Adding the right (or left) twist to tris-chelate complexes – coordination chemistry of chiral oxazolylphenolates with M^{3+} ions (M=Al or rare earth)

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Supplementary information

Synthesis of benzyl ligands

Preparation of (R)-2-amino-3-phenylpropan-1-ol
To a suspension of phenylalanine (10.0 g, 60.5 mmol) and sodium borohydride (5.03 g, 2.2 eq.) in THF (200 mL) was added under argon (Schlenk conditions not required) a solution of iodine (15.3 g, 1.0 eq.) in THF (50 mL) dropwise over 45 minutes. The solution was observed to turn brown and immediately decolourise between drops. The resultant white suspension was heated to reflux and maintained under an atmosphere of argon for 16 h, after which time it was allowed to cool. Organic solvents were removed in vacuo to afford a white foam, which was redissolved in sodium hydroxide (10 % w/v, 100 mL) and washed with diethyl ether (3 x 100 mL). Organic solvents were combined and dried over magnesium sulfate before being removed in vacuo to afford a crude, turbid oil (12.1 g) which crystallised on standing. Pure product was obtained by recrystallization in toluene to afford (R)-2-amino-3-phenylpropan-1-ol (5.49 g, 60%) as a fine white powder. FT-IR: 2927.41 (NH), 1049.09 (CO); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.06 - 7.26 (m, 5H), 3.55 (dd, J=10.9, 3.7 Hz, 1H), 3.32 (dd, J=10.8, 7.4 Hz, 1H), 2.90 - 3.11 (m, 3H), 2.69 (dd, J=13.6, 5.4 Hz, 1H), 2.47 (dd, J=13.3, 8.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 138.66, 129.65, 129.05, 126.96, 65.97, 54.68, 40.54.

Preparation of (S)-1-(4-benzyl-4,5-dihydrooxazol-2-yl)naphthalen-2-ol (Bn-Nap)
Zinc chloride (0.40 g, 0.1 eq.) was heated in a Schlenk flask under vacuum until molten, before being allowed to cool under an atmosphere of argon. To the flask was added under argon a suspension of (R)-2-amino-3-phenylpropan-1-ol (4.57 g, 1.5 eq.) and 3-hydroxy-2- naphthonitrile (5.00 g, 1.0 eq.) in chlorobenzene (30 mL). The resulting suspension was heated to reflux (130 °C) and maintained under argon for 72 h before being allowed to cool to afford a dark red suspension. Organic solvents were removed in vacuo to afford a crude brown oil, which was dissolved in dichloromethane (100 mL) and washed with hydrochloric acid (2 M, 50 mL), water (50 mL) and brine (50 mL). Prepared in an identical manner to 30a, excepting the use of (R)-2-amino-3-phenylpropan-1-ol (3.35 g, 1.5 eq.) as the amino alcohol starting material and conduction of the reaction using half the quantity of 3-hydroxy-2-naphthonitrile (2.5 g, 1.0 eq.). Crude product was isolated as a brown foam (3.91 g). Crude material was purified by flash silica chromatography, 20 % ethyl acetate in hexane (Rf = 0.56) to afford (S)-1-(4-benzyl-4,5-dihydrooxazol-2-yl)naphthalen-2-ol (0.19 g, 4 %) as a dark brown oil. M/z = 304.3 ($M+H^+$, 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.74 (d, J=8.7 Hz, 1H), 7.82 (d, J=9.0 Hz, 1H), 7.74 (dd, J=8.1, 1.2 Hz, 1H), 7.49 (ddd, J=8.7, 7.0, 1.5 Hz, 1H), 7.19 - 7.37 (m, 8H), 4.66 (ddd, J=13.5, 9.4, 7.2 Hz, 1H), 4.57 (dd, J=9.4, 8.2 Hz, 1H), 4.31 (dd, J=8.3, 7.3 Hz, 1H), 3.15 (dd, J=13.7, 6.4 Hz, 1H), 2.89 (dd, J=13.7, 7.3 Hz, 1H); ^{13}C NMR (101 MHz, CDCl3) δ ppm 168.79, 163.22, 137.87, 134.95, 129.62, 129.22, 129.10, 128.53, 128.02, 127.17,

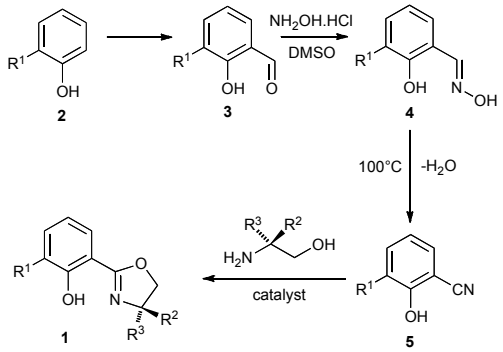
125.32, 123.46, 119.85, 71.91, 64.99, 42.35, 30.73.

Preparation of (S)-2-(4-benzyl-4,5-dihydrooxazol-2-yl)-6-methylphenol (Bn-MePh)
Prepared in an identical manner to 31a, excepting the use of (R)-2-amino-3-phenylpropan-1-ol (4.37 g, 1.50 eq.) as amino alcohol starting material. Crude product was isolated as a brown oil (6.07 g). Crude material was purified by flash silica chromatography, 10 % ethyl acetate in hexane (Rf = 0.45). Pure fractions were combined and evaporated to dryness to afford (S)-2-(4-benzyl-4,5-dihydrooxazol-2-yl)-6-methylphenol (1.79 g, 36 %) as a colourless liquid. m/z = 268.3 ($M+H^+$, 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.35 (br. s, 1H), 7.48 (dd, J=7.9, 1.2 Hz, 1H), 7.27 - 7.36 (m, 2H), 7.18 - 7.27 (m, 4H), 6.76 (t, J=7.6 Hz, 1H), 4.56 - 4.68 (m, 1H), 4.38 (dd, J=9.3, 8.6 Hz, 1H), 4.11 (dd, J=8.5, 7.5 Hz, 1H), 3.11 (dd, J=13.8, 6.4 Hz, 1H), 2.80 (dd, J=13.8, 7.6 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.25, 158.67, 138.04, 134.72, 129.60, 129.04, 127.07, 125.99, 118.47, 110.31, 71.57, 67.13, 42.32, 16.34.

Preparation of (S)-2-(4-benzyl-4,5-dihydrooxazol-2-yl)phenol (Bn-Ph)
Prepared in an identical manner to 8a, excepting the use of 2 (4.76 g, 1.5 eq.) as amino alcohol starting material. Crude product was isolated as a brown oil. Crude material was purified by flash silica chromatography, 10 % ethyl acetate in hexane. Pure fractions were combined and evaporated to dryness to afford (S)-2- (4-benzyl-4,5-dihydrooxazol-2-yl)phenol (0.65 g, 12 %) as a light red liquid.
M/z = 254.3 ($M+H^+$, 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.20 (s, 1H), 7.62 (dd, J=7.8, 1.7 Hz, 1H), 7.37 (td, J=7.8, 1.7 Hz, 1H), 7.29 - 7.35 (m, 2H), 7.01 (d, J=8.3 Hz, 1H), 6.84 - 6.90 (m, 1H), 4.56 - 4.69 (m, 1H), 4.39 (t, J=8.9 Hz, 1H), 4.14 (dd, J=8.4, 7.5 Hz, 1H), 3.11 (dd, J=13.7, 6.4 Hz, 1H), 2.81 (dd, J=13.7, 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.45, 161,23, 139.5, 133.45, 132.56, 130.63, 128.22, 129.10, 126.04, 121.56, 117.82, 74.20, 73.74, 41.54.

Investigation of Lewis acid effects on ligand synthesis

We recently reported a highly versatile and scalable synthesis of oxazolyl phenols and naphthols as shown in Scheme S1 below.[1] Reaction of the aldehyde **3** with hydroxylamine hydrochloride generates the oxime **4** which is dehydrated in situ to generate the nitrile **5**. The nitrile is then reacted with an amino alcohol in the presence of a catalyst to yield the cyclized oxazolyl phenol **1**.

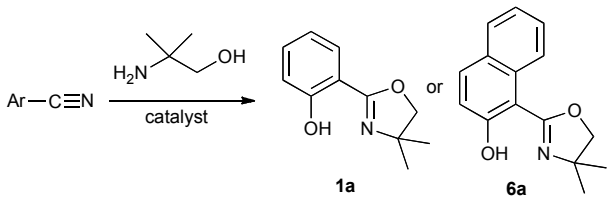


Scheme S1 Synthesis of oxazolyl ligands

[1]. H. C. Aspinall, O. Beckingham, M. D. Farrar, N. Greeves and C. D. Thomas, *Tetrahedron Lett.*, 2011, **52**, 5120-5123.

The cyclization of nitriles 5 with amino alcohols to give the oxazolyl product is generally catalyzed by $ZnCl_2$ in refluxing chlorobenzene, and there has been no systematic investigation of other possible Lewis acid catalysts for this transformation. We therefore decided to screen other Lewis acids for their activity with both phenol and naphthol substrates. The results are summarized in Table S1. We have generally found that the cyclization of naphthol substrates gives lower yields than the corresponding reactions for phenol substrates. Increasing the loading of $ZnCl_2$ from 0.1 eq. to 1.0 eq resulted in a significant decrease in iolated yield for the phenol substrate, but a modest increase in yield for the naphthol. Both $TiCl_4$ and $AlCl_3$ gave poor to modest yields at 0.1 eq., but on increasing the loading of these Lewis acids to 1.0 eq, flocculation of the reaction mixture was observed and isolated yields became vanishingly small. $Yb(OTf)_3$ had the advantage that a very low catalytic loading of 0.01 eq was required, and in the case of the naphthol substrate, the isolated yield of cyclized product 6a was higher than that achieved with $ZnCl_2$. However, in the case of the phenol substrate, $Yb(OTf)_3$ was slightly less effective than $ZnCl_2$. $Yb(OTf)_3$ also required the use of 1,2-dichlorobenzene as solvent whereas $ZnCl_2$ catalyzed cyclizations were performed in the lower-boiling chlorobenzene.

Table S1 Screening of catalysts for cyclization of nitrile compounds



Entry	Catalyst	Catalyst loading (eq)	Isolated yield **1a** (%)	Isolated yield **6a** (%)
1	$ZnCl_2$[a]	0.1	47	32
2	$ZnCl_2$[a]	1.0	26	37
3	$TiCl_4$[a]	0.1	30	4
4	$TiCl_4$[a]	1.0	0	0
5	$AlCl_3$[a]	0.1	10	2
6	$AlCl_3$[a]	1.0	6	2
7	$Yb(OTf)_3$[b]	0.01	41	41

[a] reactions performed in chlorobenzene

[b] reactions performed in 1,2-dichlorobenzene

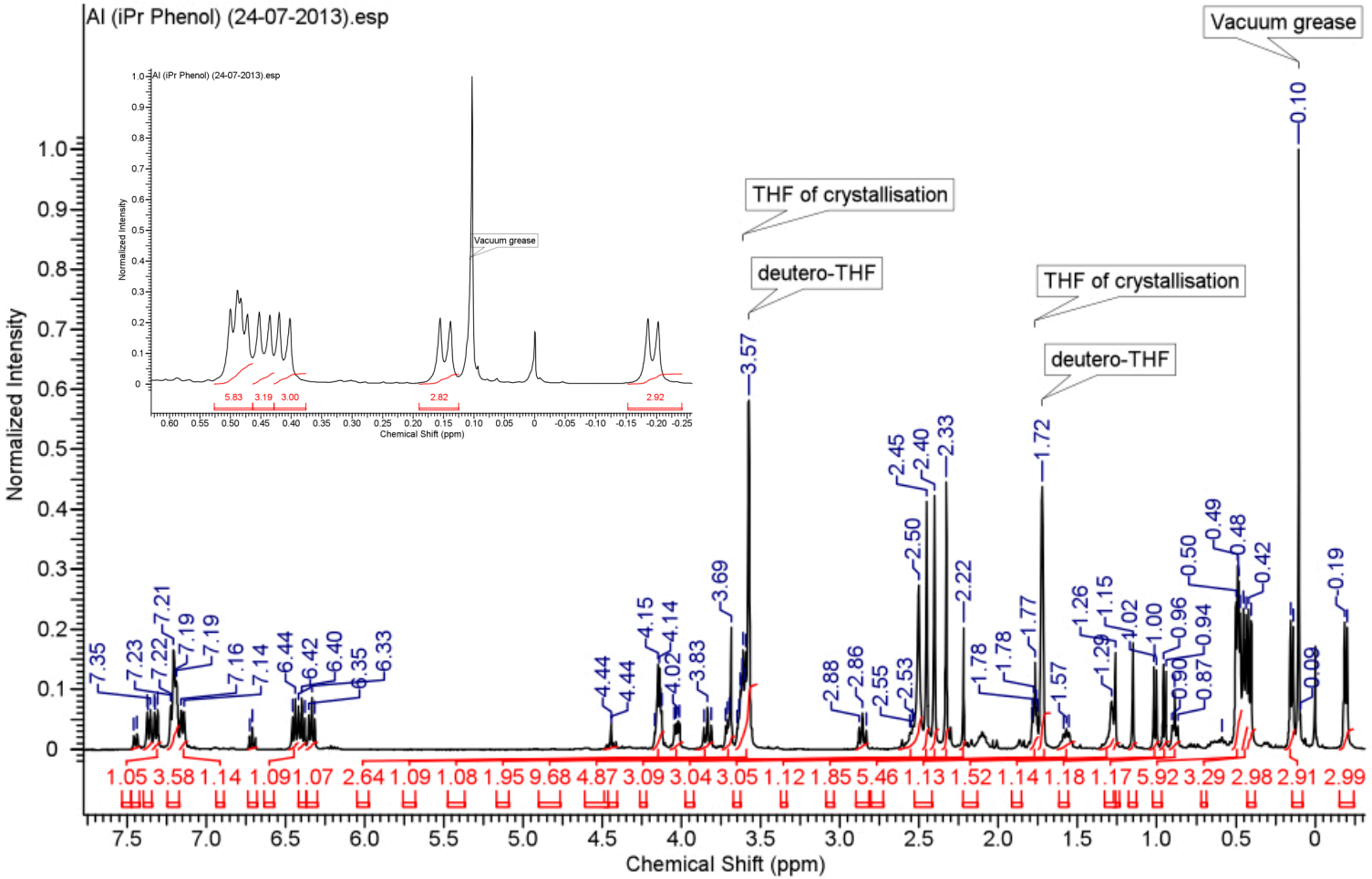
Procedure for screening of Lewis acid catalysts for cyclization of nitriles with amino alcohols
Experimental procedures for $AlCl_3$ and $TiCl_4$ were as reported previously for $ZnCl_2$ catalyzed cyclizations. A typical procedure for $Yb(OTf)_3$ catalyzed cyclizations is given below:

$Yb(OTf)_3$ catalyzed synthesis of Me_2-PhH
$Yb(OTf)_3$ (0.052g, 0.084mmol) was heated to 200 ºC under vacuum in a Schlenk flask. 2-hydroxybenzonitrile (1.0 g, 8.4 mmol) and 2-amino-2-methylpropanol (1.12 g, 12.5 mmol) in 1,2-dichlorobenzene (50 mL) were added to the reaction vessel under argon. The

reaction mixture was heated to reflux for 72 h. The reaction mixture was allowed to cool and was poured over ice (50 g) and DCM (50 mL). The two phase mixture was separated and then the organic phase was washed with water (2 x 200 mL) and dried with $MgSO_4$. The solvent was stripped to yield a brown oil. Crude yield 1.15g, 72%. The crude product was run through a silica plug with hexane and then 1:9 EtOAc in hexane. Tlc R_f=0.64. The solvent was stripped to yield a pale yellow oil which crystallized on standing to form pale yellow crystals. Yield 0.65 g, 41%. ^{1}H NMR ($CDCl_3$) δ: 7.5 (d, 1H, aryl-H), 7.245 (t, 1H, aryl-H), 6.85 (d, 1H, aryl-H), 6.7 (t, 1H, aryl-H), 3.95 (s, 2H, oxazoline CH_2), 1.3 (s, 6H, oxazoline $C(CH_3)_2$). ^{13}C NMR (d-chloroform) δ: 162.42 (aryl-C-OH), 158.74 (CN), 132.1, 126.74, 117.48, 115.47, 109.81 (aryl-C), 65.94 (CH_2), 27.29 ($C(CH_3)_2$. IR: nmax/cm^{-1}: 2973.7 (n(OH)), 1643.05 (n(C=N)), 1118.51 (n(C-O)). M/z 192.2; calcd for M+H$^+$, 192.2. Analysis: found: C, 69.1; H, 6.9; N 7.0%. Calcd. for $C_{11}H_{13}NO_2$: C, 69.1, H, 6.9, N, 7.3%.

NMR spectra

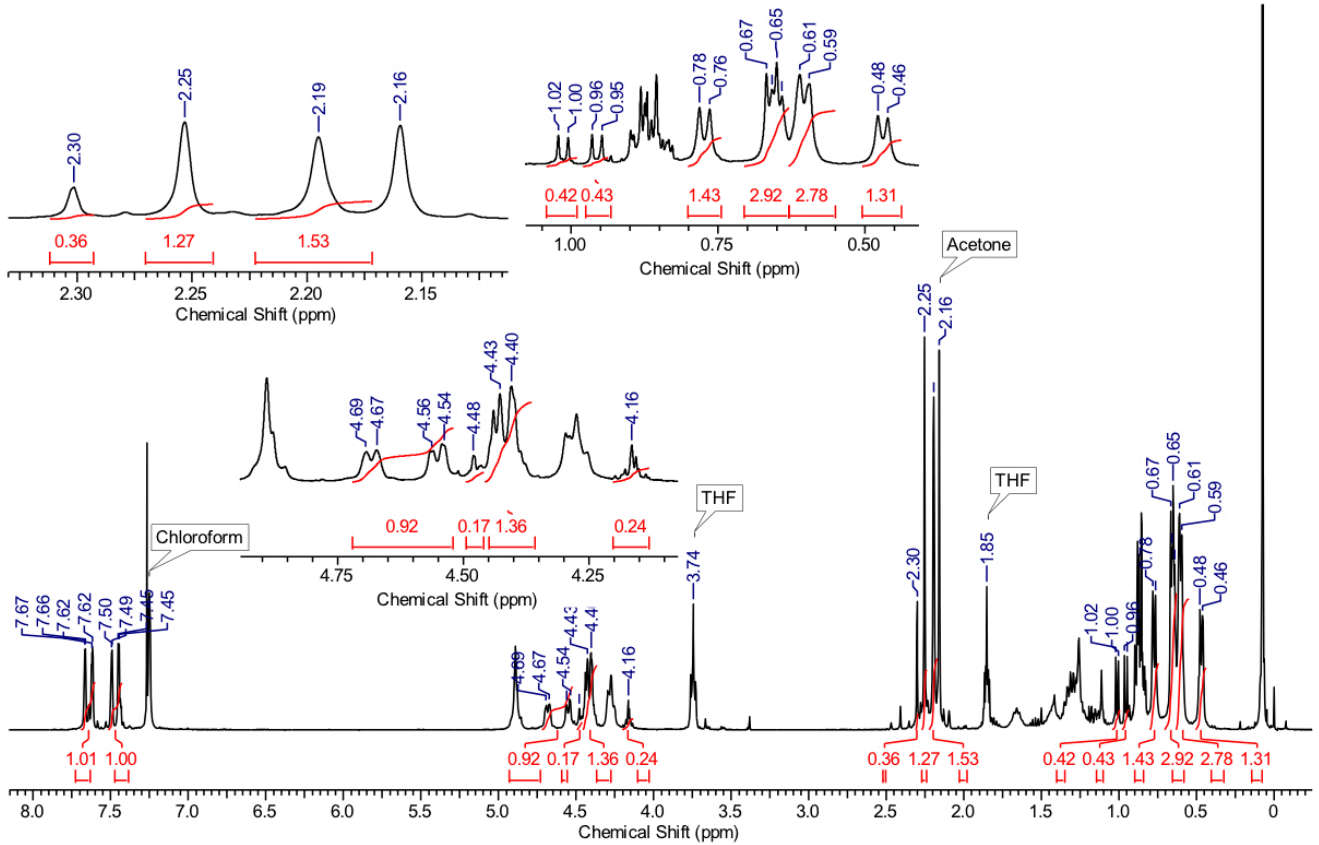
1. [Al(Pr^{i}MePh)$_3$] ^{1}H NMR spectrum



Electronic Supplementary Material (ESI) for Dalton Transactions

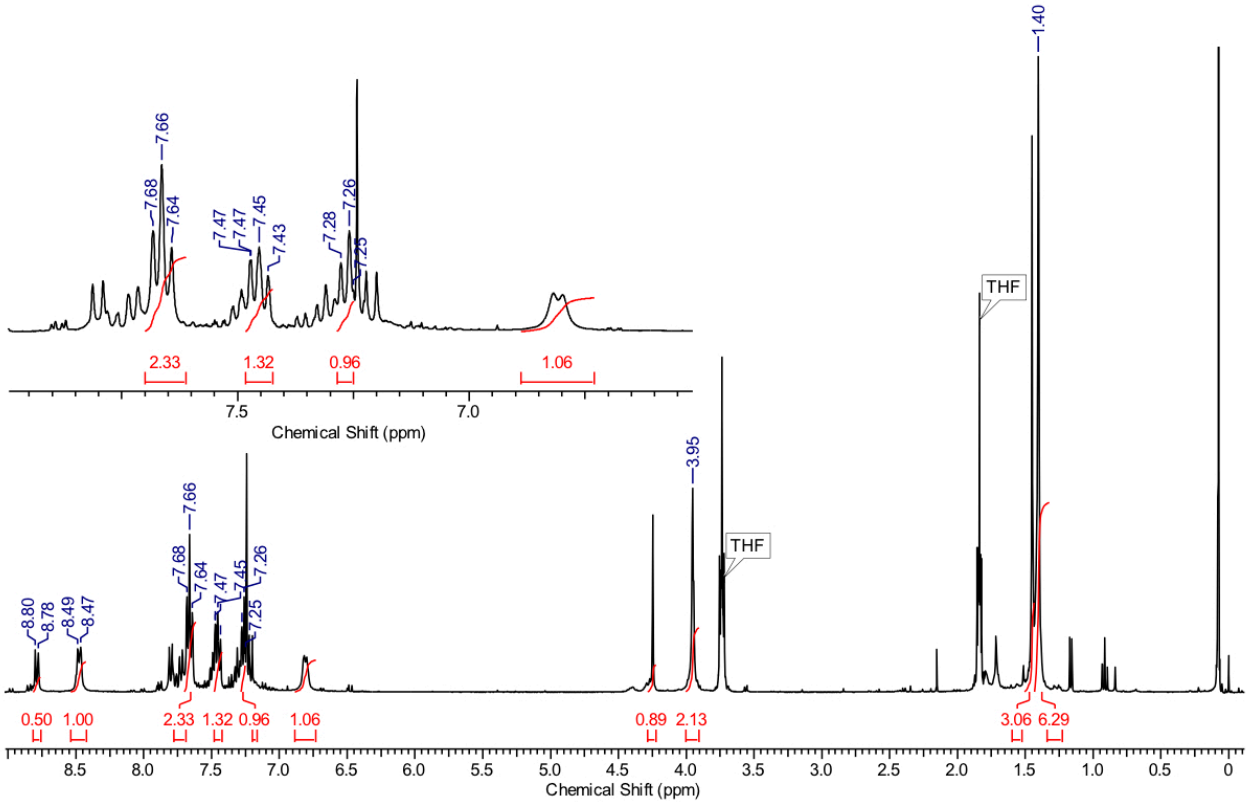
2. [Al(Pr^{i}CNPh)$_3$] ^{1}H NMR spectrum

[Al(^{i}Pr-CNPh)$_3$] – ^{1}H NMR

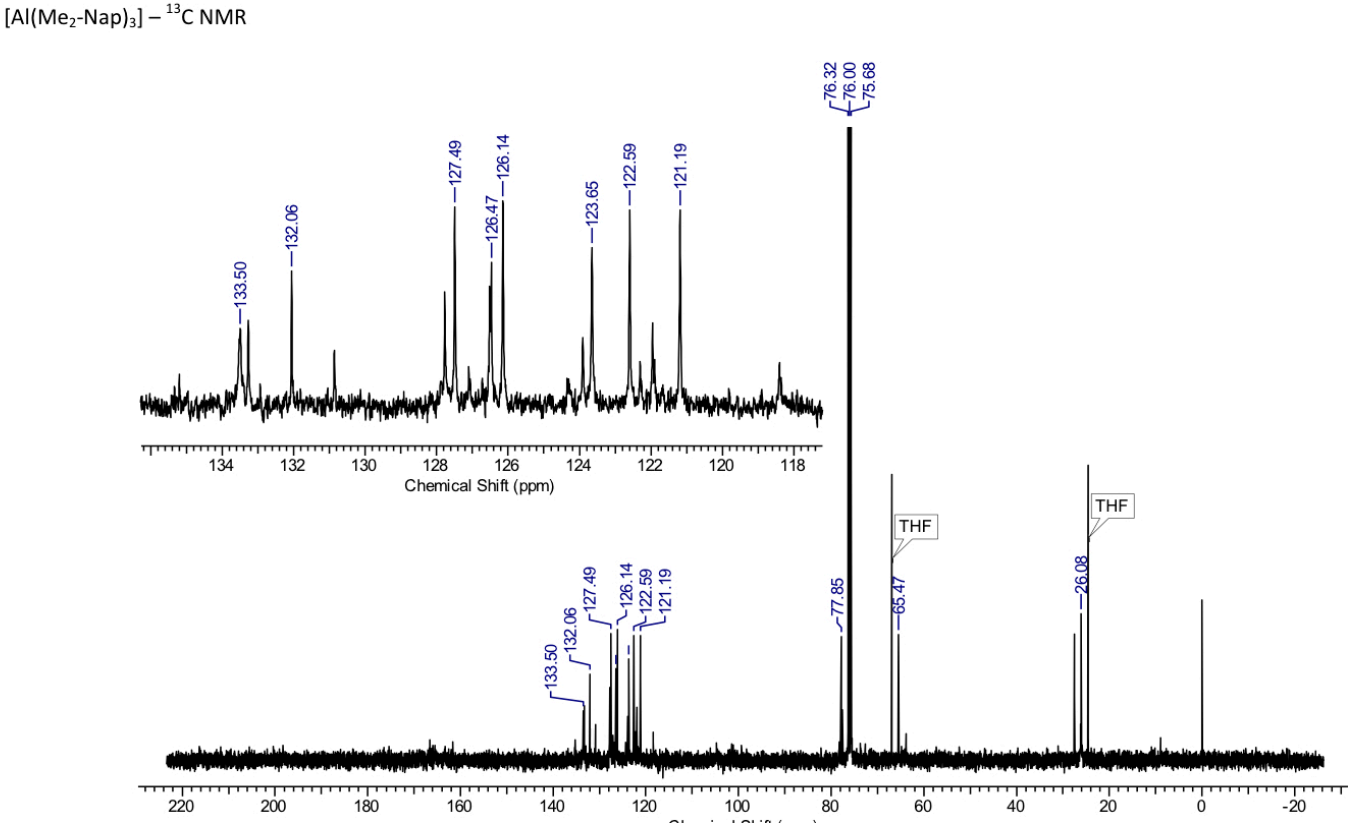


3a. $[Al(Me_2Nap)_3]$ ^1H NMR spectrum

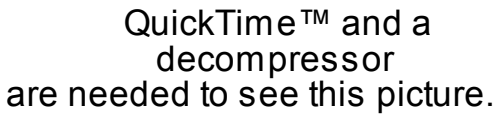
$[Al(Me_2\text{-}Nap)_3]$ – ^1H NMR



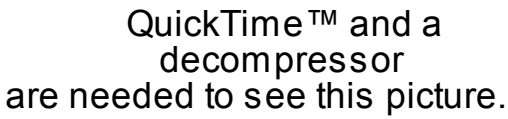
3b $[Al(Me_2Nap)_3]$ ^{13}C NMR spectrum



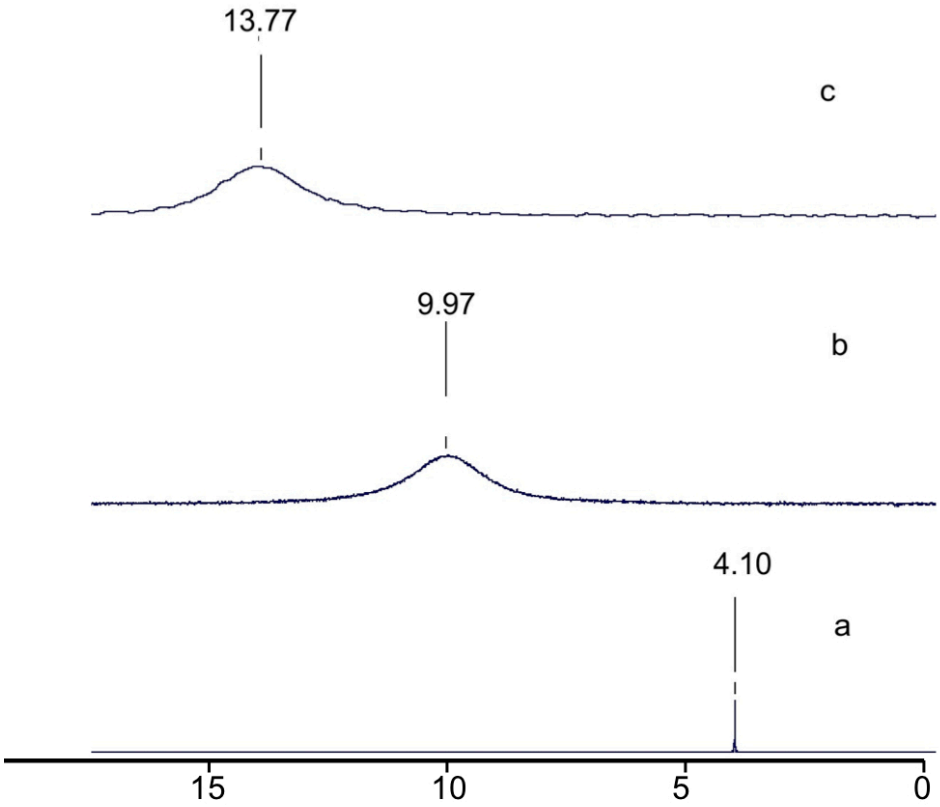
4a $[Y(Pr^iPh)_3]_2$ ^1H NMR spectrum 298K (d_8-toluene)



4b $[Y(Pr^iPh)_3]_2$ ^1H NMR spectrum 213K (d_8-toluene)



5. **^{31}P NMR spectra of (a) Free $(MeO)_3P=O$; (b)[$Yb(Pr^i\text{-}Ph)_3$] with 3 eq $(MeO)_3P=O$; (c) [$Yb(Pr^i\text{-}Ph)_3$] with 1 eq $(MeO)_3P=O$.**



Electronic Supplementary Material (ESI) for Dalton Transactions