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The synthesis of planar chiral *pseudo-gem* aminophosphine pre-ligands based on [2.2]paracyclophane

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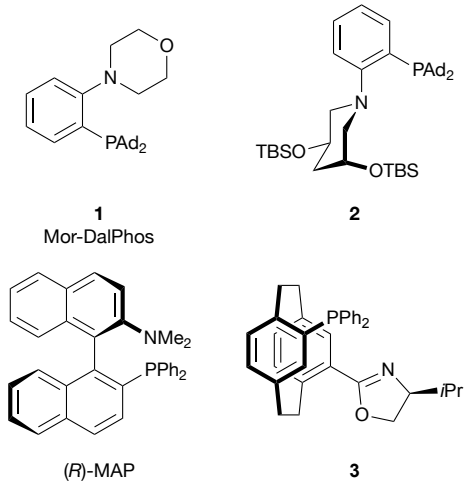
The synthesis of three planar chiral *pseudo-gem* disubstituted [2.2]paracyclophane-derived *P*,*N*-pre-ligands is reported along with preliminary results of their activity in the amination of aryl bromides and chlorides. The *pseudo-gem* aminophosphines were capable of mediating the coupling reaction at a loading of 1 mol%.

Introduction

The design and synthesis of bidentate ligands comprising of two different donor atoms has been a successful avenue of research.[1] Each donor can interact with the metal centre differently allowing modification of the properties of the catalyst in order to aid distinct steps of the catalytic cycle.



1 Mor-DalPhos

2

(*R*)-MAP

3

Figure 1: Examples of reported *P*,*N*-Pre-ligands.

Ligands bearing phosphorus and nitrogen donors (*P*,*N*-ligands) are amongst the most widely studied (Figure 1).[2] and have permitted challenging transformations to be achieved.[2c,2g,3] Regardless of these past successes there is a continued need for new *P*,*N*-ligands with different architectures. This will allow improved results to be obtained from prototypical reactions as well as the development of new synthetic transformations.

A highly successful class of *P*,*N*-ligands are the 'DalPhos' compounds, such as **1** (Figure 1), developed by the Stradiotto group.[3c,3d,4] These are based on the *ortho*-*P*,*N*-phenylene backbone and combine a bulky electron rich phosphine, normally di(1-adamantyl)phosphine, with a disubstituted amine. While the adamantyl group is undoubtedly important to the success of these pre-ligands, it is insufficient to explain their remarkable reactivity; the amine moiety is equally important, with the morpholine group of Mor-DalPhos proving particularly effective.[3a,5]

Chiral variants of DalPhos, such as **2**, have been prepared (Figure 1) and applied to gold-mediated enantioselective cyclopropanation reactions.[6] These pre-ligands include stereogenic centres on the amine substituents. This design supposes that the *P*,*N*-ligands are bidentate during the enantiodetermining step and that conformational changes keep the stereogenic centres proximal to the metal centre.

An alternate approach to chiral DalPhos analogues would incorporate the aromatic ring in a stereogenic unit. This could be achieved by using [2.2]paracyclophane to introduce planar chirality.[7] [2.2]Paracyclophane's rigid structure restricts conformational freedom resulting in well-defined ligands such as PhanePhos[8] and GemPhos.[9] These two ligands are isomeric, with PhanePhos presenting the phosphine donors in the 4,12-positions (*pseudo-ortho*) and GemPhos in the 4,13-positions (*pseudo-gem*).

We have studied a range of planar chiral heteroaromatic monophosphines[7d] formed from the combination of [2.2]paracyclophane with an imidazole ring (**4**),[10] a triazole (**5**),[11] or an indole (**6**) (Figure 2).[12] While each of these pre-ligands showed potential it was clear that the [2.2]paracyclophane moiety was a largely superfluous; if we wanted to exploit the planar chirality of [2.2]paracyclophane we needed to design bidentate derivatives.[7d,13]

Considering the potential of *P*,*N*-pre-ligands, there have been surprisingly few based on [2.2]paracyclophane. A limited

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number of monophosphines with oxazoline (*e.g.* **3**),[14] and pyridine[15] substituents have been reported but in each case the donor atoms are separated from the [2.2]paracyclophane moiety by a linker. This changes the bite angle and potentially diminishes the effect of paracyclophane.

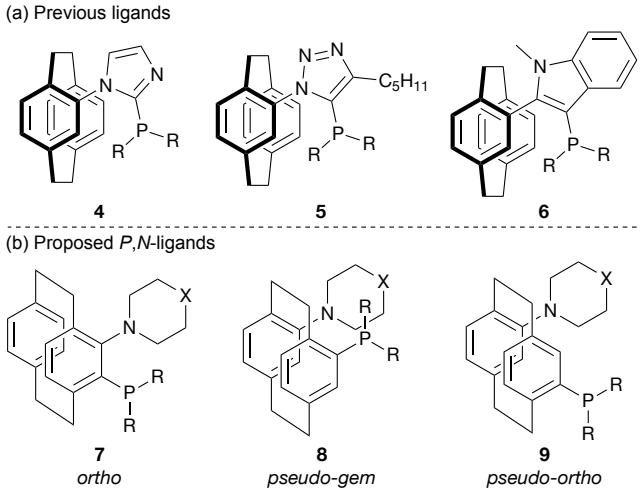


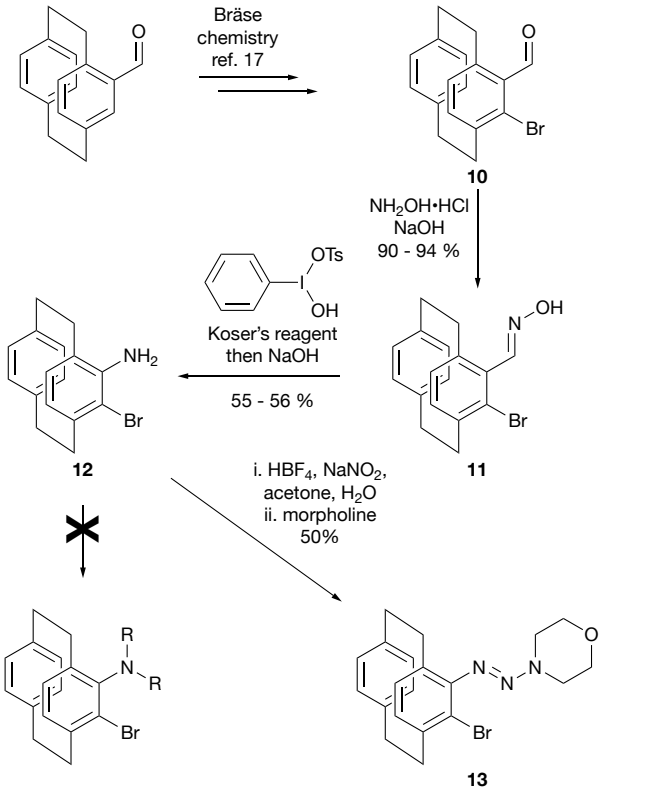
Figure 2: (a) Our previous planar chiral monophosphines and (b) proposed aminophosphine [2.2]paracyclophane derivatives.

Therefore, we targeted planar chiral analogues of Mor-DalPhos. There are three isomeric bidentate variants; the *ortho* substituted amino phosphine **7**, the *pseudo-gem* isomer (**8**), and the *pseudo-ortho* isomer (**9**) (Figure 2). This communication outlines the successful synthesis of the *pseudo-gem* isomer **8**, and the obstacles encountered attempting to prepare **7**.

Results and Discussion

Our initial target was the *ortho*-aminophosphine **7** as this most closely mirrored the structure of Mor-DalPhos. The synthesis of *ortho*-substituted [2.2]paracyclophanes can be problematic; directed *ortho*-lithiations are notoriously fickle, being prone to issues of regioselectivity (C2 *versus* C5 deprotonation)[14c,16] and chemoselectivity (1,4-addition *versus* 1,2-addition *versus* deprotonation).[14c] By combining the elegant *ortho*-bromination chemistry of Bräse[17] with a modified Lossen rearrangement,[18] we believed we could overcome these limitations and prepare the key intermediate **12** (Scheme 1). Straightforward functional group manipulations would then deliver the planar chiral aminophosphine. Unfortunately, paracyclophane chemistry frequently frustrates the best laid plans.

4-Bromo-5-formyl[2.2]paracyclophane **10** was readily prepared following the literature procedures.[17] Condensation with hydroxylamine hydrochloride gave the oxime **11** in excellent yield (Scheme 1). Treatment with Koser's reagent, hydroxy(tosyloxy)iodobenzene HTIB,[19] initiated a 'one-pot' oxidation-rearrangement that, under our optimised conditions,[18a] delivered the desired amine **12** in acceptable yield. Having installed the challenging *ortho*-substitution pattern, all that was left to achieve was elaboration of the amine. Attempts to alkylate the amine with bis(2-bromoethyl)ether in the presence of a variety of bases, and at a range of temperatures all met with failure. In each case the starting material was recovered with excellent mass balance. To simplify the reaction, we attempted methylation either by substitution or reductive amination but to no avail. Heating the aniline-derivative to reflux in neat iodomethane, while admittedly a relatively low temperature, resulted in the complete recovery of the starting material. A variety of acylations with anhydrides and acyl chlorides also returned unreacted starting material. **12** proved to be remarkably unreactive.



Scheme 1: Attempted synthesis of *ortho*-aminophosphine derivative **7**.

Only diazotisation resulted in the formation of a new product. The diazonium salt could be trapped with morpholine to give the triazene **13** (Figure 3). Attempts to prepare either the bromoiodo species or the dibromo derivative from the diazonium salt met with failure; both gave the same, as of yet, unidentified side product. Our inability to alkylate amine **12** is surprising; while anilines are less basic than alkylamines they are normally sufficiently nucleophilic to undergo derivatisation. 4-Amino[2.2]paracyclophane readily reacts with a variety of electrophiles, while a limited number of *ortho*-substituted amino[2.2]paracyclophanes have participated in cyclisation reactions.[10,18a,20] We speculate that the reduced activity is a result of increased delocalisation of the nitrogen lone pair due to the bromine substituent, and increased steric congestion around the amine. Presumably, diazotisation proceeds as the nitrosyl reagent is both highly reactive, being potentially cationic, and is small. We have observed reduced amine reactivity in *pseudo-gem* amino acids (and esters),[18a] and have attributed this to increased delocalisation as well as steric effects.

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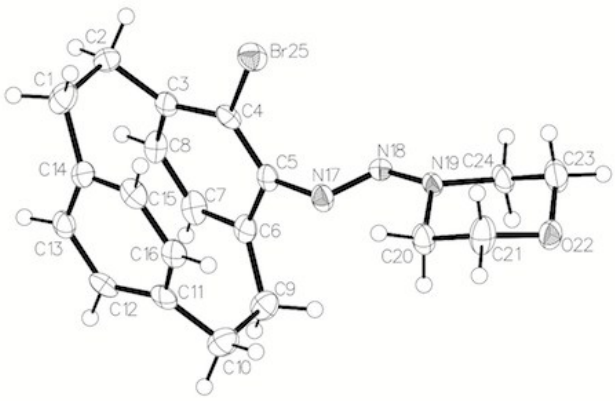
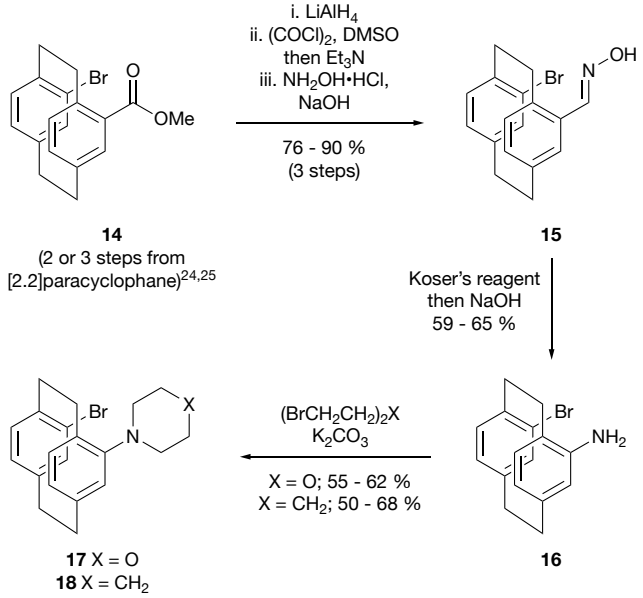


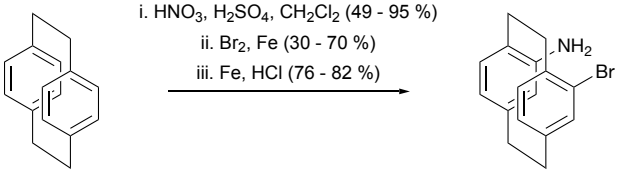
Figure 3: X-Ray structure of triazene **13** (N17–N18 = 1.263(4) Å and N18–N19 = 1.351(4) Å).[21] Ellipsoids are drawn at a 50% probability level.

The stubborn stability of the *ortho*-substituted aniline necessitated a change in target and we turned our attention to the synthesis of the *pseudo-gem* analogue **7**. Two routes were used to prepare this compound. The first route involved a 'one-pot' oxidation-rearrangement reaction (Scheme 2).[18a] The attraction of this longer route was the potential to resolve the planar chirality at either the acid,[22] or aldehyde stage.[23] [2.2]Paracyclophane-4-carboxylic acid was prepared from [2.2]paracyclophane by Friedel-Crafts acylation.[24] While this chemistry can deliver the ester directly, we always isolated a mixture of ester and acid and elected to perform the esterification in a second step. Directed bromination gave the *pseudo-gem* disubstituted derivative **14** exclusively.[25] A two-step reduction-reoxidation to the aldehyde was more reliable than partial reduction of the ester with DIBAL. The latter gives a mixture of aldehyde and alcohol. Quantitative oxime formation gave **15**, which was subjected to 'one-pot' oxidation-rearrangement to give the key aniline derivative **16**. This time the amino group was alkylated to form either the morpholine **17** or piperidine **18** derivative (Scheme 2).



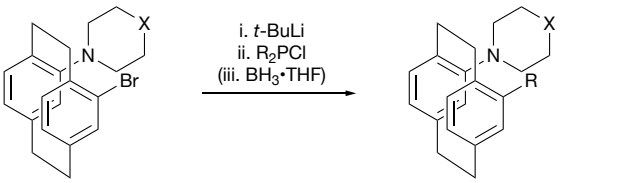
Scheme 2: Synthesis of *pseudo-gem* aminobromo derivative.

A shorter route to *pseudo-gem* aminobromo[2.2]paracyclophane **16** has been reported by Paradies, and involves nitration, followed by regioselective bromination, and reduction (Scheme 3).[26] The capricious nature of the nitration necessitated a modification of the reaction conditions; addition of a solution of [2.2]paracyclophane **19** in CH_2Cl_2 to a mixture of nitric and sulfuric acid at 0 °C minimises multiple nitrations. Careful work-up is essential as a dark orange oil often forms during the reaction. By decanting the reaction mixture from this prior to work-up avoids emulsions, which lower the yield. Under these conditions 4-nitro[2.2]paracyclophane was obtained in 49 - 95 %, which is more than satisfactory for the nitration of [2.2]paracyclophane. Regioselective bromination exploiting the transannular effect to give the *pseudo-gem* product followed by reduction was achieved following the conditions of Paradies.[26]



Scheme 3: Shorter synthesis of *pseudo-gem* aminobromo derivative.

The phosphine was introduced by metal-halogen exchange and addition to the appropriate chlorophosphine. Competing protodebromination appears to be unavoidable, and the diphenylphosphine **15** could only be obtained in 40 - 59 % yield (Scheme 3). A similar conversion was observed by ^{1}H NMR spectroscopy for the dicyclohexylphosphine derivative but it was unstable to purification, and just 8 % was isolated. *In situ* protection with borane improved the yield to a modest 33% on a small scale (< 0.1 mmol). The reaction did not proceed for di-*tert*-butylchlorophosphine. Attempts to introduce the phosphine by a palladium-mediated coupling of bromo-**17** with various disubstituted phosphines all met with failure. In keeping with all of our studies on *pseudo-gem* disubstituted [2.2]paracyclophanes[18a] we speculate that the presence of the second substituent hinders displacement of the bromide, while the highly electron rich nature of aniline-like [2.2]paracyclophane could destabilise the incipient organometallic intermediate.

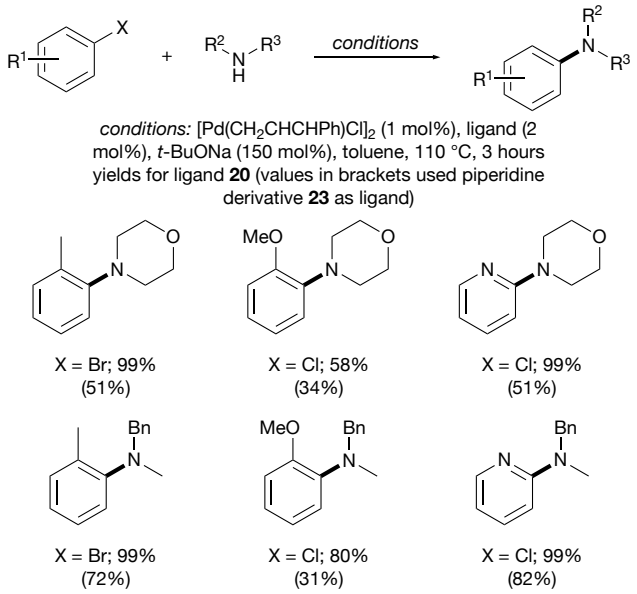


Scheme 4: Synthesis of *pseudo-gem* aminophosphine.

Applying the best conditions to the piperidine analogue permitted the synthesis of the diphenylphosphine derivative **23** in less than satisfactory yield (19 %). More protodebromination

was observed than before suggesting that the organolithium intermediate of the piperidine derivative was even less stable than its morpholine counterpart. The yield is not helped by the similarity in both the R_f and solubility of the product and debromo derivative.

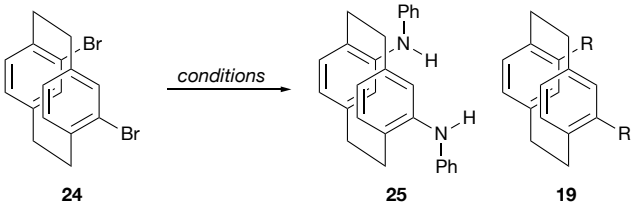
The efficacy of the new *P*,*N*-pre-ligands (**20**-**23**) in the amination of various aryl halides with morpholine was ascertained (Scheme 5).[27] Initial screening reactions suggested that the optimum conditions employed palladium(π-cinnamyl) chloride dimer (1 mol%), ligand (2 mol%), and sodium *tert*-butoxide (150 mol%) as base in toluene at 110 °C for 3 hours. The palladium source could be changed with a small decrease in yield. The base could not be altered without a dramatic drop in yield.



Scheme 5: Illustrative Buchwald-Hartwig aryl aminations.

As Scheme 5 indicates morpholine and *N*-benzylmethanamine could be coupled with electron rich (hetero)aryl bromides and chlorides in moderate to excellent yields with low catalyst loadings, and in relatively short reaction times. The range of coupling partners does appear to be limited; sterically demanding anilines, such as 2,6-dimethylaniline, fail to couple. A range of amide-like substrates including *p*-toluenesulfonamide, benzamide, and *tert*-butyl carbamate also failed to react. It is unclear if the problem arises from an incompatibility with the strong base required for the reaction or that a κ^2-complex is formed that deactivates the palladium centre.[27b]

One of the ongoing aims of our research is to identify reaction conditions that permit the controlled amination of (di)bromo[2.2]paracyclophane derivatives. There are a number of reports achieving this goal,[20a,28] but as we have detailed in an earlier publication, we have had issues reproducing many of these.[18a] As a result, we studied the amination of *pseudo-ortho* dibromo[2.2]paracyclophane **24** under our standard conditions (Scheme 6). Initially, we studied the monoamination of *pseudo-ortho*-dibromo[2.2]paracyclophane with morpholine as a means of preparing the third aminophosphine (**9**). All ligands screened, **20**, **22**, (±)-BINAP, bis(diphenylphosphino)ferrocene (dppf), and *t*-Bu_3P•HBF_4, failed. Only [2.2]paracyclophane was isolated. Protodebromination suggests that the morpholine complex is undergoing β-hydride elimination more rapidly than reductive elimination.[27b,29]



conditions: $[Pd(CH_2CHCHPh)Cl]_2$ (1 mol%), ligand (2 mol%), HNR^1R^2 (150 mol%), *t*-BuONa (150 mol%), toluene, 110 °C, 12 hours.
yields: HNR^1R^2 = morpholine; [2.2]paracyclophane **19** R = H; > 90%
HNR^1R^2 = aniline; ligand = **22**; di-**25** 37 % & **19** > 50%
HNR^1R^2 = aniline; ligand = **20**; di-**25** 21 % & **19** > 50%
HNR^1R^2 = aniline; ligand = dppf; di-**25** 30 % & **19** > 50%

Scheme 6: Trial aminations of *pseudo-ortho* dibromo[2.2]paracyclophane **24**.

To avoid β-hydride elimination we screened a number of nitrogen nucleophiles without the problematic hydrogen atoms. The only successful coupling was observed with aniline. Dppf and pre-ligands **20** and **22** furnished the *pseudo-ortho* dianiline adduct in low yield (30 %, 21 %, and 37 % respectively) along with [2.2]paracyclophane. The slight increase in yield with the dicyclohexyl derivative **22** suggests that the electron rich bulky ligand improves reactivity. Unfortunately, until a more efficient synthesis of this derivative can be developed it is unclear if this is true. No other combination of amine, amide or sulfonamide, with any of the pre-ligands tested gave any product other than [2.2]paracyclophane **19**.

Conclusion

We have synthesised three new planar chiral *pseudo-gem* aminophosphine pre-ligands. These added to the limited number of *P,N*-ligands-based on the [2.2]paracyclophane moiety. The ligands displayed promising activity in the Buchwald-Hartwig coupling reaction; they mediated the coupling of deactivated aryl chlorides in good yields at low catalyst loadings. Future work will investigate their resolution and application to enantioselective transformations. Additionally, we will study the *pseudo-ortho* derivative in order to ascertain its ease of synthesis, and to investigate any effect changing the separation of the two donor groups may have on catalytic activity.

Experimental

General Information

All starting compounds and solvents were used as received from commercial sources without further purification unless otherwise noted. All reactions were performed in oven-dried glassware under an atmosphere of argon or nitrogen unless otherwise stated. Column chromatography was carried out on silica gel (grade 60, mesh size 230-400, Scharlau). Visualisation techniques employed included using ultraviolet light (254 nm),

potassium permanganate, ethanolic phosphomolybdic acid or ninhydrin when applicable. NMR spectra were recorded at room temperature on Bruker-400 and Bruker-500 Avance instruments, with the use of the residual solvent proton as an internal standard ($CHCl_3$ = 7.26 ppm). Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Mass spectra and high resolution mass spectrometry were performed at the Waikato Mass Spectrometry Facility, The University of Waikato, New Zealand or at Massey University, using a Thermo Scientific Q Exactive Focus Hybrid Quadrupole-Orbitrap Mass Spectrometer.

4-Bromo[2.2]paracyclophane-5-carbaldehyde oxime (**11**)
To a mixture of hydroxyl amine hydrochloride (156mg, 2.25 mmol, 3.0 eq.) and sodium hydroxide (93 mg, 2.325 mmol, 3.1 eq.) in ethanol (5 ml) at reflux was added a solution of 4-bromo-5-formyl[2.2]paracyclophane (236 mg, 0.75 mmol, 1.0 eq.) in ethanol (3 ml). The resulting mixture was heated at reflux for 30 min. The mixture was cooled to rt and the solvent removed. The product was dissolved in EtOAc (10 ml) and washed with H_2O and brine, dried ($MgSO_4$) and the solvent removed under reduced pressure to give the product as a colourless solid (233 mg, 94%).
R_f (9:1 Hex:EtOAc) 0.25
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.24 (1H, s), 7.65 (1H, brs), 7.26 (1H, s), 6.98 (1H, dd, *J* = 7.8, 1.8 Hz), 6.61 (1H, d, *J* = 7.8 Hz), 6.60 (1H, dd, *J* = 7.8, 1.8 Hz), 6.53 (2H, d, *J* = 7.8 Hz), 6.52 (1H, dd, *J* = 7.8, 1.8 Hz), 3.77 (1H, ddd, *J* = 13.0, 10.1, 2.6 Hz), 3.50 (1H, ddd, *J* = 13.0, 10.3, 3.4 Hz), 3.30-2.98 (4H, m), 2.90-2.82 (2H, m)
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 151.7, 141.7, 140.1, 139.6, 139.1, 135.1, 134.1, 133.4, 133.0, 131.7, 130.3, 129.4, 128.4, 36.1, 34.8, 34.6, 33.3
HRMS (EI): *m/z* found: $[M+Na]^+$, 352.0307. $C_{17}H_{16}{}^{79}BrNO$ requires $[M+Na]^+$, 352.0313.

5-Amino-4-bromo[2.2]paracyclophane (**12**)
A mixture of finely ground 4-bromo[2.2]paracyclophane-5-carbaldehyde oxime (165 mg, 0.5 mmol, 1.0 eq.) and ground Koser's reagent (272 mg, 0.7 mmol, 1.4 eq.) in DMSO (1 ml) was allow to stirred at rt for 30 min and then heated at 80 °C for 1h. Sodium hydroxide (28 mg, 0.7 mmol, 1.4 eq.) was added and heating was continued for further 1.5 h. The mixture was cooled to rt, H_2O (1 ml) was added and the aqueous layer extracted with EtOAc (2 x 20 ml). The combined organic layers were washed with H_2O (20 ml), dried ($MgSO_4$), and the solvent was removed under reduced pressure. The resulting residue was separated by column chromatography eluting Hex:EtOAc 9:1 to afford the 5-amino-4-bromo[2.2]paracyclophane as a pale yellow solid (85 mg, 56%).
R_f (9:1 Hex:EtOAc) 0.425
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.98 (1H, dd, *J* = 7.8, 1.8 Hz), 6.92 (1H, dd, *J* = 7.8, 1.8 Hz), 6.58 (1H, d, *J* = 7.8 Hz), 6.50 (1H, dd, *J* = 7.8, 1.8 Hz), 6.37 (1H, d, *J* = 7.8 Hz), 6.18 (1H, d, *J* = 7.8 Hz), 3.95 (2H, brs), 3.35 (1H, ddd, *J* = 17.0, 10.1, 1.7 Hz), 3.15-2.93 (5H, m), 2.72-2.83 (2H, m)
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 142.7, 140.5, 138.3, 138.2, 133.3, 132.8, 132.5, 127.7, 126.4, 126.0, 124.0, 116.0, 35.8, 33.1, 33.2, 32.4
HRMS (EI): *m/z* found: $[M+H]^+$, 302.0539. $C_{16}H_{16}{}^{79}BrN$ requires $[M+H]^+$, 302.0534.

4-(4-Bromo[2.2]paracyclophan-5-yldiazenyl)morpholine (**13**)
To a solution of 4-bromo-5-amino[2.2]paracyclophane (75 mg, 0.25 mmol, 1.0 eq.) in acetone (0.1 ml), acetonitrile (0.2 ml), and H_2O (0.5 ml) at 0°C was added a solution of 50% aqueous HBF_4 (1 ml, excess). A solution of $NaNO_2$ (18 mg, 0.25 mmol, 1.0 eq.) in ice cold water (0.2 ml) was added dropwise at 0 °C. Within 10 minutes dark yellow precipitate had formed. The solid was removed by filtration and washed with cold Et_2O. The solid was mixed with morpholine (2 ml) for 2 h. The solution was diluted with CH_2Cl_2 (10 ml) and H_2O (10 ml). The layers were separated and the organic layer washed with H_2O (2 x 10 ml), dried ($MgSO_4$) and concentrated. The resulting solid was recrystallized from $CDCl_3$ (50 mg, 50%).
R_f (9:1 Hex:EtOAc) 0.70
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.06 (1H, dd, *J* = 6.8, 1.2 Hz), 6.69 (1H, dd, *J* = 6.8, 1.2 Hz), 6.58-6.53 (3H, m), 6.41 (1H, d, *J* = 7.7 Hz), 3.94-3.82 (8H, m), 3.49 (1H, ddd, *J* = 13.1, 10.3, 2.5 Hz), 3.29 (1H, ddd, *J* = 12.5, 9.8, 2.4 Hz), 3.17 (1H, ddd, 15.6, 10.3, 5.2 Hz), 3.08-3.00 (2H, m), 2.89-2.80 (2H, m), 2.67 (1H, ddd, *J* = 16.3, 10.2, 6.1 Hz)
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 146.8, 140.7, 139.3, 138.8, 133.9, 133.3, 132.9, 132.7, 131.3, 129.9, 123.9, 66.6, 48.01 (br), 35.6, 34.4, 33.5, 32.9
HRMS (EI): *m/z* found: $[M+H]^+$, 400.1048. $C_{20}H_{21}{}^{79}BrN_3O$ requires $[M+H]^+$, 400.1025.

X-Ray data of the compound **13** was recorded at low temperature (153 K) with a Rigaku-Spider X-ray diffractometer, comprising a Rigaku MM007 microfocus copper rotating-anode generator, high-flux Osmic monochromating, and focusing multilayer mirror optics ($Cu_{K\alpha}$ radiation, λ 1.5418 Å), and a curved image-plate detector. *CrystalClear*[30] was utilised for data collection and FSProcess in PROCESS-AUTO[31] for cell refinement and data reduction. Using Olex2,[32] the structure was solved with the Superflip structure solution program using Charge Flipping[33] and refined with the ShelXL[34] refinement package using least-squares minimisation. Hydrogen atoms were placed at calculated positions.

Crystal structure determination of 13
Crystal Data for $C_{20}H_{22}BrN_3O$ (*M* = 400.31 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 7.368(3) Å, *b* = 10.812(3) Å, *c* = 22.597(5) Å, *β* = 95.146(17)°, *V* = 1792.8(10) Å^3, *Z* = 4, *T* = 123 K, μ(CuKα) = 3.221 mm^{-1}, *Dcalc* = 1.483 g/cm^3, 17115 reflections measured (11.35° ≤ 2Θ ≤ 130.154°), 2883 unique (R_{int} = 0.0739, R_{sigma} = 0.0566) which were used in all calculations. The final R_1 was 0.0495 (I > 2σ(I)) and wR_2 was 0.1228 (all data).

Methyl 4-bromo[2.2]paracyclophane-13-carboxylate (**14**)[25]
A two necked round bottom flask was charged with iron filings (67 mg, 1.2 mmol, 0.3 eq.), covered with foil, and fitted with

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dropping funnel filled with a solution of Br_2 (206 µL, 4 mmol, 1.0 eq.) in CH_2Cl_2 (20 ml) (*the stock solution*). Stock solution (2 ml) was added to the iron filings and stirred for 30 min at rt. A solution of methyl [2.2]paracyclophane-4-carboxylate (1.06 g, 4 mmol, 1.0 eq.) in dry CH_2Cl_2 (20 ml) was added. The remaining stock solution was added dropwise over 1h. The resulting mixture was stirred for 1h at rt. The mixture was washed with $Na_2S_2O_3$ (30 ml) and brine (30 ml) then dried ($MgSO_4$). The solution was filtered and the solvent was removed under reduced pressure to afford the desire product as a pale yellow solid (1.28 g, 93%).

R_f (9:1 Hex:EtOAc) 0.45

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.35 (1H, d, *J* = 1.9 Hz), 6.69 (1H, dd, *J* = 7.8, 1.9 Hz), 6.60 (1H, d, *J* = 1.9 Hz), 6.57-6.54 (3H, m), 4.43-4.37 (1H, m), 3.89 (3H, s), 3.22-3.01 (1H, m) 3.15-2.92 (6H, m)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 167.5, 142.8, 141.4, 139.2, 139.2, 136.6, 136.5, 136.2, 134.9, 134.5, 131.7, 128.6, 127.3, 51.7, 35.3, 35.0, 34.7, 33.7. Data comparable to that reported in the literature.[25]

4-Bromo-13-hydroxymethyl[2.2]paracyclophane

To a suspension of $LiAlH_4$ (84 mg, 2.2 mmol, 2.2 eq.) in THF (4 ml) was slowly added a solution of methyl 4-bromo[2.2]paracyclophane-13-carboxylate (345 mg, 1.0 mmol, 1.0 eq.) in THF (6 ml) over 10 min at rt. The reaction mixture was heated to reflux for 2h then cooled to rt. The excess hydride was destroyed by addition of 2M HCl (5 ml). The reaction mixture was filtered through celite and diluted with CH_2Cl_2 (20 ml). The aqueous layer was extracted with CH_2Cl_2 (2 x 10 ml). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (10 ml), H_2O (10 ml), brine (10 ml), and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford 4-bromo-13-hydroxymethyl[2.2]paracyclophane as a colourless solid which was used in the next reaction without further purification (315 mg, quant.).

R_f (9:1 Hex:EtOAc) 0.1

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.60 (1H, dd, *J* = 7.8, 1.9 Hz), 6.55-6.45 (4H, m), 6.39 (1H, d, *J* = 1.5 Hz), 4.71 (1H, d, *J* = 12.7 Hz), 4.38 (1H, d, *J* = 12.7 Hz), 3.40 (1H, ddd, *J* = 13.1, 10.2, 2.3 Hz), 3.17-2.97 (6H, m) 2.87 (1H, ddd, *J* = 16.7, 10.8, 5.8 Hz)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 140.4, 139.9, 139.7, 139.4, 137.4, 137.6, 135.2, 133.5, 133.4, 132.5, 132.3, 132.2, 129.2, 64.7, 35.4, 35.2, 34.5, 32.9.

4-Bromo-13-formyl[2.2]paracyclophane

To a solution of oxalyl chloride (100 µL, 1.15 mmol, 1.15 eq.) in dry CH_2Cl_2 (5 ml) at -78 °C was added DMSO (170 µL, 2.4 mmol, 2.4 eq.). The solution was stirred for 15 min. A solution of 4-bromo-13-hydroxymethyl[2.2]paracyclophane (315 mg, 1 mmol, 1 eq.) in CH_2Cl_2 (5 ml) was slowly added and stirred for a further 15 min at -78 °C. Triethylamine (696 µL, 5 mmol, 5 eq.) was added to the reaction and the solution stirred for a further 1h at -78 °C. The reaction mixture was warmed to rt and diluted with CH_2Cl_2 (10 ml) and H_2O (10 ml). The aqueous layer was extracted with CH_2Cl_2 (2 x 10 ml). The combined organic layers were washed with H_2O (20 ml), dried ($MgSO_4$) and the solvent was removed under reduced pressure. The resulting residue was separated by column chromatography eluting Hex:EtOAc 9:1 to afford the 4-bromo-13-formyl[2.2]paracyclophane as a colourless solid (290 mg, 92%).

R_f (9:1 Hex:EtOAc) 0.425

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.3 (1H, s), 7.10 (1H, d, *J* = 1.9 Hz), 6.77 (1H, dd, *J* = 7.8, 1.5 Hz), 6.63 (1H, dd, *J* = 7.8, 1.5 Hz), 6.58 (1H, d, *J* = 7.8 Hz), 6.53 (1H, d, *J* = 7.8 Hz), 6.50 (1H, d, *J* = 1.5 Hz), 4.16 (1H, ddd, *J* = 10.1, 7.3, 4.2 Hz), 3.55 (1H, ddd, *J* = 10.1, 6.3, 3.2 Hz), 3.18-2.93 (6H, m)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 190.9, 143.0, 141.8, 140.2, 138.9, 138.1, 136.9, 136.4, 136.1, 135.2, 134.0, 131.5, 128.3, 35.6, 35.1, 34.9, 30.4

HRMS (EI): *m/z* found: $[M+Na]^+$, 337.0208. $C_{17}H_{15}{}^{79}BrO$ requires $[M+Na]^+$, 337.0198.

4-Bromo[2.2]paracyclophane-4-carbaldehyde oxime (**15**)

To a solution of hydroxylamine hydrochloride (208 mg, 3 mmol, 3.0 eq.) and sodium hydroxide (124 mg, 3.1 mmol, 3.1 eq.) in ethanol (10 ml) at reflux was added a solution of 4-bromo-13-formyl[2.2]paracyclophane (315 mg, 1 mmol, 1.0 eq.) in ethanol (40 ml). The resulting mixture was heated to reflux for 30 min. Then cooled to rt and the solvent removed. The residue was dissolved in EtOAc (10 ml) and washed with H_2O (10 ml) then brine (10 ml), dried ($MgSO_4$). The solvent removed under reduced pressure to give a colourless solid that was used in the next reaction without purification (325 mg, 98%).

R_f (4/1 Hex:EtOAc) 0.15

^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 10.88 (1H, s), 8.25 (1H, s), 6.79 (1H, d, *J* = 1.6 Hz), 6.67-6.61 (3H, m), 6.59 (1H, dd, *J* = 7.7, 1.6 Hz), 6.55(1H, d, *J* = 7.4 Hz), 3.72 (1H, ddd, *J* = 17.0, 13.0, 3.3 Hz), 3.38 (1H, m), 3.03-2.95 (6H,m)

^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 148.4, 141.7, 139.2, 138.1, 137.6, 135.6, 135.5, 135.2, 133.7, 132.3, 132.1, 130.6, 125.3, 34.4, 34.3, 33.9, 31.5.

HRMS-EI: *m/z* found: $[M+Na]^+$, 352.0307. $C_{17}H_{16}{}^{79}BrNO$ requires $[M+Na]^+$, 352.0313.

4-Bromo-13-amino[2.2]paracyclophane (**16**)[35]

A mixture of 4-bromo[2.2]paracyclophane-4-carbaldehyde oxime (165 mg, 0.5 mmol, 1.0 eq.) and Koser's reagent (272 mg, 0.7 mmol, 1.4 eq.) in DMSO (1 ml) was stirred at rt for 30 min and then heated at 80 °C for 1h. Sodium hydroxide (28 mg, 0.7 mmol, 1.4 eq.) was added and heating continued for further 1.5h. The mixture was cooled to rt, H_2O (1 ml) was added. The aqueous phase was extracted with EtOAc (2 x 20 ml). The combined organic layer was washed with H_2O (20 ml), dried ($MgSO_4$) and the solvent was removed under reduced pressure. The resulting residue was purified by column chromatography (eluting Hex:EtOAc 9:1) to afford the 4-bromo-13-amino[2.2]paracyclophane as a pale yellow solid (98 mg, 65%).

R_f (4/1 Hex:EtOAc) 0.525

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.83 (1H, d, *J* = 1.8 Hz), 6.47 (1H, dd, *J* = 17.7, 1.5 Hz), 6.43 (1H, d, *J* = 7.6 Hz), 6.40 (1H, d, *J* = 7.6 Hz), 6.10 (1H, dd, *J* = 7.8, 1.8 Hz), 5.70 (1H, d, *J* = 1.8 Hz), 3.69 (1H, ddd, *J* = 14.1, 9.7, 2.4 Hz), 3.33 (1H, ddd, *J* = 13.8, 10.3, 2.4 Hz), 3.13-3.00 (2H, m), 2.95-2.83 (4H, m)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 147.1, 141.1, 140.7, 138.3, 135.5, 135.5, 135.3, 132.8, 123.6, 123.2, 122.6, 121.2, 35.0, 34.8, 33.2, 31.6
HRMS-EI: *m/z* found: $[M+H]^+$, 302.0554. $C_{16}H_{16}{}^{79}BrN$ requires $[M+H]^+$, 302.0539.
Data comparable to that reported in the literature.[35]

4-Nitro[2.2]paracyclophane[26]
To a solution of [2.2]paracylophane (4.0 g, 19.2 mmol, 1.0 eq.) in CH_2Cl_2 (380 ml) at 0 °C was added H_2SO_4 (95%; 4.31 ml, 76.9 mmol, 4.0 eq.) and HNO_3 (70%; 2.29 ml, 38.5 mmol, 2.0 eq.). The mixture was allowed to warm to rt overnight. The reaction mixture was decanted onto ice, leaving any dark orange tar in reaction vessel. The biphasic mixture was stirred for 15 min. and the layers separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 ml). The combined CH_2Cl_2 layers were dried ($MgSO_4$) and concentrated. Crude mixture purified by silica gel chromatography (Hex:EtOAc 4:1) to give the title compound as a yellow powder (4.4 g, 91%).
R_f (4:1 Hex:EtOAc) 0.67
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.22 (1H, d, *J* = 1.8 Hz), 6.79 (1H, dd, *J* = 7.9, 1.8 Hz), 6.63 (2H, dd, *J* = 7.8, 2.4 Hz), 6.57 (2H, ddd, *J* = 14.0, 7.8, 1.7 Hz), 6.48 (1H, dd, *J* = 7.8, 1.8), 4.03 (1H, ddd, *J* = 13.2, 9.5, 1.9 Hz), 3.24-3.04 (6H, m), 2.90 (1H, ddd, *J* = 13.2, 9.9, 7.2 Hz).
Data comparable to that reported in the literature.[26]

4-Bromo-13-nitro[2.2]paracyclophane
A dropping funnel covered in foil was charged with Br_2 (0.25 ml, 5.0 mmol, 1.3 eq.) and CH_2Cl_2 (10 ml) (*the stock solution*). A suspension of iron filings (0.02 g, 0.4 mmol, 0.1 eq.) and 2 ml of the stock solution was stirred at rt for 1 h. A solution of 4-nitro[2.2]paracyclophane (1.0 g, 4.0 mmol, 1.0 eq.) in CH_2Cl_2 (15 ml) was added. The remaining stock solution was added dropwise over 1 h. The resulting mixture was stirred for 1 h at rt then heated to reflux for 5 h. The mixture was washed with $Na_2S_2O_3$ (30 ml) and brine (30 ml) then dried ($MgSO_4$). The solution was filtered and the solvent was removed under reduced pressure to afford the desire product as a pale yellow solid (0.93 g, 70%).
R_f (4:1 Hex:EtOAc) 0.4
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.57 (1H, d, *J* = 1.8 Hz), 6.77 (1H, dd, *J* = 7.8, 1.8 Hz), 6.71 (1H, d, *J* = 1.6 Hz), 6.65-6.61 (2H, m), 6.59 (1H, dd, *J* = 7.8, 1.7 Hz), 4.38 (1H, ddd, *J* = 13.7, 9.6, 4.1 Hz), 3.67 (1H, ddd, *J* = 13.7, 9.9, 4.1 Hz), 3.20-3.03 (6H, m).

4-Bromo-13-amino[2.2]paracyclophane (**16**)[35]
A solution of 4-bromo-13-nitro[2.2]paracyclophane (1.1 g, 3.32 mmol, 1.0 eq.) in EtOH (25 ml) and H_2O (25 ml) was stirred for 1 h at rt. Fe powder (2.23 g, 39.87 mmol, 12.0 eq.) was added and the suspension heated to reflux. Concentrated HCl (8 ml) was added dropwise over 10 min. The suspension was stirred at this temperature for a further 300 minutes then cooled to rt. The suspension was poured into a mixture of ice and sat. $NaHCO_3$ (50 ml). The aqueous layer was extracted with EtOAc (3 x 30 ml). Filtration of the suspension occasionally helped the work up. The organic layers were dried ($MgSO_4$), and concentrated under reduced pressure. The resulting residue was purified by column chromatography (eluting Hex:EtOAc 9:1) to afford the 4-bromo-13-amino[2.2]paracyclophane as a pale yellow solid (0.76 g, 76%).
Data the same as outlined above.

4-(4-Bromo[2.2]paracyclophan-13-yl)morpholine (**17**)
A mixture of 4-bromo-13-amino[2.2]paracyclophane (75.51 mg, 0.25 mmol, 1.0 eq.), bis(2-bromoethyl)ether (70 mg, 0.3 mmol, 1.2 eq.) and K_2CO_3 (76 mg, 0.55 mmol, 2.2 eq.) in DMF (2.5 ml) was heated to 80 °C for 12 hours. The mixture was cooled to rt, then partitioned between CH_2Cl_2 (5 ml) and H_2O (5 ml). The organic layer was removed and aqueous layer was extracted with CH_2Cl_2 (3 x 5 ml). The combined organic layers were dried ($MgSO_4$) and the solvent was removed. The resulting residue was separated by column chromatography eluting Hex:EtOAc 6:1 to afford 4-(4-bromo[2.2]paracyclophan-13-yl)morpholine as a pale yellow solid (58 mg, 62%).
R_f (4:1 Hex:EtOAc) 0.55
^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.57 (1H, m), 6.54 (2H, m), 6.51 (1H, d, *J* = 7.6 Hz), 6.30 (1H, dd, *J* = 7.6, 1.4 Hz), 5.93 (1H, d, *J* = 1.2 Hz), 3.93-3.85 (4H, m), 3.74-3.57 (2H, m), 3.11-2.83 (10H, m)
^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 152.4, 141.0, 140.3, 139.1, 136.1, 135.7, 135.4, 132.0, 131.5, 128.3, 123.5, 119.5, 67.1, 53.0, 35.7, 35.3, 34.8, 32.1
HRMS-EI: *m/z* found: $[M+H]^+$, 372.0950. $C_{20}H_{22}{}^{79}BrNO$ requires $[M+H]^+$, 372.0958.

4-(4-Bromo[2.2]paracyclophan-13-yl)piperidine (**18**)
A mixture of 4-bromo-13-amino[2.2]paracyclophane (100 mg, 0.33 mmol, 1.0 eq.), 1,5-dibromopentane (54 µl, 92 mg, 0.40 mmol, 1.2 eq.) and K_2CO_3 (101 mg, 0.73 mmol, 2.2 eq.) in DMF (4 ml) was heated to 80 °C for 12 hours. The mixture was cooled to rt, then partitioned between CH_2Cl_2 (5 ml) and H_2O (5 ml). The organic layer was removed and aqueous layer was extracted with CH_2Cl_2 (3 x 5 ml). The combined organic layers were dried ($MgSO_4$) and the solvent was removed. The resulting residue was separated by column chromatography eluting Hex:EtOAc 6:1 to afford 4-(4-bromo[2.2]paracyclophan-13-yl)piperidine as a pale yellow solid (122 mg, 68%).
^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 6.62 (1H, s), 6.56 (2H, s), 6.51 (1H, d, *J* = 7.5 Hz), 6.27 (1H, d, *J* = 7.5 Hz), 5.97 (1H, s), 3.76-3.72 (1H, m), 3.65-3.61 (1H, m), 3.12-3.06 (1H, m), 3.05-2.97 (2H, m), 2.96-2.81 (8H, m), 1.78 (4H, quint, *J* = 5.1 Hz), 1.57-1.52 (2H, m)
^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 153.4, 140.7, 139.8, 139.2, 135.6, 135.1, 131.7, 127.4, 123.5, 119.3, 54.0, 35.6, 35.3, 34.7, 32.0, 26.0, 24.5
HRMS-EI: *m/z* found $[M+H]^+$, 370.1162. $C_{21}H_{24}BrN$ requires $[M+H]^+$ 370.1170.

4-(4-Diphenylphosphinyl[2.2]paracyclophan-13-yl)morpholine (**20**)
A solution of *t*-BuLi (1.6M in hexanes; 148 µl, 0.24 mmol, 2.2 eq.) was added dropwise to a solution of 4-(4-bromo[2.2]paracyclophan-13-yl)morpholine (40 mg, 0.11 mmol, 1.0 eq.) in THF (10 ml) at -78 °C. The resulting clear

orange solution was stirred at -78 °C for 25 min. Chlorodiphenylphosphine (30 µl, 33 mg, 0.15 mmol, 1.4 eq.) was slowly added. The resulting mixture was warmed to rt overnight. The reaction was quenched by the addition of H_2O (30 µl), and filtered through a small pad of silica. The solvent was evaporated and the resulting residue was purified by column chromatography (eluting Hex:EtOAc 9:1) to afford 4-(4-diphenylphosphinyl[2.2]paracyclophan-13-yl)morpholine as a colourless solid (24 mg, 52%).

R_f (4:1 Hex:EtOAc) 0.575

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.35-7.18 (10H, m), 6.59 (1H, d, *J* = 7.6 Hz), 6.55-6.48 (2H, m), 6.37 (1H, dd, *J* = 7.6, 1.7 Hz), 5.90 (1H, dd, *J* = 8.0, 1.7 Hz), 5.66 (1H, d, *J* = 1.6 Hz), 4.22-4.17 (2H, m), 4.06-4.01 (2H, m), 3.61-3.54 (2H, m), 3.05-2.83 (7H, m), 2.81-2.68 (3H, m)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 143.9, 143.8, 140.7, 140.6, 140.6, 138.5, 137.8, 136.7, 136.6, 136.3, 135.9, 135.7, 134.0, 133.4, 133.4, 133.3, 132.9, 132.7, 131.6, 129.4, 128.7, 128.6, 128.3, 128.3, 128.2, 127.1, 119.2, 67.3, 67.2, 52.7, 35.1, 35.0, 33.8, 33.7

^{31}P NMR (202 MHz, $CDCl_3$): δ (ppm) -5.9

HRMS-EI: *m/z* found: $[M+O+H]^+$, 494.2243. $C_{32}H_{32}NOP$ requires $[M+O+H]^+$, 494.2171.

4-(4-Dicyclohexanylphosphinyl[2.2]paracyclophan-13-yl)morpholine (**21**)

A solution of *t*-BuLi (1.6M in hexanes; 148 µl, 0.24 mmol, 2.2 eq.) was added dropwise to a solution of 4-(4-bromo[2.2]paracyclophan-13-yl)morpholine (40 mg, 0.11 mmol, 1.0 eq.) in THF (10 ml) at -78 °C. The mixture was stirred at -78 °C for 25 min. To the resulting clear orange solution, chlorodicyclohexylphosphine (34 µl, 36 mg, 0.15 mmol, 1.4 eq.) was slowly added. The resulting mixture was warmed to rt overnight. The reaction was quenched with H_2O (30 µl), and filtered through a small pad of silica. The solvent was removed and the resulting residue was separated by column chromatography (Hex:EtOAc 15:1) to afford the 4-(4-dicyclohexanylphosphinyl[2.2]paracyclophan-13-yl)morpholine as an oil (5 mg, 8%).

R_f (4:1 Hex:EtOAc) 0.55

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.74-6.70 (1H, m), 6.61-6.52 (3H, m), 6.36 (1H, dd, *J* = 7.6, 1.2 Hz), 5.67 (1H, d, *J* = 1.2 Hz), 4.22-4.17 (1H, m), 3.95-3.85 (4H, m), 3.57-3.50 (1H, m), 3.20-3.14 (1H, m), 3.05-2.73 (9H, m), 2.23-0.96 (22H, m).

4-(4-Dicyclohexanylphosphinyl[2.2]paracyclophan-13-yl)morpholine borane complex (**22**)

A solution of *t*-BuLi (1.6M in hexanes; 148 µl, 0.24 mmol, 2.2 eq.) was added dropwise to a solution of 4-(4-bromo[2.2]paracyclophan-13-yl)morpholine (40 mg, 0.11 mmol, 1.0 eq.) in THF (10 ml) at -78 °C. The mixture was stirred at -78 °C for 25 min. To the resulting clear orange solution, chlorodicyclohexylphosphine (34 µl, 36 mg, 0.15 mmol, 1.4 eq.) was slowly added. The resulting mixture was warmed to rt overnight. A solution of borane in THF (267 µL, 0.267 mmol, 2.5 eq.) was added to the reaction mixture and stirred for 3 h at rt. The solvent was removed and the resulting residue was purified by column chromatography (Hex:EtOAc 15:1) to afford the borane complex as a colourless solid (17 mg, 33%).

R_f (25:1 Tol:EtOAc) 0.70

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.59 (1H, d, *J* = 7.6 Hz), 6.50-6.49 (2H, m), 6.38-6.36 (2H, m), 5.62 (1H, d, *J* = 1.2 Hz), 4.12-4.05 (1H, m), 3.95-3.85 (4H, m), 3.47-3.44 (1H, m), 3.05-2.73 (9H, m), 2.23-0.96 (24H, m)

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 151.4, 144.8, 144.7, 140.5, 136.5, 136.3, 135.3, 135.1, 133.9, 133.8, 132.7, 131.2, 130.3, 126.7, 117.5, 67.1, 52.5, 36.3, 36.2, 35.9, 35.8, 35.4, 35.3, 34.4, 34.2, 33.4, 33.2, 32.4, 32.2, 31.6, 31.4, 29.8, 29.0, 28.9, 28.5, 28.0, 27.9, 27.8, 27.7, 27.6, 27.5

^{31}P NMR (202 MHz, $CDCl_3$): δ (ppm) -4.12.

4-(4-Diphenylphosphinyl[2.2]paracyclophan-13-yl)piperidine (**23**)

t-BuLi (1.6M solution in hexanes; 1.32 ml, 2.11 mmol, 2.2 eq.) was added dropwise over 10 min. to a solution of 4-(4-bromo[2.2]paracyclophan-13-yl)piperidine (355 mg, 0.96 mmol, 1.0 eq.) in THF (10 ml) at -78 °C. The resulting yellow solution was stirred for 40 min. at -78 °C. Chlorodiphenylphosphine (0.17 ml, 0.96 mmol, 1.0 eq.) was added dropwise to the resulting solution over 5 min. The solution was warmed to rt overnight. The reaction mixture was quenched by the addition of H_2O (15 µl). The resulting organic phase was separated and aqueous phase was extracted with EtOAc (3 × 15 ml), the combined organics dried ($MgSO_4$) and concentrated under reduced pressure to yield a yellow residue. Purification by column chromatography on silica gel (CH_2Cl_2:Pentane 13:87) gave a white powder of 4-(4-Diphenylphosphinyl[2.2]paracyclophan-13-yl)piperidine (85 mg, 19%).

^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) 7.38-7.19 (10H, m), 6.58 (1H, d, *J* = 7.5 Hz), 6.55 (1H, dd, *J* = 7.6, 1.3 Hz), 6.52 (1H, dd, *J* = 7.6, 5.3 Hz), 6.33 (1H, dd, *J* = 7.4, 1.5 Hz), 5.91 (1H, dd, *J* = 7.8, 1.4 Hz), 5.67 (1H, d, *J* = 1.4 Hz), 3.64-3.63 (2H, m), 3.03 (1H, ddd, *J* = 13.0, 10.1, 4.0 Hz), 2.96-2.70 (10H, m), 2.10-2.06 (2H, m), 1.92-1.85 (2H, m), 1.64 (2H, quint, *J* = 5.7 Hz), 1.46-1.32 (2H, m), 0.97-0.90 (1H, m)

^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 152.8, 144.0, 140.7, 140.3, 138.6, 137.6, 136.6, 135.9, 135.8, 133.9, 133.2, 133.1, 132.7, 131.8, 129.1, 128.4, 128.0, 126.2, 119.0, 53.8, 35.0, 33.6, 33.5, 26.2, 24.7

^{31}P NMR ($CDCl_3$, 202 MHz) δ (ppm) -6.57

HRMS-EI: *m/z* $[M+H]^+$, 476.2502. $C_{33}H_{34}NP$ requires $[M+H]^+$ 476.2507.

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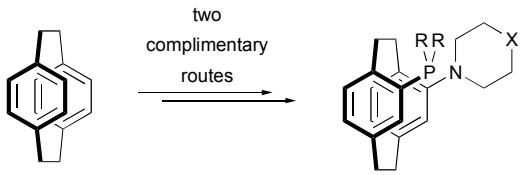

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X = O, CH_2

We have synthesized three *pseudo-gem* [2.2]paracyclophane-derived *P,N*-ligands and report preliminary activity studies for the amination of aryl bromides and chlorides.