

Scientific paper

Exploring the Synthesis, Structure, and Reactivity of Well-Defined 1-Adamantylzinc Bromide Complexes

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Abstract

The first syntheses and crystal structures of well-defined 1-adamantyl complexes of zinc are reported. The use of different ligands effects both the color and the nuclearity of the new structures. The effect of the coordination sphere of zinc on the reactivity of the new adamantylzinc nucleophiles in Negishi-like alkyl-alkyl cross-coupling reactions was also explored.

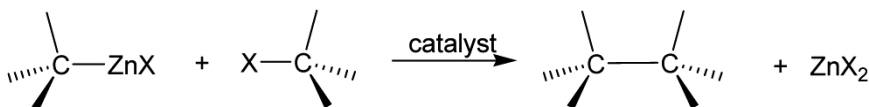
Keywords: Zinc, cross-coupling, quaternary centers.

1. Introduction

Alkyl-alkyl cross-coupling reactions are becoming important tools in synthetic chemistry.^{1–11} Ligand systems that suppress β -hydride eliminations of transition-metal alkyls have made possible catalytic transformations broad in scope and utility. Negishi protocols (Scheme 1) are particularly exciting in that they are amenable to a variety of functional groups,¹⁰ can afford high yields of cross-coupled products,^{2,8} can catalyze asymmetric cross-coupling reactions,^{5,8} and only produce non-toxic zinc dihalide co-products.

To date, much work has been done on determining the scope of reactivity of the electrophilic alkyl partner under Negishi-like conditions. Studies on halogen effects (alkyl-iodides vs. alkyl-bromides vs. alkyl-chlorides),^{2,4,11} the nature of the electrophile (halide vs. triflate vs. tosylate),^{11–13} and the steric bulk of the electrophile (primary vs. secondary)^{1,4} have all been performed. Not so much work, however, has been directed towards studying the effect of structure and electronics on the nucleophilic alkyl partner of Negishi reactions. This is surprising as recent findings

are suggesting that even small structural changes in alkylzinc reagents can dramatically effect reactivity in cross-coupling reactions,¹⁴ Knochel studied the use of secondary alkylzinc halides in nickel-catalyzed Negishi reactions,¹⁵ but to our knowledge there have been no successful reports on the use of tertiary alkylzinc halides in alkyl-alkyl cross-coupling reactions. Since a long-standing goal in synthetic chemistry is the development of a versatile way to prepare quaternary sp^3 centers, development of a cross-coupling method which employs tertiary alkyl nucleophiles would be fundamentally important. Herein we report the use of 1-adamantylzinc bromide as a model nucleophile in Negishi cross-coupling reactions. We also report the first syntheses and crystal structures of well-defined 1-adamantyl complexes of zinc, and explore the effect of the coordination sphere of zinc on the reactivity of the new adamantylzinc nucleophiles in cross-coupling reactions. The adamantyl group was chosen as a transmetalating agent because it is believed that transition-metal complexes bearing the adamantyl group are less prone to β -hydride eliminate (than a *tert*-butyl group, for instance)



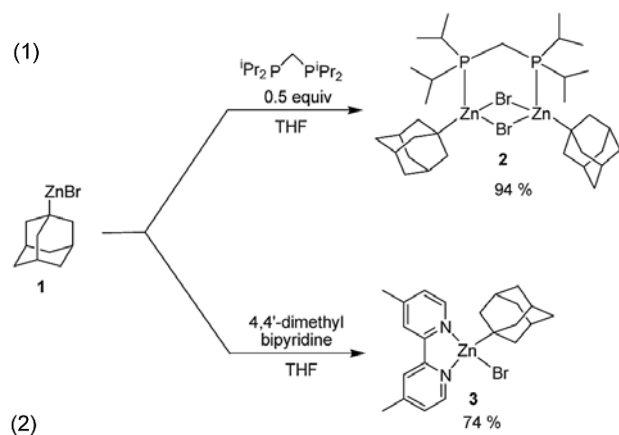
Scheme 1. General protocol for an alkyl-alkyl cross-coupling reaction under Negishi conditions.

due to the requisite formation of a bridgehead double bond.¹⁶ The 1-norbornyl group, which also has a bridgehead structure, is known to stabilize rare electronic structures of nickel,¹⁷ something which might be encountered in a catalytic cross-coupling reaction.²

2. Results and Discussion

Synthesis of well-defined 1-adamantylzinc complexes. It was found that reaction of 0.5 equivalents of 1,2-bis(di-*i*-propylphosphino)methane with 1-adamantylzinc bromide (**1**) led cleanly to the formation of the dinuclear complex **2** (Scheme 2, eq 1) by ³¹P{¹H} NMR spectroscopy. Complex **2** is stable in the solid state, and was isolated as grey/colorless powder in 94% yield. X-ray quality crystals were obtained by vapor diffusion of pentane into a THF solution of **2** at –30 °C. The ORTEP diagram of **2** is shown in Figure 1, and confirms a dinuclear zinc architecture supported by only one bridging phosphine ligand. The average Zn–C distance 1.994(8) Å found in **2** is very similar to that found for *tert*-butyl complexes of zinc.^{18–34} Each zinc atom adopts a pseudo-tetrahedral coordination sphere with the P–Zn–C angles as the largest at ~133°.

Reaction of a THF solution of **1** with 4,4'-dimethyl-2,2'-dipyridyl led to a dramatic color change in the solution from colorless to red-orange. Again, X-ray quality crystals of the ligated zinc product could be obtained by vapor diffusion of pentane into a THF solution of the bipyridine adduct (**3**, Scheme 2). The ORTEP diagram of **3** (Figure 1) describes a very different, mononuclear complex of zinc in which the zinc adopts a pseudotetrahedral conformation. The zinc-carbon bond measures 1.981(12) Å, which is shorter than that found for its closest known analogue (bpy)Zn(CH₃)₂ (2.056(5) Å)³⁵ Unlike the phosphine complex **2**, the largest bond angle at the zinc center in **3** is the C–Zn–Br angle at 124.0(4)°. We are aware of no other examples of an unsymmetrically substituted



Scheme 2. Reactivity of 1-Adamantylzinc Bromide with Two Bidentate Ligands.

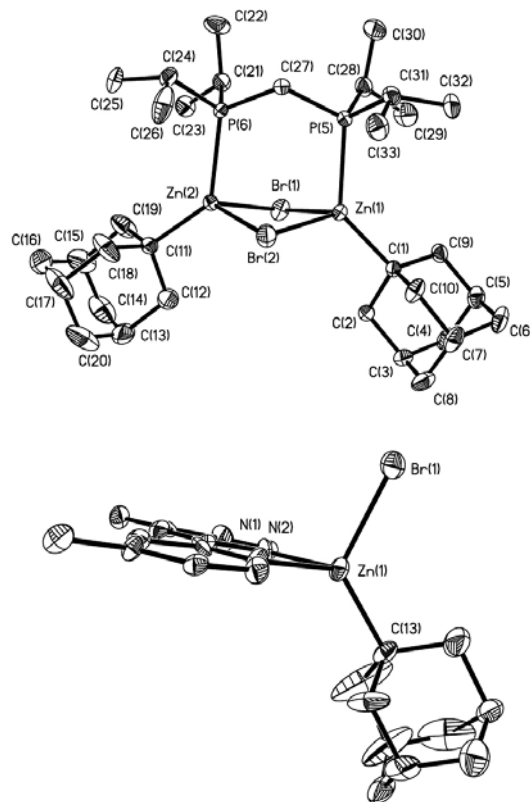
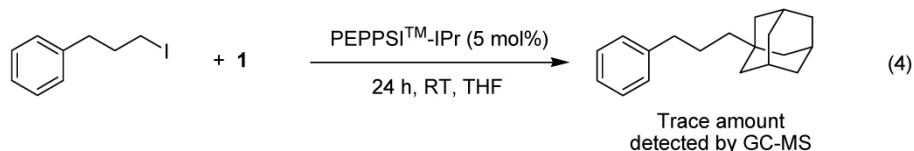
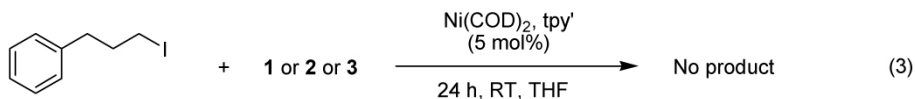


Figure 1. ORTEP diagrams of **2** (top) and **3** (bottom). Ellipsoids shown at the 50% level. Hydrogens and co-crystallized solvent molecules are omitted for clarity. Selected bond lengths (Å) for **2**: Br(1)–Zn(1) 2.5347(7); Br(1)–Zn(2) 2.5505(8); Br(2)–Zn(2) 2.5320(7); Br(2)–Zn(1) 2.5738(8); Zn(1)–C(1) 1.999(4); Zn(1)–P(5) 2.4145(12); Zn(2)–C(11) 1.989(4); Zn(2)–P(6) 2.4044(12). Selected bond angles (°) for **2**: Zn(1)–Br(1)–Zn(2) 81.93(2); Zn(2)–Br(2)–Zn(1) 81.53(2); C(1)–Zn(1)–P(5) 133.55(12); C(1)–Zn(1)–Br(1) 113.95(12); P(5)–Zn(1)–Br(1) 97.60(3); C(1)–Zn(1)–Br(2) 111.23(12); P(5)–Zn(1)–Br(2) 98.03(3); Br(1)–Zn(1)–Br(2) 95.37(2). Selected bond lengths (Å) for **3**: Br(1)–Zn(1) 2.387(3); Zn(1)–C(13) 1.981(12); Zn(1)–N(2) 2.095(10); Zn(1)–N(1) 2.095(9). Selected bond angles (°) for **3**: C(13)–Zn(1)–N(2) 117.6(5); C(13)–Zn(1)–N(1) 120.8(5); N(2)–Zn(1)–N(1) 77.5(4); C(13)–Zn(1)–Br(1) 124.0(4); N(2)–Zn(1)–Br(1) 102.8(3); N(1)–Zn(1)–Br(1) 103.7(3).

bipyridyl complex of zinc which has been crystallographically characterized.

Reactivity studies. With the new alkylzinc complexes in hand, we explored the reactivity of **1**, **2**, and **3** in the Negishi reactions outlined in eq 3 and 4. We initially used the *tpy'*-based nickel catalyst (*tpy'* = 4,4',4''-tri-*tert*-butyl-terpyridine) described in eq 3, as this ligand system is known to provide high yields of alkyl-alkyl cross-coupling products under Negishi-like conditions and is also known to provide higher yields of cross-coupled products with secondary alkyl electrophiles than primary ones.¹ To our dismay, however, **1**, **2**, and **3** were not productive nucleophiles under the conditions outlined in eq 3. A screen of other catalyst systems did not identify any metal which

could perform the cross-coupling reaction in yields >10%. In fact, the only evidence of a productive reaction was observed when the PEPPSITM palladium complex was used, in which case the adamantyl-derived product was formed in only trace amounts (eq 4).



Electrochemical study. Finally, the unique structure of **2** warranted further study of its electronic behavior. Inspired by the recent exciting discovery of ligands that can support a zinc-zinc bonding interaction,^{36–39} we were curious to see if dinuclear complex **2** could also be reduced by one electron. Such a reduction seemed at least plausible, given the fact that bis(dialkylphosphino)methane ligands are well-known to support metal-metal bonds. Electrochemistry was performed on **2** and the cyclic voltammogram is shown in Figure 2. The presence of only one irreversible reduction wave at -0.1 V vs Ag/Ag^+ (presumably that of $\text{Zn}^{2+}/\text{Zn}^0$) suggests that the ligand system found in **2** is unable to mimic the Cp^* ^{36, 38, 39} and β -diketiminat³⁷ chemistry.

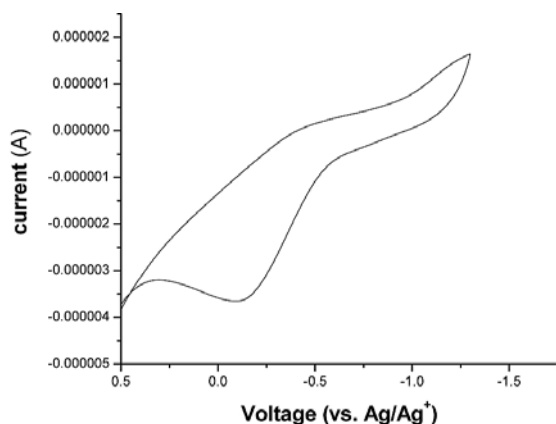


Figure 2. Cyclic voltammogram of **2** in $\text{THF}/\text{Bu}_4\text{NPF}_6$, using a scan rate of $10 \text{ mV}/\text{sec}$ and a platinum electrode.

3. Conclusions

Two new 1-adamantylzinc halide complexes were prepared and structurally characterized. These complexes are structurally quite different from each other and repre-

sent the first well-characterized adamantyl derivatives of zinc. None of the adamantyl-based zinc reagents were effective nucleophiles for nickel-mediated cross-couplings with alkyl halides under Negishi-like conditions. Palladium mediated reactions produced cross-coupling product

in trace amounts, which suggests that proper derivatization of the metal catalyst may someday lead to more efficient protocols for the cross-coupling of bulky nucleophiles.

4. Experimental Section

General Considerations. All manipulations were performed using standard Schlenk techniques or in a nitrogen-filled glovebox, unless otherwise noted. Solvents were distilled from $\text{Na}/\text{benzophenone}$ or CaH_2 . All reagents were used as received from commercial vendors unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded at ambient temperature on a Bruker Avance spectrometer and referenced to residual solvent peaks. $^{31}\text{P}\{^1\text{H}\}$ spectra were referenced to an 85% phosphoric acid external standard set to 0 ppm. Bis(di-*i*-propylphosphino)methane was prepared by published procedures.⁴¹ X-ray data were collected on a Rigaku/MSC AFC8 Mercury CCD diffractometer using Mo K α radiation. The crystal structures were solved by direct methods using SHELXS-97⁴² and refined by full-matrix least-squares procedures on F_o^2 using SHELXL-97.⁴³ All non-hydrogen atoms were refined anisotropically. The hydrogen atom positions have been refined using the atom corresponding riding model.

Synthesis of 2: To a stirred solution of 1-adamantylzinc bromide (8.1 mL of a 0.5 M solution in THF) was added dropwise 1,2-bis(di-*i*-propylphosphino)methane (500 mg in 10 mL THF) at room temperature. The solution was stirred for five minutes and then the solvents were removed. The residue was washed with pentane and then recrystallized from THF/pentane. Yield: 1.56 g (94%). ^1H NMR: (300 MHz, 25 °C, $\text{THF}-d_8$): δ 2.17–2.10 (br s, 4H), 1.95–1.56 (m, 10 H), 1.53–0.97 (m, 12 H). $^{31}\text{P}\{^1\text{H}\}$ NMR: (121.44 MHz, 25 °C, $\text{THF}-d_8$): δ -2.31 (s).

Synthesis of 3: To a solution of 1-adamantylzinc bromide (13.1 mL, 6.5 mmol, 0.5 M in THF) was added

Table 1. Crystal data and structure refinement parameters for all new compounds.⁴⁰

Compound	2-pentane	3-THF
chemical formula	C ₃₆ H ₆₇ Br ₂ P ₂ Zn ₂	C ₂₆ H ₃₅ BrN ₂ OZn
formula weight	852.40	536.84
crystal dimensions (mm)	0.45 × 0.40 × 0.30	0.25 × 0.20 × 0.05
color, habit	colorless, prism	red, plate
crystal system	monoclinic	triclinic
wavelength, Å	0.71070	0.71070
μ (mm ⁻¹)	3.393	2.745
space group, Z	P21/n, 4	P21/c, 4
a, Å	13.0146(18)	14.10(2)
b, Å	14.4779(19)	9.116(13)
c, Å	20.967(3)	19.00(2)
α (deg)	90	90
β (deg)	100.036(4)	104.16(4)
γ (deg)	90	90
vol, Å ³	3890.3(9)	2368(6)
ρ _{calc} , mg/m ³	1.455	1.506
temp, deg C	173(2)	173(2)
R indices [I > 2σ(I)]	R ₁ = 0.0575 wR ₂ = 0.1538	R ₁ = 0.1657 wR ₂ = 0.3867
R indices [all data]	R ₁ = 0.0728 wR ₂ = 0.1652	R ₁ = 0.2362 wR ₂ = 0.4401
goodness of fit	1.080	1.263
θ range, deg	2.12 to 28.00	2.21 to 28.00
number of data collected	39334	20944
number of unique data	9389	5657
R _{int}	0.0567	0.1623

4,4'-dimethyl-2,2'-dipyridyl (1.203 g, 6.5 mmol) in 50 mL of THF. The reddish-orange solution was stirred for 20 min, followed by filtration through a small pad of alumina eluting with THF. The solvent was concentrated on the high vacuum manifold to about 10 mL at which point a fine red powder was precipitated with excess pentane. The solid was collected and dried on the high vacuum manifold for 4 hr. Yield 2.25 g (74%). ¹H NMR (300 MHz, 25 °C, THF-*d*₈) δ: 8.51 (bs), 8.33 (bs), 7.37 (bs), 2.48 (bs), 2.09 (bs), 1.80 (bm), 1.59 (bs). ¹³C NMR (75.45 MHz, 25 °C, THF-*d*₈) δ: 151.8, 150.7, 149.5, 138.3, 127.1, 123.3, 46.7, 40.4, 31.0, 21.5.

Cyclic Voltammetry Measurements. Cyclic voltammetry was performed in pre-dried solutions of 3 mM zinc complex in 0.1 M TBAPF₆ in THF (TBAPF₆ = tetrabutylammonium hexafluorophosphate). The TBAPF₆ was recrystallized from THF/pentane and dried on high vacuum manifold overnight). Measurements were performed at a scan rate of 10 mV/sec under an argon atmosphere. A platinum disk (2.0 mm diameter, CH Instruments, Inc.) and a platinum flag were served as the working electrode and the counter electrode, respectively. A silver wire in a 0.01 M AgNO₃ solution of DMF (anhydrous) served as non-aqueous reference electrode which was separated from the test solution by a fine glass frit. A CH Instrument, Inc. model CHI650A potentiostat and CHI650A personal computer software controlled the electrochemical experiments. The non-aqueous reference electrode kit

(model #MF-2062) was purchased from Bioanalytical Systems, Inc..

General protocol for cross-coupling reactions: A small screw capped vial equipped with a magnetic stir bar was charged with Ni(COD)₂ (0.7 mL, 0.049 mmol, 0.07 M in THF), tpy' ligand (20 mg, 0.049 mmol), and 1-iodo-3-phenylpropane (158 μL, 0.98 mmol) in THF (7 mL). The 1-adamantylzinc bromide (0.98 mmol from a 0.5 M solution in THF) was then syringed into the stirred solution. The vial was then capped and stirred under nitrogen for 24 hours and worked-up by quenching with ethanol and filtering through a pipette packed with silica gel. The resulting solution was then analyzed by GC/MS.

5. Acknowledgement

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Povzetek

Avtorji v prispevku poročajo o sintezi in kristalni strukturi dobro definiranih 1-adamantil cinkovih kompleksov. Uporaba različnih ligandov vpliva na barvo in način tvorjenja novih struktur. Študiran je bil tudi vpliv koordinacijske sfere cinka na reaktivnost novih adamantilcinkovih nukleofilov v reakcijah Negishi-jevega tipa.