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# Synthesis of Linear and Tripoidal Oligo(phenylene ethynylene)-Based Building Blocks for Application in Modular DNA-Programmed Assembly

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Rigid linear and tripoidal organic modules based on the oligo(phenylene ethynylene) backbone having salicylaldehyde-derived termini are synthesized. A highly functionalized 5-iodosalicyl aldehyde was prepared and coupled to each ethynyl group of 1,4-diethynylbenzene or 1,3,5-triethynylbenzene in Sonogashira couplings. The two or three termini of the compounds are functionalized for incorporation in linear and branched oligonucleotide strands. For the linear module (LM), the two termini are equipped with amide spacers, and one of these was functionalized with a DMTr (dimethoxytrityl)-protected hydroxy group and the other with a phosphoramidite. One of the tripoidal modules is prepared with DMTr groups in two of its three termini. A tripoidal module is also synthesized with three different groups on its hydroxy termini: a phosphoramidite, a DMTr group, and an Fmoc group. Extended studies have shown that these rigid linear and tripoidal organic modules can be incorporated into short oligonucleotides. Several of these modules can be applied for DNA-directed assembly and covalent coupling into structures of predetermined connectivity. Such structures have potential application for molecular electronics and nanotechnology.

## Introduction

Molecular electronics have been subject to growing interest during the past few years due to the increased search for alternatives to silicon-based electronics.[1] The synthesis and testing of individual molecular electronic components have been reported;[2] however, the major obstacle to the economical production of single molecule-based electronics is our inability to connect molecular electronic components to form circuits.

In a separate paper, we reported on a new bottom-up method for the programmed assembly and formation of covalent bonds between multiple organic modules.[3] The basic building blocks are a rigid linear oligonucleotide-functionalized module (**LOM**) and a tripoidal oligonucleotide-functionalized module (**TOM**) (Scheme 1). These modules are based on an oligo(phenylene ethynylene) backbone and have salicylaldehyde-derived termini. The modules are programmed by short oligonucleotides attached to each of the two and three termini of the linear and tripoidal modules, respectively. Complementary oligonucleotides at different LOMs and/or TOMs can assemble multiple modules in a specific predetermined manner. Subsequent addition of ethylenediamine and a metal salt such as $Mn(OAc)_2$ will form metal−salen complexes between salicylaldehyde groups, which are held in close proximity by the attached DNA chains. Metal−salen formation is restricted to take place at positions between two salicylaldehyde groups attached to hybridized oligonucleotide strands.

We report here on the synthesis of the linear and tripoidal modules, which are functionalized as phosphoramidites for being incorporating into oligonucleotide chains.

## Results and Discussion

The aim of the following work is to make molecular building blocks, which can assemble and couple covalently into predetermined and geometrically well-defined macromolecular matrix, locked in a planar structure. Further demands on the system are that the individual building blocks and the covalent interconnection between them must be conducting or semiconducting because of their potential use in molecular electronics. The modules should be linear or planar tripoidal and the functionality, which connects them, should be linear. Finally, the cross-linking reaction should be compatible with the conditions under which DNA can hybridize.[4]

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(1) Joachim, C.; Gimzewski, J. K.; Aviram, A. *Nature* **2000**, *408*, 541.

(2) See, e.g.: (a) Tour, J. M. *Acc. Chem. Res.* **2002**, *33*, 791. (b) Reed, M. A.; Chen, J.; Rawlett, A. M.; Price, D. W.; Tour, J. M. *Appl. Phys. Lett.* **2001**, *78*, 3735. (c) Collier, C. P.; Mattersteig, G.; Wong, E. W.; Luo, Y.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. *Science* **2000**, *289*, 1172. (d) Park, J.; Pasupathy, A. N.; Goldsmith, J. I.; Chang, C.; Yaish, Y.; Petta, J. R.; Rinkoski, M.; Sethna, J. P.; Abruna, H. D.; McEuen, P. L.; Ralph, D. C. *Nature* **2002**, *417*, 722. (e) Liang, W.; Shores, M. P.; Bockrath, M.; Long, J. R.; Park, H. *Nature* **2002**, *417*, 725. (f) Mitchell, R. H.; Ward, T. R.; Wang, Y.; Dibble, P. W. *J. Am. Chem. Soc.* **1999**, *121*, 2601.

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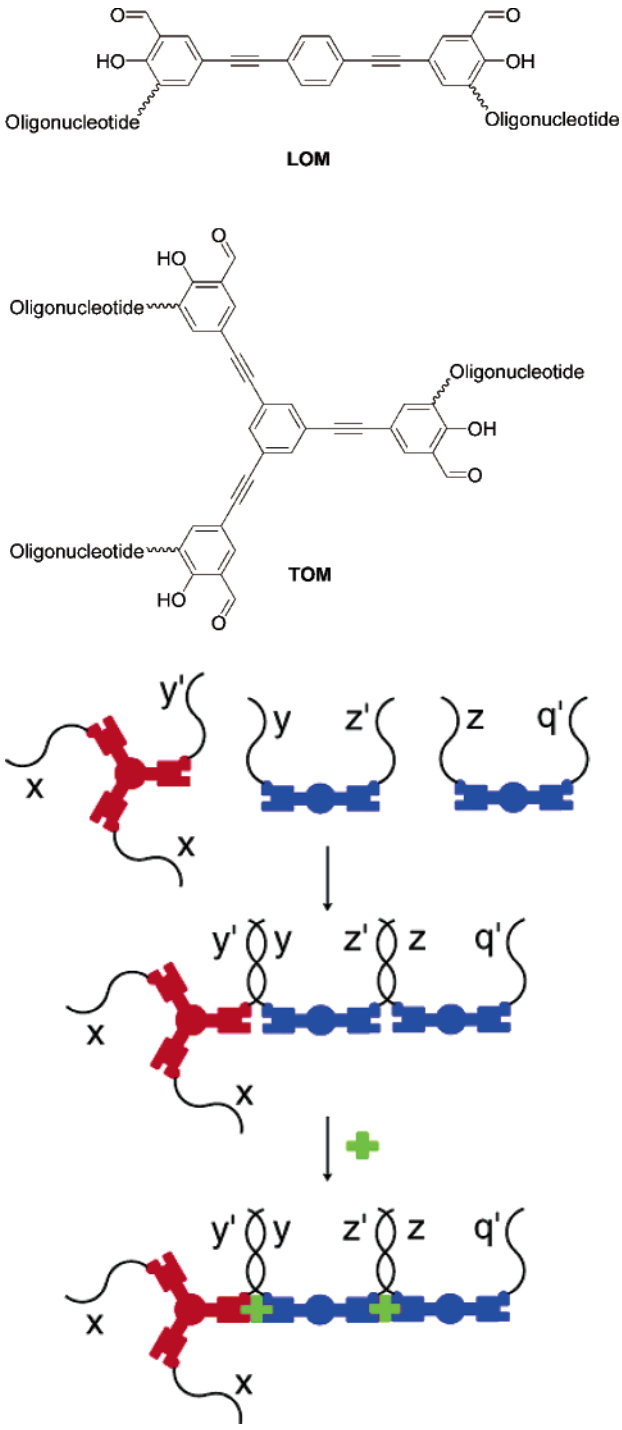
**SCHEME 1. Basic Structure of LOM and TOM Modules and Their Molecular Recognition and DNA-Directed Coupling Reaction Induced by Annealing and Addition of Ethylenediamine and $Mn(OAc)_2$[a]**




[a] Color code: **LOM**s (blue) and **TOM**s (red) are assembled by hybridization of complementary oligonucleotides (black curved lines) and coupled by ethylenediamine and $Mn(OAc)_2$ (green cross).

To form rigid and potentially conducting structures, the backbone of the modules is based on oligo(phenylene ethynylene)s as shown for the linear module in Scheme 2. Oligo(phenylene ethynylene)s have previously been extensively studied and applied as molecular wires.[2a,5] The oligonucleotide-functionalized linear module contains a salicylaldehyde-derived terminus, obtained from the corresponding DMTr- and phoshoramidite-functionalized organic module (Scheme 2). In this precursor, the aldehyde and phenol functionalities are protected since they are not compatible with oligonucleotide synthesis.[4a] This intermediate compound is obtained from the central 1,4-diethynylbenzene and two identical 5-iodosalicylaldehyde derivatives. We have previously reported on the synthesis of oligo(phenylene ethynylene)-derivatized salicylaldehydes and salen complexes.[6]

In our first approach, the spacer between the oligonucleotide chains and the organic modules was based on an ester functionality. This synthesis was initiated with the synthetic sequence illustrated in Scheme 3. The 5-iodosalicylic acid **1** was formylated in a Duff reaction[7] by treatment with hexamethylenetetramine in TFA at 90 °C in a closed vessel. Hydrolysis of the iminium intermediate was facilitated by stirring the adduct in 1 N HCl for 5 h to give **2** in 60% conversion, along with an impurity of 3,5-diiodosalicylic acid. As previously reported by Ruel et al., the outcome of this reaction was highly dependent on the temperature.[8] When the reaction was carried out at a lower temperature decreased conversion was observed, while raising the temperature above 90 °C lead to increased amounts of the byproduct. Due to the high polarity of **2**, flash chromatography proved difficult and the crude product was treated directly with 1,3-propanediol to provide after recrystallization the acetal **3** in 44% yield from **1**. Bromopropanol was protected with dimethoxytrityl chloride in a DMAP-catalyzed reaction to give **4** in 83% yield. Compound **4** was subsequently reacted with **3** and triethylamine to facilitate the ester **5** in 63% yield, which in the next step was protected at the phenol position with a benzoyl group. A study by Czlapinski and Sheppard revealed that the benzoyl group was suitable for this purpose.[4a] After benzoyl protection, the fully protected salicylaldehyde **6** was isolated in 81% yield.

The coupling between the central diethynylbenzene[9] fragment and 2 equiv of the protected 5-iodosalicylaldehydes **6** was facilitated via a Sonogashira coupling with bis(triphenylphosphine)palladium(II) chloride and copper

(4) For DNA-directed organic reactions, see: (a) Czlapinski, J. L.; Sheppard, T. L. *J. Am. Chem. Soc.* **2001**, *123*, 8618. (b) Gartner, Z. J.; Liu, D. R. *J. Am. Chem. Soc.* **2001**, *123*, 6961. (c) Gartner, Z. J.; Kanan, M. W.; Liu, D. R. *Angew. Chem., Int Ed.* **2002**, *41*, 1796. (d) Gartner, Z. J.; Kanan, M. W.; Liu, D. R. *J. Am. Chem. Soc.* **2002**, *124*, 10304. (e) Calderone, C. T.; Puckett, J. W.; Gartner, Z. J.; Liu, D. R. *Angew. Chem., Int Ed.* **2002**, *41*, 4104. (f) Gartner, Z.; Grubina, R.; Calderone, C. T.; Liu, D. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 1370. (g) Li, X.; Liu, D. R. *J. Am. Chem. Soc.* **2003**, *125*, 10188. (h) Summerer, D.; Max, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 89. (i) Eckardt, L. H.; Naumann, K.; Pankau, W. M.; Rein, M.; Schweitzer, M.; Windhab, N.; von Kiedrowski, G. *Nature* **2002**, *420*, 286.

(5) Shortell, D. B.; Palmer, L. C.; Tour, J. M. *Tetrahedron*, **2001**, *57*, 9055. (b) Bunz, U. H. F. *Acc. Chem. Res.* **2001**, *34*, 998. (c) Huang, S.; Tour, J. M. *Tetrahedron Lett.* **1999**, *40*, 3347. (d) Jones, L., II; Schumm, J. S.; Tour, J. M. *J. Org. Chem.* **1997**, *62*, 1388.

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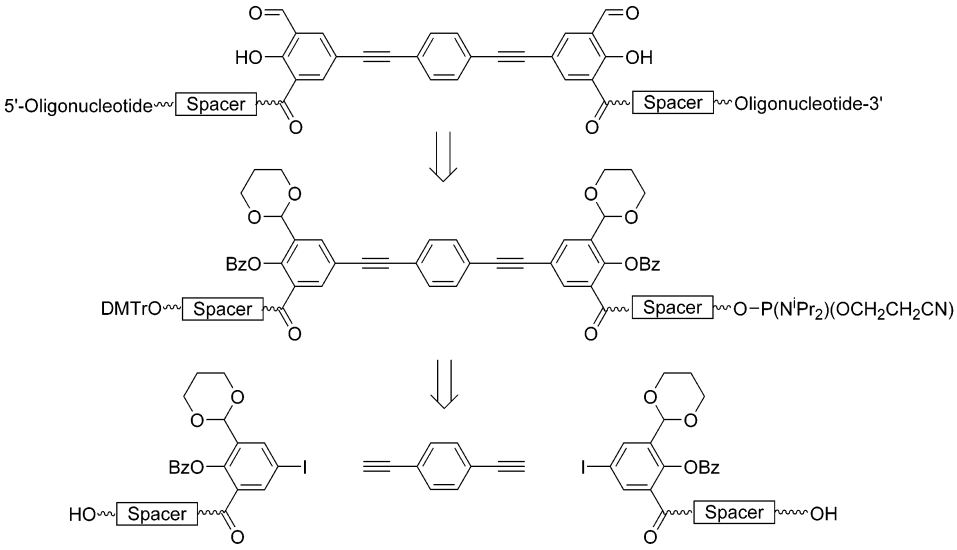
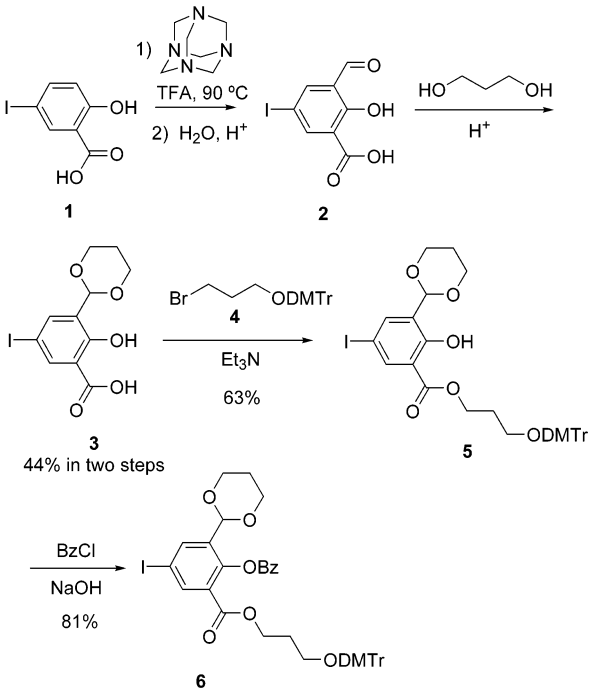
(9) (a) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627. (b) Yu, C. J.; Chong, Y.; Kayyem, J. F.; Gozin, M. *J. Org. Chem.* **1999**, *64*, 2070.

**SCHEME 2**




**SCHEME 3**




iodide as the catalysts (Scheme 4).[6,10] The coupling reaction proceeded in an overall yield of 79%, but surprisingly two products were observed. These were the expected product **7** and a product **8** carrying only one DMTr group. From TLC analysis, it was evident that the DMTr group was cleaved off during the reaction and not in the weakly acidic extraction or chromatographic separation. In several repetitions, the reaction still gave the unexpected, however convenient, single deprotection of one of the DMTr groups with identical ratios of **7** and **8**. The synthesis of the desired linear module **9** was completed by attachment of a phosphoramidite at the free hydroxyl group.[11]

It was attempted to incorporate the linear module **9** in the middle of a DNA strand consisting of 30 bases. The automated synthesis was performed using the phosphoramidite method[12] using benzoyl protecting groups for the amide groups in A, C, and G. The ester spacer used in **9** was, however, not compatible with the reaction conditions used for deprotection of the benzoyl groups. The treatment of the crude DNA-synthesis product with aqueous ammonia at 50 °C for 2 h led to complete cleavage of the oligonucleotide into fragments containing 15 bases as verified by polyacrylamide gel electrophoresis.[13]

To increase the stability of the spacer between the oligonucleotide chain and the organic module, the synthesis of a module containing the more stable amide spacer was consequently pursued. The synthesis was initiated from intermediate **3**, which was benzoyl protected and subsequently coupled with either 3-aminopropanol or *N*-methyl-3-aminopropanol to provide the amides **10a** and **10b** in moderate to good yields from **3** (Scheme 5).[14] The terminal hydroxy group was protected with a DMTr group to give **11a** and **11b** in excellent yields.

The backbone of the new linear module was assembled by a Sonogashira coupling of **11a** or **11b** with diethynylbenzene to give **12a** and **12b** (Scheme 6). Contrary to the Sonogashira reactions of the ester analogues, no loss of the DMTr protecting groups was observed in the synthesis of **12a** and **12b**. Consequently, it was necessary to selectively replace one of the DMTr groups with the phosphoramidite group. Due to hindered rotation around

(10) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3; pp 521−549.

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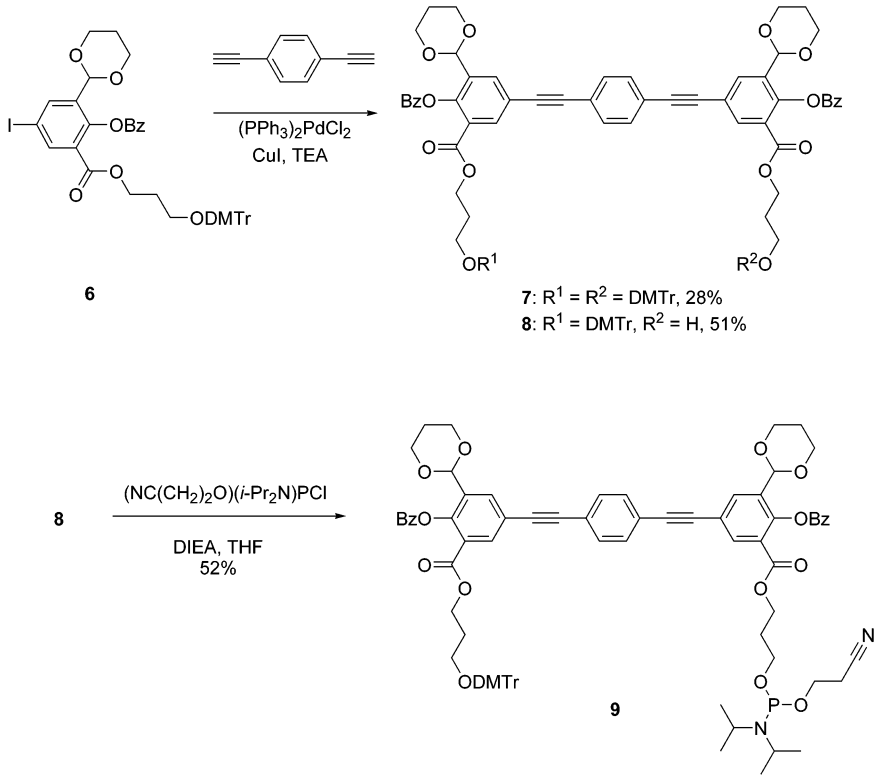
(12) Brown T.; Brown, D. J. S. In *Oligonucleotides and Analogues: A Practical Approach*; Eckstein, F., Ed.; IRL Press: Oxford, 1991; pp 1−24.

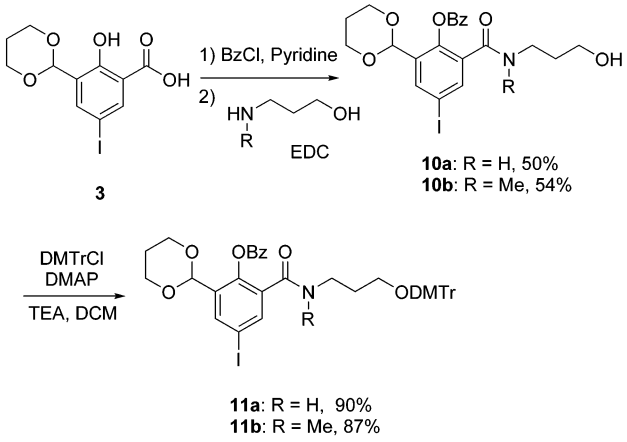
(13) This problem could be circumvented by applying other protecting groups for the bases in the DNA synthesis such as TBPA (4-*tert*-butylphenoxyacetyl), which could be removed by aqueous ammonia at room temperature. Under these conditions the desired oligonucleotide containing 15 bases on each side of the linear module could be obtained.

(14) Desai, M. C.; Stramiello, L. M. S. *Tetrahedron Lett.* **1993**, *34*, 7685.

**SCHEME 4**




**SCHEME 5**




the amide bonds in **12b**, the even distribution of *E*/*Z*-isomers gave rise to very complex $^{1}H$ and $^{13}C$ NMR spectra of the *N*-methylamides. Thus, the final steps were performed with **12a** only. The deprotection of **12a** was achieved by treatment with acetic acid to give **13** in 60% yield. The following treatment with the required phosphoramidite chloride provided the desired linear module **14** in an 85% yield.

The next target was to synthesize the tripoidal modules (TM), which are based on a central 1,3,5-trisubstituted benzene containing three phenylacetylene moieties.[15] This type of molecule will function as planar three-way branch points in the macromolecular networks. The synthesis of both symmetric and asymmetric TMs was initiated by the Sonogashira coupling between **11a** and 1,3,5-triethynylbenzene to give **15a** in 37% yield as shown in Scheme 7. The similar reaction of **11b** was also tested and gave a slightly higher yield of **15b**, compared to the synthesis of **15a**. Again, the *N*-methylamides gave rise to complex mixtures of isomers and thereby a difficult characterization. Further syntheses of the TMs were as a consequence based on only the primary amides arising from **11a**. Compound **15a** was subjected to mono-deprotection of one DMTr group by treating with 50% AcOH in $CH_2Cl_2$ for 8 min. The yield of the monohydroxy product **16** was rather low (28%) accompanied with 8% of the dihydroxy adduct **17**. More than 50% of unreacted **15a** was recovered and applied in repeated deprotections.

To obtain the symmetric tripoidal compound, functionalized for automated DNA synthesis, the free hydroxy group of compound **16** was converted into a phosphoramidite to give **18** in a high yield of 89%.

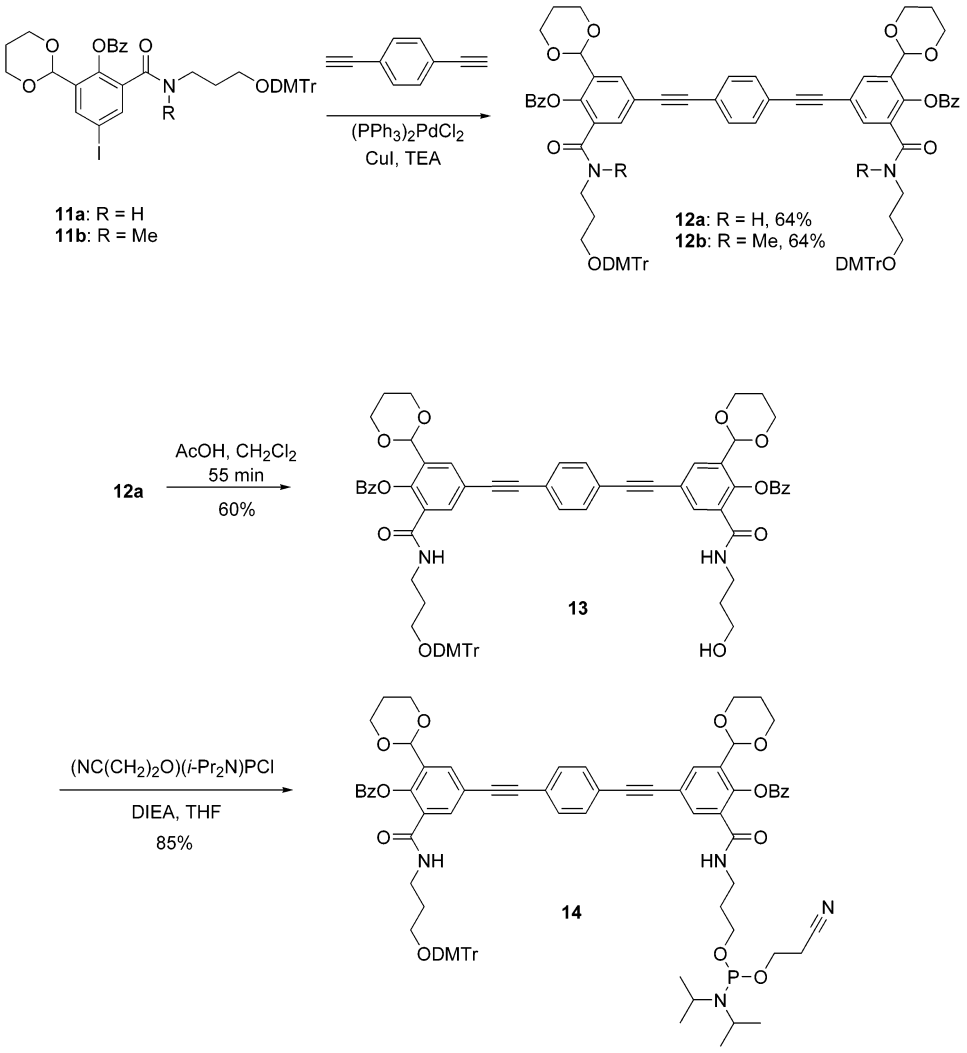
To obtain a tripoidal module to which three different nucleotide chains can be attached by automated DNA synthesis, each of the three ends has to be functionalized with different groups,[16] and for this purpose we have chosen the phosphoramidite, DMTr, and Fmoc groups. This was obtained by protecting the free hydroxyl group in **16** with FmocCl, and the protected product **19** was obtained in 74% yield.[17] Mono-deprotection of **19** was performed in 50% AcOH in $CH_2Cl_2$ for 10 min. The yield of **20** in this step was only 25%; however, more than 50% of the starting material was recovered. Finally, the

(15) (a) Weber, E.; Hecker, M.; Koepp, E.; Orlia, W.; Czugler, M.; Csöregh, I. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1251.

(16) Shchepinov, M. S.; Southern, E. M. *Russ. J. Bioorg. Chem.* **1998**, *24*, 794.

(17) (a) Johnson, T.; Quibell, M.; Owen, D.; Sheppard, R. C. *J. Chem. Soc., Chem. Commun.* **1993**, 369. (b) Seela, F.; Wenzel, T. *Helv. Chim. Acta* **1992**, *75*, 1111.

**SCHEME 6**




asymmetric tripoidal module **21** was obtained in 70% yield by converting **20** into the phosphoramidite (Scheme 8).

## Conclusion

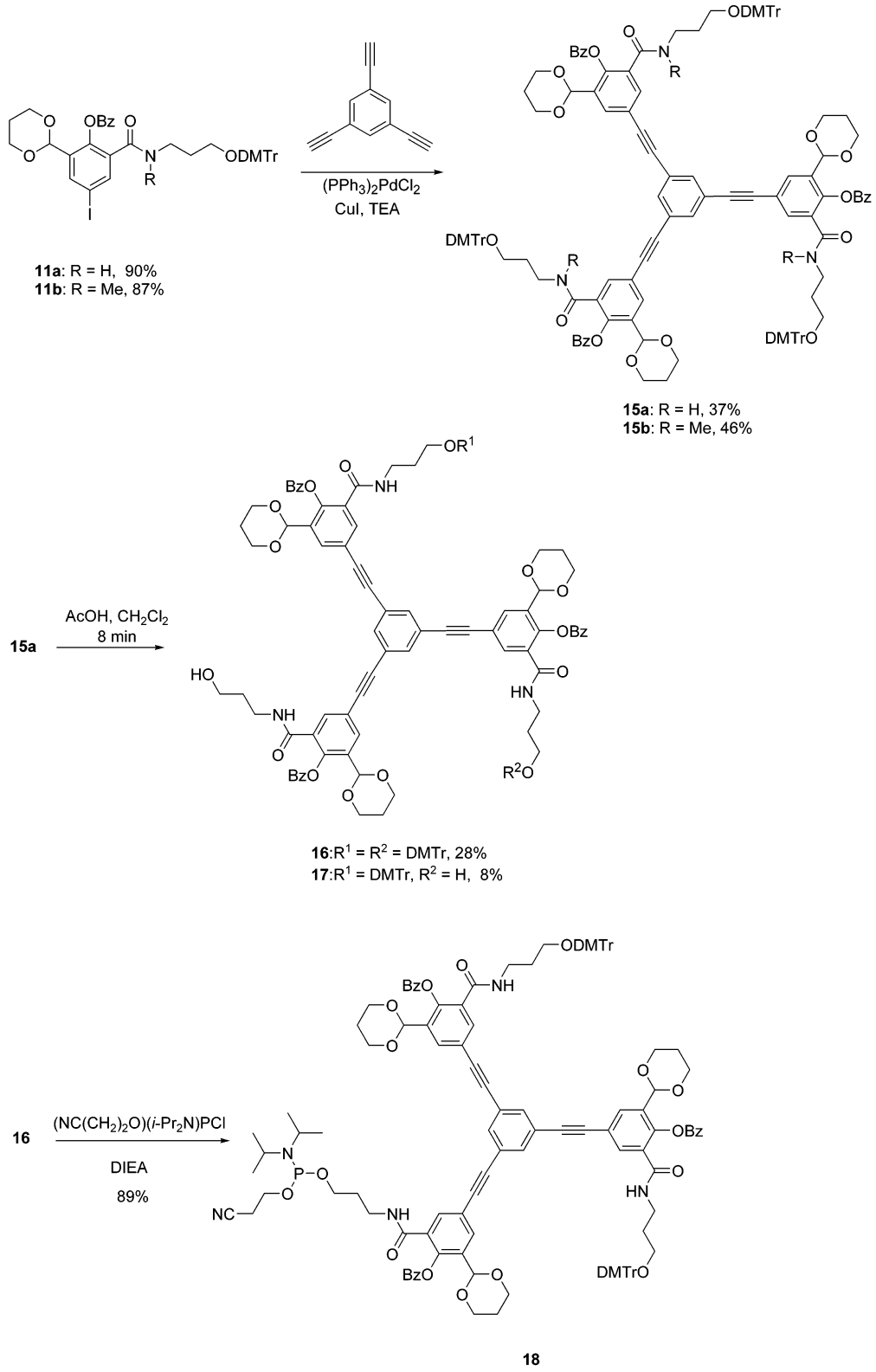
The synthesis of linear, symmetric tripoidal, and asymmetric tripoidal modules, which can be applied in automated DNA synthesis, has been demonstrated. The linear module is functionalized as a nucleoside phosphoramidite and can be incorporated in an oligonucleotide strand by automated synthesis as we have shown in a previous communication.[3] The two tripoidal modules are applied as the branch points in symmetric and asymmetric branched oligonucleotides. These oligonucleotide-functionalized organic compounds have been applied for the directed formation of metal−salen links between the individual compounds. By the functionalization with specific oligonucleotide sequences in each terminal, these modules are programmed for salen formation with other modules having complementary oligonucleotide sequences. This method is applied for the formation of predetermined nanostructures, which are potential conductors.[3]

## Experimental Procedures

**3-Formyl-2-hydroxy-5-iodobenzoic Acid (2).** A round-bottomed flask equipped with a tight screw-cap lid was charged with 2-hydroxy-5-iodobenzoic acid **1** (3.0 g, 11.3 mmol) under argon. Hexamethylenetetramine (7.0 g, 49.9 mmol) and trifluoroacetic acid (30 mL) were added, and the suspension was stirred overnight at 90 °C in the closed flask. The reaction mixture was poured into aqueous HCl (1 M, 60 mL) and stirred for 5 h. The precipitate was filtered off, washed thoroughly with aqueous HCl (1 M) and water ,and dried under vacuum. The crude material was used directly in the following reaction.

**3-(1,3-Dioxan-2-yl)-2-hydroxy-5-iodobenzoic Acid (3).** The crude product described above containing **2** (3.0 g) was suspended in toluene (30 mL) in a round-bottomed flask and then 1,3-propanediol (5.0 mL, 69 mmol) and $H_2SO_4$ (100 $\mu$L, 1.9 mmol). The reaction mixture was refluxed for 16 h, allowed to cool to rt, and neutralized with saturated aqueous $NaHCO_3$. Water (20 mL) was added, and the mixture was extracted with $CH_2Cl_2$ (5 × 20 mL). The combined organic fractions were washed with water (20 mL), dried over $MgSO_4$, and concentrated. The crude product was recrystallized twice from mixtures of toluene and pentane to yield **3** as white crystals (1.75 g, 44% from **1**): mp 88−89 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.39 (d, $J$ = 12.8, 1H), 1.91−2.06 (m, 1H), 3.89 (t, $J$ = 12.0, 2H), 4.08 (dd, $J$ = 11.2 Hz, $J$ = 4.4 Hz, 2H), 5.65 (s, 1H), 7.84 (d, $J$ = 2.0 Hz, 1H), 8.02 (d, $J$ = 2.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$,

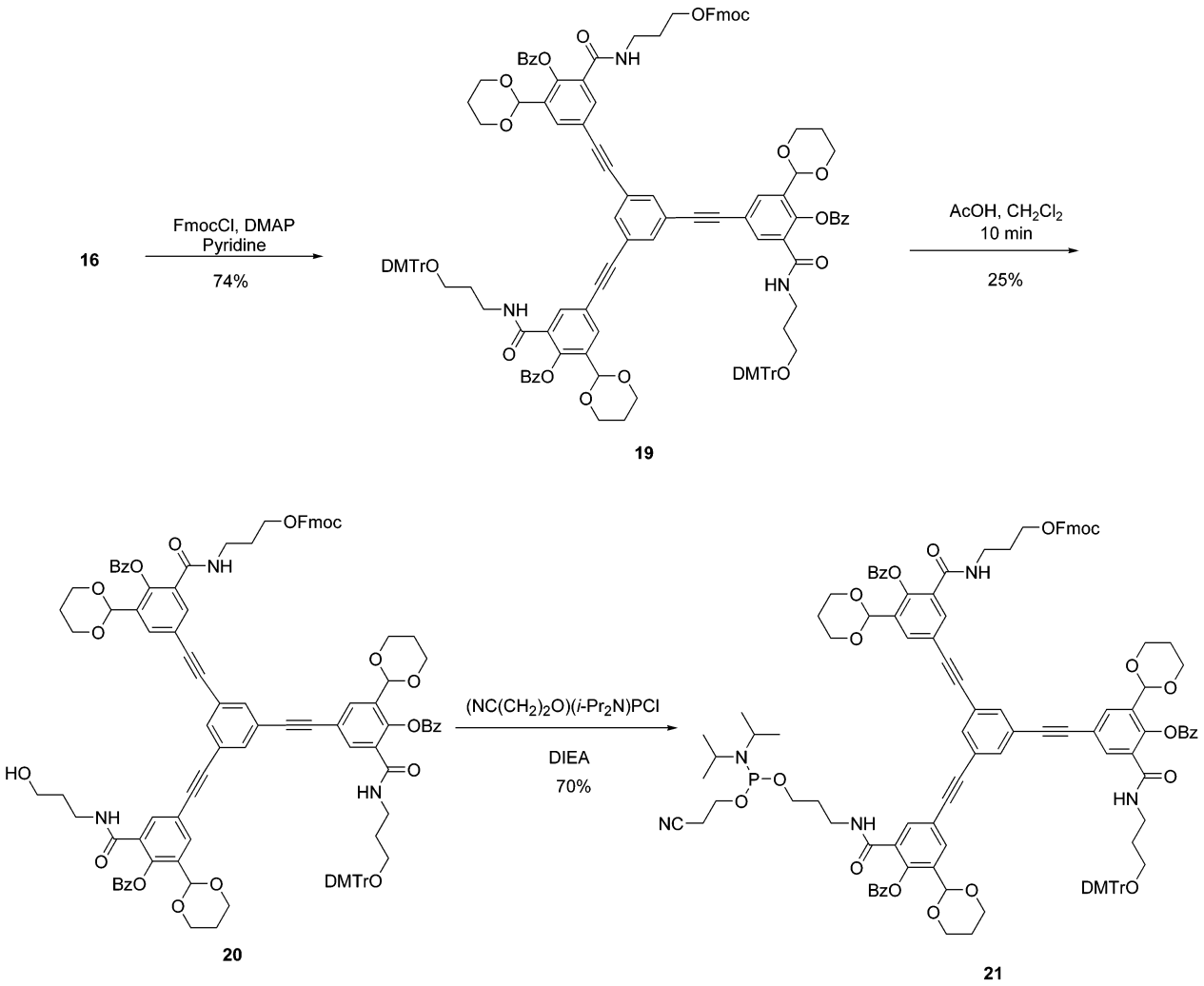
**SCHEME 7**




100 MHz) $\delta$ 26.0, 67.5, 80.9, 95.3, 116.0, 129.9, 139.1, 141.6, 158.6, 171.5; HRMS calcd 372.9549 ([M + Na]$^+$), found 372.9553.

**3-Bromo-1-(dimethoxytrityloxy)propane (4).** To a Schlenk flask charged with 3-bromo-1-propanol (256 $\mu$L, 2.95 mmol), DMTrCl (1.00 g, 2.95 mmol), and DMAP (36 mg, 0.30 mmol) in $CH_2Cl_2$ (10 mL) was added $NEt_3$ (412 $\mu$L, 2.95 mmol) dropwise while stirring. The reaction mixture was stirred at rt for 4 h and poured into water (20 mL). The organic layer was separated, and the aqueous phase was extracted with $CH_2Cl_2$ (2 × 10 mL). The combined organic fractions were washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (pentane/$Et_2O$, 9:1) to yield **4** as a reddish solid (1.078 g, 83%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.04 (qui, $J$ = 6.2 Hz, 2H), 3.13 (t, $J$ = 6.2 Hz, 2H), 3.50 (t, $J$ = 6.8 Hz, 2H), 3.72 (s, 6H),

**SCHEME 8**




6.76 (d, $J$ = 6.4 Hz, 4H), 7.14−7.25 (m, 7H), 7.35 (d, $J$ = 6.4 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 31.2, 33.7, 55.6, 61.2, 92.3, 113.3, 127.9, 129.4, 130.3, 136.5, 145.3, 158.6; HRMS calcd 463.0885 ([M + Na]$^+$), found 463.0894.

**3-(Dimethoxytrityloxy)prop-1-yl 3-(1,3-Dioxan-2-yl)-2-hydroxy-5-iodobenzoate (5).** To a Schlenk flask charged with **3** (450 mg, 1.29 mmol) and **4** (600 mg, 1.36 mmol) in DMF (2 mL) was added $NEt_3$ (190 $\mu$L, 1.36 mmol) dropwise. The reaction mixture was warmed to 40 °C and stirred for 16 h. The DMF−water mixture was poured into water (10 mL) and extracted with $Et_2O$ (3 × 10 mL). The combined organic fractions were washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel ($CH_2Cl_2$/MeOH, 98:2) to yield **5** as a colorless oil (580 mg, 63%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.45 (d, $J$ = 13.6 Hz, 1H), 2.03 (qui, $J$ = 6.0 Hz, 2H), 2.16−2.29 (m, 1H), 3.24 (t, $J$ = 5.6 Hz, 2H) 3.75 (s, 6H), 4.01 (t, $J$ = 12.0 Hz, 2H), 4.25 (dd, $J$ = 11.2 Hz, $J$ = 4.8 Hz, 2H), 4.48 (t, $J$ = 6.4 Hz, 2H), 5.84 (s, 1H), 6.79 (d, $J$ = 6.79, 4H), 7.18 (t, $J$ = 9.2 Hz, 2H), 7.24−7.32 (m, 5H), 7.41 (d, $J$ = 7.6 Hz, 2H), 7.94 (d, $J$ = 2.4 Hz, 1H), 8.06 (d, $J$ = 2.4 Hz, 1H), 11.21 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.9, 29.3, 55.3, 59.3, 63.5, 67.8, 80.4, 86.2, 95.8, 113.3, 114.7, 127.1, 128.2, 128.4, 129.0, 130.2, 136.4, 138.8, 142.0, 142.2, 145.1, 158.6, 169.2; HRMS calcd 733.1274 ([M + Na]$^+$), found 733.1277.

**3-(Dimethoxytrityloxy)prop-1-yl 2-Benzoyloxy-3-(1,3-dioxan-2-yl)-5-iodobenzoate (6).** To a Schlenk flask charged with **5** (100 mg, 0.14 mmol) dissolved in THF was added NaOH (1 M, 210 $\mu$L, 0.21 mmol) followed by dropwise addition of benzoyl chloride (25 $\mu$L, 0.21 mmol). The reaction mixture was stirred at rt for 3 min. It was then neutralized with aqueous $NH_4OH$ (20 mL) and extracted with $Et_2O$ (3 × 15 mL). The combined organic phases were dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel ($CH_2Cl_2$/MeOH, 99:1) to yield **6** as a colorless oil (93 mg, 81%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.34 (d, $J$ = 14.0 Hz, 1H), 1.74 (qui, $J$ = 5.7 Hz, 2H), 2.08−2.21 (m, 1H), 3.05 (t, $J$ = 6.0 Hz, 2H), 3.73−3.83 (m, 8H), 4.15 (dd, $J$ = 10.4 Hz, $J$ = 3.6 Hz, 2H), 4.30 (t, $J$ = 6.4 Hz, 2H), 5.57 (s, 1H), 6.78 (dd, $J$ = 6.8 Hz, $J$ = 2.0 Hz, 2H), 6.83 (dd, $J$ = 6.8 Hz, $J$ = 2.0 Hz, 2H), 7.17 (dd, $J$ = 6.8 Hz, $J$ = 2.4 Hz, 2H), 7.23−7.29 (m, 5H), 7.36 (d, $J$ = 7.2 Hz, 1H), 7.50 (t, $J$ = 7.6 Hz, 2H), 7.56 (d, $J$ = 7.6 Hz, 1H), 7.64 (t, $J$ = 7.6 Hz, 1H) 8.16 (d, $J$ = 8.4 Hz, 2H), 8.22 (d, $J$ = 2.4 Hz, 1H), 8.25 (d, $J$ = 2.4 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.6, 29.2, 55.6, 59.5, 63.3, 67.7, 86.0, 90.0, 96.6, 113.3, 128.0, 128.2, 128.4, 129.3, 129.4, 130.1, 130.2, 130.2, 130.4, 130.5, 134.7, 136.5, 141.0, 141.1, 145.2, 158.6, 163.2, 164.6; HRMS calcd 837.1537 ([M + Na]$^+$), found 837.1552.

**1,4-Bis[(4-benzoyloxy-5-(3-dimethoxytrityloxyprop-1-yloxy)carbonyl-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (7) and 1-[(4-Benzoyloxy-5-(3-dimethoxytrityloxyprop-1-yloxy)carbonyl-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-4-[(4-benzoyloxy-5-(3-hydroxyprop-1-yloxy)carbonyl-3-(1,3-dioxan-2-yl)-phenyl)ethynyl]benzene (8).** To a Schlenk flask charged with **6** (93 mg, 0.11 mmol) were added 1,4-diethynylbenzene (6.9 mg, 0.055 mmol), bis(triphenylphosphine)palladium(II) chloride (4.0 mg, 0.006 mmol), and copper

iodide (1.1 mg, 0.006 mmol), and the mixture was stirred under vacuum for 30 min. $NEt_3$ (5 mL) was added, and the reaction mixture was stirred under argon at 53 °C for 19 h. The reaction mixture was poured into 10% aqueous $NH_4Cl$ (10 mL) and extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic fractions were washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel ($Et_2O$/pentane, 9:1) to yield **7** as a yellow oil (23 mg, 28%) and **8** as a yellow oil (34 mg, 51%). **7**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.29 (d, $J$ = 12.4 Hz, 2H), 1.72 (qui, $J$ = 5.8 Hz, 4H), 2.04−2.17 (m, 2H), 3.02 (t, $J$ = 5.8 Hz, 4H), 3.67 (s, 12H), 3.76 (t, $J$ = 12.2 Hz, 4H), 4.12 (dd, $J$ = 11.2 Hz, $J$ = 4.4 Hz, 4H), 4.27 (t, $J$ = 6.4 Hz, 4H), 5.57 (s, 2H), 6.72 (d, $J$ = 8.8 Hz, 8H), 7.10 (t, $J$ = 7.4 Hz, 2H), 7.16−7.23 (m, 12H), 7.31 (d, $J$ = 7.2, 4H), 7.42−7.48 (m, 8H), 7.58 (t, $J$ = 7.4, 2H), 8.02 (d, $J$ = 2.4 Hz, 2H), 8.07 (d, $J$ = 2.4 Hz, 2H), 8.13 (d, $J$ = 7.6 Hz, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 29.2, 30.0, 55.4, 59.5, 63.2, 67.7, 86.0, 90.0, 90.3, 97.1, 113.2, 121.4, 123.2, 124.6, 126.9, 128.0, 128.4, 128.9, 129.4, 130.2, 130.5, 131.9, 133.3, 133.9, 135.1, 135.5, 136.5, 145.2, 148.4, 158.6, 163.9, 164.7; HRMS calcd 1521.5399 ([M + Na]$^+$), found 1521.5505. **8**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.35 (d, $J$ = 13.6 Hz, 2H), 1.72−1.83 (m, 4H), 2.10−2.24 (m, 2H), 3.09 (t, $J$ = 5.8 Hz, 2H), 3.61 (q, $J$ = 5.6 Hz, 2H), 3.74 (s, 6H), 3.83 (t, $J$ = 12.8 Hz, 4H), 4.18 (dd, $J$ = 4.2, $J$ = 11.8, 4H), 4.33 (t, $J$ = 6.2 Hz, 4H), 5.64 (s, 1H), 5.65 (s, 1H), 6.79 (d, $J$ = 8.8 Hz, 4H), 7.17 (t, $J$ = 6.8 Hz, 1H), 7.22−7.34 (m, 6H), 7.38 (d, $J$ = 3.6 Hz, 2H), 7.48−7.59 (m, 8H), 7.62−7.71 (m, 2H), 8.09 (d, $J$ = 2.4 Hz, 1H), 8.10 (d, $J$ = 2.4 Hz, 1H), 8.13 (d, $J$ = 2.4 Hz, 1H), 8.20 (d, $J$ = 7.8 Hz, 2H), 8.22 (d, $J$ = 2.4 Hz, 1H), 8.25 (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 Hz) $\delta$ 29.9, 30.5, 31.7, 55.4, 59.1, 59.5, 62.4, 63.2, 66.1, 67.7, 86.0, 89.9, 90.0, 90.2, 90.4, 97.1, 113.2, 121.4, 121.6, 123.1, 123.2, 124.6, 126.9, 128.0, 128.3, 128.9, 129.0, 129.4, 130.2, 130.5, 131.9, 133.3, 133.9, 134.1, 135.0, 135.2, 135.5, 136.5, 145.2, 148.2, 148.4, 158.5, 163.9, 164.5, 164.7, 164.8; HRMS calcd 1219.4092 ([M + Na]$^+$), found 1219.4094.

**1-[(4-Benzoyloxy-5-(3-dimethoxytrityloxyprop-1-yloxy)-carbonyl-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-4-[(4-benzoyloxy-5-(3-(2-cyanoethoxy-*N*,*N*-diisopropylaminophosphanyloxy)prop-1-yloxy)carbonyl-3-(1,3-dioxan-2-yl)-phenyl)ethynyl]benzene (9).** To a Schlenk flask charged with **8** (67 mg, 0.056 mmol) dissolved in THF (5 mL) was added diisopropylethylamine (49 $\mu$L, 0.28 mmol), and the solution was cooled to 0 °C. 2-Cyanoethyl diisopropylchlorophosphoramidite (44 $\mu$L, 0.20 mmol) was added dropwise while stirring. The reaction mixture was stirred under argon at rt for 16 h. The reaction was quenched by addition of MeOH (0.5 mL), and the solvent was removed by vacuum distillation. The resulting oil was dissolved in EtOAc and washed with 5.5% aqueous $NaHCO_3$ (2 × 10 mL), washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane/$NEt_3$, 4:5:1 → EtOAc/$NEt_3$, 9:1) to yield **9** as a yellow oil (41 mg, 52%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.14−1.31 (m, 14H), 1.74 (qui, $J$ = 7 Hz, 4H), 2.02−2.18 (m, 2H), 2.51 (t, $J$ = 6.4 Hz, 2H), 2.58 (t, $J$ = 7.2 Hz, 2H), 3.02 (t, $J$ = 5.6 Hz, 2H), 3.44−3.55 (m, 4H), 3.67 (s, 6H), 3.76 (t, $J$ = 11.8 Hz, 4H), 4.10 (dd, $J$ = 4.4 Hz, $J$ = 11.2 Hz, 4H), 4.19−4.29 (m, 4H), 5.566 (s, 1H), 5.572 (s, 1H), 6.71 (d, $J$ = 8.8 Hz, 4H), 7.09 (t, $J$ = 7.4 Hz, 1H), 7.15−7.22 (m, 6H), 7.31 (d, $J$ = 7.6 Hz, 2H), 7.40−7.52 (m, 8H), 7.54−7.62 (m, 2H), 8.02 (s, 2H), 8.06 (d, $J$ = 2 Hz, 1H), 8.13 (d, $J$ = 7.6 Hz, 2H), 8.15 (d, $J$ = 2.4 Hz, 1H), 8.18 (d, $J$ = 7.4 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 19.3, 23.6, 24.5, 27.9, 29.1, 42.0, 54.1, 57.4, 58.2, 58.9, 61.3, 61.9, 66.5, 84.8, 88.7, 88.8, 88.97, 89.00, 95.9, 112.0, 113.1, 120.1, 120.2, 121.9, 122.0, 123.3, 125.6, 126.7, 127.1, 127.6, 127.7, 128.2, 128.9, 129.2, 130.6, 132.0, 132.1, 132.6, 132.7, 133.8, 133.9, 134.2, 135.3, 144.0, 147.1, 147.2,157.3, 162.6, 163.4; HRMS calcd 1419.5171 ([M + Na]$^+$), found 1419.5170.

**1-Benzoyloxy-6-(1,3-dioxan-2-yl)-2-(*N*-(3-hydroxyprop-1-yl)aminocarbonyl-4-iodobenzene (10a).** To a Schlenk flask charged with **3** (513 mg, 1.47 mmol) dissolved in $CH_2Cl_2$ (20 mL) was added benzoyl chloride (170 $\mu$L, 1.47 mmol), and the mixture was cooled to 0 °C. Pyridine (237 $\mu$L, 2.93 mmol) was slowly added to the reaction mixture, which was allowed to warm to rt and stirred for 3 h under argon. 3-Amino-1-propanol (183 $\mu$L, 2.39 mmol) was then added before the mixture again was cooled to 0 °C. EDC (458 mg, 2.39 mmol) was added to the reaction mixture, which was allowed to warm to rt and stirred for 4 h under argon. The reaction mixture was poured into water (20 mL) and extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic fractions were washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane, 1:1 → EtOAc/pentane, 7:3) to yield **10a** as white crystals (374 mg, 50%): mp 64−66 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 13.6 Hz, 1H), 1.43 (qui, $J$ = 5.8 Hz, 2H), 1.95−2.10 (m, 1H), 2.62 (t, $J$ = 6.2 Hz, 1H), 3.35 (q, $J$ = 6.1 Hz, 2H), 3.43 (q, $J$ = 5.7 Hz, 2H), 3.66 (t, $J$ = 11.0 Hz, 2H), 4.02 (dd, $J$ = 4.8 Hz, $J$ = 11.2 Hz, 2H), 5.46 (s, 1H), 6.44−6.54 (m, 1H), 7.48 (t, $J$ = 7.6 Hz, 2H), 7.62 (t, $J$ = 7.4 Hz, 1H), 7.93 (d, $J$ = 2.4 Hz, 1H), 8.03 (d, $J$ = 2.4 Hz, 1H), 8.13 (d, $J$ = 8.2 Hz, 2H);$^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.5, 32.3, 36.9, 59.4, 67.6, 90.9, 97.0, 128.7, 129.1, 130.4, 132.4, 133.9, 134.5, 138.7, 138.9, 145.6, 165.3, 165.7; HRMS calcd 534.0390 ([M + Na]$^+$), found 534.0400.

**1-Benzoyloxy-6-(1,3-dioxan-2-yl)-2-[*N*-(3-hydroxyprop-1-yl)-*N*-methylaminocarbonyl]-4-iodobenzene (10b).** To a Schlenk flask charged with **3** (150 mg, 0.43 mmol) dissolved in $CH_2Cl_2$ (6 mL) was added benzoyl chloride (48 $\mu$L, 0.45 mmol) and the mixture was cooled to 0 °C. Pyridine (71 $\mu$L, 0.88 mmol) was slowly added to the reaction mixture, which was allowed to warm to rt and stirred for 3 h under argon. *N*-Methyl-3-amino-1-propanol (62 mg, 0.70 mmol) was then added before the mixture again was cooled to 0 °C. EDC (124 mg, 0.65 mmol) was added to the reaction mixture, which was allowed to warm to rt and stirred for 4 h under argon. The reaction mixture was poured into water (15 mL) and extracted with $CH_2Cl_2$ (3 × 15 mL). The combined organic fractions were washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane, 1:1 → EtOAc/pentane, 7:3) to yield **10b** as white crystals (121 mg, 54%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.25 (d, $J$ = 13.6 Hz), 1.58 (qui, $J$ = 5.8 Hz), 1.98−2.10 (m), 2.85 (s, 2. diastereomer), 2.88 (s, 1. diastereomer), 3.23 (q, $J$ = 5.9 Hz), 3.35 (t, $J$ = 6.8 Hz), 3.40−3.54 (m), 3.68 (t, $J$ = 11.0 Hz), 3.98−4.08 (m), 5.47 (s, 2 diastereomer), 5.50 (s, 1 diastereomer), 7.45 (t, $J$ = 8.0 Hz), 7.56−7.62 (m), 8.02 (d, $J$ = 2.0 Hz), 8.09 (d, $J$ = 8.4 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.6, 29.3, 30.5, 32.5, 37.2, 43.7, 48.1, 58.0, 59.5, 67.6, 90.3, 96.9, 125.8, 128.8, 129.0, 130.4, 133.0, 134.3, 134.4, 136.7, 137.7, 145.4, 164.6, 167.5; HRMS calcd 548.0546 ([M + Na]$^+$), found 548.0564.

**1-Benzoyloxy-2-(*N*-(3-dimethoxytrityloxyprop-1-yl)-aminocarbonyl)-6-(1,3-dioxan-2-yl)-4-iodobenzene (11a).** To a Schlenk flask charged with **10a** (374 mg, 0.73 mmol) dissolved in $CH_2Cl_2$ (15 mL) were added DMTrCl (452 mg, 1.33 mmol) and DMAP (16 mg, 0.13 mmol). Finally, $NEt_3$ (210 $\mu$L, 1.51 mmol) was added, and the reaction mixture was stirred under argon at rt for 4 h. The reaction mixture was poured into water (15 mL) and extracted with $CH_2Cl_2$ (3 × 15 mL). The combined organic fractions were washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane/$NEt_3$, 40:59:1) to yield **11a** as yellow crystals (494 mg, 83%): mp 78−90 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 13.0 Hz, 1H), 1.55 (qui, $J$ = 6.1 Hz, 2H), 1.96−2.10 (m, 1H), 2.99 (t, $J$ = 5.6 Hz, 2H), 3.29 (q, $J$ = 6.4 Hz, 2H), 3.66 (t, $J$ = 11.4 Hz, 2H), 3.70 (s, 6H), 4.02 (dd, $J$ = 5.0, 11.0 Hz, 2H), 5.46 (s, 1H), 6.37 (t, $J$ = 5.4 Hz, 1H), 6.70 (d, $J$ = 8.8 Hz, 4H), 7.12−7.19 (m, 7H), 7.28 (d, $J$ = 8.4 Hz, 2H), 7.43 (t, $J$ = 7.8 Hz, 2H), 7.59 (t, $J$ = 7.4 Hz, 1H), 7.83 (d, $J$ = 2.0 Hz, 1H), 8.02 (d, $J$ = 2.4 Hz, 1H), 8.04 (d, $J$ = 8.2 Hz, 2H); $^{13}$C NMR

($CDCl_3$, 100 MHz) $\delta$ 25.6, 29,5, 38.4, 55.5, 61.8, 67.6, 86.4, 90.8, 97.0, 113.3, 127.0, 128.1, 128.3, 128.9, 129.0, 130.1, 130.5, 132.9, 133.9, 134.2, 136.3, 138.5, 138.6, 144.9, 145.6, 158.6, 164.5, 164.8; HRMS calcd 836.1696 ($[M + Na]^+$), found 836.1794.

**1-Benzoyloxy-2-(*N*-(3-dimethyloxytrityloxyprop-1-yl)-*N*-methylaminocarbonyl)-6-(1,3-dioxan-2-yl)-4-iodobenzene (11b).** To a Schlenk flask charged with **10b** (120 mg, 0.23 mmol) dissolved in $CH_2Cl_2$ (5 mL) were added DMTrCl (116 mg, 0.34 mmol) and DMAP (4 mg, 0.034 mmol). Finally, $NEt_3$ (51 $\mu$L, 0.36 mmol) was added, and the reaction mixture was stirred under argon at rt for 4 h. The reaction mixture was poured into water (10 mL) and extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic fractions were washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane/$NEt_3$, 35:64:1) to yield **11b** as yellow crystals (163 mg, 87%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.22 (d, $J$ = 13.6 Hz), 1.60 (qui, $J$ = 6.9 Hz, 1 diastereomer), 1.66−1.78 (m, 2 diastereomer), 1.94−2.09 (m), 2.78 (s, 2 diastereomer), 2.80 (s, 1 diastereomer), 2.88−2.97 (m), 3.32−3.41 (m), 3.62−3.72 (m), 3.96−4.05 (m), 5.46 (s, 2 diastereomer), 5.47 (s, 1 diastereomer), 6.70−6.75 (m), 7.09−7.22 (m), 7.28 (t, $J$ = 6.6 Hz), 7.37−7.43 (m), 7.47 (d, $J$ = 2.0 Hz, 1 diastereomer), 7.50−7.56 (m, 2 diastereomer), 7.97 (d, $J$ = 1.6 Hz, 1 diastereomer), 7.99 (d, $J$ = 1.8 Hz, 2 diastereomer), 8.02−8.07 (m); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.7, 27.6, 29.3, 32.8 37.7, 45.3, 48.9, 55.5, 60.9, 61.0, 67.6, 86.0, 86.3, 90.3, 90.4, 96.9, 97.0, 113.3, 113.4, 127.0, 128.0, 128.1, 128.3, 128.4, 128.9, 129.0, 130.2, 130.5, 133.5, 133.6, 134.1, 134.3, 136.5, 136.6, 136.7, 137.3, 137.4, 145.1, 145.2, 145.3, 158.6, 164.3, 164.4, 165.8, 166.3; HRMS calcd 850.1853 ($[M + Na]^+$), found 850.1817.

**1,4-Bis[(4-benzoyloxy-5-(*N*-(3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-benzene (12a).** Bis(triphenylphosphine)palladium(II) chloride (111 mg, 0.16 mmol) and copper iodide (30 mg, 0.16 mmol) were stirred in a Schlenk flask under vacuum for 30 min, after which **11a** (1.35 g, 1.66 mmol), 1,4-diethynylbenzene (100 mg, 0.79 mmol), and THF (18 mL) were added. Finally, $NEt_3$ (7 mL) was added, and the reaction mixture was stirred under argon at 53 °C for 16 h. The reaction mixture was poured into saturated aqueous NaCl (25 mL) and extracted with $Et_2O$ (3 × 25 mL). The combined organic fractions were washed with water (25 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane, 1:1 → EtOAc/pentane, 7:3) to give **12a** as a yellow solid (753 mg, 64%): mp 118−120 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.24 (d, $J$ = 13.6 Hz, 2H), 1.59 (qui, $J$ = 6.0 Hz, 4H), 1.96−2.10 (m, 2H), 3.02 (t, $J$ = 5.4 Hz, 4H), 3.32 (q, $J$ = 6.0 Hz, 4H), 3.67 (s, 12H), 3.69 (t, $J$ = 11.6 Hz, 4H), 4.04 (dd, $J$ = 4.6, 11.4 Hz, 4H), 5.52 (s, 2H), 6.42 (t, $J$ = 5.6 Hz, 2H), 6.70 (d, $J$ = 8.8, 8H), 7.08−7.21 (m, 14H), 7.30 (d, $J$ = 7.2 Hz, 4H), 7.41 (s, 4H), 7.43 (t, $J$ = 8.0 Hz, 4H), 7.58 (t, $J$ = 7.2 Hz, 2H), 7.66 (d, $J$ = 2.0 Hz, 2H), 7.89 (d, $J$ = 2 Hz, 2H), 8.08 (d, $J$ = 7.8 Hz, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.7, 29.5, 38.5, 55.4, 61.9, 67.6, 86.5, 90.1, 90.3, 97.5, 113.3, 121.7, 123.2, 127.0, 128.1, 128.4, 129.0, 129.1, 130.1, 130.5, 131.4, 131.9, 132.6, 132.7, 132.8, 134.1, 136.4, 145.0, 145.7, 158.6, 164.9, 165.4; HRMS calcd 1519.5719 ($[M + Na]^+$), found 1519.8694.

**1,4-Bis[(4-benzoyloxy-5-(*N*-(3-(dimethoxytrityloxyprop-1-yl)-*N*-methylaminocarbonyl)-3-((1,3)-dioxan-2-yl)phenyl)ethynyl]benzene (12b).** Bis(triphenylphosphine)palladium(II) chloride (14 mg, 0.020 mmol) and copper iodide (4 mg, 0.020 mmol) were stirred in a Schlenk flask under vacuum for 30 min, after which **12b** (176 mg, 0.21 mmol), 1,4-diethynylbenzene (13 mg, 0.10 mmol), and THF (6 mL) were added. Finally, $NEt_3$ (4 mL) was added, and the reaction mixture was stirred under argon at 53 °C for 16 h. The reaction mixture was poured into saturated aqueous NaCl (10 mL) and extracted with $Et_2O$ (3 × 10 mL). The combined organic fractions were washed with water (10 mL), dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane, 1:1 → EtOAc/pentane, 7:3) to yield **12b** as a yellow foam (99 mg, 64%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.32 (d, $J$ = 12.4 Hz), 1.74 (q, $J$ = 7.0 Hz, 1 diastereomer), 1.80−1.89 (m, 2 diastereomer), 2.02−2.20 (m), 2.90 (s, 2 diastereomer), 2.93 (s, 1 diastereomer), 3.03 (t, $J$ = 5.2 Hz), 3.50 (t, $J$ = 7.8 Hz), 3.72−3.82 (m), 4.08−4.16 (m), 5.61 (s, 2 diastereomer), 5.63 (s, 1 diastereomer), 6. 82 (d, $J$ = 8.8 Hz), 7.16−7.32 (m), 7.34−7.43 (m), 7.46−7.54 (m), 7.63 (t, $J$ = 7.2 Hz), 7.92−7.96 (m), 8.17 (d, $J$ = 7.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.7, 27.6, 29.3, 32.8, 37.8, 45.3, 49.0, 55.4, 60.9, 61.0, 67.6, 67.7, 86.1, 86.3, 90.1, 90.3, 97.4, 97.5, 113.3, 121.4, 121.5, 123.2, 126.9, 128.0, 128.3, 128.4, 128.9, 129.1, 130.1, 130.2, 130.5, 130.8, 131.0, 131.6, 131.9, 132.7, 132.8, 134.0, 136.5, 136.6, 145.2, 145.26, 145.31, 158.6, 164.5, 164.6, 166.7, 167.2.

**1-[(4-Benzoyloxy-5-(*N*-(3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-4-[(4-benzoyloxy-5-(*N*-(3-hydroxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (13).** To a Schlenk flask charged with **12a** (103 mg, 0.069 mmol) dissolved in $CH_2Cl_2$ (5 mL) was added AcOH (5 mL), and reaction mixture was stirred at rt for 55 min. The reaction mixture was poured into 5.5% aqueous $NaHCO_3$ (132 mL) to obtain a pH value at 7 and then extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic fractions were washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane, 8:2) to yield **13** as a yellow solid (48 mg, 60%): mp 133−135 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.32 (d, $J$ = 13.2 Hz, 2H), 1.53 (qui, $J$ = 6.0 Hz, 2H), 1.66 (qui, $J$ = 6.0 Hz, 2H), 2.04−2.18 (m, 2H), 2.83 (t, $J$ = 6.2 Hz, 1H), 3.10 (t, $J$ = 5.4 Hz, 2H), 3.39 (q, $J$ = 6.0 Hz, 2H), 3.44 (q, $J$ = 6.3 Hz, 2H), 3.52 (q, $J$ = 5.6 Hz, 2H), 3.75 (s, 6H), 3.76 (t, $J$ = 12.4 Hz, 4H), 4.11 (dd, $J$ = 4.4, 11.6 Hz, 4H), 5.58 (s, 2H), 6.50 (t, $J$ = 5.4 Hz, 1H), 6.59 (t, $J$ = 6.4 Hz, 1H), 6.76 (d, $J$ = 8.8 Hz, 4H), 7.16−7.28 (m, 7H), 7.36 (d, $J$ = 7.2 Hz, 2H), 7.49 (s, 4H), 7.50 (t, $J$ = 8.0 Hz, 2H), 7.56 (t, $J$ = 7.8 Hz, 2H), 7.66 (t, $J$ = 7.6 Hz, 1H), 7.69 (t, $J$ = 7.6 Hz, 1H), 7.73 (d, $J$ = 2.0, 1H), 7.85 (d, $J$ = 2.4 Hz, 1H), 7.96 (d, $J$ = 2.4 Hz, 2H), 8.15 (d, $J$ = 7.6 Hz, 2H), 8.22 (d, $J$ = 7.6 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.6, 25.7, 29.5, 32.3, 36.8, 38.5, 55.4, 59,3, 61.9, 67.6, 86.5, 89.9, 90.2, 90.3, 90.5, 97.5, 113.3, 121.7, 122.0, 123.1, 123.3, 127.0, 128.1, 128.4, 128.8, 128.99, 129.05, 129.1, 130.1, 130.5, 131.0, 131.4, 131.9, 132.6, 132.7, 132.8, 132,9, 133.1, 134.1, 134.4, 136.4, 145.0, 145.6, 145.7, 158.6, 164.9, 165.4, 166.6; HRMS calcd 1217.4412 ($[M + Na]^+$), found 1217.5266.

**1-[(4-Benzoyloxy-5-(*N*-(3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-4-[(4-benzoyloxy-5-(*N*-3-(2-cyanoethoxy-*N*,*N*-diisopropylaminophosphanyloxy)prop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (14).** The alcohol **13** (300 mg, 0.25 mmol) was stirred under vacuum in a Schlenk flask for 45 min. $CH_2Cl_2$ (15 mL) and diisopropylethylamine (175 $\mu$L, 1.00 mmol) were added, and the solution was quickly cooled to 0 °C. 2-Cyanoethyl diisopropylchlorophosphoramidite (112 $\mu$L, 0.50 mmol) was added dropwise, and the reacting mixture was stirred at rt for 30 min under argon. The reacting mixture was washed with 5.5% aqueous $NaHCO_3$ (4 × 12 mL) and brine (4 × 12 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by precipitation in pentane to yield **14** as yellow crystals (299 mg, 85%): mp 109−111 °C; $^1$H NMR ($CDCl_3$, 400 Hz) $\delta$ 1.07 (d, $J$ = 7.2 Hz, 6H), 1.10 (d, $J$ = 7.2 Hz, 6H), 1.25 (d, $J$ = 13.6 Hz, 2H), 1.54−1.66 (m, 4H), 1.98−2.12 (m, 2H), 2.47 (t, $J$ = 6.6 Hz, 2H), 3.03 (t, $J$ = 5.8 Hz, 2H), 3.28−3.39 (m, 4H), 3.43−3.55 (m, 4H), 3.56−3.75 (m, 12H), 4.01−4.08 (m, 4H), 5.52 (s, 2H), 6.41 (t, $J$ = 5.6 Hz, 1H), 6.51 (t, $J$ = 5.8 Hz, 1H), 6.71 (d, $J$ = 8.8 Hz, 4H), 7.09−7.21 (m, 7H), 7.30 (d, $J$ = 7.2 Hz, 2H), 7.42 (s, 4H), 7.44 (t, $J$ = 8.0 Hz, 2H), 7.48 (t, $J$ = 8.4 Hz, 2H), 7.59 (t, $J$ = 7.6 Hz, 1H), 7.61 (t, $J$ = 7.6 Hz, 1H), 7.66 (d, $J$ = 2.0 Hz, 1H), 7.76 (d, $J$ = 2.0 Hz, 1H), 7.89 (s, 2H), 8.08 (d, $J$ = 7.8 Hz, 2H), 8.16 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100

MHz) $\delta$ 19.3, 23.6, 24.4, 28.2, 29.4, 36.5, 37.2, 41.9, 54.2, 57.2, 57.4, 60.6, 66.4, 85.2, 88.8, 88.9, 89.0, 89.1, 96.2, 112.1, 116.8, 120.4, 120.5, 121.9, 122.0, 125.8, 126.8, 127.1, 127.7, 127.8, 128.8, 129.2, 129.3, 130.1, 130.6, 131.3, 131.40, 131.44, 131.5, 131.6, 132.9, 133.0, 135.1, 143.7, 144.4, 144.5, 157.4, 163.6, 163.8, 164.1, 164.2; HRMS calcd 1417.5490 ([M + Na]$^+$), found 1417.1564.

**1,3,5-Tris[(4-benzoyloxy-5-(*N*-3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-benzene (15a).** Bis(triphenylphospine)palladium(II) chloride (148 mg, 0.211 mmol) and copper iodide (40 mg, 0.211 mmol) were stirred in a Schlenk flask under vacuum for 30 min. Then **11a** (3.44 g, 4.23 mmol), triethynylbenzene (159 mg, 1.06 mmol), and THF (90 mL) were added. Finally, $NEt_3$ (22.5 mL) was added, and the reaction mixture was stirred under argon at 52 °C for 16 h. The reaction mixture was diluted with $CH_2Cl_2$ (100 mL) and then washed with water (3 × 100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel ($CH_2Cl_2$/EtOAc, 90:10) to yield unreacted **11a** (1.06 g, 1.30 mmol) and **15a** as a white foam (866 mg, 37%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 12.8 Hz, 3H), 1.55 (qui, $J$ = 6.4 Hz, 6H), 1.99−2.12 (m, 3H), 2.99 (t, $J$ = 6.4 Hz, 6H), 3.29 (q, $J$ = 6.0 Hz, 6H), 3.67 (s, 18H), 3.7 (t, $J$ = 12.0 Hz, 6H), 4.04 (dd, $J$ = 11.2, 5.2 Hz, 6H), 5.53 (s, 3H), 6.42 (t, $J$ = 5.2 Hz, 3H), 6.70 (d, $J$ = 8.8 Hz, 12H), 7.12−7.19 (m, 21H), 7.30 (d, $J$ = 8.4 Hz, 6H), 7.44 (t, $J$ = 7.6 Hz, 6H), 7.55 (s, 3H), 7.59 (t, $J$ = 7.6 Hz, 3H), 7.67 (d, $J$ = 2.2 Hz, 3H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.7, 29.5, 38.5, 55.4, 61.9, 67.6, 86.5, 88.8, 89.5, 113.4, 121.4, 127.0, 128.1, 128.4, 129.0, 129.1, 130.1, 130.5, 131.5, 132.7, 132.8, 132.9, 134.1, 134.6, 136.4, 145.0, 145.9, 158.6, 164.9, 165.4; MALDI-TOF MS calcd 2228.84 ([M + Na]$^+$), found 2228.75.

**1,3,5-Tris[(4-benzoyloxy-5-(*N*-(3-dimethoxytrityl-oxyprop-1-yl)-*N*-methylaminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (15b).** Bis(triphenylphosphine)-palladium(II) chloride (7.7 mg, 0.011 mmol) and copper iodide (2.1 mg, 0.011 mmol) were stirred in a Schlenk flask under vacuum for 30 min. Compound **11b** (174 mg, 0.21 mmol), triethynylbenzene (8.0 mg, 0.053 mmol), and THF (8 mL) were added. Finally, $NEt_3$ (0.4 mL) was added, and the reaction mixture was stirred under argon at 52 °C for 16 h. The reaction mixture was diluted with $CH_2Cl_2$ (10 mL) and then washed with water (3 × 10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/pentane/$NEt_3$, 60:40:1) to yield unreacted **11b** (46.2 mg, 0.056 mmol) and **15b** as white foam (62.3 mg, 46%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.24 (d, $J$ = 12.6 Hz), 1.57 (qui, $J$ = 5.9 Hz), 1.99−2.12 (m), 2.82 (s, 1 diastereomer), 2.86 (s, 2 diastereomer), 2.95 (t, $J$ = 6.0 Hz), 3.37−3.45 (m), 3.64−3.71 (m), 4.04 (dd, $J$ = 11.2, 4.8 Hz), 5.54 (s, 1 diastereomer), 5.55 (s, 2 diastereomer), 6.72 (d, $J$ = 8.8 Hz), 7.12−7.19 (m), 7.27−7.33 (m), 7.40−7.46 (m), 7.53−7.63 (m), 7.84−7.90 (m, 1 and 2 diastereomer), 8.06−8.12 (m, 1 and 2 diastereomer); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.4, 27.3, 29.1, 32.5, 37.4, 44.9, 48,6, 55.1, 55.7, 60.6, 60.7, 67.2, 67.3, 85.7, 85.9, 88.1, 88.4, 89.1, 89.5, 97.0, 97.1, 112.9, 113.0, 120.6, 120.8, 123.6, 123.7, 126.6, 127.7, 128.0, 128.4, 128.5, 128.6, 128.7, 128.8, 129.8, 130.2, 130.5, 130.6. 130.7, 131.5, 131.6, 131.7, 131.8, 131.9, 132.0, 132.5, 133.7, 134.3, 135.0, 136.2, 144.8, 145.0, 158.3, 164.1, 164.2, 166.3, 166.8.

**1,3-Bis[(4-benzoyloxy-5-(*N*-3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-5-[(4-benzoyloxy-5-(*N*-(3-hydroxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (16) and 1,3-Bis[(4-benzoyloxy-5-(*N*-(3-hydroxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-5-[(4-benzoyloxy-5-(*N*-3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (17).** To a round-bottomed flask charged with **15a** (485 mg, 0.22 mmol) dissolved in $CH_2Cl_2$ (15 mL) was added dropwise glacial AcOH (15 mL). The reaction mixture was stirred for 8 min, quickly diluted with $CH_2Cl_2$ (50 mL) ,and neutralized with saturated $NaHCO_3$. The organic layer was washed with water (3 × 80 mL), dried over $MgSO_4$, and concentrated. The crude hydrolyzed mixture was purified by flash chromatography on silica gel ($CH_2Cl_2$/EtOAc, 85:15 → 60:40 → 0:100) to yield unhydrolyzed **15a** (248 mg, 0112 mmol), **16** (118 mg, 28%), and **17** (27 mg, 7.6%). **16**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 12.8 Hz, 3H), 1.48 (qui, $J$ = 6.4 Hz, 2H), 1.60 (qui, $J$ = 6.4 Hz, 4H), 1.99−2.12 (m, 3H), 2.99 (t, $J$ = 6.4 Hz, 4H), 3.29−3.42 (m, 6H), 3.47 (q, $J$ = 5.1 Hz, 2H), 3.67 (s, 12H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.04 (dd, $J$ = 11.2, 5.2 Hz, 6H), 5.53 (s, 3H), 6.42 (t, $J$ = 5.2 Hz, 2H), 6.51 (t, $J$ = 6.2 Hz, 1H), 6.70 (d, $J$ = 8.8 Hz, 8H), 7.12−7.19 (m, 14H), 7.30 (d, $J$ = 8.4 Hz, 4H), 7.42−7.51(m, 6H), 7.55−7.62 (m, 6H), 7.67 (d, $J$ = 2.2 Hz, 2H), 7.78 (d, $J$ = 2.2 Hz, 1H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 4H), 8.16 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.3, 25.4, 29.2, 32.1, 36.5, 83.2, 55.2, 59.1, 61.6, 67.3, 86.2, 88.6, 88.8, 89.0, 89.2, 97.1, 97.2, 113.1, 121.1, 121.4, 123.6, 123.7, 126.7, 127.8, 128.1, 128.6, 128.7, 128.8, 129.8, 130.2, 130.8, 131.2, 132.3, 132.4, 132.5, 132.6, 132.7, 133.0, 133.8, 134.1,-134.3, 136.1, 144.7, 145.5, 145.6, 158.4, 164.6, 165.1, 166.4; MALDI-TOF MS calcd 1926.71 ([M + Na]$^+$), found 1926.56. **17**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 12.8 Hz, 3H), 1.48 (qui, $J$ = 6.4 Hz, 4H), 1.60 (qui, $J$ = 6.4 Hz, 2H), 1.99−2.12 (m, 3H), 2.99 (t, $J$ = 6.4 Hz, 2H), 3.29−3.40 (m, 6H), 3.47 (s, br, 4H), 3.67 (s, 6H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.04 (dd, $J$ = 11.2, 5.2 Hz, 6H), 5.53 (s, 3H), 6.46 (t, $J$ = 5.2 Hz, 1H), 6.58 (t, $J$ = 6.2 Hz, 2H), 6.70 (d, $J$ = 8.8 Hz, 8H), 7.12−7.19 (m, 7H), 7.30 (d, $J$ = 8.4 Hz, 2H), 7.42−7.51 (m, 6H), 7.55−7.62 (m, 6H), 7.67 (d, $J$ = 2.2 Hz, 1H), 7.78 (d, $J$ = 2.2 Hz, 2H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 2H), 8.16 (d, $J$ = 8.0 Hz, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.4, 25.8, 28.8, 29.2, 32.0, 36.5, 38.2, 55.1, 59.0, 61.6, 67.3, 67.5, 86.1, 88.6, 88.7, 89.0, 89.2, 97.1, 113.0, 113.1, 120.9, 121.1, 121.2, 123.6, 123.7, 123.8, 123.9, 126.7, 126.9, 127.8, 127.9, 128.0, 128.4, 128.6, 128.7, 128.8, 129.5, 129.8, 130.2, 130.6, 131.0, 132.3, 132.4, 132.5, 132.5, 132.9, 133.2, 133.8, 134.0, 134.3, 135.0, 135.0, 135.9, 136.1, 144.7, 145.5, 145.6, 158.3, 158.3, 158.4, 164.6, 165.0. 165.2, 166.3; MALDI-TOF MS calcd 1624.58 ([M + Na]$^+$), found 1624.30.

**1,3-Bis[(4-benzoyloxy-5-(*N*-(3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-5-[(4-benzoyloxy-5-(*N*-(3-(2-cyanoethoxy-*N*,*N*-diisopropylaminophosphanyloxy)prop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (18).** The alcohol **16** (42.7 mg, 0.022 mmol) was a stirred under vacuum in a Schlenk flask for 45 min. $CH_2Cl_2$ (3 mL) and diisopropylethylamine (15.6 $\mu$L, 0.09 mmol) were added, and the solution was quickly cooled to 0 °C. 2-Cyanoethyl diisopropylchlorophosphoramidite (10 $\mu$L, 0.045 mmol) was added dropwise, and the reacting mixture was stirred at rt for 30 min under argon. The reacting mixture was diluted with $CH_2Cl_2$ (5 mL) and washed with saturated $NaHCO_3$ (4 × 4 mL) and brine (4 × 4 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by precipitation in pentane to yield **18** as yellow crystals (41.6 mg, 89%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.03−1.11 (m, 12H), 1.23 (d, $J$ = 12.8 Hz, 3H), 1.55−1.75 (m, 6H), 1.98−2.12 (m, 3H), 2.48 (t, $J$ = 7 Hz, 2H), 2.99 (t, $J$ = 6.4 Hz, 4H), 3.27−3.42 (m, 8H), 3.41−3.57 (m, 2H), 3.67 (s, 12H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.04 (dd, $J$ = 11.2 Hz, $J$ = 5.2 Hz, 6H), 5.53 (s, 3H), 6.42 (t, $J$ = 5.2 Hz, 2H), 6.51 (t, $J$ = 6.2 Hz, 1H), 6.70 (d, $J$ = 8.8 Hz, 8H), 7.12−7.19 (m, 14H), 7.30 (d, $J$ = 8.4 Hz, 4H), 7.42−7.51 (m, 6H), 7.55−7.62 (m, 6H), 7.67 (d, $J$ = 2.2 Hz, 2H), 7.78 (d, $J$ = 2.2 Hz, 1H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 4H), 8.16 (d, $J$ = 8.0 Hz, 2H); $^{31}$P NMR $\delta$ 148.90.

**1,3-Bis[(4-benzoyloxy-5-(*N*-3-dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-5-[(4-benzoyloxy-5-(*N*-3-(9-fluoroenylmethoxycarbonyloxy)prop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)-**

**phenyl)ethynyl]benzene (19).** To a Schlenk flask charged with 9-fluorenylmethyl chloroformate (64.2 mg, 0.25 mmol) and *N*,*N*-dimethyl-4-aminopyridine (0.76 mg, 0.0062 mmol) was added dropwise a solution of **16** (118 mg, 0.062 mmol) in pyridine (4 mL). The reaction mixture was stirred at rt for 16 h under argon, diluted with $CH_2Cl_2$ (10 mL), and washed with water (3 × 10 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel ($CH_2Cl_2$/EtOAc, 85:15) to yield **19** as white foam (98 mg, 74%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 12.8 Hz, 3H), 1.60 (qui, $J$ = 6.4 Hz, 4H), 1.74 (qui, $J$ = 6.4 Hz, 2H), 2.01−2.10 (m, 3H), 2.99 (t, $J$ = 6.4 Hz, 4H), 3.30−3.37 (m, 6H), 3.67 (s, 12H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.01−4.09 (m, 8H), 4.15 (t, $J$ = 7.7 Hz, 1H), 4.30 (d, $J$ = 7.7 Hz, 2H), 5.53 (s, 3H), 6.40−6.44 (m, 2H), 6.70 (d, $J$ = 8.8 Hz, 8H), 7.12−7.29 (m, 16H), 7.28−7.35 (m, 6H), 7.42−7.47 (m, 6H), 7.50−7.62 (m, 8H), 7.67 (d, $J$ = 2.2 Hz, 2H), 7.69 (d, $J$ = 7.7 Hz, 2H), 7.78 (d, $J$ = 2.2 Hz, 1H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 4H), 8.16 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.3, 25.4, 28.5, 29.2, 36.6, 38.2, 46.7, 55.2, 61.6, 65.5, 67.3, 69.8, 86.2, 88.6, 89.0, 89.2, 97.1, 97.2, 113.1, 120.0, 121.2, 121.4, 123.6, 123.7, 125.1, 126.7, 127.1, 127.8, 128.1, 128.6, 128.7, 128.8, 129.8, 130.9, 131.2, 132.3, 132.3, 132.5, 132.6, 133.0, 133.8, 134.0, 134.3, 136.1, 141.2, 143.3, 144.7, 145.6, 155.1, 158.3, 164.6, 164.9, 165.1, 165.4.

**1-[(4-Benzoyloxy-5-(*N*-3-dimethoxytrityloxyprop-1-yl)-aminocarbonyl)-3-(1,3-dioxan-2-yl)-phenyl)ethynyl]-3-[(4-benzoyloxy-5-(*N*-(3-hydroxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-5-[(4-benzoyloxy-5-(*N*-(3-(9-fluoroenylmethoxycarbonyloxy)prop-1-yl)-aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]benzene (20).** To a round-bottomed flask charged with **19** (114 mg, 0.054 mmol) dissolved in $CH_2Cl_2$ (5 mL) was added dropwise glacial AcOH (5 mL). The reaction mixture was stirred for 10 min, quickly diluted with $CH_2Cl_2$ (50 mL), and neutralized with saturated $NaHCO_3$. The organic layer was washed with water (3 × 80 mL), dried over $MgSO_4$, and concentrated. The crude hydrolyzed mixture was purified by flash chromatography ($CH_2Cl_2$/EtOAc, 85:15 → 60:40 → 0:100) to yield unhydrolyzed **19** (60 mg, 0.028 mmol) and **20** (24 mg, 25%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (d, $J$ = 12.8 Hz, 3H), 1.46 (qui, $J$ = 6.4 Hz, 2H), 1.60 (qui, $J$ = 6.4 Hz, 2H), 1.74 (qui, $J$ = 6.4, 2H), 1.99−2.12 (m, 3H), 2.99 (t, $J$ = 6.4 Hz, 2H), 3.29−3.43 (m, 6H), 3.47 (q, $J$ = 5.1 Hz, 2H), 3.67 (s, 6H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.04 (dd, $J$ = 11.2, 5.2 Hz, 6H), 4.15 (t, $J$ = 7.7 Hz, 1H), 4.30 (d, $J$ = 7.7 Hz, 2H), 5.53 (s, 3H), 6.45−6.51 (m, 2H), 6.68 (t, $J$ = 6.2 Hz, 1H), 6.70 (d, $J$ = 8.8 Hz, 4H), 7.12−7.29 (m, 9H), 7.27−7.34 (m, 4H), 7.42−7.62 (m, 14H), 7.67 (d, $J$ = 2.2 Hz, 1H), 7.69 (d, $J$ = 7.7 Hz, 2H), 7.78 (d, $J$ = 2.2 Hz, 1H), 7,80 (d, $J$ = 2.2 Hz, 1H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 2H), 8.16 (d, $J$ = 8.0 Hz, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 25.3, 25.4, 28.5, 29.2, 32.1, 36.5, 36.6, 38.2, 46.7, 55.1, 59.0, 61.6, 65.5, 67.3, 69.7, 86.2, 88.6, 88.7, 88.8, 88.9, 89.0, 89.2, 97.1, 97.2, 113.0, 120.0, 121.1, 121.3, 121.4, 123.6, 123.7, 125.1, 126.7, 127.1, 127.8, 128.0, 128.5, 128.6, 128.7, 128.8, 129.8, 130.2, 130.7, 130.8, 132.3, 132.4, 132.5, 132.5, 132.6, 132.9, 133.0, 133.8, 134.0, 134.1, 134.3, 136.1, 141.2, 143.2, 144.7, 145.5, 155.1, 158.3, 164.6, 165.1, 165.1, 165.4, 166.2.

**1-[(4-Benzoyloxy-5-(*N*-3-(dimethoxytrityloxyprop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-3-[(4-benzoyloxy-5-(*N*-(3-(9-fluoroenylmethoxycarbonyl)prop-1-yl)aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)-ethynyl]-5-[(4-benzoyloxy-5-(*N*-(3-(2-cyanoethoxy-*N*,*N*-diisopropylaminophosphanyloxy)prop-1-yl)-aminocarbonyl)-3-(1,3-dioxan-2-yl)phenyl)ethynyl]-benzene (21).** The alcohol **20** (25.5 mg, 0.014 mmol) was stirred under vacuum in a Schlenk flask for 45 min. $CH_2Cl_2$ (1.5 mL) and diisopropylethylamine (9.75 $\mu$L, 0.056 mmol) were added, and the solution was quickly cooled to 0 °C. 2-Cyanoethyl diisopropyl chlorophosphoramidite (6.25 $\mu$L, 0.028 mmol) was added dropwise, and the reacting mixture was stirred at rt for 30 min under argon. The reacting mixture was diluted with $CH_2Cl_2$ (3 mL), washed with saturated $NaHCO_3$ (2 × 4 mL) and brine (2 × 4 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by precipitation in pentane to yield **21** as yellow crystals (19.8 mg, 70%): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.12−1.16 (m, 12H), 1.23 (d, $J$ = 12.8 Hz, 3H), 1.46 (qui, $J$ = 6.4 Hz, 2H), 1.60 (qui, $J$ = 6.4 Hz, 2H), 1.74 (qui, $J$ = 6.4, 2H), 1.99−2.12 (m, 3H), 2.58 (t, 2H), 2.99 (t, $J$ = 6.4 Hz, 2H), 3.29−3.39 (m, 8H), 3.43−3.57 (m, 2H), 3.67 (s, 13H), 3.70 (t, $J$ = 12.0 Hz, 6H), 4.00−4.09 (m, 8H), 4.15 (t, $J$ = 7.7 Hz, 1H), 4.30 (d, $J$ = 7.7 Hz, 2H), 5.53 (s, 3H), 6.45−6.49 (m, 2H), 6.68 (t, $J$ = 6.2 Hz, 1H), 6.70 (d, $J$ = 8.8 Hz, 4H), 7.12−7.27 (m, 9H), 7.28−7.35 (m, 4H), 7.42−7.62 (m, 14H), 7.67−7.72 (m, 3H), 7.78 (d, $J$ = 2.2 Hz, 1H), 7,80 (d, $J$ = 2.2 Hz, 1H), 7.91 (d, $J$ = 2.2 Hz, 3H), 8.09 (d, $J$ = 8.4 Hz, 2H), 8.16 (d, $J$ = 8.0 Hz, 4H); $^{31}$P NMR $\delta$ 148.89.

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**Supporting Information Available:** NMR spectra of compounds **3**−**21**. This material is available free of charge via the Internet at http://pubs.acs.org.

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