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Synthesis of Dicarboxylate "C-Clamp" 1,2-Diethynylarene Compounds as Potential Transition-Metal Ion Hosts

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We report an efficient convergent synthesis of a new type of C-clamp ligand with a 1,2-diethynylarene scaffold involving a chelate host capable of binding a guest molecule in its *endo*-dicarboxylate pocket. The chemistry involves a combination of palladium-catalyzed Sonogashira, Heck, and Suzuki cross-coupling reactions. The compounds 2,3-bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]triptycene and 4,5-bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]veratrole and their 2′-carboxy-*m*-terphenyl-4-yl analogues were designed as dinucleating ligands to assemble carboxylate-bridged transition-metal complexes with a windmill geometry. The X-ray crystal structure of one such C-clamp compound containing co-crystallized water molecules reveals strong hydrogen bonds of the aqua guest to the *endo*-oriented carboxylic acid entities of the C-clamp host. In addition, two *syn*-N-donor ligands were prepared as a synthetic scaffold to mimic the geometric arrangement of N-donor atoms in carboxylate-bridged dinuclear proteins.

Introduction

Methane monooxygenase, a member of the bacterial multicomponent monooxygenase (BMM) family, catalyzes the selective oxidation of methane to methanol under ambient conditions in methanotrophic bacteria.[1] The active site of the hydroxylase component (MMOH, Figure 1) of soluble methane monooxygenase (sMMO) is embedded in a four-helix bundle that creates a hydrophobic protein environment for O_2 activation at a reduced diiron(II) site. Conversion to a high-valent diiron(IV) intermediate leads to selective oxidation of methane to methanol. The active site features a non-heme diiron center coordinated by four glutamate and two histidine residues, which coordinate in a *syn* disposition with respect to the Fe–Fe axis.[1] Other carboxylate-rich diiron enzymes like the stearoyl-acyl carrier protein Δ^9-desaturase and ribonucleotide reductase R2 (RNR-R2, Figure 1) have a similar active site composition and are responsible for fatty acid desaturation and tyrosyl radical generation, respectively.[2]

To model the structural features of these enzymes, symmetric and asymmetric carboxylate ligands, such as 2,6-bis(*p*-tolyl)benzoate ($^{-}O_2CAr^{Tol}$), 2,6-dimesitylbenzoate, 3,5-dimethyl-1,1′:3′,1′′-terphenyl-2′-carboxylate, and 2-phenylbenzoate, have been employed.[3,4] These sterically hindered carboxylates facilitate the isolation of diiron(II) complexes with double, triple, and quadruple carboxylate bridges.[5] Coordination of amino or pyridyl N-donor atoms to such complexes affords diiron complexes that recapitulate several salient features of MMOH. For example, these complexes contain four carboxylate ligands and N-donors and form reactive intermediates upon exposure to dioxygen[6] that display high oxygenation rates[7] and can oxidize hydrocarbons,[8] thioethers,[4,9] and phosphanes,[9,10] particularly when the substrates are held in close proximity to the diiron core.

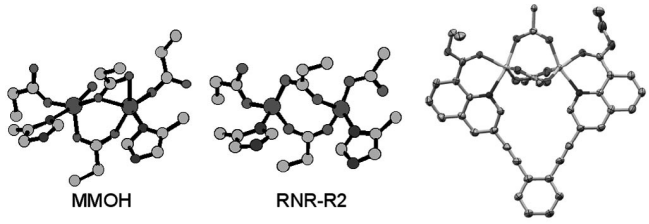

Figure 1. The reduced diiron(II) MMOH (left) and RNR-R2 (center) cores and a diiron(II) model complex $[Fe_2(Et_2BCQEB^{Et})(\mu\text{-}O_2CAr^{Tol})_3]^+$ (right) displaying the N-donors in a *syn* disposition with respect to the iron–iron vector. The location of the atoms is based on X-ray coordinates. The ethyl moieties on the phenyl ring, and the aromatic carbon atoms of the $^{-}O_2CAr^{Tol}$ ligands (except the α-carbon atoms) are omitted for clarity in the model compound.

However, the current BMM model complexes have several limitations, and efforts to prepare biomimetic oxidation catalysts continue an active area of research. A key consideration for developing functional BMM analogues is to design a synthetic platform that can stabilize high-valent (oxido)diiron species. In MMOH, the active oxidant is an oxido-bridged diiron(IV) unit, which cleaves the C–H bond

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in methane and transfers an oxygen atom from the diiron core to the substrate to form methanol. DFT calculations suggest that formation of the diiron(IV) intermediate is favored when the imidazole ligands of the MMOH active site are arranged in a *syn* disposition with respect to the Fe–Fe vector.[11] In order to mimic more closely the position of the N-donors in the native enzyme, several dinucleating ligands containing adjacent N-binding groups were prepared.[12] These *syn*-N-donor ligands have enabled the synthesis of diiron complexes, such as $[Fe_2(Et_2BCQEB^{Et})(\mu\text{-}O_2CAr^{Tol})_3]$-(OTf), where Et_2BCQEB^{Et} is 1,2-bis{2-[8-(ethoxycarbonyl)-quinol-3-yl]ethynyl}-4,5-diethylbenzene (Figure 1).[13]

Another consideration in designing synthetic model complexes for diiron enzymes is to provide a scaffold that will allow for selective binding and activation of external hydrocarbon substrates. In the native BMM enzymes, several hydrophobic cavities delineate a pathway from the protein exterior to the active-site pocket.[15] In order to incorporate such hydrophobic cavities in a synthetic system, we follow the strategy of preparing a diiron complex with a two-component ligand system. In addition to a *syn*-N-donor, which holds the two N-donors in the preferred orientation, a C-clamp ligand with two *endo*-oriented dicarboxylate groups should enforce a doubly bridging motif and allow for substrate access to the diiron core (Figure 2). Molecular recognition and substrate access play pivotal roles for selective activation of C–H bonds.[16] Here we report the preparation of *syn*-N-donor and dinucleating C-clamp ligands for use in constructing the desired doubly bridged motif. The synthesis of the latter compounds was achieved through cross-coupling reactions of a series of suitable and preorganized *endo*-dicarboxylate compounds with 2,3-diethynyltriptycene or 4,5-diethynylveratrole backbones. A retrosynthetic route is depicted in Scheme 1. The preparation of two new *syn*-N-donor compounds, according to established methods,[12] is also described.

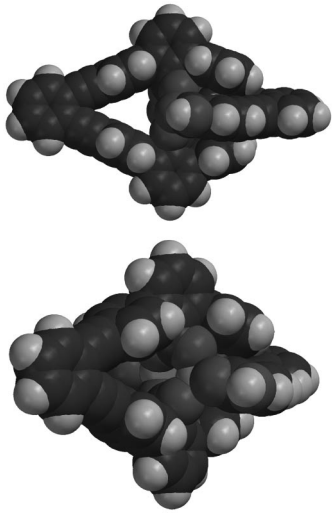
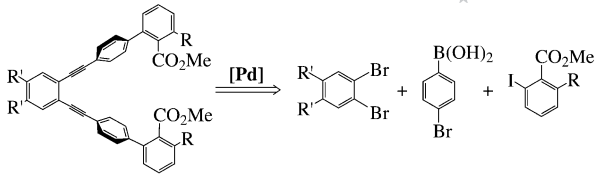


Figure 2. The energy-minimized structure[14] of $[Fe_2\{DEV(PICMe)_2\}\{DEV(terphCO_2)_2\}]$ displaying the substrate-access cavity (top) and the exposed diiron center (bottom).



Scheme 1. Synthetic route to C-clamp ligands; R = H or Ph and $R'_2C_6H_2$ = triptycene or veratrole backbone.

Results and Discussion

Structural drawings of the C-clamp and *syn*-N-donor molecules are depicted in Figure 3, and the synthetic path used to construct the former is presented in Scheme 2. The 4,5-diethynylveratrole (DEV) linker (**1**) was prepared in a manner analogous to that described for 2,3-diethynyltriptycene (DET).[12] Dual Sonogashira coupling of 4,5-dibromoveratrole with (trimethylsilyl)acetylene and $[Pd(PPh_4)_4]$/CuI (2.5 mol-% per coupling) in piperidine at elevated temperature gave the cross-coupled product. Upon desilylation with K_2CO_3 in MeOH, **1** was obtained in 67% overall yield. DEV has two significant advantages over DET: (*i*) the starting material 4,5-dibromoveratrole is commercially available in large quantities, whereas 2,3-dibromotriptycene is prepared from 1,2,4,5-tetrabromobenzene and anthracene (2.2 equiv.) in the presence of 1 equiv. of *n*BuLi in 62% yield;[17] (*ii*) C-clamp and *syn*-N-donor compounds with DEV backbones show improved solubility in organic solvents such CH_2Cl_2 and THF, which are commonly used for complexation reactions with transition-metal ions.

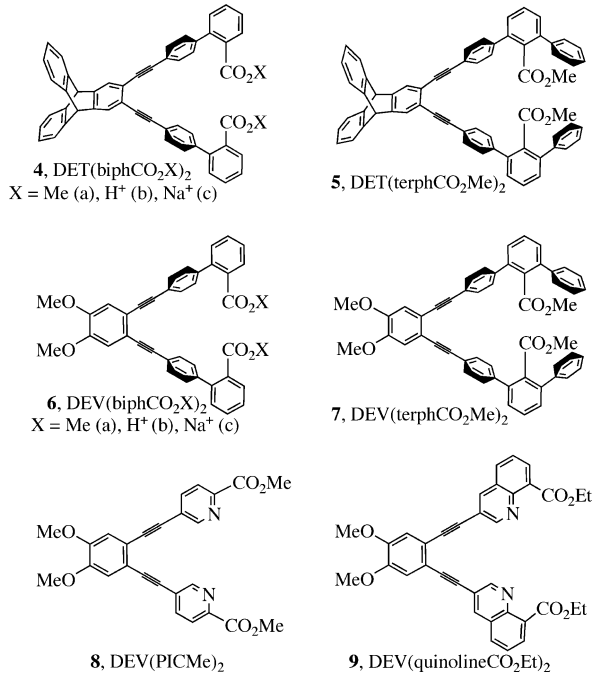
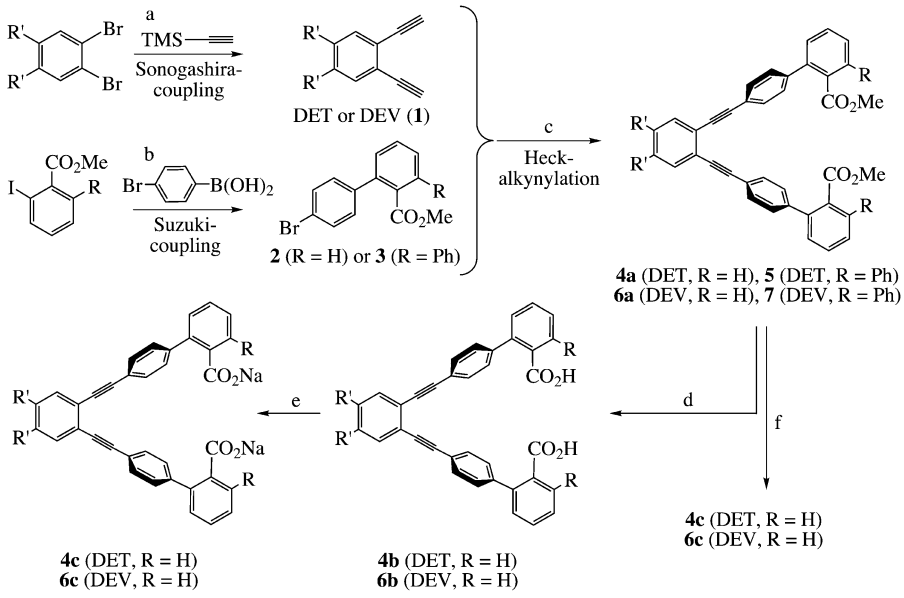


Figure 3. Graphic representation of the C-clamp (**4**–**7**) and *syn*-N-donor (**8** and **9**) ligands.



Scheme 2. Synthetic pathway to diethynylbenzene-based C-clamp ligands; $R'_2C_6H_2$ = triptycene or veratrole backbone. (a) 2 steps, 1: $[Pd(PPh_3)_4]$/CuI, piperidine, 100 °C; 2: K_2CO_3, MeOH, ref.[12]; (b) $[PdCl_2(PPh_3)_2]$, 1 M Na_2CO_3, THF, 60 °C; (c) $[Pd(PPh_3)_4]$, Et_3N, THF, 70 °C; (d) LiI, pyridine, 110 °C; (e) NaOH, MeOH, 60 °C; (f) NaOTMS, THF, 60 °C.

The aryl halide components for constructing the diethynylbenzene scaffolds were prepared by Suzuki coupling of 4-bromophenylboronic acid with methyl 2-iodobenzoate and methyl 3-iodobiphenyl-2-carboxylate with a $[PdCl_2(PPh_3)_2]$ catalyst (5 mol-%) in a mixture of THF and 1 M aqueous Na_2CO_3 at 50–60 °C to give **2** and **3** in 84 and 76% isolated yields, respectively. A 1.5 equiv. portion of the boronic acid was used to convert the aryl iodide quantitatively into the cross-coupled product, because the product and the aryl iodide are difficult to separate by column chromatography. The Suzuki reaction occurred with remarkable selectivity, and no major side-products from further coupling of the boronic acid with the bromoaryl products **2** and **3** were observed. The X-ray crystal structure of **3** is discussed below.

A dual Heck alkynylation, i.e. copper-free Sonogashira cross-coupling, between the arylalkyne DET or DEV (**1**) and the aryl bromide **2** or **3** with $[Pd(PPh_4)_4]$ (5 mol-% per coupling) in a mixture of Et_3N and THF under warming resulted in the formation of C-clamp compounds **4a**, **5**, **6a** and **7** in good isolated yields (Scheme 2). Compounds **4a** and **6a** were obtained in about 70%, but only modest yields (ca. 15%) were achieved for **5** and **7**. We do currently not have an explanation for why the cross-coupling reaction with **3** results in considerably lower yields than with **2**, although steric or conformational factors may play a role. Addition of CuI to the reaction mixture resulted in drastically reduced yields. An excess of LiI in pyridine in a pressure vessel under an inert gas at 120 °C resulted in saponification of the C-clamp esters **4a** and **6a** to give **4b** and **6b** in 73 and 56% yields, respectively. The application of commonly used bases for the ester hydrolysis, such as KOH or NaOH, did not allow for isolation of the hydrolyzed ester. Sodium salts **4c** and **6c** were isolated quantitatively by heating the carboxylic acid in MeOH with 1 equiv. of NaOH. Compounds **4c** and **6c** can also be prepared in almost quantitative yields directly from **4a** and **6a** with sodium trimethylsilanolate in THF at 60 °C. The *syn*-N-donor ligands **8** and **9** were prepared in a manner similar to that previously reported[12] for the compounds $DET(PICMe)_2$ and $DET(quinolineCO_2Et)_2$ from methyl 5-bromo-2-picolinate and ethyl 3-[(trifluoromethyl)sulfonyl]quinoline-8-carboxylate upon cross-coupling with **1** in 93 and 80% yields, respectively. The convergent synthetic strategy for the C-clamp and *syn*-N-donor compounds with its satisfying overall yields is an important advance that should facilitate future study of the coordination chemistry of this family of ligands.

The solid-state structures of **3** and **4b** were determined by X-ray crystallography and are depicted in Figures 4 and 5. The O(1)–C(1), O(1)–C(2), and O(2)–C(2) bond lengths of 1.439(2), 1.345(2), and 1.197(2) Å, respectively, and the Br(1)–C(18) distance of 1.892(2) Å in **3** are as expected. Compound **4b** crystallizes in the space group $I4_1/a$ with one half of a molecule in the asymmetric unit. Four water and two methanol molecules co-crystallize per $DEV(biphCO_2H)_2$ unit. Two solvent molecules are located between the *endo*-oriented carboxylate ligands (Figure 5), revealing that the C-clamp acid **4b** crystallizes preferentially in the desired pre-organized *endo* conformation, with the two water entities adopting the sites anticipated for potential metal–guest binding. Both of these H_2O molecules are involved in strong hydrogen bonding with the carboxylate oxygen atoms, with O(1)–O(1S) and O(2)–O(2S) distances of 2.591(6) and 2.647(4) Å, respectively. The O(1)–O(1S)–(O1A) and O(2)–O(2S)–(O2A) angles are 142.5(6) and 147.7(2)°, respectively, and the dihedral angle $\Theta_{O(2)–O(1)–(O1A)–O(2A)}$ is 57.6(3)°. Untwisting the two carboxylate ligands by rotation around the $C_{carboxylate}–C_{\alpha}$ axis

angles to $\Theta \approx 0°$ results in considerably shorter $O_{carboxylate}$–$O_{carboxylate}$ distances and shows that incorporation of two metal ions between two *endo*-oriented carboxylate ligands would result in M–$O_{carboxylate}$ distances of ca. 2.0 Å, the value required to bind 1st-row transition-metal ions.

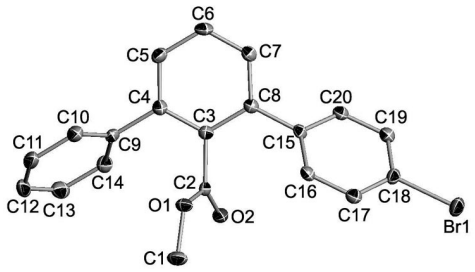


Figure 4. Molecular structure of **3**. Thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

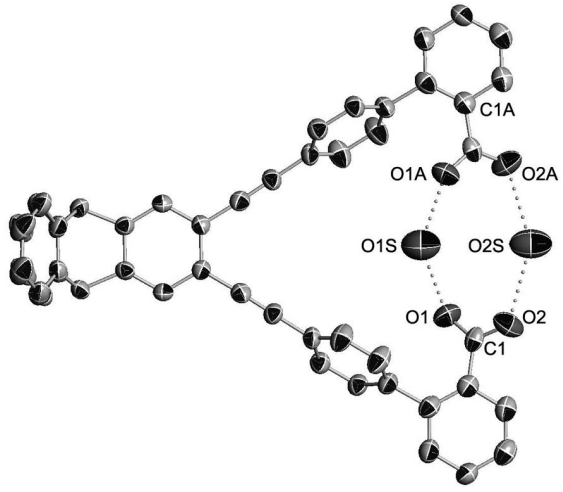


Figure 5. Molecular structure of **4b** and two co-crystallized water molecules at 100% and 50% occupancy for O2S and O1S, respectively, with strong hydrogen bonding (dotted line) between the carboxylic acid and the solvent. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms, *exo*-oriented disordered carboxylic acid moieties at 33% occupancy, two water molecules (both 25% occupancy), and two methanol solvent molecules (both 25% occupancy) are omitted for clarity.

Dicarboxylate-containing molecules with the functional groups in *endo* positions are difficult to prepare. The *syn*, *syn* configuration can be achieved when using diphenyl dibenzofuran-4,6-diylbis(acetate) (Ph_4DBA)[18] or the more rigid "*m*-xylylenediaminobis(Kemp's triacid imide)" (XDK) as a ligand.[19] For *endo* orientation of the dicarboxylate groups, macrocycles often are employed.[20,21] Such macrocyclic oligocarboxylate compounds have been investigated for host–guest chemistry because of their strong hydrogen bonding and coordinative interactions with the guests. Large chelate rings with sufficient rigidity to allow for preorganization are desired to achieve the *endo* configuration without the need for a macrocycle. C-clamp ligands have been prepared previously by reductive amination of 4-formyl-1,1′:3′,1′′-terphenyl-2′-carboxylate with the sodium salt of 1,3-bis(aminomethyl)-4,6-diisopropylbenzene.[20] The flexible 1,3-bis(aminomethyl)benzene linker, however, does not allow for convergent preorganization of the carboxylate functionalities because of steric repulsions involving the terphenyl arms, and polymerization can therefore be a major problem following addition of transition-metal ions.

The non-macrocyclic C-clamp molecules **4**–**7** feature a rigid diethynylbenzene linker that assures that both benzoate moieties are oriented in the same direction, avoiding *trans* orientation of the carboxylate entities. A hydrogen-bonding network between the C-clamp acid **4b** and guest water molecules is capable of preorganizing, at least in the solid state and most likely in solution, the two carboxylates in an *endo* configuration. The design of **4**–**7** allows for a well-positioned *endo* CO_2^-–CO_2^- pair having the proper distance to accommodate transition-metal guest ions. We are particularly interested in synthesizing diiron complexes with one *syn*-N-donor and one C-clamp ligand allowing for the two N-donors in *syn* disposition, and bridging carboxylate ligands containing an encumbered diiron center with a substrate-access cavity. Molecular modeling studies indicate the feasibility of preparing such compounds, and an energy-minimized structure[14] of [Fe_2(DEV(PICMe)$_2$)(DEV-(terphCO_2)$_2$)] is shown in Figure 2.

Conclusions

We have efficiently prepared a series of 1,2-diethynylarene C-clamp and *syn*-N-donor compounds through Sonogashira, Heck, and Suzuki palladium cross-coupling reactions using a convergent synthetic strategy. The diethynylbenzene linkers DET and DEV orient the N-donor moieties in a *syn* configuration, and the two carboxylate groups of the C-clamp ligands can prevail in an *endo* orientation when holding small guest molecules in its binding pocket. Complexation reactions of C-clamp ligands with transition-metal ions and the preparation of [Fe_2(*syn*-N-donor)(C-clamp)] compounds are underway in our laboratory. The reported compounds should be of interest as hosts or ligands for a wide variety of transition-metal ions.

Experimental Section

General Considerations: All reagents were obtained from commercial suppliers and used as received, unless otherwise noted. MP-TMT (macroporous polystyrene-2,4,6-trimercaptotriazine) was obtained from Argonaut Technologies. All cross-coupling reactions were performed under an inert gas, which was maintained either by bubbling argon through the solutions or by the freeze-pump-thaw technique to degas the reaction solutions. 2,3-Diethynyltriptycene[12] and methyl 3-iodobiphenyl-2-carboxylate[22] were prepared as described previously. Compound **1** and the acid of **2** have been reported previously, but the compounds have been prepared by different synthetic routes.[23]

Physical Methods: ^{1}H and ^{13}C NMR spectra were measured with a Varian 300 or 500 spectrometer at the Department of Chemistry Instrumentation Facility (MIT DCIF). Chemical shifts were referenced to the residual solvent peaks. Melting points were measured

with an electrothermal Mel-Temp melting-point apparatus. FTIR spectra were recorded with a Thermo Nicolet Avatar 360 spectrometer outfitted with OMNIC software. ESI-MS data were obtained with an Agilent 1100 Series LC/MSD mass spectrometer. Spartan 04 was employed for molecular modeling.[24]

X-ray Structure Determination: The X-ray structures of **3** and **4b** were obtained by mounting a single crystal covered in paratone-N oil on a glass fiber or in a nylon loop cooled under a stream of N_2 on a Bruker APEX CCD diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å), controlled by a Pentium-based PC running the SMART software package.[25] The structures were collected at 110 and 153 K for **3** and **4b**, respectively, solved by direct methods, and refined on F^2 by using the SHELXTL software package.[26] Empirical absorption corrections were applied with SADABS,[27] and the structures were validated using the PLATON software.[28] All non-hydrogen atoms were located and their positions refined with anisotropic thermal parameters. Hydrogen atoms were placed at calculated positions and their thermal parameters assigned as 1.2 times the thermal parameters of the atoms to which they were attached. Hydrogen atoms were located on difference Fourier maps for the *endo*-carboxylic acid protons and the two water molecules in the C-clamp binding pocket. The MeOH hydrogen atom, the H atom of O(3), and the disordered carboxylic acid proton at 33% occupancy of **4b** were not refined. Compound **4b** crystallized with four water molecules, one at 100%, one at 50%, and two at 25% occupancy, and two methanol molecules, both at 25% occupancy per C-clamp host. In addition, the carboxylic acid moiety is disordered over two positions, refined in a 2:1 occupancy ratio. CCDC-658787 (for **3**) and -658788 (for **4b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. **3:** $C_{20}H_{15}BrO_2$, M_r = 367.23 g/mol, *Pca*2$_1$, Z = 4, a = 9.831(4), b = 20.866(9), c = 7.811(3) Å, V = 1602.2(12) Å^3, $\rho_{calcd.}$ = 1.522 g/cm^3, size: 0.30 × 0.25 × 0.10 mm, total reflections: 23228, independent reflections: 3936, parameters: 208, R_{int} = 0.041, completeness: 98.2%, Flack parameter: 0.0135(63), GOF = 1.021, R_1 = 0.0238, wR_2 = 0.0565, largest diff. peak and hole: 0.537 and –0.215 Å^{-3}. **4b:** $C_{50.5}H_{35}O_{6.5}$, M_r = 745.79 g/mol, $I4_1/a$, Z = 8, a = 12.3624(6), b = 12.3624(6), c = 51.920(4), V = 7934.9(9) Å^3, $\rho_{calcd.}$ = 1.249 g/cm^3, size: 0.35 × 0.05 × 0.05 mm, total reflections: 43048, independent reflections: 2502, parameters: 317, R_{int} = 0.039, completeness: 99.9%, GOF = 1.090, $R1$ = 0.0684, wR_2 = 0.1940, largest diff. peak and hole: 0.356 and –0.344 Å^{-3}.

4,5-Diethynylveratrole (DEV) (1): 4,5-Dibromoveratrole (9.62 g, 32.4 mmol) and (trimethylsilyl)acetylene (15.1 mL, 109 mmol) were dissolved in piperidine (50 mL), and the solution was deoxygenated with argon for 40 min. Then [Pd(PPh$_3$)$_4$] (1.87 g, 5 mol-%) and CuI (0.31 g, 5 mol-%) were added, and the reaction mixture was deoxygenated for an additional 10 min. The yellow solution was heated at 100 °C; after ca. 0.5 h, a dark solution and a precipitate formed. The next day, the reaction mixture was cooled to room temperature, poured into H_2O (200 mL), and extracted with CH_2Cl_2 (200 mL). The organic phase was washed with aqueous NH_4Cl (200 mL) and water (200 mL), dried with $MgSO_4$, filtered, and the solvents were evaporated to dryness. To the crude silylated product [^{1}H NMR ($CDCl_3$, 20 °C): δ = 6.92 (s, 2 H), 3.89 (s, 6 H), 0.28 (s, 18 H) ppm] was added K_2CO_3 (12.6 g, 91 mmol) and MeOH (150 mL), and the suspension was stirred for 3 h. The reaction mixture was then concentrated to dryness, extracted with CH_2Cl_2 (150 mL), the extract washed with aq. NH_4Cl (2 × 150 mL), dried with $MgSO_4$, filtered, and concentrated to dryness. The product was purified by column chromatography (SiO_2; hexanes/dichloromethane, 6:4) to give an off-white powder. Yield 4.05 g (67%). M.p. 122–123 °C. R_f = 0.36 (hexanes/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 6.96 (s, 2 H, H^{Ar}), 3.89 (s, 6 H, CH_3), 3.28 (s, 2 H, C≡CH) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 20 °C): δ = 149.5 (MeOC^{Ar}), 118.2 (C^{Ar}), 114.8 (C^{Ar}), 82.2 (C≡C), 79.9 (C≡C), 56.2 (OCH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 3277 (s), 3251 (s) [ν(C≡C–H)]; 2973 (m), 2938 (w), 2912 (w) [ν(C–H)] cm^{-1}. ESI-MS (MeOH/CH_2Cl_2, 2:1): calcd. for [M + Na]$^+$ 209.1; found 208.9. $C_{12}H_{10}O_2$ (186.21): calcd. C 77.40, H 5.41; found C 77.37, H 5.23.

Methyl 4′-Bromobiphenyl-2-carboxylate, BrbiphCO$_2$Me (2): 4-Bromophenylboronic acid (5.00 g, 24.9 mmol) was added to methyl 2-iodobenzoate (4.35 g, 16.6 mmol) in THF (60 mL) and 1 M aqueous Na_2CO_3 (60 mL). The reaction mixture was deoxygenated by bubbling argon through it with stirring for 30 min, whereupon [$PdCl_2(PPh_3)_2$] (0.540 g, 5 mol-%) was added. The reaction mixture was heated to 60 °C, and the initial orange-red color turned yellow after ca. 1 h. After 6 h, the dark reaction mixture was cooled to room temperature. Water (200 mL) was added and the product extracted with CH_2Cl_2 (2 × 150 mL). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated to dryness. The product was purified by column chromatography (SiO_2; hexanes/diethyl ether, 95:5) to give a colorless oil. Yield 4.05 g (84%). R_f = 0.35 (hexanes/Et_2O, 95:5). ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 7.86 (d, J = 7.5 Hz, 1 H, H^{Ar}), 7.53 (d, J = 8.4 Hz, 2 H, H^{Ar}), 7.58–7.50 (m, 1 H, H^{Ar}), 7.44 (t, J = 7.8 Hz, 1 H, H^{Ar}), 7.34 (d, J = 7.8 Hz, 1 H, H^{Ar}), 7.19 (d, J = 8.4 Hz, 2 H, H^{Ar}), 3.68 (s, 3 H, CH_3) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 20 °C): δ = 168.8 (CO_2), 141.6 (C^{Ar}), 140.5 (C^{Ar}), 131.7 (C^{Ar}), 131.3 (C^{Ar}), 130.8 (C^{Ar}), 130.6 (C^{Ar}), 130.24 (C^{Ar}), 130.17 (C^{Ar}), 127.7 (C^{Ar}), 121.7 (C^{Ar}), 52.2 (CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 3061 (w), 3023 (m), 2993 (w), 2948 (m) [ν(C–H)]; 1728 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for [M + Na]$^+$ 313.0; found 312.9. $C_{14}H_{11}BrO_2$ (291.14): calcd. C 57.76, H 3.81; found C 57.87, H 3.55.

Methyl 4-Bromo-1,1′:3′,1′′-terphenyl-2′-carboxylate, BrterphCO$_2$Me (3): 4-Bromophenylboronic acid (1.78 g, 8.86 mmol) was added to methyl 3-iodobiphenyl-2-carboxylate (2.00 g, 5.91 mmol) in THF (20 mL) and 1 M aqueous Na_2CO_3 (15 mL). The reaction mixture was deoxygenated by bubbling argon through it for 20 min, after which [$PdCl_2(PPh_3)_2$] (0.210 g, 5 mol-%) was added. The reaction mixture was heated to 50 °C, and the brownish orange-red emulsion turned yellow after ca. 1 h. After 6 h, the reaction mixture was cooled to room temperature. Water (50 mL) was added and the product extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated to dryness. The product was purified by column chromatography (SiO_2; hexanes/diethyl ether, 95:5) to give a white powder. Yield 1.65 g (76%). M.p. 120–121 °C. R_f = 0.38 (hexanes/Et_2O, 95:5). ^{1}H NMR (300 MHz, CD_3OD, 20 °C): δ = 7.56–7.49 (m, 3 H, H^{Ar}), 7.40–7.20 (m, 9 H, H^{Ar}), 3.32 (s, 3 H, CH_3) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 20 °C): δ = 169.8 (CO_2), 140.6 (C^{Ar}), 140.4 (C^{Ar}), 139.5 (C^{Ar}), 139.2 (C^{Ar}), 131.6 (C^{Ar}), 130.2 (C^{Ar}), 129.5 (C^{Ar}), 129.3 (C^{Ar}), 128.8 (C^{Ar}), 128.3 (C^{Ar}), 128.2 (C^{Ar}), 127.8 (C^{Ar}), 122.1 (C^{Ar}), 52.0 (CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 3052 (w), 2947 (m) [ν(C–H)]; 1740 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for [M + Na]$^+$ 389.0; found 389.0. X-ray diffraction quality single crystals were grown by slow concentration from a saturated solution of the compound in CD_3OD at room temperature.

2,3-Bis{2-[2′-(methoxycarbonyl)biphenyl-4-yl]ethynyl}triptycene, DET(biphCO$_2$Me)$_2$ (4a): A portion of [$Pd(PPh_3)_4$] (0.300 g, 10 mol-%) was added to a solution of 2,3-diethynyltriptycene (0.780 g, 2.56 mmol) and methyl 4′-bromobiphenyl-2-carboxylate (**2**)

(1.50 g, 5.15 mmol) in Et_3N (4.0 mL) and THF (24 mL) in a sealed pressure vessel inside a dry box. Then the yellow-orange solution was heated at 70 °C for 36 h. After cooling to room temperature, ethyl acetate (200 mL) was added to the very dark orange reaction mixture, which contained a white precipitate, presumably (Et_3NH)-Br. After extracting twice with aq. NH_4Cl (2 × 100 mL), the organic phase was dried with $MgSO_4$, filtered, and concentrated to dryness. The product was purified by column chromatography (CH_2Cl_2/hexanes, 8:2), and further purified by stirring in dichloroethane (70 mL) in the presence of the Pd-scavenger MP-TMT (550 mg) at room temperature for 24 h. The resin was filtered off the solution, and the filtrate was concentrated to dryness to give a light yellow product. Yield 1.11 g (60%). M.p. 138–139 °C. R_f = 0.44 (hexanes/EtOAc, 7:3). ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 7.84 (d, J = 6.9 Hz, 2 H, H^{Ar}), 7.61 (s, 2 H, H^{Ar}), 7.58 (d, J = 8.7 Hz, 4 H, H^{Ar}), 7.54 (m, 2 H, H^{Ar}), 7.45–7.34 (m, 10 H, H^{Ar}), 7.29 (d, J = 8.4 Hz, 2 H, H^{Ar}), 7.05 (dd, J = 2.7, 5.4 Hz, 4 H, H^{Ar}), 5.45 (s, 2 H, CH), 3.64 (s, 6 H, CH_3) ppm. ^{13}C NMR (500 MHz, [D_6]DMSO, 20 °C): δ = 168.2 (CO_2), 146.2 (C^{Ar}), 144.3 (C^{Ar}), 141.1 (C^{Ar}), 140.4 (C^{Ar}), 131.7 (C^{Ar}), 131.2 (C^{Ar}), 130.5 (C^{Ar}), 130.4 (C^{Ar}), 129.5 (C^{Ar}), 128.7 (C^{Ar}), 127.9 (C^{Ar}), 126.8 (C^{Ar}), 125.4 (C^{Ar}), 123.9 (C^{Ar}), 121.6 (C^{Ar}), 121.1 (C^{Ar}), 92.6 (C≡C), 88.9 (C≡C), 51.97 (CH_3 or CH), 51.95 (CH_3 or CH) ppm. FTIR (KBr): $\tilde{\nu}$ = 3059 (w), 3020 (w), 2947 (m) [ν(C–H)]; 2207 (w) [ν(C≡C)]; 1745 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M + Na]^+$ 745.2; found 745.2; calcd. for $[M + K]^+$ 761.2; found 761.3. $C_{52}H_{34}O_4$ (722.82): calcd. C 86.41, H 4.74; found C 85.97, H 4.42. X-ray diffraction quality single crystals were grown from EtOAc/hexanes, and the composition of **4a** was confirmed by X-ray crystallography. However, the data set was too poor to be published.

2,3-Bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]triptycene, DET-(biphCO_2H)$_2$ (4b): The methyl ester **4a** (0.500 g, 0.69 mmol) and anhydrous lithium iodide (1.39 g, 10.4 mmol) were dissolved in anhydrous pyridine (40 mL) in a sealed tube inside a glove box. The reaction mixture was heated at 110–115 °C in the dark (Al foil) for 5 d. After cooling to room temperature, the dark solution was quenched with water (200 mL), $CHCl_3$ (150 mL) was added, and the aqueous phase acidified with 4 M HCl to pH = 1. The acidic aqueous phase was washed with $CHCl_3$ (100 mL), and the combined organic phases were washed with water (3 × 150 mL), dried with $MgSO_4$, filtered, and concentrated to dryness. The residue was washed with a small amount of cold ethyl acetate and pentane to give a white powder, which was dried under high vacuum. Yield 0.350 g (73%). M.p. 276–277 °C. R_f = 0.47 (hexanes/EtOAc, 2:8 + one drop of acetic acid). ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 12.89 (s, 2 H, CO_2), 7.78–7.43 (m, 4 H, H^{Ar}), 7.61–7.55 (m, 6 H, H^{Ar}), 7.52–7.44 (m, 6 H, H^{Ar}), 7.42–7.37 (m, 6 H, H^{Ar}), 7.06 (q, 4 H, H^{Ar}), 5.77 (s, 2 H, CH) ppm. ^{13}C NMR (500 MHz, [D_6]-DMSO, 20 °C): δ = 169.4 (CO_2), 146.2 (C^{Ar}), 144.3 (C^{Ar}), 141.6 (C^{Ar}), 140.3 (C^{Ar}), 132.1 (C^{Ar}), 131.0 (C^{Ar}), 130.4 (C^{Ar}), 129.4 (C^{Ar}), 128.9 (C^{Ar}), 127.7 (C^{Ar}), 126.9 (C^{Ar}), 125.4 (C^{Ar}), 123.9 (C^{Ar}), 121.5 (C^{Ar}), 121.0 (C^{Ar}), 92.7 (C≡C), 88.8 (C≡C), 52.0 (CH) ppm. FTIR (KBr): $\tilde{\nu}$ = 3061 (m), 3019 (w), 2962 (m) [ν(C–H)]; 2210 (m) [ν(C≡C)]; 1684 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M - H]^-$ 693.2; found 693.3; calcd. for $[M + Na]^+$ 717.2; found 717.3. $C_{50}H_{30}O_4 \cdot H_2O$ (712.8): calcd. C 84.25, H 4.52; found C 84.20, H 4.15. Recrystallization from hot MeOH resulted in single crystals suitable for X-ray diffraction studies.

2,3-Bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]triptycene Disodium Salt, DET (biphCO_2Na)$_2$ (4c). Method A: NaOH (5.8 mg, 0.14 mmol) and **4b** (50 mg, 72 μmol) were heated in MeOH (7 mL) at 50 °C for 5 h. The solution was concentrated to dryness and dried under high vacuum at 60 °C overnight. Yield 52 mg (98%). **Method B:** A reaction mixture of **4a** (0.50 g, 0.69 mmol) and sodium trimethylsilanolate (0.31 g, 2.8 mmol) in THF (30 mL) was heated at 60 °C for 24 h. After cooling the reaction mixture to room temperature, diethyl ether (100 mL) was added and the mixture stirred at room temperature for an additional 1 h. The tan-colored product was filtered off, washed with dichloromethane, diethyl ether, and dried under vacuum at 60 °C overnight. Yield 0.51 g (99%). M.p. >300 °C. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 7.75 (s, 2 H, H^{Ar}), 7.58 (d, J = 8.7 Hz, 4 H, H^{Ar}), 7.55–7.45 (m, 8 H, H^{Ar}), 7.35–7.29 (m, 2 H, H^{Ar}), 7.25–7.20 (m, 6 H, H^{Ar}), 7.05 (q, 4 H, H^{Ar}), 5.76 (s, 2 H, CH) ppm. ^{13}C NMR (500 MHz, [D_6]DMSO, 20 °C): δ = 174.0 (CO_2), 146.0 (C^{Ar}), 144.4 (C^{Ar}), 143.5 (C^{Ar}), 142.9 (C^{Ar}), 136.4 (C^{Ar}), 130.7 (C^{Ar}), 128.9 (C^{Ar}), 127.3 (C^{Ar}), 126.9 (C^{Ar}), 126.6 (C^{Ar}), 126.5 (C^{Ar}), 125.4 (C^{Ar}), 123.9 (C^{Ar}), 121.9 (C^{Ar}), 120.1 (C^{Ar}), 93.2 (C≡C), 88.3 (C≡C), 52.0 (CH) ppm. FTIR (KBr): $\tilde{\nu}$ = 3060 (m), 3018 (m), 2956 (m) [ν(C–H)]; 2203 (w) [ν(C≡C)]; 1601 (m), 1580 (s), 1559 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M - Na]^-$ 715.2; found 715.0. $C_{50}H_{28}O_4Na_2 \cdot 1.25H_2O$ (761.25): calcd. C 78.89, H 4.04; found C 78.86, H 4.07.

2,3-Bis{2-[2′-(methoxycarbonyl)-*m*-terphenyl-4-yl]ethynyl}-triptycene, DET(terphCO_2Me)$_2$ (5): A portion of $[Pd(PPh_3)_4]$ (0.040 g, 10 mol-%) was added to a solution of 2,3-diethynyltriptycene (0.103 g, 0.34 mmol) and **3** (0.250 g, 0.68 mmol) in Et_3N (0.50 mL) and THF (5 mL) in a sealed pressure vessel inside a dry box. The yellow solution was heated at 70 °C for 36 h. After cooling to room temperature, ethyl acetate (30 mL) was added to the very dark orange reaction mixture, which contained a white precipitate, presumably (Et_3NH)Br. After extracting twice with aq. NH_4Cl (2 × 25 mL), the organic phase was dried with $MgSO_4$, filtered, and stripped to dryness. The product was purified by column chromatography (EtOAc/hexanes, 25:75). The isolated material was then stirred in dichloroethane with MP-TMT (Pd-scavenger) at room temperature for 24 h. The resin was filtered off the solution, and the filtrate was concentrated to dryness to give a light yellow product. Yield 0.060 g (20%). M.p. 167–168.5 °C. R_f = 0.65 (hexanes/EtOAc, 1:1). ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 7.84 (s, 2 H), 7.67–7.60 (m, 6 H), 7.51–7.31 (m, 22 H), 7.05 (dd, 4 H), 5.78 (s, 2 H), 3.35 (s, 6 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 20 °C): δ = 169.4 (CO_2), 145.6 (C^{Ar}), 144.5 (C^{Ar}), 140.7 (C^{Ar}), 140.6 (C^{Ar}), 139.8 (C^{Ar}), 132.8 (C^{Ar}), 131.7 (C^{Ar}), 129.7 (C^{Ar}), 129.4 (C^{Ar}), 128.9 (C^{Ar}), 128.63 (C^{Ar}), 128.56 (C^{Ar}), 128.53 (C^{Ar}), 127.8 (C^{Ar}), 127.1 (C^{Ar}), 125.8 (C^{Ar}), 124.0 (C^{Ar}), 122.9 (C^{Ar}), 92.7 (C≡C), 89.6 (C≡C), 53.8 (CH or CH_3), 52.1 (CH or CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 3020 (w), 2945 (m) [ν(C–H)]; 2204 (w) [ν(C≡C)]; 1730 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH/CH_2Cl_2, 1:1): calcd. for $[M + Na]^+$ 897.3; found 897.3.

4,5-Bis{2-[2′-(methoxycarbonyl)biphenyl-4-yl]ethynyl}veratrole, DEV(biphCO_2Me)$_2$ (6a): Portions of $[Pd(PPh_3)_4]$ (0.14 g, 10 mol-%) and CuI (19 mg, 5 mol-%) were added to a deoxygenated solution of 4,5-diethynylveratrole (**1**) (0.370 g, 1.99 mmol) and methyl 4′-bromobiphenyl-2-carboxylate (**2**) (1.27 g, 4.38 mmol) in Et_3N (5.0 mL) and THF (25 mL). The reaction mixture was stirred at 70 °C for 24 h. The product was extracted with CH_2Cl_2 (2 × 100 mL) and washed with aq. NH_4Cl (100 mL). The organic phases were dried with Na_2SO_4, filtered, and the solvents evaporated to dryness. The product was purified by column chromatography (CH_2Cl_2/diethyl ether, 95:5), and further purified with the Pd-scavenger MP-TMT (0.3 g) in $CHCl_3$ (10 mL). Yield 0.920 g (76%). R_f = 0.47 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 7.85 (dd, J = 7.8, 1.2 Hz, 2 H, H^{Ar}), 7.63 (d, J = 8.1 Hz, 4 H, H^{Ar}), 7.56 (td, J = 7.8, 1.8 Hz, 2 H, H^{Ar}), 7.46–7.38 (m, 4 H, H^{Ar}), 7.31 (d, J = 8.7 Hz, 4 H, H^{Ar}), 7.07 (s, 2 H, H^{Ar}), 3.96 (s, 6 H,

OCH_3), 3.63 (s, 6 H, CO_2CH_3) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 20 °C): δ = 169.2 (CO_2), 149.2 (C^{Ar}), 141.9 (C^{Ar}), 141.5 (C^{Ar}), 131.6 (C^{Ar}), 131.4 (C^{Ar}), 130.9 (C^{Ar}), 130.7 (C^{Ar}), 130.2 (C^{Ar}), 128.6 (C^{Ar}), 127.7 (C^{Ar}), 122.6 (C^{Ar}), 119.0 (C^{Ar}), 114.1 (C^{Ar}), 92.4 (C≡C), 89.2 (C≡C), 56.2 (OCH_3), 52.2 (CO_2CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 2941 (m), 2918 (m), 2849 (w) [ν(C–H)]; 2205 (w) [ν(C≡C)]; 1726 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M + Na]^+$ 629.2; found 629.2. $C_{40}H_{30}O_6$ (606.66): calcd. C 79.19, H 4.98; found C 78.54, H 5.03.

4,5-Bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]veratrole, DEV-(biphCO_2H)$_2$ (6b): A portion of DEV(biphCO_2Me)$_2$ (**6a**) (0.600 g, 0.99 mmol) and anhydrous lithium iodide (2.00 g, 15.0 mmol) were dissolved in anhydrous pyridine (35 mL) in a sealed pressure tube inside a glove box. The reaction mixture was heated at 110 °C under protection of light (Al foil) for 6 d. After cooling to room temperature, the dark solution was quenched with water (200 mL). Then $CHCl_3$ (150 mL) was added and the aqueous phase acidified with 4 M HCl to pH = 1. The acidic aqueous phase was washed with $CHCl_3$ (100 mL), and the combined organic phases were washed with water (2 × 150 mL), dried with $MgSO_4$, filtered, and the solvents evaporated to dryness. The product was washed with pentane and dried under high vacuum. Yield 0.320 g (56%). ^1H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 11.11 (br. s, 2 H, CO_2), 7.99 (d, J = 8.5 Hz, 2 H, H^{Ar}) 7.64–7.57 (m, 6 H, H^{Ar}), 7.49–7.44 (m, 4 H, H^{Ar}), 7.37 (d, J = 8.4 Hz, 4 H, H^{Ar}), 7.08 (s, 2 H, H^{Ar}), 3.97 (s, 6 H, OCH_3) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 20 °C): δ = 175.2 (CO_2), 149.3 (C^{Ar}), 142.6 (C^{Ar}), 140.8 (C^{Ar}), 132.6 (C^{Ar}), 131.7 (C^{Ar}), 131.2 (C^{Ar}), 131.1 (C^{Ar}), 129.7 (C^{Ar}), 128.7 (C^{Ar}), 127.8 (C^{Ar}), 122.7 (C^{Ar}), 119.9 (C^{Ar}), 113.4 (C^{Ar}), 92.6 (C≡C), 88.8 (C≡C), 56.3 (OCH_3) ppm.

4,5-Bis[2-(2′-carboxybiphenyl-4-yl)ethynyl]veratrole Disodium Salt, DEV(biphCO_2Na)$_2$ (6c): A reaction mixture containing DEV-(biphCO_2Me)$_2$ (**6a**) (200 mg, 0.33 mmol) and sodium trimethylsilanolate (93.0 mg, 0.82 mmol) in THF (50 mL) was stirred at 60 °C for 3 d. After cooling to room temperature, diethyl ether (70 mL) was added to the resulting suspension, and the mixture was stirred at room temperature for an additional 1 h. The white product was filtered off, washed with diethyl ether, and dried under vacuum at room temperature. Yield 190 mg (92%). M.p. >300 °C. ^1H NMR (300 MHz, [D$_6$]DMSO, 20 °C): δ = 7.61–7.49 (m, 8 H, H^{Ar}), 7.34 (m, 2 H, H^{Ar}), 7.26 (m, 6 H, H^{Ar}), 7.19 (s, 2 H, H^{Ar}), 3.86 (s, 6 H, OCH_3) ppm. ^{13}C NMR (500 MHz, [D$_6$]DMSO, 20 °C): δ = 174.2 (CO_2), 149.2 (C^{Ar}), 143.5 (C^{Ar}), 142.5 (C^{Ar}), 136.4 (C^{Ar}), 130.6 (C^{Ar}), 128.9 (C^{Ar}), 128.8 (C^{Ar}), 127.3 (C^{Ar}), 126.8 (C^{Ar}), 126.6 (C^{Ar}), 120.4 (C^{Ar}), 118.1 (C^{Ar}), 114.0 (C^{Ar}), 92.5 (C≡C), 88.7 (C≡C), 55.8 (OCH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 2960 (w) [ν(C–H)]; 2208 (w) [ν(C≡C)]; 1600 (s), 1578 (s), 1562 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M - Na]^-$ 599.1; found 599.0; calcd. for $[M - 2\,Na + H]^-$ 577.2; found 577.2.

4,5-Bis{2-[2′-(methoxycarbonyl)-*m*-terphenyl-4-yl]ethynyl}veratrole, DEV(terCO_2Me)$_2$ (7): Solid $[Pd(PPh_3)_4]$ (0.040 g, 10 mol-%) was added to a solution of 4,5-diethynylveratrole (**1**) (0.063 g, 0.34 mmol) and **3** (0.25 g, 0.68 mmol) in Et_3N (0.50 mL) and THF (15 mL) in a sealed pressure vessel inside a dry box. The yellow solution was heated at 70 °C for ca. 36 h. After cooling to room temperature, CH_2Cl_2 (30 mL) was added to the very dark orange reaction mixture, which contained a white precipitate, presumably (Et_3NH)Br. After washing with aq. NH_4Cl (2 × 25 mL), the organic phase was dried with $MgSO_4$, filtered, and concentrated to dryness. The product was purified by column chromatography (CH_2Cl_2/hexanes, 28:12). Yield 0.22 g (9%). R_f = 0.58 (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 7.64–7.61 (m, 4 H, H^{Ar}), 7.53 (t, J = 8.4 Hz, 2 H, H^{Ar}), 7.42–7.36 (m, 18 H, H^{Ar}), 7.07 (s, 2 H, H^{Ar}), 3.96 (s, 6 H, OCH_3), 3.40 (s, 6 H, CO_2CH_3) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 20 °C): δ = 169.9 (CO_2), 149.3 (C^{Ar}), 140.7 (C^{Ar}), 140.7 (C^{Ar}), 140.6 (C^{Ar}), 139.8 (C^{Ar}), 132.9 (C^{Ar}), 131.7 (C^{Ar}), 129.7 (C^{Ar}), 129.4 (C^{Ar}), 128.9 (C^{Ar}), 128.7 (C^{Ar}), 128.6 (C^{Ar}), 128.5 (C^{Ar}), 127.8 (C^{Ar}), 122.9 (C^{Ar}), 119.0 (C^{Ar}), 114.2 (C^{Ar}), 92.3 (C≡C), 89.4 (C≡C), 56.3 (OCH_3), 52.1 (CO_2CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 2961 (m), 2945 (m) [ν(C–H)]; 2206 (w) [ν(C≡C)]; 1729 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M + Na]^+$ 781.3; found 781.3.

4,5-Bis{2-[6-(methoxycarbonyl)pyrid-3-yl]ethynyl}veratrole, DEV(PICMe)$_2$ (8): Solid $[Pd(PPh_3)_4]$ (0.27 g, 10 mol-%) was added to a deoxygenated solution of 4,5-diethynylveratrole (**1**) (0.430 g, 2.31 mmol), and methyl 5-bromo-2-picolinate (1.10 g, 5.09 mmol) in Et_3N (5.0 mL) and THF (25 mL). The yellow solution was heated at 60 °C for 36 h. The reaction mixture with some yellow precipitate was cooled to room temperature, concentrated to dryness, and dissolved in $CHCl_3$ (150 mL). The organic phase was washed with aq. NH_4Cl (150 mL), which was dried with Na_2SO_4, filtered, and the solvents were evaporated to dryness. The product was purified by column chromatography ($CHCl_3$/diethyl ether, 97:3). Yield 0.980 g (93%). M.p. 188–189 °C. R_f = 0.42 ($CHCl_3$/Et_2O, 95:5). ^1H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 8.87 (d, J = 1.8 Hz, 2 H, H^{Ar}), 8.13 (d, J = 8.1 Hz, 2 H, H^{Ar}), 7.95 (dd, J = 8.1, 1.8 Hz, 2 H, H^{Ar}), 7.09 (s, 2 H, H^{Ar}), 4.04 (s, 6 H, CH_3), 3.98 (s, 6 H, CH_3) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 20 °C): δ = 165.3 (CO_2), 152.0 (C^{Ar}), 150.1 (C^{Ar}), 146.3 (C^{Ar}), 139.1 (C^{Ar}), 124.8 (C^{Ar}), 124.0 (C^{Ar}), 118.1 (C^{Ar}), 114.3 (C^{Ar}), 94.4 (C≡C), 88.8 (C≡C), 56.3 (OCH_3), 53.3 (CO_2CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 2947 (m) [ν(C–H)]; 2205 (s) [ν(C≡C)]; 1742 (s), 1720 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M + Na]^+$ 479.1; found 479.0.

4,5-Bis{2-[8-(ethoxycarbonyl)quinol-3-yl]ethynyl}veratrole, DEV(quinolineCO_2Et)$_2$ (9): A portion of $[PdCl_2(PPh_3)_2]$ (0.14 g, 10 mol-%) and CuI (19 mg, 5 mol-%) were added to a deoxygenated solution of 4,5-diethynylveratrole (**1**) (0.370 g, 1.97 mmol) and ethyl 3-[(trifluoromethyl)sulfonyl]quinoline-8-carboxylate (1.51 g, 4.32 mmol) in Et_3N (5.0 mL) and THF (25 mL). The reaction mixture was stirred at room temperature overnight. CH_2Cl_2 (150 mL) was added to the reaction mixture, which was washed with aq. NH_4Cl (100 mL). The organic phase was dried with Na_2SO_4, filtered, and stripped to dryness. The product was purified by column chromatography (CH_2Cl_2/diethyl ether, 95:5). Yield 0.920 g (80%). M.p. 168–169 °C. R_f = 0.45 ($CHCl_3$/Et_2O, 95:5). ^1H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 9.18 (d, J = 2.1 Hz, 2 H, H^{Ar}), 8.34 (d, J = 1.8 Hz, 2 H, H^{Ar}), 8.04 (dd, J = 8.1, 1.2 Hz, 2 H, H^{Ar}), 7.88 (dd, J = 7.2, 1.2 Hz, 2 H, H^{Ar}), 7.59 (t, J = 7.8 Hz, 2 H, H^{Ar}), 7.13 (s, 2 H, H^{Ar}), 4.55 (q, J = 6.9 Hz, 4 H, CH_2), 4.00 (s, 6 H, OCH_3), 1.46 (t, J = 7.2 Hz, 6 H, CH_2CH_3) ppm. ^{13}C NMR (500 MHz, $CDCl_3$, 20 °C): δ = 167.6 (CO_2), 153.0 (C^{Ar}), 149.9 (C^{Ar}), 144.2 (C^{Ar}), 138.5 (C^{Ar}), 132.1 (C^{Ar}), 131.2 (C^{Ar}), 131.0 (C^{Ar}), 127.7 (C^{Ar}), 126.7 (C^{Ar}), 118.5 (C^{Ar}), 118.3 (C^{Ar}), 114.4 (C^{Ar}), 92.2 (C≡C), 89.6 (C≡C), 61.9 (CO_2CH_2), 56.4 (OCH_3), 14.56 (CH_2CH_3) ppm. FTIR (KBr): $\tilde{\nu}$ = 2981 (w), 2960 (m), 2937 (w), 2902 (w) [ν(C–H)]; 2209 (m) [ν(C≡C)]; 1731 (s) [ν(C=O)] cm^{-1}. ESI-MS (MeOH): calcd. for $[M + Na]^+$ 607.2; found 607.2.

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