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Regiocontrolled Synthesis and Optical Resolution of Mono-, Di-, and Trisubstituted Tribenzotriquinacene Derivatives: Key Building Blocks for Further Assembly into Molecular Squares and Cubes

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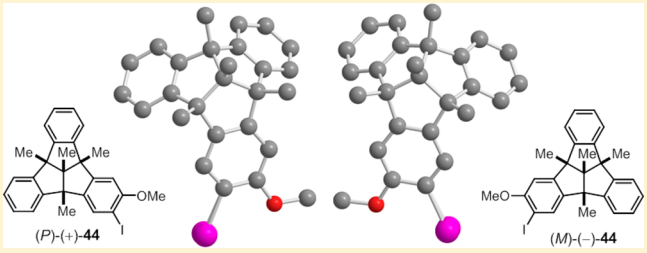
Supporting Information

ABSTRACT: The regiocontrolled syntheses of four chiral C_1- or C_3-symmetrical tribenzotriquinacene (TBTQ) derivatives bearing methoxy or hydroxy groups at the peripheral positions [(2,6-$(OMe)_2$, (±)-**18** and (±)-**20**; 2,6-$(OH)_2$, (±)-**19**; and 2,6,10-$(OMe)_3$, (±)-**21**] by two different synthesis protocols are reported. Compounds (±)-**19**, (±)-**20**, and (±)-**21** and two (already-known) monosubstituted C_1-symmetrical TBTQ analogues [2-OH (±)-**23** and 2-OMe (±)-**24**] were readily resolved by chiral HPLC, and their absolute configurations were determined by X-ray crystallography and/or circular dichroism (CD) studies. Optical resolution of three closely related TBTQ derivatives [2,6-$(OMe)_2$, (±)-**18**; 2-OMe, (±)-**22**; and 2-OH, (±)-**25**] containing the same peripheral substituents but other bridgehead residues failed. Enantiopure TBTQ derivatives of this sort are considered promising structural motifs toward the construction of molecular squares and cubes.



INTRODUCTION

Molecular self-assembly utilizing simple molecular fragments toward the synthesis of complex yet ordered molecular architectures is one of the greatest achievements in supramolecular chemistry.[1] Many of these self-organized systems have already shown applications in the fields of controlled drug delivery,[2] molecular sensing,[3,4] catalysis,[5] and host−guest complexation.[6−8] Because the self-assembly process is entropically unfavorable, the success of this approach relies heavily on the structural preorganization and geometrical matching of the various building blocks. Among the many structural motifs, the tribenzotriquinacene (TBTQ) skeletal system is of special interest. Owing to the nearly orthogonal disposition of the three indane ring systems,[9,10] TBTQ derivatives are ideally suited for the construction of molecular squares and cubes.[11] Indeed, several studies involving the use of TBTQ compounds to construct self-assembled systems have already appeared. For examples, Volkmer and co-workers demonstrated that a C_{3v}-symmetrical TBTQ host[12] and an optically pure C_3-symmetrical TBTQ host[13] can encapsulate a C_{60} guest molecule. Georghiou's and our groups also showed that C_{3v}-symmetrical TBTQ compounds can act as hosts for fullerenes such as C_{60} and C_{70}.[14,15]

To construct larger systems such as molecular squares and cubes that can accommodate larger or multiple guest molecules, designing molecular self-assembles using more than one TBTQ unit is a logical approach. Among all possible TBTQ derivatives, a limited variety of congeners, namely, 1,5- (**1**) and 2,6- (**2**) disubstituted derivatives, 1,5,9- (**3**) and 2,6,10- (**4**) trisubstituted derivatives, 1,2,5,6- (**5**) and 2,3,6,7- (**6**) tetrasubstituted derivatives, and finally 1,2,5,6,9,10- (**7**) and 2,3,6,7,10,11- (**8**) hexasubstituted derivatives that contain functional groups oriented at orthogonal geometries could serve as building blocks of molecular squares and cubes (Figure 1). Because of the high steric repulsion with the bridgehead substituents and the opposite aromatic ring, introduction of functionalities at the inner (1-, 4-, 5-, 8-, 9-, 12-) positions of the TBTQ system is difficult.[11,16] Hence, only derivatives **2**, **4**, **6**, and **8** are easily accessible targets.

However, two inherent problems have to be resolved to utilize these motifs. First, one has to develop regiocontrolled synthetic methods toward such multiply functionalized TBTQs. Based on our previous research results, it is known that the introduction of functional group(s) by electrophilic aromatic substitution of the parent TBTQ compounds **9** (R = Me or H) invariably produces mixtures of regioisomeric products. For example, two-fold formylation of the parent TBTQ derivative **9** (R = Me) gave an inseparable mixture of two C_s-symmetrical and one C_1-symmetrical diformyl derivatives **10**, **12**, and

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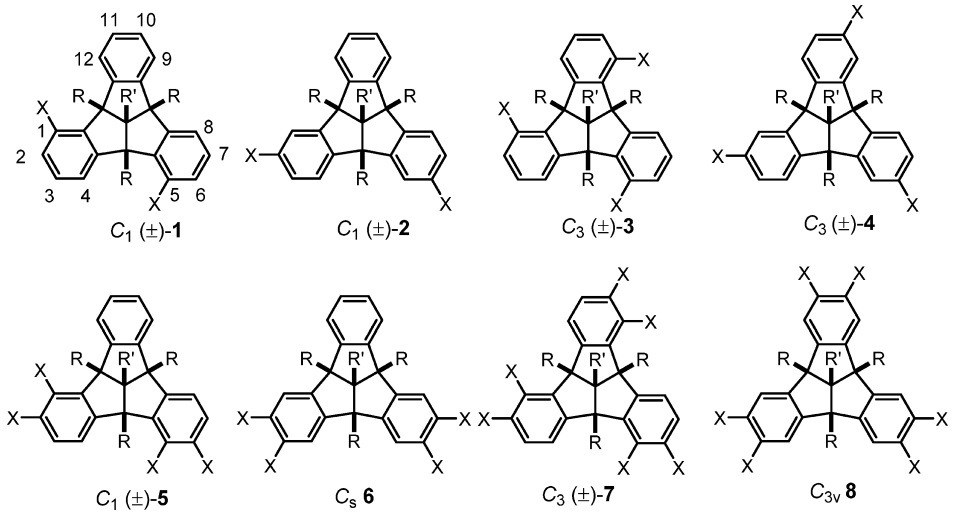

Figure 1. TBTQ derivatives that can be used to construct molecular squares and cubes.

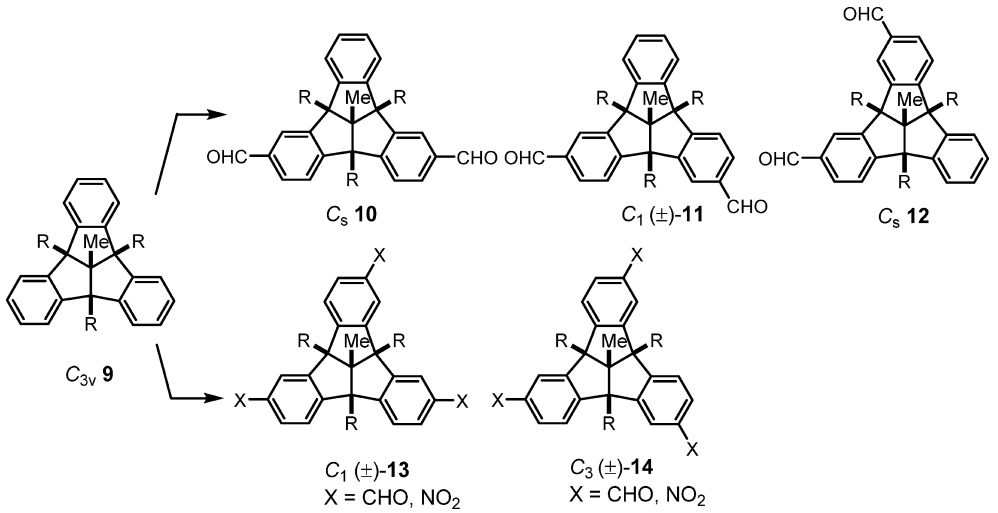

Figure 2. Synthesis of 2,6-difunctionalized TBTQ derivatives (±)-**11** and 2,6,10-trifunctionalized TBTQ derivatives (±)-**14** by electrophilic aromatic nitration or formylation.

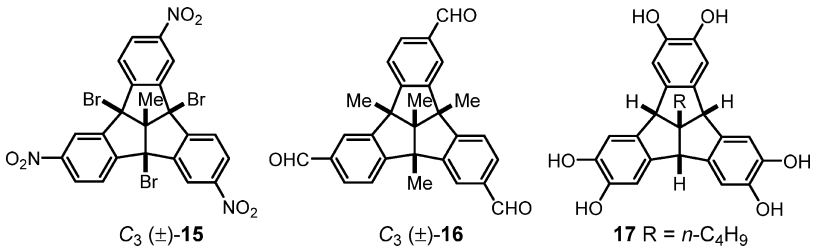

Figure 3. TBTQ derivatives used in the formation of self-assemblies containing more than one TBTQ unit.

(±)-**11** (R = Me), respectively (Figure 2).[17] Three-fold nitration of **9** (R = H[18] or Me[19]) produced a 3:1 mixture of the C_1- and C_3-symmetrical trinitro-TBTQ isomers (±)-**13** and (±)-**14** (R = H or Me, X = NO_2), respectively, whereas three-fold formylation[20] of **9** (R = Me) produced a 2:3 mixture of C_1- and C_3-symmetrical trialdehydes (±)-**13** and (±)-**14** (R = H, X = CHO), respectively. In both cases, tedious chromatographic separations were required to isolate the regioisomers in pure form. Gratifyingly, this regiochemistry issue was resolved by the recent report by Hopf and co-workers,[21] who demonstrated that the C_1-symmetric 2,6-disubstituted derivative (±)-**2** and the C_3-symmetric 2,6,10-trisubstituted analogue (±)-**4** could, in principle, be prepared in a highly regioselective manner. The second problem is associated with the inherent chirality of some of these derivatives. Whereas the tetrasubstituted **6** and hexasubstituted **8** are optically inactive, the 2,6-disubstituted derivative (±)-**2** and the 2,6,10-trisubstituted (±)-**4** analogue are inherently chiral. Hence, if the latter are to be used to construct self-assemblies containing more than one TBTQ unit, optically pure derivatives have to be used, unless a highly enantioselective self-sorting[22] could be realized during the self-assembly process involving these racemates. Such a highly

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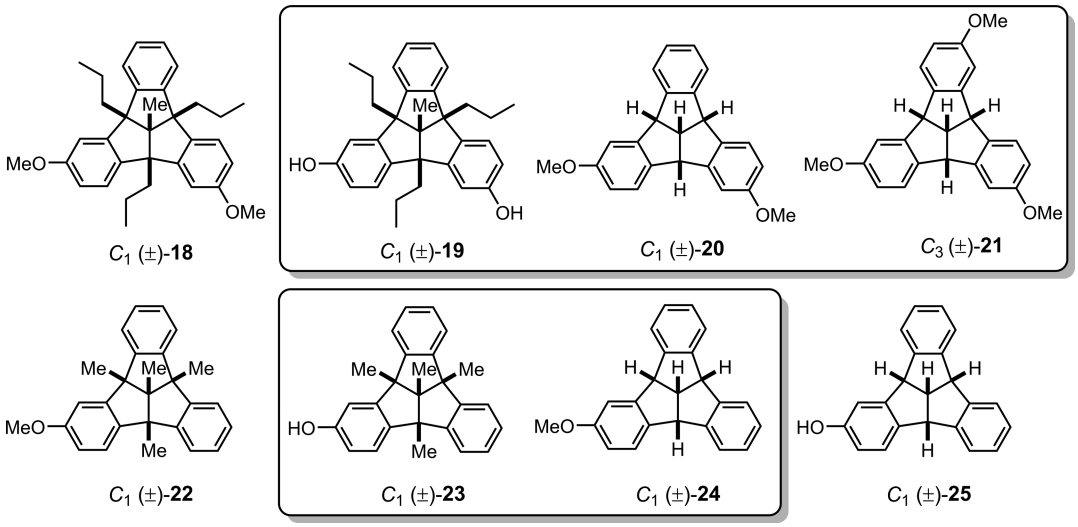


Figure 4. TBTQ derivatives synthesized in this study. Those included in the boxes are resolvable by chiral HPLC.

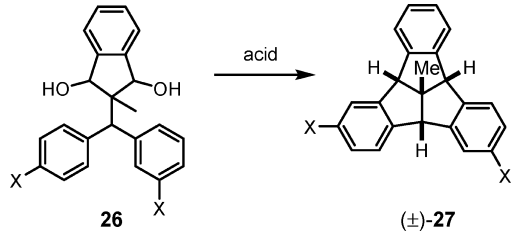
enantioselective self-sorting was observed once in our hands, but it occurred during a crystallization process. In this case, the racemic C_3-symmetrical tribromotrinitro TBTQ derivative (±)-**15** was found to form nanocubes by self-assembly of eight molecules of the same enantiomer (Figure 3).[18] However, an enantioselective self-sorting of this type has never occurred in the solution phase. For example, dynamic covalent synthesis between the racemic C_3-symmetrical trialdehyde (±)-**16** and optically pure (*S*,*S*)-diaminocyclohexane in a 2:3 molar ratio afforded a nearly statistical (~1:2:1) mixture of three cryptophane derivatives.[20] In this case, the major cryptophane product was found to contain one molecule of (+)-**16** and one molecule of (−)-**16**. Of course, the problems of both regioselectivity and optical resolution could be avoided if one employed the C_{3v}-symmetrical hexafunctionalized TBTQ compound **8** as the building block. In fact, this was recently demonstrated by Klotzbach et al. in the dynamic covalent assembly of a nanocube from the condensation of the 2,3,6,7,10,11-hexahydroxy-TBTQ derivative **17** and 1,4-diphenylenediboronic acid in a 2:3 stoichiometric ratio.[23]

To expand the application of TBTQ compounds (see Figure 4), it is necessary to develop methods that can prepare 2,6-disubstituted and 2,6,10-trisubstituted TBTQ derivatives with good regioselectivity and in optically pure form. Herein, we report some important progress toward such aims by (i) developing a regiocontrolled entry to the C_1-symmetrical 2,6-dimethoxy- and 2,6-dihydroxy-TBTQ derivatives (±)-**18** and (±)-**19**, respectively, by Kuck's method; (ii) synthesizing the C_1-symmetrical 2,6-dimethoxy-TBTQ derivative (±)-**20** and the C_3-symmetrical 2,6,10-trimethoxy-TBTQ derivative (±)-**21** based on Hopf's method; (iii) examining the possibility of resolving compounds (±)-**18**−(±)-**21** and closely related hydroxy-/methoxy-substituted TBTQ derivatives (±)-**22**−(±)-**25** by chiral HPLC; and (iv) determining the absolute configurations of the resolvable enantiomers by X-ray crystallography and/or circular dichorism (CD) spectroscopy. Conceptually, the phenolic and methyl ether groups could be conveniently transformed into the corresponding triflates, which could then be subjected to various functional-group conversions and C−C coupling reactions using transition-metal catalysis. Therefore, these new findings open up a convenient entry to a library of optically pure TBTQ molecules that could become useful toward the construction of a large variety of novel self-assembled systems.

RESULTS AND DISCUSSION

Regioselective Synthesis of C_1-Symmetrical Dimethoxy- and Dihydroxy-TBTQ Derivatives (±)-18 and (±)-19 Using Kuck's Method. In our reported synthesis of the TBTQ parent compound, the key step involved in the formation of the TBTQ skeleton **27** (X = H) was a double cyclization reaction from the 1,3-indanediol **26** (X = H) (Scheme 1).[11,24] It was envisaged that proper positioning of the

Scheme 1. Double Cyclization Strategy toward the 2,5-Difunctionalized TBTQ Skeleton by Kuck's Method



required functional groups with respect to the precursor molecule **26** before execution of this key double cyclization reaction should enable one to control both the number and positions of the introduced functionalities. In principle, C_1-symmetrical 2,6-disubstituted TBTQ derivatives (±)-**27** could be prepared from the corresponding precursors **26** having the functionalities X located at the para position of one of the phenyl rings and at the meta position of the other. Whereas cyclization involving the meta-substituted phenyl ring can incorporate the substituent X at either one of the inner or one of the outer arene positions of the emerging TBTQ framework, cyclization of the para-substituted ring introduces X exclusively at one of the outer positions. However, because of the repulsive interaction with the bridgehead hydrogen and the opposite benzene ring, incorporation of the substituent at one of the inner positions should be disfavored. As a result, the major product of the two-fold cyclization reaction should be the C_1-symmetrical, 2,6-disubstituted TBTQ derivative (±)-**27**.

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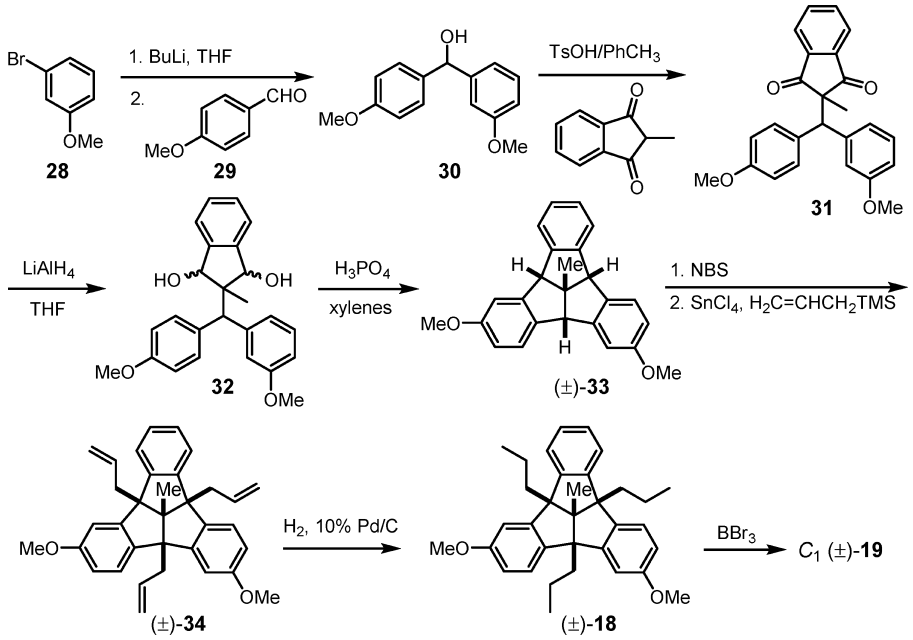
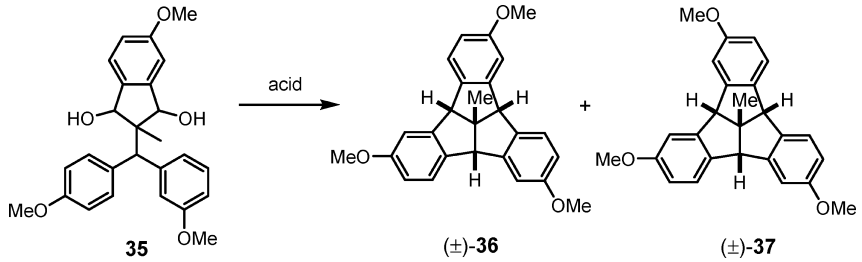
Scheme 2. Regiocontrolled Synthesis of Racemic C_1-Symmetrical 2,6-Disubstituted TBTQ Derivatives



Scheme 3. Possible Double Cyclization Strategy toward the 2,6,10- (±)-36 and 2,6,11- (±)-37 Trisubstituted TBTQ Skeletons



This idea was then executed by treatment of commercially available 3-bromoanisole **28** with 1.1 equiv of *n*-butyllithium followed by quenching with 4-methoxybenzaldehyde **29** to afford the known diarylmethanol **30**[25] in 85% yield (Scheme 2). Reaction of compound **30** and 2-methyl-1,3-indanedione in the presence of *para*-toluenesulfonic acid in refluxing toluene gave the coupling product **31** in 87% yield as a solid. The diketone **31** was then reduced to a diasteromeric mixture of diols **32** in 90% yield using lithium aluminum hydride. The mixture was then subjected to acid-catalyzed double cyclization with phosphoric acid to give the TBTQ derivative (±)-**33** in 18% yield. Although the presence of the electron-donating methoxy group should stabilize the cationic intermediates, the cyclization yield was slightly inferior to that (33%) of the reaction of the unsubstituted precursor (±)-**26** (X = H).[11,24] Incidentally, the ^{1}H and ^{13}C NMR spectra showed only the presence of isomer (±)-**33** in the isolated product. Hence, this method is clearly superior to the direct introduction of suitable electrophiles into the parent compound.

Compound (±)-**33** was then converted to the corresponding triallyl derivative (±)-**34** using the sequence of reactions reported before.[9] Hence, reaction of (±)-**33** with 4.0 equiv of *N*-bromosuccinimide (NBS) gave the crude bridgehead-substituted tribromide, which was not purified and was treated with allyltrimethylsilane in the presence of tin tetrachloride to give the triallyl derivative (±)-**34** in 33% overall yield. Catalytic hydrogenation of compound **34** in the presence of 10% palladium on charcoal in ethyl acetate furnished the tri-*n*-propyl TBTQ compound (±)-**18** in 91% yield. The three alkyl groups were essential to improve the solubility property of the TBTQ compounds. Finally, the two methyl ether groups were cleaved by boron tribromide to generate the 2,6-diphenol (±)-**19** in 90% yield.

Although Kuck's synthetic method allows the regioselective synthesis of the C_1-symmetrical (±)-2,6-disubstituted TBTQ derivative (±)-**18**, the same strategy could find problems in the synthesis of the C_3-symmetrical 2,6,10-trisubstituted TBTQ derivative (±)-**36** (Scheme 3). By introducing an additional methoxy group on the indane aromatic ring, there are now two possible double cyclization modes for substrate **35**. One cyclization route should give the desired C_3-symmetrical 2,6,10-trisubstituted product (±)-**36**, but the other should generate the C_1-symmetrical 2,6,11-trisubstituted regioisomer (±)-**37**. Knowing that Hopf's method can afford much better regiocontrol in producing the 2-substituted[26] and C_3-symmetrical TBTQ products,[21] it was therefore decided to use Hopf's method to prepare the C_1-symmetrical 2,6-dimethoxy-TBTQ derivative (±)-**20** and the C_3-symmetrical 2,6,10-trimethoxy-TBTQ analogue (±)-**21**.

Regioselective Synthesis of the C_1-Symmetrical 2,6-Dimethoxy- and C_3-Symmetrical 2,6,10-Trimethoxy-TBTQ Derivatives (±)-20 and (±)-21, Respectively, Using Hopf's Method. Treatment of the known 1,3-diketone **38**[27] and benzaldehyde **39** in the presence of piperidine and

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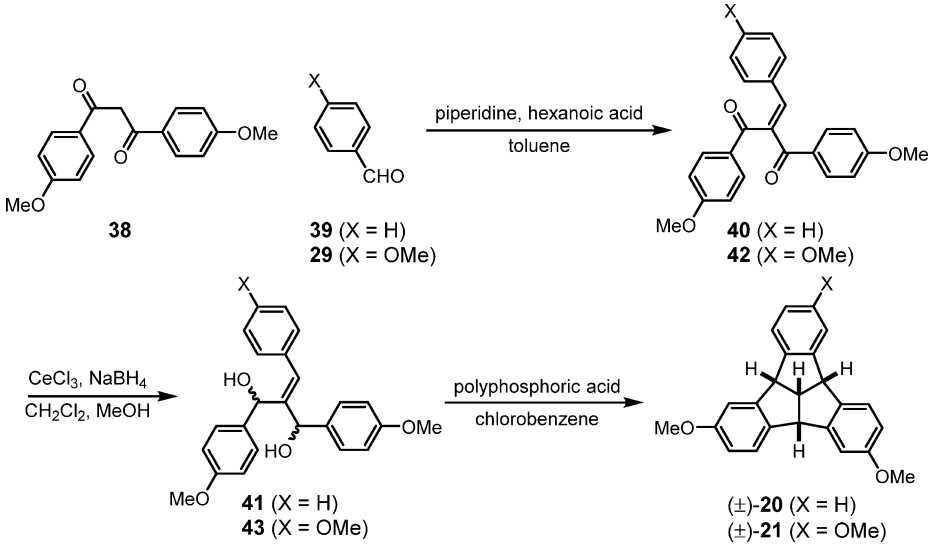
Scheme 4. Synthesis of the C_1-Symmetrical 2,6-Dimethoxy- and C_3-Symmetrical 2,6,10-Trimethoxy-TBTQ Derivatives (±)-20 and (±)-21, Respectively, Using Hopf's Method



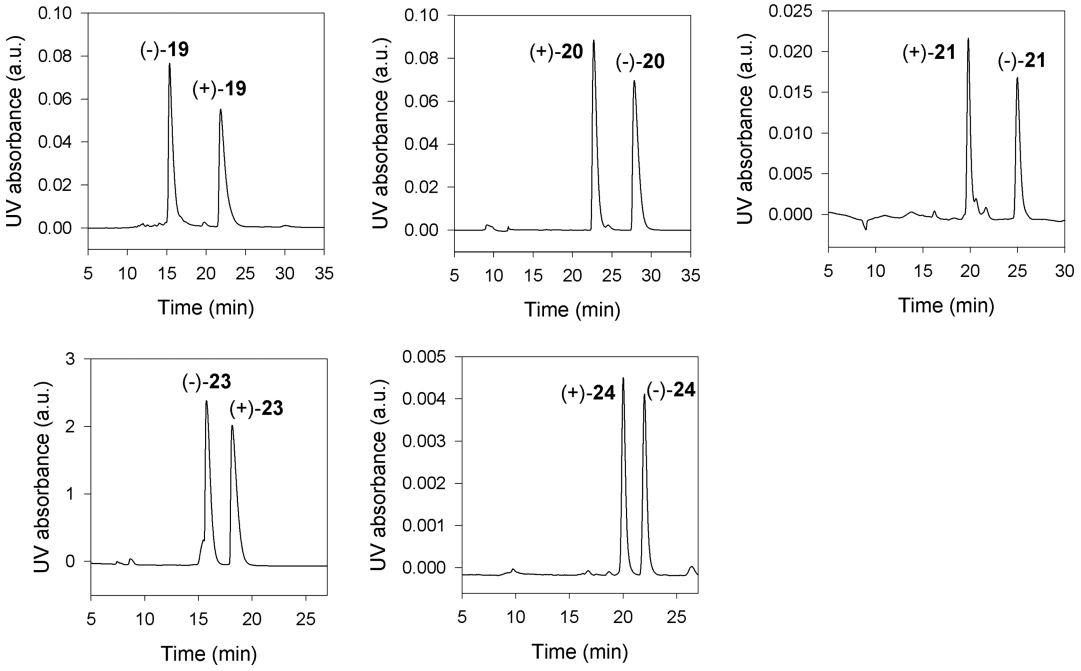


Figure 5. Chiral HPLC chromatograms of compounds (±)-**19**, (±)-**20**, (±)-**21**, (±)-**23**, and (±)-**24**.

hexanoic acid in refluxing toluene afforded the condensation product **40** as a yellow solid in 78% yield (Scheme 4). The diketone **40** was reduced to a separable mixture of diastereomeric diols **41** in 90% yield using sodium borohydride in the presence of cerium(III) chloride. Practically, the diastereomers **41** were not separated and were subjected to cyclization in the presence of polyphosphoric acid (PPA) in chlorobenzene at 130 °C to give the 2,6-dimethoxy-TBTQ derivative (±)-**20** in 6% yield after recrystallization from toluene.

The 2,6,10-trimethoxy congener (±)-**21** was similarly prepared by replacing benzaldehyde with 4-methoxybenzaldehyde **29**. The condensation product **42** and the corresponding diol **43** were obtained in yields of 77% and 87%, respectively. However, the final cyclization reaction gave the desired trimethoxy-TBTQ derivative (±)-**21** in a dismal 1% yield after recrystallization from toluene. The poor cyclization yield involving substrates containing the electron-donating methoxy group was also observed by Hopf and co-workers.[21,26] Nonetheless, the facts that both target compounds (±)-**20** and (±)-**21** could be obtained in just three steps and that no tedious chromatographic purification was required still render this route the most straightforward approach to prepare the 2,6-disubstituted and 2,6,10-trisubstituted TBTQ molecules (±)-**20** and (±)-**21**.

Structural Characterization. All synthesized compounds were fully characterized by a combination of ^{1}H and ^{13}C NMR spectroscopies and mass spectral analysis (see Supporting Information for spectra). In all cases, the spectroscopic data were fully consistent with the proposed structures. The purities

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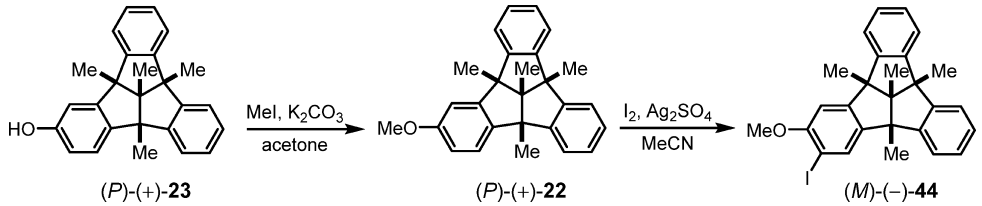
Scheme 5. Synthesis of the 2-Iodo-3-methoxy-TBTQ Derivative (*M*)-(−)-44 from (*P*)-(+)-23



(*P*)-(+)-**23** (*P*)-(+)-**22** (*M*)-(−)-**44**

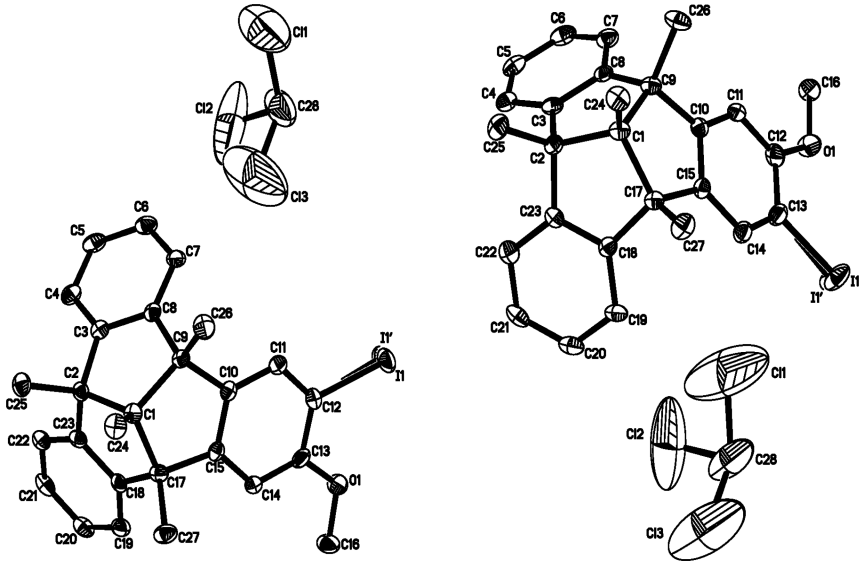


Figure 6. X-ray crystal structures of (left) (*M*)-(−)-**44** and (right) (*P*)-(+)-**44**, as obtained from hexane/$CHCl_3$, with one molecule of $CHCl_3$ per molecule of **44** (30% thermal ellipsoids).

of the compounds were also confirmed by examining the ^{1}H NMR spectra. For example, only two methoxy signals were found for the C_1-symmetrical 2,6-dimethoxy compounds (±)-**18**, (±)-**20**, and (±)-**33**, and only one methoxy signal was observed in the ^{1}H NMR spectrum of the C_3-symmetrical 2,6,10-trimethoxy compound (±)-**21**. In the case of the C_1-symmetrical compounds, the 18 carbon atoms of the three aromatic rings were all chemically different, but because of their very similar structural environments, partial signal overlapping in the ^{13}C NMR spectrum was noted. In contrast, the ^{13}C NMR spectrum of the C_3-symmetrical compound (±)-**21** was greatly simplified and was found to consist of nine signals, thus again confirming its C_3 symmetry.

Optical Resolution. Scant systematic study on the optical resolution of TBTQ derivatives is available in the literature. This is partly due to the previous lack of convenient regioselective synthetic routes to these molecules. Given that we have now secured methods for the preparation of the 2,6-dihydroxy-/dimethoxy-TBTQ derivatives (±)-**18**−(±)-**20** and the 2,6,10-trimethoxy-TBTQ derivative (±)-**21**, we decided to extend the optical resolution study to other known or readily prepared 2-hydroxy-/methoxy-TBTQ analogues such as (±)-**22**,[28] (±)-**23**,[29] (±)-**24**,[26] and (±)-**25**.[26]

All of these hydroxy-/methoxy-substituted TBTQ compounds were thus subjected to chiral HPLC analysis using a CHIRALPAK IB semipreparative column (20 mm × 250 mm) with a solvent mixture of hexane and 2-propanol in different ratios. Five compounds, namely, (±)-**19**, (±)-**20**, (±)-**21**, (±)-**23**, and (±)-**24**, were readily separable, whereas the remaining three were not (Figure 5). These eight compounds could be divided into two groups. One group (group I) contains bridgehead substituents, whereas the other (group II) does not. It was found that the hydroxy-substituted TBTQ derivatives in group I could be resolved, but the methoxy-substituted analogues were not separable. In contrast, the reverse was true for the group II derivatives: Only methoxy-substituted TBTQ derivatives in group II could be resolved, whereas the corresponding hydroxy-substituted analogues were not separable. It is not known whether this observation is just a coincidence or is due to some intriguing structural factors that we are unable to identify at this moment.

Determination of Absolute Configurations. The absolute configurations of the separated enantiomers were determined by circular dichroism (CD) spectroscopy and/or X-ray crystallography by introducing a heavy-atom scatterer into compound **23**. Hence, the (+)-**23** enantiomer, later identified to have the (*P*) absolute configuration, was converted into the corresponding methoxy derivative (*P*)-(+)-**22** in 95% yield by *O*-methylation (Scheme 5). The methoxy derivative (*P*)-(+)-**22** was then treated with iodine in the presence of silver(II) sulfate to give the 2-iodo-3-methoxy-TBTQ derivative (*M*)-(−)-**44** in 87% yield. Likewise, the (*M*)-(−)-**23** enantiomer was similarly converted into (*P*)-(+)-**44**. Both enantiomers of **44** were subjected to X-ray crystallographic analysis,[30] and thus, their absolute configurations were unambiguously established (Figure 6).

Unfortunately, similar iodination or bromination of other optically resolved TBTQ derivatives failed to produce crystals suitable for X-ray analysis. We therefore resorted to using circular dichorism (CD) spectroscopy to assign their absolute configurations. As the absolute configurations of the two enantiomers of **23** had already been confirmed, these

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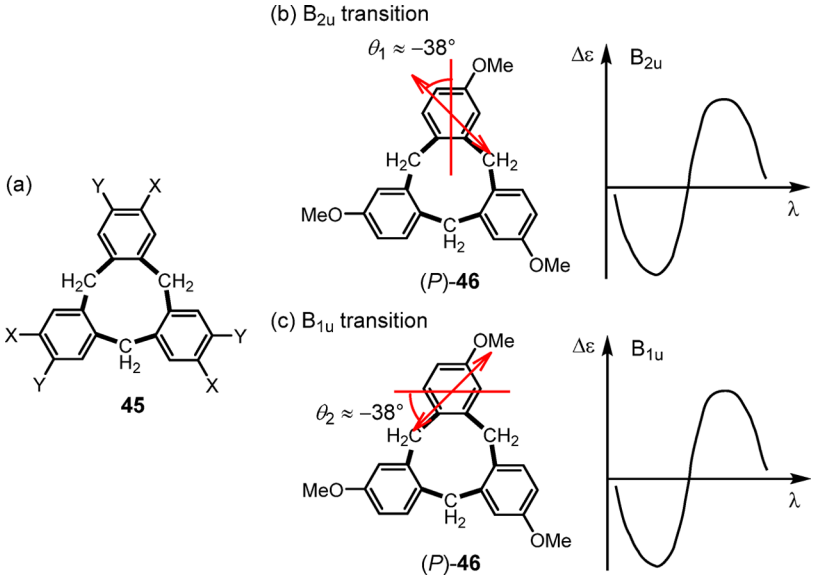

Figure 7. (a) Structure of cyclotribenzylenes **45** and (b,c) CD profiles of the (b) B_{2u} and (c) B_{1u} transitions of cyclotrianisylene derivative (*P*)-**46**.

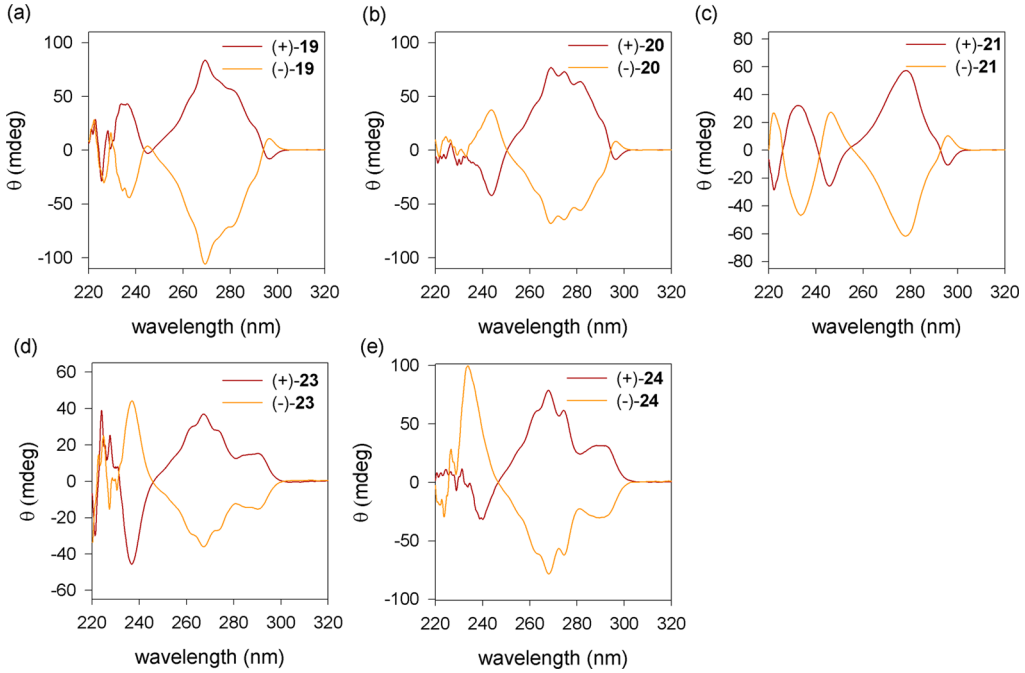

Figure 8. CD spectra (CH_2Cl_2, concentration = 1.5 mg/mL; path length = 1 mm) of the optically pure hydroxyl-/methoxy-substituted TBTQ derivatives **19**−**21**, **23**, and **24**.

enantiomers also served as testing cases to further validate the exciton model of C_3-symmetrical molecules derived from cyclotribenzylene (CTB) proposed by Collet and co-workers.[31−33] Although some of our TBTQ molecules do not exhibit C_3 symmetry, the model, being based on the exciton coupling between transition moments of the three aromatic chromophores, should be applicable to the rigid TBTQ alicyclic-aromatic skeleton that also falls into this structural category.[34] It should be noted that the exciton model was previously validated by checking with CTB derivatives of known absolute configuration.[32,35]

The CD profiles of optically active C_3-symmetric CTB **45** (X ≠ Y), especially that of the cyclotrianisylene derivative (*P*)-**46**, were thoroughly analyzed by Collet and co-workers (Figure 7).[32,33] Two key transitions, namely, B_{2u} and B_{1u}, located at approximately 290 and 240 nm, respectively, were identified in the CD spectra. The sign of each CD couplet was determined by the angle of rotation (defined as θ_1 for B_{2u} and θ_2 for B_{1u} in Figure 7) of the transition moment of B_{2u} and B_{1u}, which, in turn, was dependent on the relative magnitude of the spectroscopic moments of the substituents (OMe and H) and, hence, on the absolute configuration of the molecule. As the spectroscopic moment of H is known to be less than that of OMe and the angle of rotation (θ_1) of the transition moment (double-ended arrow in Figure 7b) responsible for the B_{2u} transition is known to fall in the range between 0° and −45° (actual value is about −38°),[32] the B_{2u} couplet generates a negative exciton pattern as shown in Figure 7b. For the B_{1u}

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transition, the transition moment is similarly known to have an angle of rotation (θ_2) of −38°. In this case, the CD profile again produces a negative exciton pattern as shown in Figure 7c. It should be noted that the CD profile is inverted for the (*M*)-enantiomer.

Examination of the CD profile of the (−)-enantiomer of the C_3-symmetric 2,6,10-trimethoxy-TBTQ derivative **21** identified two negative exciton patterns centered at around 293 nm (B_{2u}) and 242 nm (B_{1u}) (Figure 8c, yellow line). This spectral pattern matches perfectly well to that of (*P*)-**46**, and hence, (−)-**21** must exhibit a (*P*)-absolute configuration.

In the case of 2-hydroxy-TBTQ derivative **23**, it is already known from X-ray crystallography that the (+)-enantiomer exhibits the (*P*)-absolute configuration. It turns out that the spectroscopic moment of the hydroxy group is similar to that of the methoxy group.[32] As a result, the CD profile of the (*P*)-enantiomer of the 2-hydroxy-TBTQ derivative **23** should be similar to that shown in Figure 7b,c. Examination of Figure 8d shows that the (+)-**23** enantiomer gave rise to a negative exciton pattern (brown line) due to the B_{1u} transition centered at 245 nm, whereas the exciton pattern due to the B_{2u} transition at 280 nm was too weak to be identified, possibly due to the presence of just one chirally modified aromatic ring in the system. Nonetheless, this result confirms that the enantiomer (+)-**23** exhibits a (*P*)-absolute configuration, which is consistent with the X-ray data. Based on similar arguments, it was concluded that the 2-methoxy analogue (+)-**24** (Figure 8e, brown line) also has a (*P*)-absolute configuration. For the 2,6-dihydroxy **19** and 2,6-dimethoxy **20** analogues, the B_{2u} transition at 294 nm could be clearly identified. In both cases, (−)-**19** (Figure 8a, yellow line) and (−)-**20** (Figure 8b, yellow line) could be assigned to have a (*P*)-configuration. Hence, the absolute configurations of (−)-**19**, (−)-**20**, (−)-**21**, (−)-**23**, and (−)-**24** are (*P*), (*P*), (*P*), (*M*), and (*M*), respectively.

CONCLUSIONS

The C_1-symmetrical 2,6-dihydroxy-/dimethoxy-TBTQ derivatives (±)-**18**, (±)-**19**, and (±)-**20** and the C_3-symmetrical 2,6,10-trimethoxy-TBTQ derivative (±)-**21** were synthesized in a highly regioselective manner using either Kuck's or Hopf's synthetic protocol. A systematic optical resolution study of a series of 2-hydroxy-/methoxy-, 2,6-dihydroxy-/dimethoxy-, and 2,6,10-trimethoxy-TBTQ derivatives was conducted. The absolute configurations of the separated enantiomers were determined by X-ray crystallography and/or circular dichorism spectroscopy. These optically pure 2,6-disubsituted and 2,6,10-trisubstituted compounds are potentially interesting building blocks for the construction of molecular squares and cubes.

EXPERIMENTAL SECTION

General Information. All reactions that required anhydrous conditions were carried out using standard procedures under an Ar atmosphere. Commercially available reagents were used as received without further purification. Solvents were dried by distillation over the appropriate drying reagents. Column chromatography was performed through silica gel 60 (70−230 mesh) unless otherwise stated. Melting points were determined on a melting point apparatus and are uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a 400 MHz spectrometer. Chemical shift values are given in ppm, and coupling constants (*J*) are in Hz. Residual solvent signals in the ^{1}H and ^{13}C NMR spectra were used as the internal reference ($CDCl_3$: δ_H = 7.26, δ_C = 77.16 ppm). Mass spectra were recorded using either electron-impact ionization (EI) or electrospray ionization (ESI), as indicated. Accurate mass measurements were obtained on a mass spectrometer with a magnetic-sector-type mass analyzer. Single-crystal X-ray diffraction measurements were conducted on a CCD diffractometer using Mo Kα radiation. CD spectra were recorded with a spectropolarimeter. UV measurements were carried out using a UV−vis spectrophotometer. Specific rotations were measured on a polarimeter. Chiral HPLC was conducted on a CHIRALPAK IB column (20 mm × 250 mm) using an HPLC pump equipped with a UV/visible detector. For each chromatographic run, 2 mL of the racemate sample at a concentration of 10−20 mg/mL was injected into the column. The recovery yield of the separation process was about 90−95%, and the absolute amount of pure enantiomers isolated ranged from 9 to 18 mg per run.

Synthetic Procedures. *(3-Methoxyphenyl)-(4-methoxyphenyl)-methanol (**30**).*[25] *n*-BuLi (68.8 mL, 1.6 M in hexane, 110 mmol) was added to a solution of 3-bromoanisole (18.7 g, 100 mmol) in THF (100 mL) at −78 °C. After 1 h, 4-methoxybenzaldehyde (13.6 g, 100 mmol) in dry THF (10 mL) was added dropwise. After the addition, the reaction mixture was allowed to warm to 25 °C over a period of 2 h. The mixture was then poured into ice water and extracted with ether (3 × 100 mL). The combined extracts were dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate = 5/1, R_f = 0.2) to give the product **30** as a yellow oil (20.8 g, 85 mmol, 85%). ^{1}H NMR ($CDCl_3$): δ 7.32−7.28 (m, 2H), 6.99−6.96 (m, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.86−6.83 (m, 2H), 5.73 (d, *J* = 3 Hz, 1H), 3.804 (s, 3H), 3.800 (s, 3H), 2.96 (br s, 1H).

*2-[(3-Methoxyphenyl)-(4-methoxyphenyl)methyl]-2-methyl-1H-indene-1,3(2H)-dione (**31**).* A mixture of 2-methyl-1,3-indanedione (13.6 g, 85 mmol), diarylmethanol **30** (20.8 g, 85 mmol), and *p*-toluenesulfonic acid monohydrate (0.81 g, 4.3 mmol) in toluene (100 mL) was heated at 110 °C for 24 h. The mixture was cooled to 25 °C, washed with saturated K_2CO_3 solution, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/ethyl acetate = 4/1, R_f = 0.2) to give the product **31** as a colorless solid (28.6 g, 74 mmol, 87%); mp 109−110 °C. ^{1}H NMR ($CDCl_3$): δ 7.83−7.81 (m, 2H), 7.70−7.68 (m, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 7.08−7.00 (m, 3H), 6.69 (d, *J* = 8.8 Hz, 2H), 6.62 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.51 (s, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 1.29 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 204.3, 159.3, 158.3, 141.7, 141.4, 135.6, 131.8, 130.7, 129.3, 123.1, 122.0, 115.1, 113.6, 112.4, 58.2, 57.0, 55.0, 20.0. MS (ESI) *m*/*z* (%): 409 (100, $[M + Na]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{25}H_{22}O_4 + Na]^+$, 409.1410; found, 409.1416.

*2-[(3-Methoxyphenyl)-(4-methoxyphenyl)methyl]-2-methyl-2,3-dihydro-1H-indene-1,3-diol (**32**).* A solution of the diketone **31** (28.6 g, 74 mmol) in anhydrous THF (130 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (4.5 g, 118 mmol) in dry THF (20 mL) at 0 °C. After the addition was finished, the mixture was heated to reflux for 12 h. The reaction was quenched by the addition of a small amount of cool water, and the resulting suspension was filtered. The filtrate was concentrated in vacuo, and the residue purified by silica gel chromatography (hexane/ethyl acetate = 2/1, R_f = 0.2) to afford a diastereomeric mixture of product **32** as a pale yellow solid (26.0 g, 67 mmol, 90%); mp 183−184 °C. ^{1}H NMR ($CDCl_3$): δ 7.49 (d, *J* = 8.8 Hz, 2H), 7.45−7.43 (m, 2H), 7.36−7.33 (m, 2H), 7.31−7.27 (m, 1H), 7.16−7.13 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.80 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.16 (s, 1H), 4.60 (d, *J* = 7.2 Hz, 1H), 4.52 (d, *J* = 7.6 Hz, 1H), 3.811 (s, 3H), 3.809 (s, 3H), 2.26−2.23 (m, 2H), 0.84 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.8, 158.3, 144.91, 144.87, 144.0, 133.8, 131.0, 129.6, 129.3, 126.3, 122.4, 116.2, 114.0, 111.4, 81.93, 81.88, 55.33, 55.29, 53.6, 48.1, 20.6. MS (ESI) *m*/*z* (%): 413 (100, $[M + Na]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{25}H_{26}O_4 + Na]^+$, 413.1723; found, 413.1726.

*(±)-2,6-Dimethoxy-12d-methyltribenzotriquinacene [(±)-**33**].* A solution of the diol **32** (26.0 g, 67 mmol) in xylenes (200 mL) was dropped slowly into 85% orthophosphoric acid (15.6 mL, 254 mmol) at 130 °C with vigorous stirring. After the addition was complete, the mixture was heated to reflux for 20 h. The reaction mixture was cooled to 25 °C and poured into water (100 mL). The organic layer was then

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washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), filtered, and concentrated in vacuo to give an oil that was purified by column chromatography (hexane/ethyl acetate = 10/1, R_f = 0.2) to afford the product (±)- **33** as a gummy oil (4.3 g, 12 mmol, 18%). ^{1}H NMR ($CDCl_3$): δ 7.43−7.39 (m, 2H), 7.33−7.30 (m, 2H), 7.20−7.18 (m, 2H), 6.96 (d, J = 1.6 Hz, 1H), 6.91 (d, J = 1.6 Hz, 1H), 6.77−6.73 (m, 2H), 4.41 (s, 1H), 4.39 (s, 1H), 4.36 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 1.67 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.4, 158.4, 141.7, 141.5, 135.6, 131.9, 130.8, 129.4, 123.19, 123.17, 122.1, 115.2, 113.7, 112.5, 58.3, 57.1, 55.2, 20.1. MS (ESI) m/z (%): 354 (100, $M^{\bullet+}$). Accurate mass measurement (ESI) m/z: calcd for $C_{25}H_{22}O_2^{\bullet+}$, 354.1614; found, 354.1620.

*(±)-4b,8b,12b-Triallyl-2,6-dimethoxy-12d-methyltribenzotriquinacene [(±)-**34**].* A mixture of (±)-**33** (1.0 g, 2.82 mmol), benzoyl peroxide (0.11 g, 0.45 mmol), and NBS (2.0 g, 11.28 mmol) was heated to reflux in $CHCl_3$ (100 mL) under the irradiation of an infrared lamp (245 W) for 5 h. After being allowed to cool to 25 °C, the mixture was washed with saturated aqueous $Na_2S_2O_3$ solution followed by saturated aqueous $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo to give the corresponding tribromide as a yellow solid. The crude product was then dissolved in anhydrous CH_2Cl_2 (50 mL) at 0 °C, and tin tetrachloride (1.3 mL, 11.28 mmol) and allyltrimethylsilane (1.8 mL, 11.28 mmol) were slowly added in sequence. The mixture was stirred at 25 °C for 24 h, and the reaction was quenched with water. The inorganic salts were filtered off, and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo, and the residue was purified by column chromatography (hexane/ethyl acetate = 30/1, R_f = 0.2) to give compound (±)-**34** as a colorless solid (0.44 g, 0.93 mmol, 33%); mp 151−152 °C. ^{1}H NMR (400 MHz): δ 7.33−7.28 (m, 2H), 7.23−7.15 (m, 4H), 6.84 (d, J = 2.4 Hz, 1H), 6.80 (d, J = 2.4 Hz, 1H), 6.76−6.72 (m, 2 H), 5.65−5.53 (m, 3H), 5.11−5.07 (m, 3H), 4.97−4.95 (m, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.01−2.98 (m, 6H), 1.66 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.6, 149.3, 149.1, 148.1, 147.3, 140.0, 139.9, 137.42, 137.37, 137.3, 127.7, 127.5, 124.1, 123.5, 123.4, 116.5, 116.40, 116.36, 113.7, 113.5, 108.7, 108.6, 74.0, 66.1, 65.6, 65.5, 55.5, 42.8, 42.6, 17.3. MS (ESI) m/z (%): 497 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{34}H_{34}O_2 + Na]^+$, 497.2451; found, 497.2450.

*(±)-2,6-Dimethoxy-12d-methyl-4b,8b,12b-tri-n-propyltribenzotriquinacene [(±)-**18**].* A mixture of triallyltribenzotriquinance **34** (0.44 g, 0.93 mmol), 10% palladium-on-charcoal (0.15 g, 10%), and anhydrous ethyl acetate (20 mL) was stirred at 25 °C under a hydrogen atmosphere (1 atm) for 24 h. The catalyst was removed by filtration through a short pad of silica gel. The solvent was concentrated in vacuo, and the residue was purified by silica gel chromatography (hexane/ethyl acetate = 30/1, R_f = 0.2) to afford the tripropyl TBTQ (±)-**18** as a colorless solid (0.41 g, 0.85 mmol, 91%); mp 184−185 °C. ^{1}H NMR ($CDCl_3$): δ 7.28−7.24 (m, 2H), 7.17 (dd, J = 8.4, 3.2 Hz, 2H), 7.12−7.10 (m, 2H), 6.81 (d, J = 1.6 Hz, 1H), 6.76 (d, J = 2 Hz, 1H), 6.71−6.68 (m, 2H), 3.75 (s, 3H), 3.74 (s, 3H), 2.14−2.08 (m, 6H), 1.59 (s, 3H), 1.20−1.10 (m, 6H), 0.95−0.85 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 159.33, 159.29, 149.8, 149.6, 148.6, 147.8, 140.6, 140.5, 127.3, 127.1, 124.0, 123.9, 123.4, 123.3, 113.2, 113.1, 108.7, 108.5, 72.7, 67.2, 66.6, 66.5, 55.4, 41.1, 41.0, 40.9, 20.61, 20.55, 15.4, 15.3. MS (ESI) m/z (%): 503 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{34}H_{40}O_2 + Na]^+$, 503.2921; found, 503.2924.

*(±)-2,6-Dihydroxy-12d-methyl-4b,8b,12b-tri-n-propyltribenzotriquinacene [(±)-**19**].* Boron tribromide (1.9 mL, 1.87 mmoL) was added slowly to a solution of dimethoxy-TBTQ (±)-**18** (0.41 g, 0.85 mmol) in anhydrous CH_2Cl_2 (15 mL) at 0 °C. The mixture was stirred at 20 °C for 12 h. The reaction was quenched with water, and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo, and the residue was purified by column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.3) to obtain (±)-**19** as a colorless solid (0.35 g, 0.77 mmol, 90%); mp >252 °C (dec). ^{1}H NMR ($CDCl_3$): δ 7.25−7.22 (m, 2H), 7.13−7.05 (m, 4H), 6.73 (d, J = 2.0 Hz, 1H), 6.68 (d, J = 2.4 Hz, 1H), 6.60−6.55 (m, 2H), 4.91 (s, 2H), 2.10−2.04 (m, 6H), 1.58 (s, 3H), 1.22−1.17 (m, 6H), 0.92−0.89 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 155.12, 155.08, 150.2, 150.0, 148.6, 147.8, 140.6, 140.4, 127.3, 127.1, 124.2, 124.1, 123.44, 123.37, 114.92, 114.87, 109.8, 109.7, 72.8, 67.1, 66.6, 66.5, 64.8, 41.2, 40.9, 40.8, 25.4, 20.6, 20.5, 15.34, 15.27. MS (ESI) m/z (%): 475 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{32}H_{36}O_2 + Na]^+$, 475.2608; found, 475.2610.

(*P*)-(−)-**19**: Colorless solid; mp >252 °C (dec); $[\alpha]_D^{20}$ = −75.8 (c = 0.4, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.25−7.23 (m, 2H), 7.13−7.10 (m, 3H), 7.03−6.97 (m, 1H), 6.72 (s, 1H), 6.68 (d, J = 2.4 Hz, 1H), 6.59 (dd, J = 8.4, 2.0 Hz, 1H), 6.48−6.40 (m, 1H), 4.66 (br s, 1H), 4.57 (br s, 1H), 2.15−2.00 (m, 6H), 1.60 (s, 3H), 1.25−1.10 (m, 6H), 0.95−0.80 (m, 9 H). ^{13}C NMR ($CDCl_3$): δ 155.1, 155.0, 150.2, 150.0, 148.6, 147.8, 140.7, 140.5, 127.4, 127.1, 124.22, 124.16, 123.45, 123.38, 114.94, 114.88, 109.8, 109.6, 72.8, 67.1, 66.6, 66.5, 41.1, 40.90, 40.86, 20.6, 20.5, 15.4, 15.30, 15.28. MS (ESI) m/z (%): 475 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{32}H_{36}O_2 + Na]^+$, 475.2608; found, 475.2615.

(*M*)-(+)-**19**: Colorless solid; mp >252 °C (dec); $[\alpha]_D^{20}$ = +76.4 (c = 0.4, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.26−7.22 (m, 2H), 7.12−7.10 (m, 3H), 7.03 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 6.68 (d, J = 2.4 Hz, 1H), 6.60−6.51 (m, 2H), 4.61 (br s, 1H), 4.57 (br s, 1H), 2.11−2.03 (m, 6H), 1.58 (s, 3H), 1.22−1.13 (m, 6H), 0.93−0.89 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 155.1, 155.0, 150.2, 150.0, 148.6, 147.8, 140.7, 140.6, 127.4, 127.1, 124.23, 124.17, 123.45, 123.37, 115.0, 114.9, 109.8, 109.6, 72.8, 67.1, 66.6, 66.5, 41.1, 40.90, 40.87, 20.6, 20.5, 15.4, 15.30, 15.28. MS (ESI) m/z (%): 475 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{32}H_{36}O_2 + Na]^+$, 475.2608; found, 475.2610.

*2-Benzylidene-1,3-bis(4-methoxyphenyl)propane-1,3-dione (**40**).* A mixture of 1,3-bis(4-methoxyphenyl)propane-1,3-dione (20.0 g, 70 mmol) **38**,[27] benzaldehyde **39** (8.2 g, 77 mmol), piperidine (0.9 mL, 9.1 mmol), and hexanoic acid (2.2 mL, 17.5 mmol) in toluene (200 mL) was heated to reflux using a Dean−Stark trap for 20 h. The mixture was cooled to 25 °C; and washed sequentially with saturated aqueous $NaHCO_3$ solution, 5% aqueous acetic acid solution, aqueous K_2CO_3 solution, and brine; and dried ($MgSO_4$). The organic solvent was filtered and concentrated in vacuo, and the residue was recrystallized from methanol to give the product **40** as a yellow solid (20.3 g, 54.6 mmol, 78%); mp 128−129 °C. ^{1}H NMR ($CDCl_3$): δ 7.97 (d, J = 8.8 Hz, 2H), 7.94 (d, J = 8.8 Hz, 2H), 7.43 (s, 1H), 7.37−7.35 (m, 2H), 7.29−7.22 (m, 3H), 6.96 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H), 3.82 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 195.3, 193.3, 164.1, 163.4, 141.6, 140.2, 133.4, 132.1, 131.9, 130.0, 129.9, 129.6, 128.7, 114.1, 113.8, 55.5, 55.4. MS (ESI) m/z (%): 395 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{20}O_4 + Na]^+$, 395.1254; found, 395.1268.

*2-Benzylidene-1,3-bis(4-methoxyphenyl)propane-1,3-diol (**41**).* A solution of the diketone **40** (10.0 g, 26.9 mmol) was dissolved in CH_2Cl_2 (150 mL) and stirred at −78 °C under nitrogen. A methanolic solution (150 mL) of cerium chloride heptahydrate (21.0 g, 56.5 mmol) was then added, followed by sodium borohydride (3.1 g, 80.7 mmol) in small batches. The mixture was kept at −78 °C for 1 h and then allowed to warm to 25 °C over a period of 2 h. The reaction was quenched with 1.0 M hydrochloride acid, and the mixture was extracted with ether (3 × 100 mL). The organic extracts were combined, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a residue that was purified by silica gel chromatography (hexane/CH_2Cl_2/ethyl acetate = 5/3/1, R_f = 0.2 and 0.1) to afford two diastereomers of **41**. Faster-running diastereomer: Colorless solid (3.75 g, 10.0 mmol, 37%); mp 97.0−97.5 °C. ^{1}H NMR ($CDCl_3$): δ 7.34−7.25 (m, 9H), 7.04 (s, 1H), 6.89 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 5.89 (d, J = 6.4 Hz, 1H), 5.32 (d, J = 2.8 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 2.00−1.95 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 159.4, 158.8, 143.9, 136.5, 135.2, 134.6, 129.6, 128.9, 128.6, 128.5, 127.4, 127.2, 114.2, 113.8, 73.7, 71.0, 55.40, 55.38. MS (ESI) m/z (%): 399 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{24}O_4+Na]^+$, 399.1567; found, 399.1572. Slower-running diastereomer: Colorless solid (5.4 g, 14.3

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mmol, 53%); mp 126.5−127.0 °C. ^{1}H NMR ($CDCl_3$): δ 7.32−7.22 (m, 7H), 7.18 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.22 (s, 1H), 5.91 (d, J = 6.8 Hz, 1H), 5.28 (d, J = 2.8 Hz, 1H), 4.14 (d, J = 7.2 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.34 (d, J = 3.2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 159.1, 158.7, 144.0, 136.4, 134.8, 133.7, 132.4, 128.8, 128.4, 127.4, 126.9, 113.8, 113.7, 74.4, 71.8, 55.37, 55.35. MS (ESI) m/z (%): 399 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{24}O_4 + Na]^+$, 399.1567; found, 399.1570.

*(±)-2,6-Dimethoxytribenzotriquinacene [(±)-(**20**)].* A mixture of the diol **41** (3.0 g, 8.0 mmol) and polyphosphoric acid (1.5 g) in chlorobenzene (21 mL) was stirred vigorously at 130 °C. The mixture was cooled to 25 °C, and the solvent was concentrated in vacuo. The residue was chromatographed on silica gel (hexane/ethyl acetate = 20/1, R_f = 0.2) to afford a pale yellow solid that was recrystallized from toluene to yield the product (±)-**20** as a colorless solid (0.16 g, 0.48 mmol, 6%); mp >209 °C (dec). ^{1}H NMR ($CDCl_3$): δ 7.45−7.41 (m, 2H), 7.34 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.19−7.17 (m, 2H), 6.99 (s, 1H), 6.94 (s, 1H), 6.76−6.73 (m, 2H), 4.91−4.84 (m, 3H), 4.55 (q, J = 9.6 Hz, 1H), 3.783 (s, 3H), 3.776 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.7, 159.6, 147.7, 147.5, 146.4, 145.5, 138.1, 138.0, 127.5, 127.4, 124.9, 124.8, 124.39, 124.36, 113.5, 113.4, 109.7, 109.6, 56.0, 55.6, 55.21, 55.15, 52.6. MS (ESI) m/z (%): 363 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{20}O_2 + Na]^+$, 363.1356; found, 363.1352.

(*M*)-(+)-**20**: Colorless solid; mp >208 °C (dec); $[\alpha]_D^{20}$ = +144.3 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.46−7.41 (m, 2H), 7.34 (d, J = 8 Hz, 1H), 7.33 (d, J = 8 Hz, 1H), 7.19−7.17 (m, 2H), 6.99 (d, J = 2 Hz, 1H), 6.94 (d, J = 2 Hz, 1H), 6.76−6.73 (m, 2H), 4.91−4.84 (m, 3H), 4.55 (q, J = 9.6 Hz, 1H), 3.784 (s, 3H), 3.777 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.64, 159.61, 147.7, 147.5, 146.4, 145.5, 138.0, 127.6, 127.5, 124.8, 124.39, 124.36, 113.5, 113.4, 109.7, 109.6, 56.0, 55.6, 55.2, 55.1, 52.6. MS (ESI) m/z (%) 341 (45, $[M + H]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{20}O_2 + H]^+$, 341.1536; found, 341.1527.

(*P*)-(−)-**20**: Colorless solid; mp >208 °C (dec); $[\alpha]_D^{20}$ = −148.1 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.46−7.42 (m, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.20−7.18 (m, 2H), 7.0 (s, 1H), 6.95 (s, 1H), 6.77−6.73 (m, 2H), 4.91−4.84 (m, 3H), 4.55 (q, J = 9.6 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.62, 159.59, 147.7, 147.5, 146.4, 145.5, 138.04, 138.00, 127.5, 127.4, 124.9, 124.8, 124.38, 124.35, 113.5, 113.4, 109.7, 109.6, 55.9, 55.6, 55.2, 55.1, 52.6. MS (ESI) m/z (%): 341 (100, $[M + H]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{24}H_{20}O_2 + H]^+$, 341.1536; found, 341.1533.

*2-(4-Methoxybenzylidene)-1,3-bis(4-methoxyphenyl)propane-1,3-dione (**42**).* A mixture of 1,3-bis(4-methoxyphenyl)propane-1,3-dione **38**[27] (20.0 g, 70 mmol), 4-methoxybenzaldehyde **29** (10.5 g, 77 mmol), piperidine (0.9 mL, 9.1 mmol), and hexanoic acid (2.2 mL, 17.5 mmol) in toluene (200 mL) was heated to reflux with a Dean−Stark apparatus for 20 h under nitrogen. The mixture was cooled to 25 °C; washed sequentially with saturated aqueous $NaHCO_3$ solution, 5% aqueous acetic acid solution, aqueous K_2CO_3 solution, and brine; and dried ($MgSO_4$). The organic solvent was dried ($MgSO_4$), filtered, and concentrated in vacuo to give an oil that was chromatographed on silica gel (hexane/ethyl acetate = 5/1, R_f = 0.2) to afford the product **42** as a yellow oil (21.8 g, 54 mmol, 77%). ^{1}H NMR ($CDCl_3$): δ 7.97 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.32 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8 Hz, 2H), 6.89 (d, J = 9.2 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 195.9, 193.5, 164.0, 163.1, 161.1, 142.2, 137.6, 132.0, 131.9, 131.8, 130.2, 129.7, 125.8, 114.2, 114.0, 113.7, 55.42, 55.41, 55.2. MS (ESI) m/z (%): 425 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{22}O_5 + Na]^+$, 425.1359; found, 425.1359.

*2-(4-Methoxybenzylidene)-1,3-bis(4-methoxyphenyl)propane-1,3-diol (**43**).* The preparation procedure was the same as that used for compound **41**. Starting from diketone **42** (10.0 g, 24.8 mmol), cerium chloride heptahydrate (19.4 g, 52.1 mmol), and sodium borohydride (2.8 g, 74.4 mmol), the product **43** was obtained as a mixture of two diastereomers, which was separated by silica gel chromatography (hexane/CH_2Cl_2/ethyl acetate = 5/4/1, R_f = 0.2 and 0.1). Faster-running diastereomer: Colorless oil (3.0 g, 30%). ^{1}H NMR ($CDCl_3$): δ 7.30−7.26 (m, 6H), 6.94 (s, 1H), 6.89−6.84 (m, 6H); 5.89 (s, 1H), 5.31 (s, 1H), 3.81 (s, 6H), 3.80 (s, 3H), 2.07 (br s, 2H). ^{13}C NMR ($CDCl_3$): δ 159.5, 159.0, 158.8, 142.4, 135.3, 134.7, 130.3, 129.3, 128.9, 128.7, 127.3, 114.2, 113.9, 113.8, 73.9, 71.2, 55.44, 55.41. MS (ESI) m/z (%): 429 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{26}O_5 + Na]^+$, 429.1672; found, 429.1679. Slower-running diastereomer: Colorless oil (5.7 g, 57%). ^{1}H NMR ($CDCl_3$): δ 7.35 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.8 Hz, 2H), 7.20 (d, J = 9 Hz, 2H), 6.92−6.83 (m, 6H), 6.16 (s, 1H), 5.95 (d, J = 7.6 Hz, 1H), 5.30 (s, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.78 (s, 3H), 3.71 (d, J = 7.6 Hz, 1H), 2.67 (d, J = 2.8 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 159.1, 159.0, 158.7, 142.7, 134.9, 133.9, 132.0, 130.2, 128.8, 128.4, 126.9, 113.82, 113.80, 113.7, 74.5, 71.9, 55.38, 55.36, 55.3. MS (ESI) m/z (%): 429 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{26}O_5 + Na]^+$, 429.1672; found, 429.1677.

*2,6,10-Trimethoxytribenzotriquinacene [(±)-(**21**)].* The preparation procedure was similar to that used for (±)-**20**. Starting from diol **43** (3.0 g, 7.4 mmol), the product (±)-**21** was obtained as a colorless solid (27.1 mg, 72.9 μmmol, 1%) and separated by flash chromatography (hexane/ethyl acetate = 10/1, R_f = 0.2); mp >205 °C (dec). ^{1}H NMR ($CDCl_3$): δ 7.33 (d, J = 8.4 Hz, 3H), 6.95 (s, 3H), 6.74 (d, J = 8.4 Hz, 3H), 4.82 (d, J = 9.6 Hz, 3H), 4.51 (q, J = 9.6 Hz, 1H), 3.78 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 159.6, 147.8, 137.8, 124.8, 113.3, 109.6, 55.6, 55.1, 53.2. MS (ESI) m/z (%): 393 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{22}O_3 + Na]^+$, 393.1461; found, 393.1466.

(*M*)-(+)-**21**: Colorless solid; mp >205 °C (dec); $[\alpha]_D^{20}$ = +147.8 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.32 (d, J = 8.4 Hz, 3H), 6.94 (d, J = 1.2 Hz, 3H), 6.74 (dd, J = 8.4, 2.0 Hz, 3H), 4.83 (d, J = 9.6 Hz, 3H), 4.52 (q, J = 9.6 Hz, 1H), 3.78 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 159.6, 147.9, 137.8, 124.9, 113.4, 109.7, 55.6, 55.2, 53.2. MS (ESI) m/z (%): 393 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{22}O_3 + Na]^+$, 393.1461; found, 393.1462.

(*P*)-(−)-**21**: Colorless solid; mp >205 °C (dec); $[\alpha]_D^{20}$ = −136.5 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.32 (d, J = 8.4 Hz, 3H), 6.94 (d, J = 1.6 Hz, 3H), 6.73 (dd, J = 8.0, 2.4 Hz, 3H), 4.83 (d, J = 9.6 Hz, 3H), 4.52 (q, J = 9.2 Hz, 1H), 3.77 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 159.6, 147.9, 137.8, 124.9, 113.4, 109.7, 55.6, 55.2, 53.2. MS (ESI) m/z (%): 371 (100, $[M + H]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{25}H_{22}O_3 + H]^+$, 371.1642; found, 371.1646.

*(±)-2-Hydroxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene [(±)-**23**].* Compound (±)-**23** was synthesized according to a published method.[29]

(*M*)-(−)-**23**: Colorless solid; mp >250 °C (dec); $[\alpha]_D^{20}$ = −61.6 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.41−7.37 (m, 2H), 7.35−7.31 (m, 2H), 7.21−7.14 (m, 5H), 6.82 (d, J = 2.4 Hz, 1H), 6.62 (dd, J = 8.4, 2.4 Hz, 1H), 4.73 (br s, 1H), 1.68 (s, 3H), 1.65 (s, 6H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 155.4, 150.7, 149.3, 149.1, 148.8, 148.7, 141.5, 127.8, 127.69, 127.66, 127.6, 123.8, 123.1, 123.03, 123.01, 122.9, 115.3, 109.5, 70.2, 62.8, 62.7, 62.2, 26.13, 26.08, 25.9, 16.3. MS (ESI) m/z (%): 375 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{26}H_{24}O + Na]^+$, 375.1719; found, 375.1728.

(*P*)-(+)-**23**: Colorless solid; mp >250 °C (dec); $[\alpha]_D^{20}$ = +55.6 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.39−7.36 (m, 2H), 7.35−7.31 (m, 2H), 7.21−7.15 (m, 5H), 6.82 (d, J = 2.4 Hz, 1H), 6.62 (dd, J = 8.4, 2.4 Hz, 1H), 4.66 (br s, 1H), 1.67 (s, 3H), 1.65 (s, 6H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 155.4, 150.7, 149.3, 149.1, 148.8, 148.7, 141.5, 127.8, 127.78, 127.7, 123.8, 123.1, 123.04, 123.01, 122.9, 115.3, 109.5, 70.2, 62.8, 62.6, 62.2, 26.14, 26.08, 25.9, 16.3. MS (ESI) m/z (%): 375 (100, $[M + Na]^+$). Accurate mass measurement (ESI) m/z: calcd for $[C_{26}H_{24}O + Na]^+$, 375.1719; found, 375.1718.

*(±)-2-Methoxytribenzotriquinacene [(±)-(**24**)].* This compound was prepared according to the method described in the literature.[26]

(*P*)-(+)-**24**: Colorless solid; mp >213 °C (dec); $[\alpha]_D^{20}$ = +31.9 (c = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.47−7.40 (m, 4H), 7.34 (d, J = 8.0 Hz, 1H), 7.19−7.16 (m, 4H), 6.98 (d, J = 2.0 Hz, 1H), 6.74 (dd, J = 8.4, 2.0 Hz, 1H), 4.96−4.89 (m, 3H), 4.50 (q, J = 9.6 Hz, 1H), 3.78

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(s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.6, 147.4, 146.3, 146.1, 145.8, 145.7, 138.2, 127.6, 127.51, 127.49, 127.4, 124.9, 124.44, 124.40, 124.3, 113.5, 109.7, 56.0, 55.9, 55.6, 55.2, 51.9. MS (ESI) *m*/*z* (%): 333 (100, $[M + Na]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{23}H_{18}O + Na]^+$, 333.1250; found, 333.1250.

(*M*)-(−)-**24**: Colorless solid; mp >213 °C (dec); $[\alpha]_D^{20}$ = −44.1 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.48−7.41 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.20−7.17 (m, 4H), 6.99 (d, *J* = 1.6 Hz, 1H), 6.75 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.97−4.90 (m, 3H), 4.50 (q, *J* = 9.6 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.6, 147.4, 146.3, 146.1, 145.8, 145.7, 138.2, 127.6, 127.51, 127.49, 127.4, 124.9, 124.44, 124.40, 124.3, 113.5, 109.7, 56.0, 55.9, 55.6, 55.2, 51.9. MS (ESI) *m*/*z* (%): 333 (100, $[M + Na]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{23}H_{18}O + Na]^+$, 333.1250; found, 333.1250.

*(M)-(−)-2-Methoxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene [(M)-(−)-**22**].* A mixture of (*M*)-(−)-**23** (0.50 g, 1.42 mmol), K_2CO_3 (0.39 g, 2.84 mmol), and methyl iodide (97 μL, 1.56 mmol) was stirred in a sealed tube at 45 °C for 12 h. The inorganic salts were filtered, and the filtrate were concentrated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 20/1, R_f = 0.2) to obtain the product (*M*)-(−)-**22** as a colorless solid (0.49 g, 1.35 mmol, 95%); mp 236−237 °C; $[\alpha]_D^{20}$ = −64.8 (*c* = 0.4, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.42−7.35 (m, 4H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.21−7.17 (m, 4H), 6.92 (d, *J* = 2.4 Hz, 1H), 6.75 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.78 (s, 3H), 1.694 (s, 3H), 1.686 (s, 3H), 1.676 (s, 3H), 1.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.7, 150.4, 149.3, 149.1, 148.8, 148.7, 141.5, 127.8, 127.7, 127.6, 123.6, 123.1, 123.0, 122.9, 113.6, 108.3, 70.2, 62.79, 62.75, 62.2, 55.6, 26.13, 26.06, 26.0, 16.3. MS (ESI) *m*/*z* (%): 367 (100, $[M + H]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{27}H_{26}O + H]^+$, 367.2056; found, 367.2076.

*(P)-(+)-2-Methoxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene [(P)-(+)-**22**].* The synthesis procedure was the same as that used for (*M*)-(−)-**22**. Colorless solid; mp 234−235 °C; $[\alpha]_D^{20}$ = +68.6 (*c* = 0.4, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.41−7.36 (m, 4H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.21 −7.18 (m, 4H), 6.92 (s, 1H), 6.77 (dd, *J* = 8.4, 1.6 Hz, 1H), 3.79 (s, 3H), 1.70 (s, 3H), 1.69 (s, 3H), 1.68 (s, 3H), 1.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.7, 150.4, 149.3, 149.1, 148.8, 148.7, 141.5, 127.8, 127.7, 127.6, 123.6, 123.1, 123.0, 122.9, 113.6, 108.3, 70.2, 62.79, 62.75, 62.2, 55.6, 26.14, 26.06, 25.97, 16.3. MS (ESI) *m*/*z* (%): 367 (100, $[M + H]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{27}H_{26}O + H]^+$, 367.2056; found, 367.2053.

*(P)-(+)-2-Iodo-3-methoxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene [(P)-(+)-**44**].* A mixture of (*M*)-(−)-**22** (0.49 g, 1.35 mmol), silver sulfate (0.25 g, 0.81 mmol), and iodine (0.38 g, 1.49 mmol) in acetonitrile (10 mL) was stirred at 25 °C for 24 h. The reaction with excess iodine was quenched with sodium thiosulfate, and the precipitate was filtered. The filtrate was washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$), filtered, concentrated in vacuo, and purified by flash chromatography (hexane/ethyl acetate = 20/1, R_f = 0.2) to give (*P*)-(+)-**44** as a colorless solid (0.58 g, 1.17 mmol, 87%); mp 224−225 °C; $[\alpha]_D^{20}$ = +77.3 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.70 (s, 1H), 7.40−7.37 (m, 2H), 7.34−7.31 (m, 2H), 7.21−7.16 (m, 4H), 6.80 (s, 1H); 3.87 (s, 3H), 1.66 (s, 6H), 1.63 (s, 3H), 1.35 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 157.9, 150.7, 149.1, 148.7, 148.6, 148.2, 143.4, 133.7, 128.0, 127.89, 127.83, 127.8, 123.2, 123.1, 122.9, 122.7, 105.4, 85.5, 70.3, 62.8, 62.7, 62.0, 56.7, 26.1, 26.0, 25.8, 16.3. MS (ESI) *m*/*z* (%): 515 (40, $[M + Na]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{27}H_{25}IO + Na]^+$, 515.0842; found, 515.0860.

*(M)-(−)-2-Iodo-3-methoxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene [(M)-(−)-**44**].* The synthesis was the same as that used for (*P*)-(+)-**44** but starting from (*P*)-(+)-**22**. Colorless solid; mp 223−225 °C; $[\alpha]_D^{20}$ = −62.4 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.71 (s, 1H), 7.41−7.37 (m, 2H), 7.35−7.31 (m, 2H), 7.22−7.17 (m, 4H), 6.81 (s, 1H), 3.87 (s, 3H), 1.67 (s, 6H), 1.64 (s, 3H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 157.9, 150.7, 149.1, 148.7, 148.6, 148.2, 143.4, 133.7, 128.0, 127.9, 127.82, 127.78, 123.2, 123.1, 122.9, 122.7, 105.4, 85.5, 70.3, 62.8, 62.7, 62.0, 56.7, 26.1, 26.0, 25.8, 16.3. MS (ESI) *m*/*z* (%): 510 (100, $[M + NH_4]^+$). Accurate mass measurement (ESI) *m*/*z*: calcd for $[C_{27}H_{25}IO + NH_4]^+$, 510.1288; found, 510.1282.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra and mass spectra of all new compounds; chiral HPLC conditions for the optical resolution of compounds (±)-**19**, (±)-**20**, (±)-**21**, (±)-**23**, and (±)-**24**; UV spectra of compounds (±)-**19**, (±)-**20**, (±)-**21**, (±)-**23**, and (±)-**24**; and CIF files for compounds (*P*)-(+)-**44**·$CHCl_3$ and (*M*)-(−)-**44**·$CHCl_3$. 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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