Synthesis of a Hexagonal Nanosized Macrocyclic Fluorophore with Integrated Endotopic Terpyridine Metal-Chelation Sites

Paul N. W. Baxter*[a, b]

Abstract: A rigid nanosized hexagonal phenylethynyl cyclophane **5** has been prepared, which incorporates two 2,2′:6′,2″-terpyridines as integral structural units, for the purpose of binding metal ions. Macrocycle **5** was obtained by a 14-step synthesis in an overall yield of 11 %, and was characterised by spectroscopic techniques. The efficiency and ease of all transformations, and the relatively enhanced yield of the final macrocyclisation suggests that the entire synthetic pathway should be amenable to scale-up. Cyclophane **5** possesses four bulky triisopropylsilyl(TIPS)-protected ethyne substituents which serve a dual role. Firstly, they solubilise the structure thereby facilitating purification and subsequent handling. Secondly, they enable post-synthetic modification in which additional functionality may be attached to the periphery of the ring. Significantly, **5** was found to be a fluorescent chromophore, and may therefore potentially function as a new sensory platform for the detection of metal ions and H-bond donating biological substrates. The structurally well-defined nanosized morphology of **5**, coupled with its interesting spectroscopic properties, supports the expectation that **5** and related architectures will attain a wealth of future applications within the developing fields of nanochemistry and nanoscience.

Keywords: alkynes · cyclooligomerisation · cyclophanes · macrocyclic ligands · nanostructures

Introduction

Over the past two decades, synthetic organic chemistry has witnessed a gradual paradigm shift, from that of the discovery of new reactions and the synthesis of novel small molecules, to the property-targeted generation of new materials with specific functions.[1a–d] Nowhere has the quest for organic molecules with new properties been more intense than in the developing fields of nanoscience and nanochemistry. Nanosized organic molecules may exhibit novel physicochemical properties not expressed by their component parts, and in this respect constitute a reservoir of structurally and functionally complex modules from which the forthcoming generation of 21st century smart materials may be expected to emerge.[2a–h]

The relationship between morphology and function becomes especially significant when the size of a molecule enters into the nanoscopic domain. However, the preservation of molecular shape necessitates the employment of relatively rigid structural units that can collectively resist opposing external forces that would otherwise lead to solvophobic collapse of the desired superstructure. In recent years, phenylethynyl precursor units have been demonstrated to serve as particularly effective rigidifying building blocks for the conservation of nanomolecular shape.[3a–c] The latter approach has thus far enabled the creation of a structurally diverse variety of organic phenylethynyl-nanoarchitectures, such as hyperbranched and dendritic macromolecules,[4a–d] catenanes,[5] linear oligomers and nanowires,[6a–f] folded spiral[7a–e] and double helical structures,[8a,b] cages[9a,b] and macrocycles.[10a–n] With respect to phenylethynyl nanoarchitecture generation, large macrocyclic structures have attracted a considerable proportion of interest, due primarily to their ready synthetic access. The latter class of organic materials are particularly attractive candidates for nanochemical applications as they display useful functional properties, such as for example, host–guest inclusion,[11a–d] liquid crystallinity,[12a–c] solid-state porosity.[13a,b]

To expand and diversify the potential range of utilisable properties of nanosized phenylethynyl macrocycles, an especially intriguing avenue of investigation would be to endow such scaffolds with the ability to bind metal ions and complexes, either internally or externally on the outer surface of the ring.[14a–l] As well as the above-mentioned properties, rigid molecular edifices of this type may be envisioned to exhibit electrochemical, photochemical, magnetic, optical, catalytic, mechanical and sensory abilities for example.[15a–f]

In relation to the latter considerations, earlier work focused upon the syntheses of *ortho*-conjugated phenylethynyl macrocycles of the tetrabenzodehydroannulene-type, which incor-

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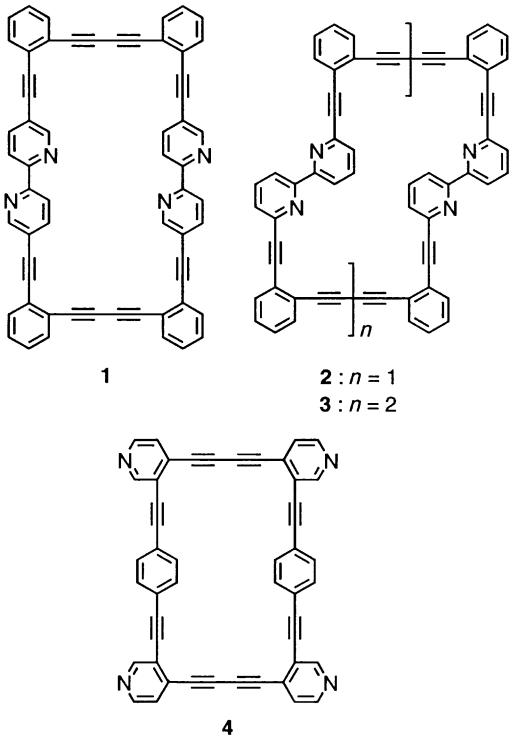
porated 2,2′-bipyridine **1**–**3**,[14f,h] and pyridine **4**,[14a] moieties for the purpose of metal ion coordination. It was anticipated that interaction of the pyridine nitrogen atoms with metal ions would initiate electron density perturbations within the



1 **2** : $n = 1$ **3** : $n = 2$ **4**

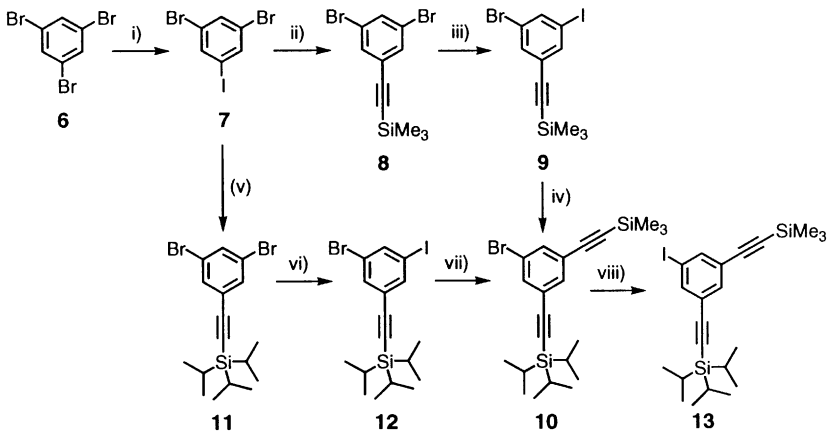
conjugated macrocyclic framework, which would in turn be accompanied by a change in properties such as redox potentials and fluorescence emission energies and intensities. The ligands would thus function as cation sensors, affording for example visual spectroscopic signal outputs characteristic of specific metals. Detailed ion-binding studies revealed that **1**–**4** did in fact function as fluorescence ion sensors, with **1** giving a chromogenic response specific to Zn^{2+} ions, **2** and **3** undergoing fluorescence quenching with Cu^{2+} and **4** displaying fluorescence quenching specific to Hg^{2+} and $PdCl_2$. It was concluded from the latter studies that subtle structural changes in the macrocyclic framework resulted in dramatic changes in ion-binding selectivity and sensory signal output. Prior to the above investigations, it was anticipated that a rigidified, nanosized macrocycle with endotopic metal ion binding sites of increased denticity, may display particularly efficient guest inclusion and therefore sensory properties, due to the inherent preorganisation of the ring. Significantly, a sensory platform of this type may be expected to signal the presence of for example, nanosized hydrogen bond donor biomolecular guests as well as cations.

Nanophane **5** (see Scheme 3) is an example of an organic molecule that embodies the latter structural requirements. The cyclophane comprises two endotopic oligopyridine 2,2′:6′,2″-terpyridine units incorporated into a conjugated hexagonal phenylethynyl macrocyclic scaffold of nanoscopic dimensions. Towards the goal of creating nanosized sensory materials, the following account describes the successful synthesis of **5**, and its characterisation by spectroscopic methods.

Results and Discussion

Nanophane **5** was constructed by using a synthetic strategy that involved three main stages. In the first stage, the phenylethynyl vertex precursor **13** was prepared from the commercially available **6** in five steps (Scheme 1). The second stage required the synthesis of the metal ion binding module **24** in seven steps starting from the commercially available **14** (Scheme 2). Finally, **13** and **24** were combined to provide the macrocycle half unit **25**, which was subsequently deprotected and cyclised to give **5** (Scheme 3).

Synthesis of vertex precursor 13: During initial attempts to prepare **13**, it was anticipated that the required unsymmetrical 1,3,5-R,R′,R″-phenyl substitution pattern could be achieved by using sequential Sonogashira coupling reactions directly upon **6** (Scheme 1). However, the 1:1 stoichiometric reaction between trimethylsilylacetylene (TMSA) in the presence of CuI and $[PdCl_2(PPh_3)_2]$ catalysts and in Et_3N/toluene solutions over a range of temperatures yielded only statistical mixtures of unreacted **6**, **8**, di- and tri-ethynylated products which were difficultly separable by column chromatography on a large scale. Pure **8** was therefore obtained by way of **7**. The reaction between **7**[16] and TMSA in Et_3N with CuI and $[PdCl_2(PPh_3)_2]$ catalysts proceeded very selectively at ambient temperature to afford **8**[17a, b] in 93% yield after work-up. Treatment of **8** with one equivalent of *n*BuLi in Et_2O at low



Scheme 1. Synthesis of phenylethynyl vertex precursor **13**. i) a) 1 equiv *n*BuLi, −78 °C, Et_2O, 3 h, b) I_2/Et_2O (84%); ii) $[PdCl_2(PPh_3)_2]$, CuI cat., TMSA, Et_3N, 20 °C, 4d (93%); iii) a) 1 equiv *n*-BuLi, −78 °C, Et_2O, 2 h, b) ICH_2CH_2I/Et_2O (95%); iv) $[PdCl_2(PPh_3)_2]$, CuI cat., TIPSA, Et_3N, 20 °C, 4.5 days (99%); v) as in (iv), (97%); vi) as in (i), (71%); vii) as in (ii), (72%); viii) as in (iii), (93%).

temperature, followed by quenching the phenyllithium intermediate with 1,2-diiodoethane provided **9** in 95% yield after chromatographic purification. The oil **9** was then coupled with triisopropylsilylacetylene (TIPSA) in Et_3N with CuI and $[PdCl_2(PPh_3)_2]$ catalysts, to give **10** as a colourless, very viscous oil in near quantitative yield after work-up.

In parallel to the above synthesis, an alternative preparative pathway to **10** was also investigated, in which the TIPSA group was introduced prior to the TMSA. Thus coupling of **7** with TIPSA under conditions similar to that used for the generation of **8**, afforded **11**[18] in 97% yield after chromatography. Selective monolithiation of **11** followed by addition of iodine to the intermediate phenyllithium, employing conditions identical those used for the generation of **7**, gave **12** in 71% yield. The reaction of **12** with TMSA in Et_3N in the presence of CuI and $[PdCl_2(PPh_3)_2]$ catalysts furnished **10** in 72% isolated yield. The syntheses of **12** and its subsequent conversion to **10** proceeded in significantly lower yields compared to the previously described route using **9**. The inferior yields of **12** were partly attributable to a side reaction in which proteo-debromination of the phenyl ring was occurring. Both the production of **12** and its reaction with TMSA involved considerably less clean transformations than those encountered during the syntheses of **9** and its conversion to **10**. Laborious and repeated column chromatographic purifications of **12**, and the **10** prepared from **12**, were thus required to obtain products that were clean by ^1H NMR spectroscopy. These latter findings demonstrated that the optimal preparative route to **10** required the introduction of the TIPSA group in the final synthetic step.

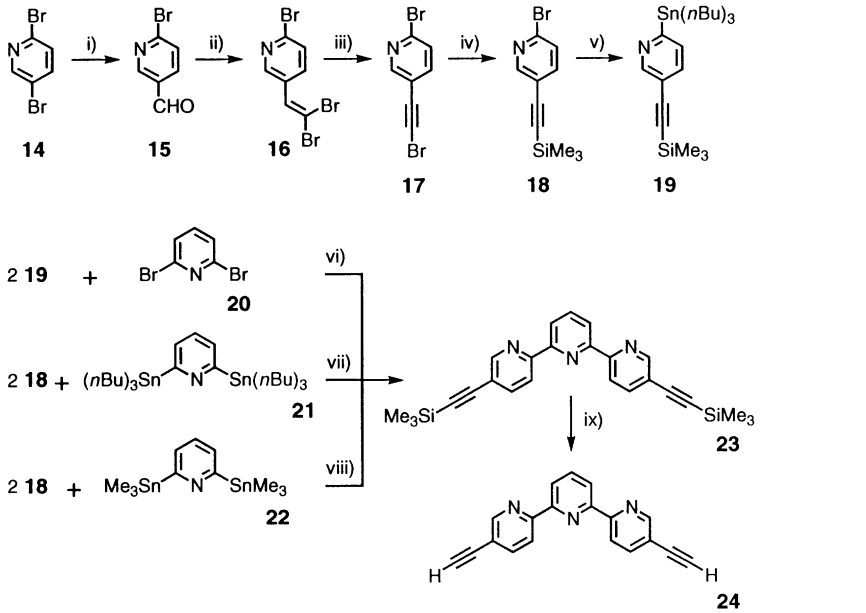
It was anticipated that later in the reaction sequence, the utilisation of iodophenyl **13**, rather than **10**, would afford bis-coupling product **25** in higher yield and greater purity.[19] Bromophenyl **10** was therefore lithiated and iodinated at low temperature in Et_2O, to furnish **13** in 93% yield after work-up.

Synthesis of terpyridine precursor 24: The terpyridine precursor **24** was synthesised by way of a seven-step pathway starting from **14** (Scheme 2). Thus **14** was converted to **15**[20a,b] and the latter compound subjected to a Corey–Fuchs reaction, in which a CH_2Cl_2 solution of CBr_4 was added to a mixture of **15**, PPh_3 and excess Et_3N in CH_2Cl_2 at $-78\,^\circ C$. The dibromovinylpyridine **16** was subsequently obtained in 93% yield after work-up. The reaction was found to be very exothermic when conducted at ambient temperature, affording considerably reduced yields of **16**. Dibromovinylpyridine **16** was dehydrobrominated with NaOMe in MeOH solution at ambient temperature, to give **17** in 85% yield after chromatography and recrystallisation.[21a–c] Bromoethyne **17** was then found to undergo a selective halogen–lithium exchange at the ethynyl-bromine with one equivalent of *n*BuLi in Et_2O at $-78\,^\circ C$. Subsequent quenching of the reaction with $ClSiMe_3$ at low temperature, provided **18** in 88% yield after work-up.

At this point it was envisioned that the tri-*n*-butylstannylpyridine **19** would also serve as a useful synthon in the preparation of ethynyl-oligopyridine molecular scaffolds.[22a, b] Accordingly, the latter stannylpyridine was synthesised by treatment of a solution of **18** in THF at $-78\,^\circ C$ with one equivalent of *n*BuLi, followed by quenching of the pyridyllithum intermediate with $ClSn(nBu)_3$, affording **19** in 68% isolated yield. Scaling-up the lithiation–stannylation reaction to quantities of **18** of greater than 2 g did however result in the isolation of significantly reduced yields of **19**. With both oligopyridine building blocks **18** and **19** in hand, exploratory investigations could then be undertaken in order to determine the optimal conditions for the generation of **23**.

To assess the potential utility of **19** for the construction of oligopyridine units, initial approaches to the synthesis of terpyridine **23** focused upon the palladium catalysed Stille reaction between **19** and 2,6-dibromopyridine **20**.[23] Thus the reaction between **19** and **20** in the presence of $Pd(PPh_3)_4$ catalyst and LiCl in toluene yielded 59% of **23**. However, reduced yields of **23** resulted when the reaction was carried out using ≥ 0.5 g of **19**.

Distannylpyridines have been described in the literature as serving as ideal substrates for the rapid and convergent construction of oligopyridines.[23, 24a–e] It was originally anticipated therefore that the use of distannylpyridines **21**[25] and **22**[24c, 26a, b] may provide the most convergent and economic



Scheme 2. Synthesis of 5,5″-diethynyl-terpyridine precursor **24**. i) a) 1 equiv *n*BuLi, $-78\,^\circ C$, Et_2O, 1.75 h, b) DMF (80%); ii) a) PPh_3, Et_3N, CH_2Cl_2, b) CBr_4/CH_2Cl_2, $-70\,^\circ C$, 1 h (93%); iii) NaOMe/MeOH, $20\,^\circ C$, 48 h (85%); iv) a) 1 equiv *n*BuLi, $-78\,^\circ C$, Et_2O, 2.5 h, b) $ClSiMe_3$ (88%); v) a) 1 equiv *n*BuLi, $-78\,^\circ C$, THF, 1 h, b) $ClSn(nBu)_3$ (68%); vi) $[Pd(PPh_3)_4]$ cat., LiCl, toluene, $120\,^\circ C$, 24 h (59%); vii) as in (vi), (35%); viii) as in (vi), (53%); ix) TBAF/THF, THF/distilled H_2O, $20\,^\circ C$, 6 h (93%).

method of access to **23**. However, reaction of a 2:1 stoichiometric ratio of **18**:**21** under conditions identical to those used for the preparation of **23** from **19** and **20**, resulted in the formation of **23** in a much reduced isolated yield of 35%. Reaction scale-up caused further reductions in the yield of **23**. When the coupling was performed using **22** in place of **21**, an enhancement in the isolated yield of **23** to 53% occurred, and the reaction was also found to be amenable to scale-up.

The above results therefore suggest that the syntheses of terpyridine **23** from **19** + **20**, and **18** + **21**, are limited primarily to small-scale preparations. The most reliable approach to **23**, using the pyridine building blocks described above is thus the reaction between **18** and **22**.

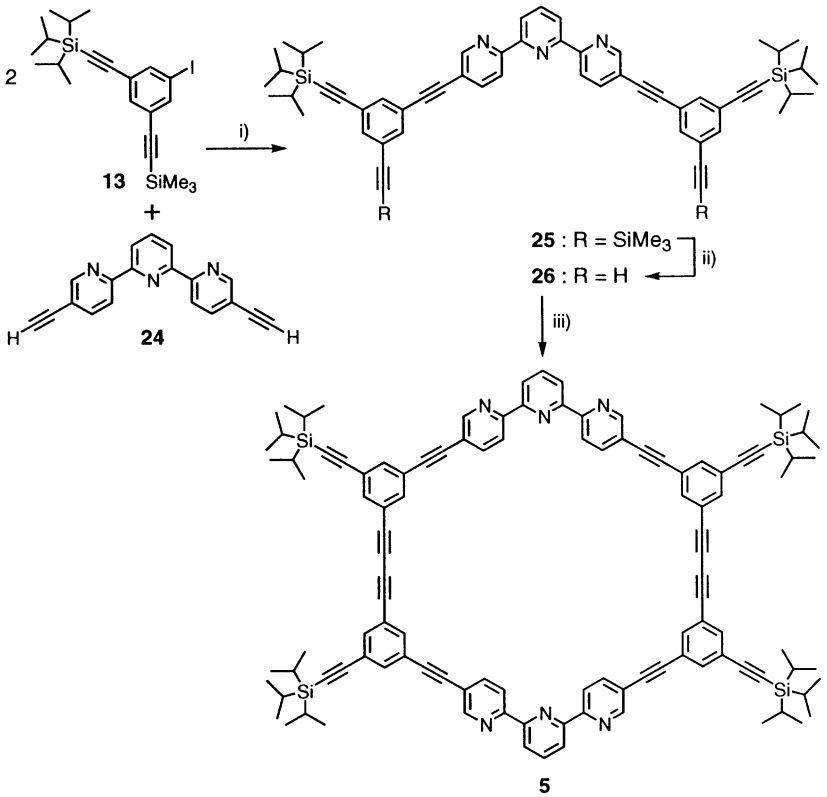
Treatment of an aqueous THF solution of **23** with TBAF, resulted in smooth desilylation to afford the deprotected diethynyl-terpyridine precursor **24**, in 93% yield.[27]

Synthesis of cyclophane 5: The third and final stage in the construction of **5** comprised the combination of the central metal ion-binding terpyridine unit **24** with **13** to give the macrocycle precursor half-unit **25** (Scheme 3). Selective deprotection of **25** followed by a metal-mediated oxidative dimerisation was then expected to result in the formation of **5**.

Thus the ambient temperature reaction between a 2:1 stoichiometric combination of **13** and **24**, in the presence of $[PdCl_2(PPh_3)_2]$ and CuI catalysts and Et_3N in pyridine,[28] afforded **25** in 62% yield. When the reaction was performed with $[PdCl_2(dppf)]\cdot CH_2Cl_2$ (dppf = 1,1′-bis(diphenylphosphino)ferrocene) in place of $[PdCl_2(PPh_3)_2]$, a product of inferior purity was obtained, which required repeated chromatography to remove the contaminants. As a result, a slightly lower yield of 59% **23** was isolated from the reaction catalysed by $[PdCl_2(dppf)]\cdot CH_2Cl_2$.

Preferential deprotection of trimethylsilylethynes in the presence of triisopropylsilylethynes has been reported to be achievable with aqueous hydroxide.[29] Surprisingly, when a solution of **25** in THF at 0 °C was treated with two equivalents of aqueous KOH in MeOH, and the reaction stirred at ambient temperature for 24 h, the deprotection occurred unselectively with the formation of a statistical distribution of four desilylated products as judged by TLC analysis. The desired terpyridine **26** was subsequently isolated from the reaction in a disappointing 53% yield. An alternative selective deprotection methodology was therefore attempted, which involved the use of K_2CO_3 in MeOH.[30] Thus, the reaction between a 1:1 stoichiometric mixture of **25** and powdered K_2CO_3 in 2:1 Et_2O/MeOH at ambient temperature resulted in the clean formation of **26**, which was isolated in 97% yield. Having successfully obtained the precursor diethynyl-terpyridine **26** in sufficient quantities, its macrocyclisation reaction to **5** could finally be undertaken.[31]

Previous ethyne-coupling macrocyclisations to give **1**–**3** suggested that cyclisation yields were strongly influenced by the coordination of the precursor bipyridine subunits to the CuCl catalyst, and/or other copper species generated therefrom.[14f,h] For example, macrocyclisations performed under similar conditions afforded a much lower yield of **2** (9–13%), compared to that of **1** (34%). The yield disparity between **1** and **2** was consistent with the presence of ion-templating phenomena.[32]



Scheme 3. Synthesis of macrocycle **5** from precursors **13** and **24**. i) $[PdCl_2(PPh_3)_2]$, CuI cat., pyridine, 20 °C, 7d (62%); ii) K_2CO_3, MeOH/Et_2O, 20 °C, 14 h (97%); iii) a) excess $[Cu_2(OAc)_4]$, pyridine, 20 °C, 8 h addition, then b) seven days, 20 °C (39%).

In the light of the aforementioned observations, it was therefore decided to explore the effectiveness of the Eglinton/Galbraith ethyne coupling protocol in the cyclisation of **26**, which uses $[Cu_2(OAc)_4]$ in place of CuCl.[31] The $[Cu_2(OAc)_4]$ would be expected to exhibit a significantly lower ambient temperature coordination affinity towards **26** compared to that of CuCl, and $Cu^{I/II}$ species generated from the latter. The relatively high concentration of $[Cu_2(OAc)_4]$ compared to **26** would also disfavour the generation of $[Cu(\mathbf{26})_2]^{I/II}$ type complexes.

Rewardingly, the cyclisation of **26** under medium/high dilution conditions in degassed pyridine with an excess of $[Cu_2(OAc)_4]$, proceeded without problem, affording a respectable 39% yield of **5** after work-up. A ^1H NMR and

MALDI TOF mass spectral analysis of the toluene extract of the crude reaction product prior to chromatographic purification, showed that **5** was formed in >50% yield. The MALDI TOF mass spectrum also exhibited three small higher mass peaks assignable to the presence of a small quantity of tetrameric, pentameric and hexameric cyclic or linear oligomers.[33]

Characterisation of nanophane 5: The structure of the product isolated from the $[Cu_2(OAc)_4]$-mediated coupling of **26** was established to be that of the macrocyclic architecture **5** (Scheme 3) on the basis of mass spectrometric, infrared, ^{1}H and ^{13}C NMR spectroscopic studies.

The FAB mass spectrum of the coupling product recorded in 10–20% $CF_3COOH/CHCl_3$ displayed a single isotope cluster peak centred at *m*/z 1681, in the *m*/*z* range of 350–2040, corresponding exactly to that calculated for the $[M^+ + H]$ isotopic envelope of macrocycle **5**. This structural assignment was further substantiated by a high-resolution FAB mass spectrometric measurement of the $[M^+ + H]$ isotopic envelope, which confirmed the exact elemental composition of the product to be $C_{114}H_{115}N_6Si_4$ in accordance with the macrocyclic structure **5** plus one hydrogen. The ^{13}C NMR spectrum of the coupling product of **26** comprised 22 peaks, consistent with the above macrocyclic structural assignment. The chemical shifts of the six peaks at $\delta = 105.0 - 75.2$ ppm correspond to the chemically and magnetically inequivalent carbon atoms of three unsymmetrically substituted alkyne groups. The remaining 14 downfield peaks at $\delta = 155.6 - 119.7$ ppm, and the two upfield peaks at $\delta = 18.7 - 11.6$ ppm, correspond to the aromatic ring and isopropyl carbon atoms, respectively.

The ^{1}H NMR spectrum of the coupling product of **26**, was also consistent with the macrocyclic structure **5**, displaying eight resonances with the expected splitting patterns between $\delta = 9.0$ and 7.5 ppm, due to aromatic protons (Figure 1). ^{1}H–^{1}H COSY and ROESY measurements also verified that it was a single compound and not a mixture of species. Peaks originating from the protons of terminal ethynes were completely absent in the ^{1}H NMR spectrum of the coupling product, lending further support for the macrocyclic identity of this compound.

Spectral assignments of **5** were made on the basis of integrations, coupling constants and comparisons with the spectra of **23**–**26**.[34]

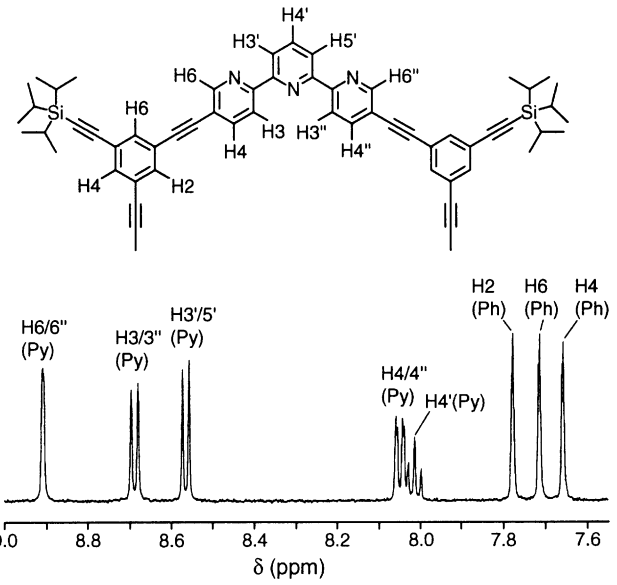


Figure 1. 500 MHz ^{1}H NMR of **5** recorded in $CDCl_2CDCl_2$ at 80 °C.

Spectroscopic properties of 5, and precursors 23–26: The UV/Vis spectra of $CHCl_3$ solutions of **23**–**26** all comprised four absorption envelopes. In the case of **25** and **26** (Figure 2), the

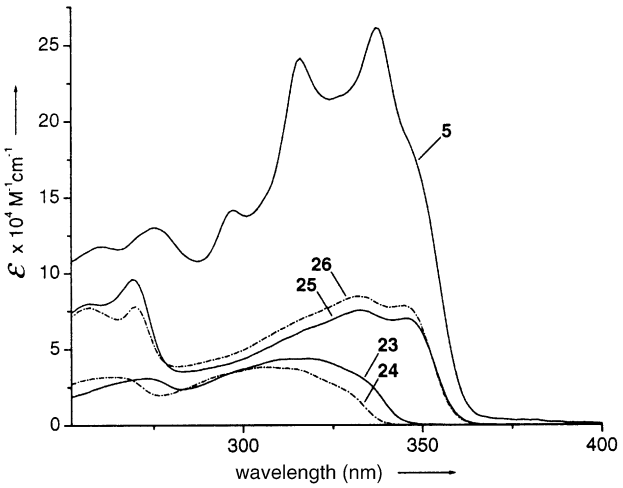


Figure 2. UV/Vis spectra of **5** and **23**–**26** in $CHCl_3$ solution at 20 °C.

two lowest energy absorptions were shifted approximately 20 to 30 nm to lower energy indicating an increased degree of conjugation within these molecules. The UV/Vis spectrum of **5** on the other hand was particularly distinctive, comprising six absorption envelopes from 261 to 348 nm (Figure 2). The absorption maxima of **5** exhibited a linear relationship between concentration and absorbance, and zero change in energies at [**5**] $\leq 1.1 \times 10^{-5}$ mol dm^{-3}, demonstrating that kinetically fast aggregation phenomena were either negligible or absent in dilute solution.

Interestingly, $CHCl_3$ solutions of macrocycle **5**, and terpyridine precursors **23**–**26** all emitted a strong purple-blue coloured fluorescence when irradiated with a UV lamp operating at 365 nm. The emission energies and intensities of all compounds remained unchanged in the presence and absence of air, showing that the excited states of **23**–**26** and **5** were insensitive to quenching by oxygen. The emission bands of the terpyridine ligands decreased in energy in the following order, **24** > **23** ≫ **25** ≈ **26** > **5** (Figure 3). The effect of the electron donating Me_3Si substituents in **23** were therefore to lower the emission energy of the conjugated terpyridine chromophore. The even greater relative decrease in the emission energy of **25**, **26** and **5** evidenced the extension of the chromophore conjugation into the peripheral phenyl rings. The fluorescence emission spectra of **25** and **26** were however, virtually identical, exemplifying the structural similarity of the excited states of these two molecules. Dilution studies

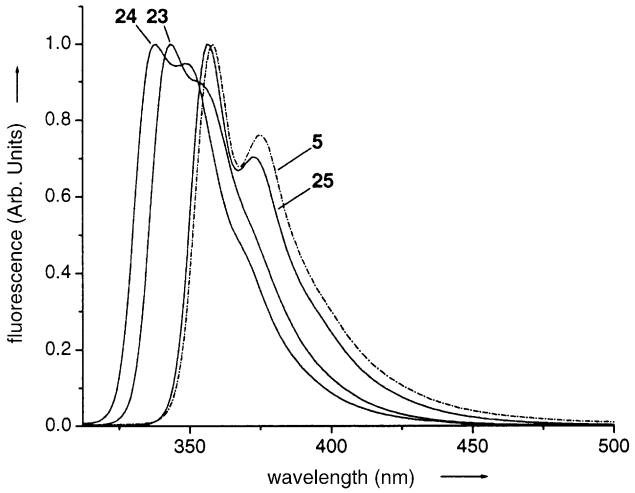


Figure 3. Normalised fluorescence emission spectra of **5** and **23**–**25** in $CHCl_3$ solution at 20 °C (300 nm excitation).

performed with $CHCl_3$ solutions of **23**–**26**, revealed that the emission energies remained constant with change in concentration below 2×10^{-5} mol dm^{-3}, showing that excited-state aggregation of these systems was absent in dilute solution. In the case of **5**, similar dilution studies demonstrated that the macrocycle was not undergoing excited-state aggregation at $[\mathbf{5}] \leq 2.9 \times 10^{-6}$ mol dm^{-3}.[35] However, the emission spectrum of a thin film of **5** comprised a broad band ($\lambda_{max} = 454$ nm) at a significantly lower energy than that of **5** in solution ($\lambda_{max} = 358$ and 375 nm), indicating that excited-state aggregation of the macrocycle was existent in the solid state.

Conclusion

The above work discloses a successful preparative strategy for the construction of a large nanosized ethynyl cyclophane, or nanophane **5**, which incorporates oligopyridine subunits for the purpose of metal ion coordination.[36] The synthesis comprised a convergent approach in which the appropriately functionalised phenylethynyl vertex **13**, and metal ion binding terpyridine **24** were independently assembled, then subsequently connected to give the macrocycle half-unit **25**. Selective deprotection of **25** to give **26**, followed by cyclisation afforded **5**, in a total of 14 steps from **6**, **14** and **22**, and in an overall yield of 11 %. Eleven of the steps proceeded in ≥ 80 % yield, and the employment of the Eglinton/Galbraith ethyne coupling protocol for the final cyclisation resulted in the isolation of a respectable 39 % yield of **5**. Furthermore, all reaction products were readily purified by conventional column chromatographic techniques. These factors collectively suggest that the entire synthetic sequence should be amenable to scale-up in order to provide gram quantities of **5**.[37]

Molecular modelling studies confirmed that **5** was a nanosized macrocyclic structure possessing a large central cavity, and with a calculated intra-terpyridyl distance of 15 Å (Figure 4).[38] Cyclophane **5** should therefore be expected to bind to a wide spectrum of guest species either by hydrogen-bonding to the terpyridyl nitrogen atoms,[39a, b] or through coordination interactions when the terpyridines are bound to metal ions. Of especial note is the fact that **5** is fluorescent when exposed to UV light. This latter physical property, coupled with potential guest inclusion abilities suggests that **5** and related structures may possibly function for example, as a new class of nanosensory materials.[40a–f]

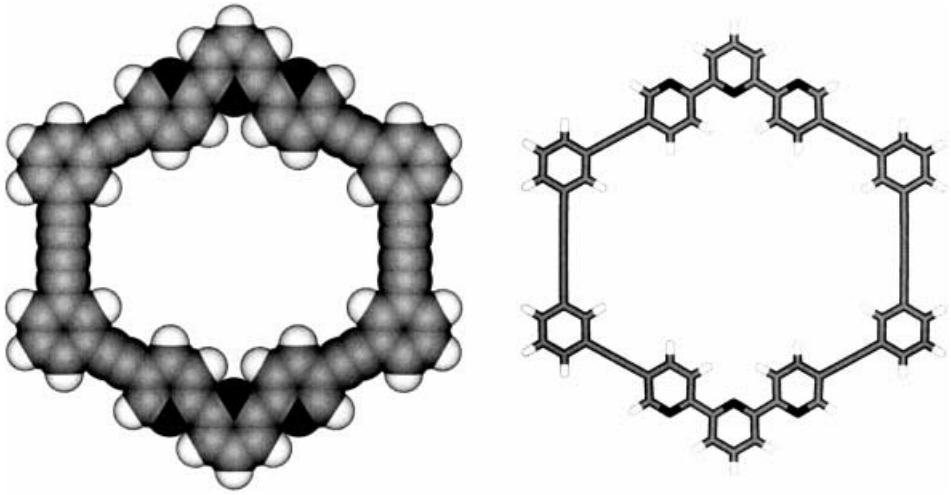


Figure 4. Energy-minimised structures of the all-planar conformation of the macrocyclic ring of **5**, without the TIPSA substituents; plan view through cavity: space-filling representation (left), stick representation (right). The minimisations were obtained by AM1 semi-empirical calculations, using SPARTAN 02 Linux/Unix, Wavefunction, Irvine CA (USA).

A design feature of particular significance is that **5** has been constructed with four outwardly projecting triisopropylsilylethynyl subunits. The latter functionality endows **5** with two important structural assets; 1) enhanced solubility in lipophilic solvents, which facilitates purification, characterisation and processing and reduces problems originating from self-aggregation phenomena, and 2) the possibility of post-synthetic-modification. In the latter case, partial or complete deprotection of the TIPS groups should enable further Sonogashira alkynyl couplings to be performed upon **5**, thereby allowing the introduction of a plethora of additional functionality, and the possibility for incorporation into larger superstructures.[41]

The synthetic approach to **5** detailed above should thus enable the creation of a palate of hybrid organic/inorganic scaffolds currently conceivable on the nanostructural hypersurface. Nanophane **5** and related structures may also be expected to contribute to the development of novel materials

with complex functional properties, within the realm of nanoscience and nanotechnology.

Experimental Section

General: Starting materials **6** and **14**, **20**, TMSA, TIPSA,[42] CuI, and $[Cu_2(OAc)_4]$ were purchased from Aldrich and used as received. The catalysts $[Pd(PPh_3)_4]$,[43] $[PdCl_2(PPh_3)_2]$,[44] $[PdCl_2(dppf)]\cdot CH_2Cl_2$,[45] were prepared according to literature procedures. Standard inert atmosphere and Schlenk techniques were employed for reactions conducted under argon. The Et_3N, toluene and pyridine solvents used in the preparation of respectively **8**, **10**, **11**, **23** and **25**, were deoxygenated by bubbling with argon for 0.5 h directly prior to use. The THF and Et_2O used in the preparation of **7**, **9**, **12**, **13**, **15**, **18** and **19** were freshly distilled off Na/benzophenone under argon. The CH_2Cl_2 solvent used in the preparation of **16** was freshly distilled off P_4O_{10} under argon. The silica used for all flash chromatography was purchased from Merck (Geduran, Silica gel Si 60, 40–60 μm). The alumina (neutral, standard activity) used in the chromatographic purification of **19** and **24** was purchased from Merck. Unless otherwise stated, all ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra at 125.8 MHz in $CDCl_3$ at 25 °C. The ^{1}H and ^{13}C NMR spectra recorded in $CDCl_3$ were referenced to the solvent peaks at $\delta = 7.26$ and 77.0 ppm, respectively. The ^{1}H and ^{13}C spectra of **5** recorded in $CDCl_2CDCl_2$ were referenced to the solvent peaks at $\delta = 6.00$ and 74.0 ppm, respectively. Intramolecular proton connectivities were determined by ^{1}H–^{1}H COSY, NOESY and ROESY NMR measurements. The fluorescence emission spectra were recorded at 20–25 °C on a Aminco, Bowman Series 2 luminescence spectrophotometer (SLM Instruments, Inc.). All fluorescence emission spectra recorded in $CHCl_3$ solution were corrected for the instrumental response. The infrared spectrum of **25** was recorded as a $CHCl_3$ evaporated thin film on a KBr disc, and that of **5** as nujol and polychlorotrifluoroethylene mulls. All the other infrared spectra were recorded as liquid thin films or KBr discs. Melting point measurements were performed on an Electrothermal Digital Melting Point apparatus calibrated with standards of known melting points. Elemental analyses were performed by the Service de Microanalyse, Institut de Chimie, Université Louis Pasteur.

(3-Bromo-5-iodophenylethynyl)trimethylsilane (9): A dried 500 mL two-necked round-bottomed flask charged with **8** (4.208 g, 1.27×10^{-2} mol), was equipped with a vacuum/argon inlet adaptor, alcohol thermometer, rubber septum and a magnetic stirrer ovoid. The flask was then evacuated and back-filled with argon four times in succession and Et_2O (125 mL), which had been freshly distilled off Na/benzophenone under argon, was added by syringe. The stirred solution was subsequently cooled to an internal temperature of −78 °C using a CO_2/acetone bath. A 1.6 M solution of *n*BuLi in hexanes (8 mL, 1.28×10^{-2} mol) was added dropwise by syringe at a rate which maintained the reaction temperature between −78 and −70 °C. During addition, the reaction solution initially became pink in colour, then changed to pale yellow and finally became almost colourless when all the *n*BuLi had been added. The reaction solution was then stirred at −78 °C for 2 h. Et_2O (25 mL) was syringed into a dried, argon-filled schlenk flask containing diiodoethane (5 g, 1.77×10^{-2} mol), and the mixture stirred until all the diiodoethane had dissolved. The diiodoethane solution was then added dropwise by syringe to the phenyllithium reaction mixture at a rate which maintained the internal temperature between −78 and −70 °C. The reaction mixture was stirred at −78 °C for a further 1 h, and was then allowed to warm to ambient temperature with continued stirring overnight. The reaction solution was extracted with distilled water (3×60 mL), and the organic layer separated, dried (anhydrous $MgSO_4$), filtered, and the Et_2O removed by distillation at ambient pressure on a water bath. The remaining oil was flash chromatographed three times on columns of silica, eluting with hexane. The product thus obtained was finally dried under dynamic vacuum (0.01 mmHg) to yield **9** (4.556g, 95%) as an odourless, colourless oil.

^{1}H NMR: $\delta = 7.797$ (t, $^4J(4,2;4,6) = 1.6$ Hz, 1H; H4), 7.731 (t, $^4J(6,2;6,4) = 1.3$ Hz, 1H; H6), 7.560 (t, $^4J(2,4;2,6) = 1.5$ Hz, 1H; H2), 0.237 ppm (s, 9H; $Si(CH_3)_3$); ^{13}C NMR: $\delta = 139.7$, 139.1, 133.9, 126.6, 122.4, 101.5, 97.6 (-C≡), 93.6 (-C≡), −0.3 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu} = 2958$ (s), 2165 (s) (C≡C), 1572 (s), 1533 (s), 1414 (s), 1397 (s), 1249 (s), 1104 (m), 893 (s), 844 (s), 760 (s), 730 (s), 670 (s), 654 cm^{-1} (m); EIMS ($CHCl_3$): *m*/*z* (%): 380 (44) [M^+], 365 (100) [$M^+ - \{CH_3\}$]; HRMS (EI, $CHCl_3$, [M^+]) calcd for $C_{11}H_{12}BrISi$: 377.8936; found: 377.8932.

1-Bromo-3-[2-(1-triisopropylsilylethynyl)]-5-[2-(1-trimethylsilylethynyl)]-benzene (10), (from 9): Et_3N (30 mL), which had been bubbled with argon, was added by syringe to a mixture of **9** (4.239 g, 1.12×10^{-2} mol) and $[PdCl_2(PPh_3)_2]$ (0.060 g, 8.55×10^{-5} mol) under an atmosphere of argon. After the mixture had been stirred for a few minutes, TIPSA (2.087 g, 1.14×10^{-2} mol) and a solution of CuI (0.060g, 3.15×10^{-4} mol) in degassed Et_3N (10 mL) were added consecutively by syringe. The mixture was stirred at ambient temperature for 4.5 days in the absence of light, during which time a copious cream precipitate formed. All solvent was subsequently removed under reduced pressure on a water bath and the residue worked-up and purified as described for **8** above. After flash chromatography on silica with hexane eluant, the product was dried under dynamic vacuum to yield **10** (4.778 g, 99%) as a colourless odourless oil.

^{1}H NMR: $\delta = 7.539$ (d, 2H; H2/6), 7.482 (t, 1H; H4), 1.120 (s, 21H; $CH(CH_3)_2$), 0.244 ppm (s, 9H; $Si(CH_3)_3$); ^{13}C NMR: $\delta = 134.6$, 134.4, 133.9, 125.4, 125.0, 121.6, 104.4 (-C≡), 102.5 (-C≡), 96.6 (-C≡), 93.2 (-C≡), 18.6 ($CH(CH_3)_2$), 11.2 ($CH(CH_3)_2$), −0.2 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu} = 2958$ (s), 2943 (s), 2892 (s), 2865 (s), 2156 (m) (C≡C), 2063 (w) (C≡C), 1550 (s), 1250 (s), 975 (s), 882 (s), 860 (s), 843 (s), 676 cm^{-1} (s); EIMS ($CHCl_3$): *m*/*z* (%): 434 (5) [M^+], 419 (5) [$M^+ - CH_3$], 391 (100) [$M^+ - \{CH(CH_3)_2\}$], 363 (22) [$M^+ - \{CH(CH_3)_2\} - 2\{CH_2\}$], 349 (25) [$M^+ - \{CH(CH_3)_2\} - 3\{CH_2\}$], 335 (49) [$M^+ - \{CH(CH_3)_2\} - 4\{CH_2\}$], 321 (63) [$M^+ - \{CH(CH_3)_2\} - 5\{CH_2\}$]; HRMS (EI, $CHCl_3$, [M^+]) calcd for $C_{22}H_{33}BrSi_2$: 432.1304; found: 432.1301.

(3,5-Dibromophenylethynyl)triisopropylsilane (11): Et_3N (25mL), which had been bubbled with argon, was added by syringe to a mixture of **7** (4.170 g, 1.15×10^{-2} mol), TIPSA (2.103 g, 1.15×10^{-2} mol) and $[PdCl_2(PPh_3)_2]$ (0.093 g, 1.32×10^{-4} mol) under an atmosphere of argon. A solution of CuI (0.083 g, 4.36×10^{-4} mol) in degassed Et_3N (4 mL) was then added by syringe and the mixture stirred at ambient temperature for four days in the absence of light. All solvent was subsequently removed under reduced pressure on a water bath and the residue worked-up and purified as described for **8** above. After flash chromatography on silica with hexane eluant, the product was dried under dynamic vacuum to yield **11** (4.681 g, 97%) as a colourless oil.

^{1}H NMR ($CDCl_3$, 500 MHz, 21 °C): $\delta = 7.608$ (t, $^4J(4,2;4,6) = 1.8$ Hz, 1H; H4), 7.531 (d, 2H; H2/6), 1.117 ppm (s, 21H; $CH(CH_3)_2$); ^{13}C NMR: $\delta =$ 134.0, 133.4, 126.8, 122.5, 103.6 (-C≡), 94.3 (-C≡), 18.6 ($CH(CH_3)_2$), 11.2 ppm ($CH(CH_3)_2$); IR: $\tilde{\nu} = 2958$ (s), 2942 (s), 2890 (s), 2864 (s), 2163 (m) (C≡C), 1578 (s), 1540 (s), 1462 (s), 1418 (s), 1400 (s), 996 (s), 896 (s), 882 (s), 855 (s), 748 (s), 680 (s), 670 (s), 651 cm^{-1} (s); EIMS ($CHCl_3$): *m*/*z* (%): 416 (22) [M^+], 373 (100) [M^+-$\{CH(CH_3)_2\}$], 345 (22) [$M^+ - \{CH(CH_3)_2\} - 2\{CH_2\}$], 331 (21) [$M^+ - \{CH(CH_3)_2\} - 3\{CH_2\}$], 317 (37) [$M^+ - \{CH(CH_3)_2\} - 4\{CH_2\}$], 303 (43) [$M^+ - \{CH(CH_3)_2\} - 5\{CH_2\}$]; HRMS (EI, $CHCl_3$, [M^+]) calcd for $C_{17}H_{24}Br_2Si$: 414.0014; found: 414.0008.

(3-Bromo-5-iodophenylethynyl)triisopropylsilane (12): The preparation of **12** was performed in a similar way to that of **9** described above. Thus Et_2O (25 mL, freshly distilled from Na/benzophenone under argon) was syringed into a dried argon filled flask containing **11** (1.730 g, 4.16×10^{-3} mol), and the stirred solution cooled to −78 °C. A 1.6 M solution of *n*BuLi in hexanes (2.6 mL, 4.16×10^{-3} mol) was added dropwise by syringe at a rate which maintained the reaction temperature between −78 and −70 °C. The resulting pale brown solution was then stirred at −78 °C for 2 h. A solution of iodine (1.06 g, 8.35×10^{-3} mol) in Et_2O (10 mL, freshly distilled from Na/benzophenone under argon) was prepared in a dried argon filled schlenk, and subsequently added dropwise by syringe to the lithiophenyl solution at a rate which maintained the reaction temperature at −70 °C. The reaction was then stirred at −78 °C for 2 h, and allowed to warm to ambient temperature overnight with continued stirring. Work-up, purification and drying as described for **9** above, yielded **12** (1.358 g, 71%) as a colourless oil.

^{1}H NMR: $\delta = 7.797$ (t, $^4J(4,2;4,6) = 1.7$ Hz, 1H; H4), 7.723 (t, $^4J(6,2;6,4) = 1.3$ Hz, 1H; H6), 7.558 (t, $^4J(2,4;2,6) = 1.6$ Hz, 1H; H2), 1.116 ppm (m, 21H; $CH(CH_3)_2$); ^{13}C NMR: $\delta = 139.5$, 139.1, 134.0, 126.9, 122.4, 103.5, 94.2 (-C≡), 93.7 (-C≡), 18.6 ($CH(CH_3)_2$), 11.2 ppm ($CH(CH_3)_2$); IR: $\tilde{\nu} = 2955$ (s), 2941 (s), 2923 (s), 2890 (s), 2864 (s), 2161 (m) (C≡C), 2063 (w) (C≡C), 1573 (s), 1533 (s), 1462 (s), 1414 (s), 1397 (s), 884 (s), 855 (s), 730 (s), 678 (s), 670 cm^{-1} (s); EIMS ($CHCl_3$): *m*/*z* (%): 464 (10) [M^+], 421 (100) [M^+ –

{$CH(CH_3)_2$}], 393 (23) [M^+ – {$CH(CH_3)_2$} – 2{CH_2}], 379 (20) [M^+ – {$CH(CH_3)_2$} – 3{CH_2}], 365 (37) [M^+ – {$CH(CH_3)_2$} – 4{CH_2}], 351 (48) [M^+ – {$CH(CH_3)_2$} – 5{CH_2}]; HRMS (EI, $CHCl_3$, [M^+]) calcd for $C_{17}H_{24}BrISi$: 461.9875; found: 461.9865.

1-Bromo-3-[2-(1-triisopropylsilylethynyl)]-5-[2-(1-trimethylsilylethynyl)]-benzene (10), (from 12): Et_3N (15mL), which had been bubbled with argon, was added by syringe to a mixture of **12** (1.356 g, 2.93×10^{-3} mol), [$PdCl_2(PPh_3)_2$] (0.030 g, 4.27×10^{-5} mol) and CuI (0.031 g, 1.63×10^{-4} mol) under an atmosphere of argon. The mixture was stirred for a few minutes, then a solution of TMSA (0.321g, 3.27×10^{-3} mol) in degassed Et_3N (4 mL) was added by syringe. The mixture was subsequently stirred at ambient temperature for four days in the absence of light. The reaction was worked up as described for **8** above. The crude product was purified by twice flash chromatographing on silica with hexane as eluant, followed by drying under dynamic vacuum to yield **10** (0.909 g, 72%) as a colourless viscous oil.

1-Iodo-3-[2-(1-triisopropylsilylethynyl)]-5-[2-(1-trimethylsilylethynyl)]-benzene (13): The preparation of **13** was performed in an identical way to that of **9** described above. Thus a 1.6 M solution of *n*BuLi in hexanes (7.0 mL, 1.12×10^{-2} mol) was added dropwise by syringe to a stirred solution of **10** (4.587 g, 1.06×10^{-2} mol) in Et_2O (140 mL), which had been previously cooled to $-78\,^{\circ}C$. The addition was conducted at a rate which maintained the reaction temperature below $-70\,^{\circ}C$. The pale yellow lithiophenyl solution was stirred at $-78\,^{\circ}C$ for 2 h, then a solution of diiodoethane (6.00 g, 2.13×10^{-2} mol) in Et_2O (50 mL) added by syringe at a rate which ensured the reaction temperature remained between -78 and $-70\,^{\circ}C$. The reaction solution was stirred at $-78\,^{\circ}C$ for 1.5 h, then allowed to warm to ambient temperature with continued stirring, and worked up as described for **9** above. The crude product was twice flash chromatographed on silica with hexane as eluant, and the isolated **13** dried under dynamic vacuum (0.01 mmHg) first at 70 °C to remove any excess diiodoethane, then at ambient temperature, to give **13** (4.710 g, 93%) as a pale yellow viscous oil.

^{1}H NMR: δ = {(7.741 (t, ^4J = 1.5 Hz, 1H), 7.732 (t, ^4J = 1.6 Hz, 1H)); H2/6}, 7.509 (t, ^4J(4,2;4,6) = 1.4 Hz, 1H; H4), 1.113 (s, 21H; $CH(CH_3)_2$), 0.237 ppm (s, 9H; $Si(CH_3)_3$); ^{13}C NMR: δ = 140.3, 140.1, 134.4, 125.3, 125.0, 104.2, 102.3 (-C≡), 96.6 (-C≡), 93.1 (-C≡), 92.9 (-C≡), 18.6 ($CH(CH_3)_2$), 11.2 ($CH(CH_3)_2$), –0.2 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu}$ = 2958 (s), 2942 (s), 2865 (s), 2155 (m) (C≡C), 2062 (w) (C≡C), 1542 (s), 1250 (s), 973 (s), 857 (s), 843 (s), 816 (s), 678 cm^{-1} (s); EIMS ($CHCl_3$): *m*/*z* (%): 480 (6) [M^+], 465 (4) [M^+ – CH_3], 437 (100) [M^+ – {$CH(CH_3)_2$}], 409 (21) [M^+ – {$CH(CH_3)_2$} – 2{CH_2}], 395 (25) [M^+ – {$CH(CH_3)_2$} – 3{CH_2}], 381 (42) [M^+ – {$CH(CH_3)_2$} – 4{CH_2}], 367 (60) [M^+ – {$CH(CH_3)_2$} – 5{CH_2}]; HRMS (EI, $CHCl_3$, [M^+]) calcd for $C_{22}H_{33}ISi_2$: 480.1166; found: 480.1157.

2-Bromo-5-(2,2-dibromovinyl)pyridine (16): A dried 500 mL two-necked round-bottomed flask charged with **15** (8.00 g, 4.30×10^{-2} mol) and PPh_3 (23.00g, 8.77×10^{-2} mol) was equipped with a vacuum/argon inlet adaptor, alcohol thermometer, rubber septum and a magnetic stirrer ovoid. The flask was then evacuated and back-filled with argon four times in succession and CH_2Cl_2 (200 mL), which had been freshly distilled off P_4O_{10} under argon, was added by syringe. The stirred solution was subsequently cooled to an internal temperature of $-78\,^{\circ}C$ using a CO_2/acetone bath, and Et_3N (6mL) added by syringe. During cooling, the **15** re-precipitated from solution. CH_2Cl_2 (40 mL) was syringed into a dried, argon-filled schlenk flask containing CBr_4 (29.00 g, 8.74×10^{-2} mol), and the mixture stirred until all solids had dissolved. The CBr_4 solution was then added dropwise by syringe to the suspension of **15** at a rate which maintained the internal temperature between -78 and $-70\,^{\circ}C$. The cream coloured mixture was stirred at $-70\,^{\circ}C$ for a further 1 h, and was then allowed to warm to 10 °C with continued stirring over 4 h. All solvent was removed by distillation on a water bath at ambient pressure, and the remaining honey coloured syrup twice flash chromatographed on silica, eluting with CH_2Cl_2. The product thus obtained was dried under dynamic vacuum to yield **16** (13.70 g, 93%) as a hard cream coloured solid. The solid could be further purified by sublimation under vacuum at 80 °C/0.01 mmHg whereby it formed jagged platy needles resembling shards of broken glass. M.p. 67.7 – 69.4 °C.

^{1}H NMR: δ = 8.439 (dd, ^4J(6,4) = 2.6 Hz, 1H; H6), 7.829 (dd, ^3J(4,3) = 8.4 Hz, ^4J(4,6) = 2.5 Hz, 1H; H4), 7.498 (d, ^3J(3,4) = 8.5 Hz, 1H; H3), 7.403 ppm (s, 1H; C*H*=CBr_2); ^{13}C NMR: δ = 149.9, 141.6, 137.2, 132.3, 130.7, 127.8, 93.3 ppm; EIMS ($CHCl_3$): *m*/z (%): 341 (100) [M^+], 262 (42) [M^+ – Br], 181 (75) [M^+ – 2Br]; HRMS (FAB, [M^+ + H]) calcd for $C_7H_5Br_3N$: 339.7972; found: 339.7965.

2-Bromo-5-[2-(1-bromoethynyl)]pyridine (17): Sodium metal (0.914 g, 3.97×10^{-2} mol) was cut into strips and added in portions to absolute MeOH (60 mL) over 2 h. During addition, the vigorous exothermic reaction was periodically moderated by immersion of the reaction flask in an ice bath when necessary. When the addition was complete, the mixture was stirred until all the sodium had reacted, and the resulting solution allowed to cool to ambient temperature. The latter NaOMe solution was then added dropwise to a solution of **16** (13.47 g, 3.94×10^{-2} mol) in MeOH (250 mL), and the mixture stirred at ambient temperature for 48 h. During stirring, a copious white suspension slowly formed. The progress of the reaction could be monitored by TLC (Silica plate/CH_2Cl_2 eluant). The solvent was then removed by distillation under reduced pressure on a water bath at 45 °C, and the residue partitioned between distilled water (200 mL) and CH_2Cl_2 (200 mL), and the aqueous phase extracted with further CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (anhydrous $MgSO_4$), filtered and the solvent removed by distillation under ambient pressure on a water bath. The crude product was then twice flash chromatographed on columns of silica, eluting with CH_2Cl_2. The last quarter of the **17** co-eluted with a contaminant, which could however be removed upon two successive recrystallisations from MeOH. The combined yield was further dried under dynamic vacuum to furnish **17** (8.741g, 85%) as cream coloured crystals. The product could also be additionally purified by sublimation under vacuum (80 °C/0.01 mmHg) to give a white crystalline solid. M.p. 132.8 – 133.5 °C.

^{1}H NMR: δ = 8.436 (d, ^4J(6,4) = 2.3 Hz, 1H; H6), 7.570 (dd, ^3J(4,3) = 8.2 Hz, ^4J(4,6) = 2.4 Hz, 1H; H4), 7.450 ppm (d, ^3J(3,4) = 8.3 Hz, 1H; H3); ^{13}C NMR: δ = 152.9, 141.5, 140.9, 127.7, 119.2, 75.8 (-C≡), 55.3 ppm (-C≡); IR: $\tilde{\nu}$ = 2199 (s) (C≡C), 1543 (s), 1459 (s), 1447 (s), 1354 (s), 1091 (s), 1022 (s), 832 cm^{-1} (s); EIMS: *m*/*z* (%): 261 (100) [M^+], 180 (54) [M^+ – Br], 101 (27) [M^+ – 2Br]; HRMS (FAB, [M^+ + H]) calcd for $C_7H_4Br_2N$: 259.8710; found: 259.8714.

2-Bromo-5-[2-(1-trimethylsilylethynyl)]pyridine (18): Compound **18** was prepared by a halogen/lithium exchange reaction in an identical way to that described above for the preparation of **9**. Thus a 1.6 M solution of *n*BuLi in hexanes (30 mL, 4.80×10^{-2} mol) was added dropwise by syringe to a stirred suspension of **17** (12.15 g, 4.66×10^{-2} mol) in Et_2O (400 mL), which had been previously cooled to $-78\,^{\circ}C$. The addition was conducted at a rate which maintained the reaction temperature below $-70\,^{\circ}C$. After the addition was complete, the resulting orange solution was stirred at $-78\,^{\circ}C$ for 2.5 h, during which time a suspended solid re-precipitated. Chlorotrimethylsilane (8.56g, 7.88×10^{-2} mol) was then added by syringe at a rate which ensured that the reaction temperature remained below $-70\,^{\circ}C$. The stirred mixture was maintained at $-78\,^{\circ}C$ for 1 h, allowed to warm to $-35\,^{\circ}C$ and held at this temperature for 1 h, then left to warm to ambient temperature overnight. The mixture was subsequently extracted with distilled water (3 × 70 mL), and the ether layer dried (anhydrous $MgSO_4$), filtered, and the solvent removed by distillation on a water bath at ambient pressure. The remaining yellow solid was flash chromatographed on silica, eluting with 10% Et_2O/hexane. The product co-eluted with a contaminant which could, however, be removed upon successive extraction of the eluate with 5 M aqueous HCl (2 × 100 mL) and distilled water (100 mL). The organic phase was then dried (anhydrous $MgSO_4$), filtered and the solvent removed by distillation under reduced pressure on a water bath. The product was finally dried under dynamic vacuum to yield **18** (10.36 g, 88%) as a pungent smelling soft white crystalline solid. M.p. 71.0 – 71.9 °C.

^{1}H NMR: δ = 8.425 (dd, ^4J(6,4) = 2.4 Hz, ^5J(6,3) = 0.8 Hz, 1H; H6), 7.572 (dd, ^3J(4,3) = 8.2 Hz, ^4J(4,6) = 2.4 Hz, 1H; H4), 7.427 (dd, ^3J(3,4) = 8.2 Hz, ^5J(3,6) = 0.8 Hz, 1H; H3), 0.254 ppm (s, 9H; $Si(CH_3)_3$); ^{13}C NMR: δ = 152.8, 141.2, 140.9, 127.5, 119.5, 100.0 (-C≡), 99.9 (-C≡), -0.2 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu}$ = 2162 (C≡C) (s), 1569 (s), 1449 (s), 1362 (s), 1251 (s), 1225 (s), 1084 (s), 1016 (s), 862 (s), 841 (s), 826 (s), 759 (s), 679 cm^{-1} (s); EIMS: *m*/*z* (%): 255 (25) [M^+], 240 (100) [M^+ – CH_3]; HRMS (FAB, [M^+ + H]) calcd for $C_{10}H_{13}BrNSi$: 254.0001; found: 254.0003.

2-(Tri-*n*-butylstannyl)-5-[2-(1-trimethylsilylethynyl)]pyridine (19): A 1.6 M solution of *n*BuLi in hexanes (5.2 mL, 8.32×10^{-3} mol) was added dropwise by syringe to a stirred solution of **18** (2.008g, 7.90×10^{-3} mol) in THF (40 mL), which had been previously cooled to $-85\,^{\circ}C$ (liq. N_2/hexane bath).

The addition was conducted at a rate which maintained the reaction temperature below −78 °C. After the addition was complete, the resulting orange-brown solution was stirred at −78 °C for 1 h, then $ClSn(nBu)_3$ (4.20 g, 1.29×10^{-2} mol) added by syringe at a rate which maintained the reaction temperature below −70 °C. The resulting pale yellow-orange solution was stirred at −78 °C for 1 h, and allowed to warm to ambient temperature overnight with continued stirring. Most of the THF was removed by distillation under reduced pressure on a water bath and the residue partitioned between distilled water and Et_2O, and extracted with distilled water (2×60 mL). The organic phase was dried (anhydrous $MgSO_4$), filtered, the solvent removed by distillation on a water bath at ambient pressure, and the remaining oil chromatographed on a short column of alumina, eluting with 5% Et_2O/hexane. The product thus obtained was dried under dynamic vacuum to yield **19** (2.504g, 68%) as a colourless oil.

^{1}H NMR: $\delta = 8.776$ (dd, $^4J(6,4) = 2.1$ Hz, $^5J(6,3) = 0.8$ Hz, 1H; H6), 7.527 (dd, $^3J(4,3) = 7.6$ Hz, $^4J(4,6) = 2.1$ Hz, 1H; H4), 7.346 (dd, $^3J(3,4) = 7.7$ Hz, $^5J(3,6) = 0.9$ Hz, 1H; H3), 1.536 (pentet, $^3J(2,1/2,3) = 7.8$ Hz, 6H; $CH_2CH_2CH_2CH_3$), 1.310 (sextet, $^3J(3,2/3,4) = 7.4$ Hz, 6H; $CH_2CH_2CH_2CH_3$), 1.111 (t, $^3J(1,2) = 8.1$ Hz, 6H; $CH_2CH_2CH_2CH_3$), 0.866 (t, $^3J(4,3) = 7.3$ Hz, 9H; $CH_2CH_2CH_2CH_3$), 0.252 ppm (s, 9H; $Si(CH_3)_3$); ^{13}C NMR: $\delta = 174.4$, 152.6, 135.6, 131.2, 118.2, 102.3 (-C≡), 97.6 (-C≡), 29.0, 27.3, 13.7, 9.9, −0.1 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu} = 2956$ (s), 2925 (s), 2871 (s), 2851 (s), 2160 (s) (C≡C), 1464 (s), 1446 (s), 1250 (s), 1022 (s), 866 (s), 843 (s), 760 cm^{-1} (s); HRMS (FAB, $[M^+ + H]$) calcd for $C_{22}H_{40}NSiSn$: 462.1947; found: 462.1945.

5,5″-bis-[2-(1-trimethylsilylethynyl)]-2,2′:6′,2″-terpyridine (23), (From 18+22): Toluene (24 mL), which had been bubbled with argon, was added by syringe to a mixture of **18** (1.816g, 7.14×10^{-3} mol), $[Pd(PPh_3)_4]$ (0.090 g, 7.79×10^{-5} mol) and anhydrous LiCl (1.820 g, 4.29×10^{-2} mol) under an atmosphere of argon. 2,6-bis(trimethylstannyl)pyridine **22** (1.331g, 3.29×10^{-3} mol) was then added by syringe, and the mixture stirred in a bath at 118 °C for 28 h. All solvent was removed under reduced pressure on a water bath and the residue flash chromatographed on a column of silica, eluting first with CH_2Cl_2. The product **23** could be visualised on the column as a purple-blue fluorescent band upon irradiation with a UV lamp operating at 365 nm. When the **23** had descended halfway down the column, the silica above the product was removed, and the **23** eluted from the column with 1% MeOH/CH_2Cl_2. If the latter procedure is not adhered to, then the impurities and **23** co-elute. The product thus obtained was briefly ultrasonicated in ice-cold MeCN (3 mL), filtered under vacuum, washed with ice-cold MeCN (2 mL), and air-dried to yield **23** (0.742 g, 53%) as a white powder. M.p. 226.9–228.6 °C.

^{1}H NMR: $\delta = 8.751$ (d, $^4J(6,4;6'',4'') = 1.4$ Hz, 2H; H6/6″), 8.551 (d, $^3J(3,4;3'',4'' = 8.2$ Hz, 2H; H3/3″), 8.452 (d, $^3J(3',4';5',4') = 7.9$ Hz, 2H; H3′/5′), 7.953 (t, $^3J(4',3';4',5') = 7.8$ Hz, 1H; H4′), 7.896 (dd, $^3J(4,3;4'',3'') = 8.2$ Hz, $^4J(4,6;4'',6'') = 2.0$ Hz, 2H; H4/4″), 0.297 (s, 18H; $Si(CH_3)_3$); ^{13}C NMR: $\delta = 154.9$, 154.7, 152.1, 139.7, 138.0, 121.6, 120.2, 101.8 (-C≡), 99.2 (-C≡), −0.2 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu} = 2957$ (s), 2160 (C≡C) (s), 1584 (s), 1543 (s), 1445 (s), 1250 (s), 1022 (s), 865 (s), 843 (s), 818 (s), 757 (s), 660 (s), 645 cm^{-1} (s); UV/Vis ($CHCl_3$): λ_{max} (ε) = 274 (30778), 298sh (35746), 312 (43496), 318 nm (43653 M^{-1}cm^{-1}); fluorescence emission ([**23**] = 2.3×10^{-6} mol dm^{-3} in $CHCl_3$, 300 nm excitation): $\lambda_{max} = 343$, 353 nm; EIMS: *m*/*z* (%): 425 (76) $[M^+]$, 410 (100) $[M^+ - CH_3]$; elemental analysis calcd (%) for $C_{25}H_{27}N_3Si_2$: C 70.54, H 6.39, N 9.87; found: C 70.50, H 6.37, N 10.03.

5,5″-Bis-[2-(1-trimethylsilylethynyl)]-2,2′:6′,2″-terpyridine (23), (From 19+20): Compound **23** was prepared and purified using a procedure identical to that described above. Thus from the reaction between **19** (0.505 g, 1.09×10^{-3} mol), **20** (0.107 g, 4.52×10^{-4} mol), $[Pd(PPh_3)_4]$ (0.017 g, 1.47×10^{-5} mol) and anhydrous LiCl (0.153 g, 3.61×10^{-3} mol), stirred and heated at 120 °C in toluene (5 mL) for 24 h, was isolated **23** (0.114 g, 59%).

5,5″-Diethynyl-2,2′:6′,2″-terpyridine (24): TBAF (2 mL, 1.0 M solution in THF, 2×10^{-3} mol) was added to a stirred solution of **23** (0.400 g, 9.40×10^{-4} mol) in THF (20 mL) and distilled water (0.5 mL). The solution was then stirred at ambient temperature in the absence of light for 6 h. All solvent was removed under reduced pressure at ambient temperature and the residue partitioned between distilled water (40 mL) and Et_2O (60 mL) and extracted with further distilled water (4×20 mL). The organic phase was then dried (anhydrous $MgSO_4$), filtered, and the solvent removed on a water bath at atmospheric pressure. The remaining solid was chromatographed on alumina, eluting with CH_2Cl_2. The solid thus obtained was briefly ultrasonicated in MeOH (3 mL), filtered under vacuum, washed with MeOH (2 mL) and finally air dried to yield **24** (0.245 g, 93%) as a white fibrous solid. M.p. 182.0–182.8 °C.

^{1}H NMR: $\delta = 8.793$ (dd, $^4J(6,4;6'',4'') = 2.1$ Hz, $^5J(6,3;6'',3'') = 0.7$ Hz, 2H; H6/6″), 8.580 (dd, $^3J(3,4;3'',4'') = 8.2$ Hz, $^5J(3,6;3'',6'') = 0.8$Hz, 2H; H3/3″), 8.466 (d, $^3J(3',4';5',4') = 7.7$ Hz, 2H; H3′/5′), 7.970 (t, $^3J(4',3';4',5') = 7.9$ Hz, 1H; H4′), 7.936 (dd, $^3J(4,3;4'',3'') = 8.2$ Hz, $^4J(4,6;4'',6'') = 2.1$ Hz, 2H; H4/4″), 3.314 ppm (s, 2H; H-C≡C); ^{13}C NMR: $\delta = 155.3$, 154.6, 152.2, 139.9, 138.0, 121.7, 120.3, 119.2, 81.4 (-C≡), 80.7 ppm (-C≡); IR: $\tilde{\nu} = 3242$ (H-C≡) (s), 2107 (C≡C) (w), 1587 (s), 1544 (s), 1478 (s), 1444 (s), 1369 (s), 1024 (s), 865 (s), 815 (s), 750 cm^{-1} (s); UV/Vis ($CHCl_3$): λ_{max} (ε) = 263 (31675), 292sh (31894), 305 (37953), 313 nm (37090 M^{-1}cm^{-1}); fluorescence emission ([**24**] = 2.8×10^{-6} mol dm^{-3} in $CHCl_3$, 300 nm excitation): $\lambda_{max} = 338$, 349 nm; EIMS: *m*/*z* (%): 281 (100) $[M^+]$, 253 (33); elemental analysis calcd (%) for $C_{19}H_{11}N_3$: C 81.12, H 3.94, N 14.94; found: C 81.23, H 3.68, N 14.81.

2,2′:6′,2″-terpyridine-5,5″-diylbis-[1-(2,1-ethynediyl)-3-(2-(1-triisopropylsilylethynyl))-5-(2-(1-trimethylsilylethynyl))benzene] (25): Argon bubbled pyridine (15 mL) was added by syringe to a mixture of **13** (0.904 g, 1.88×10^{-3} mol), **24** (0.245g, 8.71×10^{-4} mol) and $[PdCl_2(PPh_3)_2]$ (0.042g, 5.98×10^{-5} mol) under argon. After stirring the mixture for 0.1 h, a solution of CuI (0.030 g, 1.58×10^{-4} mol) in Et_3N (2 mL) was added by syringe, and the reaction stirred in the absence of light at ambient temperature for seven days. All solvent was then removed under reduced pressure, the residue extracted with hot hexane (4×35 mL), and the combined extracts filtered under vacuum through a G4 frit. The hexane was removed under reduced pressure and the residue flash chromatographed on silica, eluting with CH_2Cl_2. The product thus obtained was finally dried under vacuum (0.01 mmHg/24 h), to yield **25** (0.531g, 62%) as a cream coloured opaque glass.

^{1}H NMR: $\delta = 8.823$ (dd, $^4J(6,4;6'',4'') = 2.1$ Hz, $^5J(6,3;6'',3'') = 0.8$ Hz, 2H; pyridine H6/6″), 8.632 (dd, $^3J(3,4;3'',4'') = 8.2$ Hz, $^5J(3,6;3'',6'') = 0.8$ Hz, 2H; pyridine H3/3″), 8.491 (d, $^3J(3',4';5',4') = 7.8$ Hz, 2H; pyridine H3′/5′), 7.990 (t, $^3J(4',3';4',5') = 7.8$ Hz, 1H; pyridine H4′), 7.961 (dd, $^3J(4,3;4'',3'') = 8.2$ Hz, $^4J(4,6;4'',6'') = 2.1$ Hz, 2H; pyridine H4/4″), 7.623 (m, 4H; phenyl H2/6), 7.559 (t, $^4J(4,2;4,6) = 1.5$ Hz, 2H; phenyl H4), 1.137 (s, 42H; $CH(CH_3)_2$), 0.261 (s, 18H; $Si(CH_3)_3$); ^{13}C NMR: $\delta = 155.0$, 154.7, 151.7, 139.4, 138.0, 135.3, 134.7, 134.6, 124.3, 123.9, 123.1, 121.6, 120.5, 119.9, 105.0 (-C≡), 103.0 (-C≡), 96.0 (-C≡), 92.5 (-C≡), 91.9 (-C≡), 87.4 (-C≡), 18.6 ($CH(CH_3)_2$), 11.2 ($CH(CH_3)_2$), −0.2 ppm ($Si(CH_3)_3$); IR: $\tilde{\nu} = 2957$ (s), 2942 (s), 2924 (s), 2865 (s), 2157 (C≡C) (m), 1578 (s), 1446 (s), 1250 (s), 982 (s), 881 (s), 855 (s), 843 (s), 818 (s), 761 (s), 679 cm^{-1} (s); UV/Vis ($CHCl_3$): λ_{max} (ε) = 257 (79995), 269 (96148), 333 (75333), 345 nm (70154 M^{-1}cm^{-1}); fluorescence emission ([**25**] = 1.3×10^{-6} mol dm^{-3} in $CHCl_3$, 300 nm excitation): $\lambda_{max} = 357$, 373 nm; FABMS: (1% CF_3COOH/NBA): m/z (%): 987 (100) $[M^+ + H]$; HRMS (FAB, $[M^+ + H]$) calcd for $C_{63}H_{76}N_3Si_4$: 986.5116; found: 986.5130.

2,2′:6′,2″-terpyridine-5,5″-diylbis-[1-(2,1-ethynediyl)-3-(ethynyl)-5-(2-(1-triisopropylsilylethynyl))benzene] (26): Powdered K_2CO_3 (0.080 g, 5.79×10^{-4} mol) was added to a solution of **25** (0.571 g, 5.79×10^{-4} mol) in 2:1 Et_2O/MeOH (20 mL) and the mixture stirred at ambient temperature in the absence of light for 14 h. A copious white suspension formed, during the first hour of stirring. All solvent was removed by distillation under reduced pressure on a water bath at ambient temperature, and the residue dissolved in CH_2Cl_2 and extracted with distilled water (3×25 mL). The organic phase was dried (anhydrous $MgSO_4$), filtered, and the solvent removed by distillation on a water bath at atmospheric pressure. The remaining solid was suspended in MeOH (15 mL) and homogenised by brief ultrasonication, filtered under vacuum, washed with excess MeOH and air dried to yield **26** (0.472g, 97%) as a dusty white powder. M.p. 235.0–237.2 °C upon heating from 233.0 °C, and > 325 °C upon slow heating from ≤ 226 °C.

^{1}H NMR: $\delta = 8.827$ (d, $^4J(6,4;6'',4'') = 2.1$ Hz, 2H; pyridine H6/6″), 8.634 (d, $^3J(3,4;3'',4'') = 8.3$ Hz, 2H; pyridine H3/3″), 8.495 (d, $^3J(3',4';5',4') = 7.8$ Hz, 2H; pyridine H3′/5′), 7.988 (t, $^3J(4',3';4',5') = 7.9$ Hz, 1H; pyridine H4′), 7.967 (dd, $^3J(4,3:4'',3'') = 7.9$ Hz, $^4J(4,6;4'',6'') = 2.3$ Hz, 2H; pyridine H4/4″), 7.660 (t, $^4J(2,4;2,6) = 1.5$ Hz, 2H; phenyl H2), 7.635 (t, $^4J(6,2;6,4) = 1.6$ Hz, 2H; phenyl H6), 7.584 (t, $^4J(4,2;4,6) = 1.5$ Hz, 2H; phenyl H4),

3.126 (s, 2H; H-C≡C)), 1.141 ppm (s, 42H; $CH(CH_3)_2$); ^{13}C NMR: $\delta =$ 155.1, 154.7, 151.7, 139.4, 138.0, 135.5, 135.1, 134.6, 124.4, 123.2, 122.9, 121.7, 120.4, 119.8, 104.8 (-C≡), 92.8 (-C≡), 91.7 (-C≡), 87.6 (-C≡), 81.8 (-C≡), 78.5 (-C≡), 18.7 ($CH(CH_3)_2$), 11.2 ppm ($CH(CH_3)_2$); IR: $\tilde{\nu} = 3303$ (H-C≡) (m), 2942 (s), 2864 (s), 2156 (C≡C) (s), 1578 (s), 1446 (s), 881 (s), 817 (s), 753 (s) 680 cm^{-1} (s); UV/vis ($CHCl_3$): λ_{max} (ε) = 256 (76991), 270 (78223), 332 (84956), 345 nm ($78382\,M^{-1}cm^{-1}$); fluorescence emission ([**26**] = 1.3×10^{-6} mol dm^{-3} in $CHCl_3$, 300 nm excitation): $\lambda_{max} = 356$, 373 nm; FABMS: (1% CF_3COOH/NBA): *m*/*z* (%): 842 (100) [$M^+ + H$]; HRMS (FAB, [$M^+ + H$]) calcd for $C_{57}H_{60}N_3Si_2$: 842.4326; found: 842.4334.

Cyclophane 5: In a well-ventilated hood, [$Cu_2(OAc)_4$] (2.40g, 1.32×10^{-2} mol) was dissolved in hot pyridine (600 mL), and the solution left to cool to ambient temperature, then bubbled with argon for 2 h. A solution of **26** (0.200 g, 2.37×10^{-4} mol) in degassed pyridine (20 mL) was subsequently added dropwise to the [$Cu_2(OAc)_4$] solution over 8 h with continued stirring and argon bubbling. A white suspended solid slowly formed during the addition. After all the **26** had been added, the blue mixture was stirred under a static atmosphere of argon at ambient temperature in the absence of light for seven days. All solvent was then removed under reduced pressure on a water bath, and distilled water (200 mL) added along with excess ice, followed by the dropwise addition of concentrated aqueous KCN (10 mL). The mixture was stirred for 0.2 h, filtered under vacuum, and the collected solid washed with excess distilled water and air-dried. The product was then boiled in toluene (250 mL), gravity filtered, and the filtrate left to cool to ambient temperature. The solid which formed was isolated by filtration under vacuum, washed with toluene (4 mL), air-dried and dissolved in boiling $CHCl_3$ (500 mL). The hot solution was then successively flash chromatographed three times on silica, eluting each column first with $CHCl_3$ followed by 2% MeCN/$CHCl_3$. The progress of the chromatographic purification was best monitored using a UV lamp operating at 365 nm. Upon irradiation of the columns, the product and impurities appeared as purple fluorescent bands. The product thus obtained was suspended in acetone (4 mL), filtered under vacuum, washed with acetone and finally air dried to yield **5** (0.077 g, 39%) as a white solid. M.p. > 320 °C.

^1H NMR ($CDCl_2CDCl_2$, 500 MHz, 80 °C): $\delta = 8.871$ (d, $^4J(6,4;6'',4'') =$ 1.7 Hz, 4H; pyridine H6/6″), 8.680 (d, $^3J(3,4;3'',4'') = 8.3$ Hz, 4H; pyridine H3/3″), 8.541 (d, $^3J(3',4';5',4') = 7.8$ Hz, 4H; pyridine H3′/5′), 8.033 (dd, $^3J(4,3;4'',3'') = 8.2$ Hz, $^4J(4,6;4'',6'') = 2.1$ Hz, 4H; pyridine H4/4″), 8.003 (t, $^3J(4',3';4',5') = 7.9$ Hz, 2H; pyridine H4′), 7.749 (t, $^4J(2,4;2,6) = 1.4$ Hz, 4H; phenyl H2), 7.696 (t, $^4J(6,2;6,4) = 1.5$ Hz, 4H; phenyl H6), 7.636 (t, $^4J(4,2;4,6) = 1.5$ Hz, 4H; phenyl H4), 1.231 ppm (s, 84H; $CH(CH_3)_2$); ^{13}C NMR ($CDCl_2CDCl_2$, 125.8 MHz, 110 °C): $\delta = 155.6$, 155.0, 151.6 (C6/6″, py), 139.6 (C4/4″, py), 137.8 (C4′, py), 135.7 (C2, ph), 135.3 (C4, ph), 135.0 (C6, ph), 125.0, 123.9, 122.6, 121.8 (C3′/5′, py), 120.5 (C3/3″, py), 119.7, 105.0 (-C≡), 93.9 (-C≡), 91.7 (-C≡), 88.3 (-C≡), 80.7 (-C≡), 75.2 (-C≡), 18.7 ($CH(CH_3)_2$), 11.6 ppm ($CH(CH_3)_2$); IR: $\tilde{\nu} = 2942$ (s), 2865 (s), 2154 (C≡C) (m), 1577 (s), 1447 (s), 876 (s), 813 (s), 676 cm^{-1} (s); UV/Vis ($CHCl_3$): λ_{max} (ε) = 261 (117543), 274 (129708), 298 (141700), 317 (238469), 338 (261379), 348 sh nm ($175827\,M^{-1}cm^{-1}$); fluorescence emission ([**5**] = 2.9×10^{-7} mol dm^{-3} in $CHCl_3$, 300 nm excitation): $\lambda_{max} = 358$, 375 nm; MALDI MS (1, 8, 9-anthracenetriol matrix): *m*/*z* (%): 1681 (100) [$M^+ + H$]; HRMS (FAB, 10% $CF_3COOH/CHCl_3$, [$M^+ + H$]) calcd for $C_{114}H_{115}N_6Si_4$: 1679.8260; found: 1679.8313.

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[1] a) G. M. Whitesides, *MRS Bulletin*, **2002**, *27*, 56; b) D. N. Reinhoudt, J. F. Stoddart, R. Ungaro, *Chem. Eur. J.* **1998**, *4*, 1349; c) G. M. Whitesides, *Angew. Chem.* **1990**, *102*, 1247; *Angew. Chem. Int. Ed.* **1990**, *29*, 1209; d) D. Seebach, *Angew. Chem.* **1990**, *102*, 1363; *Angew. Chem. Int. Ed.* **1990**, *29*, 1320, and references therein.

[2] For the property-targeted synthesis of nanosized organic molecules, see for example: a) N. C. Seeman, A. M. Belcher, *Proc. Nat. Acad. Sci.* **2002**, *99*, 6451; b) M. D. Watson, A. Fechtenkötter, K. Müllen, *Chem. Rev.* **2001**, *101*, 1267; c) *Top. Curr. Chem.* **2001**, *212*, whole volume; d) *Top. Curr. Chem.* **2000**, *210*, whole volume; e) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem.* **2000**, *112*, 3484; *Angew. Chem. Int. Ed.* **2000**, *39*, 3348; f) *Top. Curr. Chem.* **1998**, *197*, whole volume; g) *Electronic Materials: The Oligomer Approach* (Eds.: K. Müllen, G. Wegner), Wiley-VCH, Weinheim, **1998**; h) N. C. Seeman, *Angew. Chem.* **1998**, *110*, 3408; *Angew. Chem. Int. Ed.* **1998**, *37*, 3220.

[3] a) J. S. Moore, *Acc. Chem. Res.* **1997**, *30*, 402; b) J. K. M. Sanders in *Comprehensive Supramolecular Chemistry* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. McNicol, F. Vögtle), *Vol. 9*, *Templating, Self-Assembly, and Self-Organisation* (Vol. Eds.: J.-P. Sauvage, M. W. Hosseini), Pergamon, Oxford, **1996**. Chapter 4, p 131; c) S. Anderson, H. L. Anderson, J. K. M. Sanders, *Acc. Chem. Res.* **1993**, *26*, 469.

[4] a) J. S. Melinger, Y. Pan, V. D. Kleiman, Z. Peng, B. L. Davis, D. McMorrow, M. Lu, *J. Am. Chem. Soc.* **2002**, *124*, 12002; b) J. Wang, M. Lu, Y. Pan, Z. Peng, *J. Org. Chem.* **2002**, *67*, 7781; c) V. J. Pugh, Q.-S. Hu, L. Pu, *Angew. Chem.* **2000**, *112*, 3784; *Angew. Chem. Int. Ed.* **2000**, *39*, 3638; for a review of earlier literature with related structures, see: d) S. M. Grayson, J. M. J. Fréchet, *Chem. Rev.* **2001**, *101*, 3819.

[5] Ö. Ünsal, A. Godt, *Chem. Eur. J.* **1999**, *5*, 1728.

[6] For recent examples of nanosized ethynyl rods and wires with aromatic bridging units, see for example: a) J. G. Rodríguez, J. L. Tejedor, *J. Org. Chem.* **2002**, *67*, 7631; b) S. H. Lee, T. Nakamura, T. Tsutsui, *Org. Lett.* **2001**, *3*, 2005; c) A. Khatyr, R. Ziessel, *J. Org. Chem.* **2000**, *65*, 3126. For reviews, see: d) U. H. F. Bunz, *Chem. Rev.* **2000**, *100*, 1605; e) P. F. H. Schwab, M. D. Levin, J. Michl, *Chem. Rev.* **1999**, *99*, 1863; f) J. M. Tour, *Chem. Rev.* **1996**, *96*, 537.

[7] a) A. Tanatani, T. S. Hughes, J. S. Moore, *Angew. Chem.* **2002**, *114*, 335; *Angew. Chem. Int. Ed.* **2002**, *41*, 325; b) T. Nishinaga, A. Tanatani, K. Oh, J. S. Moore, *J. Am. Chem. Soc.* **2002**, *124*, 5934; c) R. B. Prince, S. A. Barnes, J. S. Moore, *J. Am. Chem. Soc.* **2000**, *122*, 2758; d) R. B. Prince, J. G. Saven, P. G. Wolynes, J. S. Moore, *J. Am. Chem. Soc.* **1999**, *121*, 3114; e) J. C. Nelson, J. G. Saven, J. S. Moore, P. G. Wolynes, *Science*, **1997**, *277*, 1793.

[8] a) D. L. An, T. Nakano, A. Orita, J. Otera, *Angew. Chem. Int. Ed.* **2002**, *41*, 171; b) A. Orita, D. L. An, T. Nakano, J. Yaruva, N. Ma, J. Otera, *Chem. Eur. J.* **2002**, *8*, 2005.

[9] a) Z. Wu, J. S. Moore, *Angew. Chem.* **1996**, *108*, 320; *Angew. Chem. Int. Ed.* **1996**, *35*, 297; b) Z. Wu, S. Lee, J. S, Moore, *J. Am. Chem. Soc.* **1992**, *114*, 8730.

[10] For a selection of recent reports on the synthesis and properties of nanosized ethynylphenyl macrocyclic structures, see: a) S. Höger, S. Rosselli, A.-D. Ramminger, V. Enkelmann, *Org. Lett.* **2002**, *4*, 4269; b) S. Höger, D. L. Morrison, V. Enkelmann, *J. Am. Chem. Soc.* **2002**, *124*, 6734; c) Y. Yamaguchi, S. Kobayashi, N. Amita, T. Wakamiya, Y. Matsubara, K. Sugimoto, Z. Yoshida, *Tetrahedron Lett.* **2002**, *43*, 3277; d) Y. Tobe, N. Utsumi, K. Kawabata, A. Nagano, K. Adachi, S. Araki, M. Sonoda, K. Hirose, K. Naemura, *J. Am. Chem. Soc.* **2002**, *124*, 5350; e) Y. Tobe, N. Utsumi, A. Nagano, M. Sonoda, K. Naemura, *Tetrahedron*, **2001**, *57*, 8075; f) K. Nakamura, H. Okubo, M. Yamaguchi, *Org. Lett.* **2001**, *3*, 1097; g) S. Höger, K. Bonrad, A. Mourran, U. Beginn, M. Möller, *J. Am. Chem. Soc.* **2001**, *123*, 5651; h) P. H. Ge, W. Fu, W. A. Herrmann, E. Herdtweck, C. Campana, R. D. Adams, U. H. F. Bunz, *Angew. Chem.* **2000**, *112*, 3753; *Angew. Chem. Int. Ed.* **2000**, *39*, 3607; for reports of macrocyclic phenylethynyl belts, see: i) T. Kawase, N. Ueda, K. Tanaka, Y. Seirai, M. Oda, *Tetrahedron Lett.* **2001**, *42*, 5509; j) M. Ohkita, K. Ando, T. Tsuji, *Chem. Commun.* **2001**, 2570; k) M. Ohkita, K. Ando, T. Suzuki, T. Tsuji, *J. Org. Chem.* **2000**, *65*, 4385; for the synthesis and STM visualisation of nanosized ethynylterthiophene macrocycles, see: l) E. Mena-Osteritz, P. Bäuerle, *Adv. Mater.* **2001**, *13*, 243, and references therein; for reviews of the field up to 1999, see: m) *Top. Curr. Chem.* **1999**, *201*, whole volume; n) S. Höger, *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 2685.

[11] a) Y. Hosokawa, T. Kawase, M. Oda, *Chem. Commun.* **2001**, 1948; b) Y. Tobe, N. Utsumi, A. Nagano, K. Naemura, *Angew. Chem.* **1998**, *110*, 1347; *Angew. Chem. Int. Ed.* **1998**, *37*, 1285; c) D. L. Morrison, S. Höger, *Chem. Commun.* **1996**, 2313; d) U. Neidlein, F. Diederich, *Chem. Commun.* **1996**, 1493.

[12] a) A. Godt, S. Duda, Ö. Ünsal, J. Thiel, A. Härter, M. Roos, C. Tschierske, S. Diele, *Chem. Eur. J.* **2002**, *8*, 5094; b) S. Höger, V. Enkelmann, K. Bonrad, C. Tschierske, *Angew. Chem.* **2000**, *112*, 2355; *Angew. Chem. Int. Ed*. **2000**, *39*, 2268; c) J. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **1994**, *116*, 2655.

[13] a) K. Campbell, C. J. Kuehl, M. J. Ferguson, P. J. Stang, R. R. Tykwinski, *J. Am. Chem. Soc.* **2002**, 124, 7266; b) D. Venkataraman, S. Lee, J. Zhang, J. S. Moore, *Nature*, **1994**, *371*, 591; Interestingly, conformationally flexible nanosized ethynyl macrocycles without aromatic bridging units have also been recently demonstrated to form solvent included porous solids. See: c) D. B. Werz, R. Gleiter, F. Rominger, *J. Am. Chem. Soc.* **2002**, *124*, 10638.

[14] In particular, the construction of ethynyl macrocycles incorporating pyridine and pyridine-type units is currently the focus of rapidly growing interest. For examples of conjugated ethynyl macrocycles incorporating pyridine units, see a) P. N. W. Baxter, *Chem. Eur. J.* **2003**, *9*, 2531; b) K. Campbell, R. McDonald, N. R. Branda, R. R. Tykwinski, *Org. Lett.* **2001**, *3*, 1045; c) S.-S. Sun, A. J. Lees, *Organometallics,* **2001**, *20*, 2353; d) Y. Tobe, A. Nagano, K. Kawabata, M. Sonoda, K. Naemura, *Org. Lett.* **2000**, *2*, 3265; e) Y. Tobe, H. Nakanishi, M. Sonoda, T. Wakabayashi, Y. Achiba, *Chem. Commun.* **1999**, 1625; for examples of conjugated ethynyl macrocycles incorporating bipyridine units, see f) P. N. W. Baxter, *Chem. Eur. J.* **2002**, *8*, 5250; g) O. Henze, D. Lentz, A. Schäfer, P. Franke, A. D. Schlüter, *Chem. Eur. J.* **2002**, *8*, 357; h) P. N. W. Baxter, *J. Org. Chem.* **2001**, 66, 4170; i) O. Henze, D. Lentz, A. D. Schlüter, *Chem. Eur. J.* **2000**, *6*, 2362; j) O. Henze, U. Lehmann, A. D. Schlüter, *Am. Chem. Soc. Polym. Mater. Sci. Eng*. **1999**, *80*, 231; for a qualitative report of an ethynyl macrocycle incorporating terpyridine units, see k) U. Lehmann, O. Henze, A. D. Schlüter, *Am. Chem. Soc. Polym. Mater. Sci. Eng*. **1999**, *80*, 165; for an example of a conjugated phenylethynyl macrocycle incorporating phenanthroline units, see: l) M. Schmittel, H. Ammon, *Synlett* **1999**, 750.

[15] For examples of ethynyl macrocycles functioning as ligands in characterised coordination and organometallic complexes see; a) reference [14g]; b) reference [13a]; c) R. Gibe, J. R. Green, *Chem. Commun.* **2002**, 1550; d) M. Laskoski, W. Steffen, J. G. M. Morton, M. D. Smith, U. H, F. Bunz, *Angew. Chem.* **2002**, *114*, 2484; *Angew. Chem. Int. Ed.* **2002**, *41*, 2378; e) reference [14b]; f) W. J. Youngs, C. A. Tessier, J. D. Bradshaw, *Chem. Rev.* **1999**, *99*, 3153.

[16] P. Lustenberger, F. Diederich, *Helv. Chim. Acta*, **2000**, *83*, 2865. The 3,5-dibromoiodobenzene **7** was prepared by a slightly modified version of the above literature procedure. Thus, after the addition of 1.6 M *n*BuLi at −78 °C, the reaction solution was allowed to warm to −20 °C for 1.5 h, then recooled to −78 °C and excess iodine in Et_2O solution added slowly at between −78 °C and −70 °C. After work-up, the crude product was recrystallised from abs. EtOH (two crops of crystals were obtained) to afford **7** in 84% yield (compared to the reported 56%).

[17] a) J. S. Moore, Z. Xu, *Macromolecules*, **1991**, *24*, 5893; b) A. M. McDonagh, M. G. Humphrey, M. Samoc, B. Luther-Davies, *Organometallics*, **1999**, *18*, 5195.

[18] K. Onitsuka, M. Fujimoto, N. Ohshiro, S. Takahashi, *Angew. Chem.* **1999**, *111*, 737; *Angew. Chem. Int. Ed.* **1999**, *38*, 689. Information concerning the preparation, purification and characterisation of **11**, was however not reported. This data is therefore described above.

[19] For a recent report of an improved procedure for the coupling of terminal alkynes with aryl bromides, see: S. Thorand, N. Krause, *J. Org. Chem.* **1998**, *63*, 8551.

[20] a) T. Iida, T. Wada, K. Tomimoto, T. Mase, *Tetrahedron Lett*. **2001**, *42*, 4841; b) B. H. Lipshutz, S. S. Pfeiffer, W. Chrisman, *Tetrahedron Lett*. **1999**, *40*, 7889.

[21] For the Corey–Fuchs transformation of heterocyclic aldehydes to the corresponding 2,2-dibromovinyl analogues, and subsequent NaOMe-mediated dehydrobromination of the latter groups to bromoethynes, see: a) V. Bakthavachalam, M. d′Alarcao, N. J. Leonard, *J. Org. Chem*. **1984**, *49*, 289; b) M. d′Alarcao, N. J. Leonard, *J. Am. Chem. Soc*. **1983**, *105*, 5958. Interestingly, the direct conversion of 5-(2,2-dibromovinyl)-2,2′-bipyridine to 5-ethynyl-2,2′-bipyridine with *n*BuLi, followed by an aqueous quench, failed to proceed in high yield; c) J. Polin, E. Schmohel, V. Balzani, *Synthesis*, **1998**, 321.

[22] For the use of Stille-coupling methodology in the construction of ethynylpyridyl scaffolds, see: a) reference [14 h]; b) P. N. W. Baxter, *J. Org. Chem.* **2000**, *65*, 1257.

[23] For a pioneering investigation into the construction of oligopyridines using Sille-coupling methodology, see: Y. Yamamoto, Y. Azuma, H. Mitoh, *Synthesis*, **1986**, 564.

[24] The use of distannylpyridines for the palladium-catalysed synthesis of oligopyridines has been recently revived; a) M. Heller, U. S. Schubert, *J. Org. Chem*. **2002**, *67*, 8269; b) G. Manickam, A. D. Schlüter, *Eur. J. Org. Chem*. **2000**, 3475; c) U. S. Schubert, C. Eschbaumer, *Org. Lett*. **1999**, *1*, 1027; d) U. S. Schubert, C. Eschbaumer, C. H. Weidl, *Synlett* **1999**, 342; e) U. Lehmann, O. Henze, A. D. Schlüter, *Chem. Eur. J.* **1999**, *5*, 854.

[25] G. S. Hanan, U. S. Schubert, D. Volkmer, E. Rivière, J.-M. Lehn, N. Kyritsakas, J. Fischer, *Can. J. Chem*. **1997**, *75*, 169.

[26] a) E. F. Córsico, R. A. Rossi, *Synlett*, **2000**, 227; b) Y. Yamamoto, A. Yanagi, *Chem. Pharm. Bull*. **1982**, *30*, 1731.

[27] During manuscript preparation, a publication appeared, outlining a synthesis involving **23** and **24**. See: J. Otsuki, H. Kameda, S. Tomihira, H. Sakaguchi, T. Takido, *Chem. Lett.* **2002**, 610. However, information concerning the preparation, yields, purification and characterisation of **23** and **24**, were not reported in the latter communication. This data is therefore provided above.

[28] It was initially anticipated that the relatively strongly chelating terpyridine unit **24**, may possibly interfere with its coupling to **13**, by selective coordination and concomitant deactivation of the palladium and copper catalysts. The Sonogashira coupling between **13** and **24** was therefore conducted in pyridine in order to suppress any possible coordination of **24** to the catalysts and intermediate species derived therefrom.

[29] O. Lavastre, L. Ollivier, P. H. Dixneuf, S. Sibandhit, *Tetrahedron*, **1996**, *52*, 5495.

[30] M. L. Bell, R. C. Chiechi, C. A. Johnson, D. B. Kimball, A. J. Matzger, W. Brad Wan, T. J. R. Weakley, M. M. Haley, *Tetrahedron.* **2001**, *57*, 3507.

[31] The copper-mediated oxidative cyclisation of terminal diethynes has provided a versatile and widely exploited method for the preparation of medio- and macrocyclic ring systems. The methodology is broad in scope and tolerant to wide range of functional groups. The cyclisations are normally performed at medium to high dilution in a basic solvent such as pyridine, but reaction parameters such as co-solvents, temperature and the nature of the copper oxidant have been subject to a range of modifications. Of particular significance, is the fact that there appears to be no predictable relationship between the yield of macrocyclisation and the structure of the starting terminal diethyne. The optimal reaction parameters must be determined independently for each type of substrate. For a discussion of copper mediated ethyne coupling protocols in macrocyclisation reactions, see for example: L. Rossa, F. Vögtle, *Top. Curr. Chem.* **1983**, *113*, 72–75.

[32] In the case of **1**, molecular modelling studies showed that coordination of two precursor ligands to $Cu^{I/II}$ would juxtaposition the ethyne groups into a favourable orientation for cyclisation. Ion coordination would therefore be expected to result in an enhancement in the yield of **1**. On the other hand, the chelation of two **26** molecules to $Cu^{I/II}$ would position the ethynes of each ligand at distances out of range for intra-complex cyclisation, favouring the formation of polymeric and possibly catenated products. For a discussion of guest templating effects in the formation of ethynyl-porphyrin macrocycles, see: references [3b, c].

[33] MALDI TOF mass spectrometry has been successfully used for the characterisation of nanosized ethynylphenyl macrocycles and also their gas phase aggregation behaviour; S. Höger, J. Spickermann, D. L. Morrison, P. Dziezok, H. J. Räder, *Macromolecules*, **1997**, *30*, 3110.

[34] The aromatic resonances were assigned as follows: The doublet at $\delta =$ 8.871 ppm was the furthest downfield resonance in the ^1H NMR spectrum of **5**, and was therefore assigned to the pyridyl H6/6″ protons of the outer two pyridine rings due to their proximity to the electron-withdrawing nitrogen atoms. The doublet of doublets at $\delta = 8.033$ ppm exhibited a crosspeak with the doublet at $\delta = 8.871$ ppm in the $^1H-^1H$ COSY spectrum of **5**, and was therefore assigned to the H4/4″ protons of the outer pyridine rings. A crosspeak in the $^1H-^1H$ COSY spectrum

of **5**, between the triplet at $\delta = 8.003$ ppm due to the H4′ proton of the central pyridine, and the doublet at $\delta = 8.541$ ppm indicated that the latter resonance originated from the central pyridine H3′/H5′ protons. The remaining pyridyl doublet at $\delta = 8.680$ ppm was therefore assigned to the H3/3″ protons of the outer pyridines. This conclusion was unambiguously verified by the presence of a crosspeak in the ^{1}H–^{1}H COSY spectrum, between the latter resonance and that at $\delta =$ 8.033 ppm originating from the H4/4″ protons. The three triplets at $\delta = 7.749$, 7.696 and 7.636 ppm were assigned to the phenyl H2, H6 and H4 protons, respectively, by comparison with the spectra of **25** and **26** and on the basis of expected electronic effects translated through the adjacent ethynes. The furthest downfield phenyl resonance at $\delta =$ 7.749 ppm was thus assigned to the H2 phenyl proton, directed towards the interior of the macrocyclic cavity. The latter proton would be expected to experience the greatest downfield shifting due to its situation between the ethynes with the most electron-withdrawing substituents. The most upfield triplet at $\delta = 7.636$ ppm was assigned to the H4 proton which is positioned between the ethyne bearing the relatively electron-donating triisopropylsilyl group, and the ethyne with lesser of the two electron withdrawing substituents, that is, the butadiyne group. Finally, in the case of **5**, a ^{1}H–^{13}C HSQC experiment enabled the assignation of the proton-connected aromatic carbon atoms (see characterisation data for **5** above).

[35] It may be noted that the emission spectral energies of **23**–**26** recorded at $\leq 2 \times 10^{-7}$ mol dm^{-3}, and of **5** at $\leq 3 \times 10^{-8}$ mol dm^{-3} were particularly sensitive to the presence of trace amounts of adventitious transition metal contaminants, possibly originating from the solvent and/or the walls of the glass volumetric and measuring equipment. Repeatable results were however obtained when the dilution studies of all ligand solutions were carried out in the presence of 1×10^{-3} mol dm^{-3} NaCN (introduced as a 1:1 H_2O/MeOH solution, and 4% of the total volume of each volumetric solution). The cyanide would be expected to preferentially complex any transition metal impurities, if present. The above observation supports the expectation that **5** and related structures may function as efficient fluorescence sensors for metal ions.

[36] During completion of the manuscript, an excellent review on nano-sized ethynyl macrocycles appeared, which also reported work in progress on systems related to **5**, and undertaken concurrently with the synthesis of **5** described above; see: C. Grave, A. D. Schlüter, *Eur. J. Org. Chem*. **2002**, 3075; see also reference [14k] for work connascent with that described herein. However, the reported yields were significantly lower than that obtained for **5**. It appears therefore that the Eglinton/Galbraith ethyne macrocyclisation of precursors possessing bulky substituents, may offer a more widely applicable route to synthetically useful quantities of nanosized ethynyl macrocycles incorporating pyridine-type metal ion binding units.

[37] These factors are of crucial importance if structures such as **5** are to be considered as realistic candidates for nanomaterials research. It may also be noted that the described synthetic sequence involves the generation of a range of phenylethynyl and pyridyl synthons. These may serve as useful building blocks in their own right, for example as pivotal construction units for incorporation into alternative organic scaffolds and nanostructures.

[38] That is, the distance between the van der Waals surfaces of the terpyridine nitrogens that point towards the interior of the cavity. It may be noted that the molecular modelling studies revealed additional conformational energy minima in which the ring of **5** was non-planar. This finding suggests that **5** may be semi-flexible in solution and the gas phase, and able to oscillate through a series of puckered conformations while retaining its overall hexagonal geometry.

[39] For examples of terpyridine-organic molecule H-bonding interactions, see: a) C.-Y. Huang, V. Lynch, E. V. Anslyn, *Angew. Chem*. **1992**, *104*, 1259; *Angew. Chem. Int. Ed*. **1992**, *31*, 1244; b) M. Inouye, T. Miyake, M. Furusyo, H. Nakazumi, *J. Am. Chem. Soc*. **1995**, *117*, 12416.

[40] Literature reports of the utilisation of terpyridine chromophores for the luminescence detection of metal ions are sparse. See for example; a) W. Goodall, J. A. G. Williams, *Chem. Commun.* **2001**, 2514; b) R. Ziessel, *J. Incl. Phenomena Macrocycl. Chem.* **1999**, *35*, 369; c) M. Kimura, T. Horai, K. Hanabusa, H. Shirai, *Adv. Mater*. **1998**, *10*, 459; d) F. Barigelletti, L. Flamigni, G. Calogero, L. Hammarström, J.-P. Sauvage, J.-P. Collin, *Chem. Commun*. **1998**, 2333; e) A. P. de Silva, H. Q. N. Gunaratne, T. E. Rice, S. Stewart, *Chem. Commun*. **1997**, 1891. For an example of a terpyridine-based electrochemical anion sensor, see: f) B. Fabre, U. Lehmann, A. D. Schlüter, *Electrochim. Acta*, **2001**, *46*, 2855.

[41] The TIPS-protected ethynyl substituents should enable further synthetic addition of conjugated structures to the periphery of **5**. In this way, the global conjugation of **5** could be increased and the spectroscopic properties controllably adapted to specific applications.

[42] T. K. Jones, S. E. Denmark, *Helv. Chim. Acta*, **1983**, *66*, 2397.

[43] D. R. Coulson, L. C. Satek, S. O. Grim, *Inorg. Synth*. **1990**, *28*, 107.

[44] J. S. Brumbaugh, A. Sen, *J. Am. Chem. Soc*. **1988**, *110*, 803.

[45] B. Corain, B. Longato, G. Favero, D. Ajò, G. Pilloni, U. Russo, F. R. Kreissl, *Inorg. Chim. Acta*. **1989**, *157*, 259.

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