Synthesis and Characterisation of a Mesocyclic Tripodal Triamine Ligand

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Abstract: Meso- and macrocyclic polydentate amine ligands have been widely explored in oxidation catalysis and for the stabilization of unstable metal-superoxide, -peroxide, and -oxo intermediates. Herein we report on the design and synthesis of a novel mesocyclic, tripodal, triamine ligand that we believe will be an excellent addition to this field. We explored a number of synthetic procedures towards the mesocyclic asymmetric tetraalkylated ligand **1**. We expect that **1** will bind metals in a facially capping manner, yielding complexes that display *pseudo*-tetrahedral geometry, potentially providing access to unprecedented late transition metal-oxo complexes (metal = Co, Ni, Cu). We describe the preparation of a library of mesocyclic polyamine synthons (**8**, **16**, **17**, **18**, **19**) that are precursors in the synthesis of **1**. These synthons will be used to tailor the electronic properties of metal complexes of **1** and derivatives thereof. The X-ray crystal structures of **19** and mono- and di-protonated forms of **1b** show that the triamine crystallises in a boat-chair conformation which is undesirable for metal coordination. However, solution ¹H NMR studies show that in solution both **19** and the tetraalkylated derivative **1b** are remarkably flexible, and thus are capable of binding metals in a tridentate fashion yielding *pseudo*-tetrahedral complexes. **1b** reacted with [Cu(NCCH₃)₄](OTf) yielding a 1:1 Cu(I) complex [Cu(NCCH₃)(**1b**)]⁺.

Introduction

Iron and copper containing metalloenzymes perform a variety of oxidative conversions of inert hydrocarbon substrates.¹⁻⁵ These enzymes are capable of performing otherwise difficult oxidation reactions under ambient conditions. Terminal metal-oxo intermediates are often postulated as the reactive intermediates in these reactions. For example, in the cytochromes P450, Compound I (an Fe^{IV}=O species) performs hydrogen atom abstraction (HAA) of inert substrates.⁶ The di-copper enzyme particulate methane monooxygenase (pMMO) is capable of HAA from the strong C-H bond in methane (bond dissociation energy (BDE) = 104 kcal mol⁻¹⁽⁷⁾), ultimately yielding methanol.⁸ The HAA reagent in pMMO is likely a bis-μ-oxo dicopper(III) (Cu^{III}-O-Cu^{III}) or a terminal Cu^{III}=O species. These impressive HAA reactivities have driven synthetic chemists to develop bio-mimetic terminal metal-oxo complexes that can replicate this chemistry. While a plethora of well-characterised synthetic Fe^{IV}=O complexes has been reported,⁹⁻¹² there remains no examples of Cu^{III}=O and other terminal late transition metal-oxo (Co, Ni) complexes, although our group and others are making progress towards such species.¹³⁻¹⁶

A reason for the dearth in late transition metal-oxo complexes is that in certain geometries, *d*-electrons destabilise the metal-oxo interaction, preventing the isolation of metal-oxo's of later transition metals.^{14, 16-18} Nocera originally postulated that late transition metal-oxo's could be stabilised in complexes displaying low coordination numbers.¹⁹⁻²³ Based on this postulate, we believe that late transition metal-oxo complexes could be accessible using ancillary ligands that enforce a *pseudo*-tetrahedral geometry. We therefore set out to design and synthesise ligands and complexes that display such *pseudo*-tetrahedral geometry in order to prepare late transition metal-oxo complexes (Figure 1).

In our ligand design considerations we decided that the ligand must be tripodal and facially capping, so as to enforce a *pseudo*-tetrahedral coordination environment. Furthermore, the ligand should contain strong σ-donor atoms in order to stabilise the high oxidation state of the metal centre in metal-oxo complexes. Meso- and macro-cyclic, peralkylated amine

Figure 1 – Left: Target compound **1**, Right: a generic *pseudo* tetrahedral metal-oxo.

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ligands have been used to great success in stabilizing early transition metal-oxo complexes (metal = Mn, Fe)^{10-12, 24-26} and late transition metal-superoxide and -peroxide complexes.²⁷⁻³⁵ As well as being strong σ -donors (through their basic alkyl-amine donors) they are also oxidatively robust, because the N-donors are not as susceptible to oxygen atom transfer (OAT) compared to S- and P-donor ligands. Furthermore, meso- and macro-cyclic frameworks add further stability to complexes bearing these ligands, because of the macrocyclic effect.^{36, 37} Based on these considerations, we set-out to prepare mesocyclic ligand **1** (Figure 1). **1** is a mesocyclic tripodal triamine ligand that meets all prerequisites set-out above to stabilise late transition metal-oxo complexes.

1 is a close analogue of the tripodal acyclic ligand 1,1,1-tris(aminomethyl)ethane (TAME). The coordination chemistry of TAME and its derivatives has been extensively studied.³⁸ Due to the lack of steric bulk in this ligand, 2:1 complexes are often formed. Increasing the steric bulk via alkylation of the amine donors in TAME to give 1,1,1-tris(N,N-dimethylamino)methylethane (Me₆TAME) resulted in the ligand switching from binding to metals in a tripodal tridentate fashion, to a bidentate binding mode, with one of the ligands remaining unbound.³⁸ Similarly, the more bulky guanidine derivative of TAME, 1,1,1-tris(2N-1,1,3,3-tetramethylguanidino)methylethane (guanTAME) has been shown to exhibit variable denticity. While Chang and co-workers have isolated the *pseudo*-tetrahedral complex [Co(guanTAME)Cl](OTf) (OTf = trifluoromethanesulphonate) where GuanTAME binds as a tripodal facially capping ligand,³⁹ Wittmann and co-workers have reported a bidentate binding mode for guanTAME in both [Mn(guanTAME)(Cl)₂] and [Zn(guanTAME)(Cl)₂], with the remaining ligand arm unbound in both cases.⁴⁰ We postulate that the mesocyclic nature of **1** and the steric bulk around the putative metal-binding site will ensure **1** would bind in a tridentate fashion yielding 1:1 complexes.³⁷

1 is also a close analogue of the 1,5-diazacyclooctane (DACO) family of ligands. The unique coordination chemistry of DACO has been well studied.⁴¹ DACO forms square planar complexes [M(DACO)₂]²⁺ with Cu^{II} and Ni^{II}.³⁷ In contrast, [Co^{II}(Cl)(DACO)₂]²⁺ displayed a 5-coordinate square pyramidal structure.⁴² Analysis of the crystal structures of these complexes showed that both DACO ligands bind to the metal with the ligand displaying a boat-chair configuration.⁴³ These observations are important because we require that **1** binds to metals yielding a chair-boat configuration to ensure *pseudo*-tetrahedral geometry.

In order to introduce pendant arms containing ligating functional groups, several derivatives of DACO have been developed, exclusively through *N*-alkylation. Square pyramidal

Ni^{II}, Co^{II} and Zn^{II} complexes of 1,5-diazacyclooctane-*N,N*-diacetic acid (DACODA) were synthesised by Legg and co-workers.⁴⁴⁻⁴⁶ Darensbourg and co-workers synthesised bis-mercaptoethyl derivatives of DACO (N,N'-bis(2-mercaptoethyl)-1,5-diazacyclooctane, bme-DACO).⁴⁷⁻⁴⁹ Unusually, this square planar N₂S₂ coordination environment places the 1,5-DACO ring in a boat-boat conformation. Alkylation of the S-donor atoms results in the formation of the boat-chair conformation.⁴⁹ Halfen and co-workers have reported Fe- and Mn- complexes of the *N*-pyridyl-substituted derivative of DACO (N,N'-bis(2-pyridyl)-1,5-diazacyclooctane, DACO-py₂).⁵⁰⁻⁵² A mono-*N*-pyridyl, tridentate analogue was also developed by the same group with the capability to form mono and bi nuclear Cu(II) complexes.⁵³ Shionoya and co-workers have developed a series of *N*-functionalised phenol and imidazole functionalised derivatives of DACO.⁵⁴⁻⁵⁶ Itoh and co-workers have reported on the synthesis and reactivity of a series of Cu(I) complexes based on the DACO derivative 1-(phenethyl)-5-(2-pyridin-2-ylethyl)-1,5-diazacyclooctane.³²⁻³⁵ Overall, while many *N*-alkylated derivatives of DACO exist, few tetrahedral complexes employing DACO have been reported, and all lacking the high degree of steric bulk that we require.

We envisioned that introducing a third donor atom to DACO at the 3-position of the diazacyclooctane ring, rather than through *N*-alkylation, would present several benefits. Firstly, introduction of ligating functionalities at the 3-position would ensure a facially capping ligand (and a tetrahedral complex), whereas *N*-alkylated derivatives of DACO are mainly meridional binders. Secondly, organic functionalities can be readily introduced through *N*-alkylation in **1**, allowing us to easily modulate the electronic and steric properties of the ligand. Herein, we describe our efforts towards synthesizing the novel ligand **1** and derivatives thereof.

Results and Discussion

We identified triol 1,1,1-*tris*(hydroxymethyl)ethane (**2**, Scheme 1), as a useful starting point for the preparation of **1**. In order to prepare the asymmetric molecule **1**, we attempted to address a single arm of the tri-substituted neo-pentyl framework, leaving the other two arms to be the basis of the 8-membered mesocycle. To this end we attempted to selectively address one of the hydroxyl groups of **2** while protecting the other two hydroxyl groups. We prepared the bis-protected triol (1,3-dioxane, **3**) according to a previously published procedure.⁵⁷ The remaining hydroxyl group in **3** was then activated through reaction with one equivalent of tosyl chloride (tosyl (Ts) = 4-toluenesulphonyl) in pyridine to give the corresponding tosylate **4**.⁵⁸ The azide, **5**, was then prepared

Scheme 1 – Synthesis of 1,3-dioxane protected azide 5.

through nucleophilic substitution of the tosylate with sodium azide according to the procedure reported by Liu.⁵⁹ We subsequently pursued two avenues towards the selective derivatisation of azide 5 (Scheme 2), but neither provided us with an efficient or facile route towards 1.

In the first of these routes, we utilised the azide moiety as a masked amine. 5 was refluxed with aqueous HCl in THF for 30 minutes to cleave the dioxane protecting group.⁵⁹ The resulting diol (6) was then immediately reacted with 2.2 equivalents of tosyl chloride in the presence of aqueous sodium hydroxide in THF to give the bis-tosylate 7 in a 64 % yield. Cyclic polyamines, including DACO, are readily synthesised via the Richman-Atkins method of cyclisation.^{60, 61} In general, this involves the reaction of a di-tosylated diol (such as 7) with a deprotonated *bis*-tosylamide to facilitate cyclisation. In order to perform the cyclisation reaction of ditosylates like 6, we prepared the activated diamine *N,N'*-(propane-1,3-diyl)bis-tosylamide (12) by reacting 1,3-diaminopropane (11) with tosyl chloride according to a reported procedure (Scheme 3a).⁵¹ 12 was then deprotonated using NaH and subsequently stirred with 7, without work-up, at 145 °C in anhydrous DMF. Analysis of the post-reaction

mixture indicated none of the desired cycle 8 had formed. We attributed this to the organic azide being unstable under the high-temperature reaction conditions. The azide group may act as a leaving group under such forcing conditions.

As a result of this negative outcome, we revisited the protected azide, 5. Rather than cleaving the dioxane group we proceeded to reduce the azide moiety. This was achieved by reacting 5 with 10% wt of 5% Pd/C in the presence of ammonium formate in methanol to give the primary amine 9 in a 50% yield. We then attempted to methylate the primary amine in 9 using 2 equivalents of methyl iodide. However, ESI-MS revealed the formation of a statistical distribution of all of the possible methylation products (secondary, tertiary and quaternary), rather than a majority of the tertiary amine. These products were not separable using column chromatography. We then attempted the methylation of 9 under Eschweiler-Clarke conditions.⁶² 9 was refluxed for 6 hours in an excess of formic acid and formaldehyde. After work up, the ¹H NMR showed the disappearance of the two characteristic dioxane methyl peaks at 1.41 and 1.45 ppm, indicating that the dioxane protecting group had been cleaved under these reaction conditions, giving no indication of the formation of the desired product 10.

Given these unexpected setbacks, we decided that rather than selectively address individual arms of the triol precursor 1, we would perform cyclisation reactions on activated derivatives of triol 2, without protecting any of the hydroxide functionalities. We anticipated difficulties with this approach because of the potential formation of oligomers and polymers in the Richman-Atkins cyclisation reaction,⁶¹ however it was a necessary approach. 2 was activated through its reaction with tosyl chloride (4 equiv.) in pyridine (Scheme 3b) yielding the tris-tosylate 13 in 83% yield. While 13 can be isolated simply by precipitation after addition of ice-water followed by filtration⁶³ we found that the work-up reported by Lindhorst and co-workers, in which the product was extracted with ethyl acetate

Scheme 2 – Unsuccessful synthetic routes to target compound 1.

Scheme 3 – a) Synthesis of the activated diamine **12**; b) Synthesis of activated triols **13** and **14**.

and dried over magnesium sulphate, gave an anhydrous product.⁶⁴ This anhydrous product was better suited to the cyclisation step discussed below (Scheme 4), because it must be performed under strictly anhydrous conditions.

Importantly, we found that the *tris*-tosylate **13** was easily converted to the *tris*-bromide **14** in 76% yield by reaction between **13** and NaBr in diethylene glycol heated to 145 °C. Using this method **14** can be used without further purification, unlike the previously reported reaction of *tris*-benzenesulphonate with NaBr,⁶⁵ which we found required the product be purified by distillation. While there are several reports detailing the synthesis of **14** directly from the reaction between **2** and PBr₃,⁶⁶ we have found them difficult to

reproduce, and therefore prefer this two-step procedure for the preparation of **14**. These two activated tripodal neopentane precursors provide two useful synthons towards the preparation of **1**.

We reacted the *bis*-tosylamide, **12**, with the activated triols **13** and **14** under conditions outlined by Richman and Atkins (Scheme 4).⁶⁰ The disodium salt of **12** (**15**) was generated *in situ* by reacting **12** (0.2 M, volume??) with two equivalents of sodium hydride in anhydrous DMF. After hydrogen evolution had ceased (gas bubbles were no longer observed), the reaction mixture was heated at 100 °C under argon for one hour. A 0.1 M solution (volume??) of an activated triol (**13** or **14**) in anhydrous DMF was then added dropwise. The resulting reaction mixture was heated at 145 °C under argon flow for at least 24 h. This yielded the desired cyclised products **16a** and **16b**. **16a** and **16b** were characterised using ¹H and ¹³C NMR spectroscopies and mass spectrometry. The ¹H NMR spectra displayed resonances typical of a mesocyclic aliphatic hydrocarbon, confirming cyclisation occurred. Additionally, single crystals of **16b** suitable for x-ray diffraction were grown by slow evaporation of a solution of **16b** in chloroform (Figure 2b, Table S1). Heating at temperatures lower than 145 °C resulted in no cyclised product formation. Such forcing reaction conditions were required because of the neopentyl backbone, in which the bulky vicinal substituents sterically shield the carbon atom that the activated amine groups are attacking.⁶⁷ Furthermore, the yield of the desired cyclised product was significantly higher if *tris*-bromide **14** was used (**16b** obtained in 48% yield). The yield of **16a** from cyclisation using activated triol **13** was 10%. Additionally, while Richman and Atkins report that reaction solution concentrations for their cyclisations must be finely tuned to prevent

Scheme 4 – Cyclisation reactions and derivatisation of cyclised products.

oligomer/polymer formation,⁶⁰ we have found that the poor kinetics of this cyclisation reaction acts as an effective dilution.

After preparing the 1,5-diazacyclooctane mesocycles **16a** and **16b**, we then sought to introduce an amine functionality onto the remaining arm. We have adopted two approaches to aminating **16a** and **16b** (Scheme 4). In the first approach, we reacted the 1,5-diazacyclooctane mesocycles **16a** and **16b** with sodium azide to yield the azide **8**. Formation of **8** was confirmed using NMR spectroscopy and Mass spectrometry. In the fourier transform infra-red (FT-IR) spectrum of **8**, a strong band at 2103 cm^{-1} , which we assign as an N_3 vibrational mode, was observed. The azide group in **8** was then reduced, using 5% Pd/C and ammonium formate in methanol, to give the amine **17** as confirmed by NMR and ESI-MS. The disappearance of the FT-IR band at 2103 cm^{-1} and the appearance of the characteristic amine symmetric and asymmetric stretching frequencies at 3309 and 3151 cm^{-1} was noted, confirming reduction of the azide moiety in **8** to an amine in **17**. The *N*-tosyl protecting groups in **17** were then cleaved by heating **17** in 33% HBr/acetic acid (Scheme 4). No aromatic peaks were observed in the ^1H NMR of the triamine product **19**, which was purified as the *tris*-hydrogen bromide salt, indicating complete *N*-tosyl deprotection and isolation of the desired triamine product.

We sought an alternative synthetic route to **19**, because the azide reduction described above gave inconsistent yields. To this end, we reacted **16b** with sodium tosylamide at 145°C in anhydrous DMF to give the tosylamide **18** (Scheme 4). The formation of **18** was confirmed by ^1H NMR and ^{13}C NMR spectroscopy, which showed the aromatic and aliphatic resonances expected after the inclusion of the third tosylamide functionality. ESI-MS also confirmed the formation of **18** ($m/z = 620.1931$ for $\text{C}_{29}\text{H}_{37}\text{N}_3\text{O}_6\text{S}_3$; expected $m/z = 620.1923$). All *N*-tosyl groups were then cleaved by treatment with 33% HBr/acetic acid to give the triammonium salt **19**•3HBr in a 10% yield. The yield of the deprotection step when conc. H_2SO_4 was used instead of HBr/acetic acid was significantly

Figure 2 – a) ORTEP plot of the X-ray crystal structure of **19**•3HBr at 50% probability. Bromine and hydrogen atoms have been removed for clarity. b) ORTEP plot of the X-ray crystal structure of **16b** at 50% probability. *N*-Tosyl groups and hydrogen atoms have been omitted for clarity.

higher at 50%. This corresponds to an overall yield of 20%, much improved on the overall yield of 4% when HBr/acetic acid was used for deprotection.

Single crystals of **19**•3HBr suitable for X-ray diffraction were obtained by diffusing ethanol into a solution of **19**•3HBr in

Figure 3 – a) ^1H NOE Spectrum of the **19** irradiated at 1.72 ppm; b) ^1H Spectrum of the **19**; c) ^1H Spectrum of **1b**; d) ROESY Spectrum of **1b** irradiated at 1.63 ppm.

water. This was an important achievement as we wanted to understand the structure and structural flexibility of our mesocyclic ligands. Crystal data and refinement parameters are shown in Table S1. Analysis of the crystal structure of **19**•3HBr (Figure 2a) showed that the DACO ring in **19**•3HBr displayed a boat-chair conformation. All bond lengths were in agreement with those previously reported for diprotonated DACO rings.⁶⁸ Unusually, when compared to the other crystal structures we obtained (*vide infra*) and those previously reported in the literature for a diprotonated DACO moiety,⁶⁸ the nitrogen lone pairs in **19**•3HBr are located on opposite faces of the ring. This arrangement would disfavour complex formation. We reason that this occurs as it allows for the maximum separation of the two positively charged nitrogen atoms.

In order to promote the formation of *pseudo*-tetrahedral complexes, we required that **1** displayed the ability to form an alternative boat-chair conformation analogous to that shown by **16b** (Figure 2b), where the nitrogen atoms are primed to bind the metal in a *pseudo*-tetrahedral fashion. We therefore probed the solution behaviour of **19** further. ^1H NOE NMR studies on **19** (Figure 3, prepared by deprotonation of **19**•3HBr with KOH) were performed. The NOE spectra, with irradiation of the multiplet at 1.70 ppm (corresponding to the central CH_2 of the propylene linker ($\text{CH}_2\text{-CH}_2\text{-CH}_2$)), showed that this $-\text{CH}_2-$ displayed through space coupling to all other protons in the molecule. Of note is the through-space coupling to both the CH_3 group and CH_2NH_2 of the primary amine, indicating that the central CH_2 of the propylene linker can 'see' both faces of the mesocycle. This demonstrated that **19** retains a high degree of flexibility in solution and indicated that **1** would be sufficiently flexible to bind metals in the desired manner.

	19•3HBr	16b	[1b•H]PF ₆	[1b•2H]OTf ₂
Mean Cyclic C-C / Å	1.531	1.532	1.531	1.535
Mean C-N1 / Å	1.506	1.480	1.484	1.475
Mean C-N2 / Å	1.495	1.477	1.514	1.519
Mean C-N3 / Å	-	-	1.477	1.534
N4-N8 Distance / Å	3.6325(2)	2.8572(1)	2.6906(1)	2.8003(1)
C3-N1-C5 Fold Angle / °	N/A	115.369(2)	111.408(2)	113.050(3)
C7-N2-C9 Fold Angle / °	N/A	116.590(2)	111.466(2)	113.569(3)

Table 2 – Selected bond lengths and angles for the reported crystal structures.

We attempted to methylate **19•3HBr** to give the tetramethylated triamine product **1a** under Eschweiler-Clarke conditions.⁶² **19•3HBr** was refluxed in formic acid in the presence of an excess of formaldehyde. From this reaction we identified a mixture of products (at least 4) by ¹H NMR, none of which could be attributed to the desired peralkylated product, while suggesting that all of the starting material **19•3HBr** had been consumed. We postulated that the intermediate imine, that formed upon initial reaction between the amine groups in **19•3HBr** and formaldehyde, was not fully reduced prior to a secondary reaction between the imine and one of the other adjacent amine groups of the triamine **19**. This resulted in the formation of a cyclic amine rather than the desired permethylated product **1a**. To overcome this we attempted several reductive aminations utilising more powerful reducing agents. **19•3HBr** was refluxed with an excess of formaldehyde and acetic acid in the presence of stronger reductants (NaBH₄, KBH₄, or zinc). Unfortunately similar ¹H NMR spectra, indicative of a cyclic amine formation, were obtained in all cases. Unfortunately, permethylation of **19•3HBr** was also not possible using methyl tosylate or iodomethane as we consistently obtained over-alkylated products, in the presence of the desired product **1a** (according to ESI-MS and ¹H NMR), that were not separable by column chromatography.

Fortunately, however, we found that we were able to alkylate **19•3HBr** using benzyl bromide. The reaction of **19•3HBr** with exactly four equivalents of benzyl bromide in the presence of excess base (Na₂CO₃) gave the tetra-alkylated product **1b** (Scheme 5). Analysis of the ¹H NMR of **1b** showed the appearance of two new peaks at 3.64 ppm compared to **19**, corresponding to the benzyl CH₂ groups on the aliphatic amine. Furthermore, a multiplet at 7.4 ppm was observed, which corresponds to the phenyl groups of the benzylic functionalities. A peak in the ESI-MS was observed at m/z =

Scheme 4 - Preparation of **1b** and [Cu'(NCCH₃)(**1b**)](OTf).

518.3534 (expected m/z = 518.3535 for C₃₆H₄₄N₃), confirming the identity of **1b**. The reaction between **19•3HBr** and benzylbromide did not yield over-alkylated quaternised amine

products, whereas the reaction between **19•3HBr** and iodomethane did. We ascribe this difference in reactivity to the steric bulk of the benzyl functionality retarding the rate of the quaternisation reaction compared to methyl functionalities. This provides a strong indication that the benzyl functionalised ligand **1b** will have a sterically protected metal binding pocket.

Figure 4 – a) X-ray crystal structure of [1b•H]PF₆. Ellipsoids are shown at the 50% probability level. Only refined hydrogen atoms are shown. Counter ions have been

omitted for clarity. b) X-ray crystal structure of [1b•2H]OTf₂. Ellipsoids are shown at the 50% probability level. Only refined hydrogen atoms are shown. Counter ions have been omitted for clarity.

Similar to **19•3HBr** we assessed the solution flexibility of **1b** (Figure 3) with ¹H ROESY NMR. Irradiation of the central CH₂ of the propylene linker CH₂ of the mesocycle at 1.63 ppm showed through-space coupling to all of the other protons within the DACO ring, as well as the benzyl CH₂ groups and, importantly, the *exo*-cyclic CH₃ and CH₂ groups. This demonstrated that although we have alkylated all amine groups in **1b**, the molecule retains structural flexibility, and should bind metals in the desired *pseudo*-tetrahedral geometry.

Crystal Structures of both the monoprotonated and diprotonated congeners of **1b** were obtained (Figure 4, Table S1). Serendipitously, single crystals of [1b•H]PF₆ (Figure 4a) precipitated after layering a reaction mixture of **1b**, CuCl₂ and KPF₆ in wet acetonitrile with diethyl ether. Similarly, single crystals of [1b•2H]OTf₂ (Figure 4b) were obtained after layering of a wet acetonitrile solution of **1b** and Zn(OTf)₂ with diethyl ether. The crystal structures shown in Figure 4 unambiguously demonstrate that the cyclic amine is protonated before the acyclic amine, as would be expected based on their reported higher basicity.⁶⁹ Selected bond lengths and angles for these structures, as well as those in Figure 2, are shown in Table 1.

Figure 5 – a) ^1H NMR spectrum of **1b**, 400 MHz, CD_3CN ; b) ^1H NMR spectrum of $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$, 600 MHz, CD_3CN ; c) ^1H NMR spectrum of $[\mathbf{1b}\cdot 2\text{H}]\text{OTf}_2$, 600 MHz, CD_3CN .

The structure of $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$ consists of a discrete $\mathbf{1b}\cdot\text{H}^+$ cation and a PF_6 anion. The DACO ring adopts a boat/chair conformation, and has a C-N-C fold angle of 111° . The average cyclic C-C bond length remains similar to those found for **19**·3HBr and **16b**, (~ 1.5 Å). Protonation of N2 results in a longer mean C-N2 bond length (1.514 Å) when compared to the mean C-N1 bond length (1.484 Å), which is in agreement with the C-N bond lengths discussed above for **19**·3HBr and **16b**. The N1-N2 distance for $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$ is 2.69 Å, comparable to that measured for **16b** and significantly shorter than that measured for **19**·3HBr suggesting that monoprotection of the DACO ring allows for the nitrogen atoms to be in closer proximity. The structure of $[\mathbf{1b}\cdot 2\text{H}]\text{OTf}_2$ consists of a discrete $\mathbf{1b}\cdot 2\text{H}^+$ cation and two triflate anions. After protonation of N2 and N3 (rather than N1), the structure retains the same boat/chair conformation as in $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$. In the structures of both $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$ and $[\mathbf{1b}\cdot 2\text{H}]\text{OTf}_2$ the C-N-C fold angle is comparable to both previously reported protonated DACO moieties^{61, 68, 70, 71} as well as metal complexes containing the DACO moiety.³⁴ Furthermore, the bond lengths and angles were found to be in the region of those previously reported. This suggests that alkylation of the DACO ring at the C2, N1 and N2 positions should not hinder complex formation.

The ^1H NMR of the crystals of $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$ and $[\mathbf{1b}\cdot 2\text{H}]\text{OTf}_2$ are shown in Figure 5 and were assigned in conjunction with the corresponding HSQC and HMBC spectra (See supporting information). In the ^1H NMR of the freebase **1b** (Figure 5a) both the cyclic and acyclic benzylic protons appear as two singlets at 3.59 and 3.51 ppm as the signals for the diastereotopic protons are isochronous ($\text{H}_6 = \text{H}_{6'}$ and $\text{H}_7 = \text{H}_{7'}$). After protonation at N2 (Figure 5b), the apparent singlet at 3.59 ppm arising from $\text{H}_{6/6'}$ resolves into the pair of doublets, at 3.84 and 3.65 ppm. The coupling constant (~ 13 Hz) suggests that these doublets are a result of geminal coupling and no ^3J N-H coupling is observed. The difference of these chemical shifts (~ 0.2 ppm) indicates that these protons are fixed in a relative axial/ equatorial arrangement, with the difference in chemical shift arising from local magnetic anisotropy. This

suggests that protonation reduces the conformational flexibility in $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$ compared to **1b**. An equivalent resolution of signals is observed after protonation at N3 (Figure 5c), $\text{H}_{7/7'}$ are resolved into a pair of signals at 4.60 and 4.32 ppm. The doublet at 4.60 has a coupling constant (~ 14 Hz) indicative of geminal coupling only whereas the multiplet at 4.32 is split further, possibly by ^3J HNCH coupling. This can be interpreted as resulting from decreased rotational flexibility that promotes a preferred conformation in which $\text{H}_{7/7'}$ have different dihedral angles relative to the N-H, causing a difference in coupling constants. The change in chemical shift of the cyclic CH_2 groups upon protonation at N2 (Figure 5b) further supports a reduction in conformational flexibility. The overlapping signals for $\text{H}_{3/3'}$ (2.46–2.39 ppm) and $\text{H}_{4/4'}$ (1.54 ppm) in **1b** are resolved into pairs of multiplets for $\text{H}_{3a/3b}$ (3.10 and 2.74 ppm) and $\text{H}_{4a/4'}$ (2.07 and 1.74 ppm) in $[\mathbf{1b}\cdot\text{H}]\text{PF}_6$. As above, the difference in chemical shift (~ 0.4 ppm) for these pairs of diastereotopic protons suggests that they are fixed in a relative axial/ equatorial arrangement. Protonation at N3 (Figure 5c) maintains the splitting patterns observed for protons associated with the ring, although their chemical shifts differ slightly. Notably, a ^1H ROSEY experiment (See supporting information) where the *exo*-cyclic methyl proton H_1 , at 0.23 ppm, was irradiated shows no through space coupling to $\text{H}_{4/4'}$ indicating a significant reduction in the conformational flexibility of the DACO ring upon protonation, when compared to **1b** (*Vide Supra*).

The alkylated triamine **1b** was reacted with $[\text{Cu}^{\text{I}}(\text{NCCH}_3)_4](\text{OTf})$ in anhydrous acetonitrile. Upon addition of a solution of **1b** to the copper salt an immediate colour change from colourless to yellow was observed. ESI-MS analysis of an aliquot of this reaction mixture indicated a peak at $m/z = 621.2963$ with an isotopic pattern typical of copper, which we assign as Figure 6 – ESI-MS spectrum of $[\text{Cu}^{\text{I}}(\text{NCCH}_3)(\mathbf{1b})]^+$. Inset shows the predicted isotopic pattern.

$[\text{Cu}^{\text{I}}(\text{NCCH}_3)(\mathbf{1b})]^+$ (expected $m/z = 621.3018$, Figure 6). Encouragingly, no 2:1 (ligand:metal) species were observed in the ESI-MS spectra. After work up, $[\text{Cu}^{\text{I}}(\text{NCCH}_3)(\mathbf{1b})](\text{OTf})$ was

obtained as a pale yellow powder. These observations suggest that **1b** binds the metal centre as a tripod yielding the desired *pseudo*-tetrahedral complex. Present work in our lab is focussed on preparing further derivatives of ligand **1**, and preparing metal-oxo species derived from low-valent copper and nickel complexes of **1b**.

Conclusion

We have outlined several synthetic routes towards our target ligand **1**, a novel, mesocyclic, tripodal, triamine ligand. Our modular approach to the synthesis of **1** has provided us with a library of synthons that will allow us to tune the reactivity of metal complexes of **1**. Importantly, we have developed and optimised the synthesis of the mesocyclic fragment in **1**, utilizing a Richman-Atkins cyclisation to form **16**. We have outlined multiple routes to the further derivatisation of **16** to ultimately give the triamine skeleton **19**, which we have shown can be alkylated to give our target ligand **1b**. We have probed the conformational flexibility of both **19** and **1b** using a combination of NMR and x-ray crystallography studies. While the x-ray crystal structure obtained of **19** displays an unusual configuration, which we believe would discourage complex formation, we have shown that it maintains a high degree of flexibility in solution. Additionally, we have demonstrated that while **1b** maintains a high degree of structural flexibility in solution, protonation at both the N1 and N3 positions results in a significant loss of conformational flexibility. We have also been able to prepare $[\text{Cu}^{\text{I}}(\text{NCCH}_3)(\text{1b})]^+$ demonstrating the potential of **1b** to form *pseudo*-tetrahedral metal complexes. We expect our careful design of this ligand to lead to highly stable tridentate *pseudo*-tetrahedral complexes. Furthermore, we believe that the unique coordination chemistry offered by the mesocyclic DACO derivative will promote 1:1 complex formation, overcoming problems commonly encountered with low co-ordinate ligands.

Experimental Details

All reagents and solvents were purchased from commercial sources and used as received, unless otherwise stated. All reactions with air-sensitive materials were conducted under an inert atmosphere using either standard Schlenk techniques or a nitrogen atmosphere glove box. Anhydrous DMF and acetonitrile were purchased and used without further purification. Anhydrous THF and diethyl ether were dispensed through an Innovative Technology PureSolv EN solvent purification system and deoxygenated by purging with argon. Ammonium formate was recrystallised from ethanol before use. CDCl_3 was dried and de-acidified by stirring and subsequently storing over 4 Å molecular sieves and basic alumina. ^1H and ^{13}C NMR were recorded on either a Bruker DPX 400 MHz or Bruker Avance II 600 MHz spectrometer. ESI mass spectra were acquired using a Micromass time of flight spectrometer (tof), interfaced to a Waters 2690 HPLC. Fourier-Transform Infrared spectra were recorded using a Perkin-

Elmer Spectrum 1 FT-IR spectrometer. Thin-layer chromatography (TLC) was performed with Analytical Chromatography alumina sheets coated with silica gel (0.25mm). Spots were visualised under UV light. Flash column chromatography was conducted with Fluka Silica Gel 60 Å (230-400mesh). Compounds **3**,⁵⁷ **4**,⁵⁸ **5**,⁵⁹ **6**,⁵⁹ **13**⁶⁴ and **12**⁵¹ were synthesised according to literature procedures.

Synthesis of 2-(azidomethyl)-2-methylpropane-1,3-diyl bis-tosylate (**7**)

6 (3.53 g, 24 mmol) was dissolved in THF (50 mL) and added to a solution of NaOH (9 g) in water (9 mL). Tosyl chloride (11.6 g, 61 mmol) in THF (10 mL) was added dropwise with vigorous stirring. The reaction mixture was stirred for a further 16 h at room temperature. The mixture was diluted with water (100 mL) and then extracted with CHCl_3 (3 x 50 mL). The organic layer was washed with brine (3 x 100 mL) then dried over MgSO_4 . The solvent was removed *in vacuo* to give **7** (7.2 g, 64%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ = 0.93 (s, 3H), 2.47 (s, 6H), 3.26 (s, 2H), 3.78 (s, 4H), 7.38 (d, J =8.1, 4H), 7.76 (d, J =8.1, 4H).

^{13}C NMR (101 MHz, CDCl_3) δ = 17.0, 21.8, 39.7, 53.6, 70.7, 128.0, 130.1, 132.1, 145.4.

Synthesis of 3-(azidomethyl)-3-methyl-1,5-ditosyl-1,5-diazocane (**8**)

16a (800 mg, 1.3 mmol) was dissolved in diethylene glycol (25 mL). Sodium azide (252 mg, 3.9 mmol) was added and the reaction mixture was stirred at 135 °C for 5 days. The reaction mixture was cooled and diluted with water (25 mL). The resulting emulsion was extracted with dichloromethane (3 x 25 mL). The organic layer was collected and dried over MgSO_4 and the solvent removed *in vacuo*. The crude product was purified by column chromatography (EtOAc: Hexane: Triethylamine, 45:45:10) to give azide **8** (280 mg, 44%) as a white powder.

^1H NMR (400 MHz, CDCl_3) δ = 1.15 (s, 3H), 1.82 - 2.02 (m, 2H), 2.46 (s, 6H), 2.96 - 3.29 (m, 8H), 3.54 (s, 2H), 7.36 (d, J =8.1, 4H), 7.68 (d, J =8.1, 4H).

^{13}C NMR (101 MHz, CDCl_3) δ = 17.0, 21.8, 25.7, 39.7, 53.6, 68.0, 70.7, 128.0, 130.1, 132.1, 132.1, 145.4

$\nu_{\text{max}}/\text{cm}^{-1}$: 1156, 1335, 2103.

HRMS (m/z -ESI): Found: 492.1730 ($\text{M}^+ + \text{H}$. $\text{C}_{22}\text{H}_{30}\text{N}_5\text{O}_4\text{S}_2$ Requires: 492.1695).

Synthesis of (2,2,5-trimethyl-1,3-dioxan-5-yl)methanamine (**9**)

Azide **5** (3.52 g, 19 mmol) and ammonium formate (4.87 g, 76 mmol) were added to degassed methanol (100 mL) and stirred until the ammonium formate completely dissolved. 5% Pd/C (365 mg, 10% wt) was then added and the reaction mixture stirred for 3 hours at room temperature. The reaction mixture was then filtered through a pad of Celite and the methanol removed *in vacuo*. The residue was taken up into distilled water (10 mL) and washed with diethyl ether (3 x 20 mL). The

aqueous layer was then basified with KOH (10 g) and extracted with acetonitrile (5 x 10 mL). The organic layer was collected and dried over MgSO₄. The solvent was removed *in vacuo* to give **9** (1.50 g, 50%) as a colourless oil.

¹H NMR (600 MHz, CDCl₃) δ = 0.80 (s, 3H), 0.99 (s, 2H), 1.38 (s, 3H), 1.42 (s, 3H), 2.78 (s, 2H), 3.57 (d, *J* = 11.7, 2H), 3.62 (d, *J* = 11.7, 2H).

¹³C NMR (151 MHz, CDCl₃) δ = 17.9, 21.0, 26.5, 34.2, 46.3, 67.2, 97.8.

HRMS (*m/z* -ESI): Found: 160.1342 (*M*⁺ + H. C₈H₁₇NO₂ Requires: 160.1338).

Synthesis of 1,3-dibromo-2-(bromomethyl)-2-methylpropane (**14**)

13 (46 g, 79 mmol) and NaBr (83 g, 790 mmol) were heated in diethylene glycol (250 mL) at 145 °C for 18 hours. After cooling, the reaction mixture was diluted with deionised water (250 mL), mixed vigorously, then transferred to a separating funnel. The more dense oil (**14**) was collected. The aqueous layer was washed with diethyl ether (3 x 50 mL). The organic extracts were combined with the oil and dried over MgSO₄. The solvent was removed *in vacuo* to give **14** (18.5 g, 76%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃) δ = 1.29 (s, 3H), 3.50 (s, 6H).

Synthesis of (3-methyl-1,5-ditosyl-1,5-diazocan-3-yl)methyl tosylate (**16a**)

In a glove box, *N,N'*-(propane-1,3-diyl)bis-tosylate **12** (3.80 g, 9.93 mmol) was dissolved in anhydrous DMF (100 mL). NaH, as a 60% dispersion in mineral oil (1.0 g, 20 mmol) was added and the solution stirred until the evolution of hydrogen gas ceased. The reaction vessel was transferred to a Schlenk line and heated at 145 °C for 1 hour. A solution of **13** (5.786 g, 9.9 mmol) in anhydrous DMF (60 mL) was then added dropwise by cannula. The reaction mixture was then heated at 145 °C for a further 24 hours. The DMF was removed by distillation and the residue was taken up into CHCl₃. The organic layer was washed with water (3 x 50 mL) and brine (3 x 50 mL) then dried over MgSO₄. The solvent was removed *in vacuo*. The crude product was purified by column chromatography (EtOAc: Hexane: Triethylamine, 35:60:5) to give **16a** (591 mg, 10%) as an off-white crystalline solid.

¹H NMR (600 MHz, CDCl₃) δ = 1.14 (s, 3H), 1.92 (m, 2H), 2.44 (s, 6H), 2.45 (s, 3H), 3.11- 3.21 (m, 8H), 4.05 (s, 2H), 7.32 (d, *J* = 8.0, 4H), 7.36 (d, *J* = 8.1, 2H), 7.62 (d, *J* = 8.2, 4H), 7.84 (d, *J* = 8.3, 2H).

¹³C NMR (151 MHz, CDCl₃) δ = 21.6, 21.7, 21.8, 28.8, 39.8, 49.7, 53.2, 76.4, 127.5, 128.2, 130.0, 130.0, 132.7, 134.9, 143.9, 145.0.

*v*_{max}/cm⁻¹: 1156, 1174, 1307, 1336

HRMS (*m/z* -ESI): Found: 643.1580 (*M*⁺ + Na. C₂₉H₃₆N₂O₇S₃ Na Requires: 643.1582).

Synthesis of 3-(bromomethyl)-3-methyl-1,5-ditosyl-1,5-diazocane (**16b**)

In a glove box, *N,N'*-(propane-1,3-diyl)bis-tosylate **12** (4.7 g, 12.3 mmol) was dissolved in anhydrous DMF (200 mL). NaH, as a 60% dispersion in mineral oil (0.985 g, 24.6 mmol) was added and the solution stirred until the evolution of hydrogen gas ceased. The reaction vessel was transferred to a Schlenk line and heated at 145 °C for 1 hour. A solution of 1,3-dibromo-2-(bromomethyl)-2-methylpropane **14** (3.8 g, 12.3 mmol) in anhydrous DMF (50 mL) was then added dropwise by cannula. The reaction mixture was heated at 145 °C for a further 24 hours. The DMF was removed by distillation and the residue was taken up into Et₂O (150 mL). The ether solution was washed with water (3 x 50 mL) and brine (3 x 50 mL) and dried over MgSO₄. The solvent was removed *in vacuo*. The crude product was purified by recrystallisation in the minimum amount of boiling methanol. The product was collected by vacuum filtration and washed with cold methanol (3 x 10 mL) to give **16b** as an off white solid (3.1 g, 48%).

¹H NMR (400 MHz, CDCl₃) δ = 1.28 (s, 3H), 1.96 (m, 2H), 2.46 (s, 6H), 3.09 - 3.28 (m, 8H), 3.64 (s, 2H), 7.35 (d, *J* = 7.9, 4H), 7.69 (d, *J* = 8.0, 4H),

¹³C NMR (101 MHz, CDCl₃) δ = 21.1, 23.1, 28.1, 39.1, 43.4, 49.1, 53.8, 127.0, 129.4, 134.3, 143.4.

*v*_{max}/cm⁻¹: 547, 572, 653, 706, 755, 800, 845, 1018, 1089, 1156, 1260, 1306, 1335, 1383, 1457, 1494, 1598, 2860, 2870, 2924, 2963.

HRMS (*m/z* -ESI): Found: 551.0652 (*M*⁺ + Na. C₂₂H₂₉N₂O₄S₂Br Requires: 551.0650).

Synthesis of (3-methyl-1,5-ditosyl-1,5-diazocan-3-yl)methanamine (**17**)

8 (0.280 g, 0.57 mmol) and ammonium formate (0.144 g, 2.28 mmol) were added to degassed methanol (100 mL) and stirred until the ammonium formate completely dissolved. 5% Pd/C (0.056 g, 20% wt) was then added and the reaction mixture stirred for 18 h at room temperature. The reaction mixture was filtered through a pad of celite and the methanol removed *in vacuo*. The residue was taken up into distilled water (10 mL) and washed with diethyl ether (3 x 20 mL). The aqueous layer was basified with KOH (10 g) and extracted with acetonitrile (5 x 10 mL). The organic layer was collected and dried over MgSO₄. The solvent was removed *in vacuo* to give **17** (0.140 g, 53%).

¹H NMR (600 MHz, CDCl₃) δ = 1.06 (s, 3H), 1.87 (m, 2H), 2.43 (s, 6H), 2.70 (s, 2H), 2.93 (d, *J* = 15.1, 2H), 3.08-3.25 (m, 4H), 7.31 (d, *J* = 8.2, 4H), 7.66 (d, *J* = 8.2, 4H).

¹³C NMR (151 MHz, CDCl₃) δ = 21.5, 28.1, 40.4, 47.8, 49.8, 53.5, 127.4, 129.8, 135.1, 143.6,

*v*_{max}/cm⁻¹: 1151, 1327, 3151, 3310,

HRMS (*m/z* -ESI): Found: 466.1833 (*M*⁺ + H. C₂₂H₃₂N₃O₄S₂ Requires: 466.1790).

Synthesis of *N*-((3-methyl-1,5-ditosyl-1,5-diazocan-3-yl)methyl)tosylamide (**18**)

16b (9.0 g, 17 mmol) and sodium tosylamide (9.85 g, 51 mmol) were heated at 145 °C in anhydrous DMF (200 mL) for 4 days. Once the reaction mixture had cooled, the solvent was

removed *in vacuo*. The crude reaction mixture was recrystallised in the minimum amount of boiling methanol. The resulting white precipitate was collected by filtration and washed with cold methanol to give **18** (8.0 g, 76%).

^1H NMR (400 MHz, CDCl_3) δ = 1.09 (s, 3H), 1.85 (m, 2H), 2.41 (s, 3H), 2.43 (s, 6H), 2.7 - 3.5 (m, 8H), 3.48 (d, J =5.0, 2H), 7.27 - 7.37 (m, 4H), 7.63 (d, J =8.0, 2H), 7.77 (d, J =8.0, 2H).

^{13}C NMR (151 MHz, CDCl_3) δ = 21.7, 22.1, 28.5, 39.8, 48.1, 50.7, 127.0, 127.6, 129.9, 130.0, 134.4, 137.5, 143.2, 144.1.

HRMS (m/z -ESI): Found: 620.1931 (M^+ + H. $\text{C}_{29}\text{H}_{37}\text{N}_3\text{O}_6\text{S}_3$ Requires: 620.1931).

General Procedure for the Deprotection of *N*-Tosyl Protected Amines to give **19•3HBr** Using 33% HBr in Acetic Acid and Phenol

A solution of 33% HBr in acetic acid (1 mL) was added to the protected amine (0.25 mmol,) and phenol (1 g). The reaction mixture was heated at 90 °C for 16 hours. The temperature was lowered to 60 °C and 33% HBr in acetic acid (1 mL) was added and the reaction mixture heated for a further 5 hours. The reaction mixture was cooled in the freezer at -40°C overnight. The resulting white precipitate was collected by filtration and washed with diethyl ether (5 mL) To give **19•3HBr** as an off white solid (~10%). Crystals of **19•3HBr** suitable for X-ray diffraction were grown by slow diffusion of ethanol into a solution of **19•3HBr** in water.

19•3HBr: ^1H NMR (400 MHz, D_2O) δ = 1.24 (s, 3H), 2.23 (m, 2H), 3.14 (s, 2H), 3.46 - 3.24 (m, 8H).

^{13}C NMR (151 MHz, D_2O) δ = 18.8, 19.2, 42.6, 43.8, 45.5, 47.5.

HRMS (m/z -ESI): Found: 158.1695 (M^+ + H. $\text{C}_8\text{H}_{20}\text{N}_3$ Requires: 158.1652).

General Procedure for the Deprotection of *N*-Tosyl Protected Amines to give **19•3HBr** Using Concentrated H_2SO_4

Concentrated H_2SO_4 (1 mL) was added to the protected amine (~1 mmol). The reaction mixture was heated under argon at 160 °C for 1 hour. The reaction mixture was cooled to 0°C in an ice-bath and ethanol (10 mL) followed by diethyl ether (8 mL) was added dropwise. The reaction mixture was cooled in the fridge at 2 °C for 16 hours. The resulting brown precipitate was collected by filtration onto a pad of celite. The precipitate and the celite were then transferred to a round-bottomed flask to which water (10 mL) and activated carbon were added. The mixture was refluxed for 1.5 hours. The insoluble materials were removed by filtration and the solvent was removed under reduced pressure. The resulting brown residue was taken up into 48% hydrobromic acid (1 mL) and to this solution ethanol (20 mL) was added dropwise. The resulting white precipitate, **19•3HBr** (~50%) was collected by filtration and washed with cold diethyl ether (5 mL).

General procedure for the generation of the Freebase **19**.

19•3HBr was dissolved in an 18 M solution of KOH (~5 mL). The aqueous layer was washed with acetonitrile (5 x 5 mL). The organic layer was dried over MgSO_4 and the solvent removed under vacuum to give **19**.

^1H NMR (600 MHz, CDCl_3) δ = 0.76 (s, 3H), 1.65 - 1.77 (m, 2H), 2.58 (s, 2H), 2.58 (d, J =14.1, 2H), 2.80 (d, J =14.1, 2H), 2.84 - 3.02 (m, 4H),

^{13}C NMR (151 MHz, CDCl_3) δ = 20.98, 28.49, 38.59, 49.08, 49.2053.79.

Synthesis of *N,N*-dibenzyl-1-(*N'*,*N''*-1,5-dibenzyl-3-methyl-1,5-diazocan-3-yl)methanamine (**1b**)

19•3HBr (0.454 g, 1.1 mmol) was suspended in acetonitrile (50 mL). Benzyl bromide (0.777 g, 4.4 mmol) and K_2CO_3 (3.14 g, 22.7 mmol) were added. The reaction mixture was heated at reflux for 16 hours. After this the insoluble material was removed by filtration and the solvent was removed *in vacuo*. Remaining impurities were removed via short path distillation under vacuum to give **1b** (0.283 g, 50%).

^1H NMR (600 MHz, CDCl_3) δ = 0.95 (s, 3H), 1.55 - 1.70 (m, 2H), 2.31 - 2.56 (m, 6H), 2.58 (s, 2H), 2.71 (d, J =14.1, 2H), 3.64 (s, 4H), 3.74 (m, 4H), 6.57 - 7.93 (m, 20H),

^{13}C NMR (151 MHz, CDCl_3) δ = 22.2, 28.3, 42.5, 54.5, 60.7, 61.6, 62.1, 65.0, 126.4, 126.6, 127.9, 127.9, 128.4, 129.1, 139.9, 141.9.

HRMS (m/z -ESI): Found: 518.3530 (M^+ + H. $\text{C}_{36}\text{H}_{44}\text{N}_3$ Requires: 518.3535).

NMR Data for [**1b•H**] PF_6

^1H NMR (600 MHz, CD_3CN) δ = 0.23 (s, 3H), 1.69-1.77 (m, 2H) 2.03-2.10 (m, 2H), 2.34 (s, 2H), 2.52 (d, J = 14.2 Hz, 1H), 2.74-2.66 (m, 4H), 2.99-3.13 (m, 2H), 3.84 (d, J = 13.3 Hz, 2H), 3.65 (d, J = 14.7 Hz, 2H), 7.27-7.45 (m, 20H).

^{13}C NMR (151 MHz, CDCl_3) = 21.2, 21.4, 37.2, 56.7, 60.9, 61.7, 63.7, 129.4, 130.0, 130.0, 130.3, 131.7, 134.3, 140.4.

NMR Data for [**1b•2H**] OTf_2

^1H NMR (600 MHz, CDCl_3) δ = 0.15 (s, 3H), 1.68-1.71 (m, 2H), 1.95-1.98 (m, 2H), 2.52 (d, J = 14.5 Hz, 2H), 2.42 (d, J = 14.5 Hz, 2H), 2.65-2.75 (m, 2H), 2.98-3.13 (m, 4H), 3.76 (d, J = 13.0 Hz, 2H), 3.82 (d, J = 13.1 Hz, 2H), 4.27-4.35 (m, 2H), 4.61 (d, J = 12.6 Hz, 2H), 7.23-7.69 (m, 20H).

^{13}C NMR (151 MHz, CDCl_3) = 18.9, 20.8, 35.4, 55.7, 56.1, 59.1, 63.2, 63.6, 129.2, 130.1, 130.2, 130.4, 131.6, 131.9, 133.6, 133.7.

Synthesis of [**Cu**(**NCCH₃**)(**1b**)](**OTf**) (**21**)

In a glovebox, **1b** (0.079 g, 0.15 mmol) and [**Cu**(**NCCH₃**)₄](**OTf**) were stirred in anhydrous acetonitrile (~5 mL) for 10 minutes. The reaction mixture was then concentrated under vacuum. Anhydrous acetonitrile (1 mL) was added followed by anhydrous diethyl ether (20 mL) giving an off-white precipitate. The precipitate was collected by vacuum filtration

and washed with anhydrous diethyl ether (2 x 5 mL) to give [Cu(NCCH₃)(**1b**)](OTf) (0.045 g, 49%) as pale yellow solid. ESI-MS (*m/z* -ESI): Found: 619.0834 (*M*⁺ + K. C₃₆H₄₃N₃Cu Requires: 619.2390).

X-ray diffraction methods

See supporting information.

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