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Structural and Mechanistic Insights into the Metalation of Fluoroarenes Mediated by a Superbasic Co(II) Bis(amide) Complex

Na Jin§* and Eva Hevia*

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Abstract: Over the past decades, *s*-block metal amides including LiTMP and TMPMgCl.LiCl (TMP = 2,2,6,6-tetramethylpiperidide) have found widespread applications in the deprotonative metalation of aromatic compounds. In contrast, transition metal amides usually exhibit diminished basicity to metalate these substrates. Here we present an overview of the synthesis of a highly reactive TMP-based cobalt(II) bis(amide) complex $Co(TMP)_2$ and its relevance in the direct Co–H exchange processes with fluoroarenes. This deprotonative metalation reactivity can be further extended to cyclopentadiene to generate cobaltocene. Exhibiting an unusual reactivity, $Co(TMP)_2$ has also been found to be highly nucleophilic, as evidenced by the insertion of CO_2 molecules into both of its Co–N_{TMP} bonds.

Keywords: Amide · CO_2 insertion · Cobalt · Fluoroarenes · Metalation

Na Jin received her MRes in Drug Discovery and Development (2021) from Imperial College London where her master's thesis was carried out in the group of Prof. James Bull. She joined the group of Prof. Eva Hevia at Universität Bern as a PhD student in 2022 and is currently investigating metalation and functionalisation of *N*-heterocycles with transition metal amide complexes.

1. The TMP Amide Group in Main Group and Transition Metal Complexes

s-Block metal amides such as LiTMP or TMPMgCl.LiCl have become powerful metalating reagents in organic synthesis finding widespread applications in organic chemistry.[1,2] The presence of TMP groups seems to be key for their high reactivity. Featuring a 6-membered cyclic motif, TMP contains four methyl substituents on its α-carbon atoms, rendering the ligand more basic and sterically demanding than other synthetically relevant amide groups such as $N(SiMe_3)_2$ or N^iPr_2.[1] In addition, the use of TMP groups in alkali-metal 'ate' chemistry has shown enormous promise, as shown by Mulvey in the *meta*-magnesiation of toluene using the bimetallic base $(TMEDA)NaMg(TMP)_2{}^nBu$,[3] or more recently by our group on the C2-zincation of naphthalene employing a 2:1 combination of $KO^tBu/Zn(TMP)_2$ (Fig. 1a).[4] The latter can also promote the zincation of fluoroarenes[5] although it should be noted that $Zn(TMP)_2$ on its own is inert towards these substrates.

These studies along with others developed in this area by Knochel, Mulvey, and Uchiyama have provided evidence that the replacement of TMP by other amide groups is often detrimental to the resulting reactivities, highlighting the pivotal role of TMP in such transformations.[6]

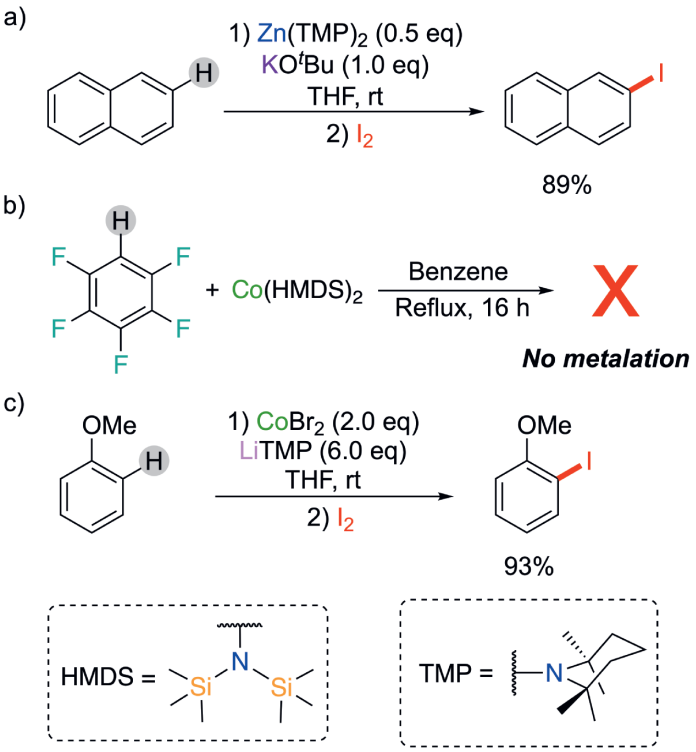

Fig. 1. a) Zincation of naphthalene. b) $Co(HMDS)_2$ inert towards metalation of pentafluorobenzene. c) Co(II)-mediated deprotonative metalation of anisole.

In terms of earth abundant transition metal chemistry, Fe(II) and Co(II) metal amides are well known, including $M(HMDS)_2$ [HMDS = $N(SiMe_3)_2$].[7,8] While they have found many applications as metal precursors in organometallic chemistry and catal-

*Correspondence: N. Jin, E-mail: na.jin@unibe.ch; Prof. E. Hevia, E-mail: eva.hevia@unibe.ch.
Departement für Chemie und Biochemie (DCBP), Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

ysis,[9] their metalating ability seems to be quite limited. Thus while they can undergo trans(amination) reactions,[10] they are inert towards C–H metalation of aromatic substrates, including activated fluoroarenes such as pentafluorobenzene (Fig. 1b).[11,12] Studies by Mongin have shown deprotonative metalation of substituted aromatics such as anisole when subjected to a 1:3 mixture of $CoBr_2$ and LiTMP, hinting at the *in situ* formation of $Co(TMP)_2$ (Fig. 1c).[13] Nevertheless, an excess of the base was required to achieve reasonable yields and the constitution of the reactive species involved in the metalation process remained elusive.

2. Cobalt(II) Bis(amide) Complexes

Inspired by these precedents, and building on our recent work on the synthesis and characterisation of Co(II) amides,[10] we focused our attention on the possible synthesis and isolation of $Co(TMP)_2$. Herein we present an overview of the synthesis, characterisation of this novel Co(II) bis(amide) and we provide the first examples of its reactivity towards fluoroarenes, uncovering its unique ability to promote Co–H exchange reactions.[14]

2.1 *Synthesis of Co(TMP)$_2$*

Building on previous studies on the synthesis of $Co(HMDS)_2$ using salt metathesis approaches,[7] $CoCl_2$ was reacted with two molar equivalents of LiTMP in THF at –30 °C to give a green solution. After solvent exchange to pentane, the by-product LiCl readily precipitated and was removed by filtration. Removing the solvent from the filtrate under vacuum led to the crude product which was purified by dynamic vacuum distillation to afford $Co(TMP)_2$ (**1**) as a dark red amorphous solid. (Fig. 2a). Alternatively, **1** could be accessed *via* trans(amidation) of $Co(HMDS)_2$ with two equivalents of NaTMP in pentane at –30 °C (Fig. 2a). The solvent adduct [(THF)Co(TMP)$_2$] (**1-THF**) could also be obtained by the salt metathesis route followed by recrystallisation from THF. X-ray crystallographic studies established the monomeric nature of **1-THF** in the solid state where the tri-coordinate cobalt centre binds to two TMP ligands and one THF molecule, displaying a distorted trigonal geometry (Fig. 2b). The ^{1}H NMR spectrum of **1** in C_6D_6 showed broad and paramagnetically shifted peaks at 186.95, 172.63 and 8.08 ppm, corresponding to the β, γ and methyl protons on the TMP substituents respectively. Solid-state variable temperature, variable field (VTVF) SQUID magnetisation measurements of **1** showed a μ_{eff} value of 5.64 B.M. at room temperature, considerably higher than the spin only value (3.87 B.M.) for one high spin (S = 3/2) Co(II) centre, which could be attributed to unquenched orbital angular momentum in the linear complex.[15]

2.2 *Metalation of Fluoroarenes with Co(TMP)$_2$*

For the metalation reactivity of **1**, we started our investigation with pentafluorobenzene as a model substrate. With a pK_a value of 29.0,[16] pentafluorobenzene is relatively active towards deprotonative metalation of its C–H bond. Nevertheless, it has been reported to undergo C–F bond activation with low valent transition metal complexes.[17] ^{1}H NMR monitoring of the reaction of equimolar amounts of **1** and pentafluorobenzene in C_6D_6 demonstrated the quantitative formation of [{Co(TMP)(C_6F_5)}$_2$] (**2**) as well as the simultaneous release of TMP(H) at room temperature, hinting at successful Co–H exchange (Fig. 3a). Complex **2** could be isolated as a crystalline solid upon cooling and X-ray crystallographic analysis confirmed its dimeric structure (Fig. 3b). Each cobalt atom exhibits a distorted trigonal planar geometry and is bound terminally to a pentafluorophenyl anion through the *ipso* carbon atom. The two cobalt centres are bridged by two TMP moieties *via* the nitrogen atoms, completing their coordination spheres and furnishing a planar {CoNCoN} ring motif. The ^{1}H NMR spectrum of **2** showed sharp and resolved peaks, although paramagnetically shifted, suggesting antiferromagnetic coupling between the two metal centres

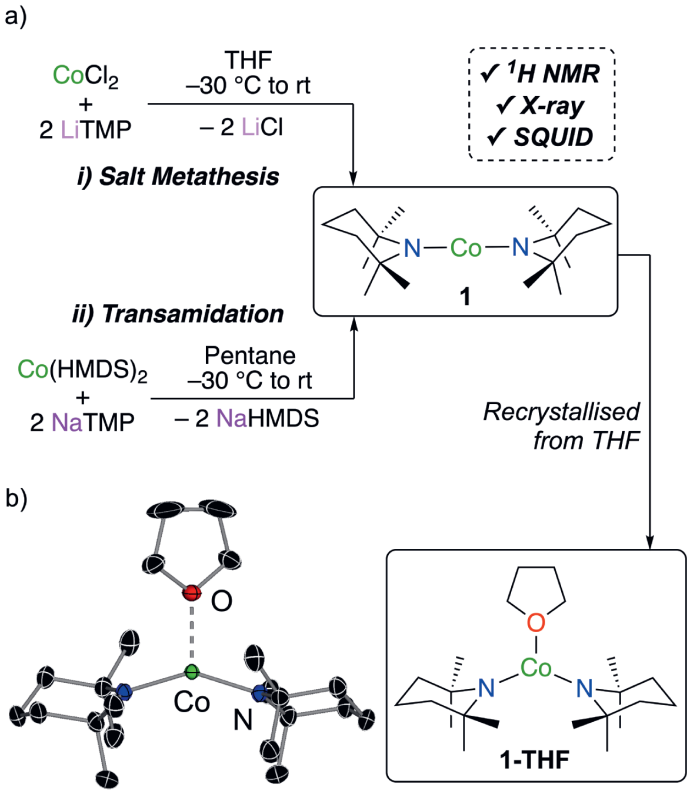

Fig. 2. a) Synthesis of **1** *via* i) salt metathesis and ii) trans(amidation). b) Molecular structure of **1-THF**, H atoms omitted for clarity and thermal ellipsoids displayed at 50% probability level.

which was substantiated by variable temperature SQUID measurements of **2** with its room temperature value reaching 1.95 B.M., much lower than the theoretical spin only value (5.47 B.M.) of two uncoupled high spin Co(II) centres.

The generation of **2** featuring two newly formed Co–C bonds corroborates the enhanced basicity of **1** compared to its HMDS analogue as no sign of fluoroarene metalation was observed with $Co(HMDS)_2$ even under forcing refluxing conditions. Although our group previously reported the metalation of fluoroarenes with the bimetallic cobaltate $NaCo(HMDS)_3$,[12] it is noteworthy that this reactivity comprises the initial sodiation of the substrate followed by rapid transmetalation onto the transition metal. Complex **2** exemplifies the first direct cobaltation of fluoroarenes to be structurally authenticated. As opposed to previously reported functionalisations of fluoroarenes *via* C–H bond activation utilising low-valent cobalt complexes which always involve a change of oxidation state at the metal centre, in our case the cobalt atom remains as Co(II) throughout the Co–H exchange process. Additionally, perfluorinated substrates commonly react with transition metal complexes *via* C–F bond activations,[17] whereas they selectively undergo C–H metalation in the presence of **1**.

When reacted with two molar equivalents of pentafluorobenzene, **1** failed to promote two-fold Co–H exchange with both of the TMP ligands to give a $CoAr_2$ species. In order to get a better understanding on the mechanism of this Co–H exchange, DFT calculations revealed the importance of coordination effects, where the fluoroarene coordinates first to the Co(II) centre *via* one of its F atoms, *ortho* to the C–H bond which is actually deprotonated by the TMP group (Fig. 3a). Furthermore, these studies showed that the formation of the dimeric product **2** greatly contributes to the overall stability of the metalated intermediate, making the overall process exothermic by 30.7 kcal mol^{-1}.[14] These studies also showed that in order to promote the activation of the remaining TMP group, cleavage of the dimeric structure of **2** is required, which is not energetically favoured.

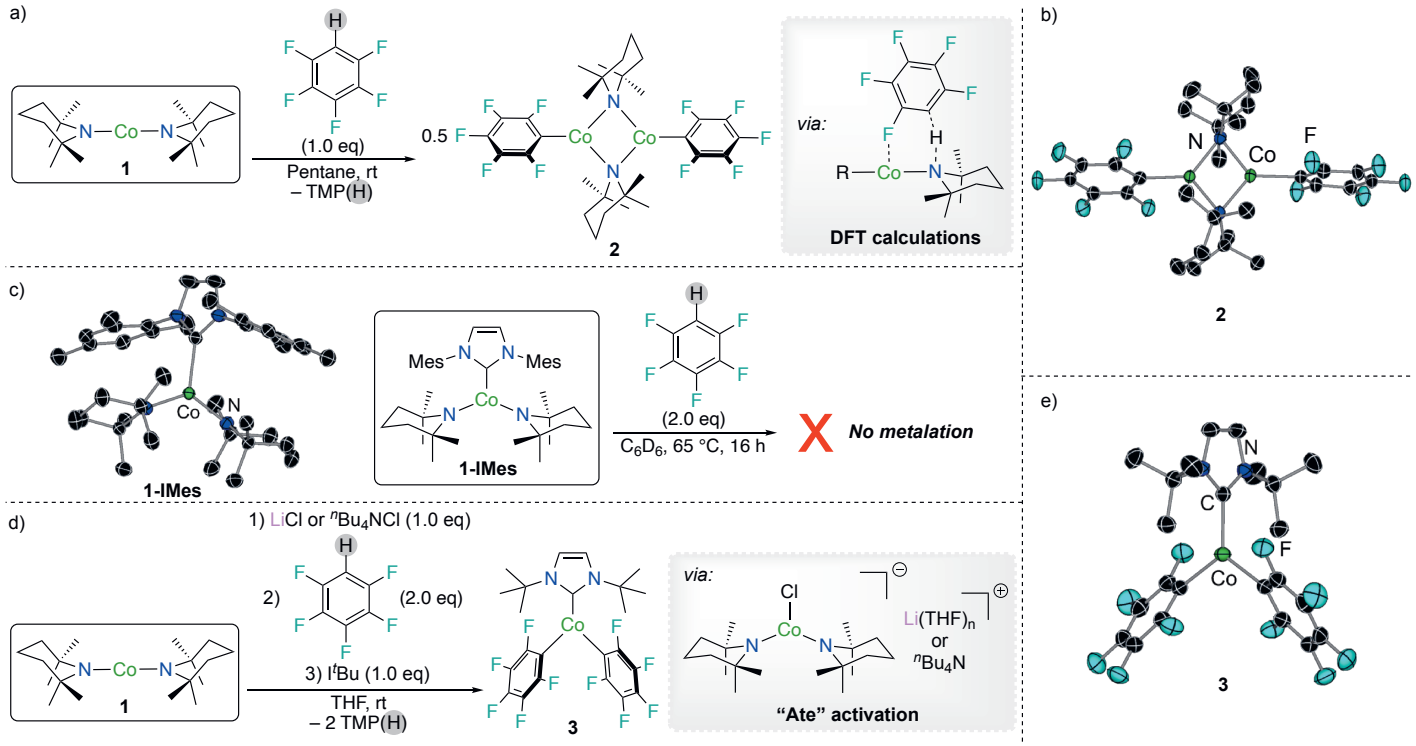

Fig. 3. a) Reaction of **1** with one equivalent of pentafluorobenzene. b) Molecular structure of **2**, H atoms omitted for clarity and thermal ellipsoids displayed at 50% probability level. c) Molecular structure of **1-IMes**, H atoms omitted for clarity and thermal ellipsoids displayed at 50% probability level. No metalation was observed for **1-IMes** and pentafluorobenzene. d) LiCl or $^{n}Bu_4NCl$ can promote two-fold Co–H exchange to form **3**. e) Molecular structure of **3**, H atoms omitted for clarity and thermal ellipsoids displayed at 50% probability level.

The importance of coordination effects in this cobaltation process was also demonstrated when the *N*-heterocyclic carbene IMes (IMes = 1,3-dimesitylimidazol-2-ylidene) was coordinated to **1** to form **1-IMes**, which was found to be completely inert towards cobaltation of pentafluorobenzene even after prolonged exposure to two equivalents of pentafluorobenzene at forcing conditions (Fig. 3c). This has been attributed to the strong coordination of IMes to Co, preventing the precoordination of the substrate to Co *via* Co···F electrostatic interactions.

Interestingly, addition of LiCl to **1** in THF allowed for the activation of both TMP arms (Fig. 3d), which could be crystallised and isolated to afford [(^{t}Bu)Co(C_6F_5)$_2$] (**3**) upon the addition of *N*-heterocyclic carbene ^{t}Bu (^{t}Bu = 1,3-di-*tert*-butylimidazol-2-ylidene) (Fig. 3e), confirming the formation of a monomeric bis(aryl) cobalt complex. It should be noted that the carbene addition takes places after the Co–H exchange and its role is to stabilise the $CoAr_2$ intermediate. NMR spectroscopic studies support the formation of an anionic cobaltate intermediate by co-complexation of **1** with LiCl, (Fig. 3d) which is expected to be kinetically more activated.[14] It is noteworthy that addition of $^{n}Bu_4NCl$ to **1** also successfully promoted two-fold Co–H exchange with both TMP groups, eliminating alkali metal effects.

2.3 *Further Reactivity Studies*

Moving away from fluoroarenes, we also found that **1** reacts with 2 equivalents of cyclopentadiene to quantitatively form cobaltocene, with concomitant elimination of TMP(H) after just five minutes at room temperature (Fig. 4a).

Furthermore, both TMP ligands on **1** exhibited significant nucleophilicity as evidenced by the insertion of two CO_2 molecules into their Co–N bonds (Fig. 4a). A pentane solution of **1** was exposed to an atmosphere of CO_2 (approx. 1 bar) overnight and the solution turned from dark red to blue. One equivalent of TMEDA (*N*,*N*,*N*',*N*'-tetramethylethylenediamine) was added to aid recrystallisation and afforded a batch of purple crystals of [(TMEDA)Co{OC(=O)TMP}$_2$] (**4**). XRD analysis established **4** as a bis(-carbamate) complex resulting from two-fold CO_2 insertion into the Co–N_{TMP} bonds in **1**, furnishing new C–N and Co–O bonds (Fig. 4b). CO_2 insertion into M–N bonds has been reported with

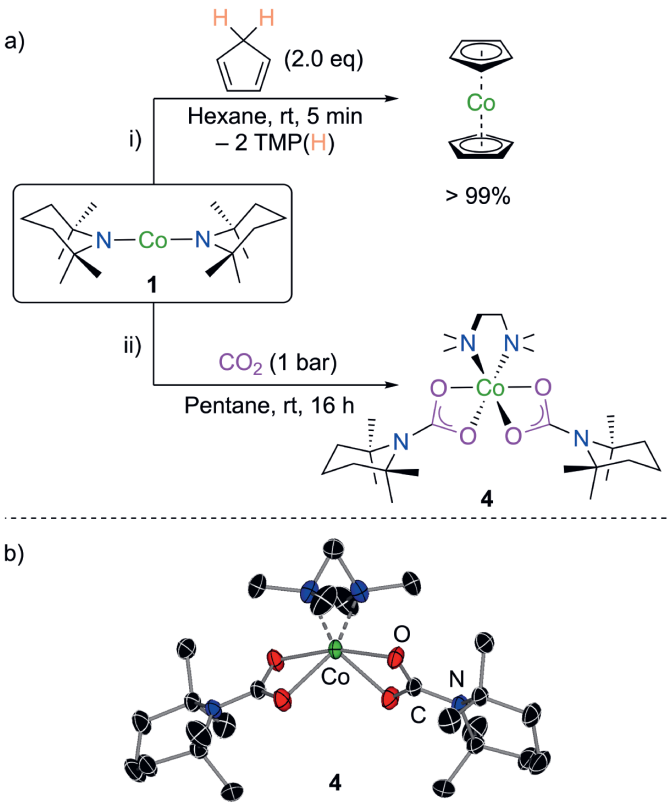

Fig. 4. a) i) Reaction of **1** with two equivalents of cyclopentadiene to synthesise cobaltocene. ii) Reaction of **1** with CO_2 to generate **4**. b) Molecular structure of **4**, H atoms omitted for clarity and thermal ellipsoids displayed at 50% probability level.

other transition metal amide complexes, although such examples remain scarcer than those with M–H or M–R (R = alkyl, alkoxide) bonds.[14]

3. Conclusions

Filling the fundamental knowledge gap related to transition metal TMP complexes, we have provided an overview of our work on the synthesis, characterisation and reactivity studies of a novel cobalt(II) bis(amide) complex. Similar to some main group metal TMP complexes, $Co(TMP)_2$ promotes selective direct Co–H exchange with polyfluoroarenes under mild conditions without changing its +2 oxidation state or cleaving C–F bonds. In addition, the TMP arms display nucleophilic behaviour and undergo CO_2 insertion under mild reaction conditions. Studies assessing the full synthetic potential of this new type of cobalt amide are currently ongoing in our group.

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