ARTICLE

OBC
www.rsc.org/obc

Acetylenic cyclodextrins for multireceptor architectures: cups with sticky ends for the formation of extension wires and junctions†

Jonathan A. Faiz, Neil Spencer and Zoe Pikramenou*

School of Chemistry, The University of Birmingham, Edgbaston, B15 2TT, UK.
E-mail: z.pikramenou@bham.ac.uk; Fax: ++44 121 414 4446 or 4403; Tel: ++44 121 414 2290

Received 17th June 2005, Accepted 19th September 2005
First published as an Advance Article on the web 25th October 2005

A mono-6-*O*-propargyl permethylated β-cyclodextrin, **3**, has been prepared by two synthetic routes as a versatile building block for the construction of cyclodextrin dimers and trimers with a core junction which is potentially electron conducting. Glaser–Hay coupling of **3** gave β-cyclodextrin dimer **6**, and Pd(0)-catalysed coupling allowed the preparation of a cyclodextrin dimer with a 1,4-phenylene bridge, **7**, and a cyclodextrin trimer based on a 1,3,5-trisubstituted benzene, **8**. All compounds have been fully characterised, and in particular, detailed analysis by 2D NMR spectroscopic techniques has provided useful insight into the identities of the compounds. The detailed full characterisation of mono-3,6-anhydro-heptakis(2,3-*O*-methyl)-hexakis(6-*O*-methyl)-β-cyclodextrin, **5**, is also described. Product **5** is formed during the methylation of compound **3**, and its formation was found to be sensitive to the reaction conditions. The absorption and fluorescence spectra of the phenylene-bridged dimer **7** and trimer **8** are also reported. They show different properties of the excited state based on the different electronic coupling imposed by the phenylene core.

Introduction

The introduction of multiple cyclodextrin recognition sites in a single supramolecular architecture has attracted interest in the field of enzymatic catalysis,[1] especially as cyclodextrin dimers have showed enhanced binding to guests compared to single cyclodextrins.[2] The potential of multi-cyclodextrin systems as components in photomolecular devices[3–10] or sensing[11,12] is less well explored. Two different strategies have been used for the formation of multi-cyclodextrin architectures. A coordination chemistry approach uses metal centres to assemble together two, three or six cyclodextrins.[12–15] Covalent bond formation has been widely used to form cyclodextrin multi-receptors, with methodologies based on thioether coupling,[16] ester,[14] amide[2,9,17–23] or ether[24] bond formation, and ring-closing metathesis.[25] The "covalent" route has led to architectures of linear dimers, dimers in macrocylic structures, trimers or tetramers built around a central core. We have been interested in the modulation of photoinduced processes by photoactive centres appended on cyclodextrin structures, with the aim of constructing wires and junctions by host–guest assembly.[3,26]

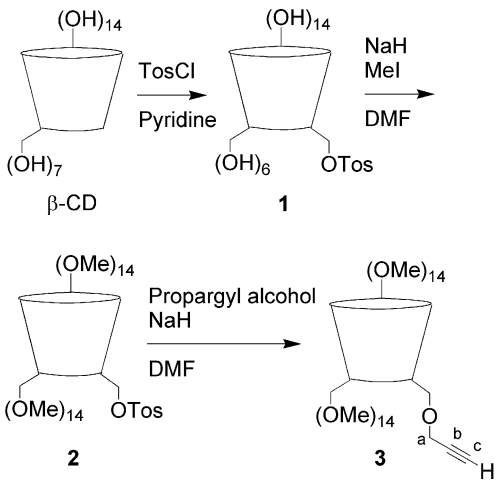
We identified the acetylenic functionality as the most ideal to append to a cyclodextrin in order to build cyclodextrin architectures with conductive acetylenic bridges. During the course of our work, a heterocyclodextrin dimer was reported based on Sonogashira coupling.[27] Here, we present the synthesis of an acetylene-functionalised cyclodextrin and its application as a building block for supramolecular arrays, is demonstrated with the synthesis of cyclodextrin dimers and trimers.

Results and discussion

Synthesis of the acetylenic cyclodextrin building block, 3

To attach a single acetylenic unit to a cyclodextrin, a precursor is required which has a single alcohol functionality, unprotected or activated, with the remaining hydroxyl groups protected. Following our approach for cyclodextrin–polypyridyl ligands, we decided to utilise monofunctionalised permethylated cyclodextrins, as this protection method makes the molecule soluble in a wide range of solvents, as well as making chromatographic purification simpler. We identified mono-6-*O*-propargyl permethylated β-cyclodextrin **3** as an ideal target for a supramolecular building block. It was prepared by two routes based on Williamson ether couplings.

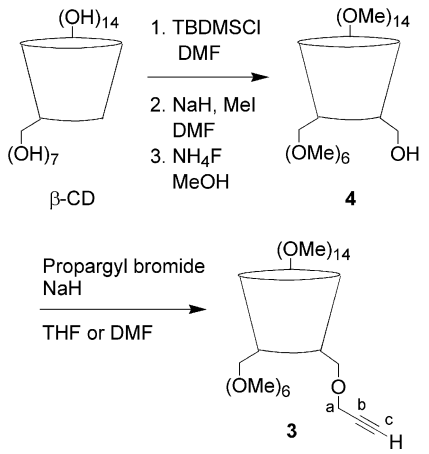
The first route investigated is shown in Scheme 1. The monotosyl derivative of β-cyclodextrin was synthesised following standard procedures.[28–30] Direct methylation of **1** with sodium hydride and methyl iodide in DMF was attempted, and was found to proceed smoothly, provided the temperature was controlled and suitable dilution was used. This reaction has been tested on a range of moderate scales, all forming **2** as the major product. The synthesis of **2** in several steps has been reported previously,[31] but we favour the direct methylation as a more straightforward approach. Reaction of **2** with propargyl alcohol and sodium hydride in DMF afforded the target acetylenic cyclodextrin **3** in 50% yield. The progress of the reaction was monitored by NMR, as it was found to be difficult to follow by TLC due to similar retention factors of reactant and product. A second route was investigated (Scheme 2), utilising the Williamson ether coupling of monohydroxy permethylated β-cyclodextrin,[13,32] based on substitution of propargyl bromide[33]



Scheme 1 Synthetic route 1 to **3** *via* a tosylated cyclodextrin derivative.

† Electronic supplementary information (ESI) available: NMR spectra of compounds **3** and **5–8**. See DOI: 10.1039/b508607h

DOI:10.1039/b508607h



Scheme 2 Synthetic route 2 to **3** *via* a hydroxy cyclodextrin derivative.

with the anion of **4**, leading to product **3** in 65%. This reaction was initially carried out in THF at elevated temperature; it was found, subsequently, that the reaction proceeded faster in DMF in the presence of tetraethylammonium iodide. Although this route is slightly higher-yielding, it is disfavoured, as the precursor **4** can be more time-consuming to synthesise and purify. Tosylation[34] of mono-6-hydroxy permethylated β-cyclodextrin **4** was also attempted, but it was not successful in our hands.

The product **3** was identified by its ^{1}H NMR spectrum (Fig. 1), and was characterised by 2D NMR studies and mass spectrometry. A triplet at 2.4 ppm corresponds to the acetylenic proton (H-c), while an apparent quartet of doublets centred at 4.2 ppm represents the methylene protons of the propargyl group (H-a). These couple in an AB pattern due to their diastereotopicity, and are further coupled with the acetylene proton by a long-range interaction mediated by the propargyl group. Analysis by DEPT and HMBC spectra shows that the acetylenic carbon atoms resonate at 80.0 ppm (C-c) and 74.5 ppm (C-b). C-6 of the cyclodextrin appears at 68.9 ppm and the propargylic methylene group (C-a) at approximately 60 ppm. The connectivity of the propargyl substitution is confirmed by the HMBC spectrum (Fig. 2), which displays correlations between the protons H-c and carbon atoms C-b, C-c and C-6 of the substituted glucose unit.

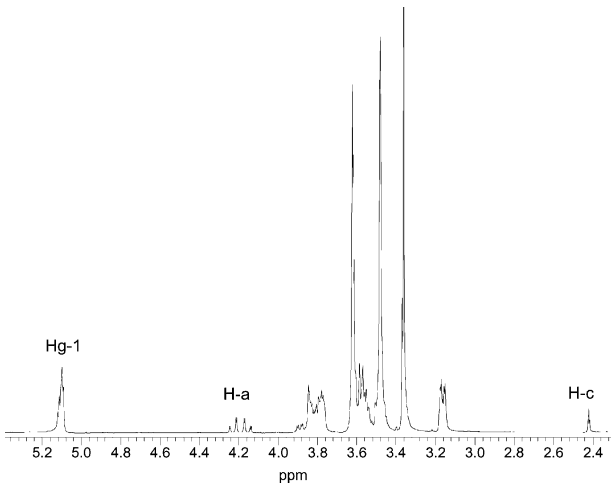


Fig. 1 The 500 MHz ^{1}H NMR spectrum of **3** in $CDCl_3$.

Mono-3,6-anhydro-heptakis(2,3-*O*-methyl)-hexakis(6-*O*-methyl)-β-cyclodextrin

During the course of the synthesis of **2** from **1**, an unexpected by-product was encountered. This methylation step was previously reported to be very sensitive to the reaction conditions, especially the regulation of temperature.[35] TLC analysis showed a small

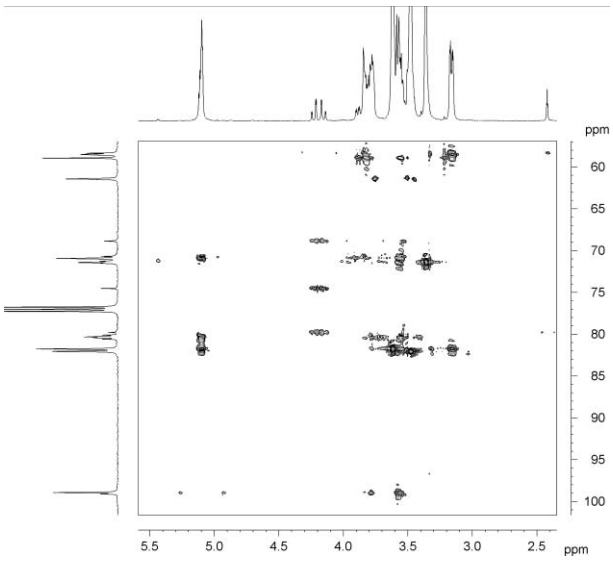
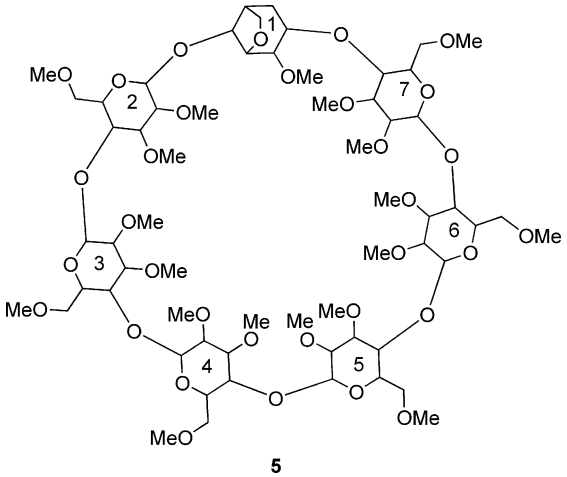


Fig. 2 HMBC plot of **3** in $CDCl_3$.

amount (maximum yield 13%) of a slow-running material, the proportion of which increased if the temperature was not controlled carefully. This product was shown to be **5** (Scheme 3), which is formed from an intramolecular displacement of the tosylate group by the alcohol at the 3-position. This product has been previously made independently by different routes for its potential chiral recognition of guests and studies of conformation effects on glycoside reactivity.[36,37] We report herein the full characterisation of **5** by elemental analysis, mass spectrometry and comprehensive NMR studies. A portfolio of NMR techniques was employed to precisely determine the structure and assign the shifts of this asymmetric compound displaying highly complex 1D spectra.



5

Scheme 3 Mono-3,6-anhydro-heptakis(2,3-*O*-methyl)-hexakis(6-*O*-methyl)-β-cyclodextrin, **5**.

The ^{1}H NMR spectrum of **5** (Fig. 3) is particularly characteristic as it contains a distinct doublet for each anomeric proton, rather than the usual multiplet seen for asymmetrically mono-functionalised permethylated cyclodextrins such as that in Fig. 1. The asymmetry of the molecule has been shown to arise from distortion of the cavity imposed by the $^1C_4$ conformation of the subunit containing the 3,6-anhydro group.[38–40] The HSQC spectrum of **5** is shown in Fig. 4. The correlation between the distinct signals for each of the anomeric positions is clearly seen around 4.9–5.5 ppm and 96–100 ppm in the ^{1}H and ^{13}C NMR spectra, respectively. In the 3.0–3.7 ppm region of the ^{1}H NMR spectrum, the methoxy signals can be distinguished by their correlation to the ^{13}C signals at 58–62 ppm, whereas the protons

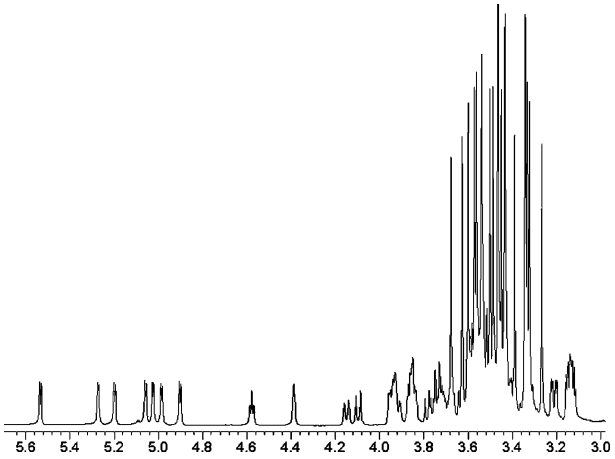


Fig. 3 The 500 MHz ^{1}H NMR spectrum of **5** in $CDCl_3$.

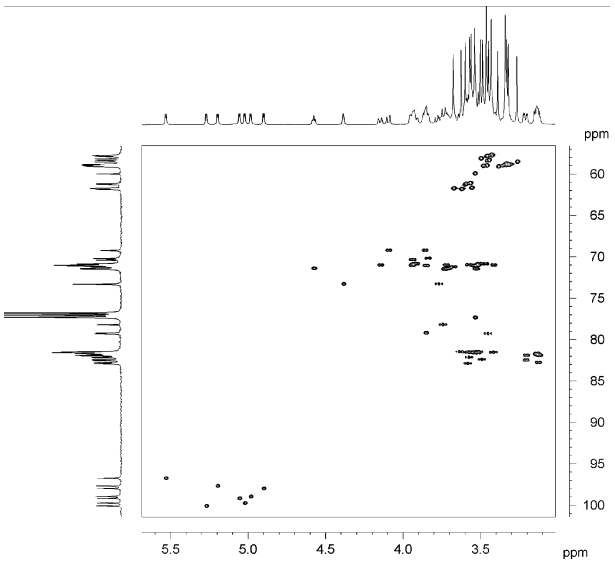
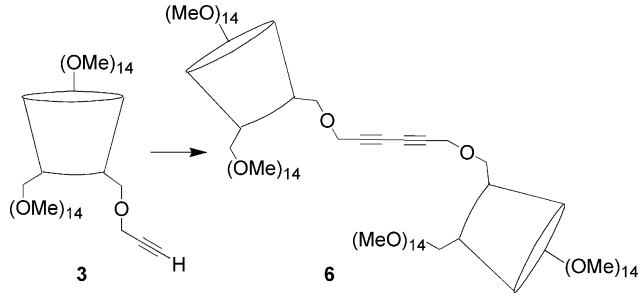


Fig. 4 HSQC NMR plot of **5** in $CDCl_3$.

between 3.3–3.1 ppm correspond to the H-2 signals of rings 2–7, correlating to the ^{13}C signals at 81–83 ppm. From the HOHAHA spectrum it can be seen that the resonances that lie outside the expected glucose regions are all associated with a single glucose ring, assigned to the anhydro ring. It is expected that distortion of this ring will lead to the shift of the glucose signals. Working from H-1 (5.26 ppm), the COSY spectrum can be used to identify H-2 (3.53 ppm), H-3 (4.57 ppm), H-4 (3.85 ppm) and H-5 (4.38 ppm). Their respective carbon resonances are identified using the HSQC spectrum. H-3 shows a three-bond coupling to H-6 (4.09–3.85 ppm), confirming the connectivity within the anhydro ring. The rings adjacent to the anhydro ring can be identified using three-bond couplings from H-1 to C-4 on neighbouring rings, while the individual protons and carbons can be subsequently located by use of COSY, HMBC and HOHAHA spectra (see Supplementary Information†). Most of the 2-, 3-, and 6-methoxy groups can be located by their three-bond couplings on the HMBC spectrum. Investigation of the through-space coupling was performed with several NOE experiments to assign the remaining methoxy signals, as well as the order and connectivity of the glucose units in the ring. The distinct diastereotopic H-6 protons of the anhydro unit were also identified by the NOE of one of the protons (4.1 ppm) to H-1.

Synthesis of acetylene-bridged cyclodextrin extension wires and junctions

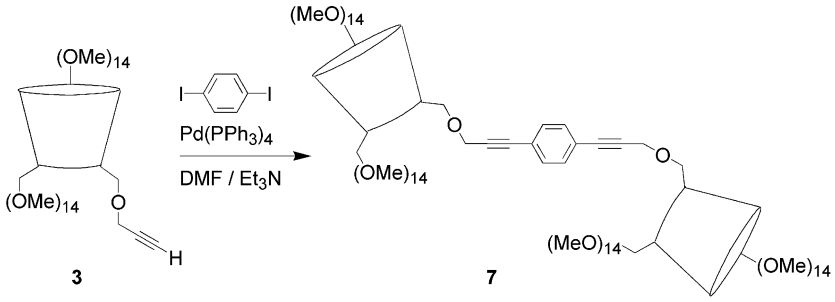
Given the potential versatility of building block **3**, attention now turned to the construction of multi-receptor arrays linked by conjugated acetylene and aromatic units. The acetylene monomer was first subjected to standard Glaser–Hay coupling conditions:[41–44] reaction with CuCl and TMEDA under dry air swiftly gave the coupled product **6**, in 52% yield (Scheme 4). Analysis of the ^{1}H NMR spectrum confirms that dimerisation has occurred, because the signal corresponding to the acetylenic proton H-c has disappeared and the quartet of doublets (H-a) at 4.2 ppm has become an AB pattern. Substitution of the triple bond is also evident from the ^{13}C NMR and DEPT spectrum (see Supplementary Information†), with the acetylenic carbons appearing as quaternary signals at 75.3 and 70.3 ppm.



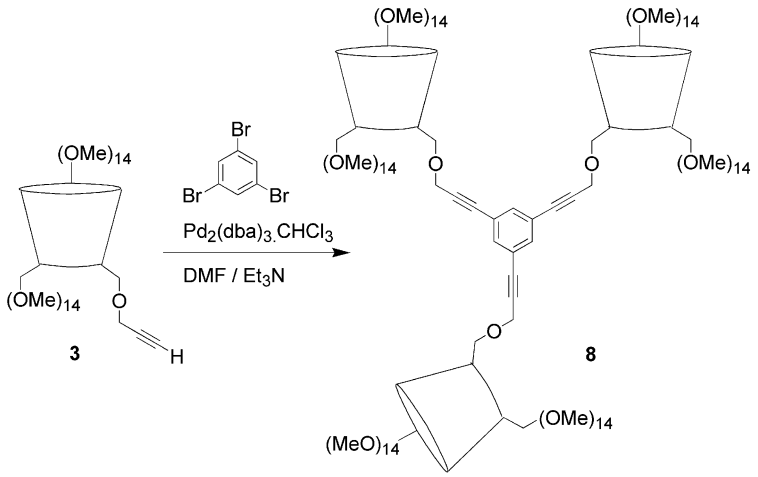
Scheme 4 Glaser–Hay coupling of **3** to form dimer **6**.

Palladium-catalysed cross-coupling reactions have been much exploited in the construction of novel architectures.[45–56] It was evident that the basic building block **3** could be reacted with aryl halides, to give spatially organised multi-receptor complexes; thus our first target was the phenyl-containing dimer **7** (Scheme 5). This was synthesised using $Pd(PPh_3)_4$ in a triethylamine/DMF mixture, following a procedure utilising acetylene-functionalised sugars.[57] The phenyl dimer **7** was found to be the major product (yield 53%), although a small amount of phenyl cyclodextrin monomer was also identified. Full substitution of the central benzene is apparent by the singlet at 7.3 ppm in the ^{1}H NMR spectrum. The acetylene carbons resonate at 87.2 and 85.5 ppm and the HMBC spectrum (Supplementary Information†) for this compound also shows correlations between the propargylic methylene protons and the aromatic carbon atoms.

Conditions used to synthesise the trimer **8** involved $Pd_2(dba)_3{\cdot}CHCl_3$ in a triethylamine/DMF mixture,[58] forming



Scheme 5 Palladium-catalysed coupling of **3** to form dimer **7**.



Scheme 6 Palladium-catalysed coupling of **3** to form trimer **8**.

the desired product in 82% yield (Scheme 6). The trisubstitution of the benzene core of **8** is confirmed by the aromatic protons appearing as a singlet at 7.3 ppm in the ^{1}H NMR spectrum (Supplementary Information†). The acetylene carbon atoms resonate at 86.7 and 84.0 ppm and further evidence for substitution can be seen in the HMBC spectrum (Fig. 5), which shows a correlation between the propargylic methylene protons (H-a) and both aromatic carbon atoms. The aforementioned conditions were found to be ideal – other attempts (including $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ with CuI in triethylamine[42,59]) gave either considerable amounts of the monomer bromobenzene cyclodextrin or **6** as products.

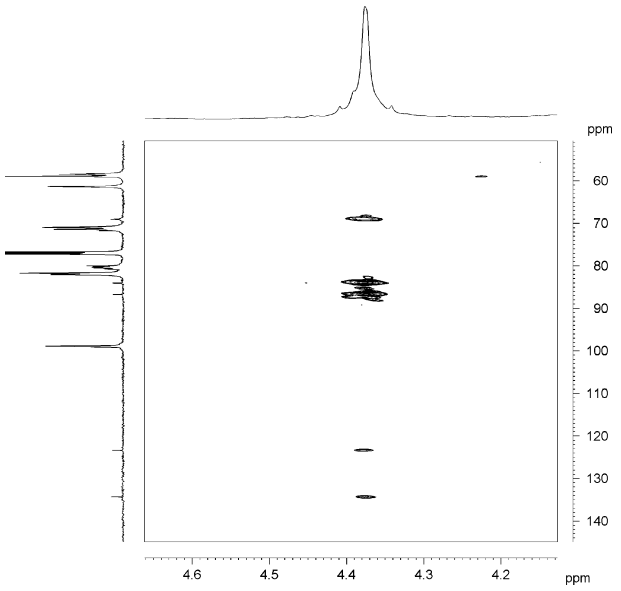


Fig. 5 HMBC plot of trimer **8** in $CDCl_3$.

An interesting feature in the preparation of the cyclodextrin dimers and trimers from the monomer **3** is the monitoring of the characteristic signal of the propargylic methylene protons at $\delta = 4.2$ ppm in compound **3**. These protons appear as an apparent quartet in dimer **6**, an AB pattern in phenyl-bridged dimer **7** and a broad singlet in trimer **8**. The apparent reduction in complexity of the NMR signals contrasts with the increased architectural complexity of these systems.

In all the cyclodextrin architectures, MALDI-TOF mass spectrometry proved to be invaluable for analysing the compounds. In all cases, well-resolved patterns have been recorded, and no signals corresponding to incomplete substitution products have been observed. IR spectra have not proved to be informative due to the large number of C–H and C–C bonds in the cyclodextrin units that overshadow the weaker acetylene signals. Weak signals have been observed for the characteristic C≡C and C–H stretches of the acetylene unit in **3**.

UV-vis and fluorescence properties of dimer 7 and trimer 8

The UV-vis absorption spectrum of the cyclodextrin dimer **7** shows a broad manifold with distinct maxima at 282 nm and 269 nm (Fig. 6). The emission spectrum is the expected mirror image of the absorption, with distinct maxima at 304 nm and 315 nm, attributed to π–π* fluorescence affected by the extensive conjugation of the 1,4-disubstituted benzene system.

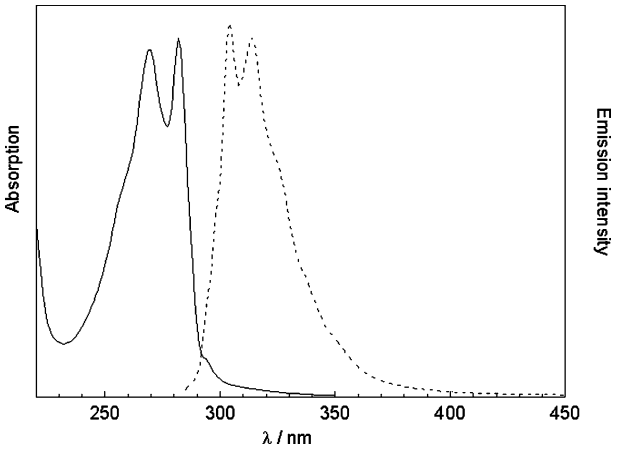


Fig. 6 UV-vis (—) and fluorescence (---) spectra of dimer **7** in MeCN (8.4×10^{-6} M).

The UV-vis spectrum of the trimer **8** (Fig. 7) shows a broad band centred around 240 nm, with a shoulder that could be attributed to an obscured sharp peak at 258 nm. Unexpectedly, the emission spectrum (Fig. 7) of the trimer **8** did not appear as the mirror image of the corresponding UV-vis spectrum. It appeared as a more structured band with distinct peaks at 326 nm and 337 nm.

The difference in the shape of the spectra and Stokes shift displayed by the trimer imply that the nature of the absorbing and emitting states are different, whereas they are the same for the dimer. The dimer **7** is fully conjugated in the ground and excited states, whereas **8**, with its *meta* substitution, does not have the acetylene units in conjugation in the ground state, but a degree of electronic coupling exists between them in the excited state. Studies on similar systems have shown that the *meta*-substituted molecule can undergo a relaxation after excitation,

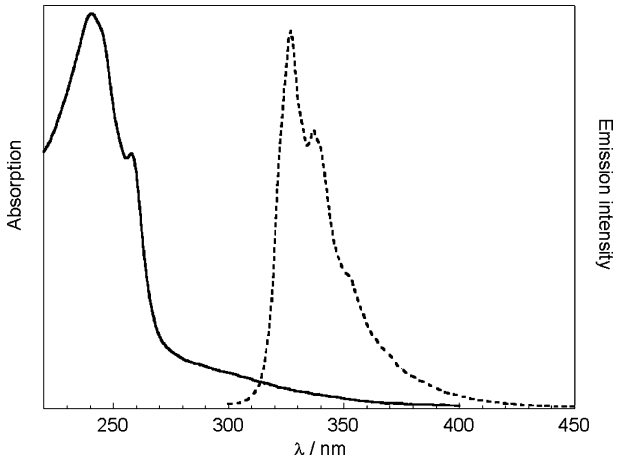


Fig. 7 UV-vis (—) and fluorescence (---) spectra of trimer **8** in MeCN (8.4×10^{-6} M).

as the excited acetylene units possess a degree of cumulenic character. This leads to a change in nuclear geometry, which in turn leads to a change in the energy of the emitting state.[60] This model explains the difference in shape of the absorption and emission spectra and Stokes shift observed between the phenyl-bridged dimer and trimer.

Conclusions

A new approach to the formation of multi-cyclodextrin architectures has been introduced, by using a new building block based on an acetylenic cyclodextrin. This versatile cyclodextrin derivative has been subjected to Glaser–Hay and Sonogashira couplings that lead to the formation of dimer and trimer architectures. The acetylenic bond provides a connection module for receptor structures that can be viewed as components in molecular electronics based on our previous work for assembly of electro-active metal centres based on cyclodextrins. The substituted benzene architectures provide a tunable luminescent core that can be modified, not only to desired lengths to control the communication with guests inside the cyclodextrins, but also to provide tailor-made photophysical properties. Further work in the participation of these cyclodextrin dimers and trimers in photophysical schemes with guests is underway.

Experimental

General

All reagents and solvents were used as supplied, unless stated otherwise. β-Cyclodextrin (Aldrich) was recrystallised from water and dried under vacuum at 80 °C for 8 h. DMF was dried over molecular sieves, pyridine was dried over KOH pellets for 24 h and subsequently molecular sieves, *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) and triethylamine were distilled from KOH, and DCM was distilled over CaH_2. NMR spectra were obtained on Bruker AC300, AV300 and DRX500 instruments. MALDI mass spectra were recorded on a Bruker Biflex IV spectrometer, and electrospray mass spectra on a VG Prospec mass spectrometer. Flash column chromatography was performed on silica gel (Fluorochem, 40–63 μm) or a Biotage prepacked silica column, and thin layer chromatography on Merck silica gel 60 F_{254} glass plates. Cyclodextrins were detected with an oxidising solution consisting of *p*-anisaldehyde–acetic acid–methanol–sulfuric acid in a 2 : 45 : 430 : 22 ratio followed by heating at around 100 °C. All reactions were carried out under a nitrogen atmosphere unless otherwise stated; standard Schlenk line techniques were used throughout. Solutions were degassed by three freeze–pump–thaw cycles. 6-*p*-Toluenesulfonyl β-cyclodextrin **1**[28–30] and 6-monohydroxy permethylated β-cyclodextrin[61] were prepared following previously published procedures. Luminescence spectra were recorded on a Photon Technology International (PTI) QM-1 emission spectrometer.[62] Fluorescence spectra were not corrected for the wavelength dependence of the photomultiplier tube response due to limitations of the correction response of the instrument.

Mono(6-*O*-*p*-toluenesulfonyl) permethylated β-cyclodextrin 2

6-*p*-Toluenesulfonyl β-cyclodextrin (2.4 g, 1.9 mmol) was dissolved in dry DMF (250 cm^3) and cooled to 0 °C. Sodium hydride (60% in mineral oil, 5.3 g, 130 mmol) was added carefully and the mixture stirred at this temperature for 1 h, and subsequently at room temperature for 1 h. The reaction mixture was then cooled to 0 °C, and methyl iodide (37.6 g, 270 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and then was left to warm slowly to room temperature. After stirring for 24 h, the mixture was cooled to 0 °C and methanol (25 cm^3) was added. The mixture was poured into ice-water (200 cm^3) and extracted with chloroform (5×100 cm^3). The organic layer was washed with 3% sodium thiosulfate (50 cm^3) and water (50 cm^3), dried over Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography on silica eluting with ethyl acetate containing 0.1% methanol to yield mono-6-*O*-*p*-toluenesulfonyl-permethylated β-cyclodextrin (2.2 g, 74%) as a white solid (Found: C, 51.9; H, 7.7. Calcd for $C_{69}H_{116}O_{37}S{\cdot}H_2O$: C, 52.2; H,7.5%). δ_H (300 MHz, $CDCl_3$) 7.76 (d, *J* 8.2, 2H), 7.36 (d, *J* 8.2, 2H), 5.18–4.99 (m, 7H), 4.47 (d, *J* 10.3, 2H), 4.0–2.96 (m, 100H), 2.45 (s, 3H); δ_C (75 MHz, $CDCl_3$) 146.6, 135.1, 131.6, 129.6, 101.0–100.1, 83.8–81.2, 73.1, 71.8, 71.2, 63.4–62.9, 60.8–59.9, 23.2; *m*/*z* (ESI) 1591.9 $(M + Na)^+$.

Mono(3,6-anhydro)-heptakis(2,3-*O*-methyl)-hexakis(6-*O*-methyl)-β-cyclodextrin 5

(Found: C, 52.8; H, 7.5. Calcd for $C_{61}H_{106}O_{34}$: C, 53.0; H, 7.7%). δ_H (500 MHz, $CDCl_3$) 5.53(d, *J* 3.6, 1H), 5.26 (d, *J* 2.5, 1H), 5.19 (d, *J* 3.1, 1H), 5.05 (d, *J* 3.2, 1H), 5.02 (d, *J* 2.8, 1H), 4.98 (d, *J* 3.3, 1H), 4.85 (d, *J* 3.7, 1H), 4.57 (t, *J* 4.7, 1H), 4.38 (br s, 1H), 4.15 (br d, *J* 10.0, 1H), 4.09 (d, *J* 10.5, 1H), 3.96–3.83 (m, 7H), 3.80–3.11 (m, 88H); δ_C (125 MHz, $CDCl_3$) 100.1, 99.7, 99.2, 99.0, 98.0, 97.7, 96.7, 82.9, 82.8, 82.5, 82.4, 82.2, 81.9, 81.8, 81.7, 81.6 81.5, 79.3, 79.2, 78.2, 77.3, 73.3, 71.5, 71.4, 71.2, 71.1, 71.0, 70.9, 70.4, 70.2, 69.3, 61.9, 61.8, 61.7, 61.3, 61.2, 60.0, 59.1, 59.0, 58.9, 58.8, 58.6, 58.4, 58.2, 57.9, 57.8, 57.7; *m*/*z* (ESI) 1405.9 $(M + Na)^+$.

Mono(6-*O*-propargyl) permethylated β-cyclodextrin 3

Synthesis by Route 1. Propargyl alcohol (0.27 g, 4.8 mmol) was dissolved in dry DMF (20 cm^3) and sodium hydride (60% in mineral oil, 153 mg, 3.8 mmol) was added. The mixture was stirred at room temperature for 4 h, cooled to 0 °C and mono(6-*O*-*p*-toluenesulfonyl) permethylated β-cyclodextrin (300 mg, 0.19 mmol) was added. The mixture was then stirred at room temperature for 20 h, water (4 cm^3) was added and the solvents removed. The residue was taken up in chloroform (30 cm^3), washed with water (2×5 cm^3), dried, and the solvent removed. Purification by column chromatography on silica (2.5% MeOH in EtOAc) yielded mono-6-*O*-propargyl permethylated β-cyclodextrin (135 mg, 49%) as white solid (Found: C, 53.8; H, 7.8. Calcd for $C_{65}H_{112}O_{35}$: C, 53.7; H, 7.8%). δ_H (500 MHz, $CDCl_3$) 5.12–5.09 (m, 7H, H-g1), 4.19 (ABX, *J* 2.3, 15.9, 21.2, 2H, H-a), 3.89 (dd, *J* 3.7, 10.6, 1H, H-g6), 3.84–3.15 (m, 101H), 2.42 (t, *J* 2.3, 1H., H-c); δ_C (125 MHz, $CDCl_3$) 99.1–99.0 (C-g1), 82.1, 81.8, 80.6–80.1, 80.0 (C-c), 74.5 (C-b), 71.4–70.7, 68.9, 61.5, 59.0–58.4; *m*/*z* (ESI) 1476 $(M + Na)^+$.

Synthesis by Route 2. Monohydroxy permethylated β-cyclodextrin (300 mg, 0.21 mmol) was dissolved in dry DMF (5 cm^3) and the solution cooled to 0 °C. Sodium hydride (60% in mineral oil, 26 mg, 0.63 mmol), was added and the mixture warmed to 50 °C for 45 min. After this time the mixture was

cooled to 0 °C and propargyl bromide (80% in toluene, 0.16 g, 1.06 mmol) and a catalytic amount of tetrabutylammonium iodide was added. The reaction mixture was stirred for 1 h at 0 °C and for 20 h at room temperature. Methanol (3 cm^3) was added at 0 °C to quench the excess NaH and the solvents were evaporated. The residue was taken up in chloroform (40 cm^3) and washed with water (5 cm^3). Purification by column chromatography on silica (1% MeOH in EtOAc) yielded mono-6-*O*-propargyl permethylated β-cyclodextrin as a white solid (199 mg, 65%).

Bis(mono-6-*O*-propargyl permethylated β-cyclodextrin)diyne 6

Copper(I) chloride (54 mg, 0.5 mmol) and TMEDA (64 mg, 0.5 mmol) were added successively to a solution of mono(6-*O*-propargyl) permethylated β-cyclodextrin (77 mg, 0.05 mmol) in dry dichloromethane (7 cm^3). The dark green mixture was stirred under dry air for 30 min, at which point water (1 cm^3) and dichloromethane (8 cm^3) were added to the reaction mixture. The organic layer was washed with water (2 × 1 cm^3) until the aqueous layer became colourless, the solvent removed and the residue purified by column chromatography on silica (5–10% MeOH in EtOAc) to yield **6** (40 mg, 52%) as a white solid (Found: C, 53.6; H, 7.8. Calcd for $C_{130}H_{222}O_{70}$: C, 53.8; H, 7.7). δ_H (500 MHz, $CDCl_3$) 5.10 (m, 10H, H-g1), 5.08 (d, *J* 3.6, 2H, H-g1), 5.05 (d, *J* 3.6, 2H, H-g1), 4.26 (AB, *J* 16.0, 30.1, 4H, H-a), 3.93 (dd, *J* 4.0, 10.7, 2H, Hg-6), 3.85–3.14 (m, 202H); δ_C (125 MHz, $CDCl_3$) 99.1–98.9 (C-g1), 82.1–81.9, 80.9, 80.5, 80.3, 80.2, 80.1, 75.3 (C≡C), 71.7, 71.4–70.8, 70.3 (C≡C), 68.9 (Cg-6), 61.5, 61.4–61.3, 58.9–58.9, 58.5–58.4, 58.3; *m/z* (MALDI, norharmane) 2931 $(M + Na)^+$.

1,4-Bis(mono-6-*O*-propargyl permethylated β-cyclodextrin)benzene 7

Mono(6-*O*-propargyl) permethylated β-cyclodextrin (100 mg, 0.1 mmol), and 1,4-diiodobenzene (10.3 mg, 0.031 mmol) were dissolved in a mixture of triethylamine (2 cm^3) and DMF (2 cm^3). The solution was degassed, $Pd(PPh_3)_4$ (3.6 mg, 3.1 μmol) was added and the mixture stirred at 60 °C for 24 h. The solvents were removed *in vacuo* and the residue was dissolved in dichloromethane (30 cm^3) and washed with water (2 × 3 cm^3). The organic phase was evaporated and purified by column chromatography on silica (4–10% MeOH in EtOAc) to yield **7** (54.2 mg, 53%) as a white solid (Found: C, 54.7; H, 7.9. Calcd for $C_{136}H_{226}O_{70}$: C, 54.5; H, 7.6%). λ_{max} (MeCN)/nm 217.7(sh) (ε/dm^3 mol^{-1} cm^{-1} 23800), 256.0(sh) (20800), 269.3 (37300), 281.8 (39100), 294(sh) (4260); δ_H (500 MHz, $CDCl_3$) 7.32 (s, 4H, H-Ar), 5.14–5.10 (m, 14H, H-g1), 4.42 (AB, *J* 16.0, 19.3, 4H, H-a), 4.01 (dd, *J* 4.0, 10.7, 2H, Hg-6), 3.88–3.14 (m, 202H); δ_C (125 MHz, $CDCl_3$) 131.5(CH-Ar), 122.7 (C-Ar), 99.0–98.9 (C-g1), 87.2 (C-b), 85.5 (C-c), 82.1–81.7, 80.6–80.1, 71.6, 71.4, 70.9, 68.8, 61.5–61.4, 59.2–58.4; *m/z* (MALDI, sinapinic acid) 3003 $(M + Na)^+$.

1,3,5-Tris(mono-6-*O*-propargyl permethylated β-cyclodextrin)benzene 8

Mono(6-*O*-propargyl) permethylated β-cyclodextrin (150 mg, 0.1 mmol), triphenylphosphine (3.6 mg, 0.014 mmol) and 1,3,5-tribromobenzene (7.23 mg, 0.02 mmol) were dissolved in a mixture of triethylamine (2 cm^3) and DMF (2 cm^3). The solution was degassed, $Pd_2(dba)_3{\cdot}CHCl_3$ (3.4 mg, 3.3 μmol) was added and the mixture stirred at 70 °C for 6 h. The solvents were removed *in vacuo* and the residue was dissolved in dichloromethane (30 cm^3) and washed with water (2 × 3 cm^3). The organic phase was evaporated and purified by column chromatography on silica (4–10% MeOH in EtOAc) to yield **8** (73.1 mg, 82%) as a light yellow solid (Found: C, 53.4; H, 7.9. Calcd for $C_{201}H_{336}O_{105}{\cdot}5H_2O$: C, 53.4, H 7.7%). λ_{max} (MeCN)/nm 240.6 (ε/dm^3 mol^{-1} cm^{-1} 50800), 258.3(sh) (32700). δ_H (500 MHz, $CDCl_3$) 7.34 (s, 3H, H-Ar), 5.14–5.08 (m, 21H, H-g1), 4.38 (br s, 6H, H-a), 4.03(dd, *J* 3.0, 10.4, 3H, Hg-6), 3.85–3.15 (m, 303H); δ_C (125 MHz, $CDCl_3$) 134.3 (CH-Ar), 123.4 (C-Ar), 99.1–98.9 (C-1), 86.7 (C-b), 84.0 (C-c), 82.1–81.7, 80.8, 80.5, 80.4, 80.3, 80.2, 80.0, 71.7–70.9, 69.0, 61.5–61.3, 59.3–59.1; *m/z* (MALDI, sinapinic acid) 4454 $(M + Na)^+$.

References

1 R. Breslow and S. D. Dong, *Chem. Rev.*, 1998, **98**, 1997.
2 D. K. Leung, J. H. Atkins and R. Breslow, *Tetrahedron Lett.*, 2001, **42**, 6255.
3 J. M. Haider, R. M. Williams, L. De Cola and Z. Pikramenou, *Angew. Chem., Int. Ed.*, 2003, **42**, 1830.
4 J. M. Haider and Z. Pikramenou, *Chem. Soc. Rev.*, 2005, **34**, 120.
5 J. S. Lock, B. L. May, P. Clememnts, S. F. Lincoln and C. J. Easton, *Org. Biomol. Chem.*, 2004, **2**, 337.
6 A. Mulder, A. Jukovic, J. Huskens and D. Reinhoudt, *Org. Biomol. Chem.*, 2004, **2**, 1748.
7 I. Banerjee, L. Yu and H. Matsui, *J. Am. Chem. Soc.*, 2003, **125**, 9542.
8 I. Hamachi, H. Takashima, Y.-Z. Hu, S. Shinkai and S. Oishi, *Chem. Commun.*, 2000, 1127.
9 K. Sasaki, M. Nagasaka and Y. Kuroda, *Chem. Commun.*, 2001, 2630.
10 N. Van Hoof, T. E. Keyes, R. J. Forster, A. McNally and N. R. Russell, *Chem. Commun.*, 2001, 1156.
11 C. M. Rudzinski, A. M. Young and D. G. Nocera, *J. Am. Chem. Soc.*, 2002, **124**, 1723.
12 H. F. M. Nelissen, M. Kercher, L. De Cola, M. C. Feiters and R. J. M. Nolte, *Chem. Eur. J.*, 2002, **8**, 5407.
13 J. M. Haider and Z. Pikramenou, *Eur. J. Inorg. Chem.*, 2001, 189.
14 Y. Liu, C. Yong, L. Li, H. Zhang, S. Liu and X. Guan, *J. Org. Chem.*, 2001, **66**, 8518.
15 H. F. Nelissen, A. F. Schut, F. Venema, M. C. Feiters and R. J. Nolte, *Chem. Commun.*, 2000, 577.
16 B. Zhang and R. Breslow, *J. Am. Chem. Soc.*, 1997, **119**, 1676.
17 F. Venema, H. F. M. Nelissen, P. Berthault, N. Birlirakis, A. E. Rowan, M. C. Feiters and R. J. M. Nolte, *Chem. Eur. J.*, 1998, **4**, 2237.
18 W.-H. Chen, J.-M. Yang, Y. Tagashira, M. Yamaguchi and K. Fujita, *Tetrahedron Lett.*, 1999, **40**, 891.
19 C. A. Haskard, C. J. Easton, B. L. May and S. F. Lincoln, *J. Phys. Chem.*, 1996, **100**, 14457.
20 E. Alvarez-Parrilla, P. Ramos Cabrer, W. Al-Soufi, F. Meijide, E. Rodriguez Nunez and J. Vazquez Tato, *Angew. Chem., Int. Ed.*, 2000, **39**, 2856.
21 H. Nakajima, Y. Sakabe, H. Ikeda and A. Ueno, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 1783.
22 T. Kikuchi, M. Narita and F. Hamada, *Tetrahedron*, 2001, **57**, 9317.
23 P. J. Skinner, A. Beeby, R. S. Dickins, D. Parker, S. Aime and M. Botta, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1329.
24 R. Deschenaux, A. Greppi, T. Ruch and H. P. Kriemler, *Tetrahedron Lett.*, 1994, **35**, 2165.
25 T. Lecourt, J. M. Mallet and P. Sinay, *Eur. J. Org. Chem.*, 2003, 4553.
26 J. M. Haider, M. Chavarot, S. Weidner, I. Sadler, R. M. Williams, L. De Cola and Z. Pikramenou, *Inorg. Chem.*, 2001, **40**, 3912.
27 O. Bistri, T. Lecourt, J. M. Mallet, M. Sollogoub and P. Sinay, *Chem. Biodiversity*, 2004, **1**, 129.
28 J. Defaye, A. Gadelle, R. Guiller and T. O'Sullivan, *Carbohydr. Res.*, 1989, **192**, 251.
29 S. Tamagaki, A. Katayama, M. Maeda and N. Yamamoto, *J. Chem. Soc., Perkin Trans. 2*, 1994, 507.
30 Y. Matsui and A. Okimoto, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 3030.
31 G. Yi, J. S. Bradshaw, B. E. Rossiter and A. Malik, *J. Org. Chem.*, 1993, **58**, 4844.
32 R. Deschenaux, M. M. Harding and T. Ruch, *J. Chem. Soc., Perkin Trans. 2*, 1993, 1251.
33 S. R. Gilbertson, G. S. Hoge and D. G. Genov, *J. Org. Chem.*, 1998, **63**, 10077.
34 K. Kano, R. Nishiyabu, T. Yamazaki and I. Yamazaki, *J. Am. Chem. Soc.*, 2003, **125**, 10625.
35 T. Kaneda, T. Fujimoto, J. Goto, K. Asano, Y. Yasufuku, J. H. Jung, C. Hosono and Y. Sakata, *Chem. Lett.*, 2002, 514.
36 F. Djedaini-Pilard, M. Gosnat, V. Brucato-Mauclaire, C. Creminon, J. P. Dalbiez, S. Pilard, W. Luijten, and B. Perly, *Proceedings of the Ninth International Symposium on Cyclodextrins*, Santiago de Compostela, Spain, 1998, p. 625.
37 C. McDonnell, O. Lopez, P. Murphy, J. G. F. Bolanos, R. Hazell and M. Bols, *J. Am. Chem. Soc.*, 2004, **126**, 12374.
38 P. R. Ashton, P. Ellwood, I. Staton and J. F. Stoddart, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 80.

39 P. R. Ashton, P. Ellwood, I. Staton and J. F. Stoddart, *J. Org. Chem.*, 1991, **56**, 7274.
40 A. Gadelle and J. Defaye, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 78.
41 M. B. Nielsen, N. F. Utesch, N. N. Moonen, C. Boudon, J. P. Gisselbrecht, S. Concilio, S. P. Piotto, P. Seiler, P. Gunter, M. Gross and F. Diederich, *Chem. Eur. J.*, 2002, **8**, 3601.
42 H. L. Anderson, C. J. Walter, A. Vidal-Ferran and R. A. Hay, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2275.
43 V. Marvaud, A. Vidal-Ferran, S. J. Webb and J. K. M. Sanders, *J. Chem. Soc., Dalton Trans.*, 1997, 985.
44 T. E. O. Screen, K. B. Lawton, G. S. Wilson, N. Dolney, R. Ispasoiu, T. Goodson, S. J. Martin, D. D. C. Bradley and H. L. Anderson, *J. Mater. Chem.*, 2001, **11**, 312.
45 Z. Xu, M. Kahr, K. L. Walker and C. L. Wilkins, *J. Am. Chem. Soc.*, 1994, **116**, 4537.
46 M. Uno and P. H. Dixneuf, *Angew. Chem., Int. Ed.*, 1998, **37**, 1714.
47 E. M. Maya, P. Vazquez, T. Torres, L. Gobbi, F. Diederich, S. Pyo and L. Echegoyen, *J. Org. Chem.*, 2000, **65**, 823.
48 Y. Pan, M. Lu, Z. Peng and J. S. Melinger, *J. Org. Chem.*, 2003, **68**, 6952.
49 U. W. Grummt, E. Birckner, E. Klemm, D. A. M. Egbe and B. Heise, *J. Phys. Org. Chem.*, 2000, **13**, 112.
50 O. Lavastre, L. Ollivier, P. H. Dixneuf and S. Sibandhit, *Tetrahedron*, 1996, **52**, 5495.
51 D. W. Price, Jr. and J. M. Tour, *Tetrahedron*, 2003, **59**, 3131.
52 I. Sato, R. Kodaka, T. Shibata, Y. Hirokawa, N. Shirai, K. Ohtake and K. Soai, *Tetrahedron: Asymmetry*, 2000, **11**, 2271.
53 J. F. Nguefack, V. Bolitt and D. Sinou, *Tetrahedron Lett.*, 1996, **37**, 5527.
54 I. P. Beletskaya, A. V. Chuchurjukin, H. P. Dijkstra, G. P. van Klink and G. van Koten, *Tetrahedron Lett.*, 2000, **41**, 1081.
55 A. H. M. Elwahy and K. Hafner, *Tetrahedron Lett.*, 2000, **41**, 4079.
56 B. G. Kim, S. Kim and S. Y. Park, *Tetrahedron Lett.*, 2001, **42**, 2697.
57 R. Roy, S. K. Das, F. Santoyo-Gonzalez, F. Hernandez-Mateo, T. K. Dam and C. F. Brewer, *Chem. Eur. J.*, 2000, **6**, 1757.
58 S. Sengupta and S. K. Sadhukhan, *Carbohydr. Res.*, 2001, **332**, 215.
59 E. C. Constable, O. Eich and C. E. Housecroft, *J. Chem. Soc., Dalton Trans.*, 1999, 1363.
60 K. M. Gaab, A. L. Thompson, J. Xu, T. J. Martinez and C. J. Bardeen, *J. Am. Chem. Soc.*, 2003, **125**, 9288.
61 Z. Chen, J. S. Bradshaw and M. L. Lee, *Tetrahedron Lett.*, 1996, **37**, 6831.
62 N. W. Alcock, P. R. Barker, J. M. Haider, M. J. Hannon, C. L. Painting, Z. Pikramenou, E. A. Plummer, K. Rissanen and P. Saarenketo, *J. Chem. Soc., Dalton Trans.*, 2000, 1447.