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Synthesis of Bis(phenanthropyrroles) via a Tandem Scholl Oxidation

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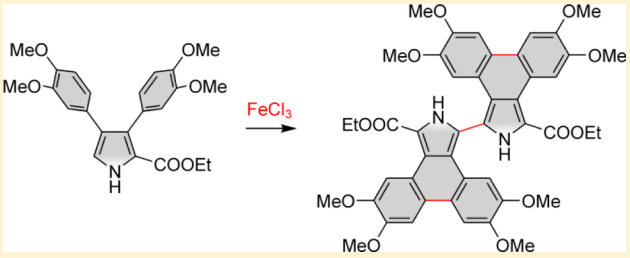
Supporting Information

ABSTRACT: An electron-rich 3,4-diarylpyrrole is shown to undergo a tandem inter- and intramolecular Scholl oxidation, providing access to bis(phenanthropyrroles), a new class of bipyrrole derivatives with extended π conjugation. Intermolecular coupling of two pyrrole molecules is found to be the initial step of this reaction. Bis(phenanthropyrroles) are characterized by restricted rotation around the $\alpha-\alpha$ bond and exhibit strong blue fluorescence and large Stokes shifts.

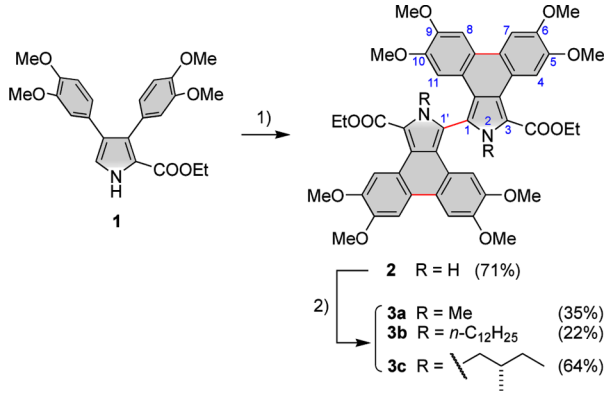


2,2′-Bipyrrole is one of the most important structural motifs in pyrrole chemistry. It occurs in certain natural products, such as prodigiosins,[1] and constitutes the trademark structural feature of several macrocyclic systems, such as sapphyrins, corroles, porphycenes, or cyclopyrroles.[2] 2,2′-Bipyrrole, the smallest system containing a direct $\alpha-\alpha$ linkage between pyrrole rings, is also the defining motif of longer oligopyrrole molecules[3] and conducting pyrrole polymers[4] and may be viewed as a potential synthetic intermediate and a convenient structural model.

In the "classical" synthetic approach to 2,2′-bipyrroles, a monopyrrole is substituted at position 2, and the substituent is transformed into the second pyrrole nucleus using various synthetic schemes.[5] Symmetrical bipyrroles are now efficiently obtained using Ullmann coupling of 2-iodopyrroles.[6] This approach is most successful for pyrroles that are thermally stable and bear electron-withdrawing substituents. N-Protection of the starting monopyrrole improves coupling yields,[6l] as it prevents the competing N-arylation reaction. Alternatively, 2-unsubstituted monopyrroles can be coupled oxidatively using a variety of reagents, such as $FeCl_3$, $Cu(NO_3)_2$, $Pd(OAc)_2$, or PIFA.[7] We have recently reported that Scholl-type oxidations of electron-rich β-aryl porphyrins provide a straightforward route to peripherally fused tetraphenanthro- and tetrakis(benzochryseno)porphyrins.[8] This reaction offers a potentially general method for preparing a variety of pyrrole-based condensed heteroaromatics. Here we show that the Scholl oxidation performed on the α-free monopyrrole **1** effects not only the intramolecular ring closure described previously but also the intermolecular $\alpha-\alpha$ coupling of two pyrrole rings. Such a tandem oxidation provides a facile and efficient route to bis(phenanthropyrrole) **2**,[9] a structurally new fluorescent bis-heterocycle (Scheme 1).

Under optimized reaction conditions, a 10 mM solution of pyrrole **1** in dry dichloromethane was treated with 4 equiv of anhydrous iron(III) chloride (33% molar excess). After 22 h of stirring and subsequent workup, bis(phenanthropyrrole) **2** was isolated in 71% yield. Pure **2** exhibits fairly low solubility (less than 140 mg/L in dichloromethane), but the crude material is not observed to precipitate under typical workup conditions. In an initial effort to obtain substituted bis(phenanthropyrrole) derivatives, **2** was reacted with several alkyl halides to produce the doubly N-alkylated compounds **3a–c**. Inconsistent yields of these reactions are a result of purification difficulties.

Scheme 1. Synthesis of Bis(phenanthropyrroles) 2 and 3a–c[a]



[a]Reagents and conditions: (1) $FeCl_3$ (4 equiv), CH_2Cl_2, 22 h, 71%; (2) RBr (**3b**) or RI (**3a**, **3c**), K_2CO_3, 18-crown-6, 22–63%.

By gradually varying the amount of oxidant used (1–4 equiv; see Supporting Information), it was found that, in the initial step of the oxidation reaction, two molecules of **1** are combined to yield tetraarylbipyrrole **4** (Scheme 2). Regardless of the exact amount of oxidant used, **4** would never become the main component of the crude reaction mixture, and consequently, isolated yields were low (ca. 5%). When 1 or 2 equiv of $FeCl_3$ was used, **4** was accompanied by a large amount of unreacted **1** and by traces of other products. Judging by the appearance of low-field singlets (above 7.5 ppm) in the ^{1}H NMR spectra of crude reaction mixtures, these products contained phenanthrene subunits. When the oxidation was performed at a lower

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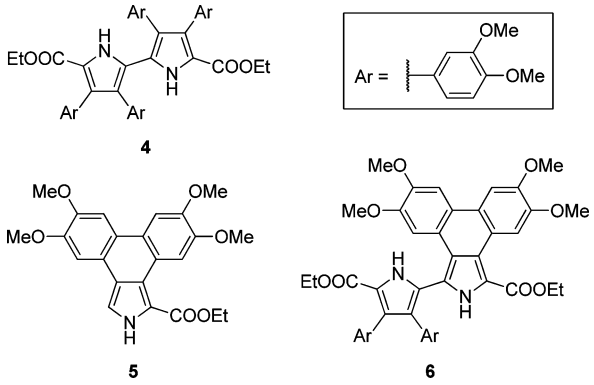
Scheme 2. Reaction Intermediates Discussed in the Text



concentration (1 mM, 2 equiv of $FeCl_3$), the conversion of the starting material was similar and, interestingly, **4** was still the dominant reaction product. Apparently, the intermolecular coupling is a rapid process and can compete with the intramolecular ring closure, suppressing the formation of phenanthropyrrole **5**. Further oxidation of **4** with additional $FeCl_3$ results in efficient formation of **2**, with no significant buildup of the expected intermediate **6**. However, when a large excess of the oxidant was used (e.g., 16 equiv), an intractable mixture of products was obtained.

The molecular structures of **2** and **3a** were confirmed by X-ray structural analyses (Figure 1). In the crystal, the molecules of both compounds are located on crystallographic C_2 axes. To accommodate the steric bulk of fused arene rings, the two phenanthropyrrole fragments are noticeably tilted relative to one another. The $NC_\alpha C_\alpha N$ torsional angle is 62.8° in the structure of **2**, corresponding to a tilted syn conformation. In the more sterically congested structure of **3a**, the $NC_\alpha C_\alpha N$ angle is nearly 90°. In the solid-state geometry of **2**, each of the two phenanthropyrrole subunits is nearly planar, including the attached carboxy group, whereas slight out-of-plane distortions are observed in the subunits of **3a**.

The geometry of **2** observed in the solid state is accurately reproduced by density functional theory (DFT) calculations (ωB97XD[10]/6-31G(d,p), Table 1, Supporting Information),

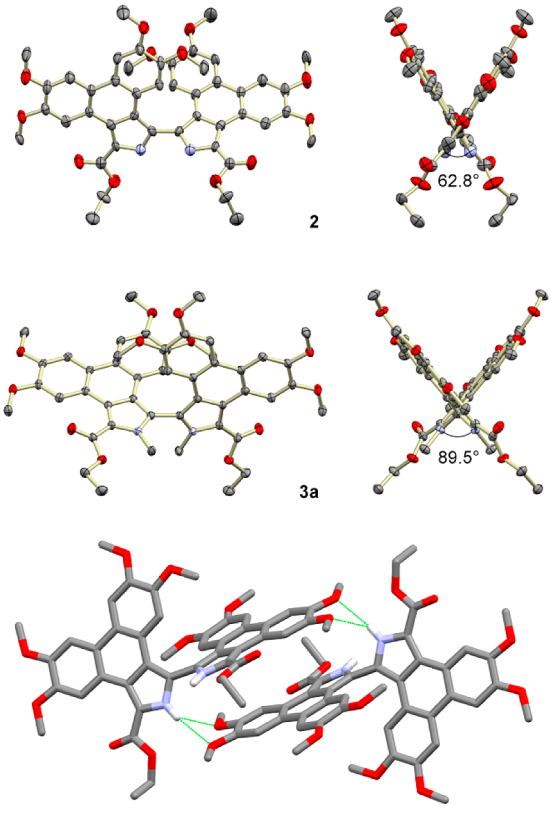


Figure 1. Molecular structures of **2** (top) and **3a** (middle) obtained from X-ray structural analyses. Thermal ellipsoids are shown at the 50% probability level. Solvent molecules, hydrogen atoms, and disordered alkoxy groups are omitted for clarity. Bottom: interaction between adjacent molecules of **2** in the solid state.

Table 1. Computational Data for Bis(phenanthropyrroles) (ωB97XD/6-31G(d,p), PCM Solvation in Dichloromethane)

species	state	E_{rel}[a] (kcal/mol)	$NC_\alpha C_\alpha N$ (deg)	C_α–C_α (Å)	S0 → S1[b] (nm)
2	S0	0.00	60.7	1.464	322
		1.19	131.0	1.457	346
	S1	1.91	24.2	1.396	466
		0.00	153.3	1.392	469
3a	S0	0.27	75.7	1.465	314
		0.00	102.5	1.463	306

[a]Relative DFT energies (S0 states) and TD-DFT energies (S1 states). [b]Lowest-energy electronic transitions for the optimized geometries.

including the relative orientation of phenanthropyrrole units. However, the calculations predict the existence of an additional, almost isoenergetic conformer, characterized by the $NC_\alpha C_\alpha N$ angle of 131°. For **3a**, two energy minima were also found, with $NC_\alpha C_\alpha N$ torsions of 103 and 76°. These values cover a narrower range of angles than observed for **2**, indicating that the torsional freedom in bis(phenanthropyrrole) is restricted upon N-substitution.

The crystal structure of **2** is stabilized by a combination of weak hydrogen bonding and π-stacking interactions (Figure 1, bottom). Each NH hydrogen of **2** interacts with a pair of adjacent OMe groups from a neighboring molecule (H···O distances of 2.38 and 2.60 Å). The π surfaces of the phenanthropyrrole units involved in H-bonding are partly overlaid, with interplane separations of 3.42–3.56 Å. This structural motif, combining π stacking with weak hydrogen bonds, is repeated infinitely in one dimension, yielding heterochiral strands of closely packed molecules.

As a consequence of their twisted conformation, compounds **2** and **3a–c** can in principle be axially chiral, but their configurational stability will depend on the rotation barrier around the α–α bond. Because of the increased steric bulk, the barrier is expected to be higher in the alkylated derivatives **3a–c**.[7a,11] In the ^{1}H NMR spectra of **2**, **3a**, and **3b**, the CH_2 signal of the ester ethyl group shows diastereotopic splitting, indicating that the rotation is slow on the NMR time scale. Separation of enantiomers could be transiently observed for **2** on a chiral HPLC column, but their racemization was very rapid. However, we were not able to observe any separation for the alkylated derivatives, probably because of insufficient column specificity.

To further explore the stereochemistry of bis(phenathropyrroles), **2** was reacted with *S*-(+)-1-iodo-2-methylbutane. The resulting dialkyl derivative **3c** was isolated as a nearly equimolar mixture of two diastereomers (SSR_a and SSS_a).

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These isomers differ in the configuration of the chirality axis and yield distinct sets of signals in the ^{1}H NMR spectrum. A sample of **3c** in *p*-xylene-d_{10} showed no signs of dynamic broadening when heated to 410 K. Likewise, exchange between the diastereomers of **3c** was not observed in the ROESY spectrum recoded under the same conditions. These results indicate that the rotation barrier in N-substituted species might be sufficiently high to ensure configurational stability at room temperature.

The electronic effects of ring fusion in bis(phenanthropyrrole) can be appreciated by comparing the absorption spectra of **2** and its nonfused analogue **4** (Figure 2). The

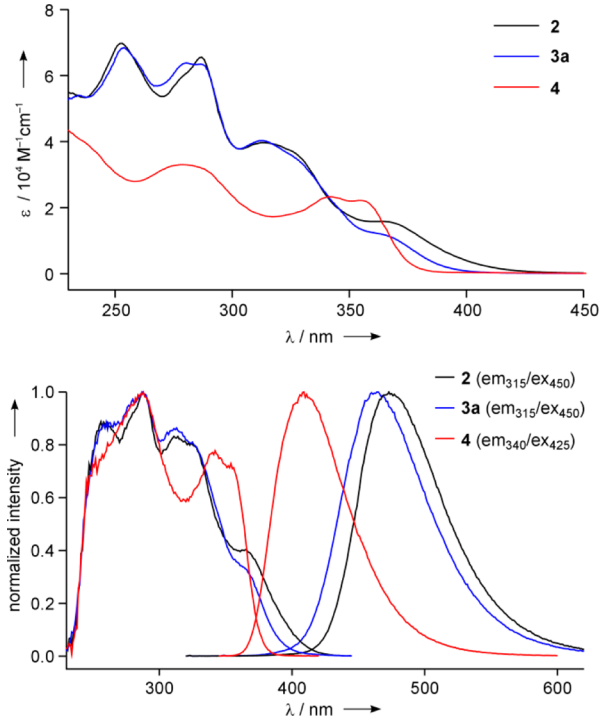

Figure 2. Top: electronic absorption spectra of bis(phenanthropyrroles) **2** and **3a** and bipyrrole **4** (293 K, dichloromethane). Bottom: normalized emission and excitation spectra of **2** and **3a** (293 K, dichloromethane).

absorption below 350 nm is significantly more intense in the spectrum of **2**, with the largest extinction coefficients reaching 70 000 M^{-1} cm^{-1}. In contrast, the longest wavelength band of **2** (364 nm) is only slightly red-shifted relative to the corresponding band in **4** (355 nm). The absorption profile of **3a** is very similar to that of **2** except for the lowest-energy band which is hypsochromically shifted and has a significantly reduced intensity. This effect can be tentatively attributed to the larger tilt of phenanthropyrrole subunits in **3a**, which reduces electronic coupling between the two π systems. Vertical excitation energies for **2** and **3a** have been calculated using time-dependent density functional theory (TD-DFT). Calculations performed at the B3LYP/6-31G(d,p) level of theory provided a significantly underestimated value of the first excitation energy (λ_{max} > 420 nm), which may result from the known deficiency of hybrid DFT functionals.[12] More realistic values could be obtained using the range-separated hybrid functional ωB97XD (Table 1).

Bis(phenanthropyrroles) display intense blue fluorescence in the solid state and in solution. In dichloromethane, the emission maxima of **2** and **3a** are 473 and 465 nm, respectively, corresponding to Stokes shifts in excess of 100 nm (Figure 2). The observed fluorescence profiles are rather insensitive to solvent polarity. The emission of bis(phenanthropyrrole) derivatives is significantly red-shifted relative to symmetrically substituted nonfused bipyrroles, which typically yield maxima in the 380−420 nm range.[6n,13] In fact, bipyrrole **4** shows the emission maximum at 409 nm, corresponding to the Stokes shift of 54 nm. Fluorescence quantum yields measured for **2** and **3a** in dichloromethane are 0.33 and 0.19, respectively.

TD-DFT geometry optimizations[12,14] show the existence of two conformations for the S1 state of **2** (Table 1, Figure 3).

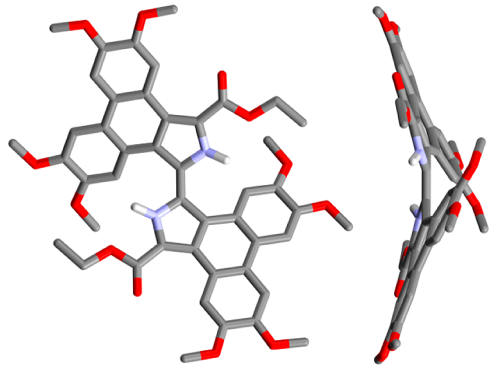

Figure 3. Optimized geometry of the lowest-energy conformer of the S1 state of **2** (ωB97XD/6-31G(d,p), dichloromethane PCM). Hydrogen atoms (except for NH) are omitted for clarity.

The two conformers have very similar energies, and the calculated S0 → S1 transitions are in very good agreement with the experimental emission wavelength. In comparison with the S0 geometries, the S1 state is characterized by more extensive π coupling between the phenanthropyrrole subunits as evidenced by the smaller deviations of the NC$_\alpha$C$_\alpha$N angles from planarity and shorter C$_\alpha$−C$_\alpha$ distances. Complete planarization of the S1 state is not possible because of steric repulsions between the polycyclic subunits, and the resulting geometry shows a characteristic puckering of the bipyrrole fragment.

The present work shows that Scholl-type oxidations provide a simple yet effective synthetic route to arene-fused 2,2′-bipyrroles. Tandem Scholl oxidations have previously been observed in oligophenylene chemistry,[15] but such reactions yield mixtures of products and are prone to oligomerization. This limitation stems from the difficulty to control the reactivity of multifunctional substrates. The success of the present approach apparently results from the intermolecular pyrrole α−α coupling being faster than other possible oxidation routes. The tandem oxidation strategy presented here can be extended in two complementary ways: by elongation of the oligopyrrole chain and by expansion of the attached polycyclic moieities. Such systems are expected to combine strong emission with high absorptivity, as already seen in **2**, making them of potential interest as electroactive materials.

EXPERIMENTAL SECTION

General. Tetrahydrofuran was dried using a commercial solvent purification system. Dichloromethane was distilled from calcium hydride when used as a reaction solvent. All other solvents and reagents were used as received. Compound **1** was synthesized as described previously.[8] ^{1}H NMR spectra were recorded on high-field spectrometers (^{1}H frequency at 500.13 or 600.13 MHz), equipped

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with broad-band inverse gradient probeheads. Spectra were referenced to the residual solvent signals (chloroform-*d*, 7.24 ppm, xylene-d_{10} assumed to be 2.30 ppm). Two-dimensional NMR spectra were recorded with 2048 data points in the t_2 domain and up to 2048 points in the t_1 domain, with a 1−1.5 s recovery delay. All 2D spectra were recorded with gradient selection, with the exception of ROESY. The ROESY spinlock time was 300 ms. ^{13}C NMR spectra were recorded with ^{1}H broad-band decoupling and referenced to solvent signals ($^{13}CDCl_3$, 77.0 ppm). High-resolution mass spectra were recorded using ESI or MALDI ionization in the positive mode. Fluorescence quantum yields were calculated following a literature procedure,[16] with quinine sulfate as a standard.[17]

Computational Methods. Density functional theory (DFT and TD-DFT) calculations were performed using Gaussian 09.[18] Ground-state DFT geometry optimizations were carried out in unconstrained C_1 symmetry, using X-ray geometries as starting models. Vertical excitation energies and excited-state geometries were calculated by means of time-dependent density functional theory (TD-DFT). DFT geometries were refined to meet standard convergence criteria, and the existence of a local minimum was verified by a normal-mode frequency calculation (the frequency calculation was not performed for the TD-DFT optimized S1 states, for which analytic second derivatives were not available). DFT calculations were performed using the hybrid functional B3LYP[19] and the range-separated ωB97XD[20] functional combined with the 6-31G(d,p) basis set.

X-ray Crystallography. X-ray quality crystals were grown by slow diffusion of methanol into a dichloromethane solution (**2**·2MeOH) and via slow evaporation o a dichloromethane solution (**3a**·3CH_2Cl_2). Diffraction measurements were performed on a κ-geometry diffractometer (ω and ϕ scans) with graphite-monochromatized Mo Kα (**2**·2MeOH) and Cu Kα radiation (**3a**·3CH_2Cl_2). Data were corrected for Lorentz and polarization effects. An analytical absorption correction was applied to the data of **3a**·3CH_2Cl_2 with the use of diffractometer software. The structures were solved by direct methods with the SHELXS-97 program and refined using SHELXL-97[21] with anisotropic thermal parameters for non-H atoms. All H atoms were found in difference Fourier maps. In the final refinement cycles, all H atoms were treated as riding atoms in geometrically optimized positions. In the structure of **2**·2MeOH, one of the methoxy groups and the ethyl group of the ester were positionally disordered.

General Procedure for the Oxidation of Ethyl 3,4-Bis(3,4-dimethoxyphenyl)-1*H*-pyrrole-2-carboxylate (1). Ethyl 3,4-bis-(3,4-bismethoxyphenyl)-1*H*-pyrrole-2-carboxylate (**1**) was dissolved in deoxygenated dichloromethane. Anhydrous iron(III) chloride was added, and the reaction mixture was stirred under argon for 20−36 h. The progress of the reaction was monitored with thin-layer chromatography. The reaction mixture was diluted with aqueous potassium thiocyanate and extracted with dichloromethane. The extracts were dried over anhydrous magnesium sulfate, and the solvent was removed on a rotary evaporator. The dark residue was crystallized from methanol/dichloromethane. The product was isolated as grayish crystals.

Diethyl 5,5′,6,6′,9,9′,10,10′-Octamethoxy-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]isoindole]-3,3′-dicarboxylate (2). Obtained from **1** (200 mg, 0.481 mmol) and anhydrous iron(III) chloride (312 mg, 1.924 mmol) in dichloromethane (48.6 mL) Reaction time was 22 h. Grayish crystals (142 mg, 71%). ^{1}H NMR (600 MHz, chloroform-*d*, 300 K): δ 10.37 (s, 2H), 9.57 (s, 2H), 7.54 (s, 4H), 7.05 (s, 2H), 4.52 (m, 4H), 4.14 (s, 6H), 4.02 (s, 6H), 3.95 (s, 6H), 2.82 (s, 6H), 1.48 (t, 6H, ^3J = 7.0 Hz). ^{13}C NMR (150 MHz, chloroform-*d*, 300 K): δ 160.6, 148.7, 148.5, 148.3, 148.1, 125.1, 124.8, 123.4, 121.7, 120.8, 120.7, 118.6, 115.4, 110.6, 105.1, 104.8, 104.3, 61.1, 56.3, 56.2, 55.9, 55.0, 14.9. UV−vis (dichloromethane, 293 K) λ [nm] (log ε in M^{-1} cm^{-1}): 253 (4.84), 287 (4.82), 313 (4.60), 364 (4.20). HR-MS (MALDI-FTMS+): *m*/*z* 816.2875 [M^+], calcd for $C_{46}H_{44}N_2O_{12}$ 816.2889; mp 330 °C (decomposition).

Diethyl 3,3′,4,4′-Tetrakis(3,4-dimethoxyphenyl)-1*H*,1′*H*-[2,2′-bipyrrole]-5,5′-dicarboxylate (4). Prepared from **1** (200 mg, 0.481 mmol) and anhydrous iron(III) chloride (234 mg, 1.443 mmol) in dichloromethane (48.6 mL). Reaction time was 20 h. Compound **4** was separated from the reaction mixture by fractional crystallization from dichloromethane/methanol as brownish crystals (9.6 mg, 4.8%). ^{1}H NMR (500 MHz, chloroform-*d*, 300 K): δ 8.98 (s, 2H), 6.87 (d, 2H, ^3J = 8.22 Hz), 6.84 (dd, 2H, ^3J = 8.12 Hz, ^4J = 1.91 Hz), 6.79 (dd, 2H, ^3J = 8.22 Hz, ^4J = 2.00 Hz), 6.73 (d, 2H, ^4J = 1.91 Hz), 6.71 (d, 2H, ^3J = 8.31 Hz), 6.67 (d, 2H, ^4J = 1.91 Hz), 4.06 (q, 4H, ^3J = 7.13 Hz), 3.87 (s, 6H), 3.81 (s, 6H), 3.70 (s, 6H), 3.62 (s, 6H), 1.09 (t, 6H, ^3J = 7.12 Hz). ^{13}C NMR (125 MHz, chloroform-*d*, 300 K): δ 159.8, 149.4, 148.7, 147.9, 147.7, 131.3, 126.6, 125.5, 123.8, 123.5, 123.3, 123.1, 117.9, 114.2, 113.9, 111.6, 110.2, 60.1, 56.0, 55.8, 55.7, 55.7, 14.0. UV−vis (dichloromethane, 293 K) λ [nm] (log ε in M^{-1} cm^{-1}): 279 (4.52), 342 (4.37), 355 (4.35). HR-MS (MALDI-FTMS+): *m*/*z* 820.3195 [M^+], calcd for $C_{46}H_{48}N_2O_{12}$ 820.3202; mp 234−235 °C.

General Procedure for the Alkylation of Diethyl 5,5′,6,6′,9,9′,10,10′-Octamethoxy-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]-isoindole]-3,3′-dicarboxylate. In a dry pressure tube equipped with magnetic stirring, diethyl 5,5′,6,6′,9,9′,10,10′-octamethoxy-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]isoindole]-3,3′-dicarboxylate (**2**, 50 mg, 0.061 mmol) was dissolved in dry tetrahydrofuran. Freshly ground anhydrous potassium carbonate (33.74 mg, 0.244 mmol) and 18-crown-6 (34.40 mg, 0.122 mmol) were added. The mixture was stirred under nitrogen for 30 min, and alkyl halide was added. The pressure tube was closed, placed in an oil bath, and heated at 90 °C for 24 h. Subsequently, the second portion of potassium carbonate (33.74 mg, 0.244 mmol) was added, and the heating was continued for the next 24 h. Hydrochloric acid (3 M solution) was used to neutralize the reaction mixture. The reaction mixture was diluted with water and extracted with dichloromethane. The extracts were dried over anhydrous magnesium sulfate, and the solvent was removed on a rotary evaporator. The product was purified by column chromatography and crystallization.

Diethyl 5,5′,6,6′,9,9′,10,10′-Octamethoxy-2,2′-dimethyl-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]isoindole]-3,3′-dicarboxylate (3a). **3a** was prepared according to the general procedure by using tetrahydrofuran (2 mL) and methyl iodide (0.122 mmol, 17.31 mg, 7.59 μL) as the alkylating agent. Reaction time was 48 h. The yellow residue was crystallized from methanol/dichloromethane. The product was isolated as pale yellow crystals (17.87 mg, 35%). ^{1}H NMR (500 MHz, chloroform-*d*, 300 K): δ 8.68 (s, 2H), 7.74 (s, 2H), 7.67 (s, 2H), 6.48 (s, 2H), 4.56 (m, 4H), 4.09 (s, 6H), 4.08 (s, 6H), 3.97 (s, 6H), 3.79 (s, 6H), 3.18 (s, 6H), 1.46 (t, 6H, ^3J = 7.1 Hz). ^{13}C NMR (125 MHz, chloroform-*d*, 300 K): δ 163.5, 148.8, 148.6, 148.2, 148.0, 124.6, 123.2, 120.9, 120.5, 120.4, 120.4, 118.6, 108.6, 105.0, 104.9, 103.7, 61.4, 56.1, 56.1, 56.0, 55.1, 35.0, 14.5. UV−vis (dichloromethane, 293 K) λ [nm] (log ε in M^{-1} cm^{-1}): 254 (4.84), 280 (4.80), 287 (4.80), 313 (4.61). HR-MS (MALDI-FTMS+): *m*/*z* 844.3196 [M^+], calcd for $C_{48}H_{48}N_2O_{12}$ 844.3202; mp 287−290 °C.

Diethyl 2,2′-Didodecyl-5,5′,6,6′,9,9′,10,10′-octamethoxy-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]isoindole]-3,3′-dicarboxylate (3b). **3b** was prepared according to the general procedure by using tetrahydrofuran (2 mL) and 1-bromododecane (0.122 mmol, 30.40 mg, 29.22 μL) as the alkylating agent. Reaction time was 48 h. The crude product was purified by column chromatography (silica gel, 1% methanol in dichloromethane). The product eluted as the third fraction. The solvent was removed on a rotary evaporator. The product was finally purified by crystallization from methanol/dichloromethane and was isolated as white crystals (15.6 mg, 22%). ^{1}H NMR (500 MHz, chloroform-*d*, 300 K): δ 8.54 (s, 2H), 7.73 (s, 2H), 7.63 (s, 2H), 6.60 (s, 2H), 4.55 (m, 4H), 4.08 (s, 6H), 4.06 (s, 6H), 3.95 (s, 6H), 3.01 (s, 6H), 1.58 (m, 4H), 1.46 (t, 6H, ^3J = 7.1 Hz), 1.07 (m, 40H), 0.83 (t, 6H, ^3J = 7.3 Hz). ^{13}C NMR (125 MHz, chloroform-*d*, 300 K): δ 164.0, 148.44, 148.41, 148.1, 147.9, 124.6, 123.04, 122.98, 120.6, 120.5, 120.2, 120.1, 117.6, 108.4, 105.0, 104.8, 104.6, 61.4, 56.04, 55.95, 55.94, 54.9, 48.0, 31.9, 31.7, 29.6, 29.5, 29.4, 29.3, 29.1, 28.9, 26.8, 22.7, 14.4, 14.1. HR-MS (MALDI-FTMS+): *m*/*z* 1152.6587 [M^+], calcd for $C_{70}H_{92}N_2O_{12}$ 1152.6645.

Diethyl 5,5′,6,6′,9,9′,10,10′-octamethoxy-2,2′-bis((*S*)-2-methylbutyl)-2*H*,2′*H*-[1,1′-bidibenzo[*e*,*g*]isoindole]-3,3′-dicarboxylate (3c). In a dry pressure tube equipped with magnetic stirring,

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compound **2** (0.037 mmol, 30 mg) was dissolved in dry tetrahydrofuran (2 mL). Freshly ground anhydrous potassium carbonate (0.148 mmol, 20.46 mg) and 18-crown-6 (0.074 mmol, 19.66 mg) were added. The mixture was stirred under nitrogen for 30 min, and *S*-(+)-1-iodo-2-methylbutane (0.148 mmol, 29.31 mg, 19.21 μL) was added. The pressure tube was closed, placed in an oil bath, and heated at 90 °C for 24 h. Subsequently, the second portion of potassium carbonate (20.46 mg, 0.148 mmol) and *S*-(+)-1-iodo-2-methylbutane (0.148 mmol, 29.31 mg, 19.21 μL) were added, and the heating was continued for the next 24 h. Hydrochloric acid (3 M solution) was used to neutralize the reaction mixture. The reaction mixture was diluted with water and extracted with dichloromethane. The extracts were dried over anhydrous magnesium sulfate, and the solvent was removed on a rotary evaporator. The crude product was analyzed by ^{1}H NMR and subjected to another round of the above alkylation procedure, in which the last heating step was extended to 48 h. The product was purified by crystallization from *n*-hexane/dichloromethane. The product was isolated as grayish crystals (22.6 mg, 64%). ^{1}H NMR (600 MHz, chloroform-*d*, 300 K, combined data for both isomers): δ 8.51 (s, 2H), 8.47 (s, 2H), 7.740 (s, 2H), 7.735 (s, 2H), 7.29 (s, 2H), 7.23 (s, 2H), 4.63 (m, 4H), 4.55 (m, 2H), 4.47 (m, 4H), 4.44 (m, 2H), 4.094 (s, 6H), 4.092 (s, 6H), 4.07 (s, 6H), 4.06 (s, 6H), 3.97 (s, 6H), 3.96 (s, 6H), 3.72 (m, 2H), 3.48 (m, 2H) 2.76 (s, 6H), 2.74 (s, 6H), 1.50 (m, 2H), 1.483 (t, 6H), 1.476 (t, 6H), 1.44 (m, 2H), 1.15 (m, 2H), 0.86 (m, 2H), 0.85 (m, 2H), 0.66 (d, 3H), 0.61 (m, 2H), 0.57 (t, 3H), 0.34 (d, 3H), 0.24 (t, 3H). ^{13}C NMR (151 MHz, chloroform-*d*, 300 K, combined data for both isomers): δ 164.42 (×2), 148.4, 148.36, 148.12, 148.10, 148.06, 148.03, 147.88, 147.86, 124.4, 124.3, 122.99, 122.97, 122.2, 122.1, 120.8, 120.61, 120.56, 120.53, 120.50, 120.48, 120.47, 120.45, 118.8, 118.5, 108.24, 108.22, 105.7, 105.4, 105.0 (×2), 104.4, 61.5, 61.4, 56.08, 56.06, 55.92, 55.90, 55.82, 55.80, 54.80, 54.77, 53.6, 52.8, 36.7, 36.5, 26.9, 26.8, 17.4, 16.9, 14.43, 14.41, 11.1, 10.7. HR-MS (MALDI-FTMS+): *m*/*z* 956.4460 [M$^+$], calcd for $C_{56}H_{64}N_2O_{12}$ 956.4454; mp (mixture of isomers) 92–97 °C.

■ ASSOCIATED CONTENT

Supporting Information

NMR and MS spectra, spectral assignments, X-ray tables, HPLC chromatograms, computational data, and Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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