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Saccharide Recognition-Induced Transformation of Pyridine−Pyridone Alternate Oligomers from Self-Dimer to Helical Complex

Hajime Abe,*[,†,‡] Hiroshi Machiguchi,[†] Shinya Matsumoto,[§] and Masahiko Inouye*[,†]

Graduate School of Pharmaceutical Sciences, University of Toyama, Toyama 930-0194, Japan, Faculty of Education and Human Sciences, Yokohama National University, Yokohama 240-8501, Japan, and PRESTO, JST, Tokyo 102-0075, Japan

abeh@pha.u-toyama.ac.jp; inouye@pha.u-toyama.ac.jp

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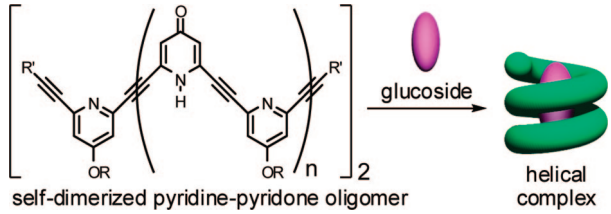

Co-oligomers involving (1*H*)-4-pyridone and 4-alkoxypyridine rings were studied, and it was found that their supramolecular transformation was caused by saccharide recognition. In the co-oligomers, pyridone and pyridine rings are alternately linked at their 2,6-position with an acetylene bond. The pyridine rings behave as a hydrogen bonding acceptor, and the pyridone rings and tautomerized 4-pyridinol work as a donor. Pyridine−pyridone−pyridine 3-mer was found to self-dimerize on the basis of vapor pressure osmometry in $CHCl_3$, and the association constant was obtained as 2.3×10^3 M^{-1} by ^1H NMR titration. Longer 5-, 7-, 9-, and 11-mer oligomers showed considerable broadening and anisotropy in the ^1H NMR spectra due to self-association. These longer oligomers recognized octyl β-D-glucopyranoside and changed their form into a chiral helical complex, showing characteristic circular dichroism.

Introduction

Hydrogen bonding builds various systems of natural[1−3] and artificial[4] host−guest associations based on effective higher-order structures, which involve helices as DNA and peptide, sheets as peptide,[5] and so on. Natural supramolecules perform their functions with motion of their structures, that is, dynamic motion of higher-order structure is necessary for dynamic function of supramolecules.

Recently, our group has developed 2,6-pyridylene ethynylene polymers "poly(*meta*-ethynylpyridines)"[6] (e.g., **I** and **II** in Figure 1a) as host molecules for saccharide recognition.[2,7−10] These polymers consist of 2,6-linked pyridine rings and can bind saccharide by multiple hydrogen bonds to form a helical complex.[11−15] The helical sense of the resulting complex is biassed by chirality of the guest saccharide to induce remarkable

* To whom correspondence should be addressed. Phone: +81-76-434-7527. Fax: +81-76-434-5049.
† University of Toyama.
‡ Yokohama National University.
§ PRESTO, JST.

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CD in the absorptive region of the host. On the other hand, without a guest saccharide, the polymeric host exists as a single string in solution, hardly showing self-association. If the ethynylpyridine polymer could self-associate and form higher-order structure by itself, its saccharide recognition will conduct more dynamic transformation from one higher-order structure to another.

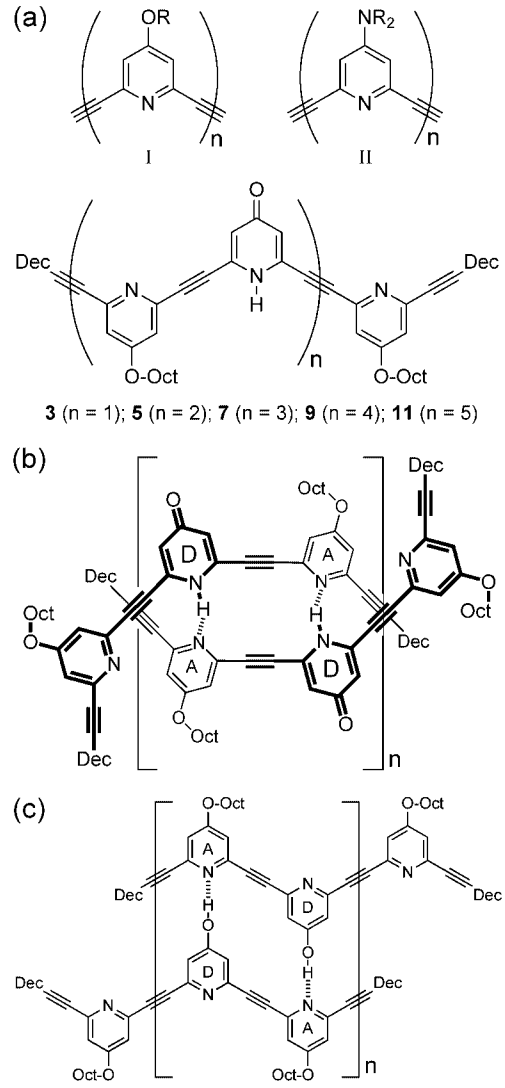

FIGURE 1. (a) The structures of *meta*-ethynylpyridine polymers **I** (alkoxy polymer), **II** (amino polymer), and *meta*-pyridine−pyridone oligomers **3**−**11**. (b,c) Two types of possible self-dimerization mode of **3**−**11** with multiple hydrogen bonds. (b) Duplex form based on 4-(1*H*)-pyridone tautomer, and (c) the linear form based on the 4-pyridinol tautomer. Oct = n-C_8H_{17}, Dec = n-$C_{10}H_{21}$, A = hydrogen bonding acceptor, D = donor.

With this in mind, we decided to introduce a new hopeful unit, 4-(1*H*)-pyridone, into our multipyridine host, producing pyridine−pyridone alternate oligomers **3**−**11** (Figure 1a). The N atoms of the 4-alkoxypyridine rings in **3**−**11** work as a hydrogen bonding acceptor (A), while the N−H groups in the pyridones work as a donor (D); therefore, the N and N−H groups are expected to interact with each other in a complementary way. For example, **3** is a trimeric module of A−D−A (pyridine−pyridone−pyridine) type and is expected to self-dimerize in an A−*D*−*A*·*A*−*D*−A way with two A·D hydrogen bonds. Undecamer **11** has potential to make an A−*D*−*A*−*D*−*A*−*D*−*A*−*D*−*A*−*D*−*A*·*A*−*D*−*A*−*D*−*A*−*D*−*A*−*D*−*A*−*D*−A dimer in which two oligomer molecules intertwist by 10 hydrogen bonds, as shown in Figure 1b (n = 5), *duplex* form.

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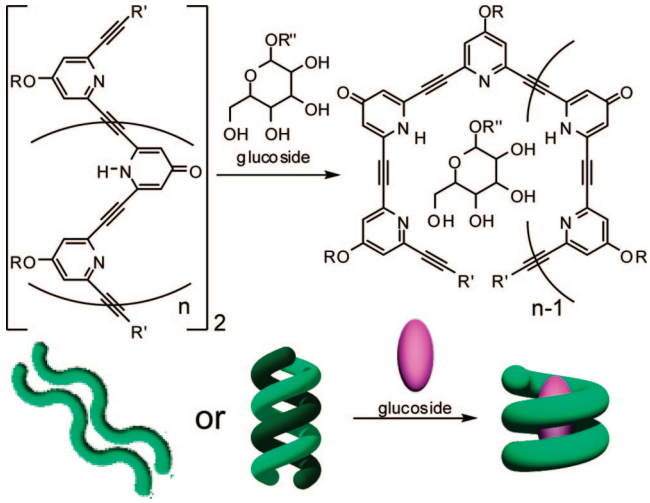
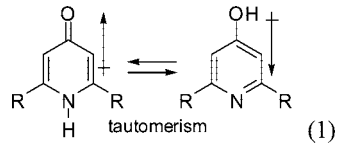
SCHEME 1. Diagram of Saccharide Recognition by the Pyridine−Pyridone Oligomer, Dynamic Structural Transformation from Self-Dimer (Duplex or Linear Form, See Figure 1b,c) into Helical Complex; The Pyridone Moiety Can Tautomerize to the Pyridinol Form



When the pyridone rings tautomerize to pyridinol as shown in eq 1,[16] the rings can still provide a hydrogen-donating OH group at the 4-position. Figure 1c outlines another possible structure of self-dimerization, *linear* form, based on the pyridinol tautomer. On the other hand, it is expected that the pyridine−pyridone oligomers associate with saccharide to form a single helical complex as well as the cases of our previous *meta*-ethynylpyridines (Scheme 1). Thus, the pyridine−pyridone oligomers have the potential to perform dynamic transformation between different types of higher-order structures by the effect of saccharide recognition. Such recognition−transformation systems which involve helical structures have been reported in the cases triggered by metal ions[12a] and cyclodextrins.[11a,12b,c]



(1)

Molecular Design of Pyridine−Pyridone Oligomers and Terms for the Oligomers and their Higher-Order Structures. The pyridine−pyridone oligomers **3**−**11** were designed in order to illustrate the concept described above. In the oligomers, 4-octoxypyridine and (1*H*)-4-pyridone rings are alternately connected at their 2,6-positions by acetylene bonds, which save moderate rigidity of the oligomer and intervals between the rings. Long alkyl chains were introduced to improve solubility. Octoxypyridine rings behave as a hydrogen-bonding acceptor, and pyridone and tautomerized pyridinol rings behave as a donor. In terms of electrostatic characteristics, octoxypyridine and pyridinol rings have polarization positive at O atoms, whereas pyridone rings have positivity at N atoms (eq 1). Thus, considering conformation of the oligomer, the cisoid form would be preferred between adjacent octoxypyridine and pyridone rings to avoid electrostatic repulsion caused by the local dipole moment at the two rings, whereas the transoid form would be preferred between octoxypyridine and pyridinol rings. These electrostatic characteristics are convenient for the higher-order structures described above. Self-duplex (Figure 1b) involves cisoid conformation with a pyridone tautomer, and a linear complex (Figure 1c) involves transoid conformation with a pyridinol tautomer. The helical complex of the oligomer with saccharide (Scheme 1) would be favorable for a pyridone tautomer which stabilizes cisoid conformation.

Strictly speaking, though the pyridine−pyridone alternate structure in Figure 1 should be called "co-oligomer", herein we would like to use the word "oligomer" for simplification. Similarly, we call the "pyridine−pyridone−pyridine oligomer" as "3-mer", and "pyridine−pyridone−pyridine−pyridone−pyridine oligomer" as "5-mer", and so on, using arabic numerals. To distinguish between a self-dimerized oligomer and a single one, we use adjectives "dimolecular" and "monomolecular" to express the number of the molecules involved. "Self-dimer" represents a self-dimerized dimolecular complex.

Results and Discussion

Preparation of the Pyridine−Pyridone Oligomers 3−11. Scheme 2 describes the preparation of building blocks for synthesizing the pyridine−pyridone oligomers **3**−**11**, and the building blocks were assembled as shown in Scheme 3. Ir-catalyzed direct boration[17] of 2,6-dibromopyridine (**1a**) followed by oxidative cleavage[17b] of the resulting C−B bonds gave 2,6-dibromo-(1*H*)-4-pyridone (**1b**). Williamson synthesis using **1b** with 1-iodooctane afforded ether **1d**, and halogen exchange[18,19] converted the dibromides **1b** and **1d** into diiodides **1c** and **1e**, respectively. The pyridones **1b**,**c** were protected by MOM groups to give **1f**,**g**. Because the MOM group can be removed by acidic treatment, the MOMO-pyridines **1f**,**g** were used as a synthon for the pyridones **1b**,**c**.[10c] The dihalides **1d**−**g** were ethynylated by Sonogashira reaction with 2-methyl-3-butyn-2-ol followed by liberation of acetone. Subsequent Sonogashira reaction and ethynylation afforded building blocks, dodecynyl ethynyl substrates **1o**, **2a**, **3c**, and **4a**, and trimeric diiodides **3a**,**b**. They were then brought to the next scheme.

The oligomers **3**−**11** were obtained as shown in Scheme 3. For example, MOM-protected 7-mer **7-MOM** was prepared by the coupling between 2 equiv of the dimeric end **2a** and 1 equiv of the trimeric center **3b**, according to the addition 2 + 3 + 2 = 7, and then acidic deprotection of the MOM groups gave **7**.

Hydrogen-Bonding Association of the Pyridine−Pyridone Oligomers. The self-association and saccharide recognition of pyridine−pyridone oligomers **3**−**11** were examined mainly in dichloromethane and chloroform. In outline, for the 3-mer **3**, the extent of self-association depends on its concentration: one kind of dimolecular complex is predominant at higher concentration, and two kinds of monomolecular tautomers appear at a lower concentration. For the longer oligomers **5**−**11**, hydrogen bonding self-association is too strong in chloroform to find monomolecular species, and the addition of alkyl glucoside into the self-associated oligomer induced the formation of a 1:1 helical complex between the oligomer and the glucoside.

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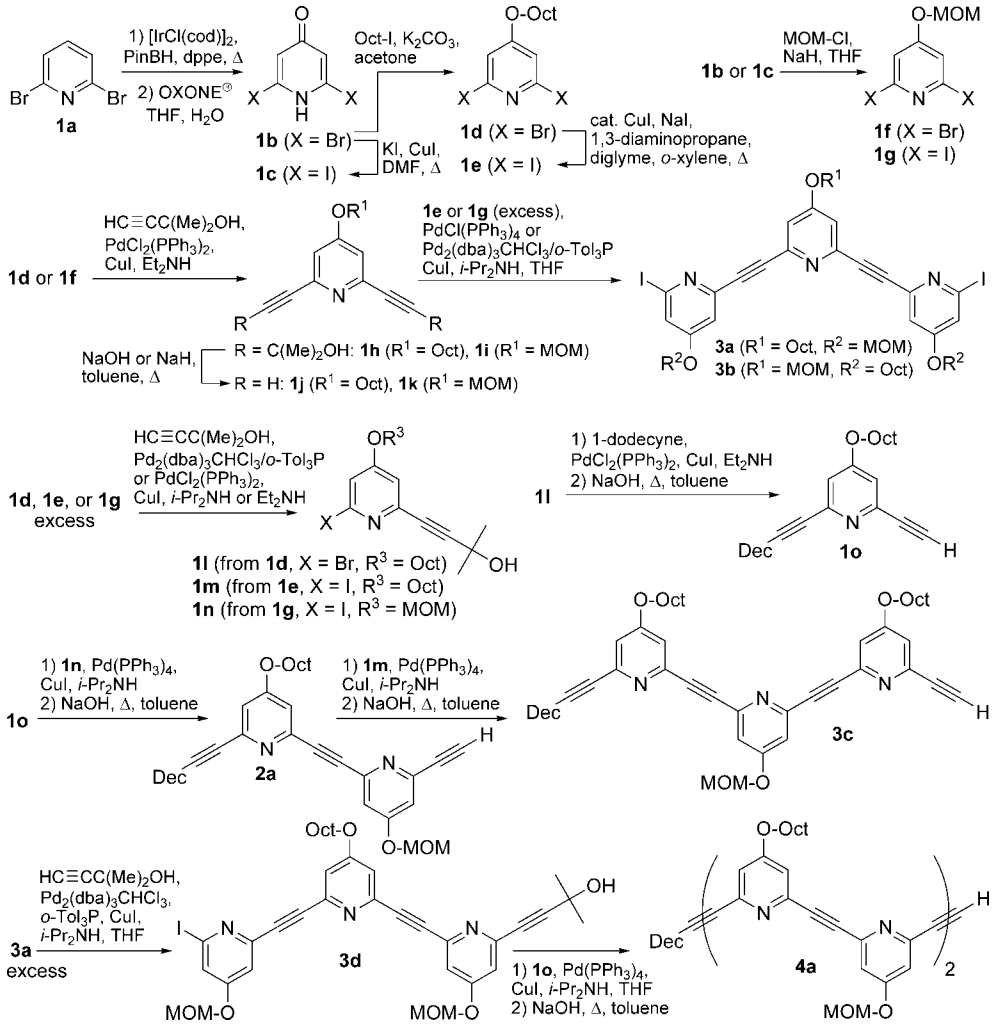
SCHEME 2. Preparation of Building Blocks of Pyridine-Pyridone Oligomers (Oct = *n*-C_8H_{17}, Dec = *n*-$C_{10}H_{21}$, MOM = methoxymethyl, cod = 1,5-cyclooctadiene, PinBH = pinacolborane, dba = dibenzylideneacetone, TFA = trifluoroacetic acid)

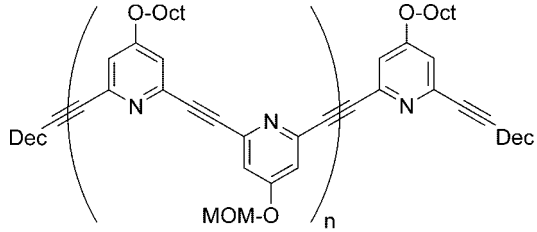


Study on Self-Dimerization of 3-mer on the Basis of VPO. Vapor pressure osmometry (VPO) studies were carried out to obtain information about self-association of the 3-mer **3** and of the MOM-protected 3-mer **3-MOM**. The ratio (observed number-average molecular weight (M_n))/(calculated molecular weight (MW) as monomer) indicates the degree of self-association under the conditions for VPO analyses. The VPO results for **3** and **3-MOM** in $CHCl_3$ at the concentration range of 6−9 mmol/kg (ca. $9-13 \times 10^{-3}$ M) are summarized in Table 1. The observed M_n/MW values for **3** and **3-MOM** are close to 2 and 1, respectively, indicating that **3** tends to exist as a dimolecular complex, whereas **3-MOM** favors a monomolecular state. The critical difference between **3** and **3-MOM** is the hydrogen-bonding nature of their center ring. The MOM-protected **3-MOM** has three pyridine rings playing only a single role as a hydrogen-bonding acceptor, whereas the central pyridone ring of deprotected **3** can serve as a donor. If a π-stacking interaction was important for the self-association, **3-MOM** would self-associate to show a higher M_n value as well as **3** in the VPO analysis. Thus, the VPO observation supports the idea that the dimerization of **3** occurs in a complementary hydrogen-bonding way, A−D−A·A−D−A, as depicted in Figure 2.

Study on Self-Dimerization of the Trimer on the Basis of ^{1}H NMR and X-ray Analysis. To acquire quantitative information on the self-dimerization of **3**, ^{1}H NMR spectra were collected in $CDCl_3$ at various concentrations ranging from 6.1×10^{-2} to 1.0×10^{-6} M. At the concentration range over 3.7×10^{-4} M, a broad signal for the N-*H* proton of the pyridone ring (or O-*H* proton of the tautomerized pyridinol ring) was observed, and its chemical shift depended on the concentration of **3** (Figure 3). By an iterative curve-fitting analysis, it was found that the results fitted well with a theoretical curve assuming self-dimerization to form a dimolecular complex. The dimerization constant was obtained as $K'_{dim} = 2.3 \times 10^3$ M^{-1}, which corresponds to $\Delta G = -19.3$ kJ/mol.

At the concentration of $\leq 6.1 \times 10^{-4}$ M, a new set of signals appeared and increased its presence as the concentration decreased (Figure 4). The integrals of the two sets of signals became comparable when the concentration of **3** was lowered to around 2.0×10^{-5} M. However, the appearance of the new signals cannot be attributed to the appearance of a monomolecular state by dissociation from the dimolecular complex. It is because, during the titration experiment as shown in Figure 3, no separation nor coalescence of signals was observed; therefore, the self-association/dissociation process of **3** is faster than the NMR time scale. Furthermore, the integral ratio does not agree with the expectation from the above K'_{dim} value, which tells us that a 0.5 mol of dissolved **3** exists as a self-dimer at $1/K'_{dim} \approx 4 \times 10^{-4}$ M. Therefore, the new set of signals should

SCHEME 3. Preparation of Pyridine-Pyridone Oligomers 3−11 (Oct = *n*-C_8H_{17}, Dec = *n*-$C_{10}H_{21}$, MOM = methoxymethyl, dba = dibenzylideneacetone, TFA = trifluoroacetic acid)



5, 7, 9, 11-MOM (n = 2,3,4,5)

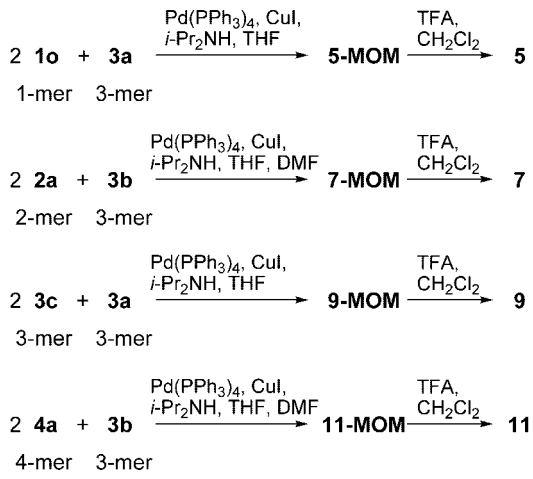


TABLE 1. M_n and MW Values Obtained from VPO Analyses of 3 and 3-MOM[a]

3-mer	MW [g/mol]	M_n [g/mol]	M_n/MW
3	882	1619	1.84
3-MOM	926	925	1.00

[a] Conditions: **3** or **3-MOM** (6−9 mmol/kg) in $CHCl_3$, 40 °C. Calibration was carried out by using benzil (2−12 mmol/kg).

be attributed to the second monomolecular species, maybe a tautomer, of which the structure is different from that involved in the self-dimer. A plausible equilibrium scheme for **3** could be drawn as Scheme 4, which contains the self-association to the self-dimer and the tautomerism occurring in the monomolecular state. As mentioned above, there would be two possible forms for the self-dimer of **3**, one is a duplex form (Figure 2a, corresponding to **3-ONE•3-ONE** in Scheme 4), and the other is a linear form (Figure 2b, corresponding to **3-OL•3-OL** in Scheme 4). At higher concentrations, one of these forms would be predominant, and at lower concentrations, the self-dimer dissociates and two kinds of monomolecular tautomers appear separately to show two comparable sets of ^{1}H NMR signals.

When a similar dilution experiment was carried out for the MOM-protected 3-mer **3-MOM** in $CDCl_3$, no meaningful change was observed for the chemical shifts of the ^{1}H NMR signals. This observation supports the importance of the center pyridone ring in **3** as a hydrogen-bonding donor for the self-association.

In order to obtain structural information for the 3-mer in a solid state, 3-mer **3e** was prepared as a model compound, in which alkyl groups in **3** were replaced by methyl groups. Using crystals of **3e** from a CH_2Cl_2/MeOH solution, X-ray crystallography showed a self-associated structure in which the

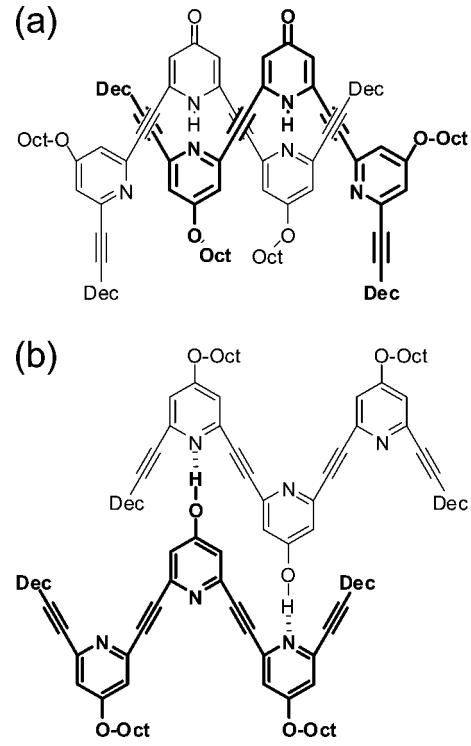


FIGURE 2. Plausible diagrams for the A−*D*−*A*•*A*−*D*−A self-dimerization of **3**. (a) Duplex form based on a pyridine−pyridone tautomer. (b) Linear form based on a pyridine−pyridinol tautomer.

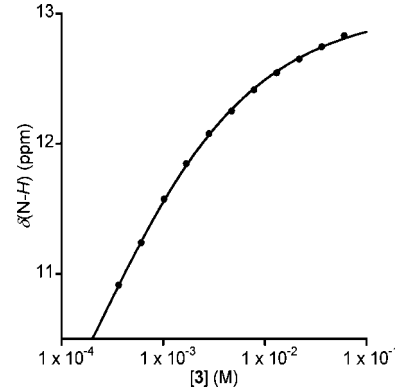


FIGURE 3. Titration curve for the NMR shift of N-*H* on dilution experiment of **3**. Solid line is the theoretical curve obtained by curve-fitting analysis.

pyridinol tautomer **3e′** exists in a planar transoid form and arranges parallel to make a layer. Methanol was found to link each of the pyridinol rings of **3e′** by hydrogen bonding (Figures 5 and S1A,B in Supporting Information).

Study on the Self-Association of the 5-mer to 11-mer. The ^{1}H NMR spectra of the pyridine−pyridone oligomers were measured in $CDCl_3$ and in $CDCl_3$/CD_3OD. In the cases of the 3-mer **3** and the 5-mer **5** in $CDCl_3$, the signals were relatively resolved and could be easily assigned. On the other hand, the shape of ^{1}H NMR spectra of the 7-mer **7** was significantly affected by solvent. The spectrum of **7** in $CDCl_3$ showed considerable broadening of signals, suggesting the formation of less mobile, self-associated species (Figure 6A), and in $CDCl_3$/CD_3OD (1:1), this broadening was almost suppressed (Figure 6B). In addition, the spectrum for **7-MOM**, which cannot make hydrogen bonding self-association, showed a

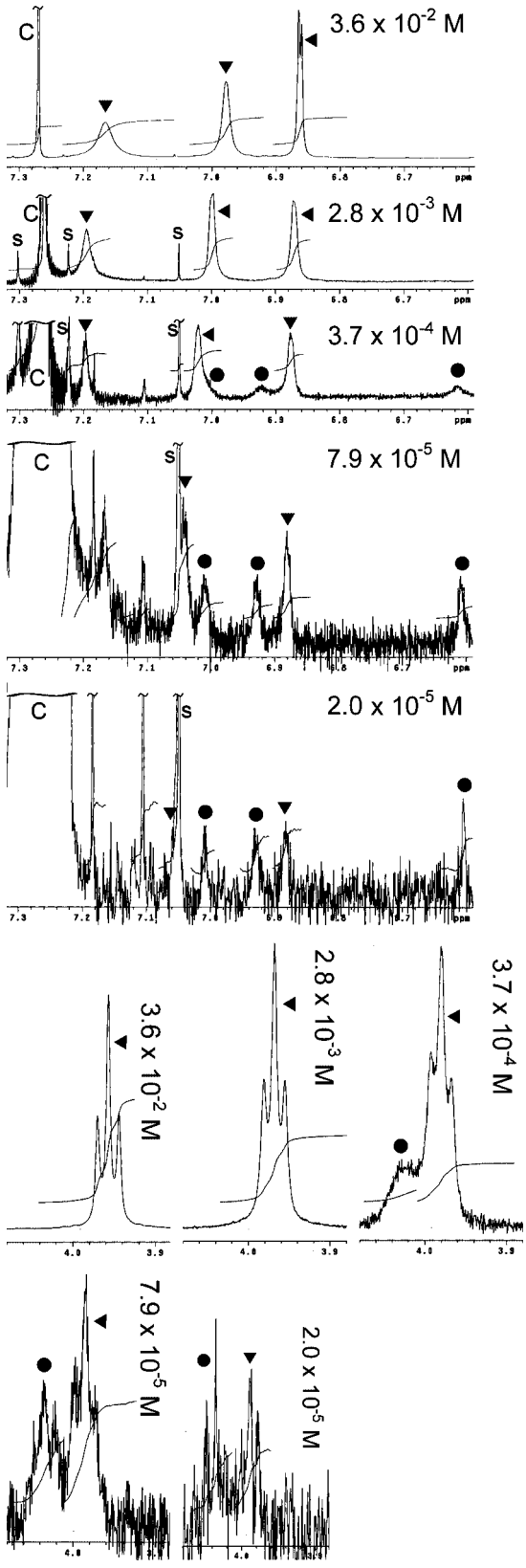
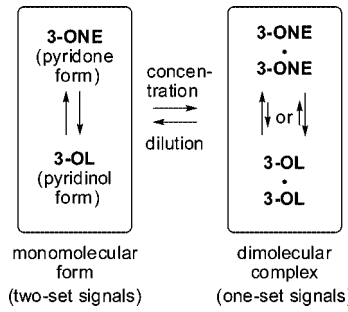


FIGURE 4. Dependence of ^{1}H NMR (500 MHz) spectra of **3** on the concentration. (Top) Signals for the aromatic region. (Bottom) Signals for $-OCH_2-$ moieties in octoxy groups. Conditions: **3** (3.6×10^{-2} to 2.0×10^{-5} M), $CDCl_3$, 22 °C, 500 MHz. Marked signals are attributed to (▼) dimolecular complex and one tautomer of monomolecular **3**, and (●) the other tautomer of monomolecular **3**; C: chloroform; s: satellite signals.

SCHEME 4. A Plausible Scheme of the Whole Equilibrium for 3 Involving the Self-Association/Dissociation and the Tautomerism



similar shape to that of **7** in $CDCl_3/CD_3OD$ without broadening (Figure 6C). This finding indicates that the hydrogen bonding self-association of **7** is collapsed by overwhelming competition by bulk CD_3OD molecules.[6d] For the longer oligomers **9** and **11**, broadening becomes more significant as does the anisotropic effect (Figure 7). The addition of CD_3OD suppressed the broadening and anisotropy as in the case of **7**. Unfortunately, quantitative evaluation for the self-association in $CDCl_3$ has not been achieved for **5**−**11** because no meaningful change has been observed in the shapes of the ^{1}H NMR spectra in the attempts of the dilution experiment under similar conditions to the experiment for **3** (Figure 4). Anyway, the observed broadening is caused by hydrogen bonding self-association of the oligomers, and the anisotropy indicates that the association is accompanied by π-interaction.

When UV−vis spectra were compared for **3**, **5**, **7**, **9**, and **11**, the absorptive band spreads to longer wavelengths as the length of the oligomer increases (Figure 8A). Our previous *meta*-ethynylpyridine oligomers lacking pyridone moieties did not

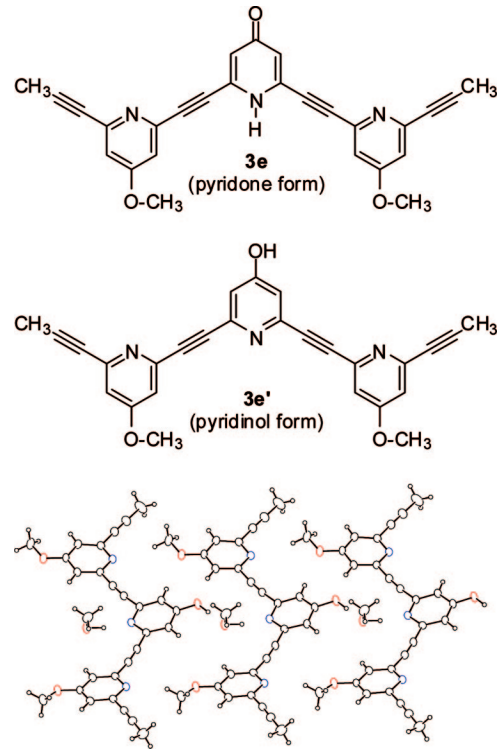


FIGURE 5. Tautomers of model 3-mer **3e** and **3e′**, and the top view of the X-ray structure of the layer consisting of **3e′** and methanol linked by hydrogen bonding.

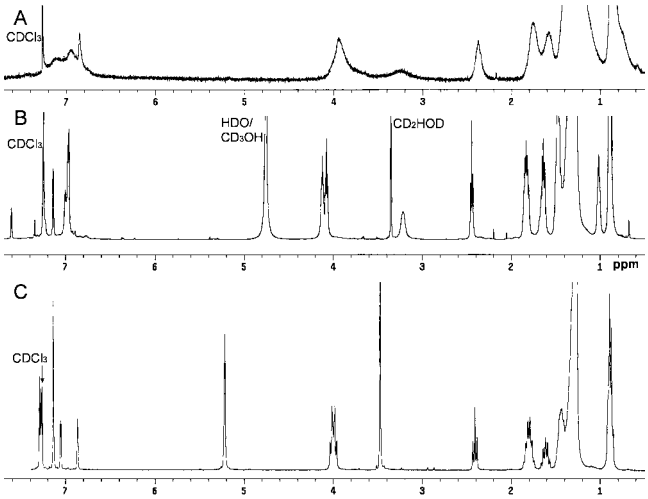


FIGURE 6. ^{1}H NMR (300 MHz) spectra for (A) **7** (ca. 1×10^{-4} M) in $CDCl_3$ after deprotection, (B) **7** (ca. 2×10^{-3} M) in $CDCl_3/CD_3OD$ (1:1), and (C) **7-MOM** (ca. 6×10^{-4} M) in $CDCl_3$, at 22 °C.

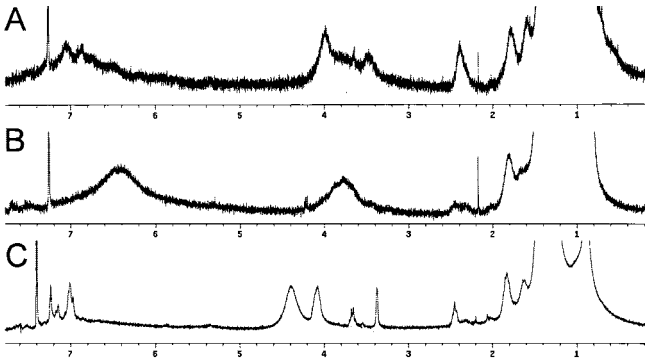


FIGURE 7. ^{1}H NMR (300 MHz) spectra for (A) **9** (ca. 5×10^{-5} M), (B) **11** (ca. 3×10^{-5} M) in $CDCl_3$, and (C) **11** (ca. 1×10^{-4} M) in $CDCl_3/CD_3OD$ = 5:1, at 22 °C.

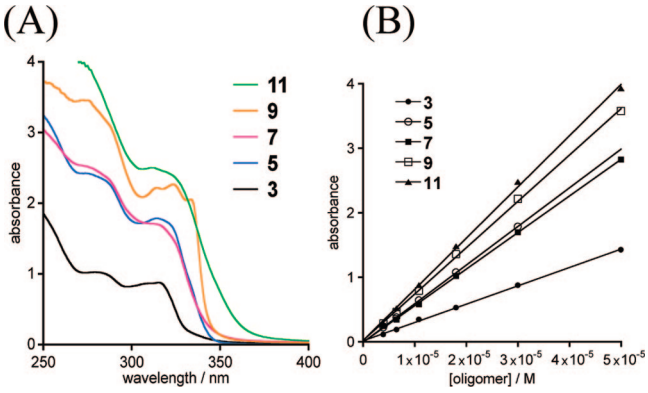
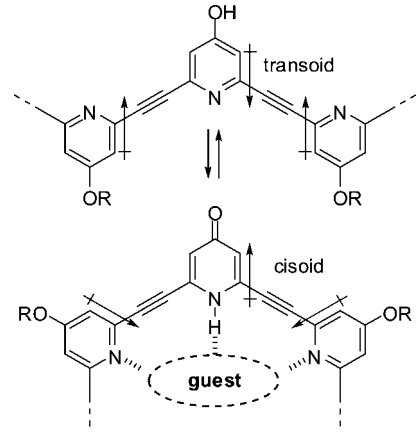


FIGURE 8. (A) UV−vis spectra for oligomers **3**−**11**. Conditions: oligomer (3.0×10^{-5} M), CH_2Cl_2, 25 °C, path length = 10 mm. (B) Beer's plots for absorbances at 315 nm for **3**−**11**. Conditions: oligomer, CH_2Cl_2, 25 °C, path length = 10 mm.

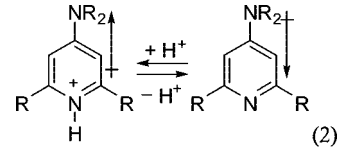
show such spreading.[6d] Therefore, the spreading observed here could be attributed to the strong self-association character of the pyridine−pyridone oligomers. The relationship between the concentration and absorbance was found to obey Beer's law (Figure 8B), suggesting that the oligomers ≥5-mer make a tight self-dimer which are stable at the examined concentration range.

SCHEME 5. Guest Recognition by Cisoid Conformation of a Pyridine−Pyridone−Pyridine Sequence



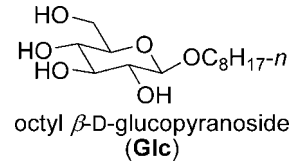
On the other hand, for **3**, the linearity in Figure 8B agrees with the results of the NMR experiment, which indicates that **3** exists in a monomolecular state at the examined concentration range for this UV measurement.

Glucoside Recognition of the Pyridine−Pyridone Oligomers. We previously reported[6c] that the half-protonation of the strong basic polymer **II** (Figure 1) enhanced its binding ability to saccharides. The change from pyridine to pyridinium form in that polymer causes the inversion of the local dipole moment



(2)

(eq 2); therefore, the adjacent pyridine−pyridinium sequence prefers a cisoid conformation and a helical higher-order structure is stabilized. Similarly, the pyridone rings in **3**−**11** are also expected to have an inverse dipole moment to stabilize the cisoid conformation and helical conformation, and the helix form has an advantage in the recognition of a guest molecule (Scheme 5). Thus, CD titration experiments in CH_2Cl_2 were performed to examine the additive effect of octyl β-D-glucopyranoside (**Glc**) on oligomers **3**−**11**.



octyl β-D-glucopyranoside (**Glc**)

When the 3-mer **3** was titrated with **Glc**, no meaningful induced CD (ICD) was observed even with the addition of an excess amount of **Glc** (Figure 9A). This observation would indicate that the oligomer length of **3** is too short to make a helical complex with **Glc**. On the other hand, the longer oligomers **5**−**11** displayed remarkable ICD bands by the addition of **Glc** (Figure 9B−E). When the 5-mer **5** (2.1×10^{-5} M) in CH_2Cl_2 was titrated with **Glc** up to 2.1×10^{-3} M (100 equiv), characteristic ICD appeared and increased at the absorptive wavelength region of **5**, as shown in Figure 9B. Because the glucoside has no absorption at that region and **5** is achiral by itself, the observed ICD must be caused by the induced chirality on the structure of **5** complexing with **Glc**.

The titration curve between the observed ellipticity and the concentration of **Glc** is shown in Figure S2. In a curve-fitting analysis, a well-fitted theoretical curve could be drawn on the basis of assumption of 1:1 complexation, and an apparent association constant was obtained as $K_a' = (1.4 \pm 0.2) \times 10^3$ M^{-1} ([**5**] $= 2.1 \times 10^{-5}$ M). On the other hand, as mentioned above, **5** proved to self-associate tightly at the concentration in this titration experiment. The strong self-association obscures the exact quantitative information, including the composition of the CD-active complex and the self-dimer of **5**, and the corresponding association constants. Nevertheless, the appearance of ICD indeed demonstrated that self-dimerized **5** changes into a 1:1 helical complex by saccharide recognition.

Also for the longer oligomers **7**, **9**, and **11**, similar CD titration experiments were performed (Figure 9C−E). In all the cases, strong ICD bands were observed around 335 nm, and apparent association constants K'_a for **7**, **9**, and **11** with **Glc** are $(1.2 \pm 0.1) \times 10^3$ M^{-1} ([**7**] $= 2.1 \times 10^{-5}$ M), $(2.3 \pm 0.2) \times 10^3$ M^{-1} ([**9**] $= 2.1 \times 10^{-5}$ M), and $(3.2 \pm 0.4) \times 10^3$ M^{-1} ([**11**] $= 2.1 \times 10^{-4}$ M), respectively, under the applied conditions. It should be pointed out that the shapes of the ICDs in Figure 9B−E resemble each other and also resemble those in the cases of poly(*meta*-ethynylpyridine)s with **Glc** as previously reported.[6] This resemblance may reflect that both the pyridine−pyridone oligomers and pyridine polymers build complexes with **Glc** in similar CD-active helical forms. Also, it was demonstrated that the glucoside recognition by **3** induced dynamic transformation interchanging between two types of higher-order structures, the self-associated dimer and the helical host−guest complex, by multiple hydrogen bonding.

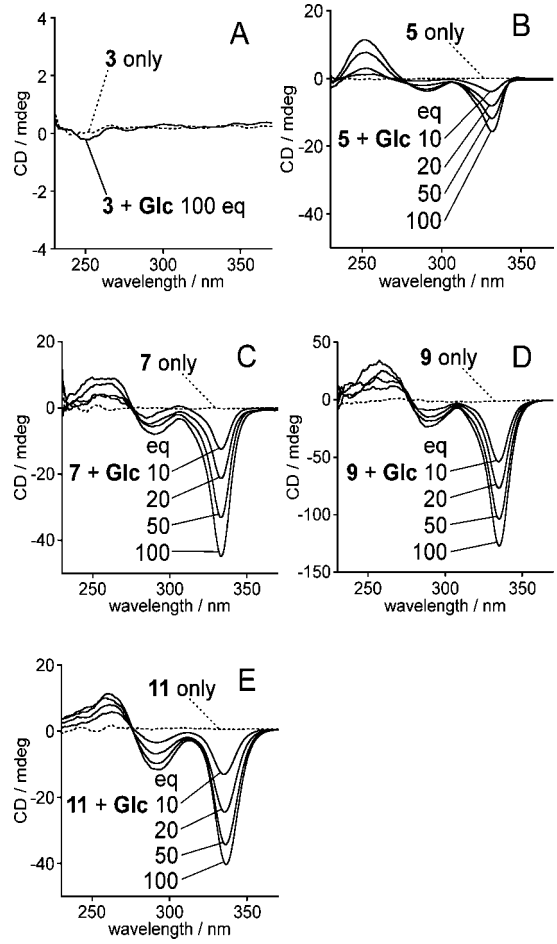


FIGURE 9. Changes of CD at the titration experiments on oligomers (A) **3**, (B) **5**, (C) **7**, (D) **9**, and (E) **11** by octyl β-D-glucopyranoside (**Glc**). Conditions: (A−D) oligomer (2.1×10^{-5} M), CH_2Cl_2, 25 °C, path length = 10 mm, (E) **11** (2.1×10^{-4} M), CH_2Cl_2, 25 °C, path length = 1 mm.

Conclusion

In summary, pyridine−pyridone alternate co-oligomers of various lengths were prepared by repeating the Sonogashira reaction. VPO and ^{1}H NMR analyses for the 3-mer **3** in chloroform quantitatively demonstrated its self-dimerization by hydrogen bonding. The longer oligomers **5**−**11** also indicated formation of a self-associated complex strongly, showing broadening and anisotropy in ^{1}H NMR. The self-associated dimer of the oligomers changed into the single helical complex by glucoside recognition, displaying characteristic induced CD. Though the length of the pyridone-containing oligomers is much shorter than that of our previous pyridine polymers, the oligomers showed good ability for glucoside recognition. We are now planning to slot pyridone units into our *meta*-ethynylpyridine polymers in hand so that the longer polymers may form inter- and intramolecular duplexes which exhibit more dynamic transformation by the detection of saccharide.

Experimental Section

General. NMR spectra were recorded using tetramethylsilane (TMS) as an internal reference. Melting points were uncorrected. THF was freshly distilled from sodium benzophenone ketyl before use, and other solvents were purified with standard methods. All of the starting materials were commercially available. 2,6-Dibromopyridine (**1a**) was purchased from TCI and used without further purification. (1*H*)-2,6-Dibromo-4-pyridone (**1b**)[20] and 2,6-dibromo-4-(methoxymethoxy)pyridine (**1f**)[10c] were prepared by the procedures in the literature.

(20) Compound **1b** is tautomerizable with 2,6-dibromo-4-pyridinol. Reference 6b describes the preparation of it.

1*H*-2,6-Diiodo-4-pyridone (1c). This compound was prepared by a modification of the published procedure by Suzuki and Inouye et al.[18] A mixture of **1b** (5 g, 19.9 mmol), CuI (87 g, 0.46 mol), and KI (179 g, 1.07 mol) in DMF (440 mL) was stirred for 24 h at 130 °C. The resulting brown mixture was concentrated in vacuo, diluted with benzene, and filtered. The precipitate was further extracted with benzene by a Soxhlet extractor, and the extract was combined with the filtrate. The combined benzene extract was evaporated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:9) to afford **1c** (5.42 g, 79%) as a brown solid: mp 214 °C (dec); IR (KBr) 2200−3200 (strong br), 1577, 1552, 1532 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.22 (s, 2 H), 11.42 (s, 1 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 117.4, 121.7, 164.4; ESI-HRMS *m*/*z* calcd for $C_5H_4I_2NO$ ($M + H^+$) 347.8382; found 347.8376.

2,6-Dibromo-4-octoxypyridine (1d). To a suspension of K_2CO_3 (44.7 g, 324 mmol) in acetone (150 mL) were added **1b** (16.7 g, 63.5 mmol) and 1-iodooctane (18.7 g, 77.7 mmol) subsequently. The mixture was refluxed for 11 h and evaporated. The resulting residue was extracted with hexane, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:48) to afford **1d** (5.1 g, 99%) as a colorless oil: IR (neat) 2926, 2855, 1574, 1536 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.9 Hz, 3 H), 1.29−1.45 (m, 10 H), 1.75 (m, 2 H), 3.99 (t, J = 6.6 Hz, 2 H), 6.96 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.8, 28.7,

29.2, 31.8, 69.2, 113.7, 140.9, 166.9; ESI-HRMS *m/z* calcd for $C_{13}H_{20}Br_2NO$ (M + H$^+$) 363.9912; found 363.9903.

2,6-Diiodo-4-octoxypyridine (1e). This compound was prepared by a modification of the published procedure by Klapars and Buchwald.[19] A mixture of **1d** (7.94 g, 21.7 mmol), CuI (207 mg, 1.09 mmol, 5.0 mol %), NaI (16.3 g, 109 mmol), diglyme (12 mL), *o*-xylene (28 mL), and 1,3-diaminopropane (161 mg, 0.10 mmol, 10 mol %) was stirred at 110 °C for 14 h under a N_2 atmosphere. The resulting suspension was allowed to reach room temperature, then water (15 mL) was added. The resulting mixture was extracted with AcOEt (3 × 15 mL), and the combined organics were washed with water followed by brine, dried over $MgSO_4$, and concentrated. The crude product was purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:49) to afford **1e** (9.27 g, 93%) as colorless plates: mp 111−113 °C (dec); IR (KBr) 2925, 2854, 1560, 1522 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.9 Hz, 3 H), 1.26−1.41 (m, 10 H), 1.76 (m, 2 H), 3.94 (t, J = 6.6 Hz, 2 H), 7.21 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.8, 28.7, 29.2, 31.8, 68.8, 115. 7, 121.1, 164.8; ESI-HRMS *m/z* calcd for $C_{13}H_{20}I_2NO$ (M + H$^+$) 459.9634; found 459.9651.

2,6-Diiodo-4-(methoxymethoxy)pyridine (1g). To a THF (2 mL) suspension of NaH (216 mg, 5.40 mmol; commercial 60% dispersion was washed thoroughly with hexane prior to use) was added a THF (4 mL) solution of **1c** (1.56 g, 4.50 mmol) dropwise at 0 °C. After stirring at that temperature for 30 min, to the solution was added chloromethyl methyl ether (441 mg, 5.40 mmol) dropwise at the same temperature. The reaction mixture was stirred at room temperature for an additional 24 h. The reaction mixture was filtered, and the filtrate was evaporated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:9) to give **1g** (1.71 g, 97%) as a colorless solid: mp 81−85 °C; IR (KBr) 2985, 2912, 1560, 1529 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.46 (s, 3 H), 5.16 (s, 2 H), 7.36 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 56.8, 94.1, 115.7, 122.2, 162.9; ESI-HRMS *m/z* calcd for $C_7H_8INO_2$ (M + H$^+$) 391.8644; found 391.8659.

2,6-Bis(3-hydroxy-3-methyl-1-butynyl)-4-octoxypyridine (1h). To an Et_2NH (130 mL) suspension of $PdCl_2(PPh_3)_2$ (740 mg, 1.06 mmol) and CuI (101 mg, 0.53 mmol) were added **1d** (9.70 g, 26.6 mmol) and 2-methyl-3-butyn-2-ol (4.90 g, 58.5 mmol) subsequently. The mixture was stirred for 3 h at room temperature and evaporated. The evaporated residue was diluted with ether, and the insoluble salts were filtered off. The filtrate was concentrated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:1) to afford **1h** (9.67 g, 98%) as a yellow solid: mp 90−91 °C; IR (KBr) 3402, 3295 (br), 2927, 2854, 2231, 1580, 1554 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.8 Hz, 3 H), 1.23−1.40 (m, 10 H), 1.62 (s, 12 H), 1.65−1.79 (m, 2 H), 3.97 (t, J = 6.5 Hz, 2 H), 4.1 (br s, 2 H), 6.84 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.9, 28.8, 29.21, 29.24, 31.1, 31.8, 65.0, 68.4, 80.9, 94.5, 112.9, 143.9, 165.1; ESI-HRMS *m/z* calcd for $C_{23}H_{34}NO_3$ (M + H$^+$) 372.2539; found 372.2535.

2,6-Bis(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)pyridine (1i). To an Et_2NH (20 mL) suspension of $PdCl_2(PPh_3)_2$ (110 mg, 0.157 mmol) and CuI (15 mg, 0.00783 mmol) were added **1f** (1.16 g, 3.91 mmol) and 2-methyl-3-butyn-2-ol (0.724 g, 8.61 mmol) subsequently. The mixture was stirred for 18 h at room temperature and evaporated. The evaporated residue was diluted with ether, and the insoluble salts were filtered off. The filtrate was concentrated, and the crude product was purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:1) to afford **1i** (1.01 g, 85%) as a yellow solid: mp 87−88 °C; IR (KBr) 3410, 3367 (br), 2985, 2932, 2229, 1579, 1557 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.62 (s, 12 H), 3.46 (s, 3 H), 4.03 (br s, 2 H), 5.20 (s, 2 H), 6.99 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 31.1, 56.6, 65.0, 80.7, 93.8, 94.7, 114.2, 144.0, 163.3; ESI-HRMS *m/z* calcd for $C_{17}H_{22}NO_4$ (M + H$^+$) 304.1549; found 304.1536.

2,6-Diethynyl-4-octoxypyridine (1j). To a NaH (23 mg, 0.578 mmol; commercial 60% dispersion was washed thoroughly with hexane prior to use) suspension in toluene (40 mL) was added **1h** (2.14 g, 5.77 mmol). The mixture was refluxed for 30 min and evaporated. The evaporated residue was purified by silica gel column chromatography (eluent: CH_2Cl_2) to afford **1j** (0.917 g, 62%) as a brownish solid: mp 81−83 °C; IR (neat) 3283, 3169, 2927, 2851, 1583, 1552 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.7 Hz, 3 H), 1.24−1.46 (m, 10 H), 1.74−1.83 (m, 2 H), 3.10 (s, 2 H), 4.00 (t, J = 6.5 Hz, 2 H), 6.97 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.9, 28.8, 29.2, 29.3, 31.8, 68.5, 77.1, 82.2, 114.0, 143.5, 165.1; ESI-HRMS *m/z* calcd for $C_{17}H_{22}NO$ (M + H$^+$) 256.1701; found 256.1702.

2,6-Diethynyl-4-(methoxymethoxy)pyridine (1k). To a pulverized NaOH (342 mg, 8.54 mmol) suspension in toluene (15 mL) was added **1i** (259 mg, 0.854 mmol). The mixture was stirred at 80 °C for 1 h, filtrated, and evaporated. The evaporated residue was purified by silica gel column chromatography (eluent: AcOEt/hexane = 3:17) to afford **1k** (104 mg, 65%) as a brownish solid: mp 83−85 °C; IR (neat) 3286, 3186, 2966, 2921, 2107, 1586, 1552 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.13 (s, 2 H), 3.47 (s, 3 H), 5.23 (s, 2 H), 7.12 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 56.6, 82.0, 93.9, 115.1, 143.6, 163.3; ESI-HRMS *m/z* calcd for $C_{11}H_{10}NO_2$ (M + H$^+$) 188.0712; found 188.0710.

2-Bromo-6-(3-hydroxy-3-methyl-1-butynyl)-4-octoxypyridine (1l). To an Et_2NH (100 mL) suspension of $PdCl_2(PPh_3)_2$ (317 mg, 0.452 mmol) and CuI (43 mg, 0.226 mmol) were added **1d** (20.6 g, 56.6 mmol) and 2-methyl-3-butyn-2-ol (0.960 g, 11.3 mmol) subsequently. The mixture was stirred for 3 h at room temperature and evaporated. The evaporated residue was diluted with ether, the insoluble salts were filtered off. The filtrate was concentrated, and the crude product was subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:49) to recover **1d** (16.5 g, 80% recovery) and (AcOEt/hexane = 1:4) to afford **1l** (3.64 g, 87%) as a yellow oil: IR (neat) 3375 (br), 2927, 2856, 2233, 1581, 1540 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3 H), 1.29−1.43 (m, 10 H), 1.61 (s, 6 H), 1.73−1.82 (m, 2 H), 2.46 (br s, 1H), 3.98 (t, J = 6.6 Hz, 2 H), 6.89 (m, 1 H), 6.93 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.8, 28.7, 29.2, 31.1, 31.8, 65.4, 68.8, 80.4, 94.5, 113.4, 113.6, 142.2, 143.6, 166.0; ESI-HRMS *m/z* calcd for $C_{18}H_{27}BrNO_2$ (M + H$^+$) 368.1225; found 368.1240.

2-(3-Hydroxy-3-methyl-1-butynyl)-6-iodo-4-octoxypyridine (1m). To an *i*-Pr_2NH (70 mL) suspension of $PdCl_2(PPh_3)_2$ (198 mg, 0.283 mmol) and CuI (27 mg, 0.141 mmol) were added **1e** (16.2 g, 35.3 mmol) and 2-methyl-3-butyn-2-ol (0.594 g, 7.07 mmol) subsequently. The mixture was stirred for 10 h at room temperature and evaporated. The evaporated residue was diluted with ether, and the insoluble salts were filtered off. The filtrate was concentrated and subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:49) to recover **1e** (13.0 g, 80% recovery) and (AcOEt/hexane = 3:17) to afford **1m** (2.93 g, 100%) as a yellow oil: IR (neat) 3366 (br), 2926, 2855, 2234, 1573, 1535 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3 H), 1.29−1.44 (m, 10 H), 1.61 (s, 6 H), 1.72−1.81 (m, 2 H), 2.58 (br s, 1H), 3.96 (t, J = 6.5 Hz, 2 H), 6.90 (m, 1 H), 7.18 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.8, 28.8, 29.2, 31.1, 31.8, 65.4, 68.6, 80.5, 94.6, 113.8, 117.4, 120.6, 143.9, 164.8; ESI-HRMS *m/z* calcd for $C_{18}H_{27}INO_2$ (M + H$^+$) 416.1086; found 416.1075.

2-(3-Hydroxy-3-methyl-1-butynyl)-6-iodo-4-(methoxymethoxy)-pyridine (1n). To an *i*-Pr_2NH (100 mL) and THF (25 mL) suspension of $Pd_2(dba)_3 \cdot CHCl_3$ (203 mg, 0.196 mmol), (*o*-Tol)$_3$P (239 mg, 0.785 mmol), and CuI (37 mg, 0.196 mmol) were added **1g** (19.2 g, 49.1 mmol) and 2-methyl-3-butyn-2-ol (825 mg, 9.81 mmol) subsequently. The mixture was stirred for 4 h at room temperature and evaporated. The evaporated residue was diluted with ether, and the insoluble salts were filtered off. The filtrate was concentrated and subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:19) to recover **1g** (15.6 g, 80% recovery) and (AcOEt/hexane = 7:13) to afford **1n** (3.41 g, 100%) as a yellow oil: IR (neat) 3375 (br), 2981, 2933, 2234, 1574, 1538 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.61 (s, 6 H), 2.22 (br, 1 H), 3.47 (s, 3 H), 5.19 (s, 2 H), 7.04 (d, J = 2.1 Hz, 1 H), 7.34 (d, J = 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 31.1, 56.7, 65.4, 80.3, 93.9, 94.9, 114.8, 117.2, 122.0, 144.1, 162.9; ESI-HRMS *m/z* calcd for $C_{12}H_{15}INO_3$ (M + H$^+$) 348.0097; found 348.0109.

2-(1-Dodecynyl)-6-(3-hydroxy-3-methyl-1-butynyl)-4-octoxypyridine (1o-pre). To an Et_2NH (100 mL) suspension of $PdCl_2(PPh_3)_2$

(442 mg, 0.629 mmol) and CuI (60 mg, 0.315 mmol) were added **1l** (5.74 g, 15.7 mmol) and 1-dodecyne (3.14 g, 18.9 mmol) subsequently. The mixture was stirred for 2.5 h at room temperature and evaporated. The evaporated residue was diluted with ether, and the insoluble salts were filtered off. The filtrate was concentrated and subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:9) to afford **1o-pre** (7.13 g, 100%) as a brownish oil: IR (neat) 3357 (br), 2925, 2855, 2231, 1582, 1554 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.91 (m, 6 H), 1.27−1.42 (m, 24 H), 1.55−1.65 (m, 8 H), 1.73−1.82 (m, 2 H), 1.89 (br s, 1 H), 2.39 (t, J = 7.2 Hz, 2 H), 3.97 (t, J = 6.5 Hz, 2 H), 6.82 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.16, 14.19, 19.4, 22.70, 22.73, 25.9, 28.3, 28.8, 29.1, 29.19, 29.22, 29.3, 29.4, 29.55, 29.63, 31.2, 31.8, 31.9, 65.4, 68.3, 80.0, 81.4, 91.1, 93.1, 112.5, 112.8, 143.8, 145.0, 165.00; ESI-HRMS *m*/*z* calcd for $C_{30}H_{48}NO_2$ (M + H^+) 454.3685; found 454.3672.

2-(1-Dodecynyl)-6-ethynyl-4-octoxypyridine (1o). To a pulverized NaOH (414 mg, 10.4 mmol) suspension in toluene (15 mL) was added **1o-pre** (940 mg, 2.07 mmol). The mixture was stirred at 80 °C for 30 min and evaporated. The evaporated residue was subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:9) to afford **1o** (683 mg, 83%) as a brownish oil: IR (neat) 3309, 2925, 2854, 2236, 2108, 1579 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.91 (m, 6 H), 1.27−1.45 (m, 24 H), 1.55−1.65 (m, 2 H), 1.73−1.82 (m, 2 H), 2.40 (t, J = 7.1 Hz, 2 H), 3.06 (s, 1 H), 3.98 (t, J = 6.5 Hz, 2 H), 6.86 (d, J = 2.5 Hz, 1 H), 6.90 (d, J = 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.18, 14.21, 19.4, 22.7, 22.8, 25.9, 28.3, 28.8, 29.1, 29.2, 29.3, 29.4, 29.55, 29.64, 31.8, 31.9, 68.3, 79.9, 82.5, 91.2, 113.0, 113.1, 143.1, 145.2, 165.0; ESI-HRMS *m*/*z* calcd for $C_{27}H_{42}NO$ (M + H^+) 396.3266; found 396.3250.

2-(6-Dodecynyl-4-octoxy-2-pyridyl)-6-(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)pyridine (2a-pre). To an *i*-Pr_2NH (20 mL) suspension of $Pd(PPh_3)_4$ (107 mg, 0.0926 mmol) and CuI (9.0 mg, 0.0463 mmol) were added **1n** (804 mg, 2.32 mmol) and **1o** (1.01 g, 2.548 mmol) subsequently. The mixture was stirred for 17 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 3:7) to afford **2a-pre** (879 mg, 100%) as a brownish solid: mp 74−77 °C; IR (KBr) 3378, 3271 (br), 2923, 2854, 2239, 1585, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.92 (m, 6 H), 1.27−1.44 (m, 24 H), 1.63 (m, 8 H), 1.74−1.83 (m, 2 H), 2.41 (t, J = 7.1 Hz, 2 H), 2.48 (br s, 1H), 3.47 (s, 3 H), 3.99 (t, J = 6.6 Hz, 2 H), 5.22 (s, 2 H), 6.88 (d, J = 2.6 Hz, 1 H), 7.06 (m, 2 H), 7.23 (d, J = 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.70, 22.73, 25.9, 28.3, 28.8, 29.0, 29.19, 29.22, 29.3, 29.4, 29.5, 29.6, 31.1, 31.2, 31.8, 31.9, 56.6, 65.4, 68.4, 79.8, 81.1, 86.7, 87.8, 91.3, 93.8, 93.9, 113.1, 113.6, 114.7, 115.2, 143.3, 143.8, 144.3, 145.1, 163.3, 165.0; ESI-HRMS *m*/*z* calcd for $C_{39}H_{55}N_2O_4$ (M + H^+) 615.4162; found 615.4134.

2-(6-Dodecynyl-4-octoxy-2-pyridyl)-6-ethynyl-4-(methoxymethoxy)-pyridine (2a). To a pulverized NaOH (133 mg, 3.32 mmol) suspension in toluene (7 mL) was added **2a-pre** (408 mg, 0.664 mmol). The mixture was stirred at 85 °C for 30 min and evaporated. The evaporated residue was subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:4) to afford **2a** (370 mg, 100%) as a brownish oil: IR (neat) 3306, 2925, 2854, 2232, 2108, 1582, 1551 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85−0.92 (m, 6 H), 1.24−1.41 (m, 24 H), 1.57−1.66 (m, 2 H), 1.74−1.83 (m, 2 H), 2.41 (t, J = 7.1 Hz, 2 H), 3.14 (s, 1 H), 3.47 (s, 3 H), 3.99 (t, J = 6.5 Hz, 2 H), 5.22 (s, 2 H), 6.88 (d, J = 2.2 Hz, 1 H), 7.06 (d, J = 2.2 Hz, 1 H), 7.12 (d, J = 2.2 Hz, 1 H), 7.28 (d, J = 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.70, 22.73, 25.9, 28.3, 28.8, 29.0, 29.19, 29.22, 29.3, 29.4, 29.5, 29.6, 31.8, 31.9, 56.6, 68.4, 77.3, 79.9, 82.1, 86.6, 87.8, 91.2, 93.9, 113.1, 113.7, 115.3, 115.4, 143.3, 143.6, 144.0, 145.1, 163.3, 165.0; ESI-HRMS *m*/*z* calcd for $C_{36}H_{49}N_2O_3$ (M + H^+) 557.3743; found 557.3730.

2,6-Bis(6-iodo-4-(methoxymethoxy)pyridylethynyl)-4-octoxypyridine (3a). To an *i*-Pr_2NH (60 mL) and THF (50 mL) suspension of $Pd(PPh_3)_4$ (291 mg, 0.252 mmol) and CuI (48 mg, 0.126 mmol) were added **1g** (23.8 g, 60.9 mmol) and **1j** (1.61 g, 6.31 mmol) subsequently. The mixture was stirred for 3.5 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and subjected to silica gel column chromatography (eluent: CH_2Cl_2/hexane = 3:7) to recover **1g** (19.3 g, 81% recovery) and (AcOEt/hexane = 3:1) to afford **3a** (4.93 g, 100% based on **1j**) as a brownish solid: mp 141−142 °C; IR (KBr) 2924, 2853, 1580, 1533 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, J = 6.7 Hz, 3 H), 1.31−1.46 (m, 10 H), 1.77−1.86 (m, 2 H), 3.47 (s, 6 H), 4.02 (t, J = 6.6 Hz, 2 H), 5.20 (s, 4 H), 7.14 (s, 2 H), 7.27 (m, 2 H), 7.39 (d, J = 2.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.9, 28.7, 29.2, 31.8, 56.7, 68.8, 86.4, 88.2, 94.3, 114.6, 115.7, 117.5, 122.4, 143.5, 143.6, 163.0, 165.1; ESI-HRMS *m*/*z* calcd for $C_{31}H_{34}I_2N_3O_5$ (M + H^+) 782.0588; found 782.0602.

2,6-Bis(6-iodo-4-octoxypyridylethynyl)-4-(methoxymethoxy)pyridine (3b). To an *i*-Pr_2NH (50 mL) and THF (50 mL) suspension of $Pd_2(dba)_3 \cdot CHCl_3$ (187 mg, 0.183 mmol), (*o*-Tol)$_3$P (220 mg, 0.721 mmol), and CuI (69 mg, 0.361 mmol) were added **1e** (24.8 g, 54.1 mmol) and **1k** (1.67 g, 9.02 mmol) subsequently. The mixture was stirred for 7 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and subjected to silica gel column chromatography (eluent: CH_2Cl_2/hexane = 1:4) to recover **1e** (17.7 g, 71% recovery) and (AcOEt/hexane = 1:4) to afford **3b** (3.9 g, 52% based on **1k**) as a brownish oil: IR (neat) 2925, 2855, 1575, 1538 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 6 H), 1.29−1.43 (m, 20 H), 1.74−1.81 (m, 4 H), 3.49 (s, 3 H), 3.98 (t, J = 6.6 Hz, 4 H), 5.24 (s, 2 H), 7.11 (d, J = 2.1 Hz, 2 H), 7.24 (d, J = 2.1 Hz, 2 H), 7.28 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.6, 25.7, 28.6, 29.1, 31.7, 56.6, 68.7, 68.9, 86.7, 87.7, 94.0, 114.3, 115.7, 117.5, 121.3, 143.2, 143. 6, 163.3, 164.7; ESI-HRMS *m*/*z* calcd for $C_{37}H_{46}I_2N_3O_4$ (M + H^+) 850.1578; found 850.1617.

2-(6-(1-Dodecynyl)-4-octoxy-2-pyridynylethynyl)-6-(6-(3-hydroxy-3-methyl-1-butynyl)-4-octoxy-2-pyridynylethynyl)-4-(methoxymethoxy)pyridine (3c-pre). To an *i*-Pr_2NH (25 mL) suspension of $Pd(PPh_3)_4$ (83 mg, 0.0718 mmol) and CuI (6.8 mg, 0.0359 mmol) were added **1m** (746 mg, 1.80 mmol) and **2a** (1.10 g, 1.98 mmol) subsequently. The mixture was stirred for 5 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and subjected to silica gel column chromatography (eluent: AcOEt/hexane = 1:2) to afford **3c-pre** (1.38 g, 87%) as a brownish oil: IR (neat) 3337, 2925, 2855, 2232, 1582, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.92 (m, 9 H), 1.27−1.44 (m, 34 H), 1.57−1.63 (m, 8 H), 1.75−1.82 (m, 4 H), 2.42 (t, J = 6.5 Hz, 2 H), 2.56 (br s, 1 H), 3.48 (s, 3 H), 4.00 (t, J = 6.5 Hz, 4 H), 5.23 (s, 2 H), 6.88 (d, J = 2.5 Hz, 1 H), 6.93 (d, J = 2.2 Hz, 1 H), 7.07 (d, J = 2.5 Hz, 1 H), 7.10 (d, J = 2.5 Hz, 1 H), 7.28 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.69, 22.72, 25.9, 28.3, 28.8, 29.0, 29.21, 29.24, 29.4, 29.5, 29.6, 31.2, 31.8, 31.9, 56.6, 65.3, 68.4, 68.6, 79.9, 81.1, 86.6, 87.1, 87.5, 87.8, 91.3, 93.7, 94.0, 113.1, 113.6, 113.7, 113.9, 115.6, 115.7, 143.3, 143.5, 143.8, 144.0, 144.2, 145.2, 163.4, 165.0, 165.1; ESI-HRMS *m*/*z* calcd for $C_{54}H_{74}N_3O_5$ (M + H^+) 844.5628; found 844.5597.

2-(6-(6-(1-Dodecynyl)-4-octoxy-2-pyridylethynyl)-4-(methoxymethoxy)-2-pyridylethynyl)-6-ethynyl-4-octoxypyridine (3c). To a pulverized NaOH (91 mg, 2.29 mmol) suspension in toluene (7 mL) was added **3c-pre** (386 mg, 0.457 mmol). The mixture was stirred at 100 °C for 15 min and evaporated. The evaporated residue was purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:3) to afford **3c** (104 mg, 85%) as a brownish solid: mp 28−30 °C; IR (KBr) 3307, 2926, 2854, 2232, 2108, 1581, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.92 (m, 9 H), 1.24−1.44 (m, 34 H), 1.57−1.67 (m, 2 H), 1.78−1.83 (m, 4 H), 2.42 (t, J = 7.1 Hz, 2 H), 3.13 (s, 1 H), 3.48 (s, 3 H), 4.00 (m, 4 H), 5.23 (s, 2 H), 6.89 (d, J = 2.2 Hz, 1 H), 7.00 (d, J = 2.5 Hz, 1 H), 7.07 (d, J = 2.5 Hz, 1 H), 7.14 (d, J = 2.5 Hz, 1 H), 7.28 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 14.4, 22.68, 22.73, 25.9, 28.3, 28.7, 28.8, 29.0, 29.2, 29.3, 29.4, 29.6, 31.8, 31.9, 56.6, 68.4, 68.6, 77.1, 79.9, 82.2, 86.6, 87.1, 87.4, 87.8, 91.3, 94.0, 113.1, 113.6, 113.9, 114.5, 115.6, 115.7, 143.3, 143.4, 143.7, 143.8, 144.0,

145.2, 163.4, 165.0, 165.1; ESI-HRMS *m/z* calcd for $C_{51}H_{68}N_3O_4$ ($M + H^+$) 786.5210; found 786.5184.

2-(6-(6-Iodo-4-(methoxymethoxy)-2-pyridylethynyl)-4-octoxy-2-pyridylethynyl)-6-(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)pyridine (3d). To an *i*-Pr_2NH (60 mL) and THF (40 mL) suspension of $Pd_2(dba)_3 \cdot CHCl_3$ (33.8 mg, 0.00327 mmol), (*o*-Tol)$_3$P (45 mg, 0.131 mmol), and CuI (6.2 mg, 0.00327 mmol) were added **3a** (6.38 g, 8.17 mmol) and 2-methyl-3-butyn-2-ol (137 mg, 1.63 mmol) subsequently. The mixture was stirred for 5 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and subjected to silica gel column chromatography (eluent: CH_2Cl_2/hexane = 1:1) to recover **3a** (4.95 g, 78% recovery) and (AcOEt/hexane = 2:3) to afford **3d** (589 mg, 87% based on 2-methyl-3-butyn-2-ol) as a brownish solid: mp 89−91 °C; IR (KBr) 3209 (br), 2927, 2855, 2229, 1582, 1535 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (m, 3 H), 1.26−1.46 (m, 10 H), 1.64 (s, 6 H), 1.79−1.86 (m, 2 H), 2.39 (br s, 1 H), 3.48 (s, 6 H), 4.02 (t, J = 6.6 Hz, 2 H), 5.20 (s, 2 H), 5.23 (s, 2 H), 7.08 (br s, 1 H), 7.14 (s, 2 H), 7.25 (br s, 1 H), 7.27 (br s, 1H), 7.39 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 25.9, 28.7, 29.2, 29.3, 31.1, 31.2, 31.8, 56.6, 56.7, 65.4, 68.8, 77.2, 81.0, 86.3, 87.2, 87.3, 88.3, 93.9, 94.0, 114.5, 114.6, 114.8, 115.2, 115.7, 117.5, 122.4, 143.5, 143.58, 143.61, 143.7, 144.3, 163.0, 163.3, 165.1; ESI-HRMS *m/z* calcd for $C_{36}H_{41}IN_3O_6$ ($M + H^+$) 738.2040; found 738.2011.

2,6-Bis(6-dodecynyl-4-octoxy-2-pyridylethynyl)-4-(methoxymethoxy)pyridine (3-MOM). To an *i*-Pr_2NH (15 mL) and THF (10 mL) suspension of $Pd_2(dba)_3 \cdot CHCl_3$ (30 mg, 0.0286 mmol), (*o*-Tol)$_3$P (35 mg, 0.1144 mmol), and CuI (5.0 mg, 0.0286 mmol) were added **3b** (1.21 g, 1.43 mmol) and 1-dodecyne (547 mg, 3.28 mmol) subsequently. The mixture was stirred for 8 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: AcOEt/hexane = 1:9) to afford **3-MOM** (1.14 g, 86%) as a brownish oil: IR (neat) 2925, 2854, 2233, 1580, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.92 (m, 12 H), 1.27−1.46 (m, 48 H), 1.57−1.67 (m, 4 H), 1.74−1.84 (m, 4 H), 2.39−2.44 (t, J = 7.0 Hz, 4 H), 3.48 (s, 3 H), 3.99 (t, J = 6.6 Hz, 4 H), 5.22 (s, 2 H), 6.88 (d, J = 2.5 Hz, 2 H), 7.07 (d, J = 2.2 Hz, 2 H), 7.27−7.28 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.16, 14.19, 19.4, 22.69, 22.73, 25.9, 28.3, 28.8, 29.0, 29.19, 29.22, 29.4, 29.4, 29.55, 29.63, 31.8, 31.9, 56.6, 68.4, 79.9, 86.7, 87.8, 91.3, 94.0, 113.1, 113.6, 115.6, 143.3, 144.0, 145.2, 145.3, 163.3, 165.0; ESI-HRMS *m/z* calcd for $C_{61}H_{88}N_3O_4$ ($M + H^+$) 926.6775; found 926.6738.

2,6-Bis(6-dodecynyl-4-octoxy-2-pyridylethynyl)-1*H*-4-pyridone (3). To **3-MOM** (810 mg, 0.874 mmol) in CH_2Cl_2 (10 mL) was added trifluoroacetic acid (7 mL). The mixture was stirred for 3 h and quenched by the addition of an aqueous $NaHCO_3$ solution. The mixture was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by HPLC (eluent: AcOEt/CH_2Cl_2 = 7:3) to afford **3** (772 mg, 91%) as a brownish oil: IR (neat) 2200−3200 (strong br), 2925, 2854, 2234, 1583, 1551 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, J = 6.5 Hz, 12 H), 1.24−1.39 (m, 48 H), 1.51−1.60 (m, 4 H), 1.73−1.79 (m, 4 H), 2.37 (t, J = 7.1 Hz, 4 H), 3.92−3.98 (m, 4 H), 6.86 (d, J = 2.4 Hz, 2 H), 6.97 (s, 2 H), 7.13 (br s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.06, 14.08, 19.3, 22.60, 22.64, 25.8, 28.2, 28.7, 28.9, 29.1, 29.15, 29.21, 29.3, 29.5, 29.6, 31.8, 31.9, 68.5, 79.3, 86.7 (br), 87.8 (br), 92.2, 113.1, 114.0, 116.8 (br), 143.2 (br), 144.8, 165.5, 165.8 (br); ESI-HRMS *m/z* calcd for $C_{59}H_{84}N_3O_3$ ($M + H^+$) 882.6513; found 882.6480.

2-(6-(6-(6-(1-Dodecynyl)-4-octoxy-2-pyridylethynyl)-4-(methoxymethoxy)-2-pyridylethynyl)-4-octoxy-2-pyridylethynyl)-6-(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)pyridine (4a-pre). To an *i*-Pr_2NH (50 mL) and THF (300 mL) suspension of $Pd(PPh_3)_4$ (219 mg, 0.189 mmol) and CuI (18 mg, 0.0946 mmol) were added **3d** (3.49 g, 4.73 mmol) and **1o** (2.81 g, 7.10 mmol) subsequently. The mixture was stirred for 6 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and subjected to silica gel column chromatography (eluent: AcOEt/hexane = 7:13) to afford **4a-pre** (4.34 g, 91%) as a brownish solid: mp 80−81 °C; IR (KBr) 3398 (br), 2925, 2854, 2232, 1538, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.92 (m, 9 H), 1.27−1.44 (m, 34 H), 1.57−1.64 (m, 8 H), 1.75−1.84 (m, 4 H), 2.40−2.46 (m, 3 H), 3.48 (s, 6 H), 4.01 (m, 4 H), 5.23 (s, 4 H), 6.89 (d, J = 2.5 Hz, 1 H), 7.07 (d, J = 2.2 Hz, 2 H), 7.14 (m, 2 H), 7.26 (d, J = 2.5 Hz, 1 H), 7.29 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.6, 22.7, 25.9, 28.3, 28.7, 28.8, 29.0, 29.21, 29.24, 29.4, 29.5, 29.6, 31.2, 31.8, 31.9, 56.6, 65.4, 68.4, 68.7, 79.9, 81.0, 86.6, 87.2, 87.3, 87.9, 91.3, 93.9, 94.0, 113.1, 113.6, 114.5, 114.8, 115.2, 115.6, 143.3, 143.6, 143.7, 143.8, 144.0, 144.3, 145.2, 163.3, 163.4, 165.0, 165.1; ESI-HRMS *m/z* calcd for $C_{63}H_{81}N_4O_7$ ($M + H^+$) 1005.6105; found 1005.6092.

2-(6-(6-(6-(1-Dodecynyl)-4-octoxy-2-pyridylethynyl)-4-(methoxymethoxy)-2-pyridylethynyl)-4-octoxy-2-pyridylethynyl)-6-(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)pyridine (4a). To a pulverized NaOH (135 mg, 3.38 mmol) suspension in toluene (7 mL) was added **4a-pre** (680 mg, 0.676 mmol). The mixture was stirred at 95 °C for 20 min and evaporated. The evaporated residue was subjected to silica gel column chromatography (eluent: AcOEt/hexane = 3:7) to afford **4a** (616 mg, 96%) as a brownish solid: mp 103−105 °C; IR (KBr) 3308, 2925, 2854, 2232, 2106, 1583, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.90 (m, 9 H), 1.27−1.46 (m, 34 H), 1.57−1.62 (m, 2 H), 1.75−1.84 (m, 4 H), 2.42 (t, J = 7.1 Hz, 2 H), 3.15 (s, 1 H), 3.48 (s, 6 H), 4.01 (m, 4 H), 5.23 (s, 4 H), 6.89 (d, J = 2.2 Hz, 1 H), 7.08 (d, J = 2.5 Hz, 1 H), 7.14 (m, 3 H), 7.30 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.7, 25.8, 28.3, 28.7, 28.8, 29.0, 29.2, 29.3, 29.5, 29.6, 31.8, 31.9, 56.6, 68.4, 68.7, 77.2, 79.8, 82.1, 86.6, 87.0, 87.1, 87.3, 87.8, 91.3, 93.9, 94.0, 113.1, 113.6, 114.5, 114.6, 115.4, 115.5, 115.6, 143.3, 143.60, 143.64, 143.76, 143.79, 144.0, 145.1, 163.3, 165.0, 165.1; ESI-HRMS *m/z* calcd for $C_{60}H_{75}N_4O_6$ ($M + H^+$) 947.5687; found 947.5718.

MOM-Protected 5-mer 5-MOM. To an *i*-Pr_2NH (15 mL) and THF (10 mL) suspension of $Pd(PPh_3)_4$ (42 mg, 0.0362 mmol) and CuI (1.7 mg, 0.00901 mmol) were added **3a** (354 mg, 0.453 mmol) and **1o** (394 mg, 0.996 mmol) subsequently. The mixture was stirred for 7 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: CH_2Cl_2) to afford **5-MOM** (548 mg, 92%) as a brownish solid: mp 101−103 °C; IR (KBr) 2925, 2853, 2233, 1583, 1550 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.90 (m, 15 H), 1.28−1.44 (m, 58 H), 1.57−1.67 (m, 4 H), 1.75−1.84 (m, 6 H), 2.42 (t, J = 7.0 Hz, 4 H), 3.49 (s, 6 H), 4.01 (m, 6 H), 5.23 (s, 4 H), 6.89 (d, J = 2.2 Hz, 2 H), 7.08 (d, J = 2.2 Hz, 2 H), 7.15 (s, 2 H), 7.28−7.31 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.69, 22.73, 25.9, 28.3, 28.7, 28.8, 29.0, 29.2, 29.3, 29.4, 29.5, 29.6, 31.8, 31.9, 56.6, 68.4, 68.7, 77.2, 79.9, 86.7, 87.2, 87.4, 87.9, 91.3, 94.0, 113.1, 113.6, 114.5, 115.65, 115.69, 143.3, 143.7, 143.8, 144.0, 145.2, 163.4, 165.0, 165.1; ESI-HRMS *m/z* calcd for $C_{91}H_{129}N_6O_7$ ($M +$ *i*-$Pr_2NH + H^+$) 1417.9923; found 1417.9886.

Pyridine−Pyridone 5-mer 5. To **5-MOM** (149 mg, 0.113 mmol) in CH_2Cl_2 (5 mL) was added trifluoroacetic acid (2 mL). The mixture was stirred for 2 h and quenched by the addition of an aqueous $NaHCO_3$ solution. The mixture was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (eluent: CH_2Cl_2/EtOH = 10:1) to afford **5** (139 mg, 100%) as a yellow solid: mp 81−83 °C; IR (KBr) 2200−3200 (strong br), 2925, 2854, 2233, 1584, 1550 cm^{-1}. ^1H NMR ($CD_3OD/CDCl_3$ = 2: 3, 300 MHz) δ 0.86−0.90 (m, 15 H), 1.19−1.47 (m, 58 H), 1.59−1.69 (m, 4 H), 1.78−1.85 (m, 6 H), 2.45 (t, J = 7.0 Hz, 4 H), 4.05−4.15 (m, 6 H), 6.97 (s, 6 H), 7.14 (d, J = 2.2 Hz, 2 H), 7.25 (s, 2 H); ^{13}C NMR ($CD_3OD/CDCl_3$ = 2: 3, 75 MHz) δ 19.5, 23.96, 22.99, 26.2, 28.6, 29.1, 29.3, 29.45, 29.53, 29.56, 29.64, 29.8, 29.9, 32.1, 32.2, 57.7, 69.1, 69.4, 79.6, 84.8 (br), 89.2 (br), 92.6, 114.16, 114.21, 115.4, 118.7 (br), 139.1 (br), 142.5, 143.3, 145.4, 166.0, 166.1, 171.3 (br); ESI-HRMS *m/z* calcd for $C_{81}H_{106}N_5O_5$ ($M + H^+$) 1228.8194; found 1228.8142.

MOM-Protected 7-mer 7-MOM. To an *i*-Pr_2NH (20 mL), DMF (10 mL), and THF (2 mL) suspension of $Pd(PPh_3)_4$ (50 mg, 0.0431 mmol) and CuI (2.0 mg, 0.0108 mmol) were added **3b** (458 mg, 0.539 mmol) and **2a** (660 mg, 1.19 mmol) subsequently. The mixture was stirred for 4 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: CH_2Cl_2) to afford **7-MOM** (548 mg, 62%) as a brownish solid: mp 156−158 °C; IR (KBr) 2925, 2854, 2233, 1583, 1549 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.90 (m, 18 H), 1.27−1.44 (m, 68 H), 1.57−1.67 (m, 4 H), 1.75−1.85 (m, 8 H), 2.42 (t, J = 7.1 Hz, 4 H), 3.49 (s, 9 H), 4.01 (m, 8 H), 5.24 (s, 6 H), 6.89 (d, J = 2.2 Hz, 2 H), 7.08 (d, J = 2.2 Hz, 2 H), 7.16 (s, 4 H), 7.30−7.32 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.67, 22.72, 25.9, 28.3, 28.7, 28.8, 29.0, 29.19, 29.24, 29.3, 29.5, 29.6, 31.8, 31.9, 56.6, 68.4, 68.7, 79.8, 86.6, 87.9, 87.2, 87.36, 87.42, 87.8, 91.3, 94.0, 113.1, 113.6, 114.5, 115.7, 143.3, 143.7, 143.76, 143.82, 144.0, 145.1, 163.4, 165. 0, 165.1; ESI-HRMS *m/z* calcd for $C_{109}H_{140}N_7O_{10}$ ($M + H^+$) 1707.0662; found 1707.0581.

Pyridine−Pyridone 7-mer 7. To **7-MOM** (103 mg, 0.0603 mmol) in CH_2Cl_2 (7 mL) was added trifluoroacetic acid (3 mL). The mixture was stirred for 1 h and quenched by the addition of an aqueous $NaHCO_3$ solution. The mixture was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purifed by GPC to afford **7** (95 mg, 86%) as a brownish solid: mp 141 °C (dec); IR (KBr) 2200−3200 (strong br) 2925, 2854, 2232, 1583, 1550 cm^{-1}; ^1H NMR ($CD_3OD/CDCl_3$ = 1: 1, 500 MHz) δ 0.87−0.96 (m, 18 H), 1.28−1.48 (m, 68 H), 1.61−1.67 (m, 4 H), 1.79−1.86 (m, 8 H), 2.43−2.46 (t, J = 7.1 Hz, 4 H), 4.06−4.13 (m, 8 H), 6.89−7.00 (m, 8 H), 7.14 (s, 2 H), 7.25 (s, 4 H); ^{13}C NMR ($CD_3OD/CDCl_3$ = 1: 1, 125 MHz) δ 14.2, 19.6, 23.07, 23.09, 26.3, 28.7, 29.2, 29.4, 29.6, 29.66, 29.71, 29.8, 29.96, 30.03, 32.3, 32.4, 57.3 (br), 69.3, 69.6, 82.7 (br), 89.0 (br), 92.8, 96.9 (br), 114.5, 115.6, 118.4 (br), 124.4 (br), 142.6 (br), 143.7 (br), 145.8, 146.2, 166.4, 166.5, 171.9 (br); ESI-HRMS *m/z* calcd for $C_{103}H_{128}N_7O_7$ ($M + H^+$) 1574.9875; found 1574.9932.

MOM-Protected 9-mer 9-MOM. To an *i*-Pr_2NH (10 mL) and THF (5 mL) suspension of $Pd(PPh_3)_4$ (11.4 mg, 0.00983 mmol) and CuI (1.0 mg, 0.00492 mmol) were added **3a** (77.3 mg, 0.0983 mmol) and **3c** (193 mg, 0.246 mmol) subsequently. The mixture was stirred for 6 h at room temperature, and the insoluble salts were filtered off. The filtrate was evaporated and purified by silica gel column chromatography (eluent: *i*-PrOH/CH_2Cl_2 = 1:400) to afford **9-MOM** (139 mg, 68%) as a brownish solid: mp 175−177 °C; IR (KBr) 2925, 2854, 2232, 1583, 1549 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86−0.90 (m, 21 H), 1.11−1.44 (m, 78 H), 1.57−1.67 (m, 4 H), 1.77−1.85 (m, 10 H), 2.42 (t, J = 7.1 Hz, 4 H), 3.49 (m, 12 H), 4.01 (m, 10 H), 5.24 (m, 8 H), 6.89 (d, J = 2.5 Hz, 2 H), 7.08 (d, J = 2.2 Hz, 2 H), 7.16 (s, 6 H), 7.28−7.32 (m, 8 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 22.7, 22.73, 28.3, 28.7, 28.8, 29.0, 29.2, 29.3, 29.4, 29.55, 29.63, 31.8, 31.9, 56.6, 68.4, 68.7, 79.9, 86.6, 87.1, 87.2, 87.36, 87.44, 87.9, 91.3, 94.0, 113.1, 113.6, 114.6, 115.8, 143.3, 143.7, 143.77, 143.84, 144.0, 145.2, 163.4, 165.02, 165.11; ESI-HRMS *m/z* calcd for $C_{133}H_{166}N_9O_{13}$ ($M + H^+$) 2097.2605; found 2097.2621.

Pyridine−Pyridone 9-mer 9. To **9-MOM** (48 mg, 0.0229 mmol) in CH_2Cl_2 (7 mL) was added trifluoroacetic acid (4 mL). The mixture was stirred for 1 h and quenched by the addition of an aqueous $NaHCO_3$ solution. The mixture was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by GPC to afford **9** (44 mg, 100%) as a brownish solid: mp 150 °C (dec); IR (KBr) 2200−3200 (strong br), 2925, 2854, 2232, 1585, 1550 cm^{-1}; ^1H NMR ($CD_3OD/CDCl_3$ = 2: 3, 500 MHz) δ 0.87−0.93 (br m, 21 H), 1.16−1.47 (br m, 78 H), 1.61−1.66 (br m, 4 H), 1.82−1.85 (br m, 10 H), 2.44−2.46 (br m, 4 H), 4.06−4.13 (br m, 10 H), 6.87−7.31 (br m, 18 H); ^{13}C NMR ($CD_3OD/CDCl_3$ = 2: 3, 125 MHz) δ 14.1, 19.4, 22.9, 26.1, 28.5, 29.0, 29.25, 29.4, 29.51, 29.54, 29.6, 29.8, 29.9, 30.032.1, 32.2, 69.5 (br), 114.4 (br), 115.5 (br), 143.5 (br), 166.2 (br); ESI-HRMS *m/z* calcd for $C_{125}H_{150}N_9O_9$ ($M + H^+$) 1921.1556; found 1921.1516.

MOM-Protected 11-mer 11-MOM. To an *i*-Pr_2NH (10 mL), DMF (7 mL), and THF (3 mL) suspension of $Pd(PPh_3)_4$ (19.6 mg, 0.00852 mmol) and CuI (0.8 mg, 0.00213 mmol) were added **3b** (90.5 mg, 0.107 mmol) and **4a** (222 mg, 0.234 mmol) subsequently. The mixture was stirred for 7 h at room temperature, evaporated, and the resulting residue was purified by GPC to afford **11-MOM** (165 mg, 62%) as a brownish solid: mp 200 °C (dec); IR (KBr) 2925, 2854, 2232, 1583, 1549 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.87−0.90 (m, 9 H), 1.26−1.45 (m, 88 H), 1.61−1.64 (m, 4 H), 1.78−1.84 (m, 12 H), 2.42 (t, J = 7.0 Hz, 4 H), 3.49 (m, 15 H), 4.01 (m, 12 H), 5.25 (m, 10 H), 6.89 (d, J = 2.0 Hz, 2 H), 7.08 (d, J = 1.5 Hz, 2 H), 7.17 (d, J = 2.5 Hz, 8 H), 7.31−7.33 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.12, 14.14, 19.4, 22.66, 22.69, 25.8, 25.9, 28.3, 28.7, 28.8, 29.0, 29.17, 29.20, 29.23, 29.3, 29.5, 29.6, 31.8, 31.9, 56.6, 68.5, 68.8, 79.9, 86.7, 87.2, 87.3, 87.47, 87.54, 88.0, 91.4, 94.1, 113.3, 113.8, 114.7, 115.8, 115.8, 115.9, 143.5, 143.87, 143.90, 143.97, 144.04, 144.2, 145.4, 163.6, 163.6, 165.3, 165.4; ESI-HRMS *m/z* calcd for $C_{157}H_{191}N_{11}O_{16}$ (M^+) 2486.4470; found 2486.4520.

Pyridine−Pyridone 11-mer 11. To **11-MOM** (115 mg, 0.0462 mmol) in CH_2Cl_2 (5 mL) was added trifluoroacetic acid (3 mL). The mixture was stirred for 3 h and quenched by the addition of an aqueous $NaHCO_3$ solution. The mixture was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by GPC to afford **11** (101 mg, 96%) as a brownish solid: mp 165 °C (dec); IR (KBr) 2200−3200 (strong br), 2925, 2853, 2230, 1584, 1550 cm^{-1}; ^1H NMR ($CD_3OD/CDCl_3$ = 1: 5, 300 MHz) δ 0.10−2.00 (br m, 128 H), 2.40−2.50 (br m, 4 H), 4.00−4.20 (br m, 12 H), 6.00−8.00 (br m, 22 H); ^{13}C NMR ($CD_3OD/CDCl_3$ = 1: 5, 75 MHz) δ 14.1, 22.7, 25.8 (br), 29.2 (br), 31.8 (br); ESI-HRMS *m/z* calcd for $C_{147}H_{172}N_{11}O_{11}$ ($M + H^+$) 2267.3238; found 2267.3269.

Supporting Information Available: Experimental details of analyses for VPO and association constants, Figures S1 and S2, preparation of **3e**, and experimental details and CIF file for X-ray analysis of **3e′**. This material is available free of charge via the Internet at http://pubs.acs.org.

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