

Tri(1-adamantyl)phosphine: Expanding the Boundary of Electron-Releasing Character Available to Organophosphorus Compounds

Liye Chen, Peng Ren, and Brad P. Carrow*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544, United States

S Supporting Information

ABSTRACT: We report here the remarkable properties of PAd_3 , a crystalline air-stable solid accessible through a scalable $\text{S}_{\text{N}}1$ reaction. Spectroscopic data reveal that PAd_3 , benefiting from the polarizability inherent to large hydrocarbyl groups, exhibits unexpected electron releasing character that exceeds other alkylphosphines and falls within a range dominated by N-heterocyclic carbenes. Dramatic effects in catalysis are also enabled by PAd_3 during Suzuki–Miyaura cross-coupling of chloro(hetero)arenes (40 examples) at low Pd loading, including the late-stage functionalization of commercial drugs. Exceptional space-time yields are demonstrated for the syntheses of industrial precursors to valsartan and boscalid from chloroarenes with $\sim 2 \times 10^4$ turnovers in 10 min.

The capacity of ancillary ligands to tune the activity, selectivity, and stability of homogeneous metal catalysts has played a central role in the development of many modern synthetic methods.¹ Phosphines constitute one of the most utilized among various ligand types due in large part to the sensitivity of the electron density and steric environment about phosphorus towards substituent perturbations. The many areas of synthetic chemistry that utilize organophosphines, including emerging fields such as organocatalysis,² bioorthogonal reactions,³ nanomaterials,⁴ polymerization,⁵ and frustrated Lewis pairs,⁶ could thus benefit from expansion of accessible stereo-electronic properties beyond classical boundaries. Several recent discoveries that highlight this potential include Alcarazo's phosphine cations' ability to greatly accelerate π -acid catalysis,⁷ Radosevich's T-shaped phosphines' oxidative additions,⁸ and Dielmann's imidazolin-2-ylidenaminophosphines' reversible CO_2 fixation.⁹

Another enabling aspect of organophosphine chemistry has been the development of quantitative descriptors of their electronic and steric properties such as Tolman's electronic parameter (TEP) and cone angle, respectively,¹⁰ which aid both in mechanistic understanding and prediction of reactivity. A typical response of the TEP to increased α -carbon branching in the homoleptic series $\text{P}\{\text{C}[(\text{H})_{3-n}(\text{CH}_3)_n]\}_3$ ($n = 0-3$) can be seen in Figure 1a (open circles). Tolman rationalized such a trend as arising from steric repulsion of larger substituents, which raises the HOMO energy as phosphorus adopts a more planar geometry (Figure 1b). However, a curious enhancement in donor strength that is not readily explained by geometric effects is evident for phosphines that possess alkyl substituents at the more distant β -position (e.g., PBu_3 and PCy_3) rather than β -

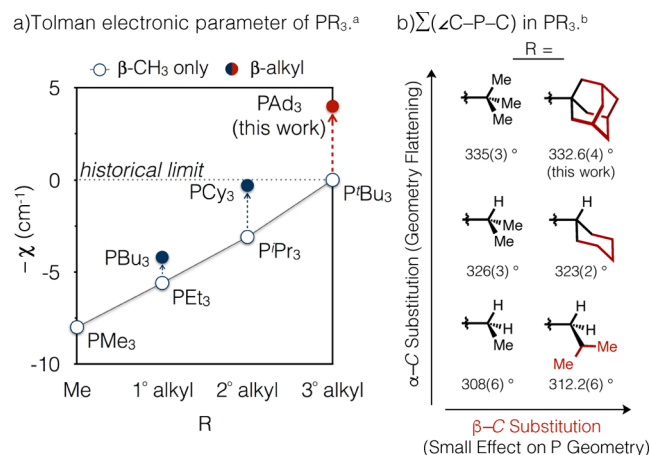


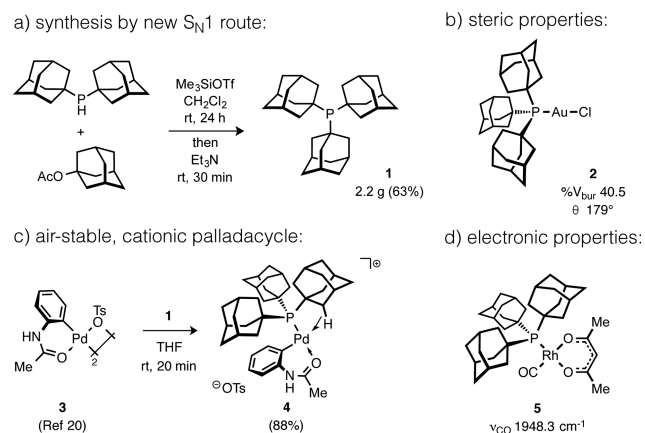
Figure 1. Examples of β -substituent effects on the (a) TEP and (b) geometry of homoleptic phosphines. (a) $\chi = \nu_{\text{CO}}(\text{A}_1) - 2056.1 \text{ cm}^{-1}$ for $\text{Ni}(\text{CO})_3(\text{PR}_3)$. (b) From solid-state data for $\text{Au}(\text{PR}_3)\text{Cl}$.¹²

methyl groups (e.g., PEt_3 and $\text{P}(i\text{-Pr})_3$). We report here the first synthesis of tri(1-adamantyl)phosphine (PAd_3), which appears to capitalize on this effect more than existing phosphines to access electron-releasing properties exceeding a boundary for organophosphines that has persisted over many decades.¹¹

Numerous syntheses of phosphines with two 1-adamantyl (Ad) substituents have been developed, many of which have found wide success in catalysis.¹³ Installation of a third hindered Ad group, however, has remained challenging. In fact, any tri-*tert*-alkylphosphine for which all β -carbon positions are alkyl rather than methyl groups is, to the best of our knowledge, unprecedented. We found that reaction of ClPAd_2 and AdMgBr in the presence of a CuI/LiBr catalyst¹⁴ led to complete consumption of the electrophile over 15 h but gave only trace amounts of PAd_3 (**1**). This is consistent with a noncatalyzed $\text{S}_{\text{N}}2$ route attempted by Whitesides.¹⁵ An alternative strategy (Scheme 1a) to forge the final hindered P–C bond in PAd_3 that proved surprisingly facile involved instead an $\text{S}_{\text{N}}1$ reaction with Ad cation.¹⁶ A mixture of the commercial reagent HAd_2 , AdOAc (1.1 equiv), and Me_3SiOTf (1.2 equiv) cleanly generated protonated PAd_3 over 24 h at rt.¹⁷ Neutralization of **1**·HOTf with Et_3N formed a colorless precipitate, pure PAd_3 , that was simply filtered under air in good yield (63%) on a multigram scale. We were surprised to then discover that negligible oxidation of solid PAd_3 occurred during storage under air over a period of three

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Scheme 1. Synthesis and Properties of PAd₃ (1)

months, as determined from periodic analysis of aliquots by ³¹P NMR spectroscopy.¹⁸ This behavior contrasts starkly with many other alkylphosphines that are air-sensitive and in the case of P(*t*-Bu)₃, pyrophoric.

Comparison of the Charton steric parameter (*v*) for the Ad group (1.33) compared to, for instance, a *t*-Bu group (1.24) intuitively suggests that PAd₃ should be more sterically hindered than other trialkylphosphines.¹⁹ We thus synthesized (PAd₃)-AuCl (2) (Scheme 1b) and the air-stable cationic complex 4, prepared in one step by coordination of 1 to palladacycle 3 (Scheme 1c),²⁰ to quantitatively establish the steric properties of PAd₃. The cone angle (θ) calculated from the solid-state structure of 2 (179°) is similar to the reported value for P(*t*-Bu)₃ (182°).^{10b} Similarly, the buried volume parameter (%V_{bur}) of PAd₃ in 2 (40.5) calculated using the SambVca program²¹ is close to that for P(*t*-Bu)₃ (40.0) in an analogous gold complex.^{10b,22} Values for PAd₃ in 4 (40.3) versus P(*t*-Bu)₃ in Pd[P(*t*-Bu)₃](Ph)(Br) (39.3)²³ are also similar. We thus conclude PAd₃ and P(*t*-Bu)₃ are best described as isosteric, which contrasts common proposals about the differences of Ad- and *t*-Bu-phosphine congeners.²⁴

The electronic properties of PAd₃ (Scheme 1d) were next established from the carbonyl stretching frequency of 5 (ν_{CO} 1948.3 cm⁻¹), which occurs at a uniquely low frequency among alkylphosphines. Analogous Rh complexes (S3–S5) ligated by P(*t*-Bu)₃ (ν_{CO} 1956.4 cm⁻¹), PAd₂(*n*-Bu) (ν_{CO} 1956.9 cm⁻¹), or PCy₃ (ν_{CO} 1958.7 cm⁻¹) all exhibit distinctly higher frequencies indicative of reduced electron releasing ability of these compared to PAd₃.²⁵ The TEP for PAd₃ (2052.1 cm⁻¹), indirectly calculated from the relationship between ν_{CO} for Ni(CO)₃(L) and Rh(acac)(CO)(L) complexes (Figure S5),²⁶ is significantly red-shifted compared to P(*t*-Bu)₃ (2056.1 cm⁻¹) and other alkylphosphines.^{10a,c} In fact, PAd₃ approaches a range typical of N-heterocyclic carbenes (e.g., IPr; 2051.5 cm⁻¹)²⁷ that are generally regarded as superior σ donors to transition metals.²⁸ Additional theoretical and experimental data that corroborate this spectroscopic data include a higher calculated HOMO energy for PAd₃ (+0.20 eV) relative to P(*t*-Bu)₃, a larger pK_a^{THF} of the conjugate acid of PAd₃ (11.6) compared to P(*t*-Bu)₃ (10.7),²⁹ and a smaller ¹J(³¹P-⁷⁷Se) coupling constant for Ad₃PSe (669.9 Hz) than for (*t*-Bu)₃PSe (688.2 Hz).³⁰

Several effects were considered that might account for the unique electronic properties of PAd₃. The average C _{α} –C _{β} bond length of PAd₃ in 2 (1.551(4) Å) is slightly longer than the average C _{β} –C _{γ} (1.537(4) Å) and C _{γ} –C _{δ} (1.530(4) Å) bond lengths. A hyperconjugative effect would be expected to contract

the C _{α} –C _{β} bonds,³¹ which is clearly not the case. The sum of the C–P–C angles about PAd₃ (332.6(4)°) determined from solid-state data for 2 are slightly less compared to P(*t*-Bu)₃ in the analogous gold complex (335(3)°).^{12a} The C–P–C angles in 4 and the known complex Pd[P(*t*-Bu)₃](Ph)(Br) are also similar.²⁰ These data show that planarization of phosphorus also does not account for the properties of PAd₃. However, London dispersion could explain the slight contraction of the C–P–C bond angles in PAd₃,¹¹ and this possibility led us to further consider van der Waals forces.^{11,32} The larger Taft polarizability parameter (σ_a) of Ad (–0.95) compared to *t*-Bu (–0.75) indicates the former is better able to facilitate electron donation from phosphorus by stabilizing a more polarized P–M dative bond.³³ In fact, a general correlation is observed between σ_a and the TEP of a series of homoleptic alkylphosphines (eq 1). This correlation suggests to us that van der Waals forces might account for the trend that phosphines possessing large β -alkyl groups are more electron-releasing than the β -methyl analogues (Figure 1a).¹¹

$$\nu_{\text{CO}}(A_1) = (20.234 \times \sigma_a) + 2071.5; \quad R^2 = 0.995 \quad (1)$$

Because transition states are generally more polarizable than are ground states,³⁴ we wanted to assess effects of PAd₃ within a catalytic manifold. We chose as a challenging test case the room temperature Suzuki–Miyaura cross-coupling (SMC) of *p*-chloroanisole (0.50 mmol), 1-naphthylboronic acid (0.55 mmol), and KOH (1.1 mmol) in the presence of palladacycle 3 and a phosphine (0.05 mol % Pd; L/Pd = 1 in all cases) in THF/toluene (eq 2). The use of P(*t*-Bu)₃, PAd₂(*n*-Bu), or PCy₃, each of which is used extensively for SMC,³⁵ led to low yields (<10%) of 1-(*p*-anisyl)naphthalene (6) over 8 h (Figure 2). In

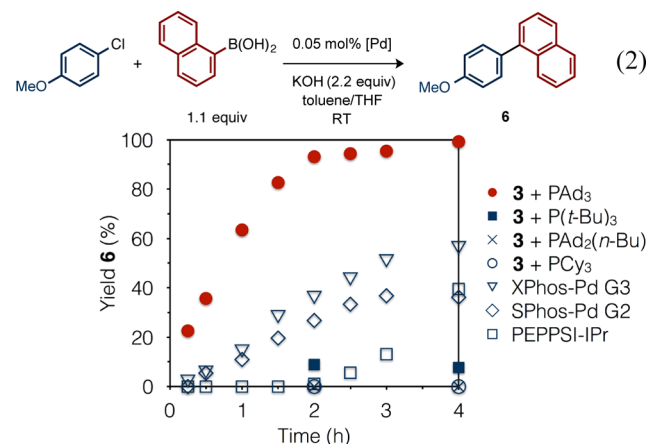


Figure 2. Yield of 6 from reactions in eq 2. L/Pd = 1 in all cases.

contrast, the reaction catalyzed by the combination of 3 and PAd₃ under identical conditions proceeded to 99% yield within 4 h. The yield of 6 at 10 min (99%) using 0.25 mol % 3 and 0.5 mol % PAd₃ corresponds to a turnover frequency (TOF) of 1.2×10^4 h⁻¹ at rt even with this quintessential deactivated substrate for SMC; an analogous reaction using P(*t*-Bu)₃ was slower and stalled at ~33% yield (Figure S3). The reactivity of 3 and PAd₃ compared favorably even head-to-head against state-of-the-art precatalysts such as SPhos-Pd G2, XPhos-Pd G3, and PEPPSI-IPr.³⁶ Note that these data only sample the ensemble of ligand effects on catalyst initiation, innate reactivity, and stability that affect the overall catalyst performance. We do believe the high reactivity of the PAd₃-Pd catalyst in this SMC reflects the

donicity and polarizability of PAd_3 , but a related PAd_3 -Pd complex (**S1**) was also found to be very stable toward cyclometalation (Figure S1). Thus, catalyst stability differences might also contribute to these observations.

The stark contrast of the catalytic effects of PAd_3 versus, for instance, $\text{PAd}_2(n\text{-Bu})$ in this SMC is surprising given the structural similarities. We considered that Tolman's proposal of substituent additivity (eq 3)^{10a} could be used to evaluate if in fact the number of Ad groups exerts a proportional effect on the phosphine properties. We thus determined χ_{Ad} (eq 4) in PAd_3 (-1.3 cm^{-1}), $\text{PAd}_2(n\text{-Bu})$ (-0.20 cm^{-1}), and PAd_2Bn (-1.0 cm^{-1}) using known χ_{R} and TEP values.^{10a} The variance in χ_{Ad} indicates that, contrary to Tolman's proposal,^{10c} the influence of the Ad group is actually dependent on the exact phosphine structure and also that phosphorus apparently gains more electron density per Ad group in the case of PAd_3 .

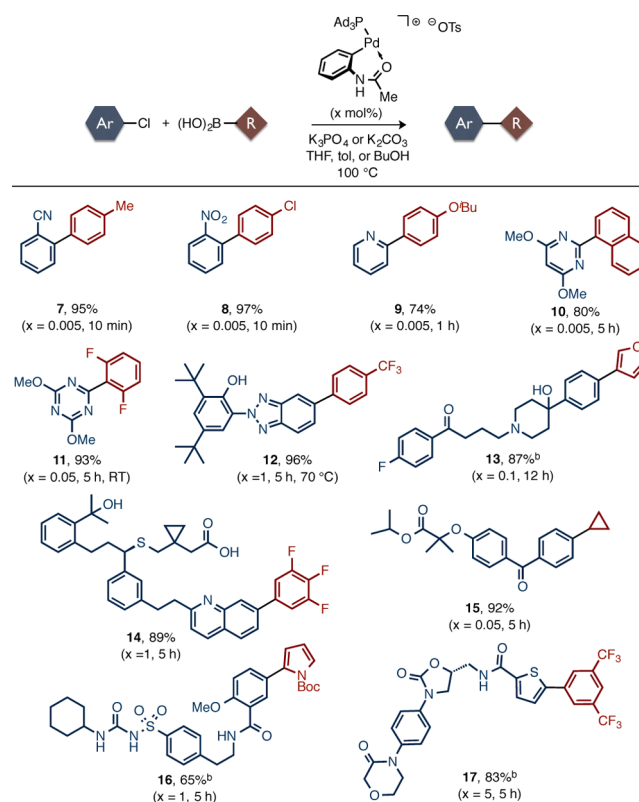
$$\nu_{\text{CO}}(\text{A}_1) - 2056.1 \text{ cm}^{-1} = \chi = \sum_{i=1}^3 \chi_i \quad (3)$$

$$\text{For } \text{P}(\text{Ad})_2\text{R}: \chi_{\text{Ad}} = \frac{(\chi - \chi_{\text{R}})}{2} \quad (4)$$

Lastly, we broadened our investigation of the SMC to establish if PAd_3 -Pd catalysts might be broadly applicable at low Pd loading ($\leq 0.1 \text{ mol } \%$),³⁷ which is desirable for industrial applications yet remains challenging using chloroarenes.³⁸ A limited selection of solvents (THF, toluene, or *n*-BuOH) and bases (K_3PO_4 or K_2CO_3) using **4** as catalyst was sufficient to achieve high yields across 40 diverse combinations of chloro-(hetero)arene and organoboronic acid. Representative examples are shown in Scheme 2 with the remainder listed in Figure S4. Complex **4** retained high activity in the presence of *N*-heteroaryl substrates including pyridine, pyrrole, pyrazine, pyrimidine, isoxazole, triazine, and thiadiazole fragments giving high yields within 1–12 h using 0.05–0.1 mol % [Pd]. Products from reactions with organoboron compounds that are notoriously sensitive to protodeboronation such as 2-pyrrolyl, 2-furyl, 2-thienyl, and 2,6-difluorophenyl boronic acids also formed in high yields even at low catalyst loadings.³⁹ Reactions that formed industrial precursors (**7**, **8**) to valsartan and boscalid proceeded to high yield (95–97%) within 10 min at 100 °C using 0.005 mol % [Pd].^{37b} These turnover numbers (TON) of $\sim 2 \times 10^4$ and exceptional TOFs exceeding $1 \times 10^5 \text{ h}^{-1}$ highlight that high space-time yield are accessible using less reactive chloroarenes and low Pd loading. High TON within 1–5 h are also observed for reactions of *N*-heteroarenes (**9–11**). Lastly, functionalization by SMC of the C–Cl bond in haloperidol, fenofibrate, montelukast, glibenclamide, and 5-*R*-rivaroxaban with methyl, cyclopropyl, heteroaromatic, or fluoroaromatic fragments occurred in uniformly good yields (65–92%). We were very encouraged by the observations that PAd_3 , a simple compound readily prepared from inexpensive reagents, engenders catalytic properties rivaling some of the most important methods developed for SMC reactions.

In conclusion, a facile and scalable synthesis of PAd_3 has been developed. Spectroscopic data reveal PAd_3 is significantly more donating than $\text{P}(t\text{-Bu})_3$, thus redefining the limit of electron-releasing character accessible to alkylphosphines that has persisted for half a century. Preliminary investigations to establish how the electronic properties and chemical stability of PAd_3 might be leveraged revealed that a PAd_3 -palladacycle catalyzes Suzuki–Miyaura coupling of chloro(hetero)arenes

Scheme 2. Illustrative Examples of **4** as a General Catalyst for Suzuki–Miyaura Coupling of Chloro(hetero)arenes^a



^aSee SI for 28 additional examples and full experimental details. ^bYield determined by NMR.

with exceptional TOF and high TON. A strong correlation between the Tolman electronic and Taft σ_{a} parameters argues the special properties of PAd_3 originate from the substantial polarizability inherent to large hydrocarbyl groups like adamantyl. These results support the hypothesis that access to phosphine steric or electronic properties beyond historical limits can enable unique reactivity in catalysis and also contribute to a growing number of examples for which weak van der Waals forces can in fact contribute significantly to both structure and reactivity.¹¹

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b03215.

Experimental details and data (PDF)

Crystallographic data (CIF)

Crystallographic data (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*bcarrow@princeton.edu

Notes

The authors declare the following competing financial interest(s): A patent application was filed by Princeton University, which is not yet published.

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REFERENCES

- (1) Selected reviews and preeminent examples of phosphine effects in catalysis: (a) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713. (b) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1703. (c) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27. (d) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (e) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (f) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336. (g) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543. (h) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887. (i) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759.
- (2) (a) Wei, Y.; Shi, M. *Acc. Chem. Res.* **2010**, *43*, 1005. (b) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535.
- (3) Sletten, E. M.; Bertozzi, C. R. *Acc. Chem. Res.* **2011**, *44*, 666.
- (4) (a) Kim, S.; Lim, Y. T.; Soltesz, E. G.; De Grand, A. M.; Lee, J.; Nakayama, A.; Parker, J. A.; Mihaljevic, T.; Laurence, R. G.; Dor, D. M.; Cohn, L. H.; Bawendi, M. G.; Frangioni, J. V. *Nat. Biotechnol.* **2004**, *22*, 93. (b) Walter, M.; Akola, J.; Lopez-Acevedo, O.; Jadzinsky, P. D.; Calero, G.; Ackerson, C. J.; Whetten, R. L.; Grönbeck, H.; Häkkinen, H. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 9157.
- (5) Myers, M.; Connor, E. F.; Glauser, T.; Möck, A.; Nycy, G.; Hedrick, J. L. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 844.
- (6) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 46.
- (7) Petušková, J.; Patil, M.; Holle, S.; Lehmann, C. W.; Thiel, W.; Alcarazo, M. *J. Am. Chem. Soc.* **2011**, *133*, 20758.
- (8) Dunn, N. L.; Ha, M.; Radosevich, A. T. *J. Am. Chem. Soc.* **2012**, *134*, 11330.
- (9) (a) Buß, F.; Mehlmann, P.; Mück-Lichtenfeld, C.; Bergander, K.; Dielmann, F. *J. Am. Chem. Soc.* **2016**, *138*, 1840. (b) Wünsche, M. A.; Mehlmann, P.; Witteler, T.; Buß, F.; Rathmann, P.; Dielmann, F. *Angew. Chem., Int. Ed.* **2015**, *54*, 11857.
- (10) (a) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2953. (b) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313. (c) Bartik, T.; Himmler, T.; Schulte, H. G.; Seevogel, K. *J. Organomet. Chem.* **1984**, *272*, 29.
- (11) Wagner, J. P.; Schreiner, P. R. *Angew. Chem., Int. Ed.* **2015**, *54*, 12274.
- (12) (a) Schmidbaur, H.; Brachthäuser, B.; Steigelmann, O.; Beruda, H. *Chem. Ber.* **1992**, *125*, 2705. (b) Angermaier, K.; Zeller, E.; Schmidbaur, H. *J. Organomet. Chem.* **1994**, *472*, 371. (c) Tiekink, E. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1989**, *45*, 1233. (d) Muir, J. A.; Muir, M. M.; Pulgar, L. B.; Jones, P. G.; Sheldrick, G. M. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1985**, *41*, 1174. (e) Bowen, R. J.; Caddy, J.; Fernandes, M. A.; Layh, M.; Mamo, M. A. *Polyhedron* **2004**, *23*, 2273.
- (13) (a) Fleckenstein, C. A.; Plenio, H. *Chem. Soc. Rev.* **2010**, *39*, 694. (b) Agnew-Francis, K. A.; Williams, C. M. *Adv. Synth. Catal.* **2016**, *358*, 675.
- (14) (a) Rampf, F.; Militzer, H.-C. EP1354886 A1, October 22, 2003. (b) Maehara, S.; Iwazaki, H. Int. Pat. WO2003066643 A1, August 14, 2003.
- (15) Hackett, M.; Whitesides, G. M. *Organometallics* **1987**, *6*, 403.
- (16) Prabagar, J.; Cowley, A. R.; Brown, J. M. *Synlett* **2011**, *2011*, 2351.
- (17) (a) No, B. I.; Zotov, Y. L.; Karev, V. N. *Zh. Obshch. Khim.* **1990**, *60*, 1795. (b) Goerlich, J. R.; Schmutzler, R. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, *81*, 141. (c) Sasaki, T.; Nakanishi, A.; Ohno, M. *J. Org. Chem.* **1982**, *47*, 3219.
- (18) The stability of pure **1** may be related to its crystallinity (mp 357 °C, dec), because a solution of **1** does oxidize when exposed to air.
- (19) Charton, M. In *Steric Effects in Drug Design*; Springer: Berlin, 1983; Vol. 114, p 57–91.
- (20) Giri, R.; Lam, J. K.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 686.
- (21) Poater, A.; Cosenza, B.; Correa, A.; Giudice, S.; Ragone, F.; Scarano, V.; Cavallo, L. *Eur. J. Inorg. Chem.* **2009**, *2009*, 1759.
- (22) (a) Müller, T.; Mingos, D. M. *Transition Met. Chem.* **1995**, *20*, 533. (b) Clavier, H.; Nolan, S. P. *Chem. Commun.* **2010**, *46*, 841.
- (23) Stambuli, J. P.; Incarvito, C. D.; Bühl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 1184.
- (24) (a) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369. (b) an der Heiden, M.; Plenio, H. *Chem. Commun.* **2007**, *972*. (c) Sergeev, A. G.; Spannenberg, A.; Beller, M. *J. Am. Chem. Soc.* **2008**, *130*, 15549. (d) Gowrisankar, S.; Sergeev, A. G.; Anbarasan, P.; Spannenberg, A.; Neumann, H.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 11592. (e) Su, M.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 4710.
- (25) (a) Kühnl, O. *Coord. Chem. Rev.* **2005**, *249*, 693. (b) Rahman, M. M.; Liu, H. Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1989**, *8*, 1.
- (26) Serron, S.; Huang, J.; Nolan, S. P. *Organometallics* **1998**, *17*, 534.
- (27) Nelson, D. J.; Nolan, S. P. *Chem. Soc. Rev.* **2013**, *42*, 6723.
- (28) (a) Spokoiny, A. M.; Lewis, C. D.; Teverovskiy, G.; Buchwald, S. L. *Organometallics* **2012**, *31*, 8478. (b) Mohr, B.; Lynn, D. M.; Grubbs, R. H. *Organometallics* **1996**, *15*, 4317.
- (29) (a) Allman, T.; Goel, R. G. *Can. J. Chem.* **1982**, *60*, 716. (b) Abdur-Rashid, K.; Fong, T. P.; Greaves, B.; Gusev, D. G.; Hinman, J. G.; Landau, S. E.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 9155.
- (30) Pinnell, R. P.; Megerle, C. A.; Manatt, S. L.; Kroon, P. A. *J. Am. Chem. Soc.* **1973**, *95*, 977.
- (31) Laube, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 349.
- (32) Lyngvi, E.; Sanhueza, I. A.; Schoenebeck, F. *Organometallics* **2015**, *34*, 805.
- (33) (a) Hehre, W. J.; Pau, C. F.; Headley, A. D.; Taft, R. W.; Topsom, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 1711. (b) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
- (34) Ngola, S. M.; Dougherty, D. A. *J. Org. Chem.* **1996**, *61*, 4355.
- (35) (a) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555. (b) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4153.
- (36) See SI for a comparison of PAd₃ and XPhos under conditions optimized for the later.
- (37) (a) Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027. (b) de Vries, J. G. *Top. Organomet. Chem.* **2012**, *42*, 1.
- (38) (a) Bedford, R. B.; Cazin, C. S. J.; Hazelwood, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 4120. (b) Handa, S.; Andersson, M. P.; Gallou, F.; Reilly, J.; Lipshutz, B. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 4914.
- (39) Kinzel, T.; Zhang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 14073.