Synthesis of an elongated linear oligo(phenylene ethynylene)-based building block for application in DNA-programmed assembly†‡

Peter Blakskjær[a,b] and Kurt V. Gothelf*[a]

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The synthesis of an elongated linear oligonucleotide-functionalised module (ELOM) is described. The ELOM structure is based on an oligo(phenylene ethynylene) backbone substituted with two decyloxy groups. The two termini constitute two salicylaldehyde moieties acting as chemical cross-linkers. Before incorporation into an oligonucleotide sequence the organic part of the module, the elongated linear module (ELM), is functionalised with a dimethoxytrityl group and a phosphoramidite group. This enables incorporation into the middle of 30-mer oligonucleotide sequences by automated DNA synthesis. The obtained ELOMs were characterised by polyacrylamide gel electrophoresis and MALDI-TOF mass spectrometry. In analogy with previously reported LOM and TOM structures the coupling reactions of the ELOM modules were tested.

Introduction

The interest in using molecular building blocks for assembly of geometrically well-defined and functional molecular nanostructures has led to the search for new ways to assemble organic molecules into supra- or macromolecular structures as an alternative to conventional organic synthesis. The formation of large and well-defined molecular assemblies from a relatively simple set of building blocks is of great interest for the field of molecular electronics.[1] During the past few years a number of molecular electronic components and wires have been synthesised and evaluated for their electronic behaviour.[2] Reliable methods for the controlled assembly of these devices into nanostructures have, however, not yet been developed. In recent years much interest has been focused on the application of DNA as an encodable material for the spatial positioning of molecules and materials.[3,4] In addition, DNA-programmed chemistry has proven to be an efficient tool to assemble *and* couple organic molecules.[5,6]

As part of an ongoing programme addressing this problem we recently published a new bottom-up method for the programmed assembly and covalent coupling of multiple organic modules.[6–10] The building blocks used in these reactions were linear (LOM) and tripoidal (TOM) oligo(phenylene ethylene)-based structures containing terminal salicylaldehyde moieties (Scheme 1). They were encoded with short (15 nt) oligonucleotides at their termini. Annealing of the structures followed by imine formation of the aldehyde moieties using ethylenediamine in the presence of a metal salt such as $Mn(OAc)_2$ led to structures consisting of up to four segments linked by metal–salen complexes.[7] The imines could alternatively be reduced with $NaBH_3CN$ which gave the corresponding amine-linked structures.[10]

One limitation associated with this procedure is that more than four modules could not be assembled in satisfactory yields. We imagine that this may be caused by steric interactions of the very large oligonucleotide duplexes. The diameter of the DNA duplex is 2 nm, and the LOMs are also about 2 nm long. Thus, the multiple duplexes formed in these nanostructures are expected to induce steric strain as the structures grow. We therefore rationalised that if this reason is prevalent, then one way of solving the problem may be by extending the length of the linear module.

Here we report on the synthesis of an elongated linear module (ELM) designed to be incorporated into oligonucleotides by automated DNA synthesis. We have previously shown that compounds of this type functionalised as a nucleoside phosphoramidite can be efficiently incorporated into an oligonucleotide strand by automated oligonucleotide synthesis.[4,7] This ELM meets the requirements previously stated for the linear modules (LM's), *i.e.* it is rigid and potentially conducting.[11] It is appropriately functionalised both to be incorporated into oligonucleotides and to undergo salen-formation. The aldehydes and the phenols have to be protected since they are not compatible with the oligonucleotide synthesis.[1,12] The amide bonds provide a stable linkage to the oligonucleotides[7,8] and the C_{10} chains have been added to aid solubility of the oligo(phenylene ethylene) backbone.[13]

Results and discussion

The synthesis of the salicylaldehyde building block **3** for preparation of the functional end groups in ELM has previously been reported by us (Scheme 2).[8] The most obvious way to build up the ELM oligo(phenylene ethylene) backbone is by a series of Sonogashira couplings and the synthesis was carried out in a straightforward manner according to Scheme 3.[14] First, the TMS-protected 4-(ethynyl)-1-iodobenzene building block **4** was prepared from (4-bromophenylethynyl)-trimethylsilane. The (4-bromophenylethynyl)-trimethylsilane is commercially available from Aldrich, but it was easily synthesised in high yield (85%)

[a]*Center for Catalysis and Interdisciplinary Nanoscience Center (iNANO), Department of Chemistry, University of Aarhus, Langelandsgade, 140, Denmark. E-mail: kvg@chem.au.dk; Fax: +45 86196199; Tel: +45 89423907*
[b]*Vipergen, Fruebjergvej 3, DK-2100, Copenhagen, OE, Denmark*

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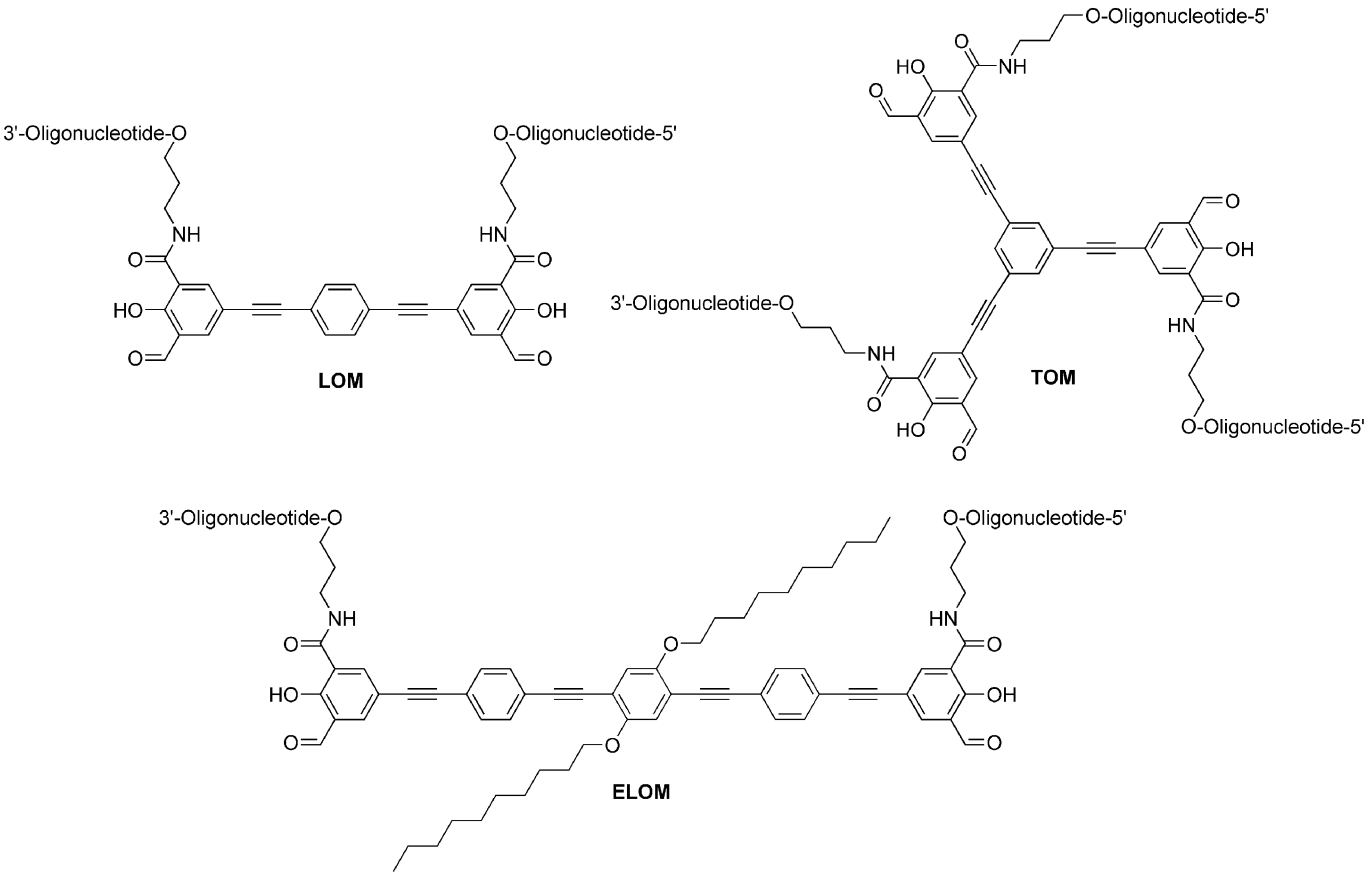
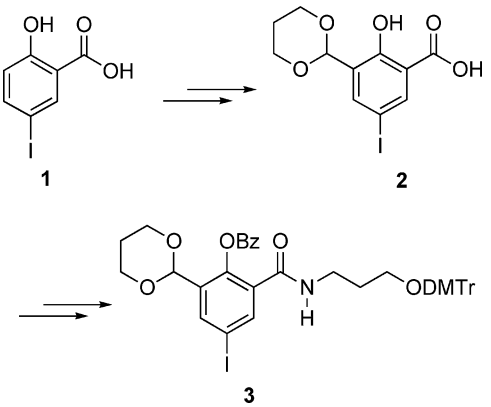
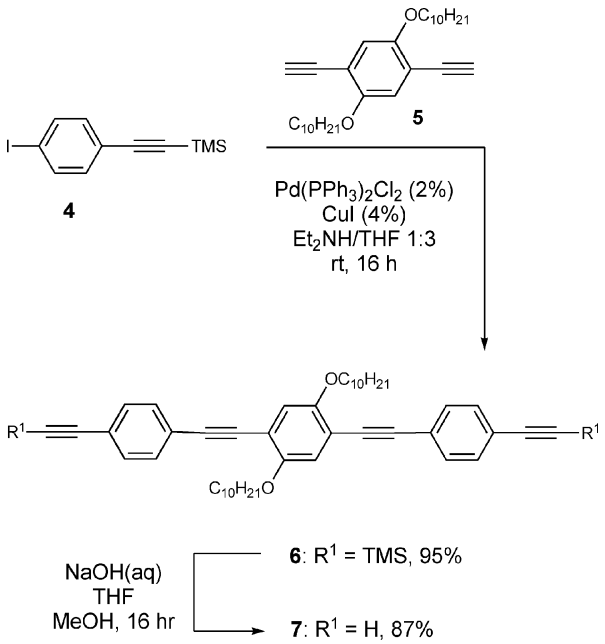


Scheme 1 Chemical structures of the linear oligonucleotide-functionalised module (LOM), the tripoidal oligonucleotide-functionalised module (TOM) and the elongated linear oligonucleotide-functionalised module (ELOM).

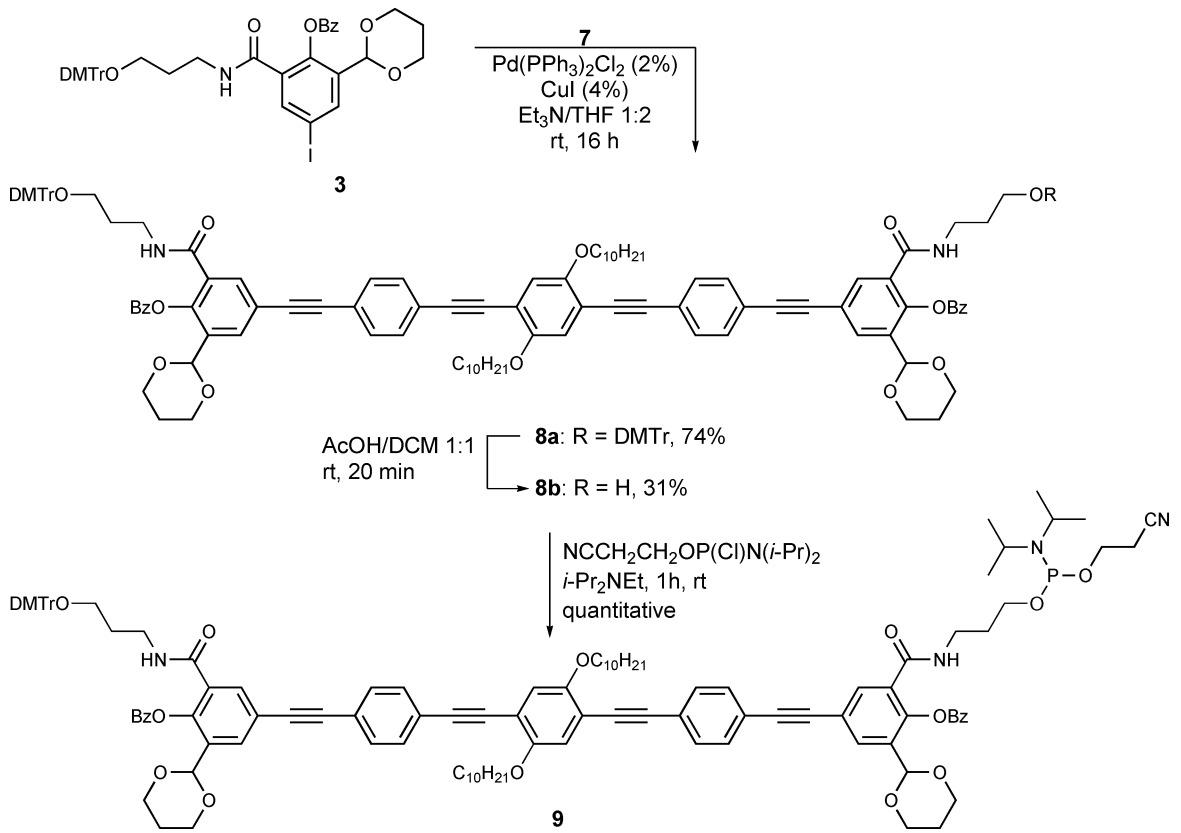


Scheme 2 Synthesis of the protected salicylaldehyde head group.



Scheme 3 Preparation of the linear backbone by Sonogashira reactions.

by a Sonogashira coupling between 4-bromo-1-iodobenzene and trimethyl-silylacetylene catalysed by bis(triphenyl-phosphine)-palladium(II) chloride and copper(I) iodide in the presence of diethylamine.[15] Lithiation of the bromide facilitated by treatment with two equivalents of *tert*-butyllithium at −78 °C followed by addition to molecular iodine gave the corresponding iodide **4** in essentially quantitative yield.[16] The central 1,4-bis-decyloxy-2,5-diethynylbenzene (**5**) was synthesised according to a known literature procedure.[13c] The conjugated backbone was assembled by a Sonogashira coupling, using almost the same conditions as in the first coupling, of the diacetylene **5** with two equivalents of the iodide **4**. The appearance of a strongly fluorescent solution indicated the formation of the conjugated backbone and compound **6** was isolated in an excellent yield of 95%. Removal of



Scheme 4 Preparation of the elongated linear module (ELM) **9**, functionalised as a phosphoramadite.

the trimethylsilyl groups in aqueous base gave the oligo(phenylene ethylene) **7** in 87% yield.

A final Sonogashira coupling with the 5-iodosalicylic aldehyde derivative **3** constructed the ELM backbone **8a** in good yield (Scheme 4). One of the DMTr groups was removed by 50% acetic acid in dichloromethane for 20 min. This reaction was carefully monitored by thin layer chromatography and stopped as soon as the product in which both DMTr groups were removed was observed. Chromatography gave the desired mono-deprotected derivative **8b** in a moderate yield of 31%. However, 60% of the starting material could easily be recovered and applied in repeated deprotections. A following treatment with the required phosphoramidite chloride and Hünigs base provide phosporamidite **9** which was isolated quantitatively by precipitation in pentane (overall yield for two steps of 31%). We had previously shown that phosporamidites of this type would partly decompose during chromatography on silica gel.[8] The precipitated material was analysed by ^{31}P NMR and showed only minor impurities and the sample was therefore not further purified but used directly for automated oligonucleotide synthesis.

Phosphoramidite **9** was used as precursor for the elongated linear oligonucleotide-functionalised module ELOM. The phosphoramidites were incorporated by standard automated oligonucleotide synthesis into the middle of an oligonucleotide containing 30 nucleotides. After basic removal of the base protecting groups the conjugates were purified by FPLC. The 5′-terminal DMTr group was removed, the phenol moiety was deprotected in 25% aqueous ammonia at 50 °C and finally the acetal protecting group was removed in NaOAc buffer at pH 4. In this manner we have prepared the three ELOM modules **11–13** listed in Table 1. This table also includes LOM compound **14**, which has been described previously.[7,8]

Table 1 DNA-sequences and MALDI-TOF mass spectrometry characterization of ELOM and LOM structures

Module		DNA sequences	Calc. mass (Da)[a]	Observed mass (Da)[b]
ELOM **11**	a-ELM-b′	5′-ATTGATCTAGTTGAT-ELM-TGTACATCTACACTT-3′	10413.11	10480
ELOM **12**	b-ELM-c′	5′-AAGTGTAGATGTACA-ELM-ACTTCAGTTGGTCGT-3′	10528.13	10616
ELOM **13**	c-ELM-d′	5′-ACGACCAACTGAAGT-ELM-CTGTAGACATATGTT-3′	10466.14	10552
LOM **14**[c]	b-LM-c′	5′-AAGTGTAGATGTACA-LM-ACTTCAGTTGGTCGT-3′		

[a] Mass spectra were recorded before removal of the acetal protecting groups. [b] The reported values represents the max. height of the peak; the peaks are broad with a width at half max. height of approximately 400 Da. [c] This linear module is described in ref. 7.

The resulting ELOM modules were characterised by MALDI-TOF mass spectrometry and by denaturing polyacrylamide gel electrophoresis.

The mass peaks are relatively broad with a width at half max. height of around 400 Da, as it appears from the example on the MALDI-TOF spectrum of ELOM **11** in Fig. 1A. Thus the calculated masses fall well within the observed mass peaks. The ELOMs were also analysed by denaturing polyacrylamide gel electrophoresis (PAGE) in a 8 M urea buffer (Fig. 1B). The mobility of the ELOM modules are shown in lanes 1–3 and 9 and they show well-defined bands with a slightly lower mobility than the previously reported LOM modules (lane 8).[7] Additionally, the purity and UV absorption of the three ELOMSs were determined by HPLC (see: electronic supplementary information‡).

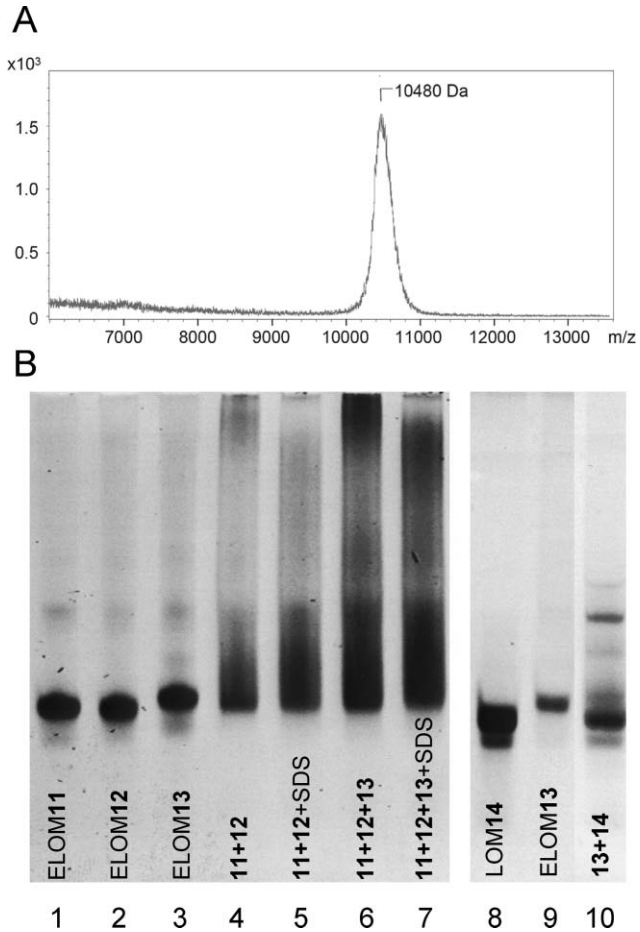
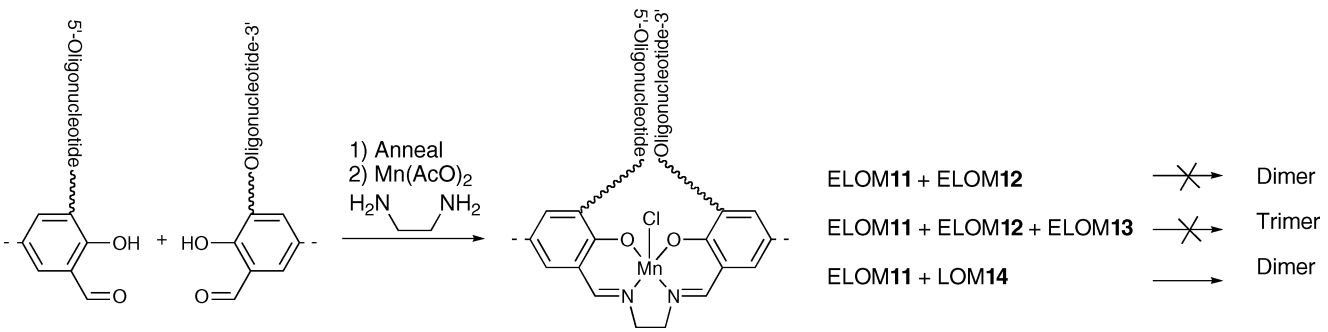


Fig. 1 Analysis of ELOM and LOM and their coupling reactions. (A) MALDI-TOF mass spectrum of ELOM **11** with a calc. mass of 10413 Da and an obs. mass of 10480 Da. (B) Denaturing polyacrylamide gel electrophoresis in 8 M urea of the coupling products. Reactions were performed in the presence of 1.0 mM EDA and 0.5 mM $Mn(OAc)_2$. Lanes 1–3: ELOM monomers, lanes 4–7 coupling reactions of ELOM modules in the absence and presence of SDS as indicated, lanes 8–9 LOM and ELOM monomers, coupling between LOM **14** and ELOM **13**.

The coupling reaction between ELOM modules by a DNA-programmed reaction between the salicylaldehyde moieties was attempted in the presence of ethylenediamine and $Mn(OAc)_2$ (Scheme 5). This approach was very efficient for the coupling of up to four LOM modules.[6,7,9,10] Our attempts to couple two or three ELOM modules were unfortunately unsuccessful (Fig. 1B, lanes 4–7), whereas the coupling between ELOM **13** and LOM **14** was successful and resulted in a well-defined product band (lane 10). For the ELOM dimerisations and trimerisations in lanes 4 and 6, no well-defined product bands result from the PAGE analysis. A smear is observed at the top of the gel close to the ELOM monomer. Native PAGE did not improve the appearance of the gels. We speculate that the lacking ability of the ELOM structures to undergo dimerisation is due to aggregation of the ELOM moieties. In addition to the length, a major difference between the LOM/TOM structures and the ELOM structure is the two decyloxy substituents in the ELOM structure. The decyloxy groups were added to improve solubility of the ELM in organic solvents. As a consequence, however, the ELOM structure may behave as an amphiphile due to the hydrophilic DNA-sequences and the hydrophobic decyloxy groups. Hence, the ELOM structures may aggregate by hydrophobic interactions during the coupling reactions leading to formation of higher order oligomeric structures. To suppress the aggregation it was attempted to perform the dimerisation and trimerisation reactions in the presence of sodium dodecyl sulfate (lanes 5 and 7). However, this did not improve the coupling reactions and the smearing was only slightly reduced or the mobility of smeared bands changed.

Future studies will show if it is possible to circumvent these problems by substitution of the decyloxy side chains with *e.g.* ethyleneglycol oligomers. However, it will also be investigated if we can take advantage of the amphiphilic nature of the ELOM. For example, by testing the assembly and coupling of ELOM structures in the interface between water and a hydrophobic solvent. It has been reported that oligo(phenylene ethynylene)s with alkyl side chains absorb and align on the surface of carbon nanotubes.[17] We will explore the possible DNA-programmed



Scheme 5 DNA-programmed coupling between two salicylaldehyde head groups by manganese salen formation (left) and the results of basic couplings between ELOMs and LOM (right).

assembly of the ELOM structures in the presence of carbon nanotubes.

Conclusion

In conclusion, an efficient synthesis of a highly functionalised elongated linear module containing an oligo(phenylene ethynylene) backbone has been developed. This ELM is functionalised as a nucleoside phosporamidite which can be incorporated into oligonucleotides by automated synthesis. The assembly and coupling between a LOM structure and an ELOM structure was successful, however, it was not possible to induce DNA-programmed ELOM dimerisation or trimerisation. It is proposed that this is due to the amphiphilic nature of the ELOMs. Future studies may reveal if the amphiphilic nature of the ELOM can be used for assembly and coupling at interfaces.

Experimental

General methods

The ^{1}H NMR, ^{31}P NMR and ^{13}C NMR were recorded at 400, 160 and 100 MHz, respectively. Chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for ^{1}H NMR, relative to the central $CDCl_3$ resonance ($\delta = 77.16$) for ^{13}C NMR and relative to 85% H_3PO_4 ($\delta = 0$) for ^{31}P NMR. All reactions were carried out under an argon atmosphere using standard Schlenk equipment and vacuum line techniques unless otherwise stated.

Materials

Solvents were dried according to standard procedures and distilled under an atmosphere of argon or nitrogen prior to use. (4-Bromophenylethynyl)-trimethylsilane[14] is commercially available from Aldrich but was synthesised from 1-bromo-4-iodobenzene (Aldrich). (4-iodophenylethynyl)trimethylsilane,[16] 1,4-bis-decyloxy-2,5-diethynylbenzene[13c] and 1-benzoyloxy-2-(*N*-(3-dimethoxytrityloxyprop-1-yl)-aminocarbonyl)-6-(1,3-dioxan-2-yl)-4-iodobenzene (**3**)[8] were synthesised according to literature procedures.

1,4-Bis-decyloxy-2,5-bis-(4-trimethylsilanylethynyl-phenylethynyl)-benzene (6). To a Schlenk flask charged with 1,4-bisdecyloxy-2,5-diethynylbenzene (**5**) (87.7 mg, 0.20 mmol), (4-iodophenylethynyl)-trimethylsilane (**4**) (132.1 mg, 0.44 mmol), $Pd(PPh_3)_2Cl_2$ (2.8 mg, 0.004 mmol) and CuI (1.5 mg, 0.008 mol) was added THF (3.0 mL) and diethylamine (1.0 mL). This solution was stirred at room temperature for 19 h. The solvents were evaporated and the residue diluted with CH_2Cl_2 and satd. NaCl solution. The aqueous solution was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$) and evaporated. The crude material was purified by flash chromatography on silica gel using CH_2Cl_2–pentane 1 : 9 → 1 : 4 as eluents to yield the title compound as a yellow fluorescent crystalline solid (149.0 mg, 95%). ^{1}H NMR ($CDCl_3$) δ (ppm) 7.44 (center of an AB spin system, 8H, J_{AB} = 8.4 Hz), 6.99 (s, 2H), 4.02 (t, 4H, $J = 6.4$ Hz), 1.84 (quint, 4H, $J =$ 6.8 Hz), 1.53 (quint, 4H, $J = 6.8$ Hz), 1.38–1.10 (m, 24H), 0.88 (t, 6H, $J = 6.8$ Hz), 0.25 (s, 18H). ^{13}C NMR ($CDCl_3$) δ (ppm) 153.8, 132.0, 131.4, 123.6, 123.0, 116.9, 114.1, 104.8, 96.4, 94.7, 88.0, 69.7, 32.0, 29.8, 29.7, 29.5, 29.4 (2 signals), 26.2, 22.8, 14.2, 0.0. MALDI-TOF $C_{52}H_{70}O_2Si_2$ [M$^+$]; calculated: 782.49 found: 799.26. UV/VIS (abs. ethanol) λ_{max}/nm 256, 323, 385.

1,4-Bisdecyloxy-2,5-bis(4-ethynylphenylethynyl)-benzene (7). 1,4-Bisdecyloxy-2,5-bis(4-trimethylsilanylethynyl-phenylethynyl)-benzene (**6**) (162.2 mg, 0.207 mmol) dissolved in a mixture of THF (5.0 mL) and methanol (3.0 mL) and was cooled to 0 °C and treated with 5 M $NaOH_{(aq)}$ (0.25 mL, 1.25 mmol). This mixture was warmed to room temperature and stirred for 16 h. Then water and CH_2Cl_2 were added and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic phase was dried ($MgSO_4$) and evaporated which gave the desired product as a yellow fluorescent solid (114.5 mg, 87%). ^{1}H NMR ($CDCl_3$) δ (ppm) 7.48 (s, 8H), 7.01 (s, 2H), 4.02 (t, 4H, $J = 6.4$ Hz), 3.19 (s, 2H), 1.85 (quint, 4H, $J = 7.6$ Hz), 1.54 (quint, 4H, $J = 7.6$ Hz), 1.40–1.22 (m, 24H), 0.88 (t, 6H, $J = 7.2$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm) 153.9, 132.3, 131.7, 124.1, 122.1, 117.0, 114.1, 94.7, 88.2, 83.5, 79.2, 69.8, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 26.3, 22.9, 14.4.

MALDI-TOF $C_{46}H_{54}O_2$ [M$^+$]; calculated: 638.41 found: 634.82.

DMTrO-ELM-ODMTr (8a). To a Schlenk flask charged with $Pd(PPh_3)_2Cl_2$ (2.2 mg, 3.1 μmol) and CuI (1.2 mg, 6.2 μmol) was added 1,4-bisdecyloxy-2,5-bis-(4-ethynyl-phenylethynyl)-benzene (**7**) (109.7 mg, 0.172 mmol) dissolved in THF (4.0 mL) and 1-benzoyloxy-2-(*N*-(3-dimethoxytrityloxyprop-1-yl)-aminocarbonyl)-6-(1,3-dioxan-2-yl)-4-iodobenzene (**3**) (279.9 mg, 0.344 mmol) dissolved in THF (4.0 mL). To this solution was added triethylamine (4.0 mL) and the mixture was stirred for 24 h at room temperature. The solvents were evaporated and a 1 : 1 mixture of EtOAc and CH_2Cl_2 was added. Filtration through a plug of silica gel and evaporation gave a residue that was purified by flash chromatography on silica gel using EtOAc–CH_2Cl_2–pentane 1 : 1 : 3 → 5 : 4 : 11 as eluents. This gave the desired product as a yellow fluorescent foamy solid (255.4 mg, 74%). ^{1}H NMR ($CDCl_3$) δ (ppm) 8.15 (dd, 4H, $J = 7.2$, 1.2 Hz), 7.95 (d, 2H, $J = 2$ Hz), 7.74 (d, 2H, $J = 2$), 7.67 (tt, 2H, $J =$ 7.6, 1.2 Hz), 7.53–7.47 (m, 12H), 7.36 (dd, 4H, $J = 7.2$, 1.2 Hz), 7.30–7.21 (m, 12H), 7.19 (tt, 2H, $J = 7.2$, 1.2 Hz), 7.03 (s, 2H), 6.77 (d, 8H, $J = 8.8$ Hz), 6.49 (t, 2H, $J = 6.0$ Hz), 5.59 (s, 2H), 4.14–4.09 (m, 4H), 4.05 (t, 4H, $J = 7.0$ Hz) 3.81–3.72 (m, 4H), 3.76 (s, 12H), 3.40 (q, 4H, $J = 6.0$ Hz), 3.09 (t, 4H, $J = 6.0$ Hz), 2.18–2.06 (m, 2H), 1.87 (quint, 4H, $J = 7.0$ Hz), 1.66 (quint, 4H, $J = 6.0$ Hz), 1.56 (quint, 4H, $J = 7.0$ Hz), 1.40–1.24 (m, 26H), 0.88 (t, 6H, $J = 7.0$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm) 165.2, 164.7, 158.4, 153.7, 145.4, 144.7, 136.2, 133.9, 132.6, 132.5, 132.3, 131.61, 131.55, 131.2, 130.3, 129.9, 129.2, 128.8, 128.1, 127.9, 126.8, 123.5, 122.7, 121.6, 116.8, 113.9, 113.1, 97.6, 94.7, 90.2, 89.9, 88.1, 86.2, 69.6, 67.4, 61.6, 55.2, 38.2, 32.0, 29.7, 29.6, 29.5, 29.41, 29.37, 29.3, 26.1, 25.5, 22.8, 14.2. MALDI-TOF $C_{130}H_{132}N_2O_{18}$ [M + Na$^+$]; calculated: 2031.94 found: 2032.58 UV/VIS (CH_2Cl_2): λ_{max}/nm (log ε): 237 (4.83), 277 (4.32), 332 (4.37), 389 (4.40)

DMTrO-ELM-OH (8b). To a 50 mL roundbottomed flask charged with DMTrO-ELM-ODMTr (**8a**) (109.7 mg, 54.6 μmol) was added a 1 : 1 solution of acetic acid and dichloromethane (7.5 mL). This solution was stirred for 20 min. at room temperature and then poured into satd. $NaHCO_3$ and extracted with dichloromethane (3 × 20 mL), dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography on silica gel using EtOAc–pentane 1 : 1 → 4 : 1 as eluents. This

gave the desired alcohol **8b** as a yellow fluorescent solid (28.8 mg, 31%) together with the starting material (66 mg, 60%). ^{1}H NMR (CD_2Cl_2) δ (ppm) 8.12 (d, 2H, $J = 7.6$ Hz), 8.04 (d, 2H, $J = 7.6$ Hz), 7.86 (s, 2H), 7.78 (d, 1H, $J = 2.0$ Hz), 7.67 (d, 1H, $J = 2.0$ Hz), 7.63 (t, 1H, $J = 7.5$ Hz), 7.61 (t, 1H, $J = 7.5$), 7.49 (t, 4H, $J = 7.5$ Hz), 7.45 (s, 8H), 7.28 (d, 2H, $J = 7.5$ Hz), 7.19–7.11 (m, 2H), 7.16 (d, 4H, $J = 8.4$ Hz), 6.97 (s, 2H), 6.69 (d, 4H, $J = 8.4$ Hz), 6.50 (br m, 1H), 6.40 (br m, 1H), 5.53 (s, 2H), 4.04–3.94 (m, 8H), 3.73–3.65 (m, 4H), 3.66 (s, 6H), 3.39 (m, 2H), 3.31 (q, 2H, $J = 6.2$ Hz), 3.26 (q, 2H, $J = 6.2$ Hz), 2.98 (t, 2H, $J = 5.6$ Hz), 2.57 (br s, 1H), 2.06–1.94 (m, 2H), 1.78 (quint, 4H, $J = 7.2$ Hz), 1.56–1.38 (m, 8H), 1.34–1.12 (m, 26H), 0.80 (t, 6H, $J = 6.8$ Hz). ^{13}C NMR was not obtained of this compound. MALDI-TOF $C_{109}H_{114}N_2O_{16}$ [M + Na^+]; calculated: 1729.81 found: 1730.24.

DMTrO-ELM-OP(N^iPr_2)O(CH_2)$_2$CN (9). DMTrO-ELM-OH (**8b**) (104.0 mg, 0.061 mmol) was dissolved in CH_2Cl_2 (10 mL) in a Schlenk flask and cooled to 0 °C then diisopropylethylamine (74.2 µL, 0.43 mmol) was added followed by dropwise treatment with diisopropyl-chlorophosphoramidite (40.8 µL, 0.18 mmol). This mixture was stirred at this temperature for 10 min then allowed to reach room temperature and stirred for another 1 h followed by dilution with CH_2Cl_2 (20 mL) and washed twice with satd. $NaHCO_3$ and once with water. Drying over Na_2SO_4 and concentration gave a yellow oil that was precipitated into pentane to give the desired phosphoramidite as a yellow fluorescent chunky solid (116.1 mg, 100%) after removal of the liquid and a wash with pentane followed by drying *in vacuo*. ^{1}H NMR (CD_2Cl_2) δ (ppm) 8.13 (dd, 2H, $J = 8.0$, 1.2 Hz), 8.04 (dd, 2H, $J =$ 8.0 Hz), 7.87 (d, 1H, $J = 2.0$ Hz), 7.86 (d, 1H, $J = 2.0$ Hz), 7.75 (d, 1H, $J = 2.0$ Hz), 7.67 (d, 1H, $J = 2.0$ Hz), 7.65–7.60 (m, 2H), 7.50 (t, 4H, $J = 8.0$ Hz), 7.46 (centre of an AB spin system, 8H, $J_{AB} = 7.2$ Hz), 7.28 (d, 2H, $J = 8.0$ Hz), 7.19–7.10 (m, 2H), 7.17 (d, 4H, $J = 8.8$ Hz), 6.97 (s, 2H), 6.69 (d, 4H, $J = 8.8$ Hz), 6.45 (t, 1H, $J = 5.6$ Hz), 6.39 (t, 1H, $J = 5.6$ Hz), 5.53 (s, 2H), 4.20–4.00 (m, 10H), 3.82–3.70 (m, 4H), 3.72 (s, 6H), 3.70–3.24 (m, 6H), 3.05 (t, 2H, $J = 5.6$ Hz), 2.55 (t, 2H, $J = 6.5$ Hz), 2.18–2.01 (m, 2H), 1.85 (quint, 4H, $J = 7.2$ Hz), 1.68–1.38 (m, 8H), 1.44–1.10 (m, 26H), 1.15 (d, 6H, $J = 7.0$ Hz), 1.10 (d, 6H, $J = 7.0$ Hz), 0.85 (t, 6H, $J = 6.8$ Hz). ^{31}P NMR (CD_2Cl_2) δ (ppm) 148.8.

Synthesis of elongated linear oligonucleotide-functionalised modules (ELOMs)

The ELOMs were prepared by incorporation of phosphoramidite **9** into nucleotides by standard automated oligonucleotide synthesis (DNA Technology, Aarhus, Denmark) on a 0.2 µmol scale using TBPA (4-*tert*-butylphenoxyacetyl) protection for nucleotides A, C and G. Removal of the base protection groups was performed in 25% aqueous ammonia at 25 °C for 2 h. The benzoyl protection groups were not removed during this basic deprotection step. After purification by FPLC the 5′ terminal DMTr group was removed in 70% aqueous AcOH at 25 °C for 20 min. Removal of the benzoyl protection groups was achieved in 25% aqueous ammonia at 50 °C for 4 h. Removal of dioxane protecting groups from the crude DNA-conjugate was carried out in 0.5 M NaOAc (pH 4.0), 1 mM EDTA for 2 h at 37 °C. Sufficient 1.5 M CAPS (pH 10.4) buffer was added to adjust the pH to 7.0. The oligonucleotides were recovered by precipitation overnight with 3 volumes of ethanol at −20 °C and centrifugation (15 min at 10 000*g*). Resulting pellets were washed and centrifuged three times with 75% (v/v) ethanol and stored in 10 mM EPPS (pH 8.0) at −20 °C.

DNA-programmed coupling between the modules

A solution (10 µl) of the two or three ELOM or LOM modules (5 µM each) in 100 mM KCl, 50 mM EPPS (pH 8.0) were heated to 60 °C for 5 min and cooled slowly to rt in a water bath. The coupling reactions were performed by addition of 0.25 mM ethylenediamine, 1 mM $Mn(OAc)_2$ and incubation for 2 h at 30 °C. Analysis of the reaction products was performed by electrophoresis at 90 V in 7.5% polyacrylamide gels (30 : 1.6) in 50 mM Tricine (pH 8.1) and 8 M urea. Samples were loaded in 8 M urea without heating and addition of dyes. Gels were fixed in 50% (v/v) ethanol, stained with ethidium bromide and photographed in UV light.

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