Organic & Biomolecular Chemistry

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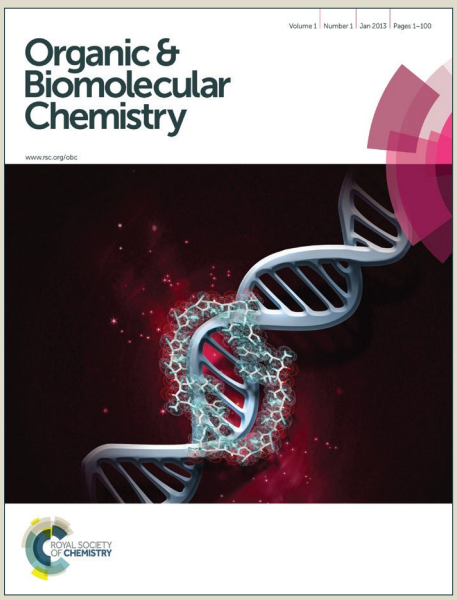

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ARTICLE

Synthesis and Characterisation of a Mesocyclic Tripodal Triamine Ligand

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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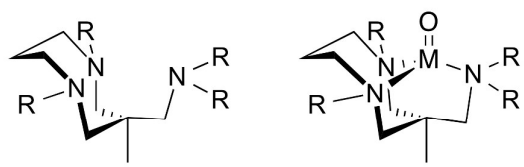
Abstract: Meso- and macrocyclic polydentate amine ligands have been widely explored in oxidation catalysis and for the stabilization of unstable metal-superoxide, -peroxide, and -oxo intermediates. Herein we report on the design and synthesis of a novel mesocyclic, tripodal, triamine ligand that we believe 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 mescocylcic 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 crystalises in a boat-chair conformation which is undesirable for metal coordination. However, solution ^{1}H NMR studies show that in solution both **19** and the tetraalkylated derivative **1b** are remarkably flexible. **1b** reacted with $[Cu^{I}(NCCH_3)_4](OTf)$ yielding a 1:1 copper(I) complex $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$.

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.[9] 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,[10-13] 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. [14-17]

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.[15, 17-19] Nocera postulated that late transition metal-oxo's could be stabilised in complexes displaying low coordination numbers.[20-24] 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 a *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



1, R = Me (**1a**), CH_2Ph (**1b**)

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

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Electronic Supplementary Information (ESI) available: X-ray diffraction methods and all NMR spectra are provided. See DOI: 10.1039/x0xx00000x

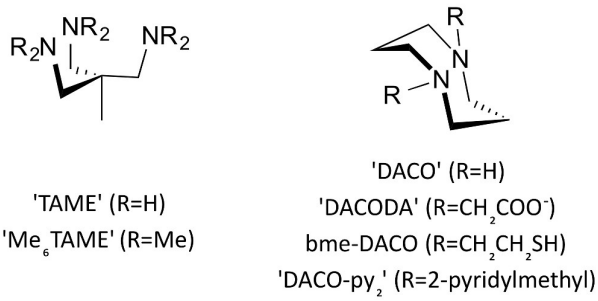


Figure 2 – Chemdraw representations of the ligands related to **1b**.

ligands have been used to great success in stabilizing early transition metal-oxo complexes (metal = Mn, Fe)[11-13, 25-27] and late transition metal-superoxide and -peroxide complexes.[28-36] Meso- and macro-cyclic frameworks add further stability to complexes bearing these ligands, because of the macrocyclic effect.[37, 38] Based on these considerations, we set-out to prepare mesocyclic ligand **1** (Figure 1).

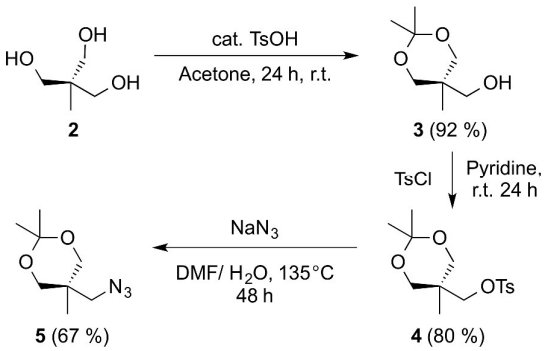
1 is a close analogue of the tripodal acyclic ligand 1,1,1-tris(aminomethyl)ethane (TAME, Figure 2). Due to the lack of steric bulk in TAME, 2:1 complexes are often formed. Increasing the steric bulk via *N*-alkylation to give 1,1,1-tris(N,N-dimethylamino)methylethane (Me_6TAME, Figure 2) resulted in the ligand switching from binding to metals in a tridentate fashion, to a bidentate binding mode, with one of the nitrogens remaining unbound.[39] Similarly, the more bulky guanidine derivative of TAME, 1,1,1-tris(*2N*-1,1,3,3-tetramethylguanidino)methylethane (guanTAME, Figure 2) has been shown to exhibit variable denticity.[40, 41] 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.[38]

1 is also a close analogue of the 1,5-diazacyclooctane (DACO, Figure 2) family of ligands.[38, 42, 43] DACO ligands tend to bind to the metal with the DACO framework displaying a boat-chair configuration.[44] These observations are important because we require that **1** binds to metals yielding a chair-boat configuration to ensure *pseudo*-tetrahedral geometry. Several derivatives of DACO have been developed, exclusively through *N*-alkylation (Figure 2).[33-36, 45-53] In general, these ligands yield square planar complexes. Overall, while many N-alkylated derivatives of DACO exist, few tetrahedral complexes employing DACO have been reported, and all are 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 DACO 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 *pseudo*-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

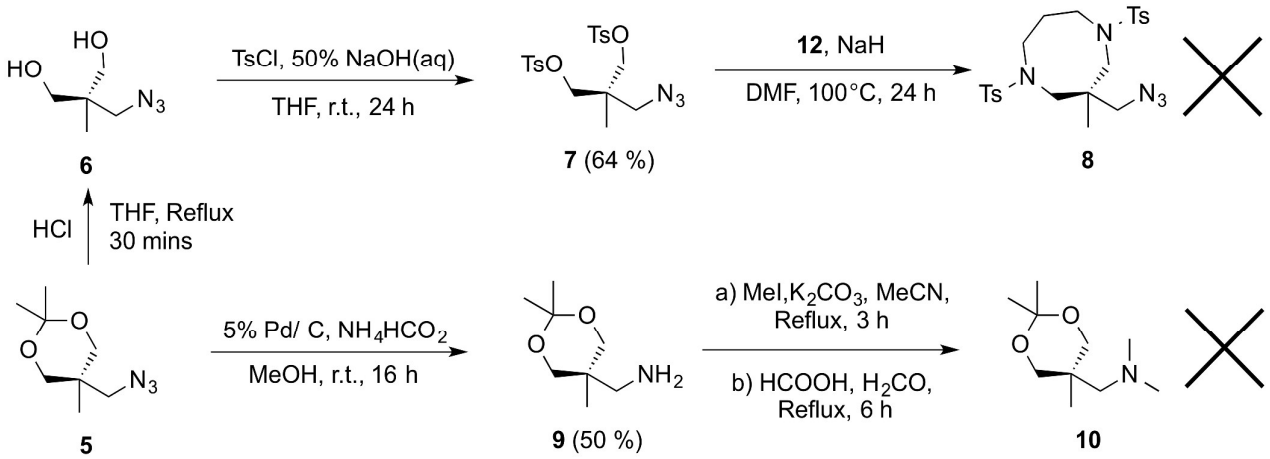
We identified triol 1,1,1-*tris*(hydroxymethyl)ethane (**2**, Scheme 1), as a useful starting point for the preparation of **1**. In order to prepare the asymmetric molecule **1**, we attempted to address a single arm of the tri-substituted neo-pentyl framework, leaving the other two arms to be the basis 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.[54] 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**.[55] The azide, **5**, was then prepared through nucleophilic substitution of the tosylate with sodium azide according to the procedure reported by Liu.[56] We subsequently pursued two avenues towards the selective derivitisation 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 tetrahydrofuran (THF) for 30 minutes to cleave the dioxane protecting group.[56] 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.[57, 58] 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 **7**, 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).[52] **12** was then deprotonated using NaH and subsequently stirred with **7**, without work-up,



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

Scheme 2 – Unsuccessful synthetic routes towards target compound **1**.

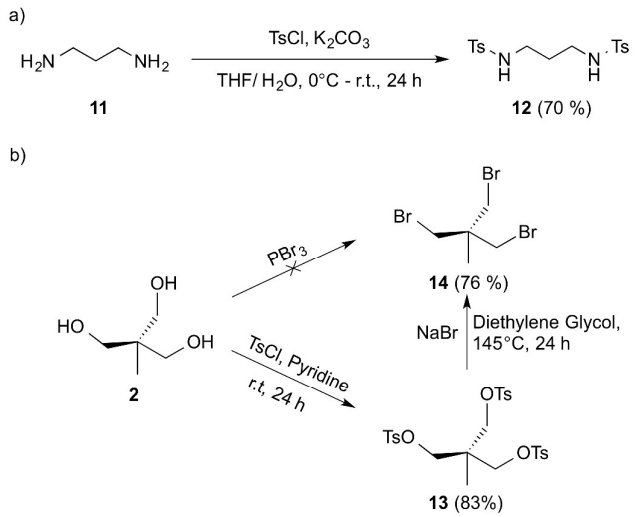


at 145 °C in anhydrous dimethylformamide (DMF). Analysis of the post-reaction mixture indicated none of the desired cycle **8** had formed. We attributed this to the organic azide being unstable under the high-temperature reaction conditions. The azide group may act as a leaving group under such forcing conditions.

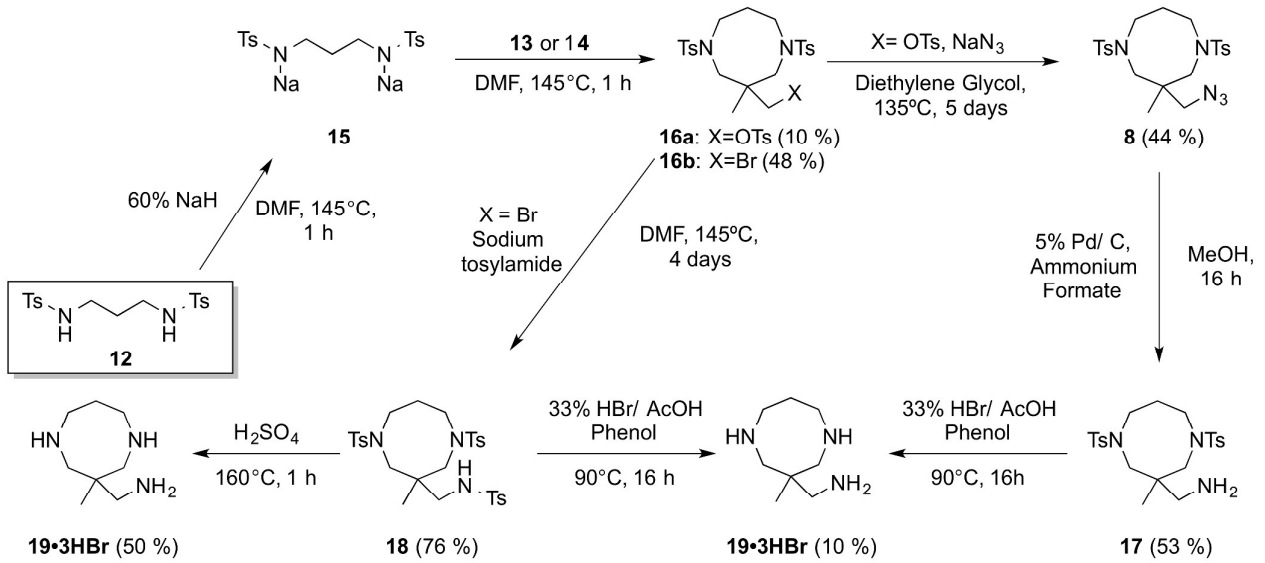
As a result of this negative outcome, we revisited the protected azide, **5.** Rather than cleaving the dioxane group we proceeded to reduce the azide moiety. This was achieved by reacting **5** with 10% wt of 5% Pd/C in the presence of ammonium formate in methanol to give the primary amine **9** in 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.[59] **9** was refluxed for 6 hours in an excess of formic acid and formaldehyde. After work up, the ^{1}H 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 hydroxyl functionalities. We anticipated difficulties with this approach because of the potential formation of oligomers and polymers in the Richman-Atkins cyclisation reaction,[58] 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 filtration[60] we found that the work-up reported by Lindhorst and co-workers, in which the product was extracted with ethyl acetate and dried over magnesium sulphate, gave an anhydrous product.[61] 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 the *tris*-benzenesulphonate analogue of **13** with NaBr,[62] 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 PBr_3,[63] 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**.



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



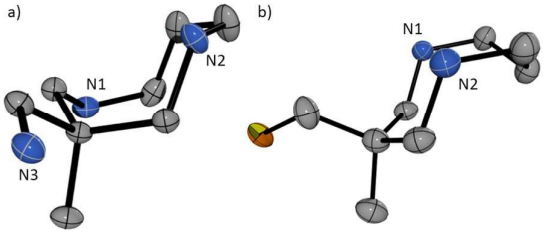
Scheme 4 – Cyclisation reactions and derivatisation of cyclised products.

We reacted the *bis*-tosylamide, **12**, with the activated triols **13** and **14** under conditions outlined by Richman and Atkins (Scheme 4).[57] The disodium salt of **12** (**15**) was generated *in situ* by reacting **12** (0.1 M, 100 mL) 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 0.2 M solution (50 mL) 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 ^{1}H and ^{13}C NMR spectroscopies and mass spectrometry. The ^{1}H 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 $CHCl_3$ (Figure 3b, 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.[64] 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 oligomer/polymer formation,[57] 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 ^{1}H 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.

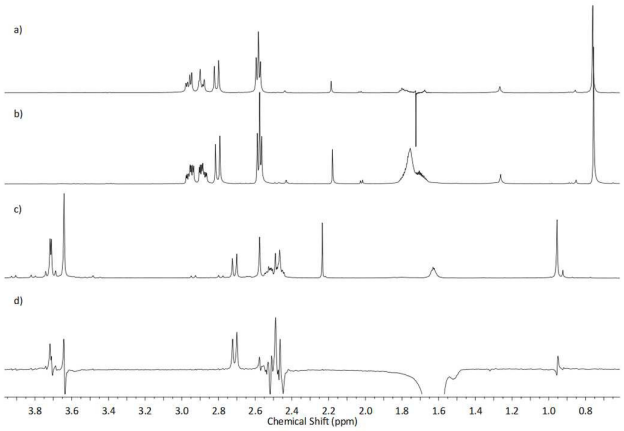
We sought an alternative synthetic route to **19**, because the azide reduction described above gave inconsistent yields. To this end, we reacted **16b** with sodium tosylamide at 145 °C in anhydrous DMF to give the tosylamide **18** (Scheme 4). The formation of **18** was confirmed by ^{1}H NMR and ^{13}C NMR spectroscopy, which showed the aromatic and aliphatic

Figure 3 – a) ORTEP plot of the X-ray crystal structure of **19**•3HBr at 50% probability. Bromine and hydrogen atoms have been omitted 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.

Figure 4 – a) ^{1}H NOE Spectrum of the **19** irradiated at 1.72 ppm; b) ^{1}H Spectrum of the **19**; c) ^{1}H Spectrum of **1b**; d) ROESY Spectrum of **1b** irradiated at 1.63 ppm.



resonances expected after the inclusion of the third tosylamide functionality. ESI-MS also confirmed the formation of **18** (m/z = 620.1931 for $C_{29}H_{37}N_3O_6S_3$; expected m/z = 620.1923). All *N*-tosyl groups were then cleaved by treatment with 33% HBr/acetic acid to give the triamonium 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 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 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 3a) 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.[65] Unusually, when compared to the other crystal structures we obtained (*vide infra*) and those previously reported in the literature for a diprotonated DACO moiety,[65] 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.

	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)

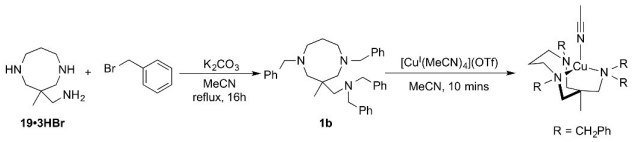
Table 1 – Selected bond lengths and angles for the reported crystal structures.

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 3b), where the nitrogen atoms are primed to bind the metal in a *pseudo*-tetrahedral fashion. We therefore probed the solution behaviour of **19** further. ^{1}H NOE NMR studies on **19** (Figure 4, 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 (CH_2-C*H*$_2$-CH_2)), showed that this -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.

We attempted to methylate **19**•3HBr to give the tetramethylated triamine product **1a** under Eschweiler-Clarke conditions.[59] **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 ^{1}H 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 an 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 aminal containing cyclic amines 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 ($NaBH_4$, KBH_4, or zinc). Unfortunately similar ^{1}H NMR spectra, indicative of aminal 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 ^{1}H 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 (Na_2CO_3) gave the tetra-alkylated product **1b**

Scheme 5 - Preparation of **1b** and $[Cu^I(NCCH_3)(\mathbf{1b})](OTf)$.

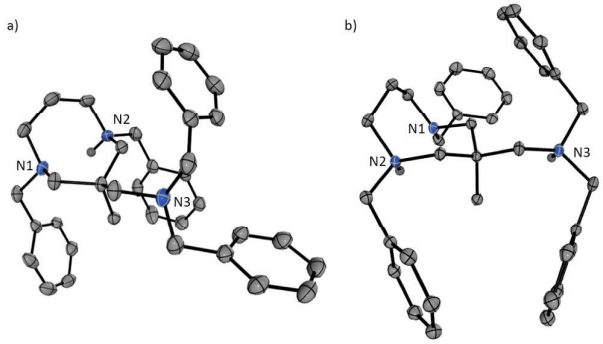


(Scheme 5). Analysis of the ^{1}H NMR of **1b** showed the appearance of two new peaks at 3.64 ppm compared to **19**, corresponding to the benzyl CH_2 groups on the aliphatic amine.

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 = 518.3534 (expected m/z = 518.3535 for $C_{36}H_{44}N_3$), confirming the identity of **1b**. The reaction between **19**•3HBr and benzyl bromide 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.

Similar to **19**•3HBr we assessed the solution flexibility of **1b** (Figure 4) with ^{1}H Rotating-frame Overhauser Effect Spectroscopy (ROESY) NMR. Irradiation of the central CH_2 of the propylene linker CH_2 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 CH_2 groups and, importantly, the *exo*-cyclic CH_3 and CH_2 groups. This demonstrated that although we have alkylated all amine groups in **1b**, the molecule retains is structural flexibility, and should bind metals in the desired *pseudo*-tetrahedral geometry.

Figure 5 – a) X-ray crystal structure of [**1b**•H]PF_6. 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]$(OTf)_2$. Ellipsoids are shown at the 50% probability level. Only refined hydrogen atoms are shown. Counter ions have been omitted for clarity.

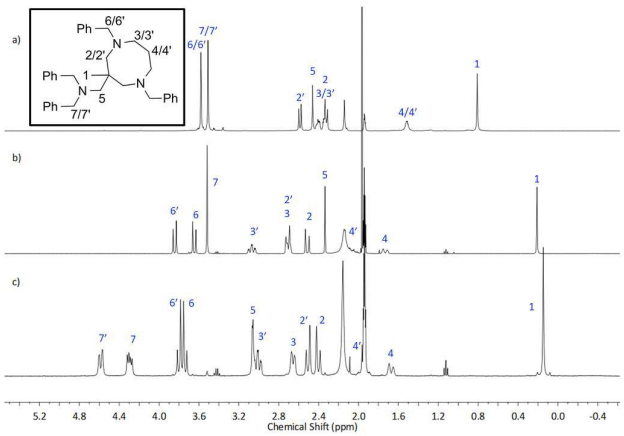


Crystal Structures of both the monoprotonated and diprotonated congeners of **1b** were obtained (Figure 5, Table S1). Serendipitously, single crystals of [**1b**•H]PF_6 (Figure 5a) precipitated after layering a reaction mixture of **1b**, $CuCl_2$ and KPF_6 in wet acetonitrile (CH_3CN) with diethylether (Et_2O). Similarly, single crystals of [**1b**•2H]$(OTf)_2$ (Figure 5b) were obtained after layering of a wet CH_3CN solution of **1b** and $Zn(OTf)_2$ with Et_2O. The crystal structures shown in Figure 5 unambiguously demonstrate that the cyclic amine was protonated before the acyclic amine, as would be expected based on their reported higher basicity.[66] Selected bond lengths and angles for these structures, as well as those in Figure 3, are shown in Table 1.

The structure of [**1b**•H]PF_6 consists of a discrete **1b**•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 [**1b**•H]PF_6 is 2.69 Å, comparable to that measured for **16b** and significantly shorter than that measured for **19**•3HBr suggesting that monoprotonation of the DACO ring allows for the nitrogen atoms to be in closer proximity. The structure of [**1b**•2H]$(OTf)_2$ consists of a discrete **1b**•$2H^+$ cation and two triflate anions. After protonation of N2 and N3 (rather than N1), the structure retains the same boat/chair conformation as in [**1b**•H]PF_6. In the structures of both [**1b**•H]PF_6 and [**1b**•2H]$(OTf)_2$ the C-N-C fold angle is comparable to both previously reported protonated DACO moieties[58, 65, 67, 68] as well as metal complexes containing the DACO moiety.[35] 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 ^{1}H NMR of the crystals of [**1b**•H]PF_6 and [**1b**•2H]$(OTf)_2$ are shown in Figure 6 and were assigned in conjunction with the corresponding heteronuclear single quantum coherence (HSQC) and heteronuclear multiple bond correlation HMBC spectra (See supporting information, Figures S30-35). The ^{1}H NMR of the freebase **1b** and of [**1b**•H]PF_6 are shown in Figure 6a and 6b respectively. The spectra show that upon protonation at N2 (Figure 6b), the apparent singlet at 3.59 ppm arising from $H_{6/6'}$ in **1b** resolves into the pair of doublets, at 3.84 and 3.65 ppm in [**1b**•H]PF_6. The coupling constant (~13 Hz) indicates that these doublets are a result of geminal coupling and no ^{3}J N-H coupling is observed. The difference between these chemical shifts (~0.2 ppm) is a result of the relative axial/equatorial arrangement of these diastereotopic protons, arising from a change in local magnetic anisotropy brought about by protonation. An equivalent resolution of signals is observed after protonation at N3 (Figure 6c), $H_{7/7'}$ 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

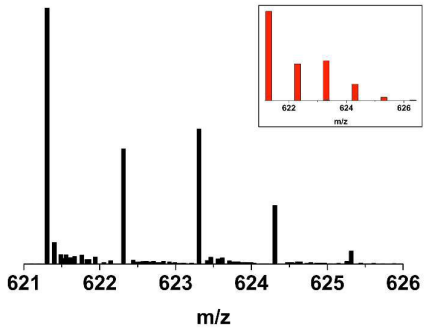
Figure 6 – a) ^{1}H NMR spectrum of **1b**, 400 MHz, CD_3CN; b) ^{1}H NMR spectrum of [**1b**•H]PF_6, 600 MHz, CD_3CN; c) ^{1}H NMR spectrum of [**1b**•2H]$(OTf)_2$, 600 MHz, CD_3CN.



further, possibly by ^{3}J HNCH coupling. The overlapping signals for $H_{3/3'}$ (2.46 - 2.39 ppm) and $H_{4/4'}$ (1.54 ppm) in **1b** are resolved into pairs of multiplets for $H_{3/3'}$ (3.10 and 2.74 ppm) and $H_{4/4'}$ (2.07 and 1.74 ppm) in [**1b**•H]PF_6. As above, the difference in chemical shift (~0.4 ppm) for these pairs of diastereotopic protons is a result of their relative axial/ equatorial arrangement. Protonation at N3 (Figure 6c) maintains the splitting patterns observed for protons associated with the ring, although their chemical shifts differ slightly. Notably, a ^{1}H Nuclear Overhauser Effect Spectroscopy (NOESY) experiment (See supporting information, Figures S33) indicates no through space coupling between H_1 and $H_{3/3'}$, in contrast to analogous experiments conducted on **19** and **1b** (Figure 4). Furthermore, only through space coupling is observed to one of the diastereotopic pair $H_{2/2'}$ whereas coupling to both can be observed in a selective ^{1}H-NOSEY of **1b** (See supporting information Figure S29). We postulate that this is most likely due to a slight reduction in the conformational flexibility of the DACO ring upon protonation.

Figure 7 – ESI-MS spectrum of $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$. Inset shows the predicted isotopic pattern.

The alkylated triamine **1b** was reacted with $[Cu^{I}(NCCH_3)_4](OTf)$ in anhydrous CH_3CN. 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 $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$ (expected m/z = 621.3018, Figure 7). Encouragingly, no 2:1 (ligand:metal) species were observed in the ESI-MS spectra. These observations suggest that **1b** binds the metal centre as a tripod yielding a four-coordinate complex. Unfortunately, work-up of this reaction mixture did not yield the desired complex. Consequently, the same reaction was repeated utilising dichloromethane (DCM) as the reaction solvent (CH_3CN was eliminated from the reaction as we suspect the complex is unstable in CH_3CN). Figure 8 shows the ^{1}H NMR spectrum of the yellow solid obtained from the DCM reaction mixture. The signal assignments shown in Figure 8 were made in combination with HSQC spectra (Figure S38). The splitting of the diastereotopic signals resembles that observed after protonation of **1b**, however, the new material displayed resonances distinct from those of **1b**, [**1b**•H]PF_6, and [**1b**•2H]$(OTf)_2$, indicating complexation of Cu^{I} by **1b** had occurred. Notably, a resonance at 2.42 (corresponding to 3 protons) was observed. We assigned this to a coordinated CH_3-CN ligand (uncoordinated CH_3CN = 2.01 ppm). This assignment was confirmed by the presence of a high-field signal at 2.9 ppm in the ^{13}C NMR, typical of a nitrile methyl group. Integration of the resonances in Figure 8 showed a 1:1 ratio of **1b** to CH_3CN, and thus a coordination number of four. This is further corroborated by our ESI-MS data that indicated the formation of $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$. Complexes containing the DACO moiety tend to form four or five coordinate complexes (*vide supra*)[33-36, 38, 42, 43, 45-52] and six coordinate complexes are unprecedented. Furthermore, Cu(I) complexes prefer to sit in tetrahedral geometry. We are therefore confident in our assignment of this spectrum as a *pseudo*-tetrahedral species $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$.

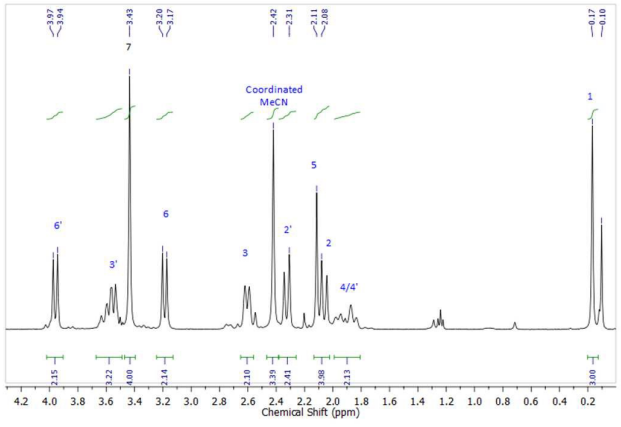


Figure 8 – ^{1}H NMR spectrum of $[Cu^{I}(NCCH_3)(\mathbf{1b})]^{+}$, $CDCl_3$, 400 MHz.

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 for **19** displayed an unusual configuration, 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 the N1 position results in a loss of conformational flexibility. We have also been able to prepare $[Cu^{I}(NCCH_3)(\mathbf{1b})]^+$ demonstrating the potential of **1b** to form *pseudo*-tetrahedral metal complexes. 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**.

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 CH_3CN were purchased and used without further purification. Anhydrous THF and Et_2O were dispensed through an Innovative Technology PureSolv EN solvent purification system and deoxygenated by purging with argon. Ammonium formate was recrystalised 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 MHx 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**,[54] **4**,[55] **5**,[56] **6**,[56] **12**[52] and **13**[61] were synthesised according to literature procedures. Compounds **9**[69] and **14**[62] were prepared by modified literature procedures as described below. X-ray diffraction refinement details and refinement parameters along with all NMR spectra are provided in the supporting information.

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 a colourless oil. The crude product was purified by column chromatography (Hexane: EtOAc, 4:1) to give **7** (7.2 g, 64%) as an off-white solid.

^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.

ν_{max} /cm^{-1}: 3068, 2981, 2951, 2927, 2895, 2530, 2220, 2111, 1980, 1925, 1809, 1654, 1597, 1495, 1471, 1451, 1410, 1399, 1368, 1289, 1211, 1191, 1175, 1121, 1098, 1034, 1017, 964, 934, 917, 893, 866, 840, 831, 814, 804, 794, 706, 664, 629, 603, 568, 553.

HRMS (*m/z* -ESI): Found: 476.0961 (M^+ + Na predicted mass: 476.0926 $C_{19}H_{23}N_3O_6S_2Na$)

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 DCM (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

ν_{max} /cm^{-1}: 1156, 1335, 2103.

HRMS (*m/z* -ESI): Found: 492.1730 (M^+ + H. $C_{22}H_{30}N_5O_4S_2$ predicted mass: 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 Et_2O (3 x 20 mL). The aqueous layer was then basified with KOH (10 g) and extracted with CH_3CN (5 x 10 mL). The organic layer was collected and dried over $MgSO_4$. The solvent was removed *in vacuo* to give **9** (1.50 g, 50%) as a colourless oil.

^{1}H NMR (600 MHz, $CDCl_3$) 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).
^{13}C NMR (151 MHz, $CDCl_3$) δ = 17.9, 21.0, 26.5, 34.2, 46.3, 67.2, 97.8.
HRMS (*m/z* -ESI): Found: 160.1342 (M^+ + H. $C_8H_{17}NO_2$ predicted mass: 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 Et_2O (3 x 50 mL). The organic extracts were combined with the oil and dried over $MgSO_4$. The solvent was removed *in vacuo* to give **14** (18.5 g, 76%) as a pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) 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 $CHCl_3$. The organic layer was washed with water (3 x 50 mL) and brine (3 x 50 mL) then dried over $MgSO_4$. 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.
^{1}H NMR (600 MHz, $CDCl_3$) 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).
^{13}C NMR (151 MHz, $CDCl_3$) 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.
ν_{max} /cm^{-1}: 1156, 1174, 1307, 1336
HRMS (*m/z* -ESI): Found: 643.1580 (M^+ + Na. $C_{29}H_{36}N_2O_7S_3Na$ predicted mass: 643.1582).
Melting point: 86-88°C

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 Et_2O (150 mL). The Et_2O solution was washed with water (3 x 50 ml) and brine (3 x 50 ml) and dried over $MgSO_4$. The solvent was removed *in vacuo*. The crude product was purified by recrystalisation 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%).
^{1}H NMR (400 MHz, $CDCl_3$) 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),
^{13}C NMR (101 MHz, $CDCl_3$) δ = 21.1, 23.1, 28.1, 39.1, 43.4, 49.1, 53.8, 127.0, 129.4, 134.3, 143.4.
ν_{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. $C_{22}H_{29}N_2O_4S_2Br$ predicted mass: 551.0650).
Melting point: 140-143°C

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 Et_2O (3 x 20 mL). The aqueous layer was basified with KOH (10 g) and extracted with CH_3CN (5 x 10 mL). The organic layer was collected and dried over $MgSO_4$. The solvent was removed *in vacuo* to give **17** (0.140 g, 53%).
^{1}H NMR (600 MHz, $CDCl_3$) 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).
^{13}C NMR (151 MHz, $CDCl_3$) δ = 21.5, 28.1, 40.4, 47.8, 49.8, 53.5, 127.4, 129.8, 135.1, 143.6,
ν_{max} /cm^{-1}: 1151, 1327, 3151, 3310,
HRMS (*m/z* -ESI): Found: 466.1833 (M^+ + H. $C_{22}H_{32}N_3O_4S_2$ predicted mass: 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 recrystalised 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%). The crude product was then recrystalised from acetone.
^{1}H 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.
ν_{max} /cm^{-1}: 3290, 2925, 2286, 2050, 1980, 1598, 1494, 1458, 1382, 1328, 1305, 1216, 1153, 1089, 1017, 967, 847, 811, 752, 739, 705, 653, 567.
HRMS (*m/z* -ESI): Found: 620.1931 (M^+ + H. $C_{29}H_{37}N_3O_6S_3$ predicted mass: 620.1931).
Melting point: 110-114°C

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 Et_2O (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: ^{1}H 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. $C_8H_{20}N_3$ predicted mass: 158.1652).
Melting Point: Decomposes at ~255°C

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 Et_2O (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 Et_2O (5 mL).

General procedure for the generation of the Freebase 19.

19•3HBr was dissolved in the minimum amount of deionised water. NaOH (10 e.q) and toluene (~20 mL) were then added. The toluene solution was then heated under reflux with a Dean-Stark trap for 24 hours. After cooling, the any insoluble material was removed by filtration and the solvent removed under vacuum to give **19** as a colourless oil.
^{1}H 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.
ν_{max} /cm^{-1}: 3295, 2903, 2862, 1595, 1459, 1393, 1365, 1293, 1230, 1146, 1069, 880, 845, 810, 769, 747, 692, 639, 623, 616, 609, 601, 593, 585, 578, 570, 563, 555.
HRMS (*m/z* -ESI): Found: 158.1674 (M^+ + H. $C_8H_{20}N_3$ predicted mass: 158.1652).

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

19•3HBr (1.1 g, 2.7 mmol) was suspended in CH_3CN (30 mL). Benzyl bromide (1.88 g, 1.3 mL, 11.0 mmol) and K_2CO_3 (7.6 g, 55 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*. The resulting yellow oil was dissolved in H_2O (5 mL) and added to a suspension of sodium hydroxide (5 g) in toluene (50 mL). The toluene solution was then heated under reflux with a Dean-Stark trap for 24 hours. After cooling, the insoluble material was removed by filtration and the solvent removed under vacuum to give **1b** (0.988 g, 70%) as a white solid.
^{1}H 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.
ν_{max} /cm^{-1}: 3084, 3063, 3025, 2965, 2949, 2939, 2922, 2888, 2814, 2780, 2711, 2049, 1940, 1870, 1803, 1602, 1585, 1493, 1468, 1451, 1357, 1332, 1302, 1283, 1243, 1212, 1192, 1176, 1145, 1115, 1090, 1071, 1062, 1045, 1027, 984, 972, 935, 922, 906, 888, 861, 838, 821, 760, 744, 731, 695, 632, 613, 583, 569, 555.
HRMS (*m/z* -ESI): Found: 518.3530 (M^+ + H. $C_{36}H_{44}N_3$ predicted mass: 518.3535).
Melting point: 88-90°C

NMR Data for [1b•H]PF_6

^{1}H 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)$_2$

^{1}H 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^I(NCCH$_3$)(1b)](OTf) (21)

In a glovebox, **1b** (0.079 g, 0.15 mmol) and [Cu^I(NCCH$_3$)$_4$](OTf) (0.063 g, 0.17 mmol) were stirred in anhydrous CH_3CN (~5 mL) for 10 minutes. The reaction mixture was then concentrated under vacuum. Anhydrous CH_3CN (1 mL) was added followed by anhydrous Et_2O (20 mL) giving an off-white precipitate. The precipitate was collected by vacuum filtration and washed with anhydrous Et_2O (2 x 5 mL) to give [Cu^I(NCCH$_3$)(**1b**)](OTf) (0.045 g, 49%) as pale yellow solid.
ESI-MS (*m/z* -ESI): Found: 619.0834 (M^+ + K. $C_{36}H_{43}N_3Cu^0K$ predicted mass: 619.2390).
Air sensitive compound, no melting point determined.

Synthesis of [Cu^I(NCCH$_3$)(1b)](PF$_6$) (22)

In a glovebox, **1b** (0.050 g, 0.09 mmol) and [Cu^I(NCCH$_3$)$_4$](PF$_6$) (0.040 g, 0.1 mmol) were stirred in anhydrous DCM (2 mL) for 10 minutes. Anhydrous Et_2O (15 mL) was added resulting in the formation of a pale yellow precipitate. The supernatant was decanted and the precipitate dissolved in the minimum amount of DCM. The resulting solution was layered with anhydrous Et_2O and the product recrystalised to give **1b** as pale yellow needles (0.048 g, 65 %).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.17 (s, 3H), 1.84-1.98 (m, 2H), 2.04-2.11 (m, 4H), 2.33 (d, *J*= 14.5 Hz, 2H), 2.42 (s, 3H), 2.55-2.63 (m, 2H), 3.19 (d, *J* = 12.3 Hz, 2H), 3.43 (s, 4H), 3.50-3.63 (m, 2H), 3.96 (d, *J* = 12.3 Hz, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) = 2.9, 23.8, 24.4, 30.9, 38.4, 59.2, 59.4, 61.7, 62.2, 67.1, 127.5, 128.4, 128.6, 129.3, 130.9, 131.6, 134.8, 139.3.

Acknowledgements

This publication has emanated from research supported in part by the European Union (FP7-333948) and a research grant from Science Foundation Ireland (SFI/12/RC/2278). We thank Dr. John O'Brien (NMR) and Dr. Brendan Twamley (XRD) for technical support. Dr. Brendan Twamley acknowledges PRTLI and ERDF for funding.

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