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Synthesis of enantiomeric bridgehead substituted bisnoradamantane derivatives

Carles Ayats,[a] Pelayo Camps,[a,*] Mercè Font-Bardia,[b] Xavier Solans[b] and Santiago Vázquez[a,*]

[a]*Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, Av. Diagonal, 643, Barcelona E-08028, Spain*
[b]*Serveis Cientifico-Tècnics, Universitat de Barcelona, Av. Martí Franquès, s/n, Barcelona E-08028, Spain*

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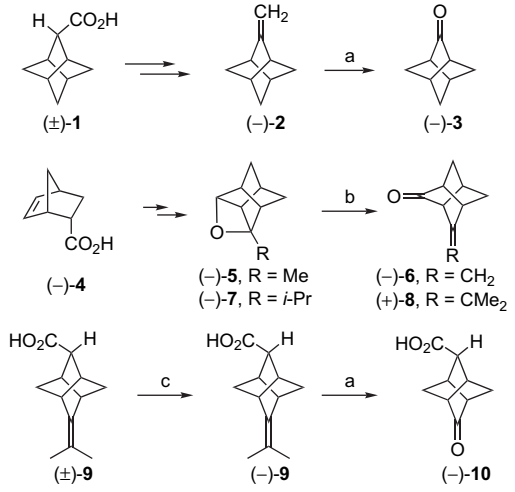
Abstract—The preparation of (+)- and (−)-**12** by resolution of (±)-**12** with (*R*)-*N*-phenylpantolactam, (*R*)-**13**, is described. From (+)- and (−)-**12** a series of chiral bisnoradamantane derivatives, whose chirality stems from substitution at the bridgehead positions, have been obtained in both enantiomeric forms.

1. Introduction

Tricyclo[3.3.0.0^{3,7}]octane, also called bisnoradamantane or natane, is an aesthetically pleasing, high-symmetry cage-shaped molecule with achiral D_{2d} symmetry.[1] The molecular geometry of bisnoradamantane results in two sets of homotopic methylene groups, and the sets are in turn enantiotopic. The molecule can be desymmetrized by differentiation of one set of enantiotopic methylene groups from the other set and a variety of bisnoradamantane derivatives have been prepared in an optically active form.

The most simple chiral bisnoradamantane derivatives are monosubstituted such as **1**, **2**, and **3**. Naemura and Nakazaki's group achieved the resolution of (±)-**1**, from which (−)-**2** and (−)-**3** were obtained.[2] Some disubstituted enantiopure bisnoradamantane derivatives have also been synthesized. For example, starting from enantiopure (−)-**4**, oxetanes (−)-**5** and (−)-**7** were prepared, and treatment with $LiNEt_2$ followed by oxidation led to (−)-**6** and (+)-**8**, respectively.[3] Finally, coaxially disubstituted derivatives were also prepared in optically active form. Optical resolution of (±)-**9** was accomplished via the (+)-2-(1-aminoethyl)naphthalene salt to furnish (−)-**9**, which was converted into (−)-**10** (Scheme 1).[4]

Worthy of note, substituted bisnoradamantanes of general structure **11** are chiral tricyclo[3.3.0.0^{3,7}]octane derivatives (Fig. 1). All of them contain four stereogenic centers, which correspond to the bridgehead positions. However, in a more simple way, they can be considered as having a chiral axis passing by the middle of the C1–C5 and C3–C7 bonds. Their chirality could then be defined as *R* or *S*, in the same way as for chiral allenes, and requires only different substitutions at the vicinal bridgehead positions.



Scheme 1. Several chiral bisnoradamantanes. (a) O_3, then Zn/H_3O^+. (b) $LiNEt_2$, benzene, Δ; then, CrO_3, pyridine. (c) Resolution.

Although several bridgehead substituted chiral bisnoradamantanes are known,[5] efforts directed toward their preparation as single enantiomers have not been described.

In this paper, we report the preparation of (+)- and (−)-**12** from racemic (±)-**12** by using (*R*)-*N*-phenylpantolactam,

* Corresponding authors. Tel.: +34 934024536; fax: +34 934035941 (P.C.); tel.: +34 934024533; fax: +34 934035941 (S.V.); e-mail addresses: camps@ub.edu; svazquez@ub.edu

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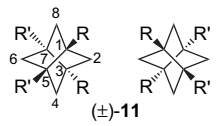


Figure 1. Bridgehead substituted chiral bisnoradamantanes.

13, a chiral auxiliary developed by our group.[6] From (+)- and (−)-**12** a series of enantiomeric bisnoradamantane derivatives have been prepared.

2. Results and discussion

Reaction of the easily available (±)-**12**,[5c] with (*R*)-*N*-phenylpantolactam, **13**, gave a diastereomeric mixture of diesters **14**, from which diesters (+)-**14** and (−)-**14** were isolated and fully characterized after column chromatography. The absolute configuration of (−)-**14** was established as (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14** by X-ray diffraction analysis (Fig. 2), thus allowing us to establish also the absolute configuration of (+)-**14** as (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-**14** (Scheme 2).[7]

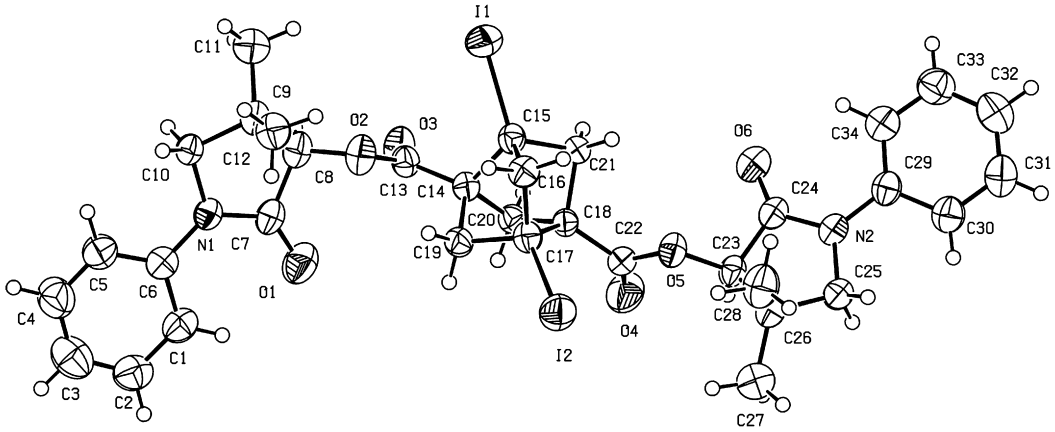
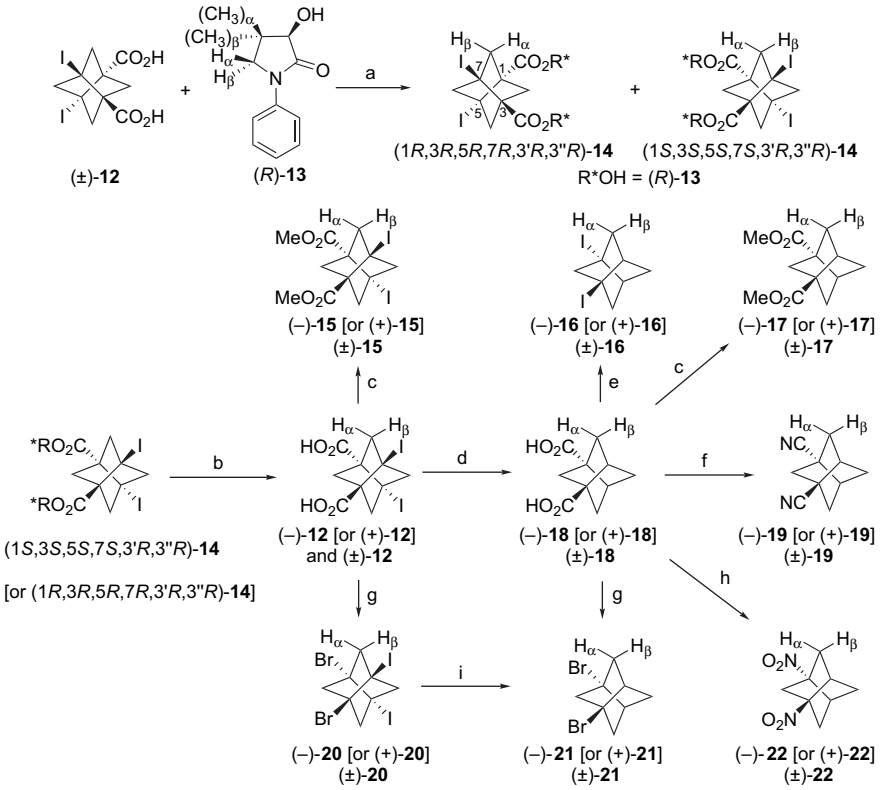


Figure 2. X-ray diffraction structure (ORTEP) of (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14**.



Scheme 2. Synthesis of enantiopure bridgehead substituted bisnoradamantanes. (a) DCC, DMAP, anhydrous THF, 0 °C–rt, 21 h, 27% of (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-**14**; 30% of (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14**, after silica gel column chromatography. (b) LiOH·H_2O, H_2O_2, THF, 0 °C–rt, 48 h, 87% of (−)-**12**, 92% of (+)-**12**. (c) MeOH, H_2SO_4, Δ, 18 h, 86% of (−)-**15**, 89% of (+)-**15**, 90% of (±)-**17**, 88% of (−)-**17**, 86% of (+)-**17**. (d) Li, *t*-BuOH, Δ, 6 h, 75% of (−)-**18**, 65% of (+)-**18**. (e) IBDA, I_2, acetonitrile, hν, 20 h, 57% of (−)-**16**, 56% of (+)-**16**. (f) Acetonitrile, H_2SO_4, Δ, 6 h, 38% of (±)-**19**, 26% of (−)-**19**, 29% of (+)-**19**. (g) HgO, Br_2, CH_2Br_2, Δ, 3 h, 88% of (±)-**20**, 94% of (−)-**20**, 88% of (+)-**20**, 53% of (±)-**21**, 71% of (−)-**21**, 71% of (+)-**21**. (h) $SOCl_2$, Δ, 2 h; then NaN_3, H_2O, acetone, 0 °C–rt, 3 h; then anhydrous toluene, Δ, 5 h; then DMD, H_2O, acetone, rt, 12 h, 48% of (±)-**22**, 41% of (−)-**22**, 44% of (+)-**22**. (i) H_2, Pd/C, MeOH, H_2O, approx. 83% of (±)-**21**, approx. 79% of (−)-**21**, approx. 85% of (+)-**21**.

Worthy of note, attempted resolution of diacid (±)-**18** as described for (±)-**12**, failed.

Hydrolysis of (−)-**14** gave the enantiopure diacid (−)-**12** in 87% yield, while hydrolysis of (+)-**14** gave diacid (+)-**12** in 92% yield. The absolute configuration of (−)-**12** must be (1*S*,3*S*,5*S*,7*S*). As a compound having a chiral axis, it would be more easily defined as (*S*)-**12**.

Very recently, we have described that reduction of (±)-**12** with Li/*t*-BuOH gave the diacid (±)-**18**,[5b] whose double iododecarboxylation led to racemic (±)-**16** in 76% yield.[5d] Starting from (−)-**12**, and following the aforementioned procedures, (−)-**18** and (−)-**16** were obtained in high yields.

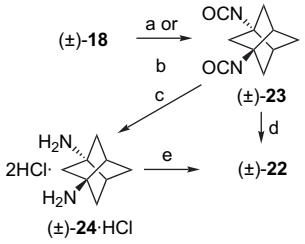
On the other hand, esterification of (−)-**12** with methanol led to the diester (−)-**15** in 86% yield. Racemic (±)-**15**, had been previously obtained by our group following a different synthetic approach.[5c] Similarly, (+)-**15**, (+)-**16**, and (+)-**18** were obtained from (+)-**12** (Scheme 2).

In order to further explore the chemistry of enantiomeric bridgehead substituted bisnoradamantanes we envisaged the new compounds **17** and **19**–**22**. Firstly, the synthesis of these compounds was planned as racemic mixtures starting from (±)-**12**. Thus, double bromodecarboxylation of (±)-**12** and (±)-**18** using HgO/Br_2 in CH_2Br_2 led to (±)-**20** and (±)-**21** in 88 and 53% yields, respectively. Both new compounds were fully characterized and the structure of (±)-**20** was unequivocally established by X-ray diffraction analysis (Fig. 3).[8]

While Fischer esterification of (±)-**18** with methanol gave (±)-**17** in 90% yield, obtention of (±)-**19** from (±)-**18** was troublesome. Initial attempts to obtain (±)-**19** from (±)-**18** by using Barton's decarboxylative cyanation met with failure.[9] Also, a one-pot three-step procedure involving conversion of (±)-**18** into the corresponding bisacyl chloride, diamide formation and dehydration gave (±)-**19** in very low yield. Fortunately, reaction of (±)-**18** with H_2SO_4 in acetonitrile, conditions very recently applied by Mlinarić-Majerski and co-workers to adamantane-1,3-dicarboxylic acid, led to (±)-**19** in 38% yield.[10]

Although application of Yamada's modification of the classical Curtius reaction to (±)-**18** gave the dihydrochloride of diamine (±)-**24**·**2HCl** in only 22% yield, we carried out its oxidation with an acetone solution of dimethyldioxirane (DMD) to give the dinitroderivative (±)-**22** in 67% yield.

More conveniently, (±)-**22** was prepared in 48% yield by oxidation of the corresponding diisocyanate, (±)-**23**, with dimethyldioxirane in wet acetone (Scheme 3), following a procedure first reported by Eaton in the synthesis of 1,4-dinitrocubane.[11]



Scheme 3. Synthesis of (±)-**22**. (a) $SOCl_2$, Δ, 2 h; then NaN_3, H_2O, acetone, 0 °C–rt, 3 h; then anhydrous toluene, Δ, 5 h. (b) $(C_6H_5O)_2PON_3$, Et_3N, toluene, Δ, 3 h. (c) 6 N HCl, Δ, 24 h, 22% from (±)-**18**. (d) DMD, acetone, H_2O, rt, 12 h, 48% of (±)-**22** from (±)-**18**. (e) DMD, acetone, rt, 16 h, 67%.

Following the aforementioned procedures in the racemic series and starting from enantiopure diacid (−)- or (+)-**12**, enantiopure (−)- or (+)-**17**, **19**–**22**, respectively, were prepared and fully characterized.

The enantiopurity of (+)- and (−)-**19** and of (+)- and (−)-**21** was established by chiral GC/MS using a 30-m column containing permethylated β-cyclodextrine as the chiral stationary phase. Only one stereoisomer was observed in each case. The enantiopurity of (+)- and (−)-**19**, implies also that of their precursors, (+)-**12** and (+)-**18**, and (−)-**12** and (−)-**18**, respectively. We were not able to resolve esters (±)-**15** and (±)-**17**, and compounds (±)-**20** and (±)-**22** by chiral GC. However, chemoselective hydrogenation of (−)- and (+)-**20** in alkaline methanol led to enantiopure (−)- and (+)-**21**, respectively, thus establishing the enantiopurity of the first compounds.

Since esterification of **12** and **18** and the conversion of **18** to **22** are not expected to take place with racemization, the enantiopurity of compounds (+)-**15**, (+)-**17**, and (+)-**22** must be the same as their common precursor (+)-**12**. The same is true in the enantiomeric series.

It should be noted that the density of (±)-**22** is quite high, 1.46 g mL^{-1}, as determined from its X-ray diffraction analysis (Fig. 4).[12] Polynitro cage compounds have raised interest as high-energetic materials as has beautifully been illustrated by Eaton[13] and Marchand.[14]

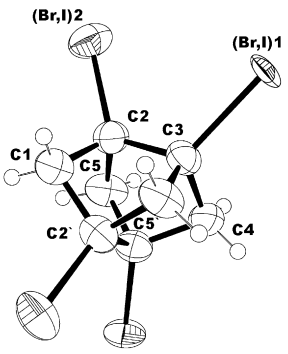


Figure 3. X-ray diffraction structure (ORTEP) of (±)-**20**.

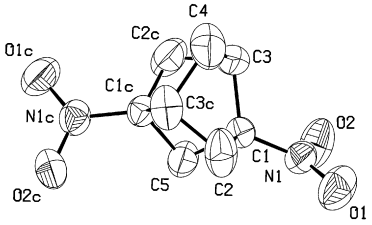


Figure 4. X-ray diffraction structure (ORTEP) of (±)-**22**.

Taking into account the high density of (±)-**22**, we attempted the obtention of 1,3,5,7-tetranitrotricyclo-[3.3.0.0^{3,7}]octane from the known tricyclo[3.3.0.0^{3,7}]-octane-1,3,5,7-tetracarboxylic acid,[5c] following a synthetic sequence similar to that shown in Scheme 3 for (±)-**22**. However, a complex mixture of products not containing the expected tetranitro derivative was obtained.

3. Conclusions

In conclusion, an easy entry to unprecedented enantiomeric bridgehead substituted bisnoradamantane derivatives by resolution of diacid (±)-**12** via diastereomeric esters of (*R*)-*N*-phenylpantolactam has been developed. These compounds constitute particular cases of axial chirality.

4. Experimental section

4.1. General methods

Melting points were determined in open capillary tubes. Unless otherwise stated, NMR spectra were recorded in $CDCl_3$: ^{1}H NMR (500 MHz), ^{13}C NMR (75.4 MHz). Chemical shifts (δ) are reported in parts per million related to internal tetramethylsilane (TMS). Assignments given for the NMR spectra are based on DEPT, COSY ^{1}H/^{1}H, HETCOR ^{1}H/^{13}C (HSQC and HMBC sequences for one bond and long range ^{1}H/^{13}C heterocorrelations, respectively), and NOESY experiments for selected compounds. Diastereotopic methylene protons in tricyclo[3.3.0.0^{3,7}]octane derivatives are referred as H_α and H_β as shown in the corresponding structures. ^{1}H NMR and ^{13}C NMR spectra are given only for the new racemic compounds, while only the 300 MHz ^{1}H NMR spectra are given for the enantiomeric compounds. For the routine MS and GC/MS analyses the sample was introduced directly or through a gas chromatograph. For achiral GC/MS analyses a 30-m column [5% diphenyl-95% dimethylpolysiloxane, conditions: 10 psi, initial temperature: 35 °C (2 min), then heating at a range of 8 °C min^{-1} till 300 °C, then isothermic at 300 °C] was used. For chiral GC/MS analyses a 30-m (0.25 mm internal diameter) chiral column [containing permethylated β-cyclodextrine as the chiral stationary phase, conditions: 10 psi, initial temperature: 50 °C (2 min), then heating at a range of 10 °C min^{-1} till 240 °C, then isothermic at 240 °C] was used. In both cases, the electron impact (70 eV) or chemical ionization (CH_4) techniques were used. Only significant ions are given: those with higher relative abundance, except for the ions with higher *m*/*z* values. Accurate mass measurements were obtained using EI, CI or ESI techniques. Absorption values in the IR spectra are given as wavenumbers (cm^{-1}). Rotatory powers were determined on a polarimeter using 1-cm cells. Column chromatography was performed on silica gel 60 Å (35–70 mesh). For the thin layer chromatography (TLC) aluminum-backed sheets with silica gel 60 F_{254} were used and spots were visualized with UV light and/or 1% aqueous solutions of $KMnO_4$.

4.1.1. Bis[(3*R*)-1-phenyl-4,4-dimethyl-2-oxopyrrolidin-3-yl] (1*R*,3*R*,5*R*,7*R*)- and (1*S*,3*S*,5*S*,7*S*)-5,7-diiodotricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylate, (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-14 and (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-14. Dicyclohexylcarbodiimide (DCC, 1.84 g, 8.92 mmol) was added in portions to a solution of (±)-**12** (2.0 g, 4.46 mmol) in anhydrous THF (15 mL) at 0 °C and the mixture was stirred at this temperature for 30 min. A solution of (*R*)-3-hydroxy-4,4-dimethyl-1-phenylpyrrolidin-2-one [(*R*)-**13**, 1.83 g, 8.92 mmol] in anhydrous THF (15 mL) and 4-(dimethylamino)pyridine (DMAP, 30 mg, 0.24 mmol) was added and the mixture was stirred at room temperature for 21 h. The precipitated dicyclohexylurea (DCU) was filtered through Celite® washing the solid with CH_2Cl_2 (5×10 mL). The combined filtrate and washings were concentrated under reduced pressure, H_2O (150 mL) and brine (30 mL) were added and the mixture was extracted with CH_2Cl_2 (3×150 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure to give a diastereomeric mixture of (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)- and (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14** (4.72 g, dr=50:50, by ^{1}H NMR), which was submitted to flash column chromatography [silica gel, (480 g), 8 cm internal diameter of the column, mixture hexane/AcOEt (3:1)] obtaining in order of elution: (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-**14** (1.62 g), which after recrystallization from EtOH (4 mL) gave the analytical sample (1.00 g, 27% yield from (±)-**12**, dr >98, by ^{1}H NMR) and (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14** (1.69 g), which was washed with hot EtOH (8 mL) to give the analytical sample (1.09 g, 30% yield from (±)-**12**, dr >98, by ^{1}H NMR), both as white solids. (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-**14**: mp 124–125 °C (EtOH); TLC (silica gel), R_f 0.61 [hexane/AcOEt (1:1)]; $[\alpha]_D^{20}$ +22.7 (CH_2Cl_2, *c* 0.50); IR (KBr) ν 2964, 2931, 2875, 1741, 1717, 1598, 1500, 1481, 1409, 1385, 1324, 1264, 1217, 1158, 1124, 1100, 1075, 759, 691 cm^{-1}; ^{1}H NMR δ: 1.23 [s, 6H, 4′(4″)-α-CH_3], 1.42 [s, 6H, 4′(4″)-β-CH_3], 2.35 [dm, *J*= 10.3 Hz, 2H, 4(8)-H_β], 2.46 [br s, 2H, 2-H_2], 2.66 [br s, 2H, 6-H_2], 2.69 [dm, *J*=10.3 Hz, 2H, 4(8)-H_α], 3.54 [d, *J*= 9.5 Hz, 2H, 5′(5″)-H_α], 3.65 [d, *J*=9.5 Hz, 2H, 5′(5″)-H_β], 5.54 [s, 2H, 3′(3″)-H], 7.17 [tt, *J*=7.5 Hz, *J*′=1.0 Hz, 2H, Ar–H*para N*-phenyl], 7.37 [m, 4H, Ar–H*meta N*-phenyl], 7.62 [m, 4H, Ar–H*ortho N*-phenyl]. ^{13}C NMR δ: 21.5 [CH_3, 4′(4″)-α-CH_3], 24.9 [CH_3, 4′(4″)-β-CH_3], 27.8 [C, C5(7)], 37.4 [C, C4′(4″)], 51.0 [CH_2, C2], 57.7 [CH_2, C5′(5″)], 60.6 [CH_2, C4(8)], 61.2 [C, C1(3)], 69.0 [CH_2, C6], 78.9 [CH, C3′(3″)], 119.4 [CH, Ar–C*ortho N*-phenyl], 124.9 [CH, Ar–C*para N*-phenyl], 128.9 [CH, Ar–C*meta N*-phenyl], 138.9 [C, Ar–C*ipso N*-phenyl], 168.2 [C, C2′(2″) and 1(3)-CO_2]; MS (EI), *m*/*z* (%): 695 ([M−I]$^+$, 1), 568 ([M−2I]$^{\bullet+}$, 1), 362 ([M−I−HI−$C_{12}H_{15}NO_2$]$^+$, 6), 285 ([M−I−2$C_{12}H_{15}NO_2$]$^+$, 11), 206 (17), 188 (18), 174 (14), 158 ([M−2I−2$C_{12}H_{15}NO_2$]$^{\bullet+}$, 17), 131 (11), 127 (12), 119 (13), 106 (21), 105 (26), 104 (42), 103 (17), 77 (41), 69 (100). Anal. Calcd for $C_{34}H_{36}I_2N_2O_6$ (822.47): C 49.65, H 4.41, N 3.41, I 30.86. Found: C 49.54, H 4.34, N 3.38, I 30.77. (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14**: mp 278–279 °C (EtOH); TLC (silica gel), R_f 0.47 [hexane/AcOEt (1:1)]; $[\alpha]_D^{20}$ −23.0 (CH_2Cl_2, *c* 0.55); IR (KBr) ν 2962, 2929, 1741, 1716, 1699, 1626, 1599, 1500, 1488, 1411, 1388, 1345, 1325, 1304, 1286, 1264, 1223, 1157, 1125, 1079, 757, 688 cm^{-1}; ^{1}H NMR δ: 1.23 [s, 6H, 4′(4″)-α-CH_3], 1.41 [s, 6H, 4′(4″)-β-CH_3], 2.41 [br s, 2H, 2-H_2], 2.44 [dm, *J*= 10.5 Hz, 2H, 4(8)-H_β], 2.64 [br s, 2H, 6-H_2], 2.66 [dm, *J*= 10.5 Hz, 2H, 4(8)-H_α], 3.54 [d, *J*=9.5 Hz, 2H, 5′(5″)-H_α], 3.64 [d, *J*=9.5 Hz, 2H, 5′(5″)-H_β], 5.52 [s, 2H, 3′(3″)-H], 7.17 [tt, *J*=7.5 Hz, *J*′=1.0 Hz, 2H, Ar–H*para N*-phenyl],

7.38 [m, 4H, Ar–H*meta N*-phenyl], 7.63 [m, 4H, Ar–H*ortho N*-phenyl]. ^{13}C NMR δ: 21.4 [CH_3, 4′(4″)-α-CH_3], 24.8 [CH_3, 4′(4″)-β-CH_3], 27.6 [C, C5(7)], 37.4 [C, C4′(4″)], 51.2 [CH_2, C2], 57.6 [CH_2, C5′(5″)], 60.6 [CH_2, C4(8)], 60.7 [C, C1(3)], 69.2 [CH_2, C6], 79.0 [CH, C3′(3″)], 119.3 [CH, Ar–C*ortho N*-phenyl], 124.9 [CH, Ar–C*para N*-phenyl], 128.9 [CH, Ar–C*meta N*-phenyl], 139.0 [C, Ar–C*ipso N*-phenyl], 168.2 (C) and 168.4 (C) [C2′(2″) and 1(3)-CO_2]; MS (EI), *m/z* (%): 568 ([M−2I]$^{\bullet+}$, 1), 362 (3), 285 (7), 206 (12), 188 (14), 174 (10), 158 (15), 131 (10), 127 (9), 119 (11), 106 (19), 105 (21), 104 (35), 103 (14), 77 (36), 69 (100). Anal. Calcd for $C_{34}H_{36}I_2N_2O_6$ (822.47): C 49.65, H 4.41, N 3.41, I 30.86. Found: C 49.70, H 4.45, N 3.35, I 30.77.

4.1.2. (−)(1*S*,3*S*,5*S*,7*S*)-5,7-Diiodotricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid, (−)-12.[5c] To a cold (0 °C) suspension of (1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14** (681 mg, 0.83 mmol) in THF (15 mL), H_2O_2 30% w/v (0.8 mL, 7.06 mmol) and LiOH·H_2O (0.18 g, 4.30 mmol) were added and the mixture was stirred at room temperature for 48 h. The suspension was cooled in an ice-bath and aqueous Na_2SO_3 (1.5 N, 7 mL, pH≈9) was added. The mixture was extracted with AcOEt (3×60 mL) and the combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure to give (*R*)-**13** (340 mg, quantitative recovery, >99% ee by chiral HPLC). The aqueous phase was cooled in an ice-bath, made acidic to pH≈1–2 with 5 N HCl (4 mL) and the mixture was extracted with AcOEt (5×60 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure to give diiodo diacid (−)-**12** (322 mg, 87% yield) as a white solid, mp >300 °C (dec); $[\alpha]_D^{23}$ −24.0 (MeOH, *c* 2.06); IR (KBr) *ν* 3200–2200 (max. at 3007, 2919, 2712, 2599), 1713, 1698, 1472, 1421, 1327, 1306, 1269, 1235, 1173, 1119, 1058, 989, 963, 947, 899, 801, 750, 723, 701, 638 cm^{-1}; MS (EI), *m/z* (%): 448 (M$^{\bullet+}$, 2), 430 ([M−H_2O]$^{\bullet+}$, 3), 321 ([M−I]$^+$, 4), 304 (11), 303 ([M−I−H_2O]$^+$, 100), 277 (14), 275 ([M−I−HCO_2H]$^+$, 58), 176 ([M−2I−H_2O]$^{\bullet+}$, 24), 149 (21), 148 ([M−2I−HCO_2H]$^{\bullet+}$, 49), 105 (22), 104 (28), 103 (41), 77 (36); MS (CI), *m/z* (%): 449 ([M+H]$^+$, 7), 448 (M$^{\bullet+}$, 1), 403 (35), 321 ([M−I]$^+$, 41), 304 (30), 303 ([M−I−H_2O]$^+$, 92), 277 (82), 276 (91), 275 ([M−I−HCO_2H]$^+$, 100), 231 (43), 194 (25), 193 (61), 177 (30), 176 ([M−2I−H_2O]$^{\bullet+}$, 59), 175 (42), 150 (34), 149 (82), 148 ([M−2I−HCO_2H]$^{\bullet+}$, 66), 147 (22), 131 (20), 105 (37), 104 (38), 103 (39). Accurate mass measurement (ESI+) calcd for [$C_{10}H_{10}O_4I_2$+H]$^+$: 448.8741. Found: 448.8738.

4.1.3. (+)(1*R*,3*R*,5*R*,7*R*)-5,7-Diiodotricyclo[3.3.0.0^{3,7}]-octane-1,3-dicarboxylic acid, (+)-12.[5c] This reaction was carried out as described for the preparation of diiodo diacid (−)-**12**. From (1*R*,3*R*,5*R*,7*R*,3′*R*,3″*R*)-**14** (816 mg, 0.99 mmol), H_2O_2 30% w/v (0.95 mL, 8.38 mmol), and LiOH·H_2O (0.22 g, 5.24 mmol) in THF (18 mL), (*R*)-**13** (390 mg, 96% recovery, >99% ee by chiral HPLC) and diiodo diacid (+)-**12** (409 mg, 92% yield) were obtained as white solids, mp >300 °C (dec); $[\alpha]_D^{23}$ +27.9 (MeOH, *c* 1.98); IR (KBr) *ν* 3500–2200 (max. at 3008, 2920, 2714, 2599), 1713, 1698, 1472, 1421, 1328, 1305, 1269, 1235, 1173, 1119, 1058, 989, 963, 947, 899, 869, 801, 749, 723, 701, 638 cm^{-1}; MS (EI), *m/z* (%): 448 (M$^{\bullet+}$, 2), 430 ([M−H_2O]$^{\bullet+}$, 3), 321 ([M−I]$^+$, 4), 303 ([M−I−H_2O]$^+$, 100), 275 ([M−I−HCO_2H]$^+$, 65), 176 ([M−2I−H_2O]$^{\bullet+}$, 25), 149 (25), 148 ([M−2I−HCO_2H]$^{\bullet+}$, 57), 105 (29), 104 (38), 103 (62), 91 (26), 77 (54). Accurate mass measurement (ESI+) calcd for [$C_{10}H_{10}O_4I_2$+Na]$^+$: 470.85607. Found: 470.85657.

4.1.4. (−)-Dimethyl (1*S*,3*S*,5*S*,7*S*)-5,7-diiodotricyclo-[3.3.0.0^{3,7}]octane-1,3-dicarboxylate, (−)-15.[5c] A solution of diiodo diacid (−)-**12** (100 mg, 0.22 mmol) in anhydrous MeOH (2 mL) and concd H_2SO_4 (0.2 mL) was heated under reflux for 18 h. The mixture was allowed to cool to room temperature and concentrated under reduced pressure to remove MeOH. The residue was taken in CH_2Cl_2 (20 mL) and the organic solution was washed with H_2O (3×5 mL) and saturated aqueous $NaHCO_3$ solution (2×5 mL). Evaporation of the solvent from the dried organic phase (anhydrous Na_2SO_4) under reduced pressure gave a yellow oil, which was washed with a small amount of *n*-pentane to give diiodo diester (−)-**15** (90 mg, 86% yield) as a white solid. The analytical sample was obtained by crystallization from AcOEt, mp 87–89 °C; $[\alpha]_D^{24}$ −21.1 (CH_2Cl_2, *c* 2.05); IR (KBr) *ν* 3000, 2952, 2899, 1734, 1479, 1435, 1315, 1268, 1226, 1158, 1125, 1057, 942 cm^{-1}; MS (EI), *m/z* (%): 349 ([M−I]$^+$, 8), 317 ([M−I−CH_3OH]$^+$, 49), 289 ([M−I−HCO_2-CH_3]$^+$, 61), 190 (38), 189 (31), 162 ([M−2I−HCO_2CH_3]$^{\bullet+}$, 95), 131 (28), 104 (30), 103 ([M−2I−HCO_2CH_3−CO_2CH_3]$^+$, 100), 102 (44), 91 (31), 78 (33), 77 (65), 59 ([CO_2CH_3]$^+$, 68). Accurate mass measurement (ESI+) calcd for [$C_{12}H_{14}O_4I_2$+Na]$^+$: 498.8874. Found: 498.8875.

4.1.5. (+)-Dimethyl (1*R*,3*R*,5*R*,7*R*)-5,7-diiodotricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylate, (+)-15.[5c] This reaction was carried out as described for the preparation of diiodo diester (−)-**15**. From (+)-**12** (102 mg, 0.23 mmol), anhydrous MeOH (2 mL), and concd H_2SO_4 (0.2 mL), diiodo diester (+)-**15** (97 mg, 89% yield) was obtained as a white solid. The analytical sample was obtained by crystallization from AcOEt, mp 97–98 °C; $[\alpha]_D^{24}$ +21.0 (CH_2Cl_2, *c* 1.00); IR (KBr) *ν* 3002, 2953, 2851, 1733, 1724, 1480, 1435, 1316, 1269, 1227, 1126, 1058, 943 cm^{-1}; MS (EI), *m/z* (%): 349 [(M−I)$^+$, 8], 317 ([M−I−CH_3OH]$^+$, 42), 289 ([M−I−HCO_2CH_3]$^+$, 55), 190 (34), 189 (30), 162 ([M−2I−HCO_2CH_3]$^{\bullet+}$, 93), 131 (28), 104 (30), 103 ([M−2I−HCO_2CH_3−CO_2CH_3]$^+$, 100), 102 (45), 91 (31), 78 (32), 77 (68), 59 ([CO_2CH_3]$^+$, 76). Accurate mass measurement (ESI+) calcd for [$C_{12}H_{14}O_4I_2$+Na]$^+$: 498.8874. Found: 498.8873.

4.1.6. (−)(1*S*,3*S*,5*S*,7*S*)-1,3-Diiodotricyclo[3.3.0.0^{3,7}]octane, (−)-16.[5d] A mixture of diacid (−)-**18** (37 mg, 0.19 mmol), iodine (0.11 g, 0.45 mmol), and iodosobenzenediacetate (IBDA, 0.15 g, 98% content, 0.45 mmol) in anhydrous acetonitrile (4 mL) was irradiated under reflux with a 100 W tungsten lamp in an argon atmosphere for 4 h. More iodine (0.11 g, 0.45 mmol) and IBDA (0.15 g, 0.45 mmol) were added and irradiation under reflux was continued for 20 h more. The resulting solution was distilled under atmospheric pressure through a Vigreux column (10 cm). The residue was taken in diethyl ether (10 mL) and the organic solution was washed with aqueous $Na_2S_2O_3$ solution (10%, 3×10 mL), saturated aqueous $NaHCO_3$ solution (3×10 mL), and brine (2×10 mL). The organic phase was dried (anhydrous Na_2SO_4) and the solvent was distilled under atmospheric pressure through a Vigreux column

(10 cm). Most of the iodobenzene formed in the reaction was distilled using a rotary microdistillation equipment at 70–80 °C/30 Torr. The light yellow residue (128 mg) was submitted to column chromatography [silica gel (25 g), hexane]. The solvent of the chromatographic fractions was distilled off at atmospheric pressure through a Vigreux column (10 cm) to afford diiodide (−)-**16** (43 mg) as a light yellow liquid, which was further purified by distillation on a rotary microdistillation equipment at 100–110 °C/30 Torr to give pure (−)-**16** (39 mg, 57% yield) as a colorless liquid; $[\alpha]_D^{25}$ −40.4 (CH_2Cl_2, *c* 0.86); IR (NaCl) *ν* 2992, 2940, 2893, 1477, 1282, 1266, 1249, 1209, 1195, 1067, 1000, 944, 921, 809 cm^{-1}; MS (EI), *m/z* (%): 360 [$M^{\bullet+}$, <1], 233 ([M−I]$^+$, 22), 106 ([M−2I]$^{\bullet+}$, 100), 105 (48), 91 (41), 79 (28), 78 (32), 77 (19). Anal. Calcd for $C_8H_{10}I_2$ (359.98): C 26.69, H 2.80, I 70.51. Found: C 27.07, H 2.74, I 69.36.

4.1.7. (+)(1*R*,3*R*,5*R*,7*R*)-1,3-Diiodotricyclo[3.3.0.0^{3,7}]octane, (+)-16.[5d] This reaction was carried out as described for the preparation of diiodide (−)-**16**. From (+)-**18** (70 mg, 0.36 mmol), iodine [2×(0.20 g, 0.78 mmol)], and iodosobenzenediacetate [IBDA, 2×(0.26 g, 98% content, 0.78 mmol)] in anhydrous acetonitrile (7 mL), diiodide (+)-**16** (72 mg, 56% yield) was obtained as a colorless liquid; $[\alpha]_D^{28}$ +41.2 (CH_2Cl_2, *c* 0.47); IR (NaCl) *ν* 2992, 2940, 2893, 1477, 1282, 1252, 1208, 1196, 1067, 1000, 944, 921, 809 cm^{-1}; MS (EI), *m/z* (%): 360 ($M^{\bullet+}$, 2), 233 ([M−I]$^+$, 39), 106 ([M−2I]$^{\bullet+}$, 100), 105 (40), 91 (39), 79 (24), 78 (27). Anal. Calcd for $C_8H_{10}I_2$ (359.98): C 26.69, H 2.80, I 70.51. Found: C 27.17, H 2.82, I 70.45.

4.1.8. (−)(1*S*,3*S*,5*S*,7*S*)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid, (−)-18.[5d] To a boiling solution of (−)-**12** (640 mg, 1.43 mmol) in a mixture of *t*-BuOH (8.2 mL, 86 mmol) and anhydrous THF (30 mL) kept under argon, lithium in small pieces (600 mg, 86 mmol) was added, and the mixture was heated under reflux for 6 h. The mixture was allowed to cool to room temperature and poured onto ice-water (70 g). The aqueous solution was washed with diethyl ether (3×25 mL), cooled with an ice-water bath, made acidic (pH≈1–2) with aqueous 5 N HCl (35 mL), and extracted with AcOEt (5×25 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure to give a light yellow residue (280 mg), which was washed with a small amount of cold diethyl ether to give (−)-**18** (210 mg, 75% yield) as a white solid, mp 189–190 °C (diethyl ether); $[\alpha]_D^{24}$ −8.0 (CH_3OH, *c* 0.44); IR (KBr) *ν* 3500–2250 (max. at 2997, 2950, 2903, 2716, 2612), 1706, 1483, 1419, 1319, 1289, 1258, 1219, 1140, 1088, 1030, 887, 757, 748 cm^{-1}; MS (EI), *m/z* (%): 178 ([M−H_2O]$^{\bullet+}$, 27), 150 ([M−HCO_2H]$^{\bullet+}$, 100), 134 (29), 133 ([M−HCO_2H−OH]$^+$, 80), 132 (40), 123 (31), 111 (87), 110 (17), 106 (29), 105 (100), 104 ([M−2HCO_2H]$^{\bullet+}$, 34), 103 (29), 93 (55), 91 (49), 83 (20), 79 (75), 78 (30), 77 (70), 67 (53), 66 (29), 65 (52). Accurate mass measurement (ESI−) calcd for [$C_{10}H_{12}O_4$−H]$^-$: 195.06628. Found: 195.06587.

4.1.9. (+)(1*R*,3*R*,5*R*,7*R*)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid, (+)-18.[5d] This reaction was carried out as described for the preparation of diacid (−)-**18**. From (+)-**12** (1.43 g, 3.19 mmol), *t*-BuOH (18.5 mL, 195 mmol), anhydrous THF (65 mL), and lithium in small pieces (1.33 g, 192 mmol), diacid (+)-**18** (410 mg, 65% yield) was obtained as a white solid, mp 190–191 °C (diethyl ether); $[\alpha]_D^{25}$ +7.7 (CH_3OH, *c* 2.03); IR (KBr) *ν* 3500–2250 (max. at 2996, 2950, 2903, 2713, 2612), 1698, 1483, 1420, 1319, 1289, 1259, 1219, 1127, 1088, 887, 747 cm^{-1}; MS (EI), *m/z* (%): 178 ([M−H_2O]$^{\bullet+}$, 1), 150 ([M−HCO_2H]$^{\bullet+}$, 19), 133 ([M−HCO_2H−OH]$^+$, 10), 132 (10), 111 (13), 110 (10), 106 (18), 105 (68), 104 ([M−2HCO_2H]$^{\bullet+}$, 20), 103 (29), 93 (19), 91 (53), 79 (66), 78 (40), 77 (100), 67 (45), 66 (44), 65 (68). Accurate mass measurement (ESI−) calcd for [$C_{10}H_{12}O_4$−H]$^-$: 195.06628. Found: 195.06665.

4.1.10. (±)-Dimethyl tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylate, (±)-17. This reaction was carried out as described for the preparation of diiodo diester (−)-**15**. From (±)-**18** (123 mg, 0.62 mmol), anhydrous MeOH (3 mL), and concd H_2SO_4 (0.3 mL), diester (±)-**17** (125 mg, 90% yield) was obtained as a white solid, mp 42–43 °C (*n*-pentane); IR (KBr) *ν* 3002, 2951, 2902, 2849, 1726, 1483, 1460, 1436, 1333, 1318, 1280, 1251, 1229, 1215, 1205, 1120, 1105, 1090, 1068, 1050, 1004, 934, 886, 873, 808, 783, 752, 737 cm^{-1}; ^1H NMR *δ*: 1.64 [br s, 2H, 6-H_2], 1.74 [dt, *J*=9.5 Hz, *J*′=2.0 Hz, 2H, 4(8)-H_α], 1.91 [dm, *J*=9.5 Hz, 2H, 4(8)-H_β], 2.02 [t, *J*=2.0 Hz, 2H, 2-H_2], 2.73 [m, 2H, 5(7)-H], 3.71 [s, 6H, 1(3)-CO_2CH_3]. ^{13}C NMR *δ*: 42.8 [CH, C5(7)], 46.5 [CH_2, C6], 50.5 [CH_2, C4(8)], 51.7 [CH_3, 1(3)-CO_2CH_3], 52.7 [C, C1(3)], 53.7 [CH_2, C2], 174.6 [C, 1(3)-CO_2CH_3]; MS (EI), *m/z* (%): 192 ([M−CH_3OH]$^{\bullet+}$, 33), 165 (26), 164 ([M−HCO_2CH_3]$^{\bullet+}$, 61), 133 ([M−HCO_2CH_3−CH_3O]$^+$, 66), 132 (24), 125 (63), 105 (100), 104 (31), 93 (73), 79 (40), 77 (25), 65 (25), 59 ([CO_2CH_3]$^+$, 42). Anal. Calcd for $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19. Found: C 64.11, H 7.13.

4.1.11. (−)-Dimethyl (1*S*,3*S*,5*S*,7*S*)-tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylate, (−)-17. This reaction was carried out as described for the preparation of diiodo diester (−)-**15**. From (−)-**18** (25 mg, 0.13 mmol), anhydrous MeOH (1 mL), and concd H_2SO_4 (0.1 mL), diester (−)-**17** (25 mg, 88% yield) was obtained as a white solid, mp 45–46 °C (*n*-pentane); $[\alpha]_D^{25}$ −10.0 (CH_2Cl_2, *c* 0.60); IR (KBr) *ν* 3002, 2951, 2902, 2848, 1726, 1483, 1436, 1420, 1333, 1318, 1279, 1251, 1228, 1205, 1120, 1090, 1069, 1050, 1004, 934, 887, 782 cm^{-1}; MS (EI), *m/z* (%): 192 ([M−CH_3OH]$^{\bullet+}$, 18), 165 (16), 164 ([M−HCO_2CH_3]$^{\bullet+}$, 39), 133 ([M−HCO_2-CH_3−CH_3O]$^+$, 51), 132 (21), 125 (45), 105 (100), 104 (30), 93 (67), 79 (45), 77 (32), 65 (34), 59 ([CO_2CH_3]$^+$, 48). Anal. Calcd for $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19. Found: C 64.02, H 7.18.

4.1.12. (+)-Dimethyl (1*R*,3*R*,5*R*,7*R*)-tricyclo[3.3.0.0^{3,7}]-octane-1,3-dicarboxylate, (+)-17. This reaction was carried out as described for the preparation of diiodo diester (−)-**15**. From (+)-**18** (39 mg, 0.20 mmol), anhydrous MeOH (2 mL), and concd H_2SO_4 (0.2 mL), diester (+)-**17** (38 mg, 86% yield) was obtained as a white solid, mp 51–52 °C (*n*-pentane); $[\alpha]_D^{25}$ +9.5 (CH_2Cl_2, *c* 0.78); IR (KBr) *ν* 2983, 2951, 2902, 2853, 1732, 1484, 1452, 1436, 1330, 1319, 1283, 1253, 1229, 1213, 1178, 1135, 1117, 1087, 1067, 1050, 874, 783 cm^{-1}; MS (EI), *m/z* (%): 192 ([M−CH_3OH]$^{\bullet+}$, 21), 165 (18), 164 ([M−HCO_2CH_3]$^{\bullet+}$, 42), 133 ([M−HCO_2CH_3−CH_3O]$^+$, 54), 132 (21), 125 (47), 105 (100), 104 (33), 93 (73), 79 (52), 77 (36), 65 (39), 59 ([CO_2CH_3]$^+$, 57). Anal. Calcd for $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19. Found: C 63.98, H 7.28.

4.1.13. (±)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarbonitrile, (±)-19. To a suspension of diacid (±)-**18** (150 mg, 0.76 mmol) in acetonitrile (7 mL), concd H_2SO_4 (0.8 mL) was added dropwise and the mixture was heated under reflux for 6 h. The mixture was allowed to cool to room temperature and was concentrated under reduced pressure. The residue was taken in CH_2Cl_2 (30 mL) and H_2O (30 mL), the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3×30 mL). The combined organic phase and extracts were washed with brine (2×30 mL), dried with anhydrous Na_2SO_4, and concentrated under reduced pressure to give a colorless oil, which was subjected to column chromatography [flash silica gel (3 g), hexane/AcOEt]. On elution with hexane/AcOEt in the ratio of 5:1 (50 mL), dinitrile (±)-**19** (46 mg, 38% yield) was obtained as a white solid. The analytical sample was obtained by crystallization from diethyl ether/*n*-pentane (1:1), mp 120–121 °C; IR (KBr) ν 3004, 2957, 2906, 2237, 1484, 1311, 1287, 1269, 1025, 889, 778 cm^{-1}; ^{1}H NMR δ: 1.75 [quint, J=2.0 Hz, 2H, 6-H$_2$], 1.92 [dt, J=10.0 Hz, J'=2.0 Hz, 2H, 4(8)-H$_\alpha$], 2.05 [dq, J=10.0 Hz, J'=2.0 Hz, 2H, 4(8)-H$_\beta$], 2.19 [t, J=2.0 Hz, 2H, 2-H$_2$], 2.87 [q, J=2.0 Hz, 2H, 5(7)-H]. ^{13}C NMR δ: 35.4 [C, C1(3)], 44.4 [CH, C5(7)], 46.1 [CH$_2$, C6], 51.1 [CH$_2$, C4(8)], 55.2 [CH$_2$, C2], 120.1 [C, 1(3)-*C*N]; MS (EI), *m*/*z* (%): 158 (M$^{\bullet+}$, 2), 157 ([M−H]$^+$, 13), 131 ([M−HCN]$^{\bullet+}$, 8), 130 (12), 117 (15), 116 (17), 104 (10), 92 (100), 91 (14), 79 (24), 65 (27). Chiral GC/MS analysis (retention time): (+)-**19** (40.34 min) and (−)-**19** (40.59 min). Accurate mass measurement (ESI+) calcd for [$C_{10}H_{10}N_2$+H]$^+$: 159.0922. Found: 159.0917.

4.1.14. (−)(1*S*,3*S*,5*S*,7*S*)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarbonitrile, (−)-19. This reaction was carried out as described for the preparation of dinitrile (±)-**19**. From (−)-**18** (56 mg, 0.29 mmol), acetonitrile (3 mL), and concd H_2SO_4 (0.3 mL), dinitrile (−)-**19** (12 mg, 26% yield) was obtained as a white solid. The analytical sample of (−)-**19** was obtained by crystallization from diethyl ether/*n*-pentane (1:1), mp 112–114 °C; $[\alpha]_D^{24}$ −17.7 (CH_2Cl_2, *c* 0.52); IR (KBr) ν 3004, 2954, 2926, 2906, 2854, 2236, 1482, 1302, 1268, 1212, 1055, 1030, 890, 799, 776 cm^{-1}; MS (EI), *m*/*z* (%): 158 (M$^{\bullet+}$, 4), 157 [(M−H)$^+$, 20], 130 (11), 130 (10), 116 (25), 104 (10), 92 (100), 86 (22), 84 (26). Chiral GC/MS analysis (retention time): (−)-**19** (40.59 min). Accurate mass measurement (EI) calcd for [$C_{10}H_{10}N_2$]$^{\bullet+}$: 158.0844. Found: 158.0841.

4.1.15. (+)(1*R*,3*R*,5*R*,7*R*)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarbonitrile, (+)-19. This reaction was carried out as described for the preparation of dinitrile (±)-**19**. From (+)-**18** (80.5 mg, 0.41 mmol), acetonitrile (4 mL), and concd H_2SO_4 (0.4 mL), dinitrile (+)-**19** (19 mg, 29% yield) was obtained as a white solid. The analytical sample of (+)-**19** was obtained by crystallization from diethyl ether/*n*-pentane (1:1), mp 116–117 °C; $[\alpha]_D^{24}$ +17.3 (CH_2Cl_2, *c* 0.95); IR (KBr) ν 3004, 2954, 2905, 2236, 1482, 1302, 1266, 1212, 1030, 890, 776 cm^{-1}; MS (EI), *m*/*z* (%): 158 (M$^{\bullet+}$, 8), 157 ([M−H]$^+$, 23), 149 (29), 130 (23), 129 (24), 117 (30), 116 (33), 109 (23), 106 (20), 105 (37), 104 (23), 98 (38), 97 (35), 92 (100), 85 (22), 84 (34), 83 (28), 78 (34), 77 (29), 71 (51), 63 (21). Chiral GC/MS analysis (retention time): (+)-**19** (40.34 min). Accurate mass measurement (EI) calcd for [$C_{10}H_{10}N_2$]$^{\bullet+}$: 158.0844. Found: 158.0840.

4.1.16. (±)-1,3-Dibromo-5,7-diiodotricyclo[3.3.0.0^{3,7}]octane, (±)-20. To a stirred suspension of red HgO (140 mg, 0.65 mmol) in anhydrous CH_2Br_2 (15 mL) in a Dean–Stark distillation system maintained under an argon atmosphere, diiodo diacid (±)-**12** (200 mg, 0.45 mmol) was added. The mixture was heated while distilling part of the solvent (5 mL). A solution of bromine (0.047 mL, 0.93 mmol) in anhydrous CH_2Br_2 (5 mL) was added and the mixture was heated under reflux for 3 h. The mixture was allowed to cool to room temperature and the suspension was filtered through Celite® washing the solid with CH_2Cl_2 (3×5 mL). The combined filtrate and washings were washed with aqueous $Na_2S_2O_3$ solution (10%, 3×5 mL), 2 N NaOH (3×5 mL), and brine (2×5 mL). The organic phase was dried (anhydrous Na_2SO_4) and the solvent was removed under reduced pressure to give (±)-**20** (205 mg, 88% yield) as a yellow solid. The analytical sample of (±)-**20** was obtained by crystallization from CH_2Cl_2 to give (±)-**20** as a white solid, mp 232–233 °C (CH_2Cl_2); IR (KBr) ν 2996, 2941, 1471, 1265, 1242, 1230, 1126, 994, 963, 874, 787 cm^{-1}; ^{1}H NMR δ: 2.52 [t, J=2.5 Hz, 2H, 2-H$_2$], 2.58 [dt, J=10.0 Hz, J'=2.0 Hz, 2H, 4(8)-H$_\alpha$], 2.64 [dt, J=10.0 Hz, J'=2.0 Hz, 2H, 4(8)-H$_\beta$], 2.71 [t, J=2.5 Hz, 2H, 6-H$_2$]. ^{13}C NMR δ: 36.3 [C, C5(7)], 60.5 [C, C1(3)], 64.0 [CH$_2$, C2], 66.7 [CH$_2$, C4(8)], 69.4 [CH$_2$, C6]; MS (EI), *m*/*z* (%): 439 (3) and 437 (3) ([M−Br]$^+$), 393 (8), 391 (16) and 389 (8) ([M−I]$^+$), 312 (37) and 310 (37) ([M−Br−I]$^{\bullet+}$), 266 (8), 264 (15) and 262 (8) ([M−2I]$^{\bullet+}$), 185 (58) and 183 (62) ([M−Br−2I]) 104 (100), 103 (72), 78 (29), 77 (35); MS (CI), *m*/*z* (%): 521 (2), 519 (4) and 517 (2) ([M+H]$^+$), 439 (52) and 437 (54) ([M−Br]$^+$), 393 (17), 391 (36) and 389 (19) ([M−I]$^+$), 312 (53) and 310 (55) ([M−Br−I]$^{\bullet+}$), 311 (55) and 309 (50) ([M−HBr−I]$^+$), 266 (11), 264 (21) and 262 (11) ([M−2I]$^{\bullet+}$), 265 (14), 263 (24) and 261 (12) ([M−HI−I]$^+$), 231 ([M−2Br−I]$^+$, 28), 186 (12), 185 (97) and 183 (100) ([M−Br−2I]$^+$), 184 (30), 182 (18), 105 (16), 104 (28), 103 (18). Accurate mass measurement (ESI+) calcd for [$C_8H_8{}^{79}Br^{81}BrI_2$+H]$^+$: 518.714005. Found: 518.714032.

4.1.17. (−)(1*R*,3*R*,5*S*,7*S*)-1,3-Dibromo-5,7-diiodotricyclo[3.3.0.0^{3,7}]octane, (−)-20. This reaction was carried out as described for the preparation of (±)-**20**. From (−)-**12** (195 mg, 0.44 mmol), red HgO (140 mg, 0.65 mmol) in anhydrous CH_2Br_2 (15 mL) and bromine (0.047 mL, 0.93 mmol) in anhydrous CH_2Br_2 (5 mL), (−)-**20** (214 mg, 94% yield) was obtained as a yellow solid. The analytical sample of (−)-**20** was obtained by crystallization from CH_2Cl_2, mp 233–234 °C (CH_2Cl_2); $[\alpha]_D^{24}$ −6.4 (CH_2Cl_2, *c* 2.00); IR (KBr) ν 2995, 2935, 2888, 1470, 1265, 1242, 1230, 1125, 993, 963, 873, 860, 804, 785, 635 cm^{-1}; MS (EI), *m*/*z* (%): 393 (1), 391 (3) and 389 (1) ([M−I]$^+$), 312 (10) and 310 (10) ([M−Br−I]$^{\bullet+}$), 266 (3), 264 (6) and 262 (3) ([M−2I]$^{\bullet+}$), 185 (33) and 183 (37) ([M−Br−2I]$^+$), 104 (100), 103 (71), 78 (33), 77 (46), 63 (23). Accurate mass measurement (EI) calcd for [$C_8H_8{}^{79}Br^{81}BrI_2$]$^{\bullet+}$: 517.7062. Found: 517.7048.

4.1.18. (+)(1*S*,3*S*,5*R*,7*R*)-1,3-Dibromo-5,7-diiodotricyclo[3.3.0.0^{3,7}]octane, (+)-20. This reaction was carried out as described for the preparation of (±)-**20**. From (+)-**12** (200 mg, 0.45 mmol), red HgO (140 mg, 0.65 mmol) in anhydrous CH_2Br_2 (15 mL) and bromine (0.047 mL,

0.93 mmol) in anhydrous CH_2Br_2 (5 mL), (+)-**20** (205 mg, 88% yield) was obtained as a yellow solid. The analytical sample of (+)-**20** was obtained by crystallization from CH_2Cl_2, mp 232–233 °C (CH_2Cl_2); $[\alpha]_D^{24}$ +6.3 (CH_2Cl_2, *c* 1.99); IR (KBr) *ν* 2992, 2938, 1473, 1266, 1242, 1230, 1125, 993, 963, 873, 860, 801, 785, 634 cm^{-1}; MS (EI), *m/z* (%): 439 (1) and 437 (1) ($[M-Br]^+$), 393 (3), 391 (6) and 389 (3) ($[M-I]^+$), 312 (13) and 310 (14) ($[M-Br-I]^{\bullet+}$), 266 (4), 264 (8) and 262 (4) ($[M-2I]^{\bullet+}$), 185 (38) and 183 (42) ($[M-Br-2I]^+$), 104 (100), 103 (69), 77 (48), 66 (23). Accurate mass measurement (EI) calcd for $[C_8H_8{}^{79}Br^{81}BrI_2]^{\bullet+}$: 517.7062, found: 517.7075.

4.1.19. (±)-1,3-Dibromotricyclo[3.3.0.0^{3,7}]octane, (±)-21.

4.1.19.1. Method A. To a stirred suspension of red HgO (320 mg, 1.47 mmol) in anhydrous CH_2Br_2 (30 mL) in a Dean–Stark distillation system maintained under an argon atmosphere, diacid (±)-**18** (200 mg, 1.02 mmol) was added. The mixture was heated and part of the solvent (10 mL) was distilled off. A solution of bromine (0.11 mL, 2.10 mmol) in anhydrous CH_2Br_2 (10 mL) was added and the mixture was heated under reflux for 3 h. The mixture was allowed to cool to room temperature and the suspension was filtered through Celite® washing the solid with CH_2Cl_2 (3×5 mL). The combined filtrate and washings were washed with aqueous $Na_2S_2O_3$ solution (10%, 3×5 mL), 2 N NaOH (3×5 mL), and brine (2×5 mL). The organic phase was dried (anhydrous Na_2SO_4) and the solvent was distilled under atmospheric pressure through a Vigreux column (10 cm). The oily residue (352 mg) was submitted to column chromatography [silica gel (50 g), hexane]. On elution with hexane (60 mL), dibromide (±)-**21** (145 mg, 53% yield) was obtained as a light yellow liquid. The analytical sample of (±)-**21** was obtained by distillation on a rotary microdistillation equipment at 60–70 °C/30 Torr; IR (NaCl) *ν* 2999, 2946, 2898, 1480, 1284, 1256, 1211, 1204, 1004, 947, 933, 824 cm^{-1}; ^1H NMR *δ*: 1.74 [quint, *J*=2.0 Hz, 2H, 6-H_2], 1.81 [dt, *J*=9.5 Hz, *J′*=2.0 Hz, 2H, 4(8)-H_α], 2.24 [dq, *J*=9.5 Hz, *J′*=2.0 Hz, 2H, 4(8)-H_β], 2.30 [t, *J*=2.0 Hz, 2H, 2-H_2], 2.54 [q, *J*=2.0 Hz, 2H, 5(7)-H]. ^{13}C NMR *δ*: 46.4 [CH_2, C6], 48.4 [CH, C5(7)], 52.9 [C, C1(3)], 56.2 [CH_2, C4(8)], 64.7 [CH_2, C2]; MS (EI), *m/z* (%): 187 (26) and 185 (27) ($[M-Br]^+$), 106 (27), 105 ($[M-Br-HBr]^+$, 100), 91 (20), 79 (36), 78 (20), 77 (31), 65 (32); MS (CI), *m/z* (%): 187 (55) and 185 (57) ($[M-Br]^+$), 107 (14), 106 (16), 105 ($[M-Br-HBr]^+$, 100), 87 (18), 85 (28), 79 (36). Chiral GC/MS analysis (retention time): (+)-**21** (22.14 min) and (−)-**21** (22.34 min). Anal. Calcd for $C_8H_{10}Br_2$ (265.97): C 36.13, H 3.79, Br 60.08. Found: C 36.09, H 3.75, Br 59.77.

4.1.19.2. Method B. A suspension of (±)-**20** (42 mg, 0.08 mmol), 10% Pd/C (7 mg), and NaOH (10 mg, 0.25 mmol) in MeOH (2 mL) was hydrogenated at atmospheric pressure for 16 h. The suspension was filtered through Celite® washing the solid with MeOH (1 mL). Water (5 mL) was added to the combined filtrate and washings and the mixture was extracted with CH_2Cl_2 (5×5 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and the solvent was distilled under atmospheric pressure through a Vigreux column (10 cm), to give dibromide (±)-**21** (18 mg, approx. 83% yield) as a colorless liquid.

4.1.20. (−)(1*S*,3*S*,5*S*,7*S*)-1,3-Dibromotricyclo[3.3.0.0^{3,7}]-octane, (−)-21.

4.1.20.1. Method A. This reaction was carried out as described for the preparation of dibromide (±)-**21** (method A). From (−)-**18** (50 mg, 0.25 mmol), red HgO (78 mg, 0.36 mmol) in anhydrous CH_2Br_2 (8 mL) and bromine (0.03 mL, 0.58 mmol) in anhydrous CH_2Br_2 (3 mL), dibromide (−)-**21** (47 mg, 71% yield) was obtained as a light yellow liquid. The analytical sample of (−)-**21** was obtained by distillation on a rotary microdistillation equipment at 60–70 °C/30 Torr; $[\alpha]_D^{25}$ −19.0 (CH_2Cl_2, *c* 0.54); IR (NaCl) *ν* 3000, 2946, 2898, 2858, 1480, 1284, 1256, 1211, 1004, 947, 933, 824 cm^{-1}; MS (EI), *m/z* (%): 226 (3), 224 (6) and 222 (3) ($[M-C_3H_6]^{\bullet+}$), 187 (24) and 185 (25) ($[M-Br]^+$), 145 (11), 106 ($[M-2Br]^{\bullet+}$, 34), 105 (100), 91 (23), 79 (47), 78 (20), 77 (30), 65 (38). Chiral GC/MS analysis (retention time): (−)-**21** (22.34 min). Anal. Calcd for $C_8H_{10}Br_2$ (265.97): C 36.13, H 3.79, Br 60.08. Found: C 35.97, H 3.62, Br 60.26.

4.1.20.2. Method B. This reaction was carried out as described for the preparation of dibromide (±)-**21** (method B). From (−)-**20** (42 mg, 0.081 mmol), 10% Pd/C (7 mg), and NaOH (10 mg, 0.25 mmol) in MeOH (2 mL), dibromide (−)-**21** (17 mg, approx. 79% yield) was obtained as a colorless liquid.

4.1.21. (+)(1*R*,3*R*,5*R*,7*R*)-1,3-Dibromotricyclo[3.3.0.0^{3,7}]-octane, (+)-21.

4.1.21.1. Method A. This reaction was carried out as described for the preparation of dibromide (±)-**21** (method A). From (+)-**18** (99 mg, 0.51 mmol), red HgO (160 mg, 0.73 mmol) in anhydrous CH_2Br_2 (15 mL) and bromine (0.054 mL, 1.05 mmol) in anhydrous CH_2Br_2 (5 mL), dibromide (+)-**21** (96 mg, 71% yield) was obtained as a light yellow liquid. The analytical sample of (+)-**21** was obtained by distillation on a rotary microdistillation equipment at 60–70 °C/30 Torr; $[\alpha]_D^{25}$ +19.4 (CH_2Cl_2, *c* 1.02); IR (NaCl) *ν* 3000, 2946, 2898, 1480, 1284, 1259, 1211, 1004, 949, 933, 824 cm^{-1}; MS (EI), *m/z* (%): 226 (3), 224 (6) and 222 (3) ($[M-C_3H_6]^{\bullet+}$), 187 (23) and 185 (23) ($[M-Br]^+$), 106 ($[M-2Br]^{\bullet+}$, 34), 105 (100), 91 (23), 79 (47), 78 (20), 77 (30), 65 (38). Chiral GC/MS analysis (retention time): (+)-**21** (22.14 min). Anal. Calcd for $C_8H_{10}Br_2$ (265.97): C 36.13, H 3.79, Br 60.08. Found: C 36.02, H 3.68, Br 60.12.

4.1.21.2. Method B. This reaction was carried out as described for the preparation of dibromide (±)-**21** (method B). From (+)-**20** (40 mg, 0.078 mmol), 10% Pd/C (7 mg), and NaOH (10 mg, 0.25 mmol) in MeOH (2 mL), dibromide (+)-**21** (18 mg, approx. 85% yield) was obtained as a colorless liquid.

4.1.22. (±)-1,3-Dinitrotricyclo[3.3.0.0^{3,7}]octane, (±)-22.

4.1.22.1. Method A. A suspension of diacid (±)-**18** (100 mg, 0.51 mmol) in $SOCl_2$ (2 mL) was heated under reflux for 2 h. The mixture was allowed to cool to room temperature and was concentrated under reduced pressure to give a white solid (121 mg). To a cold (0 °C) solution of NaN_3 (0.22 g, 3.37 mmol) in H_2O (1.5 mL), a solution of the above white solid (121 mg) in acetone (1.5 mL) was added dropwise for 15 min and the mixture was stirred at

room temperature for 3 h. The mixture was diluted with H_2O (2 mL) and was extracted with AcOEt (3×5 mL). The combined organic extracts were washed with aqueous $NaHCO_3$ solution (5%, 2×5 mL) and H_2O (2×5 mL), dried (anhydrous Na_2SO_4), and concentrated under reduced pressure to give a colorless oil (114 mg). A solution of the above colorless oil (114 mg) in anhydrous toluene (2 mL) was added for 30 min to anhydrous toluene (14 mL) under reflux and the residue was stirred under reflux for 5 h. The mixture was allowed to cool to room temperature and the solvent was distilled under atmospheric pressure through a Vigreux column (10 cm) to give (±)-**23** (96 mg) as a yellow wax. To (±)-**23** (96 mg) a solution of dimethyldioxirane (DMD) in acetone (0.073 N, 70 mL, 5.1 mmol) and H_2O (13 mL) was added and the mixture, protected from light, was stirred under an argon atmosphere for 12 h at room temperature. Acetone was removed in vacuo and the precipitated white solid was filtered in vacuo and washed with H_2O (2 mL) to give (±)-**22** (36 mg) as a white solid. The combined filtrate and washings were extracted with CH_2Cl_2 (3×5 mL), dried (anhydrous Na_2SO_4), and concentrated under reduced pressure to give a yellow oil (34 mg), which was washed with diethyl ether to give more (±)-**22** (12 mg, global yield 48%), mp 135–137 °C (H_2O); IR (KBr) ν 3020, 2957, 2909, 1534, 1483, 1427, 1376, 1291, 1146, 1032, 900, 886, 806, 780 cm^{-1}; ^1H NMR δ: 2.01 [br s, 2H, 6-H_2], 2.26 [dt, J=10.0 Hz, J'=2.0 Hz, 2H, 4(8)-H_α], 2.54 [dm, J=10.0 Hz, 2H, 4(8)-H_β], 2.84 [t, J=2.0 Hz, 2H, 2-H_2], 3.14 [br s, 2H, 5(7)-H]. ^{13}C NMR δ: 44.4 [CH, C5(7)], 45.5 [CH_2, C6], 51.0 [CH_2, C4(8)], 54.7 [CH_2, C2], 86.0 [C, C1(3)]; MS (CI), *m/z* (%): 180 ([M−HNO_2+C_2H_5]$^+$, 8), 169 (15), 153 (11), 152 ([M−NO_2]$^+$, 100), 106 (20), 105 (44), 93 (16), 91 (19), 79 (63); MS (EI), *m/z* (%): 198 ($M^{\bullet+}$, 0.3), 152 ([M−NO_2]$^+$, 2), 121 (29), 107 (15), 105 (87), 104 (50), 103 (35), 94 (22), 93 (61), 92 (20), 91 (54), 80 (15), 79 (100), 78 (39), 77 (71), 65 (15). Accurate mass measurement (EI) calcd for [$C_8H_{10}N_2O_4$]$^{\bullet+}$: 198.0641. Found: 198.0641.

4.1.22.2. Method B. To (±)-**24·2HCl** (10.4 mg, 0.049 mmol), a solution of dimethyldioxirane in acetone (0.08 N, 12 mL, 0.96 mmol) was added and the mixture, protected from light, was stirred under an argon atmosphere for 16 h at room temperature. The solvent was removed in vacuo to give a yellow wax (10 mg), which was washed with CH_2Cl_2 (3×2 mL), filtered and the combined filtrate and washings were concentrated under reduced pressure to give a white solid (9 mg), which was washed with a small amount of diethyl ether to give (±)-**22** (6.5 mg, 67% yield) as a white solid.

4.1.23. (−)(1*S*,3*S*,5*S*,7*S*)-1,3-Dinitrotricyclo[3.3.0.0^{3,7}]-octane, (−)-22. This reaction was carried out as described for the preparation of (±)-**22** (method A). From (−)-**18** (31 mg, 0.16 mmol), (−)-**22** (13 mg, 41% yield) was obtained as a white solid, mp 149–151 °C (H_2O); $[\alpha]_D^{25}$ −3.6 (CH_2Cl_2, *c* 0.32); IR (KBr) ν 3026, 2958, 2910, 1540, 1484, 1378, 1137, 1046, 808 cm^{-1}; MS (EI), *m/z* (%): 152 ([M−NO_2]$^+$, 1), 121 (66), 107 (14), 105 (98), 104 (81), 103 (65), 94 (26), 93 (93), 92 (28), 91 (84), 80 (16), 79 (100), 78 (69), 77 (94), 65 (18). The molecular ion was not observed. Accurate mass measurement (EI) calcd for [$C_8H_{10}NO_2$]$^+$ corresponding to [M−NO_2]$^+$: 152.0712. Found: 152.0715.

4.1.24. (+)(1*R*,3*R*,5*R*,7*R*)-1,3-Dinitrotricyclo[3.3.0.0^{3,7}]-octane, (+)-22. This reaction was carried out as described for the preparation of (±)-**22** (method A). From (+)-**18** (71 mg, 0.36 mmol), (+)-**22** (31 mg, 44% yield) was obtained as a white solid, mp 141–142 °C (H_2O); $[\alpha]_D^{25}$ +3.4 (CH_2Cl_2, *c* 0.91); IR (KBr) ν 3025, 2960, 2923, 2853, 1540, 1378, 1136, 1046, 884, 807 cm^{-1}; MS (EI), *m/z* (%): 152 ([M−NO_2]$^+$, 0.4), 151 (0.8), 121 (24), 107 (10), 105 (93), 104 (47), 103 (30), 94 (16), 93 (75), 92 (14), 91 (53), 80 (10), 79 (100), 78 (35), 77 (87), 65 (11). The molecular ion was not observed. Accurate mass measurement (EI) calcd for [$C_8H_{10}NO_2$]$^+$ corresponding to [M−NO_2]$^+$: 152.0712. Found: 152.0709.

4.1.25. (±)-Tricyclo[3.3.0.0^{3,7}]octane-1,3-diamine dihydrochloride, (±)-24·2HCl. To a solution of (±)-**18** (200 mg, 1.02 mmol) in toluene (6 mL), Et_3N (0.38 mL, 2.73 mmol) and $(PhO)_2P(O)N_3$ (0.67 mL, 3.0 mmol) were added and the mixture was heated under reflux for 3 h. The mixture was allowed to cool to room temperature and was washed with 1 N HCl (10×10 mL) at 0 °C. Then, 6 N HCl (10 mL) was added to the organic phase and it was heated under reflux for 24 h. The solution was allowed to cool to room temperature and the phases were separated. The aqueous layer was washed with diethyl ether (3×8 mL) and the aqueous solution was concentrated under reduced pressure to give a brown solid (239 mg), which was washed with a small amount of hot 2-propanol to give (±)-**24·2HCl** (150 mg) as a yellow solid. A solution of (±)-**24·2HCl** (150 mg, 0.71 mmol) was added to an aqueous solution of NaOH (0.70 N, 2 mL) and the solution was extracted with AcOEt (10×20 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and distilled under atmospheric pressure through a Vigreux column (10 cm) to a final volume of approx. 5 mL. Diethyl ether/HCl was added (until no more precipitate was formed) and the mixture was filtered to give (±)-**24·2HCl** (47 mg, 22% yield) as a yellow solid, mp >300 °C (dec); IR (KBr) ν 3600–2200 (max. at 3413, 2995, 2947, 2900, 2749, 2594), 1593, 1571, 1509, 1492, 1319, 1286, 1265, 1244, 1181, 1163, 1086, 1055 cm^{-1}; ^1H NMR (CD_3OD) δ: 1.85 [m, J=2.0 Hz, 2H, 4(8)-H_α], 1.86 [m, 2H, 6-H_2], 2.17 [m, 2H, 4(8)-H_β], 2.18 [m, 2H, 2-H_2], 2.55 [br s, 2H, 5(7)-H], 4.86 (br s, mobile H). ^{13}C NMR (100.6 MHz, CD_3OD) δ: 43.1 [CH, C5(7)], 46.6 [CH_2, C6], 49.9 [CH_2, C4(8)], 52.8 [CH_2, C2], 60.1 [C, C1(3)]; MS (EI), *m/z* (%): 138 (5), 137 ([M−H]$^+$, 36), 120 (32), 109 (100), 97 (21), 96 (94), 95 (41), 94 (27), 82 (39), 81 (99), 80 (86). Accurate mass measurement (ESI+) calcd for [$C_8H_{14}N_2$+H]$^+$: 139.12297. Found: 139.12245.

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References and notes

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7. A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on an Enraf–Nonius CAD4 four-circle diffractometer. Unit-cell parameters were determined from automatic centering of 25 reflections ($12<\theta<21^\circ$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation; 9861 reflections were measured in the range $2.17\leq\theta\leq29.99$; 7836 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. Three reflections were measured every two hours as orientation and intensity control, significant intensity decay was not observed. Lorentz-polarization but no absorption corrections were made. The structure was solved by direct methods, using SHELXS computer program[15] and refined by full-matrix least-squares method with SHELX-97 computer program,[16] using 9861 reflections (very negative intensities were not assumed). The minimized function was $\sum w||F_0|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.0524P)^2+0.2022P]^{-1}$ and $P=(|F_0|^2+2|F_c|^2)/3$, f, f', and f'' were taken from International Tables of X-ray Crystallography.[17] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 times the equivalent temperature factor of the atom to which it is linked. The final R(on F) factor was 0.031, wR(on $|F|^2$)=0.080 and goodness of fit=1.022 for all observed reflections. Number of refined parameters was 397. Max. shift/esd=0.00, mean shift/esd=0.00. Max. and min. peaks in final difference synthesis were 0.696 and −0.517 eÅ^{-3}, respectively.
8. A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on a MAR345 diffractometer with an image plate detector. Unit-cell parameters were determined from 2210 reflections ($3<\theta<31^\circ$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation; 1679 reflections were measured in the range $3.35\leq\theta\leq29.99$; 1479 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. Lorentz-polarization but no absorption corrections were made. The structure was solved by direct methods, using SHELXS computer program[15] and refined by full-matrix least-squares method with SHELX-97 computer program,[16] using 1679 reflections (very negative intensities were not assumed). The minimized function was $\sum w||F_0|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.1251P)^2+2.1488P]^{-1}$, and $P=(|F_0|^2+2|F_c|^2)/3$, f, f', and f'' were taken from International Tables of X-ray Crystallography.[17] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 times the equivalent temperature factor of the atom to which it is linked. The final R(on F) factor was 0.071, wR(on $|F|^2$)=0.1160 and goodness of fit=1.088 for all observed reflections. Number of refined parameters was 77. Max. shift/esd=0.00, mean shift/esd=0.00. Max. and min. peaks in final difference synthesis were 0.698 and −1.065 eÅ^{-3}, respectively.[18]
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12. A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on a MAR345 diffractometer with an image plate detector. Unit-cell parameters were determined from 125 reflections ($3<\theta<31^\circ$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation; 3697 reflections were measured in the range $3.60\leq\theta\leq29.92$; 542 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. Three reflections were measured every two hours as orientation and intensity control, significant intensity decay was not observed. Lorentz-polarization but no absorption corrections were made. The structure was solved by direct methods, using SHELXS computer program[15] and refined by full-matrix least-squares method with SHELX-97 computer program,[16] using 619 reflections (very negative intensities were not assumed). The minimized function was $\sum w||F_0|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.1120P)^2+0.0532P]^{-1}$, and $P=(|F_0|^2+2|F_c|^2)/3$, f, f', and f'' were taken from International Tables of X-ray Crystallography.[17] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 times the equivalent temperature factor of the atom to which it is linked. The final R(on F) factor was 0.061, wR(on $|F|^2$)=0.167 and goodness of fit=1.079 for all observed reflections. Number of refined parameters was 66. Max. shift/esd=0.00, mean shift/esd=0.00. Max. and min. peaks in final difference synthesis were 0.141 and −0.216 eÅ^{-3}, respectively.[18]
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18. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 641679 [(1*S*,3*S*,5*S*,7*S*,3′*R*,3″*R*)-**14**], CCDC 641677 [(±)-**20**], and CCDC 641678 [(±)-**22**]. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].