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# Synthesis of *trans*-1, *trans*-2, *trans*-3, and *trans*-4 Bisadducts of $C_{60}$ by Regio- and Stereoselective Tether-Directed Remote Functionalization

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**Abstract:** The double Bingel reaction of fullerene $C_{60}$ with bismalonates attached to a Tröger base derived tether afforded *trans*-1, *trans*-2, *trans*-3, and *trans*-4 bisadducts with excellent regioselectivity. In particular, enantiomerically pure bisadducts with inherently chiral *trans*-2 or *trans*-3 addition patterns were prepared starting from enantiomerically pure bismalonates. The absolute configuration of the *trans*-2 and *trans*-3 bisadducts was established from their CD spectra. The excellent diastereoselectivity in the double additions to give the *trans*-2 bisadducts is particularly remarkable given the large distance between the two reacting bonds in opposite hemispheres of the fullerene that is spanned by the tether. Now, all inherently chiral double addition patterns are readily available by tether-directed functionalization using appropriate chiral, nonracemic spacers.

**Keywords:** CD spectra · chiral auxiliaries · cyclic voltammetry · cycloaddition · fullerene · regioselectivity

## Introduction

Regio- and, in the event, stereoselective multiple functionalization of fullerenes is a key issue to be addressed to prepare pure adducts with well-defined addition patterns on a reasonable scale and without tedious purification. However, stepwise multiple additions suffer from very low regioselectivity. Thus, the second addition of diethyl malonate to a monoadduct of $C_{60}$ gives a mixture of seven out of eight theoretically possible regioisomers.[1] Also, some interesting addition patterns are hardly available by simple, consecutive additions due to the intrinsic reactivity of fullerene derivatives.[2] In the search for a rational approach to the regioselective formation of multiadducts of $C_{60}$ and other fullerenes, Diederich and co-workers introduced the tether-directed remote functionalization in 1994.[3] Since that time, this versatile and powerful synthetic methodology has become the method of choice for selective multiple additions to fullerenes.[4]

An interesting aspect of *cis*-3, *trans*-3, and *trans*-2 addition patterns of $C_{60}$ is their inherent chirality, that is, even addition of two identical addends without chirality elements of their own gives a chiral molecule.[5] Several syntheses of optically active *cis*-3 bisadducts of $C_{60}$ using bismalonates attached to optically pure threitol or 2,3-butanediol tethers have been published.[6] However, the asymmetric synthesis of $C_2$-symmetrical *trans*-2 or *trans*-3 bisadducts, with the addends located in opposite hemispheres of $C_{60}$, remained unknown until recently.[7] The main challenge consisted in finding a large but conformationally constrained chiral tether. Very recently, we reported in a preliminary communication the first example of a regio- and stereoselective synthesis of *trans*-2 bisadducts of $C_{60}$ using chiral tethers with the structural motif of the Tröger base.[8]

Tröger base (**1**) is a chiral amine with two bridgehead nitrogen atoms as stereogenic centers.[9] Rigidity, $C_2$ symmetry, and a folded geometry with nearly perpendicular planes of two aromatic rings made derivatives of the Tröger base very attractive for applications in supramolecular chemistry and molecular recognition.[10] Here, we report the regio- and stereoselective synthesis of biscyclopropanated derivatives of $C_{60}$ with inherently chiral *trans*-2 and *trans*-3 addition patterns starting from bismalonates connected by the core of the Tröger base. In addition, we describe the high-yielding,

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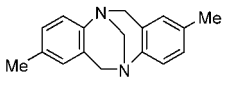
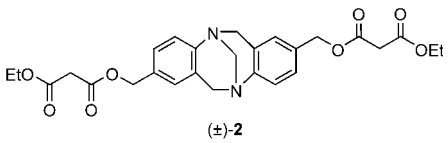


(±)-**1**



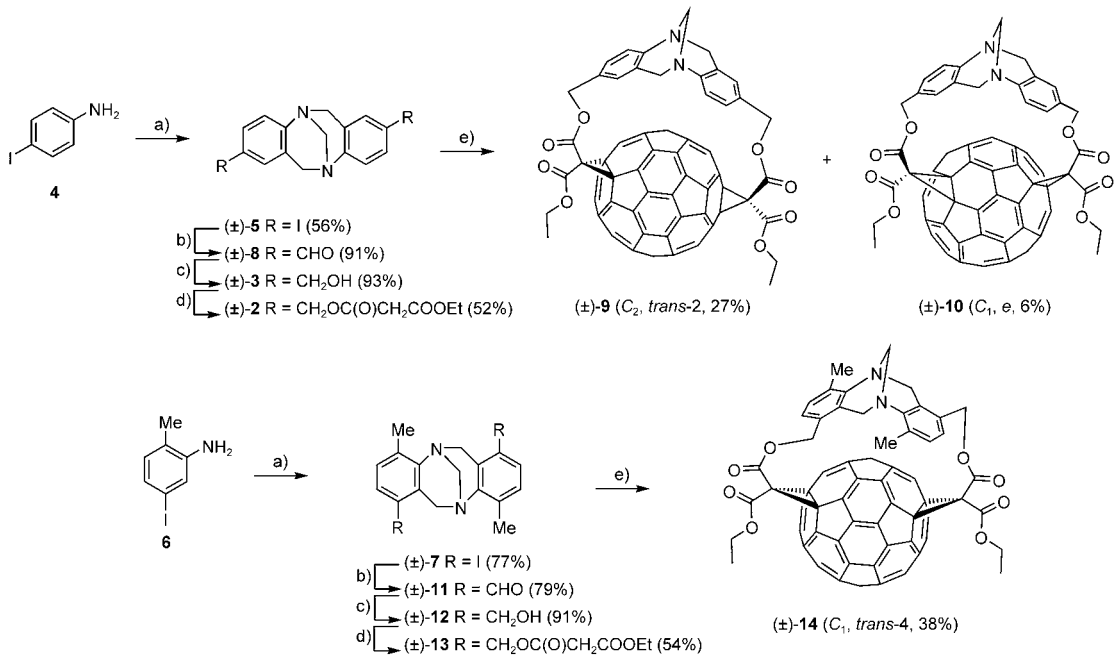
(±)-**2**

regioselective synthesis of *trans*-4 and *trans*-1 bisadducts of $C_{60}$ by the same approach.

## Results and Discussion

**Synthesis of racemic bisadducts of $C_{60}$**: The synthesis of the new fullerene bisadducts is outlined in Scheme 1 and Scheme 2. We have chosen malonate (±)-**2** as a first candidate to be tested in the tether-directed remote functionalization. It should be mentioned that the intermediate diol (±)-**3** cannot be prepared by direct condensation of the corresponding aromatic amine with formaldehyde or a synthetic equivalent thereof, the most practical route to analogues of the Tröger base, due to acid-catalyzed formation of polymeric products.[11] It was also accepted until recently, that electron-withdrawing substituents in any position of the aniline ring are not allowable for the successful condensation to give derivatives of the Tröger base.[11] Fortunately, Wärnmark and co-workers recently found a solution to this problem by performing the condensation of 4-iodoaniline (**4**) and other halogeno-substituted anilines in trifluoroacetic acid (TFA), using paraformaldehyde as a source of $CH_2O$.[12] Probably, the concentration of electrophilic, protonated formaldehyde and, therefore, the rate of key steps of the condensation to give a derivative of the Tröger base is increased in TFA compared to the frequently applied protocol that uses formalin and aqueous HCl in ethanol.[12b] It was also demonstrated later that strict temperature control is extremely important, particularly when the reaction scale exceeds 1 mmol.[13] We have further optimized the published procedure by changing, first of all, the order of addition of the reagents. When a mixture of **4** and paraformaldehyde was added to TFA at −15 °C (the melting point of TFA), the corresponding diiodo derivative of the Tröger base, (±)-**5**, was isolated in well reproducible 56–62 % yield on a 20 to 100 mmol scale (Scheme 1). Furthermore, we concluded that long reaction times are less practical as they lead to formation of unidentified side products, whereas the condensation to give derivatives of the Tröger base is completed within 24 h. We also applied the optimized protocol to prepare the previously unknown diiodide (±)-**7** from 5-iodo-2-methylaniline (**6**). In agreement with previous literature accounts, an additional electron-donating methyl group in the *ortho* position with respect to the nitrogen atom increases the reactivity of the aniline and the yield of the Tröger base derivative.[11a] Additionally, the *ortho*-methyl group is important to block the attack of the electrophile at this position and prevent the unwanted formation of other regioisomers.

The availability of halo derivatives of the Tröger base provides the opportunity to use the great variety of reactions




Scheme 1. Synthesis of bisadducts (±)-**9**, (±)-**10**, and (±)-**14**. a) $(H_2CO)_n$, $CF_3COOH$, 0 °C, 24 h; b) *n*BuLi, THF, −78 °C, 10 min, then DMF, THF, −78 °C → RT, 30 min; c) $LiAlH_4$, THF, RT 1 h; d) $EtOOCCH_2COCl$, DMAP, THF, 0 °C, 16 h; e) $C_{60}$, $I_2$, DBU, toluene, 0 °C, 1 h. DMAP = 4-(dimethylamino)pyridine, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DMF = dimethylformamide.

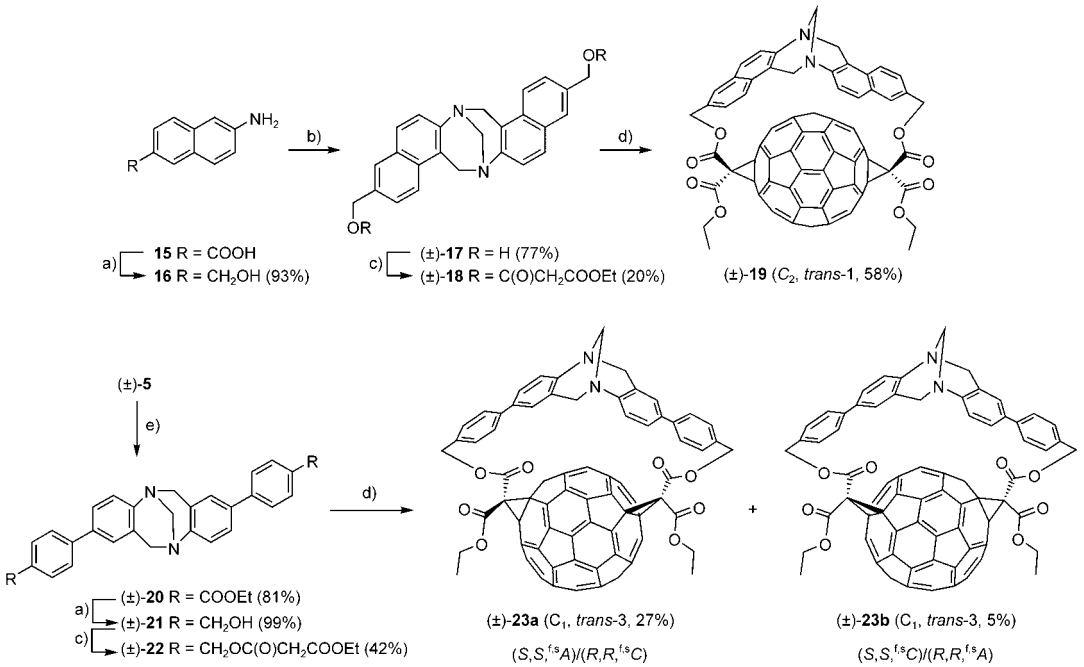
with organometallics or transition-metal catalysts for further transformations. Thus, iodine–lithium exchange in (±)-**5**, followed by the reaction of the dilithiated intermediate with DMF afforded the corresponding dialdehyde (±)-**8**, which was reduced ($LiAlH_4$) to diol (±)-**3** and then transformed into bismalonate (±)-**2** by the action of $EtO_2CCH_2COCl$ in the presence of DMAP. A modified Bingel reaction[14] of (±)-**2** with $C_{60}$ afforded the *trans*-2 bisadduct (±)-**9** as a major product (27%). In addition, a minor amount (5%) of the regioisomeric bisadduct (±)-**10** with *equatorial* (*e*) addition pattern was obtained. Both regioisomers were isolated by simple flash chromatography on $SiO_2$. Diiodide (±)-**7** was converted by the same approach via dialdehyde (±)-**11** and diol (±)-**12** into bismalonate (±)-**13** (see Supporting Information for the X-ray crystal structure of (±)-**13**). The Bingel reaction of the latter with $C_{60}$ afforded exclusively the *trans*-4 configured bisadduct (±)-**14**.

We were also interested in testing a larger tether derived from a naphthalene analogue of the Tröger base. Diol (±)-**17** (Scheme 2) was prepared by direct condensation[11] of amino alcohol **16** (synthesized by reduction of the commercially available amino acid **15**) with formaldehyde in HCl and then converted to bismalonate (±)-**18**. Subsequent Bingel reaction of (±)-**18** with $C_{60}$ afforded exclusively *trans*-1 bisadduct (±)-**19** in remarkable 58% yield. It should be noted that *trans*-1 biscyclopropanated adducts of $C_{60}$ have been prepared previously with the aid of crown ether-derived tethers which require relatively tedious synthesis,[15] while preparation of diol (±)-**17** is very simple and high-yielding.

The addition patterns of bisadducts (±)-**9**, (±)-**10**, (±)-**14**, and (±)-**19** were unequivocally established using UV/Vis and NMR spectroscopy. The absorption spectra of malonate bisadducts of $C_{60}$ in the region between 400 and 800 nm are mainly determined by the structure of the fullerene chromophore and nearly independent of the structure of addends. Therefore, they can be used as "fingerprints" for the identification of addition patterns (see Supporting Information).[7b,c] For all synthesized derivatives (±)-**9**, (±)-**10**, (±)-**14**, and (±)-**19**, the absorption spectra were almost identical to those reported for the corresponding bis(diethyl malonate) adducts $C_{62}(COOEt)_4$.[16] The $^1H$ and $^{13}C$ NMR spectra perfectly reflect the $C_2$ symmetry of (±)-**9** and (±)-**19**, and the $C_1$ symmetry of (±)-**10** and (±)-**14**.

In theory, the described tether-directed double addition to $C_{60}$ can give various diastereoisomers with respect to the relative orientation of the ethoxycarbonyl residues at the two methano-bridge atoms.[17] There are three (*in–in*, *in–out*, and *out–out*) potential isomers for *trans*-2 and *trans*-4 adducts; *trans*-1 addition can yield two (*out–out* and *in–out*) diastereoisomers, and four diastereoisomers exist for the *e* pattern. However, all bisadducts (±)-**9**, (±)-**10**, (±)-**14**, and (±)-**19** were isolated as single racemates, and the *out-out* configuration (as depicted in Scheme 1 and 2) was assigned for all compounds.

The configuration of *trans*-1 bisaduct (±)-**19** was also confirmed by X-ray crystal structure analysis (Figure 1). Surprisingly, only one, namely the (*R*,*R*)-configured enantiomer crystallized out of a solution of (±)-**19** in a mixture of $CH_2Cl_2$ and $CHCl_3$. The absolute configuration was clearly established by X-ray analysis, that is, by determining the absolute structure parameter. Thus we observed a relatively rare example of spontaneous resolution of a racemic mixture. To the best of our knowledge, this is the first example




Scheme 2. Synthesis of bisadducts (±)-**19**, (±)-**23a**, and (±)-**23b**. a) $LiAlH_4$, THF, reflux, 2 h; b) $H_2CO/H_2O$, HCl, EtOH, RT, 24 h; c) $EtOOCCH_2COCl$, DMAP, THF or DMF, 0°C, 16 h; d) $C_{60}$, $I_2$, DBU, toluene, 0°C, 1 h; e) 4-(Ethoxycarbonyl)phenylboronic acid, $[Pd(PPh_3)_4]$, $K_2CO_3$, toluene/EtOH/$H_2O$, reflux, 1.5 h.

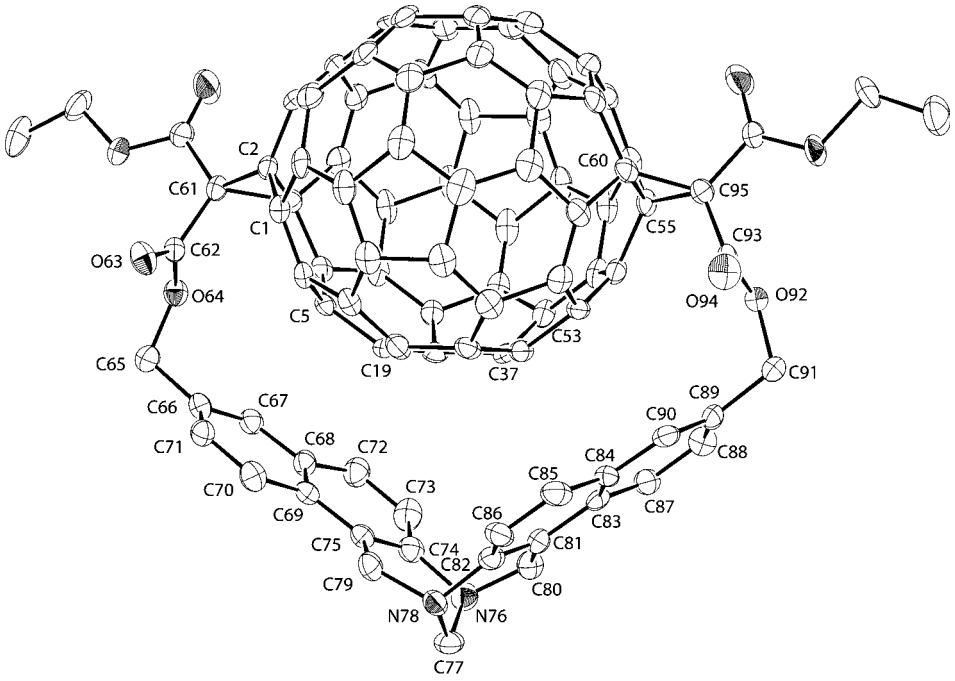



Figure 1. Crystal structure of *trans*-1 bisadduct (*R*,*R*)-**19**. Molecules of $CH_2Cl_2$ are omitted for clarity. Atomic displacement parameters obtained at 238 K are drawn at the 30% probability level.

for a chiral fullerene. In this connection it should be mentioned that crystallization of this compound is difficult and time-consuming. For the present analysis, only one suitable crystal was available and thus we cannot exclude that crystals of the (*S*,*S*)-enantiomer and the racemic compound can be obtained.

The symmetry of the fullerene bisadduct (*R*,*R*)-**19** is approximately $C_2$. With respect to the free $C_{60}$ skeleton (with a mean diameter of ca. 7.07 Å), the bridgehead atoms C1, C2, C55, C60 of the cyclopropane rings protrude out by about 0.13 Å, as observed, for example, in a hexakisadduct of $C_{60}$.[18] Semiempirical calculations[19] of malonate (*R*,*R*)-**18** gave a distance of 12.86 Å between the two methylene groups attached to the naphthyl moieties of the modified Tröger base tether. The calculated value deviates only slightly from the observed corresponding distance of 12.80 Å between C65 and C91. This result indicates very small strain in the spacer which probably accounts for the observed high yield of the double Bingel cycloaddition. The planar naphthyl subunits C66–C75 and C81–C90 are in close contact with the $C_{60}$ skeleton. The [6,5] bond C5–C19 is nearly on top of the six-membered ring C66–C71, making four short intramolecular contacts between 3.22 and 3.33 Å. On the other side, there are also four short contacts between the [6,5] bond C37–C53 and the six-membered ring C83–C90, with distances between 3.26 and 3.37 Å.

The crystal packing based on its calculated density (1.625 g cm$^{-3}$), as well as on the analysis of intermolecular contacts is quite compact, as expected. The overall arrangement of a hexagonal close-packed layer, with solvent molecules sitting in the cavities, is shown in Figure 2 (note that only the ordered solvent molecules are considered here). Each fullerene molecule makes a short O···C contact of 3.09 Å to a neighboring molecule of solvent. In addition, each fullerene is involved in 29 intermolecular contacts (3.12 to 3.50 Å) to neighbouring fullerenes. The shortest intermolecular contact between a naphthyl unit and the $C_{60}$ sphere of 3.12 Å is indicated in Figure 2 as a dashed line.

To prepare bisadducts with the *trans*-3 addition pattern, we explored biphenyl derivatives of the Tröger base, since they offer the opportunity for fine-tuning both geometry and extension of the tether by placing reactive groups in various positions of the terminal phenyl rings. Suzuki cross-coupling is the most powerful and most frequently used synthetic route to biaryls.[20] Reaction of diiodide (±)-**5** with 4-(ethoxycarbonyl)phenylboronic acid in the presence of [Pd(PPh$_3$)$_4$] afforded diester (±)-**20** in 81% yield. Subsequent reduction with LiAlH$_4$ gave diol (±)-**21**, which was converted to bismalonate (±)-**22** by the same method as described above (see Supporting Information for the X-ray crystal structure of (±)-**22**). Bingel reaction of bismalonate (±)-**22** with $C_{60}$ afforded two diastereoisomeric bisadducts (±)-**23a** and (±)-**23b** in a 5.4:1 ratio which demonstrate identical absorption spectra and have, therefore, the same addition pattern,

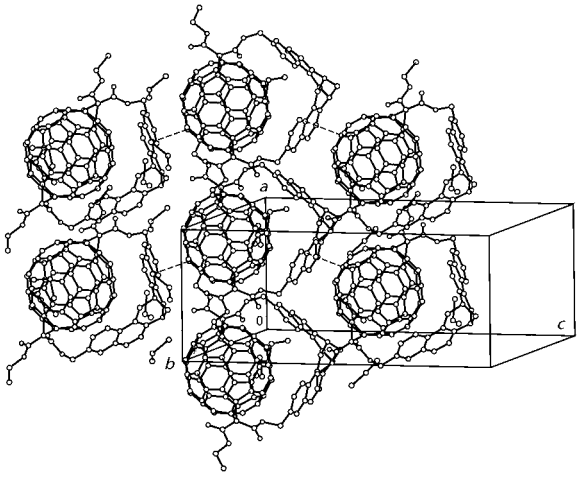



Figure 2. Crystal packing of (*R*,*R*)-**19**. Only ordered molecules of $CH_2Cl_2$ are shown for clarity. The shortest intermolecular contact between the naphthyl unit of a spacer and a $C_{60}$ sphere (3.12 Å) is shown as a dashed line.

identified as *trans*-3. The $^1$H NMR spectra of (±)-**23a** and (±)-**23b** clearly indicated $C_1$-symmetry for both products. In addition, in the $^{13}$C NMR spectra of the major product, (±)-**23a**, 75 of expected 76 signals in the C(sp$^2$)-region were observed, thus undoubtedly confirming $C_1$ symmetry.

The formation of three (*in–in*, *in–out*, and *out–out*) isomers is theoretically possible also for the *trans*-3 bisadduct of $C_{60}$.[17] However, both *in–in* and *out–out* adducts should have $C_2$ symmetry due to the matching of the $C_2$ symmetry of the Tröger base unit with the same symmetry of the *trans*-3 addition pattern, and have to be excluded on the basis of the NMR data. Therefore, both isolated bisadducts, (±)-**23a** and (±)-**23b** must have the *in–out trans*-3 configuration. Accordingly, they are diastereoisomeric pairs of enantiomers with (*S*,*S*,$^{f,s}$*A*)/(*R*,*R*,$^{f,s}$*C*) and (*S*,*S*,$^{f,s}$*C*)/(*R*,*R*,$^{f,s}$*A*) configurations (Scheme 2).[21] Absolute configurations of **23a**/**23b** were established later with the aid of enantiomerically pure **22** (see below).

**Enantiomerically pure bismalonates and bisadducts of $C_{60}$**: Since the *trans*-2 and *trans*-3 addition patterns are inherently chiral, it was particularly attractive to prepare the corresponding bisadducts using nonracemic **2** and **22**. It was known since the work of Prelog and Wieland[9c] that the resolution of the Tröger base via diastereoisomeric salts with optically active acids is generally not feasible due to relatively rapid racemization in the acidic media. Consequently, in a pioneering approach, the authors developed the first resolution of the Tröger base by chromatography on a chiral stationary phase (CSP) consisting of a specially prepared lactose.[9c] We succeeded in separating the enantiomers of bismalonate **2** on a Chiralcel OJ HPLC column with a tris(4-methylbenzoyl)cellulose derivative as CSP. In the case of **22**, separation of enantiomers was achieved on the (*S*,*S*)-Whelk O1 stationary phase with a covalently bound chiral selector derived from a 3,4-disubstituted 1,2,3,4-tetrahydrophenanthrene.

The absolute configuration of (+)-**2** was assigned as (*S*,*S*) based on the close similarity of its CD spectrum with that of (+)-(*S*,*S*)-**1** (see Supporting Information). The absolute configuration of the latter was undoubtedly determined previously from the X-ray structure of the salt with (−)-1,1′-binaphthalene-2,2′-diyl hydrogen phosphate.[22] Similarly, we assigned the absolute configurations of (−)-**22** and (+)-**22** as (*R*,*R*) and (*S*,*S*), respectively, based on the sign of the Cotton effect for the longest-wavelength absorption band in their CD-spectra (see Supporting Information). However, this assignment should be treated with some caution, since the structure of the chromophore in **22** is somewhat different from that in **1** or **2**.

Double Bingel addition of enantiomerically pure (*S*,*S*)-**2** and (*R*,*R*)-**2** to $C_{60}$ afforded two enantiomeric adducts (*S*,*S*,$^{f,s}$*A*)-**9** (for NMR spectra, see Supporting Information) and (*R*,*R*,$^{f,s}$*C*)-**9**, respectively, with perfect diastereoselectivity.[21] Double addition of (*S*,*S*)-**2** to $C_{60}$ resulted in the formation of the bisadduct with a ($^{f,s}$*A*)-configured fullerene moiety, which was established by comparison of its CD spectrum (Figure 3) with those of previously reported optically pure *trans*-2 derivatives of $C_{60}$.[7] Accordingly, double addition of (*R*,*R*)-**2** gave exclusively (*R*,*R*,$^{f,s}$*C*)-**9**.

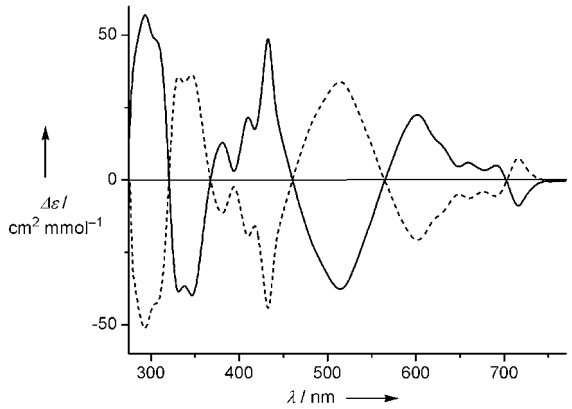



Figure 3. CD spectra of (*S*,*S*,$^{f,s}$*A*)-**9** (solid line) and (*R*,*R*,$^{f,s}$*C*)-**9** (dashed line) in $CHCl_3$.

The high asymmetric induction in the double addition of (*S*,*S*)-**2** and (*R*,*R*)-**2** to $C_{60}$ is remarkable given the very large distance between the two reacting fullerene bonds that is spanned by the tether. It was rationalized by using semiempirical PM3 calculations of the optimized geometries and heats of formation of the potential diastereoisomeric bisadducts.[19] Bisadduct (*S*,*S*,$^{f,s}$*A*)-**9** was calculated to be dramatically more favorable ($\Delta\Delta H = 29.4$ kcal mol$^{-1}$) than its theoretically possible diastereoisomer (*S*,*S*,$^{f,s}$*C*)-**9** (Figure 4). The

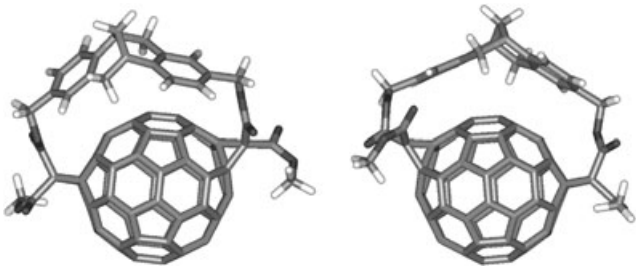


Figure 4. Energy-minimized structures of (*S*,*S*,$^{f,s}$*A*)-**9** (left) and (*S*,*S*,$^{f,s}$*C*)-**9** (right). Ethyl esters have been substituted by methyl esters for clarity.

calculated stereoselectivity is in perfect agreement with the experimental finding, assuming that the thermodynamic stability of the bisadducts is reflected in the transition state of the second cyclopropanation step that leads to macrocyclization and determines the absolute configuration of the addition pattern.[6a]

As described above, double Bingel addition of racemic bismalonate (±)-**22** leads to two diastereoisomeric pairs of enantiomers (±)-**23a**/(±)-**23b**. We repeated this addition with enantiomerically pure bismalonates (*S*,*S*)-**22** and (*R*,*R*)-**22**, isolated all four diastereoisomers (*S*,*S*,$^{f,s}$*A*)-**23a**, (*S*,*S*,$^{f,s}$*C*)-**23a**, (*R*,*R*,$^{f,s}$*A*)-**23b**, and (*R*,*R*,$^{f,s}$*C*)-**23b**, and assigned their absolute configuration from their CD spectra (Figure 5). As

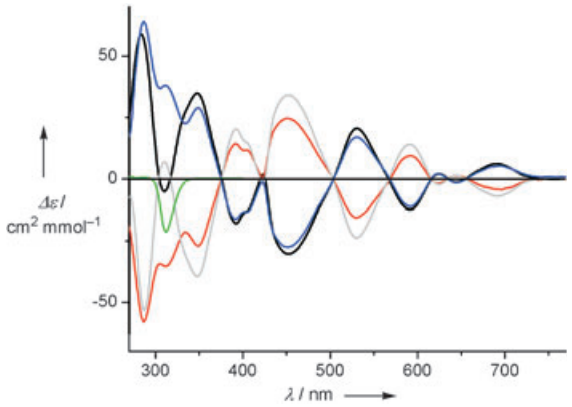



Figure 5. CD spectra of ($R$,$R$,$^{f,s}C$)-**23a** (black), ($R$,$R$,$^{f,s}A$)-**23a** (red), ($S$,$S$,$^{f,s}A$)-**23b** (gray), ($S$,$S$,$^{f,s}C$)-**23b** (blue), and ($R$,$R$)-**22** (green) in $CHCl_3$.

expected, *enantiomeric* pairs of bisadducts ($S$,$S$,$^{f,s}A$)-**23a**/($R$,$R$,$^{f,s}C$)-**23b** or ($S$,$S$,$^{f,s}C$)-**23a**/($R$,$R$,$^{f,s}A$)-**23b** display opposite Cotton effects over the entire spectral range. On the other hand, *diastereoisomeric* pairs ($S$,$S$,$^{f,s}A$)-**23a**/($S$,$S$,$^{f,s}C$)-**23a** or ($R$,$R$,$^{f,s}A$)-**23b**/($R$,$R$,$^{f,s}C$)-**23b** show some deviation from mirror image in the range 270–340 nm due to the own Cotton effect of the Tröger base unit, which has *the same* configuration in each pair of diastereoisomers while configurations of fullerene chromophores are *opposite*. Subtraction of the spectrum of ($S$,$S$)-**22** from the spectra of ($S$,$S$,$^{f,s}A$)-**23a** and ($S$,$S$,$^{f,s}C$)-**23a** gave "pure" CD spectra of the oppositely configured fullerene chromophores (Figure 6). They are

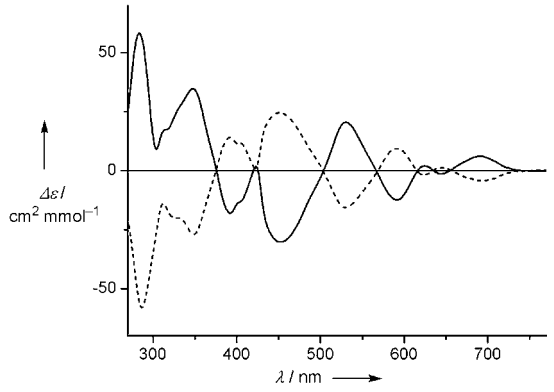



Figure 6. CD spectra of ($^{f,s}C$) (solid line) and ($^{f,s}A$) (dashed line) configured fullerene chromophores with *trans*-3 addition pattern, obtained by subtraction of the CD spectrum of ($R$,$R$)-**22** from the spectra of ($R$,$R$,$^{f,s}C$)-**23a** and ($R$,$R$,$^{f,s}A$)-**23a**, respectively.

merely identical to the previously published CD spectra of enantiomerically pure *trans*-3 bis(diethyl malonate) adducts $C_{62}(COOEt)_4$,[7] thus allowing assignment of the absolute configuration of the fullerene chromophore. The major product from addition of ($S$,$S$)-**22** to $C_{60}$ has ($S$,$S$,$^{f,s}A$), and the minor one ($S$,$S$,$^{f,s}A$) configuration. According to calculations of optimized geometries and heats of formation,[19] ($S$,$S$,$^{f,s}A$)-**23a** is indeed by 0.9 kcal mol$^{-1}$ more favorable than ($S$,$S$,$^{f,s}C$)-**23a**, thus supporting the correct assignment of the relative and absolute configuration. Definitely, these results should also be treated with some caution, as the energy difference between two diastereoisomers is very small. However, the results of the calculation are in good agreement with the experimentally found moderate diastereoselectivity (d.r. 85:15) in favor of the ($^{f,s}A$) addition pattern in the case of the ($S$,$S$)-configured bismalonate.

The very high yield obtained in the synthesis of *trans*-1 bisadduct (±)-**19**, together with the X-ray crystallographic analysis (Figure 1), suggested the possibility of a special intramolecular interaction between the naphthalene moieties of the tether and the fullerene core, not present in other conjugates, which could contribute to the stereoselectivity of the Bingel macrocyclization reaction. To probe this further, electrochemical experiments were performed with the *trans*-1, *trans*-2, and *trans*-4 bisadducts (±)-**19**, (±)-**9**, and (±)-**14**, using cyclic voltammetry (CV), Osteryoung square wave voltammetry (OSWV), and controlled potential electrolysis (CPE).

The CVs of the three compounds are presented in Figure 7, and the potential scale is referenced to internal ferrocene, shown at 0 V. In all three cases, the first reduction process is chemically and electrochemically reversible (see Table 1). However, on the CV time scale, the second reduction process for the *trans*-2 and *trans*-4 bisadducts (±)-**9** and (±)-**14** is chemically irreversible, as evidenced by the appearance of decreased anodic currents on the return scan, and the appearance of extra anodic waves. This is the expected result, since malonate adducts are known to be unstable at the second reduction process, a transformation we discovered and called retro-Bingel or retro-cyclopropanation reaction.[23] Interestingly, *trans*-1 adduct (±)-**19** exhibits perfectly reversible behavior for the first two reduction processes, on the CV time scale. This indicates higher stability of this malonate adduct relative to the others, at least under electron-reducing conditions, possibly the result of the naphthalene–fullerene interaction. However, the first reduction potential of *trans*-1 bisadduct (±)-**19** is identical to

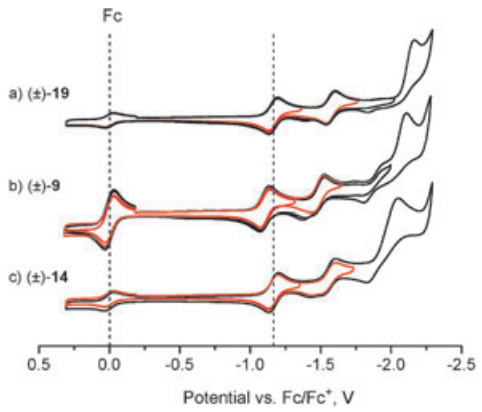



Figure 7. CV of a) 0.2 mM (±)-**19**, b) 0.2 mM *trans*-2 (±)-**9**, and c) 0.2 mM (±)-**14** in $CH_2Cl_2$, 0.1 M $Bu_4NPF_6$, scan rate 100 mV s$^{-1}$, room temperature.

Table 1. Electrochemical potentials (V) and $\Delta E_{pp}$ (mV, in parentheses) versus $Fc/Fc^+$, scan rate 100 mV $s^{-1}$.

| | $C_{60}$[a] | *trans*-1 ((±)-**19**)[b] | *trans*-2 ((±)-**9**)[b] | *trans*-4 ((±)-**14**)[b] | *trans*-1 (**24**)[c] | *trans*-1 ((±)-**25**)[c] | *trans*-2 ((±)-**26**)[c] |
|---|---|---|---|---|---|---|---|
| $E^1_{1/2}$ | −0.98 (65) | −1.17 (69) | −1.11(65) | −1.17(70) | −0. 94(77) | −1.04(70) | −1.02(79) |
| $E^2_{1/2}$ | −1.37 (67) | −1.57(66) | −1.52[d] | −1.61[d] | −1.36[d] | −1.51[d] | −1.48[d] |

[a] In $CH_3CN$/toluene, taken from reference [24]. [b] In $CH_2Cl_2$ in the presence of 0.1 M $Bu_4NPF_6$. [c] In $CH_3CN$/$CH_2Cl_2$ in the presence of 0.1 M $Bu_4NPF_6$, taken from reference [15a]. [d] Only cathodic potential is given.

that of (±)-**14**, while (±)-**9** is easier to reduce by 60 mV. The origin of these differences is not clear at the present time. Due to the irreversible nature of the second reduction process for (±)-**9** and (±)-**14**, it is not possible to report $E^2_{1/2}$ values, but based on the peak potentials observed, *trans*-1 and *trans*-4 bisadducts (±)-**19** and (±)-**14** seem to have comparable values for the second reduction potential, while *trans*-2 compound (±)-**9** is again easier to reduce to its corresponding dianion. The first reduction potentials $E^1_{1/2}$ are all more negative than that of the non-tethered *trans*-1 reference bisadduct **24** (Table 1).[15a] It thus appears as if the tethers in all cases, including those on the dibenzo[18]crown derivative analogues (±)-**25** and (±)-**26** (Figure 8), result in cathodic shifts for the first reduction potential, expected if they all exhibit some intramolecular donor–acceptor interactions.

To further probe the stability of these compounds upon electron reductions, CPEs were performed for (±)-**9**, (±)-**14**, and (±)-**19** (see Supporting Information for details). While CV showed that the *trans*-1 bisadduct (±)-**19** is kinetically much more stable than (±)-**9** and (±)-**14**, even after two-electron reduction, CPE resulted in the decomposition of all adducts back to the parent $C_{60}$. Thus on the CV time scale (seconds), *trans*-1 bisadduct (±)-**19** is more stable than the others when reduced, but all three bisadducts are unstable on the CPE time scale (minutes).

## Conclusion

In this paper, we report the first diastereoselective synthesis of enantiomeric bisadducts of $C_{60}$ with the inherently chiral *trans*-2 and *trans*-3 addition patterns by tether-directed remote functionalization using novel Tröger base derivatives as optically active spacers. Now, all inherently chiral bisaddition patterns of $C_{60}$ are readily available by this versatile methodology. This result from extensive research efforts is not only of fundamental but also of technological interest since enantiomerically pure fullerene derivatives are becoming promising building blocks for supramolecular applications.[25] To the best of our knowledge, there are no other examples of asymmetric syntheses using the structural motif of the Tröger base as a chiral auxiliary. In addition, we describe the use of derivatives of the Tröger base in the regio- and diastereoselective (with respect to *in–out* isomerism) tether-directed remote functionalization to give *trans*-4 and *trans*-1 bisadducts of $C_{60}$ in remarkably high yields. Spontaneous resolution of the *trans-1* derivative afforded the enantiomer in which the fullerene sphere is bridged by an (*R,R*)-configured Tröger base tether as shown by X-ray crystallography: it is the first such example in the field of fullerene chirality. We are now applying the novel tethers to the regio- and stereoselective multiple functionalization of higher fullerenes, a nearly unexplored field.[26]

## Experimental Section

**General methods**: All chemicals and solvents were obtained from commercial sources (Fluka, Aldrich, Merck) and used without further purification unless stated otherwise. Technical grade solvents were distilled before use. THF was distilled over sodium/benzophenone. DMF was stored over flame-dried molecular sieves (4 Å). Reactions were carried out under dry $N_2$ or Ar. TLC: precoated $SiO_2$ plates Alugram $UV_{254}$ (Macherey-Nagel). Column chromatography: Kieselgel 60 (Fluka, particle size 0.040–0.063 mm). HPLC: Merck-Hitachi L-6250 Intelligent Pump, L-4000 A UV-detector, and D-2500 Chromato-Integrator. FT-IR spectra: Perkin Elmer Spectrum BX Spectrometer. NMR: 300 MHz $^1$H NMR and 75 MHz $^{13}$C NMR spectra were recorded on a Varian Gemini 300 spectrometer; 500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR spectra were measured on a Bruker AMX 500 spectrometer; chemical shifts ($\delta$) are given in ppm relative to TMS; coupling constants ($J$) are given in Hz; solvent signals were used as internal references. EI-MS (70 eV): Micromass Auto-Spec Ultima mass spectrometer; ESI-MS (solvent $CH_2Cl_2$/$CH_3OH$) and MALDI-MS (2-[(2*E*)-3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile (DCTB) matrix): Ion Spec 4.7 Ultima mass spectrometer. UV-visible spectra: Varian CARY 500 spectrophotometer. Circular

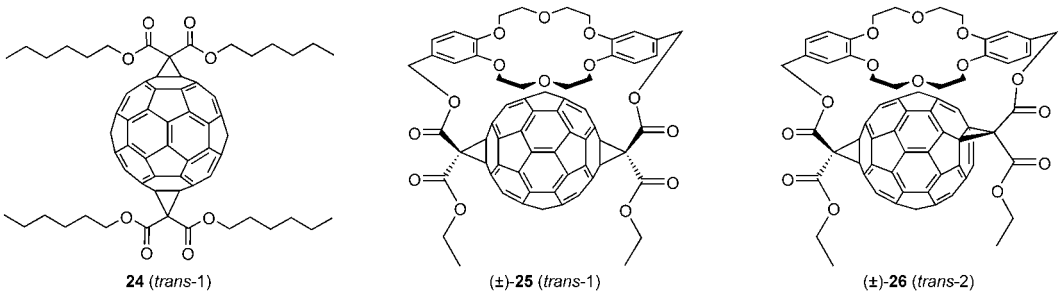



Figure 8. Reference compounds for electrochemical studies: non-tethered *trans*-1 bisadduct **24** and *trans*-1 and *trans*-2 bisadducts (±)-**25** and (±)-**26** with crown ether spacers.

dichroism (CD) spectra: Jasco J 715 spectropolarimeter. Optical rotations: Perkin-Elmer 241 polarimeter, $[\alpha]_D$ values are given in $10^{-1}$ deg cm$^2$ g$^{-1}$. Melting points: Büchi B-540 instrument in open capillaries.

**(±)-2,8-Diiodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine ((±)-5)**:[12b] A mixture of **4** (6.59 g, 30 mmol) and paraformaldehyde (1.81 g, 60 mmol) was added in portions under vigorous stirring to TFA (50 mL) at −15 °C. The resulting mixture was allowed to reach room temperature and stirred for 40 h, then slowly added to a stirred mixture of ice and an excess of concentrated aqueous $NH_3$. Extraction with $CH_2Cl_2$ (3× 100 mL), drying of the organic layer over $MgSO_4$, and removal of the solvent in vacuo gave a crude product which was purified by flash chromatography (AcOEt/$CH_2Cl_2$ 1:10) to give (±)-**5** (3.98 g, 56 %). $R_f$ (AcOEt/$CH_2Cl_2$ 1:10) = 0.26 ; m.p. 178.5–180 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.45 (dd, $J$ = 8.4, $J$ = 1.9 Hz, 2H; Ar-H), 7.23 (d, $J$ = 1.9 Hz, 2H; Ar-H), 6.87 (d, $J$ = 8.4 Hz, 2H; Ar-H), 4.62 (d, $J$ = 16.8 Hz, 2H; *exo*-$CH_2$N), 4.24 (s, 2H; $NCH_2$N), 4.08 ppm (d, $J$ = 16.8 Hz, 2H; *endo*-$CH_2$N); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 147.47, 136.34, 135.63, 130.07, 126.93, 87.60, 66.54, 58.16 ppm; ESI-MS: 475 (100, $[M$H$]^+$), 497 (9, $[M$+Na$]^+$).

**(±)-1,7-Diiodo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine ((±)-7)**: Prepared as described for (±)-**5** from **6** (4.46 g, 19.1 mmol). Yield 3.72 g (77 %); $R_f$ = 0.67 ($CH_2Cl_2$); m.p. 208.5–210.0 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.44 (d, $J$ = 8.1 Hz, 2H; Ar-H), 6.81 (d, $J$ = 7.8 Hz, 2H; Ar-H), 4.25 (d, $J$ = 17.1 Hz, 2H; *exo*-$CH_2$N), 4.20 (s, 2H; $NCH_2$N), 3.84 (d, $J$ = 17.1 Hz, 2H; *endo*-$CH_2$N), 2.42 ppm (s, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 147.71, 134.32, 133.63, 130.66, 129.84, 95.33, 66.91, 61.24, 17.20 ppm; FT-IR (neat): $\tilde{\nu}$ = 2937, 2879, 1571, 1446, 1426, 1389, 1211, 1118, 963, 939, 798 cm$^{-1}$; HR-ESI-MS: $m/z$: calcd for $C_{17}H_{17}I_2N_2$ ($[M$H$]^+$): 502.9481; found: 502.9468.

**(±)-6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-dicarbaldehyde ((±)-8)**:[12a] A solution of (±)-**5** (474 mg, 1.0 mmol) in dry THF (5 mL) was treated dropwise with a 1.6 M solution of *n*BuLi in hexane (1.6 mL, 2.5 mmol) at −80 °C. The mixture was stirred for 5 min at −78 °C, then dry DMF (0.2 mL, 2.6 mmol) was added. The mixture was allowed to reach room temperature, then water (10 mL) was added. Extraction with $CH_2Cl_2$ (3×25 mL), drying of the organic layer over $MgSO_4$ and removal of the solvent in vacuo gave a crude product which was purified by flash chromatography (AcOEt/$CH_2Cl_2$ 1:3) to give (±)-**8** (253 mg, 91 %). $R_f$ = 0.39 (AcOEt/$CH_2Cl_2$ 1:3); m.p. 161–162 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.83 (s, 2H; CHO), 7.69 (dd, $J$ = 8.4, $J$ = 1.5 Hz, 2H; Ar-H), 7.47 (d, $J$ = 1.5 Hz, 2H; Ar-H), 7.27 (d, $J$ = 8.4 Hz, 2H; Ar-H), 4.81 (d, $J$ = 16.8 Hz, 2H; *exo*-$CH_2$N), 4.29–4.36 ppm (m, 4H; $NCH_2$N, *endo*-$CH_2$N); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 190.76, 153.80, 132.41, 128.99, 128.90, 128.00, 125.50, 66.49, 58.65 ppm; ESI-MS: 279 ($[M$H$]^+$).

**(±)-4,10-Dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine-1,7-dicarbaldehyde ((±)-11)**: Prepared as described for (±)-**8** from (±)-**7** (502 g, 1.0 mmol) with the following amendment: 50 mL THF was used due to limited solubility of (±)-**7** at low temperature. Yield 241 mg (79 %); $R_f$ = 0.26 (AcOEt/$CH_2Cl_2$ 1:20); m.p. 240–242 °C (decomp); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.90 (s, 2H; CHO), 7.40 (d, $J$ = 8.1 Hz, 2H; Ar-H), 7.27 (d, $J$ = 8.1 Hz, 2H; Ar-H), 4.82 (d, $J$ = 18.0 Hz, 2H; *exo*-$CH_2$N), 4.59 (d, $J$ = 18.0 Hz, 2H; *endo*-$CH_2$N), 4.27 (s, 2H; $NCH_2$N), 2.54 ppm (s, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 192.94, 147.20, 140.63, 131.47 (2 overlapped signals), 130.06, 129.09, 65.62, 54.47, 18.39 ppm; FT-IR (neat): $\tilde{\nu}$ = 2894, 2729, 1678 (C=O), 1568, 1426, 1218, 1100, 950, 935, 820, 751 cm$^{-1}$; ESI-MS: $m/z$: 307 (55, $M$H$^+$), 279 (100, $[M$H−CO$]^+$). HR-MALDI-MS: $m/z$: calcd for $C_{19}H_{19}N_2O_2$ ($[M$H$]^+$): 307.1447; found: 307.1445.

**(±)-(8-Hydroxymethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocin-2-yl)-methanol ((±)-3)**: A solution of (±)-**8** (556 g, 2.0 mmol) in dry THF (20 mL) was slowly added to a suspension of $LiAlH_4$ (114 mg, 3.0 mmol) in dry THF (20 mL). The mixture was stirred for 2 h at room temperature, then quenched by slow addition of water. The inorganic precipitate was filtered and the filtrate dried over $MgSO_4$ and concentrated to give (±)-**3** (524 mg, 93 %) which was used without further purification. M.p. 194.5–196.5 °C; $^1$H NMR (300 MHz, $CDCl_3$/$CD_3OD$): $\delta$ = 7.02 (dd, $J$ = 8.4 Hz, 1.9, 2H; Ar-H), 6.97 (d, $J$ = 8.4 Hz, 2H; Ar-H), 6.76 (d, $J$ = 1.9 Hz, 2H; Ar-H), 4.52 (d, $J$ = 16.8 Hz, 2H; *exo*-$CH_2$N), 4.35 (s, 4H; $OCH_2$); 4.17 (s, 2H; $NCH_2$N), 4.02 ppm (d, $J$ = 16.8 Hz, 2H; *endo*-$CH_2$N); $^{13}$C NMR (75 MHz, $CDCl_3$/$CD_3OD$): $\delta$ = 146.05, 137.02, 127.10, 126.17, 125.36, 124.57, 66.54, 63.85, 58.48 ppm; FT-IR (neat): $\tilde{\nu}$ = 3410, 3150, 2920, 2872, 1612, 1576, 1492, 1205, 1008, 841, 831 cm$^{-1}$; HR-MALDI-MS: $m/z$: calcd for $C_{17}H_{19}N_2O_2$ ($[M$H$]^+$): 283.1447; found: 283.1437.

**(±)-(4,10-Dimethyl-7-hydroxymethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocin-1-yl)methanol ((±)-12)**: Prepared as described for (±)-**3** from (±)-**11** (367 mg, 1.2 mmol). Yield 338 mg (91 %); m.p. 222–223 °C; $^1$H NMR (300 MHz, $CDCl_3$/$CD_3OD$): $\delta$ = 6.99 (d, $J$ = 8.2 Hz, 2H; Ar-H), 6.85 (d, $J$ = 8.2 Hz, 2H; Ar-H), 4.50 (d, $J$ = 17.5 Hz, 2H; *exo*-$CH_2$N), 4.37 (s, 4H; $OCH_2$), 4.16 (s, 2H; $NCH_2$N), 4.11 (d, $J$ = 17.5 Hz, 2H; *endo*-$CH_2$N), 2.61 (br. s, 2H; OH), 2.38 ppm (s, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$/$CD_3OD$): $\delta$ = 145.94, 135.19, 132.45, 128.67, 126.21, 123.30, 66.33, 61.98, 52.47, 17.29 ppm; FT-IR (neat): $\nu$ = 3550–3260 (OH), 2863, 1579, 1446, 1407, 1217, 977, 942, 817 cm$^{-1}$; HR-MALDI-MS: $m/z$: calcd for $C_{19}H_{23}N_2O_2$ ($[M$H$]^+$): 311.1760; found: 311.1754.

**(6-Aminonaphthyl)methanol (16)**: Acid **15** (1.87 g, 10 mmol) was added in portions to a suspension of $LiAlH_4$ (1.14 g, 30 mmol) in dry THF (50 mL) at 0 °C. After the addition was completed, the mixture was stirred for 1 h at room temperature and then heated to reflux for 2 h. The mixture was allowed to reach room temperature and carefully quenched by slow addition of water. The inorganic precipitate was filtered and the filtrate dried over $MgSO_4$ and concentrated to give **16** (1.61 g, 93 %) as a slightly brownish solid which was used without further purification; m.p. 166–168 °C (decomp); $^1$H NMR (300 MHz, $(CD_3)_2SO$): 7.53–7.57 (m, 2H; Ar-H), 7.46 (d, $J$ = 8.4 Hz, 1H; Ar-H), 7.25 (dd, $J$ = 8.4, 1.6 Hz, 1H; Ar-H), 6.92 (dd, $J$ = 8.7, 2.2 Hz, 1H; Ar-H), 6.81 (d, $J$ = 2.2 Hz, 1H; Ar-H), 5.30 (s, 2H; $CH_2$), 5.15 (br. s, 1H; OH), 4.53 ppm (s, 2H; $NH_2$); $^{13}$C NMR (75 MHz, $(CD_3)_2SO$): $\delta$ = 146.11, 134.67, 133.93, 128.17, 125.91, 125.40, 124.28, 124.55, 118.25, 105.83, 63.21 ppm; FT-IR (neat): $\tilde{\nu}$ = 3370 ($NH_2$), 3195 (OH), 2923, 2863, 1630, 1607, 1508, 1483, 1178, 1011, 882, 821 cm$^{-1}$; HR-EI-MS: $m/z$: calcd for $C_{11}H_{11}NO$ ($[M]^+$): 173.0841; found: 173.0835.

**(±)-(11-Hydroxymethyl-8*H*,16*H*-7,15-methanodinaphtho[2,1-*b*][2′,1′-*f*][1,5]-diazocin-3-yl)methanol ((±)-17)**: A suspension of **16** (865 mg, 5.0 mmol) in EtOH (10 mL) was treated at 0 °C first with formaldehyde solution (37 % in water; 2.5 mL, ca. 30 mmol) and then with concentrated HCl solution (32 % in water, 2.0 mL). After stirring at room temperature for 2 h, the mixture turned to clear yellow solution, then a white solid precipitated slowly. After 16 h, water (30 mL) was added and the pH adjusted to 14 with conc. aqueous $NH_3$. The formed precipitate was filtered, washed excessively with $H_2O$, then with $CH_2Cl_2$, and dried in vacuo to give (±)-**17** (736 mg, 77 %) which was used without further purification. M.p.: decomposes above 290 °C; $^1$H NMR (300 MHz, $(CD_3)_2SO$): 7.63–7.72 (m, 6H; Ar-H), 7.42 (d, $J$ = 8.6 Hz, 2H; Ar-H), 7.35 (d, $J$ = 8.7 Hz, 2H; Ar-H), 5.26 (t, $J$ = 5.6 Hz, 2H; OH), 4.94 (d, $J$ = 16.8 Hz, 2H; *exo*-$CH_2$N), 4.69 (d, $J$ = 16.8 Hz, 2H; *endo*-$CH_2$N), 4.58 (d, $J$ = 5.6 Hz, 4H; C$H_2$OH), 4.42 ppm (s, 2H; $NCH_2$N); $^{13}$C NMR (75 MHz, $(CD_3)_2SO$): $\delta$ = 144.80, 138.57, 129.89, 129.76, 126.92, 125.45, 124.79, 124.54, 121.14, 121.03, 66.01, 62.69, 55.15 ppm; FT-IR (neat): $\tilde{\nu}$ = 3360–3180 (OH), 2909, 2847, 1597, 1471, 1389, 1210, 1017, 935, 896, 821 cm$^{-1}$; ESI-MS: 383 ($[M$H$]^+$); HR-MALDI-MS: $m/z$: calcd for $C_{25}H_{23}N_2O_2$ ($[M$H$]^+$): 383.1760; found: 383.1759.

**(±)-Diethyl 4,4′-(6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diyl)dibenzoate ((±)-20)**: A suspension of 4-(ethoxycarbonyl)phenylboronic acid (1.076 g, 5.55 mmol) in ethanol (8 mL) and a solution of $K_2CO_3$ (3.317 g, 24.00 mmol) in $H_2O$ (4 mL) were added to a solution of (±)-**3** (948 mg, 2.00 mmol) and $[Pd(PPh_3)_4]$ (231 mg, 0.20 mmol) in toluene (40 mL). The resulting mixture was heated to reflux for 1.5 h under Ar, then cooled to room temperature and partitioned between $CH_2Cl_2$ (100 mL) and $H_2O$ (50 mL). The organic layer was separated, washed with $H_2O$ (2×50 mL), dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (AcOEt/$CH_2Cl_2$ 1:10–1:5) afforded (±)-**20** (835 mg, 81 %) as colorless solid. $R_f$ (AcOEt/$CH_2Cl_2$ 1:5) = 0.24; m.p. 209–211 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.05 (d, $J$ = 8.7 Hz, 4H; Ar-H), 7.54 (d, $J$ = 8.7 Hz, 4H; Ar-H), 7.44 (dd, $J$ = 8.4 Hz, 2.2, 2H; Ar-H), 7.25 (d, $J$ = 8.4 Hz, 2H; Ar-H), 7.19 (d, $J$ = 1.9 Hz; 2H; Ar-H), 4.81 (d,

2H, $J$=16.5 Hz, 2H; *exo*-$NCH_2$), 4.39 (s, 2H; $NCH_2N$)), 4.38 (q, $J$=7.2 Hz, 4H; $CH_3CH_2$), 4.31 (d, $J$=16.8, 2H; *endo*-$NCH_2$), 1.40 ppm (t, $J$=7.2 Hz, 6H; $CH_3CH_2$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=166.33, 148.10, 144.76, 135.72, 129.94, 128.87, 128.18, 126.51, 126.32, 125.70, 125.51, 67.00, 61.00, 58.90, 14.51 ppm; FT-IR (neat): $\tilde{\nu}$=2956, 2898, 1705 (C=O), 1606, 1267, 1180, 1102, 962, 942, 747 cm$^{-1}$; HR-ESI-MS: $m/z$: calcd for $C_{33}H_{30}N_2NaO_4$ ([$M$+Na]$^+$): 541.2103; found: 541.2098.

**(±)-[6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diylbis(4,1-phenylene)]dimethanol ((±)-21)**: A solution of (±)-**20** (835 mg, 1.6 mmol) in THF (20 mL) was added dropwise to a suspension of $LiAlH_4$ (190 mg, 5.0 mmol) in THF (10 mL). The mixture was heated to reflux for 2 h under Ar, then cooled to 0 °C and carefully quenched by slow addition of water. The inorganic precipitate was filtered and the filtrate dried over $MgSO_4$ and evaporated in vacuo to give (±)-**21** (700 mg, 100 %) which was used without further purification. M.p. 243.5–245 °C. $^1$H NMR (300 MHz, $(CD_3)_2SO$): $\delta$=7.50 (d, $J$=8.4 Hz, 4H; Ar-H), 7.42 (dd, $J$=8.4 Hz, 2.2, 2H; Ar-H), 7.33 (d, $J$=8.4 Hz, 4H; Ar-H), 7.25 (d, $J$=1.9 Hz, 2H; Ar-H), 7.19 (d, $J$=8.4 Hz, 2H; Ar-H), 5.17 (t, $J$=5.8 Hz, 2H; OH), 4.70 (d, $J$=16.8 Hz, 2H; *exo*-$NCH_2$), 4.49 (d, $J$=5.9 Hz, 4H; $CH_2O$), 4.28 (s, 2H; $NCH_2N$), 4.23 ppm (d, $J$=17.1 Hz, 2H; *endo*-$NCH_2$); $^{13}$C NMR (75 MHz, $(CD_3)_2SO$): $\delta$=147.28, 141.06, 138.03, 135.07, 128.33, 126.76, 125.79, 125.10, 125.03, 124.69, 66.22, 62.55, 58.24 ppm; FT-IR (neat): $\tilde{\nu}$=3250 (OH), 2950, 2899, 2848, 1611, 1479, 1320, 964, 941, 841, 764 cm$^{-1}$; ESI-MS: $m/z$ (%): 435 (100) ([$M$H]$^+$), 457 (12) ([$M$+Na]$^+$); HR-ESI-MS: $m/z$: calcd for $C_{29}H_{27}N_2O_2$ ([$M$H]$^+$): 435.2073; found: 435.2061.

**(±)-1,1′-Diethyl 3,3′-(6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diyl)dimethylene Dimalonate ((±)-2)**: A solution of (±)-**3** (282 mg, 1.0 mmol) and DMAP (488 mg, 4.0 mmol) in dry THF (50 mL) was treated at 0 °C with EtOOCCH$_2$COCl (0.50 mL; 4.0 mmol). The mixture was stirred at room temperature for 16 h, then the solvent was removed in vacuo. Column chromatography of the residue afforded (±)-**2** (267 mg, 52 %). Viscous colorless oil. $R_f$ (AcOEt/$CH_2Cl_2$ 1 : 2)=0.26; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.15 (dd, $J$=8.1 Hz, 1.9, 2H; Ar-H), 7.11 (d, $J$=8.1 Hz, 2H; Ar-H), 6.90 (d, $J$=1.9 Hz, 2H; Ar-H), 5.03 (s, 4H; $OCH_2$), 4.68 (d, $J$=16.8 Hz, 2H; *exo*-$CH_2N$), 4.28 (s, 2H; $NCH_2N$), 4.10–4.17 (m, 6H; *endo*-$CH_2N$, $CH_2CH_3$), 3.36 (s, 4H; $CH_2CO$), 1.20 ppm (t, $J$=7.2 Hz, 6H; $CH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=166.23, 166.19, 148.11, 130.76, 127.77, 127.64, 127.17, 125.18, 66.89, 66.72, 61.55, 58.57, 41.61, 14.09 ppm; FT-IR (neat): $\tilde{\nu}$=2980, 2945, 2900, 1742 sh, 1724 (C=O), 1616, 1493, 1326, 1263, 1204, 1143, 1029, 834 cm$^{-1}$; HR-ESI-MS: $m/z$: calcd for $C_{27}H_{30}N_2O_8Na$ ([$M$+Na]$^+$): 533.1900; found: 533.1901.

(*R*,*R*)-**2** and (*S*,*S*)-**2** were isolated by preparative HPLC on a Daicel Chiralcel OJ column (250×20 mm, eluent ethanol, flow rate 15 mL min$^{-1}$, detection at 254 nm). (*R*,*R*)-**2**: $[\alpha]_D$=−195 ($c$=0.25, chloroform); (*S*,*S*)-**2**: $[\alpha]_D$=+203 ($c$=0.48, chloroform).

**(±)-1,1′-Diethyl 3,3′-(8*H*,16*H*-7,15-Methanodinaphtho[2,1-*b*][2′,1′-*f*][1,5]diazocin-3,11-diyl)dimethylene Dimalonate ((±)-18)**: Prepared as described for (±)-**2** from (±)-**17** (382 mg, 1.0 mmol). Viscous colorless oil. Yield 123 mg (20 %); $R_f$ (AcOEt/$CH_2Cl_2$ 1:5)=0.20; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.64–7.71 (m, 6H; Ar-H), 7.42 (dd, $J$=8.6 Hz, 1.7, 2H; Ar-H), 7.35 (d, $J$=9.0 Hz, 2H; Ar-H), 5.27 (s, 4H; 2 $OCH_2Ar$), 5.00 (d, $J$=16.8 Hz; 2H; *exo*-$NCH_2$), 4.73 (d, $J$=16.8 Hz; 2H; *endo*-$NCH_2$), 4.50 (s, 2H; $NCH_2N$), 4.17 (q, $J$=7.2 Hz, 4H; $CH_2CH_3$), 3.40 (s, 4H; $COCH_2$), 1.22 ppm (t, $J$=7.2 Hz, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=166.26, 145.69, 131.48, 131.02, 130.44, 128.20, 127.83, 126.48, 121.64, 121.09, 67.17, 66.72, 61.58, 55.66, 41.65, 14.14 ppm; FT-IR (neat): $\tilde{\nu}$=2980, 2899, 1741 sh, 1725 (C=O), 1599, 1474, 1327, 1264, 1144, 1027, 819, 732 cm$^{-1}$; HR-MALDI-MS: $m/z$: calcd for $C_{35}H_{35}N_2O_8$ ([$M$H]$^+$): 611.2393; found: 611.2378.

**(±)-1,1′-Diethyl 3,3′-[6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diylbis(4,1-phenylenemethylene)] Dimalonate ((±)-22)**: Prepared as described for (±)-**2** from (±)-**21** (218 mg, 0.50 mmol). Yield 139 mg (42 %); $R_f$ (AcOEt/$CH_2Cl_2$ 1:2)=0.47; m.p. 123–125 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.48 (*d*, $J$=8.4 Hz, 4H; Ar-H), 7.36–7.42 (*m*, 6H; Ar-H), 7.23 (*d*, $J$=8.4 Hz, 2H; Ar-H), 7.14 (d, $J$=1.9 Hz, 2H; Ar-H), 5.19 (s, 4H; $CH_2OAr$), 4.80 (d, $J$=16.5 Hz, 2H; *exo*-$NCH_2$), 4.38 (s, 2H; $NCH_2N$), 4.29 (d, $J$=16.8 Hz, 2H; *endo*-$NCH_2$), 4.19 (q, $J$=7.2 Hz, 4H; $CH_3CH_2$), 3.42 (s, 4H; $COCH_2$), 1.24 ppm (t, $J$=7.2 Hz, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=166.33, 166.27, 147.55, 140.73, 136.32, 133.90, 128.71, 128.09, 126.91, 126.15, 125.44, 66.96, 61.65, 58.85, 41.72, 14.18 ppm; FT-IR (neat): $\tilde{\nu}$=2963, 2925, 1723 (C=O), 1612, 1485, 1191, 1149, 1024, 826, 816 cm$^{-1}$; ESI-MS: 663 (100, [$M$H]$^+$), 685 (39, [$M$+Na]$^+$); HR-ESI-MS: $m/z$: calcd for $C_{39}H_{39}N_2O_8$ ([$M$H]$^+$): 663.2706; found: 663.2702.

(*R*,*R*)-**22** and (*S*,*S*)-**22** were isolated by preparative HPLC on a Regis (*S*,*S*)-Whelk-O1 column (250×10 mm, eluent hexane/AcOEt/EtOH 83:5:12, flow rate 7 min$^{-1}$, detection at 290 nm). (*R*,*R*)-**22**: $[\alpha]_D$=−434 ($c$=0.80, chloroform); (*S*,*S*)-**22**: $[\alpha]_D$=+456 ($c$=0.76, chloroform).

**(±)-1,1′-Diethyl 3,3′-(4,10-Dimethyl-6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-1,7-diyl)dimethylene Dimalonate ((±)-13)**: Prepared as described for (±)-**2** from (±)-**12** (310 mg, 1.0 mmol). Viscous colorless oil, which crystallized very slowly upon standing; yield 288 mg (54 %); m.p. 92–93.5 °C; $R_f$ (AcOEt/$CH_2Cl_2$ 1:5)=0.32; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.08 (d, $J$=7.8 Hz, 2H; Ar-H), 7.00 (d, $J$=7.8 Hz, 2H; Ar-H), 5.01 (s, 4H; $OCH_2Ar$), 4.57 (d, $J$=17.1 Hz, 2H; *exo*-$CH_2N$), 4.28 (s, 2H; $NCH_2N$), 4.16 (qd, $J$=7.2, 2.0 Hz; 4H; $CH_2CH_3$), 4.06 (d, $J$=17.1 Hz, 2H; *endo*-$CH_2N$), 3.36 (s, 4H; $CH_2CO$), 2.42 (s, 6H; $CH_3$), 1.23 ppm (t, $J$=7.2 Hz, 6H; $CH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=166.17, 166.09, 146.40, 133.99, 129.52, 128.85, 127.03, 125.13, 66.35, 64.47, 61.61, 52.58, 41.56, 17.45, 14.11 ppm; FT-IR (neat): $\tilde{\nu}$=2946, 2899, 1744 (C=O), 1728 (C=O), 1580, 1330, 1142, 1094, 1023, 977, 810, 747 cm$^{-1}$; HR-ESI-MS: $m/z$: calcd for $C_{29}H_{34}N_2O_8Na$ ([$M$+Na]$^+$): 561.2213; found: 561.2213.

***out*,*out*-3′,3″-Diethyl (*S*,*S*)-3′,3″-(6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diyldimethylene) ($^{f,s}$*A*)-3′*H*,3″*H*-Dicyclopropa[1,9:49,59](C$_{60}$-*I*$_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate and *out*,*out*-3′,3″-Diethyl (*S*,*S*)-3′,3″-(6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diyldimethylene) 3′*H*,3″*H*-Dicyclopropa[1,9:16,17](C$_{60}$-*I*$_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate ((*S*,*S*,$^{f,s}$*A*)-9 and (*S*,*S*)-10)**: A well-degassed solution of (*S*,*S*)-**2** (44 mg, 0.086 mmol) and $C_{60}$ (54 mg, 0.075 mmol) in toluene (100 mL) was treated at 0 °C with a solution of $I_2$ (48 mg, 0.19 mmol) in toluene (5 mL) and then with DBU (0.07 mL, 0.45 mmol). The resulting mixture was stirred for 1 h at 0 °C, then filtered and applied on a $SiO_2$ column. Elution with $CH_2Cl_2$/AcOEt 5:1 afforded (*S*,*S*,$^{f,s}$*A*)-**9** (25 mg, 27 %), then (*S*,*S*)-**10** (5 mg, 6 %). Analogously, (*R*,*R*,$^{f,s}$*C*)-**9** (25 %), and (*R*,*R*)-**10** (6 %) were prepared starting from (*R*,*R*)-**8**.

**(*S*,*S*,$^{f,s}$*A*)-9**: UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$=405 (sh, 4950), 432 (4000), 488 (2000), 636 (550), 701 nm (400); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.28 (m, overlap with $CHCl_3$, 2H, Ar-H), 6.99 (d, $J$=8.1, 2H; Ar-H), 6.94 (s, 2H; Ar-H), 5.87 (d, $J$=11.5 Hz, 2H; $OCH_2Ar$), 4.96 (d, $J$=11.5 Hz, 2H; $OCH_2Ar$), 4.70 (q, $J$=7.2 Hz, 4H; $CH_2CH_3$), 4.59 (d, $J$=17.1 Hz, 2H; $NCH_2Ar$), 3.91 (s, 2H; $NCH_2N$), 3.85 (d, $J$=17.1 Hz, 2H; $NCH_2Ar$), 1.62 ppm (t, $J$=7.2 Hz, 6H; $CH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=164.04, 163.48, 149.65, 146.88, 146.87, 146.20, 145.98, 145.30, 145.23, 144.91, 144.85, 144.67, 144.59, 144.32, 144.00, 143.74, 143.40, 143.30, 143.14, 142.78, 142.16, 142.12, 142.04, 141.98, 141.88, 141.63, 141.31, 140.78, 139.75, 136.07, 135.24, 130.35, 129.33, 128.93, 127.95, 125.61, 70.89, 70.79, 67.84, 65.33, 63.76, 56.17, 49.06, 14.54 ppm; FT-IR (neat): $\tilde{\nu}$=2975, 2878, 1739 (C=O), 1607, 1490, 1222, 1106, 1055, 942, 828, 734, 702 cm$^{-1}$; HR-MALDI-MS: $m/z$: calcd for $C_{87}H_{26}N_2O_8$ ([$M$]$^+$): 1226.1689; found 1226.1696.

**(*S*,*S*)-10**: UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$=409 (sh, 2700), 422 (2300), 480 nm (2670); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=7.09–7.15 (m, 3H; Ar-H), 6.92 (s, 1H; Ar-H), 6.87(s, 1H; Ar-H), 6.76 (d, 1H; Ar-H), 5.67 (d, $J$=11.0 Hz, 1H; $OCH_2Ar$), 5.54 (d, $J$=13.2 Hz, 1H; $OCH_2Ar$), 5.10 (d, $J$=13.2 Hz, 1H; $OCH_2Ar$), 5.01 (d, $J$=11.0 Hz, 1H; $OCH_2Ar$), 4.40–4.63 (m, 6H, $OCH_2CH_3$, $NCH_2Ar$), 4.30 (s, 2H; $NCH_2N$), 4.14 (d, $J$=17.1 Hz, 1H; $NCH_2Ar$), 3.68 (d, $J$=17.1 Hz, 1H; $NCH_2Ar$), 1.39–1.46 (m, 6H, $OCH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=163.38, 163.06, 162.99, 162.27, 148.99, 148.42, 147.17, 147.10, 146.99, 146.91, 146.50, 146.29, 146.27, 146.16, 145.87, 145.85, 145.82, 145.47, 145.34, 144.92, 144.91, 144.85, 144.80, 144.69, 144.63, 144.51, 144.47, 144.43, 144.38, 144.31, 144.10, 143.79, 143.76, 143.63, 143.56, 143.54, 143.51, 143.50, 143.50, 143.50, 143.29, 143.15, 142.95, 142.67, 142.28, 142.10, 141.81, 141.73,

141.61, 141.53, 141.52, 141.45, 141.30, 140.64, 138.37, 138.17, 137.89, 137.83, 71.57, 71.28, 71.09, 68.54, 67.67, 66.99, 63.39, 63.34, 59.37, 58.89, 53.16, 51.19, 14.33 ppm; FT-IR (neat): $\tilde{\nu}$ = 2976, 2898, 1738 (C=O), 1614, 1492, 1225, 1205, 1097, 1058, 831, 731, 701 $cm^{-1}$; HR-MALDI-MS: *m/z*: calcd for $C_{87}H_{26}N_2O_8$ ($[M]^+$): 1226.1689; found 1226.1672.

***out*,*out*-3′,3″-Diethyl (±)-3′,3″-(4,10-Dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine-1,7-diyldimethylene) 3′*H*,3″*H*-Dicyclopropa[1,9:32,33]($C_{60}$-$I_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate ((±)-14)**: Prepared as described for (*S*,*S*,$^{f,s}$*A*)-**9** from (±)-**13** (129 mg, 0.24 mmol). Yield 95 mg (38%); UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$ = 416 (2900), 472 (2100), 628 (470), 692 nm (310); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.96 (d, *J* = 7.8 Hz, 1H; Ar-H), 6.84–6.89 (m, 2H; Ar-H), 6.74 (d, *J* = 7.6 Hz, 1H; Ar-H), 5.70 (d, *J* = 11.5 Hz, 1H; $OCH_2$Ar), 5.42 (d, *J* = 11.8 Hz, 1H; $OCH_2$Ar), 5.26 (d, *J* = 11.8 Hz, 1H; $OCH_2$Ar), 4.88–4.97 (m, 2H; $NCH_2$Ar, $OCH_2$Ar), 4.51–4.70 (m, 6H; C$H_2$$CH_3$, $NCH_2$Ar), 4.24 (d, *J* = 16.5 Hz, 1H; $NCH_2$Ar), 4.14 (s, 2H; $NCH_2$N), 2.48 (s, 3H; $CH_3$-Ar), 2.26 (s, 3H; $CH_3$-Ar), 1.51 ppm (t, *J* = 7.1 Hz, 6H; $CH_2$C$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 163.52, 163.33, 163.17, 163.00, 147.91, 146.85, 146.78, 146.06, 145.93, 145.88, 145.78, 145.64, 145.35, 145.31, 145.24, 145.09, 145.06, 144.93, 144.88, 144.82, 144.76, 144.71, 144.50, 144.32, 143.95, 143.91, 143.83, 143.78, 143.77, 143.14, 142.99, 142.91, 142.81, 142.75, 142.58, 142.56, 142.41, 141.99, 141.86, 141.85, 141.64, 141.58, 141.50, 141.18, 141.11, 141.03, 140.97, 140.73, 140.61, 140.13, 139.45, 139.19, 138.92, 138.42, 138.15, 134.32, 134.27, 133.96, 133.30, 129.04, 129.00, 128.94, 128.83, 127.46, 126.71, 125.84, 125.25, 70.94, 70.75, 70.53, 70.22, 66.41, 63.64, 63.40, 62.17, 52.68, 52.25, 50.21, 49.23, 17.60, 17.51, 14.54 ppm; FT-IR (neat): $\tilde{\nu}$ = 2956, 2889, 1732 (C=O), 1442, 1365, 1223, 1093, 1060, 805 $cm^{-1}$; HR-MALDI-MS: *m/z*: calcd for $C_{89}H_{30}N_2O_8$ ($[M]^+$): 1254.2002; found 1254.1986.

***out*,*out*-3′,3″-Diethyl (±)-3′,3″-(8*H*,16*H*-7,15-methanodinaphtho[2,1-*b*][2′,1′-*f*][1,5]diazocin-3,11-diyldimethylene) 3′*H*,3″*H*-Dicyclopropa[1,9:52,60]($C_{60}$-$I_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate ((±)-19)**: Prepared as described for (*S*,*S*,$^{f,s}$*A*)-**9** from (±)-**18** (121 mg, 0.20 mmol) with the following amendment: acylation was performed in DMF (5 mL). Yield 128 mg (58%); UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$ = 405 (sh, 4950), 440 (2500), 470 (3700), 575 (sh, 500), 650 nm (sh, 200); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.93 (s, 2H; Ar-H), 7.56–7.62 (m, 6H, Ar-H), 7.29 (d, *J* = 8.7 Hz, 2H; Ar-H), 5.89 (d, *J* = 10.9 Hz, 2H; $OCH_2$Ar), 5.70 (d, *J* = 10.9 Hz, 2H; $OCH_2$Ar), 5.00 (d, *J* = 17.1 Hz, 2H; $NCH_2$Ar), 4.65 (q, *J* = 7.2 Hz, 4H; $OCH_2CH_3$), 4.48 (d, *J* = 17.1 Hz, 2H; $NCH_2$Ar), 4.33 (s, 2H; $NCH_2$N), 1.58 ppm (t, *J* = 7.2 Hz, 6H; $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 164.27, 164.15, 147.24, 145.09, 145.02, 144.93, 144.45, 144.38, 143.88, 143.61, 143.30, 143.09, 143.01, 142.98, 142.83, 142.77, 142.73, 142.57, 142.41, 142.11, 142.09, 142.00, 141.82, 140.90, 140.73, 140.58, 140.56, 140.44, 140.13, 136.34, 135.91, 132.24, 131.91, 131.53, 131.18, 129.25, 128.48, 125.65, 121.76, 121.47, 69.73, 69.65, 69.08, 65.81, 63.65, 54.88, 44.83, 14.46 ppm; FT-IR (neat): $\tilde{\nu}$ = 2920, 2850, 1727 (C=O), 1596, 1470, 1362, 1237, 1207, 1165, 1065, 1013, 806, 734 $cm^{-1}$; HR-MALDI-MS (DCTB): *m/z*: calcd for $C_{95}H_{30}O_8N_2$ ($[M]^+$): 1326.2002; found: 1326.1980.

***in*,*out*-3′,3″-Diethyl (*S*,*S*)-3′,3″-[6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diylbis(4,1-phenylenemethylene)] ($^{f,s}$*A*)-3′*H*,3″*H*-Dicyclopropa[1,9:34,35]($C_{60}$-$I_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate and *in*,*out*-3′,3″-Diethyl (*S*,*S*)-3′,3″-[6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine-2,8-diylbis(4,1-phenylenemethylene)] ($^{f,s}$*C*)-3′*H*,3″*H*-Dicyclopropa[1,9:34,35]($C_{60}$-$I_h$)[5,6]fullerene-3′,3′,3″,3″-tetracarboxylate ((*S*,*S*,$^{f,s}$*A*)-23a and (*S*,*S*,$^{f,s}$*C*)-23a)**: Prepared as described for (*S*,*S*,$^{f,s}$*A*)-**9** from (*S*,*S*)-**22**. Column chromatography (AcOEt/$CH_2Cl_2$ 1:10) afforded a mixture of diastereoisomers which were separated by preparative HPLC on a Regis Bucky Clutcher column (500×21 mm, eluent toluene/AcOEt 93 : 7, flow rate 15 $min^{-1}$, detection at 350 nm), to give (*S*,*S*,$^{f,s}$*A*)-**23a** (16.5 mg, 27%) and (*S*,*S*,$^{f,s}$*C*)-**23a** (4.5 mg, 5%). Similarly, (*R*,*R*,$^{f,s}$*C*)-**23b** and (*R*,*R*,$^{f,s}$*A*)-**23b** were prepared starting from (*R*,*R*)-**22**.

**(*S*,*S*,$^{f,s}$*A*)-23a**: Retention time (analytical HPLC: Regis Bucky Clutcher column, 250×4.6 mm, eluent toluene/AcOEt 93 : 7, flow rate 1 mL $min^{-1}$, detection at 350 nm): 19.9 min; $R_f$ (AcOEt/$CH_2Cl_2$ 1:10) = 0.20; UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$ = 413 (2480), 423 (2010), 490 (1680), 618 nm (440); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 7.60 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H; Ar-H), 7.43 (d, *J* = 8.1 Hz, 2H; Ar-H), 7.37 (dd, *J* = 8.4, 2.2 Hz, 1H; Ar-H), 7.24–7.31 (m, overlap with $CHCl_3$, 3H; Ar-H), 7.21 (d, *J* = 1.9 Hz, 1H; Ar-H), 7.14 (d, *J* = 8.4 Hz, 1H; Ar-H), 7.02 (d, *J* = 8.1 Hz, 1H; Ar-H), 6.90 (d, *J* = 1.9 Hz, 1H; Ar-H), 6.10 (d, *J* = 10.6 Hz, 1H; $OCH_2$Ar), 5.90 (d, *J* = 10.9 Hz, 1H; $OCH_2$Ar), 5.08 (d, *J* = 10.6 Hz, 1H; $OCH_2$Ar), 5.02 (d, *J* = 10.9 Hz, 1H; $OCH_2$Ar), 4.71 (d, *J* = 16.2 Hz, 2H; *exo*-$NCH_2$), 4.41–4.58 (m, 6H; $CH_3$C$H_2$, $NCH_2$N), 4.16 (d, *J* = 16.5 Hz, 1H; *endo*-$NCH_2$), 4.07 (d, *J* = 16.5 Hz, 1H; *endo*-$NCH_2$), 1.51 (t, *J* = 7.0 Hz, 3H; C$H_3$$CH_2$), 1.42 ppm (t, *J* = 7.2 Hz, 3H; C$H_3$$CH_2$); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 163.79, 163.52, 163.39, 162.57, 147.45, 147.38, 147.24, 146.86, 146.81, 146.65, 146.60, 146.52, 146.48, 146.35, 146.23, 145.67, 145.37, 145.34, 145.28, 145.24, 145.07, 144.96, 144.94, 144.86, 144.69, 144.50, 144.40, 144.35, 144.28, 144.23, 144.20, 143.96, 143.77, 143.43, 143.25, 143.24, 143.20, 143.14, 143.09, 142.81, 142.60, 142.59, 142.30, 141.87, 141.85, 141.80, 141.53, 141.36, 141.32, 141.23, 140.68, 140.59, 140.52, 140.24, 140.03, 139.65, 138.94, 137.80, 136.11, 135.41, 135.35, 133.97, 133.79, 132.33, 131.30, 129.04, 129.00, 128.61, 128.51, 128.23, 128.05, 127.36, 126.82, 126.49, 126.29, 126.02, 125.31, 124.80, 124.61, 71.68, 71.56, 71.00, 70.86, 69.36, 68.45, 67.56, 63.49, 63.44, 60.64, 59.86, 51.54, 51.30, 14.29, 14.19 ppm (1 C missing due to signal overlap); FT-IR (neat): $\tilde{\nu}$ = 2961, 2848, 1742 (C=O), 1607, 1485, 1246, 1227, 1207, 962, 753 $cm^{-1}$; HR-MALDI-MS: *m/z*: calcd for $C_{99}H_{34}N_2O_8$ ($[M]^+$): 1378.2315; found 1378.2295.

**(*S*,*S*,$^{f,s}$*C*)-23b**: Retention time (analytical HPLC): 23.6 min; $R_f$ (AcOEt/$CH_2Cl_2$ 1:10) = 0.20; UV/Vis ($CHCl_3$): $\lambda_{max}(\varepsilon)$ = 413 (2400), 423 (1950), 491 (1700), 620 nm (420); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.58 (d, *J* = 8.5 Hz, 2H; Ar-H), 7.02–7.47 (m, overlap with $CHCl_3$, 11H; Ar-H), 6.87 (d, *J* = 1.9 Hz, 1H; Ar-H), 5.80 (d, *J* = 11.0 Hz, 1H; $OCH_2$Ar), 5.70 (d, *J* = 11.0 Hz, 1H; $OCH_2$Ar), 5.45 (d, *J* = 10.7 Hz, 1H; $OCH_2$Ar), 5.07 (d, *J* = 11.0 Hz, 1H; $OCH_2$Ar), 4.68 (d, *J* = 16.8 Hz, 2H; *exo*-$NCH_2$), 4.43–4.58 (m, 6H; $CH_3$C$H_2$, $NCH_2$N), 4.13 (d, *J* = 16.5 Hz, 1H; *endo*-$NCH_2$), 3.94 (d, *J* = 16.5 Hz, 1H; *endo*-$NCH_2$), 1.49 (*t*, *J* = 7.1 Hz, 3H; C$H_3$$CH_2$), 1.43 ppm (t, *J* = 7.1 Hz, 3H; C$H_3$$CH_2$); FT-IR (neat): $\tilde{\nu}$ = 2921, 2850, 1741 (C=O), 1610, 1485, 1226, 1207, 1174, 1103, 962, 771, 753 $cm^{-1}$; HR-MALDI-MS: *m/z*: calcd for $C_{99}H_{34}N_2O_8$ ($[M]^+$): 1378.2315; found 1378.2329.

**X-ray crystal structure analyses:** (±)-**13**: Crystal data at 220(2) K: $C_{29}H_{34}N_2O_8$, $M_r$ = 538.58, triclinic, space group $P\bar{1}$ (no. 2), $\rho_{calcd}$ = 1.341 g $cm^{-3}$, *Z* = 2, *a* = 8.3728(2), *b* = 12.3137(2), *c* = 13.5893(3) Å, $\alpha$ = 106.060(1), $\beta$ = 97.703(1), $\gamma$ = 98.613(1)°, *V* = 1334.29(5) $Å^3$. Bruker-Nonius CCD diffractometer, $Mo_{K\alpha}$ radiation, $\lambda$ = 0.7107 Å. A colorless crystal was obtained by very slow evaporation of a solution of (±)-**13** in $CH_2Cl_2$. The structure was solved by direct methods (SIR97)[27] and refined by full-matrix least-squares analysis (SHELXL-97),[28] using an isotropic extinction correction, and $w = 1/[\sigma^2(F_o^2) + (0.1092P)^2 + 0.5140P]$, where $P = (F_o^2 + 2F_c^2)/3$. C29 is disordered over two orientations, only one orientation is shown (see Supporting Information). All heavy atom were refined anisotropically, hydrogen atoms isotropically, whereby hydrogen positions are based on stereochemical considerations. Final $R(F)$ = 0.060, $wR(F^2)$ = 0.171 for 385 parameters and 5036 reflections with $I > 2\sigma(I)$ and $3.14 < \theta < 27.47°$ (corresponding *R* values based on all 5897 reflections are 0.069 and 0.181 respectively).

**(*R*,*R*)-19**: Crystal data at 238(2) K: $C_{95}H_{30}O_8N_2{\cdot}2\,CH_2Cl_2$, orthorhombic, space group $P2_12_12_1$ (no. 19), $\rho_{calcd}$ = 1.625 g $cm^{-3}$, *Z* = 4, *a* = 10.3913(13), *b* = 23.387(8), *c* = 25.187(7) Å, *V* = 6121(3) $Å^3$. Nonius CAD4 diffractometer, $Cu_{K\alpha}$ radiation, $\lambda$ = 1.5418 Å. A black crystal was obtained by very slow evaporation of a solution of (±)-**19** in a mixture of $CH_2Cl_2$ and $CHCl_3$. It was cut to linear dimensions of about 0.32×0.25×0.22 mm and mounted at low temperature to prevent evaporation of enclosed solvents. The structure was solved by direct methods (SIR97)[27] and refined by full-matrix least-squares analysis (SHELXL-97),[28] using an isotropic extinction correction, and $w = 1/[\sigma^2(F_o^2) + (0.1932P)^2 + 2.4285P]$, where $P = (F_o^2 + 2F_c^2)/3$. One of the two $CH_2Cl_2$ molecules, included in the crystal packing, is disordered over four orientations. All heavy atoms of (*R*,*R*)-**19** were refined anisotropically, hydrogen atoms isotropically, whereby hydrogen positions are based on stereochemical considerations. Final $R(F)$ = 0.078, $wR(F^2)$ = 0.209 for 1050 parameters and 4485 reflections with $I > 2\sigma(I)$ and $2.58 < \theta < 66.96°$ (corresponding *R* values based on all 5751 reflections are 0.098 and 0.242, respectively).

**(±)-22**: Crystal data at 200(2) K: $C_{39}H_{38}N_2O_8$, $M_r = 662.71$, monoclinic, space group $C2/c$ (no. 15), $\rho_{calcd} = 1.343\ g\,cm^{-3}$, $Z = 4$, $a = 25.1985(6)$, $b = 5.5400(1)$, $c = 23.6427(5)$ Å, $\beta = 96.801(1)°$, $V = 3277.29(12)$ Å$^3$. Bruker-Nonius Kappa-CCD diffractometer, $Mo_{K\alpha}$ radiation, $\lambda = 0.7107$ Å. A colorless crystal (linear dimensions about $0.25 \times 0.21 \times 0.15$ mm) was obtained by slow diffusion of hexane into solution of (±)-**22** in $CH_2Cl_2$. The structure was solved by direct methods (SIR97)[27] and refined by full-matrix least-squares analysis (SHELXL-97),[28] using an isotropic extinction correction, and $w = 1/[\sigma^2(F_o^2) + (0.0718P)^2 + 5.7134P]$, where $P = (F_o^2 + 2F_c^2)/3$. All heavy atoms of (±)-**22** were refined anisotropically, hydrogen atoms isotropically, whereby hydrogen positions are based on stereochemical considerations. Final $R(F) = 0.061$, $wR(F^2) = 0.153$ for 240 parameters and 2953 reflections with $I > 2\sigma(I)$ and $3.26 < \theta < 27.47°$ (corresponding $R$ values based on all 3726 reflections are 0.077 and 0.165, respectively).

CCDC-257155 ((±)-**13**), CCDC-257156 ((*R*,*R*)-**19**), and CCDC-257157 ((±)-**22**) 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.

**Cyclic voltammetry**: Electrochemical measurements were performed at room temperature in a three-electrode cell containing 0.1 M $Bu_4NPF_6$ in $CH_2Cl_2$. A mini-glassy carbon electrode (CHI, 1 mm diameter) was used as the working electrode, platinum wire was used as the counter electrode, and $Ag/AgNO_3$ as reference electrode. Ferrocene was added as an internal standard, and all potentials were measured relative to the $Fc/Fc^+$ couple. Solutions were stirred and degassed with argon prior to each measurement.

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