Opening the Black Box of Mixed-Metal TMP Metallating Reagents: Direct Cadmation or Lithium-Cadmium Transmetallation?

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Supporting Information

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Experimental

General experimental

All reactions and manipulations were carried out under a protective argon atmosphere using either standard Schlenk techniques or a glove box. All solvents were dried over Na/benzophenone and freshly distilled prior to use. [Li(TMP)·THF]$_2$ [1] and lithiated anisole [2] were prepared by literature methods. nBuLi and iodine were purchased from Aldrich and used as received. Anisole was dried over 4Å molecular sieves. LiCl and CdCl$_2$ were dried under vacuum at 110°C for 6h and stored under argon prior to use. ^{1}H, ^{13}C and ^{113}Cd NMR spectra were recorded on a Bruker AV400 MHz spectrometer (operating at 400.03 MHz for ^{1}H, 100.58 MHz for ^{13}C and 88.72 MHz for ^{113}Cd). All ^{13}C NMR spectra were proton decoupled.

Cd(TMP)$_2$ 2

16 mmol of LiTMP was prepared in THF (10mL) at room temperature from TMP(H) (2.72 mL, 16 mmol) and ^{n}BuLi (10 mL, 1.6 M in hexane, 16 mmol). CdCl$_2$ (1.46 g, 8 mmol) was added and this was stirred at room temperature for one hour to give a yellow solution and a dark precipitate. All solvents were removed *in vacuo* and hexane (30mL) was added. This was filtered and the solvent removed with the application of heat. After cooling to -35°C, a waxy yellow solid remained (2.40 g, 76 %).

^{1}H NMR (C$_6$D$_6$) 300K: 1.71 (m, 4H, TMP γ), 1.43 (t, $^3J_{HH}$ = 6.4 Hz, 8H, TMP β), 1.25 ppm (s, 24H, TMP Me). ^{13}C NMR (C$_6$D$_6$) 300K: 54.0 (TMP α), 39.4 (TMP β, $^3J_{CdC}$ = 38 Hz), 38.2 ppm (TMP Me), 19.7 (TMP γ). ^{113}Cd (C$_6$D$_6$) 300K: 363 ppm.

Cd(o-C$_6$H$_4$OMe)$_2$·TMEDA 3

Li(o-C$_6$H$_4$OMe) (0.228 g, 2 mmol), CdCl$_2$ (0.183 g, 1 mmol) and TMEDA (0.15 mL, 1 mmol) were stirred in hexane (5mL) giving a suspension. THF was added dropwise with stirring until a homogenous solution resulted (~ 10 mL required). Upon cooling to -35°C a crop of colourless crystals precipitated (0.151 g, 34 %).

^{1}H NMR (C$_6$D$_6$) 300K: 7.79 (dd, $^3J_{HH}$ = 6.7 Hz, $^3J_{CdH}$ = 46 Hz, 2H, aromatic CH), 7.34 (dt, $^3J_{HH}$ = 7.7 Hz, 2H, aromatic CH), 7.21 (t, $^3J_{HH}$ = 7.3 Hz, $^4J_{CdH}$ = 24 Hz, 2H, aromatic CH), 6.78 (d, $^3J_{HH}$ = 8.2 Hz, $^4J_{CdH}$ = 27 Hz, 2H, aromatic CH), 3.43 (s, 6H,

OMe), 2.06 (s, 12H, TMEDA Me), 1.95 ppm (s, 4H, TMEDA CH$_2$). ^{13}C NMR (C$_6$D$_6$) 300K: 165.9 (quaternary aromatic), 151.0 (quaternary aromatic), 140.7, 127.0, 121.2, 108.7 (all aromatic CH), 57.5 (TMEDA CH$_2$), 54.6 (OMe), 46.8 (TMEDA Me). ^{113}Cd (C$_6$D$_6$) 300K: 469 ppm. Satisfactory elemental analyses could not be obtained due to a small amount of LiCl by-product precipitating along side the desired product.

General procedure for anisole metallation reactions

Anisole (2mL of a pre-prepared 1 M solution in THF, 2 mmol) was added to a THF solution containing 1 mmol of the appropriate metallating agent. This was allowed to stir for two hours at room temperature before an excess of I$_2$ in THF was added. The following day a large excess of saturated NaS$_2$O$_3$ in H$_2$O was added. Ethyl acetate was added, the organic fraction was separated and dried with anhydrous MgSO$_4$. Ferrocene (37.2 mg, 0.2 mmol) was added as an inert integration standard and an aliquot of this mixture was removed for NMR analysis (in CDCl$_3$) upon removing the organic solvents under reduced pressure.

DOSY experiments

The Diffusion-Ordered Spectroscopy (DOSY) NMR experiments were performed on a Bruker AVANCE 400 NMR spectrometer operating at 400.13 MHz for proton resonance under TopSpin (version 2.0, Bruker Biospin, Karlsruhe) and equipped with a BBFO-z-atm probe with actively shielded z-gradient coil capable of delivering a maximum gradient strength of 54 G/cm. Diffusion ordered NMR data was acquired using the Bruker pulse program dstegp3s employing a double stimulated echo with three spoiling gradients. Sine-shaped gradient pulses were used with a duration of 3 ms together with a diffusion period of 100 ms. Gradient recovery delays of 200 μs followed the application of each gradient pulse. Data was accumulated by linearly varying the diffusion encoding gradients over a range from 2% to 95% of maximum for 64 gradient increment values. DOSY plot was generated by use of the DOSY processing module of TopSpin. Parameters were optimized empirically to find the best quality of data for presentation purposes. Diffusion coefficients were calculated by fitting intensity data to the Stejskal-Tanner expression with estimates of errors taken from the variability in the calculated diffusion coefficients by consideration of different NMR responses for the same molecules of interest (except TMS).

Diffusion study of (1): ^1H DOSY NMR experiment of $CdCl_2$ and Li(TMP) with internal references present (tetraphenylnaphthalene TPhN, phenylnaphthalene PhN and tetramethylsilane, TMS) was recorded at 27°C in d_8-THF. All the different components of the mixture separate clearly in the diffusion dimension with a relative size sequence of TPhN > $Cd(TMP)_2$ >> PhN > TMP(H) > TMS (Figure 5), according to their increasing D values [D(TPhN) = 7.84 x 10^{-10} m^2 s^{-1} < D("Li(TMP)") = 8.55 x 10^{-10} < D("$Cd(TMP)_2$") = 9.46 x 10^{-10} << D(PhN) = 1.39 x 10^{-9} m^2 s^{-1} < D(TMPH) = 1.54 x 10^{-9} m^2 s^{-1} << D(TMS) = 1.92 x 10^{-9} m^2 s^{-1} (Table 2)].

Diffusion study of (2): ^1H DOSY NMR experiment of $Cd(TMP)_2$ with internal references present (tetraphenylnaphthalene TPhN, phenylnaphthalene PhN and tetramethylsilane, TMS) was recorded at 27°C in d_8-THF. All the different components of the mixture separate clearly in the diffusion dimension with a relative size sequence of TPhN > "Li(TMP)" > "$Cd(TMP)_2$" >> PhN > TMP(H) > TMS (Figure S2), according to their increasing D values [D(TPhN) = 8.40 x 10^{-10} m^2 s^{-1} < D($Cd(TMP)_2$) = 1.06 x 10^{-9} << D(PhN) = 1.32 x 10^{-9} m^2 s^{-1} < D(TMPH) = 1.63 x 10^{-9} m^2 s^{-1} << D(TMS) = 2.00 x 10^{-9} m^2 s^{-1} (Table S1)].

Crystal structure determinations

Crystallographic data was collected at 123(2) K on an Oxford Diffraction Diffractometer with $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). Structure was solved using SHELXS-97 [3] and refined to convergence on F^2 against all independent reflections by the full-matrix least-squares using the SHELXL-97 [3] program. CCDC-xxxxxx contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal data for **2**: $C_{18}H_{36}CdN_2$, M_r = 392.89, monoclinic, space group $P2_1/n$, a = 11.8651(4), b = 11.5596(3), c = 15.5090(6) Å, β = 112.201(4)°, V = 1969.45(13) $Å^3$, Z = 4, μ = 1.107 mm^{-1}, T = 123(2) K; 11 745 reflections, 4834 unique, R_{int} = 0.0255; final refinement to convergence on F^2 gave R = 0.0284 (F, 3850 obs. data only) and R_w = 0.0555 (F^2, all data), GOF = 1.050.

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Computational details

Calculations were performed using the Gaussian 03 package [4] and B3LYP density functionals.[5] The DZVP [6] basis set was used for Cd while the 6-31G* [7] basis set was used for all other atoms. A frequency analysis was carried out on all the optimised structures. The total energy values quoted include the zero point energy contribution.
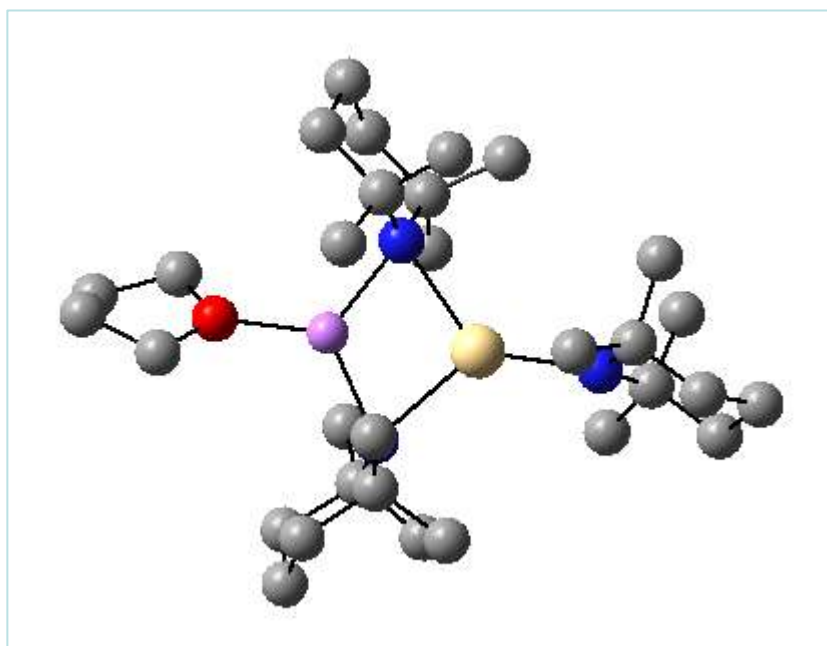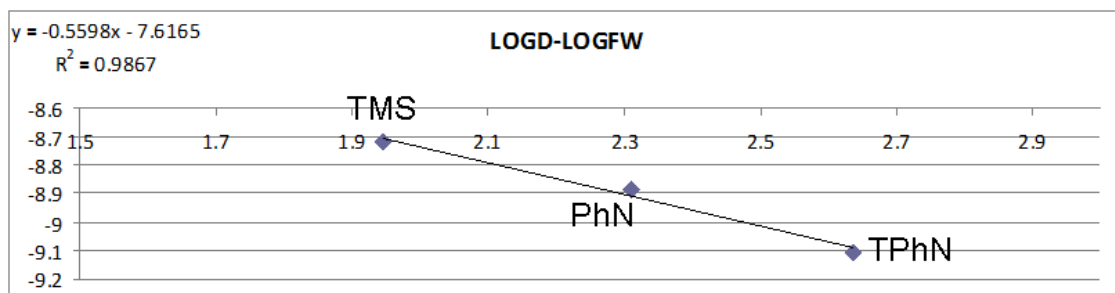
Figure S1 Calculated structure of putative **1**·THF

Selected bond lengths (Å) and angles (°)

Li-O	2.004
Li-N	2.077
	2.072
Cd-N_{br}	2.369
	2.376
Cd-N_{ter}	2.202
Li-N-Cd	73.5
	73.4
N-Li-N	116.8
N-Cd-N	96.3

Graph S1 log D – log FW representation from the ^{1}H DOSY NMR data obtained for the mixture of CdCl$_2$ and 3Li(TMP), and the standards TPhN, PhN, TMS at 27 °C in d$_8$-THF.
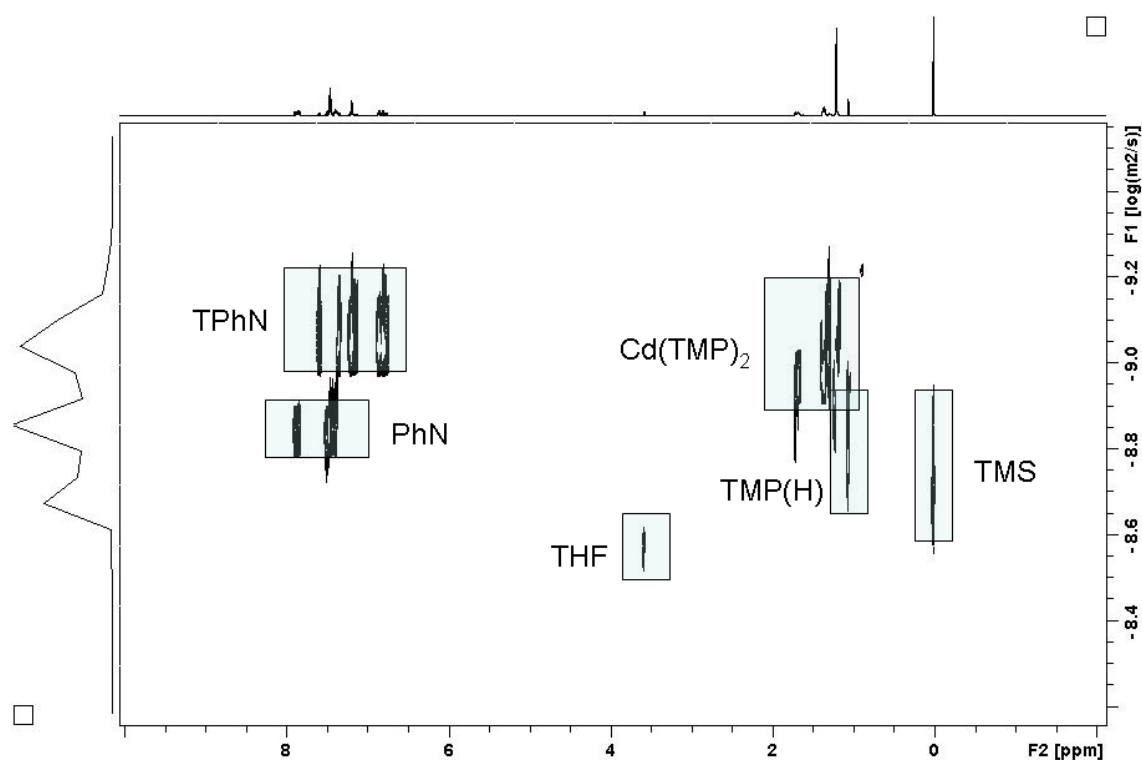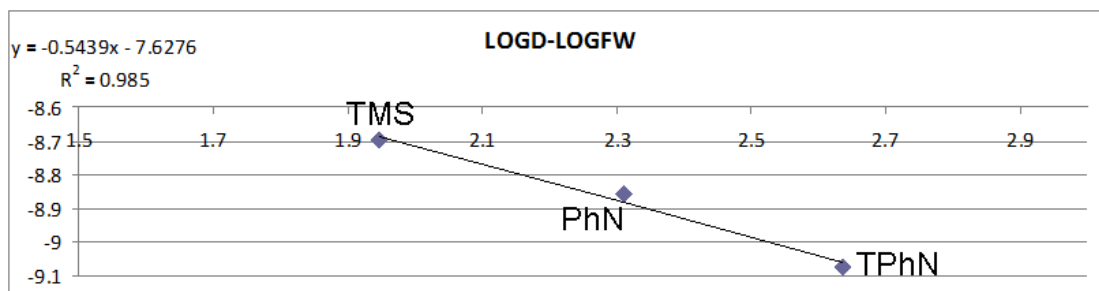

Figure S2 ^{1}H DOSY NMR spectrum of Cd(TMP)$_2$ in d$_8$-THF at 27°C in the presence of the inert standards tetraphenylnaphthalene (TPhN), phenylnaphthalene (PhN) and tetramethylsilane (TMS).

Compound	10^{-10} D(m^2/s)
TPhN	8.40
PhN	13.89
TMS	20.02
Cd(TMP)$_2$	10.57
TMP(H)	16.32

Table S1 Diffusion coefficients obtained from ^{1}H DOSY NMR experiment

Graph S2 log D – log FW representation from the ^{1}H DOSY NMR data obtained for Cd(TMP)$_2$, and the standards TPhN, PhN, TMS at 27 °C in d$_8$-THF.
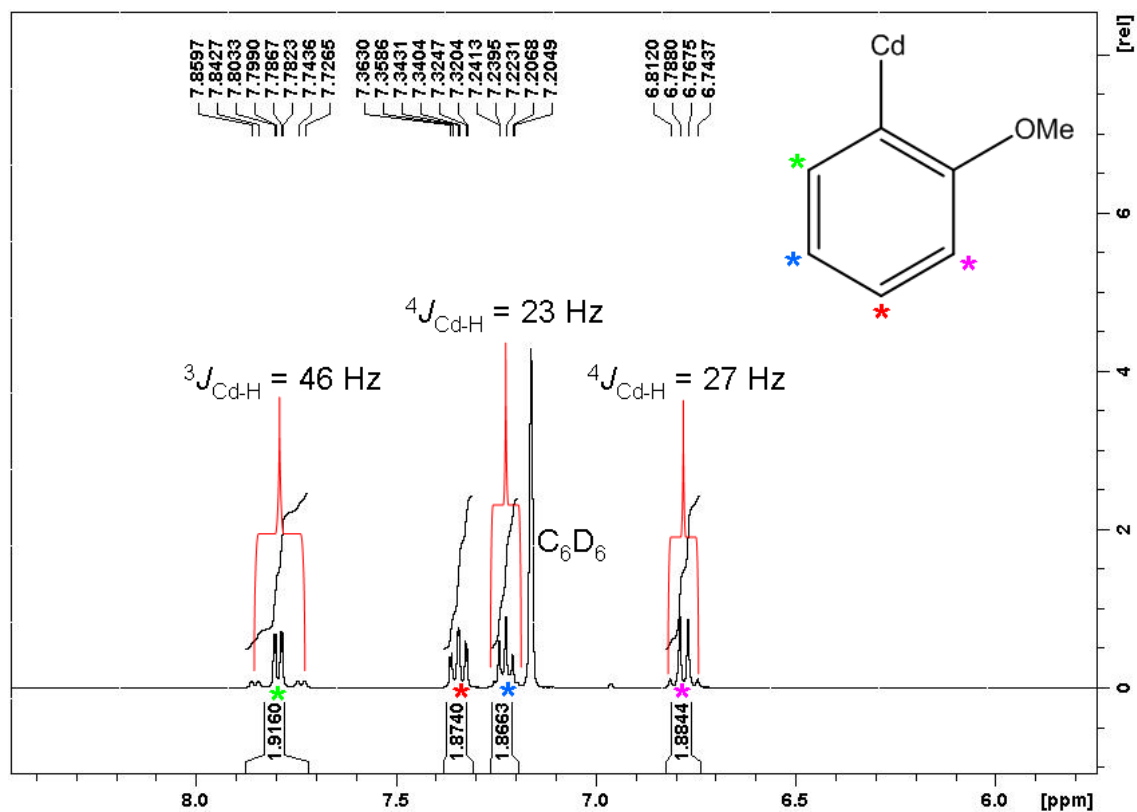
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Figure S3 Expansion of aromatic region of ^{1}H NMR spectrum of (anisolyl)$_2$Cd·TMEDA (**3**) in C$_6$D$_6$ with ^{113}Cd satellites highlighted.
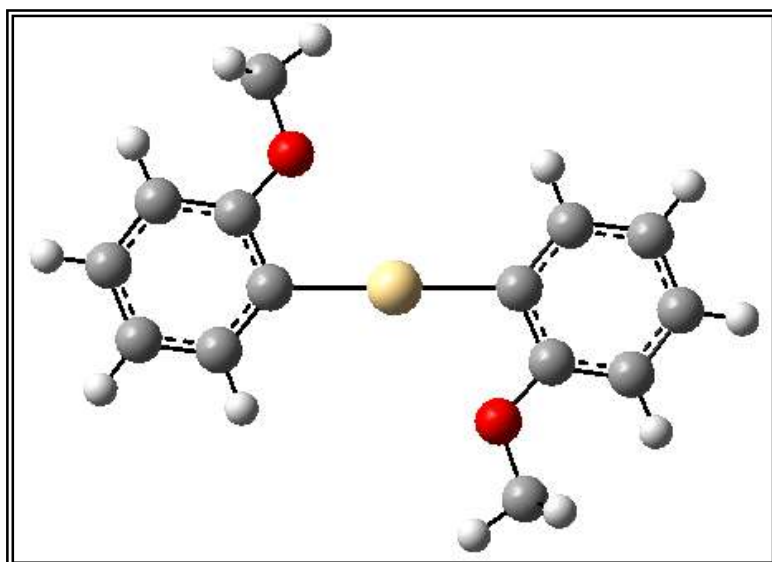
Figure S4 Optimized structure of (MeOC$_6$H$_4$)$_2$Cd

Selected bond lengths (Å) and angles (^{o})

Cd-C	2.166
C-C	1.405
C-O	1.385
O..Cd	2.935
C-Cd-C	179.9
Cd-C-C	113.7
	129.0
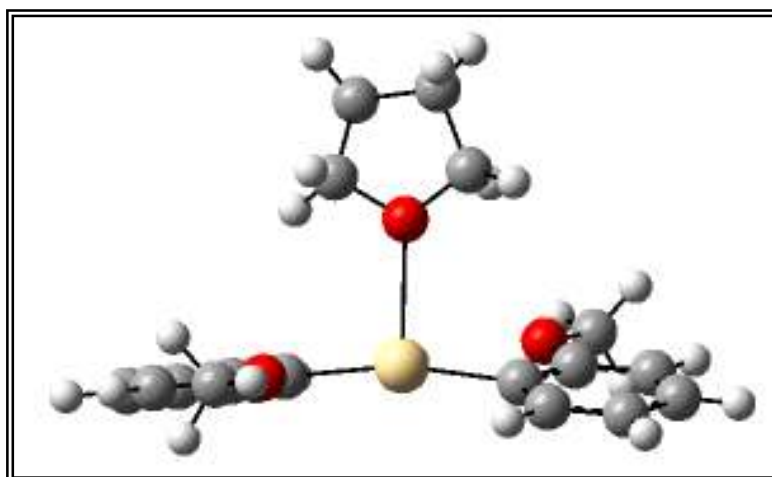
Figure S5 Optimized structure of $(MeOC_6H_4)_2Cd \cdot THF$

Selected bond lengths (Å) and angles (^{o})

Cd-C	2.183
	2.192
C-C	1.404
	1.405
C-O	1.389
	1.391
O..Cd	2.930
	2.981
Cd-O	2.570
C-Cd-C	167.3
Cd-C-C	113.2
	129.9
	114.5
	128.8
O-Cd-C	95.8
	96.8
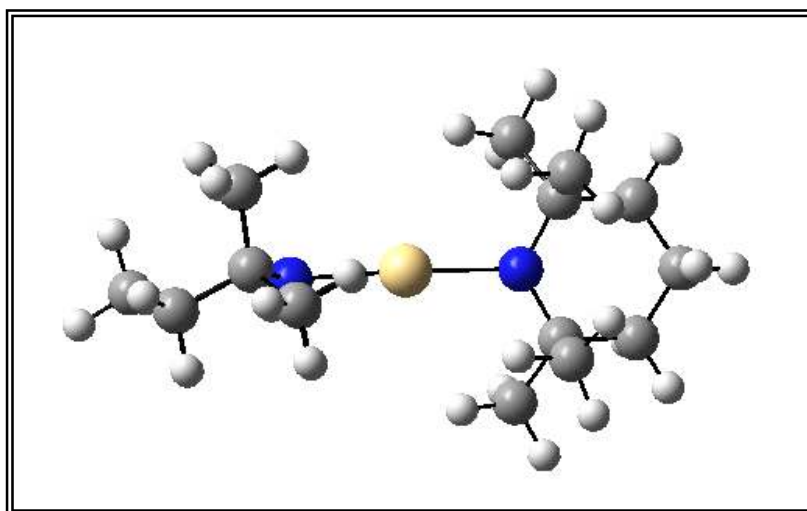
Figure S6 Optimized structure of Cd(TMP)$_2$

Selected bond lengths (Å) and angles (^{o})

Cd-N	2.093
N-C	1.476
	1.476
N-Cd-N	174.6
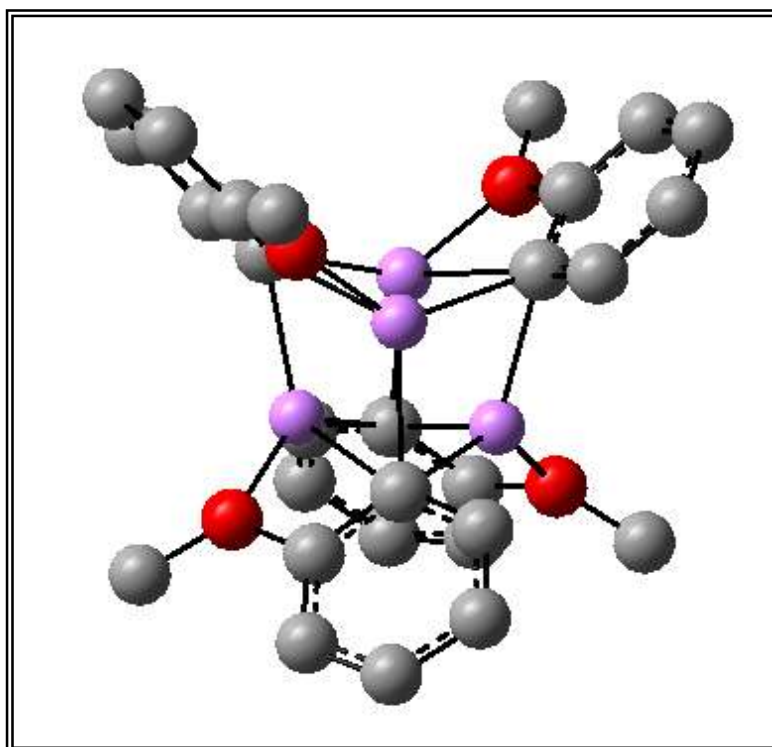
Figure S7 Optimized structure of [(MeOC$_6$H$_4$)Li]$_4$

Selected bond lengths (Å) and angles (^{o})

Li-C	2.213
	2.247
	2.422
Li-O	1.915
C-O	1.409
C-Li-C	107.4
	104.6
	112.3
Li-C-Li	67.9
	69.7
	66.0
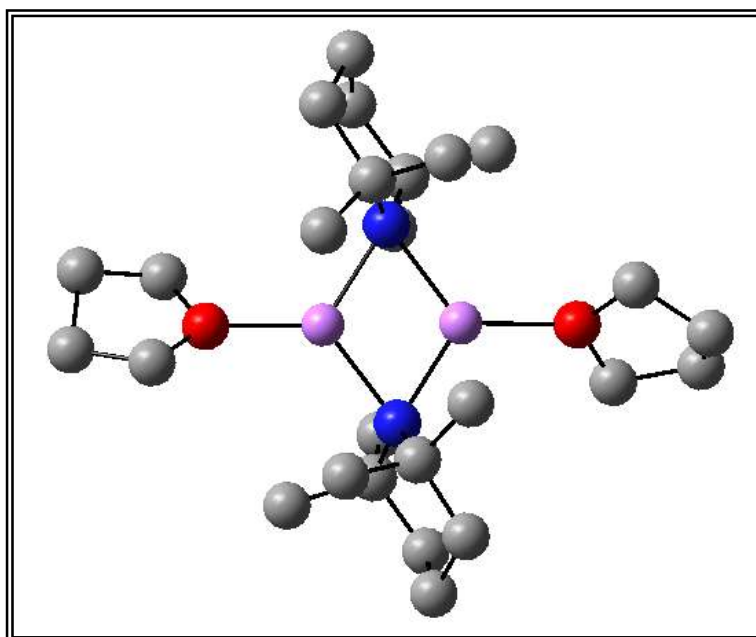
Figure S8 Optimized structure of [Li(TMP)·THF]$_2$

Selected bond lengths (Å) and angles ($^\circ$)

Li-N	2.119
	2.116
	2.040
	2.040
Li-O	2.021
	2.023
N-Li-N	110.6
	110.7
Li-N-Li	69.3
	69.2

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