One-step assembly of a chiral palladium bis(acyclic diaminocarbene) complex and its unexpected oxidation to a bis(amidine) complex†

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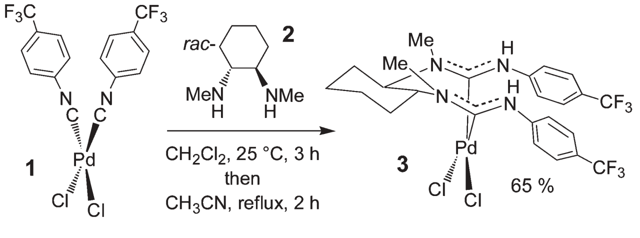
Addition of *trans-N,N′*-dimethyl-1,2-diaminocyclohexane to a palladium bis(arylisocyanide) complex leads to the one-step formation of the first chiral bis(acyclic diaminocarbene) complex, which is thermally stable under N_2 but undergoes slow oxidation to a bis(amidine) complex under air.

In recent years, N-heterocyclic carbenes (NHCs) derived from imidazole have defined the cutting edge of ligand design for homogeneous catalysis.[1] Their ability to promote a range of useful catalytic reactions has often been attributed to a combination of strong σ-donor ability, thermal robustness, and unique steric properties.[2] Related acyclic diaminocarbenes (ADCs)[3] have been reported to act as even stronger σ-donors toward transition metals than NHCs,[4] but to date only a limited number of ADCs have been investigated as ligands.[4–7] The use of ADCs in catalysis remains largely unexplored. However, a few recent reports indicate that ADC-based catalysts can show some of the same favorable attributes as those containing NHC ligands, such as air-stability[8] and high activity for activation of aryl chlorides in Suzuki–Miyaura coupling[9] and Buchwald–Hartwig amination[10] reactions. Further investigations of ADC ligands with novel structures are clearly warranted. In particular, no chiral ADCs have appeared, in contrast to the substantial number of chiral NHC ligands.[11] Furthermore, common procedures for ADC metalation involving oxidative addition[10] or *in situ* deprotonation[5] of amidinium salts appear to have significant limitations. For example, Herrmann recently reported that an attempt to prepare a chelated bis(ADC) complex by the latter route was unsuccessful.[7]

A potentially versatile synthetic route to ADCs is the nucleophilic addition of amines to coordinated isocyanides.[12] We have reported that an array of Pd complexes of Chugaev carbenes—unusual chelating bis(ADC)s[8,13]—can be conveniently prepared by Pd-templated addition of hydrazines to alkylisocyanides and screened to identify an air-stable Suzuki–Miyaura coupling catalyst.[14] We envisioned that a similar procedure could be used for the facile preparation of chiral bis(ADC) ligands from readily available chiral diamines. This ligand synthesis strategy is appealing because it affords a new chiral ligand in single step, opening the possibility of rapidly generating a structurally diverse library of such ligands without multistep syntheses. Herein, we report the one-step synthesis of the first chiral ADC complex, demonstrating that this isocyanide-based approach is a viable strategy for rapid construction of novel ADCs with potential catalytic utility.[15] We also report the unexpected oxidative conversion of the chiral bis(acyclic carbene) ligand to a bis(amidine), identifying a previously unrecognized decomposition route that will be a consideration in future ADC ligand designs.

Bis(arylisocyanide) palladium dichloride complex **1** (Scheme 1), readily prepared by reaction of (COD)$PdCl_2$ with two equiv. of the isocyanide, was chosen as a test synthon for one-step assembly of new bis(ADC) ligands. We expected that the trifluoromethyl substituents would enhance the susceptibility of the isocyanide carbon to nucleophilic attack, allowing us to prepare bis(ADCs) from a range of diamine precursors and examine the influence of the chiral backbone on chelate geometry. Reaction of **1** with racemic *trans-N,N′*-dimethyl-1,2-diaminocyclohexane **2** for 2 h in CH_2Cl_2 led to precipitation of chiral bis(ADC) complex **3** as a pale yellow solid. For preparative scale reactions (>100 mg), both purity and yield were maximized by slow syringe pump addition of the diamine followed by refluxing in CH_3CN for 2 h. NMR data indicated a structure having two inequivalent carbene units, with two carbene signals at 190.3 and 184.4 ppm in the ^{13}C NMR spectrum and two sets of NH and NMe signals in the ^1H NMR spectrum.‡

X-Ray diffraction analysis of a crystal obtained by slow evaporation of a MeOH solution of **3** revealed a C_1-symmetric geometry for the bis(ADC) ligand (Fig. 1). The Pd–C bond lengths of 1.975(6) and 1.985(6) Å are in the expected range for Pd bis(carbene) complexes,[16] and the N–$C_{carbene}$–N angles of 117.5(5) and 116.0(6)° are comparable to known ADC ligands.[4,15] Despite the twist imparted by the chiral backbone, the four N-substituents are nearly coplanar with the carbene NCN units, as shown by the average $NC_{carbene}NC_{Me}$ and $NC_{carbene}NC_{cyclohex}$ torsion angles of −6.8(6) and 179.7(4)°, respectively. Because a more pronounced C_2 chirality is typically considered favorable for asymmetric catalysis,[17] we turned to density functional theoretical calculations to understand why the C_2 symmetry of diamine **2** is lost upon



Scheme 1 One-step assembly of a chiral palladium bis(acyclic diaminocarbene) complex.

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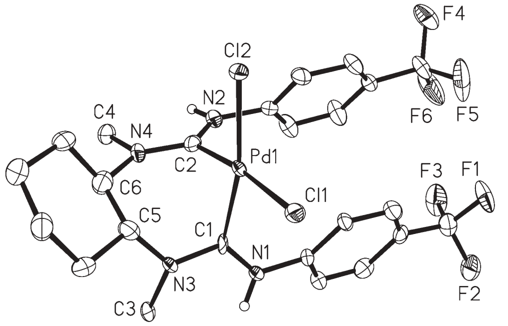


Fig. 1 Molecular structure of **3** with 50% probability ellipsoids. Selected bond lengths (Å), angles (°), and torsion angles (°): Pd1–C1 1.975(6), Pd1–C2 1.985(6), Pd1–Cl1 2.3942(16), Pd1–Cl2 2.3901(16), C1–N1 1.346(7), C1–N3 1.331(7), C2–N2 1.350(8), C2–N4 1.333(7); N1–C1–N3 117.5(5), N2–C2–N4 116.0(6), C1–Pd1–C2 82.3(2); N1–C1–N3–C3 −10.3(8), N2–C2–N4–C4 −3.3(8), N1–C1–N3–C5 180.8(5), N2–C2–N4–C6 178.5(5). Non-NH hydrogen atoms are omitted for clarity.

formation of **3**. Optimization of the C_1 conformation of **3** at the B3LYP/SBK(d) level of theory (Fig. 2(a)) reproduced key features of the crystallographically determined ligand geometry, including average carbene NCN angles of 115.8° (*vs.* 116.8(4)° experimental) and near-planar carbene moieties ($NC_{carbene}NC_{Me}$ torsions $\leqslant 7°$; $NC_{carbene}NC_{cyclohex}$ torsions within 1.1° of 180°), although the predicted Pd–C distances are slightly larger than the experimental values (av. 2.025 Å *vs.* 1.980(4) Å, experimental). The most stable C_2 form of the bis(carbene) ligand (Fig. 2(b)) is disfavored by 17.9 kcal mol^{-1} relative to the optimized X-ray geometry. This is apparently due to the severe distortions required of the sp^2-hybridized carbene unit in order to adopt a C_2 conformation (av. $NC_{carbene}NC_{Me}$ torsion −149°, av. $NC_{carbene}NC_{cyclohex}$ torsion 64°), which results in pyramidalization of the N(Me) nitrogens (sum of angles 351°) and loss of conjugation ($C_{carbene}$–N(Me) 1.396 Å). Thus, **3** likely adopts a C_1 conformation in order to accommodate a planar carbene geometry that maximizes π-overlap within the NCN units.

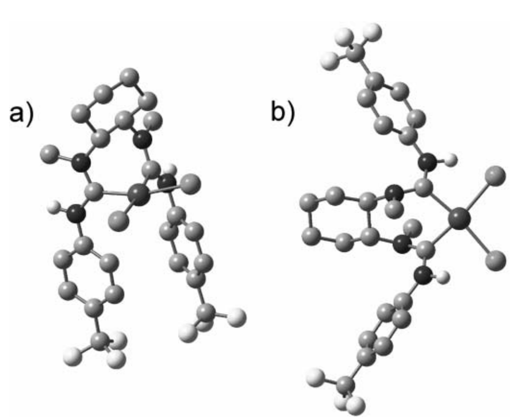


Fig. 2 Geometries of two conformations of **3** optimized at the B3LYP/SBK(d) level of theory: (a) C_1 conformation starting from X-ray coordinates; (b) lowest energy C_2 conformation. Non-NH hydrogens are omitted for clarity. Selected bond angles and torsion angles (°): $NC_{carbene}N$: (a) 116.0, 115.6; (b) 119.6; $NC_{carbene}NC_{Me}$: (a) −2.7, −7.0; (b) −149.8; $NC_{carbene}NC_{cyclohex}$: (a) 179.8, 178.9; (b) 64.4. A full tabulation of geometric parameters is included in the ESI.†

Complex **3** is air- and moisture-stable as a solid and reasonably robust in solution, showing only 26% decomposition by ^1H NMR spectroscopy upon heating at 80 °C for 5 d in degassed DMSO-d_6. However, leaving a concentrated DMSO solution of **3** under air for 30 d at 25 °C resulted in the formation of red–orange crystals of a new compound **4**. X-Ray diffraction analysis revealed **4** to be a complex containing a new nitrogen-bound chelate ligand resulting from a two-electron oxidation of the bis(carbene) of **3** (Fig. 3), with formal loss of two hydrogen atoms from the NH groups accompanied by coupling of the carbene carbons. The carbon–nitrogen distances are consistent with a bis(amidine) ligand having π-conjugated NCN moieties (*e.g.* C1–N1 1.316(3) Å, C1–N3 1.343(11) Å). This oxidative coupling of two carbene ligands is without precedent. However, a related conversion of monodentate ADC ligands to amidines was recently reported by Herrmann and co-workers.[6]

Complex **4** was obtained preparatively by oxidation of **3** with excess iodosobenzene (2 equiv.) in DMF (Scheme 2).§ Samples of **4** were characterized by elemental analysis, crystallographic indexing of several crystals, and comparison of decomposition points versus a sample prepared by air oxidation, but NMR data could not be obtained due to the insolubility of **4** in all common solvents. Attempts to form a soluble bis(methylisocyanide) adduct resulted in release of the free bis(amidine) **5**, which was isolated and structurally characterized (Fig. 4; see ESI† for analytical data). We hypothesize that derivatives of **4** are unstable toward ligand loss in solution due to a large distortion of one Pd-bound amidine moiety that disrupts the NCN π-conjugation (N1–C1–N3–C3 torsion 29.9(10)°, N1–C1–N3–C7 torsion −150.8(5)). This strain is relieved upon decoordination to give the free bis(amidine) **5** (av. N–C–N–C_{Me} torsion −2.6(4)°, av. N–C–N–$C_{cyclohex}$ torsion −159.6(2)°).

In summary, we report the synthesis of the first chiral ADC complex by a convenient, one-step procedure that can be scaled to >600 mg preparations based on this initial study. The observation that a chelating bis(ADC) with near-planar carbene units is preferentially formed will guide future ligand design efforts using this synthetic route. Given that a wide range of chiral diamines and substituted arylisocyanides[18] are available, this procedure could potentially provide access to a diverse class of new bis(ADC)

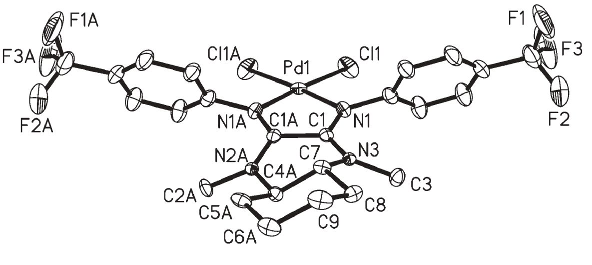
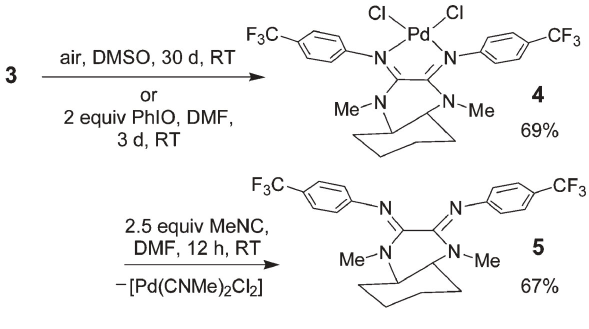


Fig. 3 Molecular structure of **4** with 50% probability ellipsoids. The compound is disordered about a crystallographic mirror plane bisecting the Cl1–Pd1–Cl1A angle, with only one enantiomer shown here. Atoms labeled "A" are located at the symmetry equivalent position (x, ½ − y, z). Selected bond lengths (Å) and angles (°): Pd1–N1 2.036(2), Pd1–N1A 2.036(2), Pd1–Cl1 2.2848(7), Pd1–Cl1A 2.2848(7), C1–N1 1.316(3), C1–N3 1.343(11), C1A–N1A 1.316(3), C1A–N2A 1.340(11), C1–C1A 1.502(5); N1–C1–N3 128.0(5), N1A–C1A–N2A 125.5(4), N1–Pd1–N1A 79.60(12). Hydrogen atoms are omitted for clarity.



Scheme 2 Oxidation of bis(carbene) complex **3** to bis(amidine) complex **4** and decoordination of the bis(amidine).

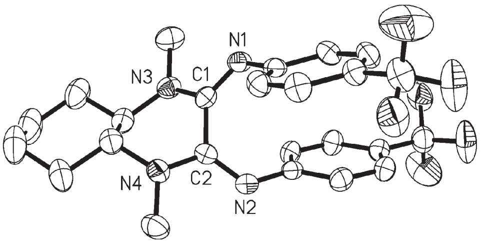


Fig. 4 Molecular structure of **5** with 30% probability ellipsoids. Selected bond lengths (Å) and angles (°): C1–N1 1.288(4), C1–N3 1.359(4), C2–N2 1.289(4), C2–N4 1.347(5), C1–C2 1.512(5); N1–C1–N3 121.2(4), N2–C2–N4 121.4(4). Hydrogen atoms are omitted for clarity.

ligands having tunable steric and electronic properties without multistep syntheses. The newly identified oxidation of the NH-containing bis(carbene) ligand to a bis(amidine) represents a pitfall that must be overcome to produce robust catalysts; however, published procedures for the alkylation of cyclic NH-containing carbenes suggest a strategy to solve this problem.[19] Our efforts to address this issue and to utilize enantiopure bis(ADC) ligands in asymmetric catalysis will be reported in due course.

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Notes and references

‡ *Synthesis* of **3**: To a stirred solution of **1** (885 mg, 1.7 mmol; see ESI† for synthetic details) under Ar in 70 mL of CH_2Cl_2 at 25 °C was added a solution of **2** (244 μL, 220 mg, 1.55 mmol) in 12 mL of CH_2Cl_2 *via* syringe pump over a period of 1 h. After stirring for a further 2 h, the solvent was removed under reduced pressure, anhydrous CH_3CN (30 mL) was added to the residue, and the mixture was refluxed under Ar for 2 h. The pale yellow precipitate was collected by filtration, washed with CH_3CN, and dried in vacuo (661 mg, 65%).

Selected analytical data for **3**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.62 (1H, s, N*H*), 9.05 (1H, s, N*H*), 8.25 (2H, d, *J* = 8.3 Hz, Ar), 7.71 (2H, d, *J* = 7.7 Hz, Ar), 7.55 (2H, d, *J* = 8.3 Hz, Ar), 7.42 (1H, m, ^{c}Hex *ipso* C*H*), 7.19 (2H, d, *J* = 7.7 Hz, Ar), 3.68 (1H, m, ^{c}Hex *ipso* C*H*), 3.20 (3H, s, NCH_3), 3.10 (3H, s, NCH_3), 2.36–2.22 (1H, m, ^{c}Hex), 2.22–2.08 (1H, m, ^{c}Hex), 2.04–1.78 (4H, m, ^{c}Hex), 1.63–1.38 (2H, m, ^{c}Hex). ^{13}C NMR (101 MHz, DMSO-d_6): δ 190.3 (carbene), 184.4 (carbene), 144.4 (*ipso*-Ar), 143.6 (*ipso*-Ar), 125.6 (q, $^2J_{CF}$ = 31.2 Hz, *p*-Ar), 125.4 (q, $^3J_{CF}$ = 4.1 Hz, *m*-Ar), 124.8 (q, $^2J_{CF}$ = 32.5 Hz, *p*-Ar), 124.4 (q, $^3J_{CF}$ = 3.8 Hz, *m*-Ar), 124.2 (q, $^1J_{CF}$ = 272 Hz, CF_3), 124.2 (q, $^1J_{CF}$ = 272 Hz, CF_3), 123.8 (*o*-Ar), 123.5 (*o*-Ar), 67.9, 66.9 (NCH_3), 40.7, 31.7, 31.4, 29.9, 25.3, 24.6 (^{c}Hex). Anal. Calc. for $C_{24}H_{26}Cl_2F_6N_4Pd$: C, 43.56; H, 3.96; N, 8.47%. Found: C, 43.41; H, 3.93; N, 8.63%.

Crystal data for **3**: $C_{24}H_{26}Cl_2F_6N_4Pd\cdot 2CH_3OH$, *M* = 725.87, triclinic, non-merohedral twin (twin law 1 0 0, 0.92 −1 0, 0.25 0 −1, BASF 0.45), space group $P\bar{1}$, *a* = 8.0588(4), *b* = 14.0376(8), *c* = 14.1642(8) Å, α = 84.861(4), β = 85.869(4), γ = 74.662(4)°, *U* = 1537.11(15) Å^3, *Z* = 2, D_c = 1.568 g cm^{-3}, μ(Mo-Kα) = 0.844 mm^{-1}, *T* = 100(2) K, 9760 total reflections, 4285 independent (R_{int} = 0.057). Final *R*1 [$I > 2\sigma(I)$] = 0.0510, *wR*2 (all data) = 0.1141. CCDC 625246. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b703769d

§ See ESI for detailed synthetic procedures and analytical data for **1**, **4** and **5**, as well as details of crystallographic determinations. CCDC 625247 (**4**), 625248 (**5**). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b703769d .

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