THF at 298 K. Singlet-triplet spin-crossing (SC) points, also called minimum energy crossing points (MECP), were located using the algorithm developed by Harvey et al. in conjunction with Gaussian 09.⁴¹ The 3D ball and stick structures were rendered using CYLview.⁴²

Ground State Ligand Coordination in (PC_{sp3}^HP)NiBr₂. To begin, we have explored tetrahedral as well as cis and trans square-planar coordination geometries for the mononuclear nonmetalated species $(PC_{sp}^{HP})NiBr_2$ 1 (Figure 1). As expected, structures featuring square-planar geometries (¹trans-1, ¹trans-1-twist, and ¹cis-1) are singlet species, while the tetrahedral species ³tetra-1 is a triplet. Interestingly, ³tetra-1 was found to be the lowest energy structure at the M06 level of theory, being 4.7, 4.4, and 3.7 kcal/mol lower than ¹cis-1, ¹trans-1, and ¹trans-1-twist, respectively; this difference in stability was found to be even greater (by ca. 10 kcal/mol) when the B3LYP functional was used. The observed order of stabilities, which is contrary to the usual preference for squareplanar structures in (PR₃)₂NiX₂, arises mostly from the minimization of CH₂-CH₂ eclipsing interactions in the highly twisted configuration adopted in 3 tetra-1 by the PC_{sp} ${}^{{}^{3}H}$ P ligand backbone. Among the square-planar structures, the eclipsing interactions seem to be highest in ¹cis-1, followed by ¹trans-1



Figure 1. Lowest energy square-planar and tetrahedral ground-state complexes for the nonmetalated $(PC_{sp}{}^{3H}P)NiBr_2$. Free energies are relative to 3 tetra-1 (kcal/mol).

and ¹trans-1-twist. Another important factor is the smaller than ideal P–Ni–P angles in ¹trans-1 (157°) and ¹trans-1-twist (148°) structures in comparison to the nearly ideal P–Ni–P angle of ca. 106° in ³tetra-1. The closest C–H…Ni distance (at 2.367 Å in ¹trans-1) does not induce any C–H bond elongation, implying that none of these nonmetalated structures involves η^2 C–H agostic interactions.

The structures depicted in Figure 1 are for 1:1 $PC_{sp}^{3H}P:NiBr_2$ species. Exploring the energetics of 2:2 species has led us to the structure *trans,trans-*($PC_{sp}^{3H}P)_2Ni_2Br_4$ (¹trans,trans-1) shown in Figure 2.⁴³ The conversion of 2 equiv of ³tetra-1 into ¹trans,trans-1 is exergonic by 7.5 kcal/mol at the M06 level of theory (eq 2), because this dinuclear structure can adopt a



nearly optimal square-planar geometry with P–Ni–P angles of ca. 176°. In contrast, B3LYP predicted that conversion of ³tetra-1 to ¹trans,trans-1 should be endergonic by 1.3 kcal/ mol. However, this endergonic estimate is likely the result of B3LYP overestimating the high-spin state. When *i*-Pr₂P groups were modeled instead of Me₂P, ³tetra-1 was found to be more stable than ¹trans,trans-1 even by M06 ($\Delta G = 2.1$ kcal/mol), indicating that the steric bulk plays a significant role in whether dimeric or monomeric nickel species are favored. It is worth noting that if ¹trans,trans-1 is formed, either as a kinetic product or in equilibrium, it must convert to a mononuclear species prior to metalation. In other words, factors leading to stabilization of dimeric structures will likely hinder the metalation step.⁴⁴

Mechanism of $(PC_{sp}^{3H}P)NiBr_2$ Metalation. The first mechanism we explored for the metalation of (PC_{sp}^{3H}P)NiBr₂ involves oxidative addition of the central C-H bond of the coordinated ligand onto the Ni^{II} metal center to give an octahedral, tetravalent hydrido-pincer intermediate (Scheme 4a). Oxidative addition is typically a closed-shell process and is unlikely to proceed from the triplet species ³tetra-1. Accordingly, the lowest energy oxidative addition transitionstate structure located for the bromo precursor (X = Br) is the closed-shell singlet ¹trans-OXadd, which leads to the hydridopincer intermediate ¹trans-INT (Figure 3). The free energy barrier for this process is 20.7 kcal/mol relative to ³tetra-1, and the hydrido-pincer intermediate is endergonic by 19.7 kcal/mol relative to ³tetra-1. It is also worth noting that ¹trans-INT faces a reductive elimination barrier of only 1.4 kcal/mol; such shallow M-H intermediates have also been detected in other oxidative addition reactions analyzed by DFT.45

The reaction pathway leading to ¹trans-OXadd goes through the singlet species ¹trans-2 (Figure 4), which resembles ¹trans-1 except for the proximity of the nickel center to the methylene group that eventually undergoes metalation. At 1.958 Å, the C– H…Ni distance in ¹trans-2 is typical of an agostic type interaction, but the relatively nonperturbed C–H bond (1.108 Å) and the higher energy of ¹trans-2 relative to ³tetra-1 (by 9.9 kcal/mol) indicate that the C–H bond does not participate in an agostic interaction. This is a reasonable conclusion, because there is no low-lying and geometrically accessible vacant orbital on the nickel center. Unexpectedly, ¹trans-2 was found to be a spin-contaminated species ($\langle S^2 \rangle = 0.17$), and its reoptimization as a triplet gave the nearly equally energetic structure ³trans-2 (10.0 kcal/mol, Figure 4). The possible pathways leading to ¹trans-2 and ³trans-2 are shown in Scheme 5.



Figure 2. Possible nonmetalated trans-dinuclear species.

Scheme 4





Figure 3. Oxidative addition transition structure and nickel hydride intermediate for sp 3 PCP metalation. Free energies are expressed in kcal/mol relative to 3 tetra-1.



Figure 4. Singlet and triplet intermediates prior to sp³ PCP ligand metalation. Free energies are expressed in kcal/mol relative to **³tetra-1**.

The next mechanism we explored was σ -bond metathesis that would directly generate the metalated product (PC_{sp}:P)-NiBr and HBr (Scheme 4b). All attempts to locate a transition state for the bromo precursor traversing this pathway converged on the structure ¹trans-TS (Figure 5), for which the free energy was found to be lower than that of ¹trans-OXadd by 3.3 kcal/mol (M06) or 10.6 kcal/mol (B3LYP). The most significant feature of ¹trans-TS is the completely dissociated character of the bromide ion during the deprotonation of the C–H bond. This aspect differentiates the C–H nickelation scheme operating in the present system from analogous mechanistic schemes in which the base remains coordinated to the metal center throughout the metalation process (cf. concerted metalation deprotonation⁴⁶ and ambiphilic metal–ligand activation^{21b,47}).

Modeling the transition structure with *i*- Pr_2P moieties leads to a greater predicted activation free energy for the two-step ionic pathway (17.4 vs 21.2 kcal/mol), which is not surprising given the congested transition state. It should be noted, however, that oxidative addition remains the higher energy pathway (29.4 vs 21.2 kcal/mol), even with *i*- Pr_2P moieties. The closed-shell structure ¹trans-TS does not have a lower energy unrestricted energy solution; a similar transition structure was also identified on the triplet energy surface, but this triplet structure (³trans-TS, Figure 5) is 24.9 kcal/mol higher in free energy than the singlet transition structure.

The imaginary vibrational frequency in ¹trans-TS suggests that this structure connects an ion pair intermediate to the metalated product and liberated HBr. However, calculation of the forward and reverse intrinsic reaction coordinates (IRC) only showed product formation, while optimization of a slightly perturbed ¹trans-TS structure gave ¹trans-2. Since the IRC calculations were not definitive, we explored the homolytic and heterolytic Ni-Br bond dissociation energies (BDE). The unreasonably large BDE value for homolytic cleavage of the Ni-Br bond (53.0 kcal/mol relative to ¹trans-2) indicates that all scenarios requiring such a step can be discounted. Heterolytic cleavage of the Ni-Br bond (24.7 kcal/mol relative to ¹trans-2) is significantly lower than homolytic cleavage but higher than ¹trans-TS, suggesting that the bromide anion likely undergoes an incomplete dissociation prior to ¹trans-TS to form a tight ion pair intermediate between ¹trans-2 and ¹trans-TS. To explore this possibility, we carried out Ni-Br bond scans on ¹trans-2 from 2.40 to 4.00 Å, which revealed that a closed-shell minimum energy structure ion-pair (Scheme 5) exists at a Ni-Br bond length of 3.90 Å.

The tight **ion-pair** intermediate is generated from an associative type transition structure where the incoming C–H bond begins to form an agostic interaction with concomitant displacement of the bromide ion via ¹trans-TSassoc (Figure 5). In this transition structure, the C–H bond is lengthened to 1.135 Å from 1.108 Å in ¹trans-2, and the Ni–Br bond increases by 0.3 Å to an elongated bond length of 2.674 Å. IRC calculations for ¹trans-TSassoc indeed confirm the connection between ¹trans-2 and ion-pair. The activation free energy of ¹trans-TSassoc is 0.4 kcal/mol higher than the activation free energy of ¹trans-TS.

Scheme 5. Proposed Free Energy Surface for Conversion of $(PC_{sp}^{3H}P)NiBr_2$ to the Pincer Species $(PC_{sp}^{3}P)NiBr^2$



^aGrey lines indicate the triplet surface, and blue lines indicate the singlet surface. SC = singlet-triplet energy surface crossings. All energies are expressed in kcal/mol.



Figure 5. Singlet and triplet transition structures for sp³ PCP ligand metalation. Free energies are relative to ³tetra-1 (kcal/mol).

Scheme 5 outlines a computed free energy surface for metalation of $(PC_{sp}{}^{3H}P)NiBr_2$ starting with ³tetra-1. The structural transformation of this species from a tetrahedral to a square-planar geometry prior to C–H bond cleavage can proceed via two possible triplet–singlet spin crossing points. The first crossing can occur as ³tetra-1 converts into ¹trans-1-twist (SC-1, Scheme 2). Alternatively, it is also possible that the structures ¹trans-1-twist and ¹trans-1 are bypassed and ³tetra-1 is directly converted into ¹trans-2 via SC-2. In this mechanism the spin crossing likely occurs near the geometry of trans-2, since the singlet and triplet energies are degenerate at this geometry. Indeed, the located minimum energy crossing point SC-2 and its geometry and energy are nearly identical with those of ¹trans-2 and ³trans-2 (see the Supporting Information for the structure).

The ¹trans-2 structure is then a branching point for the oxidative addition and the stepwise ion pair pathways. As

discussed above, the lower energy pathway goes through a tight ion pair intermediate (ion-pair) that forms via an associative type transition state featuring a rupturing Ni-Br bond. The C-H bond is then cleaved via ¹trans-TS to liberate HBr and generate the pincer species. Interestingly, the overall free energy of the nickelation reaction to give (PC_{sp}³P)NiBr and HBr is endergonic by 12.1 kcal/mol relative to ³tetra-1; moreover, this free energy decreases by only 0.5 kcal/mol when *i*-Pr₂P groups are modeled. All other density functionals tested also indicate that this metalation reaction is endergonic: B3LYP predicts a slightly higher reaction free energy, while BP86 and MPWPW91 functionals predict the reaction free energy to be endergonic by only 2-3 kcal/mol. These results indicate that the added base likely plays an important thermodynamic role in quenching the 1 equiv of HBr generated in the metalation reaction. In THF, the acid-base reaction equilibrium between NEt₃ and HBr to give $Et_3NH^+Br^-$ is computed to be -15.6

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kcal/mol, which would render the overall process exergonic. Alternatively, it is feasible that excess phosphine ligand plays a role as the base required to quench the generated HBr.

Comparing Metalation of $(PC_{sp}{}^{*H}P)NiBr_2$ and $(PC_{sp}{}^{*H}P)-NiBr_2$. Investigating the nickelation of arene-based pincer ligands revealed a similar mechanism for C–H activation in comparison to the reaction of their saturated hydrocarbon analogues, the major difference being the barrier heights for C–H bond cleavage. The lower barrier for metalation of these aromatic ligands is in part due to the fact that $PC_{sp}{}^{2H}P$ also coordinates less favorably with NiBr₂ to give either a tetrahedral triplet complex or a trans singlet complex, both of which are less stable than the corresponding nonmetalated intermediates in the metalation of $PC_{sp}{}^{3H}P$. The greater ground state energy of $(\kappa^{P,P'}-PC_{sp}{}^{2H}P)NiBr_2$ might explain the lower barrier for the metalation of these aromatic ligands. Despite the more favorable Ni–C(sp²) bond present in the final product, M06 predicts the overall reaction free energy to be endergonic by 10.5 kcal/mol with Me₂P and 5.4 kcal/mol with *i*-Pr₂P moieties. This implies that here, too, the base plays a crucial role in rendering the C–H metalation thermodynamically favorable.

Figure 6 shows the monomeric tetrahedral triplet $(\kappa^{P,P'} - PC_{sp}^{-H}P)$ NiBr₂ complex ³tetra-3 and the singlet C–H bond



Figure 6. Tetrahedral intermediate and transition structure for $(PC_{sp}^{HP})NiBr_2$ nickelation.

cleavage transition structure ¹trans-TS3. The M06 activation free energy for ¹trans-TS3 is 13.9 kcal/mol, 3.5 kcal/mol lower than the ¹trans-TS discussed above. As before, this reaction pathway is favored over oxidative addition that has a free energy barrier of 24.3 kcal/mol. The lower barrier for sp² vs sp³ C–H bond metalation likely results from forming a shorter and stronger Ni–C bond (1.946 Å) and a more stabilized anionic sp² C as the reaction proceeds through the ionic pathway. These transition effects combine with the above-mentioned favorable ground state effects to facilitate the metalation of sp² C–H bonds.

We note that, despite significant effort, we were unable to locate either an associative transition-state structure or a tight ion pair intermediate on the potential energy surface. Nevertheless, by analogy to the free energy surface shown in Scheme 5 for metalation of $PC_{sp}^{3H}P$, we assume that the free energy for an associative-like transition structure for $PC_{sp}^{2H}P$ would be very similar to ¹trans-TS3, since the bromide is dislodged from the nickel center.

Comparing Nickelation of PCP and POCOP Ligands. The competition experiments discussed earlier have revealed that PCP-type ligands are metalated more readily than their POCOP counterparts. To explore the kinetic and thermodynamic roots of this phenomenon, we have computed the ionic reaction pathway for the sp³ POCOP ligand in order to allow a comparison to the nickelation of $PC_{sp}^{,H}P$. The geometrics of the triplet tetrahedral ground state for $(\kappa^{P,P'}-POC_{sp}^{,H}OP)NiBr_2$ (³tetra-4, Figure 7) are nearly identical with those of its PCP



Figure 7. Triplet tetrahedral ground state and closed-shell ionic transition structures and intermediate for nickelation of $POC_{sp}^{H}OP$.

analogue ³tetra-1. In THF solvent, coordination to tetrahedral nickel is 3.3 kcal/mol more favorable in ³tetra-4 relative to ³tetra-1 (eq 3), whereas the opposite order of stabilities is observed for the trans species (eq 4).



As before, the ionic pathway mechanism begins with an associative transition structure, ¹trans-TS4assoc, that induces an agostic C–H bond interaction with the nickel metal center and results in cleavage of the Ni–Br bond to give the tight ion pair structure ¹trans-4ion. The free energy barrier for ¹trans-TS4assoc relative to ³tetra-4 is 27.4 kcal/mol, and the ion pair intermediate free energy is 23.5 kcal/mol. This activation free energy is ~10 kcal/mol higher than the free energy barrier for the associative transition structure for nickelation of PC_{sp}³HP. This substantially higher barrier can be understood in terms of the significantly weaker donor character of phosphinite-type donor moieties relative to phosphines, which would not allow

an effective stabilization of a transition state involving substitution of the bromide ligand by a weakly donating C-H bond.

The C-H bond cleavage transition structure ¹trans-TS4 shows marked differences in comparison to ¹trans-TS. The breaking C-H bond distance is shorter by 0.22 Å and the forming Ni-C bond is also shorter by 0.03 Å, while the forming H-Br bond is 0.09 Å longer. This comparison indicates that the C-H bond cleavage transition structure for POC_{sp}^{3H}OP is "earlier" along the reaction coordinate than the corresponding $PC_{sp}^{3H}P$ transition structure. The activation free energy for ¹trans-TS4 is 28.3 kcal/mol, 0.9 kcal/mol higher than ¹trans-TS4assoc. The barrier for C-H cleavage relative to the ¹trans-4ion intermediate is 4.8 kcal/mol, which is similar to the 3.4 kcal/mol barrier for the analogous step in the nickelation of PC_{sp}^{3H}P; this confirms that the most energetically important step is the Ni–Br bond rupture. As before, formation of the pincer species ($\kappa^{P,C,P'}$ -POC_{sp}³O)PNiBr is endergonic with a reaction free energy of 14.2 and 7.8 kcal/mol for Me₂P and *i*-Pr₂P moieties, respectively. Finally, we have also found that the pincer complex featuring the PC_{sp}³P ligand is slightly more stable (by 1.1 kcal/mol) in comparison to its POC_{sp}³OP analogue.

CONCLUSION

The combined experimental and computational investigations described above have shed some light on the relative rates and mechanisms of the direct nickelation of the PCP- and POCOP-type pincer ligands studied. We have confirmed and quantified the more facile nickelation of PCP vs POCOP ligands and aromatic vs aliphatic backbones. The more facile metalation of the aromatic C–H bonds is related to their more effective coordination to the electrophilic Ni center and better stabilization of the developing Ni–C bond, as well as to the absence of dinuclear species in the ground states of the aromatic ligands. The preference for PCP vs POCOP nickelation likely results from the better chelation of the phosphine moieties; the importance of chelation is also reflected in the preference for $P(t-Pr)_2$ vs $P(t-Bu)_2$ and PPh_2 moieties.

The experimental finding that electron-releasing substituents favor the nickelation of aromatic POCOP ligands is consistent with a mechanism resembling electrophilic aromatic substitution, which is in stark contrast to what has been observed for direct C-H palladation reactions of aromatic substrates.^{31,32} Our DFT calculations indicate that oxidative addition is higher in energy than a two-step pathway characterized by a bromide dissociation to give a tight-ion pair followed by bromide deprotonation of the C-H bond. The crucial stabilization of the electron-depleted metal center in such a pathway explains the importance of Ni-C(H) interactions and hence the preference for electron-rich aromatic ligands. These features, namely the preference for activation of more electron rich C-H bonds and the complete dissociation of the internal H acceptor (Br⁻), distinguish the direct metalation process in our Nipromoted systems from the much more extensively investigated Pd-based systems wherein electron-deficient C-H bonds are metalated preferentially and the H transfer involves Pd-bound acceptors (halides, acetate, carbonate, etc.).

Future studies will be directed at examining the C-H metalation of other pincer ligands (PCN, POCN, NCN, etc.). If these investigations confirm the main findings of the current study, it should be possible to develop successful strategies for

facilitating C–H nickelation reactions by using more electronrich aromatic substrates and Ni precursors featuring more easily ionized Ni–X bonds.

EXPERIMENTAL SECTION

General Procedures. Unless otherwise indicated, all manipulations were carried out under nitrogen using standard Schlenk procedures and a drybox. Solvents were dried by passage over molecular sieves contained in MBRAUN systems. Triethylamine was dried by distillation over CaH₂. The reagents isobutyronitrile, nickel powder, bromine, $ClP(i-Pr)_2$, $ClP(t-Bu)_2$, $ClP(Ph)_2$, 5-methyl-1,3-benzenediol, 4,6-dichloro-1,3-benzenediol, methyl 2,4-dihydroxybenzoate, methyl 3,5-dihydroxybenzoate, and NaH were purchased from Aldrich and used without further purification. 5-Methoxyresorcinol is purchased from Chemsavers. 4-Methoxyresorcinol has been synthesized following a published procedure.⁴⁸ The synthesis and characterization of the ligands and their Ni complexes used in the present study have been described in previously published reports.²² The Ni–Cl analogue of 1c' and the *t*-Bu₂P analogues of ligands 1e and 1i have been reported previously.^{11d}

Most NMR spectra were recorded at 400 (¹H) and 161.9 MHz (³¹P) using a Bruker AV400rg spectrometer, or at 400 (¹H) and 100.56 MHz (¹³C{¹H}) using a Bruker ARX400 spectrometer. The ³¹P{¹H} NMR spectrum of complex **1** h' was recorded at 202.5 MHz using a Bruker AV500 spectrometer. Chemical shift values are reported in ppm (δ) and referenced internally to the residual solvent signals (¹H and ¹³C: 7.26 and 77.16 ppm for CDCl₃; 7.16 and 128.06 ppm for C₆D₆) or externally (³¹P, H₃PO₄ in D₂O, δ = 0). Coupling constants are reported in Hz. UV/vis spectra were measured on a Varian Cary 500i.

General Procedure for Competition Reactions. Ligands 1*a*–*j*. A THF solution (650 μ L) containing approximately equimolar quantities of ligands 6 (0.175 mmol, 60 mg) and 1 (0.175 mmol, 65 mg) was analyzed by ³¹P NMR to confirm the molar ratio of the ligands, and then added to a homogeneous THF solution (650 μ L) containing {(*i*-PrCN)NiBr₂}_n (0.132 mmol, 38 mg) and NEt₃ (49 μ L, 0.35 mmol). The initial blue color of the reaction mixture changed instantly, turning to brown first and then yellow, and a white precipitate formed over time. The mixture was stirred for 5 min at room temperature and samples were withdrawn over regular intervals for analysis by ³¹P NMR. Reaction progress was determined on the basis of the relative intensities of the ³¹P signals for the ligands and the in situ formed complexes. To confirm the irreversible nature of the nickelation process, the samples were also analyzed after 24 h.

Ligands 3 and 4. Applying the above procedure to the aliphatic ligands (but in Toluene instead of THF) results in formation of a homogeneous, dark brown solution, which was heated over three days at 100 $^{\circ}$ C before analysis by ³¹P NMR.

ASSOCIATED CONTENT

S Supporting Information

Full citation for ref 36 and a plot showing the free energy relationship between relative nickelation rates for substituted aromatic POCOP ligands and Hammett σ parameters. Free of charge at http://pubs.acs.org. 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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DEDICATION

[†]This report is dedicated to Prof. Kenneth G. Caulton as a tribute to his numerous and significant contributions to organometallic chemistry.

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(28) The molar mass of $(MeCN)_nNiBr_2$ is somewhat uncertain because of the poorly defined acetonitrile content that varies considerably as a function of the sample's age and the specific protocol used for the recrystallization and drying steps. This uncertainty in the molar mass is not a major concern when conducting preparative experiments wherein the precursor is often used in excess, but this issue is crucial for the kinetic measurements reported in this study.

(29) It should be noted that nickelation of the aliphatic ligands 3 and 4 proceeds sufficiently slowly to allow direct rate measurements, but using large excess of Ni and NEt₃, as required under pseudo-first-order conditions, often led to variable amounts of unidentified side products and gave irreproducible rates. In contrast, nickelation reactions using small excesses of NEt₃ and Ni do not generate side products.

(30) One of the reviewers of our paper urged us to explore the possibility that in some instances the initially formed pincer complexes might react with unreacted ligands to generate new pincer complexes; these types of "trans-cyclometalation" reactions have been observed earlier between (NCN)PtCl complexes and PC^HP ligands to generate (PCP)PtCl and NC^HN ligands. See: Albrecht, M.; Dani, P.; Lutz, M.; Spek, A. L.; van Koten, G. J. Am. Chem. Soc. 2000, 122, 11822. We can confirm here that trans-cyclometalation reactions do not take place with aliphatic ligands/complexes even under forcing conditions. For instance, heating a mixture of preformed 3' and excess 4 at 100 °C over 15 h showed no sign of reaction. On the other hand, transcyclometalation does occur with aromatic ligands under forcing conditions. For instance, heating a mixture of preformed complex 2' and 7 equiv of ligand 1a in toluene at 100 °C for 18 h showed the formation of ligand 2 and complex 1a' (final ratio 2':1a \approx 3:2 by ³¹P NMR). It should be emphasized, however, that the nickelation ratios reported here for the aromatic ligands/complexes are invariable under the conditions of the kinetic experiments: i.e., equimolar quantities of ligands reacting with a slight deficiency of $\{(i-PrCN)NiBr_2\}_n$ at room temperature.

(31) We have proposed that this nonmetalated intermediate is the dinuclear species ${trans-(\mu-3)NiBr_2}_2$ featuring a 16-membered metallacycle.¹⁸ Such complexes have also been isolated during the attempted nickelation of the PC_{sp}?P ligand ${i-Pr_2P(CH_2)_2}_2CH_2$ and fully characterized.^{10b}

(32) Plotting σ_p vs ln(relative rates) gave a Hammett reaction constant of -2.87, which indicates a positive charge developing on the *p*-C atom during nickelation (see the Supporting Information).

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(35) A reviewer of our paper has suggested that substituents located at the meta position with respect to the central C–H bond would be expected to favor nickelation by sterically restricting the conformational freedom of the donor moiety in its proximity and hence increasing its rate of coordination to the Ni center. This explanation is consistent with the relative nickelation rates we have observed for ligands 1g,h and hence should be taken into consideration when discussing the impact of meta substituents on the nickelation of aromatic POCOP ligands.

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(44) We have obtained a calculated ΔG value of 34.7 kcal/mol for a single C–H nickelation from the dinuclear intermediate, confirming that nickelation pathways going through a prior dissociation of the dinuclear intermediates into mononuclear species are significantly more favorable. This preference for nickelation from the mononuclear species can be ascribed to the significant contortion of the PCP ligand and the formation of a highly distorted geometry around the Ni center required for bringing the C–H bond into the coordination sphere of the Ni center in the dinuclear species.

(45) See, for instance, the proposed mechanism for C–H activation reactions of (tris(pyrazolyl)borate)Ru(PH₃)CH₃: Lam, W. H.; Jia, G. C.; Lin, Z. Y.; Lau, C. P.; Eisenstein, O. *Chem. Eur. J.* **2003**, *9*, 2775.

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