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# Atropo-Enantioselective Synthesis of a Simplified Analog of Mastigophorenes A and B

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***Abstract***: A first approach to the atroposelective total synthesis of mastigophorenes is described, the directed preparation of a structurally slightly modified analog of mastigophorenes A and B, with a *tert*-butyl instead of a substituted, chiral cyclopentyl residue. Its (partially protected) monomeric half is dimerized by oxidative (phenolic) coupling to give the corresponding biphenyl in a racemic form, or atropo-enantioselectively *via* the corresponding biaryl lactone, to give the *M*- or, optionally, the *P*-enantiomeric form, by stereoselective ring opening and subsequent standard transformations.


## INTRODUCTION

Mastigophorenes A (*P*-**1**) and B (*M*-**1**)[2] are novel 'dimeric'[3] sesquiterpenoid biaryl natural products from the liverwort, *Mastigophora diclados*, co-occurring with their monomeric phenolic precursor, herbertenediol (**2**), and the mono- or bis-sidechain coupled analogs **3** (mastigophorene C) and **6** (mastigophorene D).[2] Mastigophorenes A (*P*-**1**), B (*M*-**1**), and D (**6**) are characterized by pronounced nerve growth and network

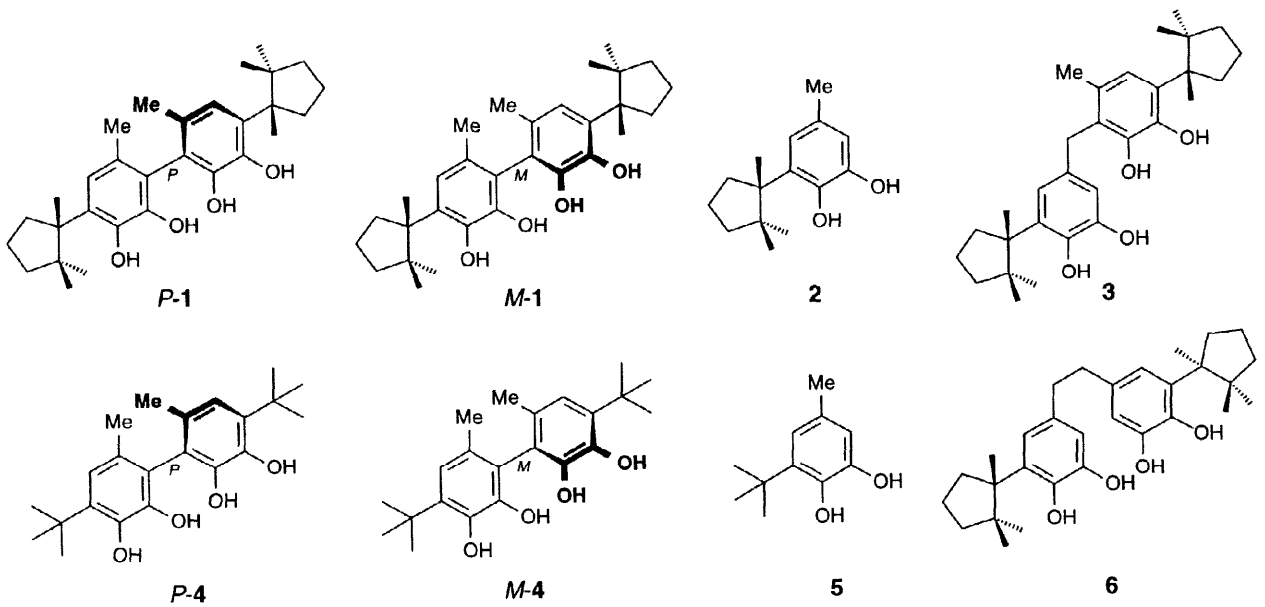


**Fig. 1.** Natural mono- and dimeric phenolic terpenoids and their simplified unnatural analogs.

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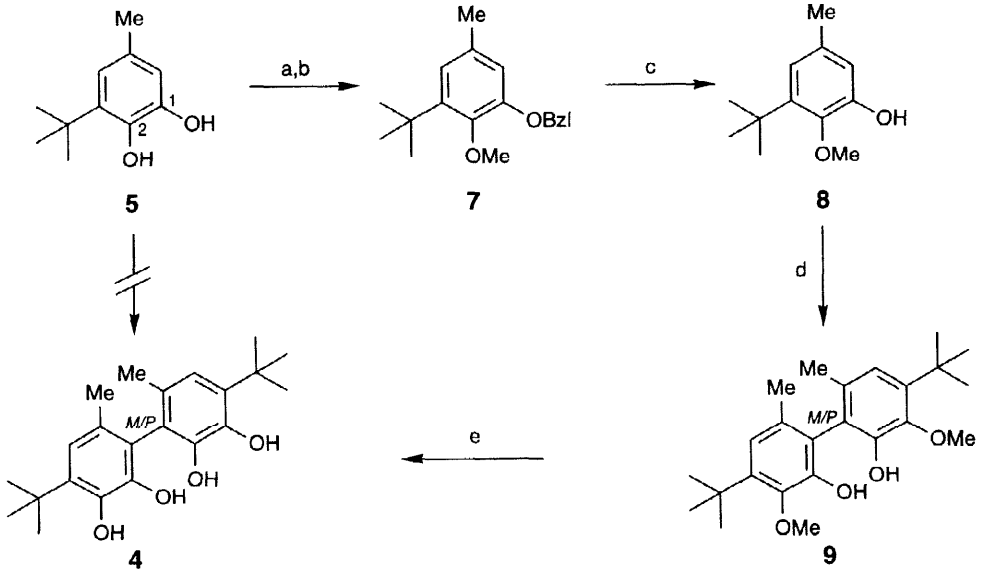
formation stimulating activity, whereas **3** was shown to suppress neuritic differentiation.[2] Despite these interesting activities, no total synthesis of **1** or any related analog has so far been described. Recently Fukuyama *et al.* reported the synthesis of racemic **2**.[4] In this paper, we describe the atropo-enantioselective coupling of a closely related achiral analog **5** of herbertenediol (**2**) to give *P*-**4** or, optionally, *M*-**4** as the first synthetic analogs of mastigophorenes A (*P*-**1**) and B (*M*-**1**).

## RESULTS AND DISCUSSION

In order to elaborate strategies for the directed construction of the stereogenic biaryl axis of mastigophorene A (*P*-**1**) by regio- and stereoselective coupling of its molecular halves, we chose the known[5] simplified analog **5** instead of the authentic natural precursor **2**. In this analog **5**, the lipophilic cyclopentyl residue, with its stereocenter, is replaced by an achiral, but comparably lipophilic *tert*-butyl group, so that, if likewise biologically active, it would simultaneously constitute of a simplified analog for the production of this active compound on an larger scale for extended biological tests.

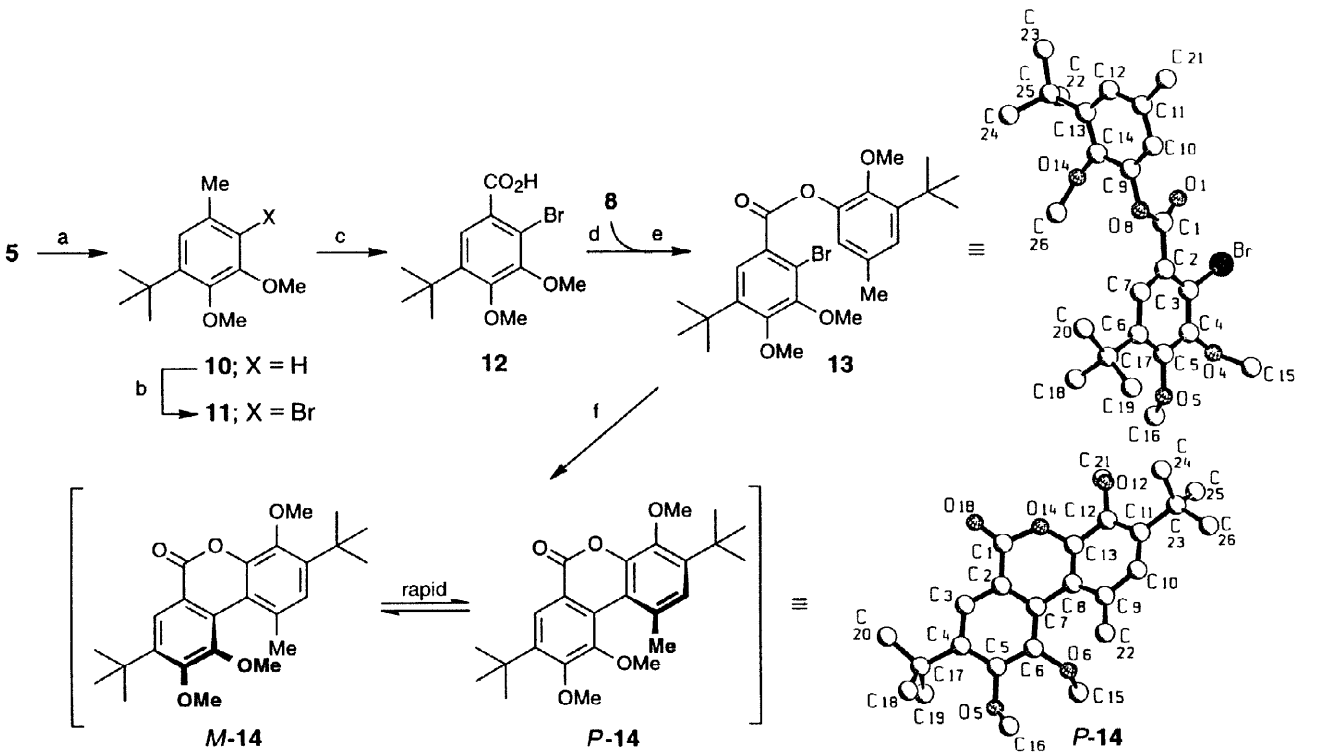
For a first synthesis of the dimer **4**, the preparatively useful and biosynthetically relevant principle of oxidative phenolic coupling[6] appeared to be the method of choice, although here to be applied to an unnatural analog. Yet, various attempts for a direct oxidative dimerization, using a variety of known oxidants such as $FeCl_3$, $Pb(OAc)_4$, $Ag_2O$, and (*tert*-$BuO)_2$ failed, giving rise to a broad spectrum of as yet unidentified products. A more promising (since less reactive) monophenolic coupling precursor, should be compound **8**, with a free phenolic group, as required for the oxidative dimerization reaction, *ortho* to the scheduled




**Scheme 1.** Synthesis of the monophenolic analog **8** of **5** and its oxidative coupling to give **4**. Reaction conditions: a) BzlBr, $K_2CO_3$, acetone, rt; b) $Me_2SO_4$, $K_2CO_3$, Bzl(*n*-Bu)$_3$NBr, acetone, rt, 94% from **5**; c) $H_2$, Pd/C (10%), EtOH/AcOEt, 1 atm, rt, 76%; d) (*tert*-$BuO)_2$, $C_6H_5Cl$, reflux, 80%; e) $BBr_3$, $CH_2Cl_2$, 0 °C, 80%.

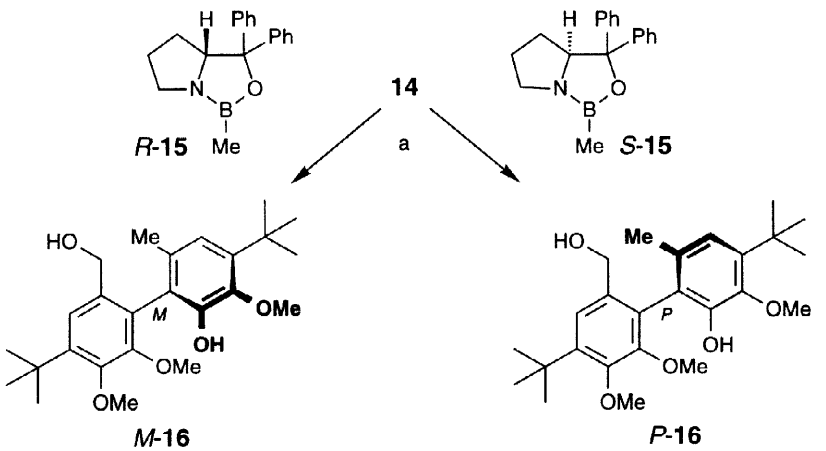
coupling site, while the other oxygen function is blocked by *O*-alkylation. Its synthesis is outlined in Scheme 1. Reaction of **5** with benzyl bromide allowed specific protection of the less hindered 1-oxygen, due the steric demand of the *tert*-butyl group. Subsequent methylation of O-2 to give **7** and hydrogenolytic cleavage of the benzyl group gave **8**. Coupling of this mono-*O*-alkylated analog **8** of **5** was best done with (*tert*-BuO)$_2$ in refluxing chlorobenzene,[7] leading to the biaryl **9** in 80% yield. *O*-Deprotection with $BBr_3$ in $CH_2Cl_2$ gave the (as yet racemic) target biaryl **4**.

For the synthesis of **4** in enantiomerically pure form, we chose our 'lactone methodology',[8-11] which allows the regio- and atroposelective construction of biaryl axes, *via* configuratively unstable biaryl lactones. For the preparation of such an 'axially prostereogenic'[12] lactone **14**, the required building blocks were **8** (as already prepared above), and **12**, which was synthesized by double *O*-alkylation of **5** to give **10** and bromination to give **11**, and subsequent Co-mediated benzylic oxidation with elemental oxygen.[13] Reaction of **8** with **12** (*via* its acid chloride) gave the ester **13**, whose structure, including the correct position of the halogen, was rigorously proven by an X-ray structure analysis.[14] Subsequent Pd-catalyzed intramolecular aryl coupling gave the lactone **14** as the stereochemically labile key compound of the synthesis. Its anticipated structure, including the helical distortion of the molecule, was confirmed by an X-ray structure analysis.[14] In the crystal, both helimeric forms, *P*-**14** and *M*-**14**, are found (two molecules each per crystal unit, along with two molecules of *n*-hexane). For reasons of clarity, only *P*-**14** is shown in Scheme 2.



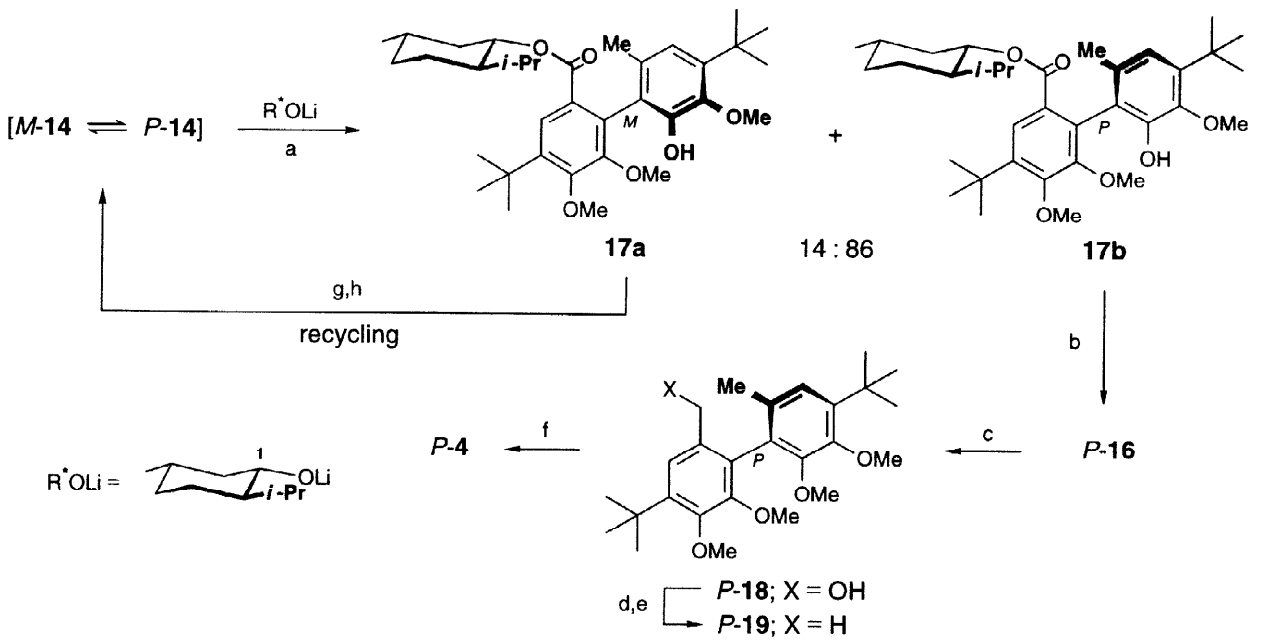

**Scheme 2.** Synthesis of the stereochemically labile key compound **14**. Reaction conditions: a) $Me_2SO_4$, NaOH, Bzl(*n*-Bu)$_3$NBr, $H_2O/CH_2Cl_2$, rt, 87%; b) $Br_2$, $CH_2Cl_2$, 0 °C, 76%; c) Co(II)(OAc)$_2$, $O_2$, 2-butanone, HOAc, 120 °C, 92%; d) $SOCl_2$, rt; e) NaH, THF, rt, 76% from **12**; f) Pd(OAc)$_2$, $Ph_3P$, NaOAc, dimethylacetamide, 130 °C, 32% (48% of **13** recovered).

For the atropo-enantioselective cleavage of **14**, we first chose the oxazaborolidine technique previously elaborated.[11,15] Thus, reduction of **14** with *R*-**15**·$BH_3$ in THF at 0 °C gave one of the two possible enantiomeric diols **16**, preferentially. The stereoanalysis, which was first optimized with a synthetic racemate (as obtained by reduction of **14** with $LiAlH_4$), was best done by HPLC on a chiral phase, giving up to 94:6 e.r. in favor of the *M*-enantiomer (for the stereochemical attribution of the two atropo-enantiomers, see below). As expected, reduction of the same configuratively unstable lactone **14**, now with the enantiomeric reagent, *S*-**15**, gave rise to the other atropisomer, *P*-**16**, in a likewise good enantiomeric ratio (8:92 e.r.), thus allowing the enantiodivergent optional synthesis of **16**, both in its *M*- or *P*-configured form. Attempts to further enhance the enantiomeric purity *e.g.* of *M*-**16** by crystallization of the enantiomerically enriched material, as an alternative to a preparative HPLC separation, gave the biaryl in a virtually stereopure form (e.r. ≥ 99:1), yet only by enrichment in the mother liquor, with the crystals containing a higher degree of racemization.



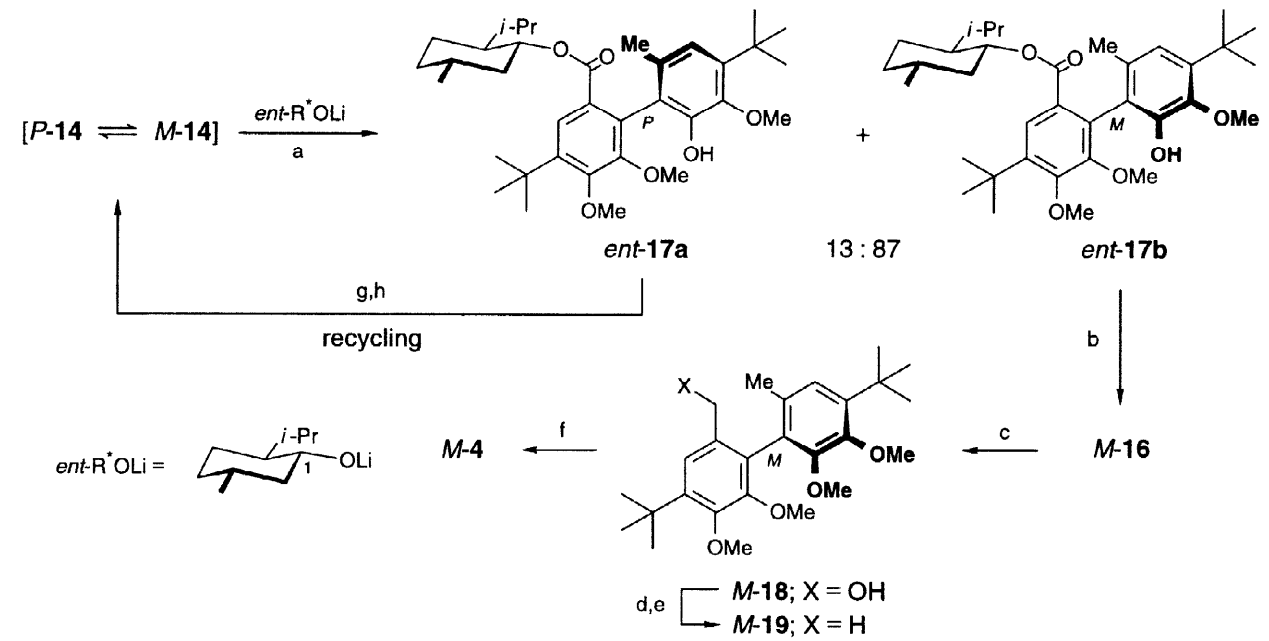

**Scheme 3.** Atropo-enantioselective ring cleavage of **14** to give *M*- or, optionally, *P*-**16**. Reaction conditions: a) THF, $BH_3$, 0 °C, 68%.

For the preparative synthesis of truly enantiopure material of **16**, the stereoselective ring opening of **14** with chiral *O*-nucleophiles seemed preferable, allowing for the option of now purifying *diastereomeric* intermediates and the recycling of the undesired minor atropodiastereomer, as elaborated previously.[16] Indeed, ring cleavage of **14** with the lithium 1*S*-mentholate in toluene at 0 °C delivered *P*-configured **17b** in a good atropo-diastereoselectivity (d.r. 86:14, analyzed by HPLC). From this diastereomeric mixture, **17b** was obtained by a simple chromatographic resolution. Reduction of pure **17b** gave *P*-**16**, likewise in a stereochemically homogeneous (here enantiomerically pure) form. In this procedure, the minor atropisomer, here **17a**, is not lost, but can be recycled, by recyclization back to the configuratively unstable lactone **14**, and renewed ring opening reaction - chiral economy with respect to atropisomerism.[12,17] From enantiomerically pure *P*-**16**, the stereochemically homogeneous target molecule *P*-**4** was finally obtained by further standard transformations, first optimized with the racemic compound, yielded by reduction of **14** with $LiAlH_4$.




**Scheme 4a.** Atropo-diastereoselective ring opening of **14** and transformation to *P*-**4**. Reaction conditions: a) toluene, 0 °C, 63% **17b**; b) $LiAlH_4$, THF, 98%; c) $K_2CO_3$, $Me_2SO_4$, acetone, rt, 97%; d) $C_2Br_2Cl_4$,[18] $PPh_3$, $CH_2Cl_2$, rt; e) $LiAlH_4$, THF, 0 °C, 79% from *P*-**18**; f) $BBr_3$, $CH_2Cl_2$, 0 °C, 95%; g) 2N NaOH, dioxan; h) 150 °C, vacuum, 78% from **17a**.

By the use of 1*R*- (instead of 1*S*-) mentholate for the ring opening (d.r. 87:13) and application of the same series of transformations as above, *M*-**4** became available in an enantiopure form, too (Scheme 4b).




**Scheme 4b.** Optional directed preparation of *M*-**4** by using 1*R*-menthol as a chiral source. Reaction conditions as in Scheme 4a.

The stereochemical attribution of *P*-**19** was done by comparison of the experimental CD spectrum with the ones quantumchemically calculated[19] for *M*- and *P*-**19**. The good agreement of the experimental CD with that of *P*-**19**, and the near-opposite spectrum calculated for the *M*-atropisomer of **19** show the synthesized compound to be *P*-configured at the axis as anticipated in Scheme 4a.

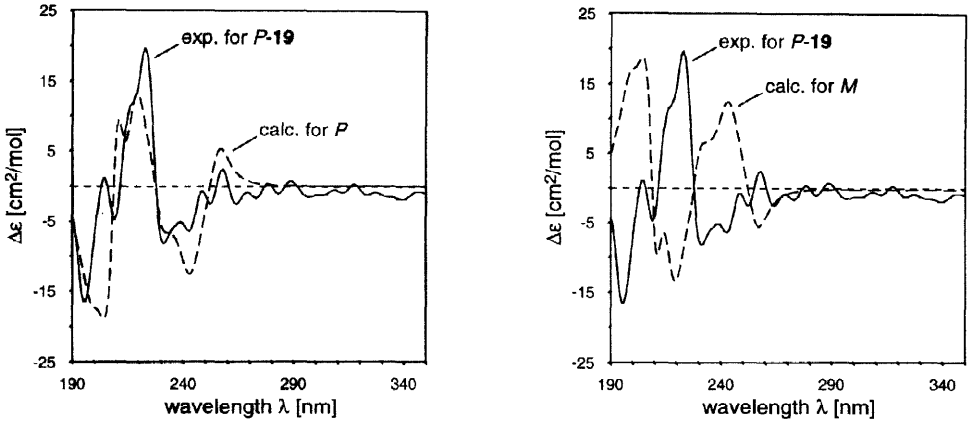



**Fig. 2.** Experimental CD spectrum of *P*-**19** and the spectra calculated for the absolute *P*- and *M*-stereostructures.

Furthermore, the comparison of the CD spectrum of *P*-**4** showed an excellent conformity with that of natural mastigophorene A (*P*-**1**), thus verifying the previous stereochemical attribution of the natural product.[2]

The presented work constitutes the first stereoselective synthesis of a mastigophorene-like biaryl and establishes the key methodology for the scheduled stereoselective total synthesis of the natural products, mastigophorenes A (*P*-**1**) and B (*M*-**1**). Given the availability of the authentic molecular half **2** both from natural resources (in an enantiomerically pure form)[2,20] and through synthesis (as yet racemic),[4] the coupling strategies presented in this paper should provide a promising strategy for the directed synthesis of authentic *P*-**1** and *M*-**1**. The biological evaluation of the now available simplified analogs *P*- and *M*-**4** is in progress.[21]

## EXPERIMENTAL

The melting points were determined with an Kofler hot plate apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1420 infrared spectrophotometer and reported in wave numbers ($cm^{-1}$). The $^1H$ NMR and $^{13}C$ NMR spectra were recorded on a Bruker AC 200 (200 MHz) or AC 250 (250 MHz). The chemicals shift are given in parts per million (ppm) with the deuterated solvent as internal reference for $^1H$ and $^{13}C$ NMR. The coupling constants, *J*, are given in Hertz. Mass spectra were recorded on a Finnigan MTA 8200 spectrometer at 70 eV in the EI mode. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. CD spectra were recorded in ethanolic solution on Jobin Yvon Model CD6 spectrograph at room temperature within the range of 190 - 350 nm. HPLC analyses of **16** were carried out with a combination of a Waters M 510 pump, a Chiracel OD-H column (Daicel Chem. Ind. Ltd., 4.6 mm x 250 mm) and an ERC-7215 UV-detector, using *n*-hexane / *i*-PrOH (99:1) as eluent. **4** was analyzed with the same combination but with *n*-hexane / *i*-PrOH (9:1) as eluent. The HPLC analyses of the esters **17** were done with the combination of a Knauer-64 pump, a Waters μPorasil™ column (125 Å, 10 μm, 3.9 mm x 300 mm) and a Waters Lamda-

Max 481 UV detector with petroleum ether / $CH_2Cl_2$ / HCOOH (60:40:0.05) as eluent. The X-ray structure analyses of compounds **13** and **14** were obtained with a Siemens R3m/V four-circle diffractrometer (MoKα, Wyckoff-scan, empirical absorption correction). The structures were solved by direct phase determination (Siemens, SHELXTL-PLUS).

**3-Benzyloxy-5-*tert*-butyl-4-methoxytoluene (7).** To a solution of **5**[5] (22.5 g, 125 mmol) in acetone (400 ml), BzlBr (21.5 g, 125 mmol) and $K_2CO_3$ (69.0 g, 500 mmol) were added. After 3 d stirring at room temperature, $(n\text{-Bu})_4NCl$ (2 g) and $Me_2SO_4$ (23.6 g, 187 mmol) were added and stirring was continued for further 2 d. The mixture was then cooled to 0 °C and after addition of conc. aqueous $NH_3$ (180 ml) the organic solvent was removed under reduced pressure and the aqueous layer was extracted with petroleum ether. The extract was dried ($Na_2SO_4$) and evaporated to yield **7** (34.0 g, 94%) as a yellow brown solid, which may be used directly for the next step. Recrystallization from petroleum ether gave colorless crystals: mp 53 °C; IR (KBr): $\tilde{\nu}$ 3040, 2930, 2890, 2840, 1565, 1305, 1000, 830, 735, 695; $^1H$ NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 9H, $C(CH_3)_3$], 2.30 (s, 3H, $ArCH_3$), 3.90 (s, 3H, $OCH_3$), 5.09 (s, 2H, $PhCH_2$), 6.73 (br. s, 1H, 2-H or 6-H), 6.75 (br. s, 1H, 2-H or 6-H), 7.31-7.51 (m, 5H, Ph-H); $^{13}C$ NMR (63 MHz, $CDCl_3$): δ = 21.55 ($ArCH_3$), 30.61 [$C(CH_3)_3$], 34.99 [$C(CH_3)_3$], 60.51 ($OCH_3$), 70.79 ($PhCH_2$), 113.2, 119.8, 127.4, 127.8, 128.5, 132.2, 137.3, 143.0, 146.7, 152.1 (Ar-C); MS: *m/z* (%) = 284 (30) [$M^+$], 228 (13) [$M^+ - C_4H_8$], 193 (35) [$M^+ - PhCH_2$], 91 (100) [$PhCH_2$]; Anal. calcd. for $C_{19}H_{24}O_2$ (284.4): C, 80.24; H, 8.51. Found: C, 80.57; H, 8.40.

Data of the intermediate 2-benzyloxy-6-*tert*-butyl-4-methylphenol, as obtained by workup before the addition of $Me_2SO_4$ and $(n\text{-Bu})_4NCl$: mp 89-90 °C (from petroleum ether); IR (KBr): $\tilde{\nu}$ 3500, 3020, 3000, 2945, 2940, 2890, 2845, 1570, 1280, 1030, 825, 740, 680; $^1H$ NMR (250 MHz, $CDCl_3$): δ = 1.44 [s, 9H, $C(CH_3)_3$], 2.32 (s, 3H, $ArCH_3$), 5.09 (s, 2H, $PhCH_2$), 5.92 (br. s, 1H, OH), 6.72 (d, *J* = 1.5, 1H, 3-H or 5-H), 6.76 (d, *J* = 1.2, 1H, 3-H or 5-H), 7.34-7.48 (m, 5H, Ph-H); $^{13}C$ NMR (63 MHz, $CDCl_3$): δ = 22.62 ($ArCH_3$), 29.41 [$C(CH_3)_3$], 34.61 [$C(CH_3)_3$], 71.28 ($PhCH_2$), 110.6, 119.7, 127.8, 128.3, 128.7, 129.0, 135.4, 136.6, 142.1, 145.8 (Ar-C); MS: *m/z* (%) = 270 (7) [$M^+$], 214 (6) [$M^+ - C_4H_8$], 179 (3) [$M^+ - PhCH_2$], 91 (100) [$PhCH_2$]; Anal. calcd. for $C_{18}H_{22}O_2$ (270.2): C, 80.01; H, 8.14. Found: C, 79.75; H, 8.35.

**3-*tert*-Butyl-2-methoxy-5-methylphenol (8).** A solution of **7** (11.5 g, 40.5 mmol) in a 1:1 mixture of EtOH and ethylacetate (200 ml) was hydrogenated with $H_2$ at atmospheric pressure for 5 h after addition of Pd/C (10%) (500 mg). Then the suspension was filtered through silica gel, the solvent was removed and the residue purified by sublimation *in vacuo* (100 °C) and subsequent crystallization from petroleum ether gave **8** (5.90 g, 76%): mp 104 °C; IR (KBr): $\tilde{\nu}$ 3290, 3030, 2980, 2930, 2900, 2840, 1580, 1305, 990, 830; $^1H$ NMR (250 MHz, $CDCl_3$): δ = 1.38 [s, 9H, $C(CH_3)_3$], 2.27 (br. s, 3H, $ArCH_3$), 3.81 (s, 3H, $OCH_3$), 5.23 (s, 1H, OH), 6.67 (br. s, 2H, 4-H and 6-H); $^{13}C$ NMR (63 MHz, $CDCl_3$): δ = 21.27 ($ArCH_3$), 30.98 [$C(CH_3)_3$], 34.96 [$C(CH_3)_3$], 61.01 ($OCH_3$), 115.0, 119.53, 133.6, 142.8, 144.5, 149.3 (Ar-C); MS: *m/z* (%) = 194 (60) [$M^+$], 179 (100) [$M^+ - CH_3$], 164 (24) [179 - $CH_3$]; Anal. calcd. for $C_{12}H_{18}O_2$ (194.3): C, 74.19; H, 9.34. Found: C, 73.90; H, 9.45.

***rac*-4,4'-Di-*tert*-butyl-2,2'-dihydroxy-3,3'-dimethoxy-6,6'-dimethylbiphenyl (9).** To a solution of **8** (452 mg, 2.33 mmol) in chlorobenzene (20 ml) di-*tert*-butylperoxide (860 µl, 4.66 mmol) was added under $N_2$

and the mixture was refluxed for 4 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel with petroleum ether / ethylacetate (5:1) as eluent. The crude product was recrystallized from petroleum ether to give **9** (360 mg, 80%): mp 177 °C; IR (KBr): $\tilde{\nu}$ 3360, 3040, 2980, 2940, 2900, 2840, 1400, 830; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.42 [s, 18H, $C(CH_3)_3$], 1.97 (s, 6H, $ArCH_3$), 3.88 (s, 6H, $OCH_3$), 4.87 (s, 2H, OH), 6.82 (s, 2H, ArH); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 19.46 ($ArCH_3$), 30.64 [$C(CH_3)_3$], 35.05 [$C(CH_3)_3$], 60.38 ($OCH_3$), 119.5, 119.9, 132.0, 143.3, 144.9, 147.1 (Ar-C); MS: *m/z* (%) = 386 (100) [$M^+$], 371 (5) [$M^+ - CH_3$], 330 (30) [$M^+ - C_4H_8$], 315 (46) [$M^+ - CH_3 - C_4H_8$]; Anal. calcd. for $C_{24}H_{34}O_4$ (386.5): C, 74.58; H, 8.87. Found: C, 74.25; H, 8.68.

***rac*-4,4'-Di-*tert*-butyl-2,2',3,3'-tetrahydroxy-6,6'-dimethylbiphenyl (4).** To a cooled (0 °C) solution of **9** (240 mg, 622 µmol) in dry $CH_2Cl_2$ (5 ml), a 1M $BBr_3$ solution in $CH_2Cl_2$ (2.50 ml, 2.50 mmol) was added under $N_2$ and the mixture was stirred for 3 h. Then MeOH (2 ml) was added and the solvent was evaporated. Purification of the residue by column chromatography on silica gel ($CH_2Cl_2$ / MeOH 20:1) and recrystallization from *n*-hexane gave **4** (178 mg, 80%) as fine needles: mp 249 °C; IR (KBr): $\tilde{\nu}$ 3460, 3040, 2980, 2940, 2900, 2850, 1215, 815; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.44 [s, 18H, $C(CH_3)_3$], 1.95 (s, 6H, $ArCH_3$), 4.66 (s, 2H, OH), 5.56 (s, 2H, OH), 6.81 (s, 2H, ArH); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 19.13 ($ArCH_3$), 29.41 [$C(CH_3)_3$], 34.72 [$C(CH_3)_3$], 117.1, 120.3, 127.4, 136.6, 140.6, 141.0 (Ar-C); MS: *m/z* (%) = 358 (48) [$M^+$], 302 (52) [$M^+ - C_4H_8$], 287 (75) [$M^+ - CH_3$], 246 (56) [$M^+ - C_4H_8$], 57 (100) [$C_4H_9^+$]; Anal. calcd. for $C_{22}H_{30}O_4$ (358.5): C, 73.71; H, 8.44. Found: C, 73.43; H, 8.44.

**3-*tert*-Butyl-1,2-dimethoxy-5-methylbenzene (10).** To a cooled (0 °C) solution of **5** (22.5 g, 125 mmol) in a mixture of $CH_2Cl_2$ (160 ml) and water (80 ml), NaOH (20.0 g, 508 mmol) and $Me_2SO_4$ (26.4 ml, 383 mmol) were added. After stirring at room temperature over night, conc. aqueous $NH_3$ (50 ml) was slowly added and the organic solvent was removed under reduced pressure. The aqueous layer was extracted with petroleum ether, the organic extract was dried ($Na_2SO_4$) and the solvent was evaporated. The obtained oil was purified by distillation *in vacuo* (98-100 °C) to afford **10** (22.7 g, 87%): IR (KBr): $\tilde{\nu}$ 3030, 2960, 2870, 2840, 1580, 840; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.41 [s, 9H, $C(CH_3)_3$], 2.35 (s, 3H, $ArCH_3$), 3.87 (s, 3H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), 6.68 (d, *J* = 1.8, 1H, 4-H or 6-H), 6.75 (d, *J* = 1.8, 1H, 4-H or 6-H); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 21.54 ($ArCH_3$), 30.52 [$C(CH_3)_3$], 34.89 [$C(CH_3)_3$], 55.55, 60.29 ($OCH_3$), 111.3, 119.2, 132.2, 142.8, 146.1, 152.9 (Ar-C); MS: *m/z* (%) = 208 (56) [$M^+$], 193 (100) [$M^+ - CH_3$], 178 (51) [193 - $CH_3$]; Anal. calcd. for $C_{13}H_{20}O_2$ (208.3): C, 74.96; H, 9.68. Found: C, 74.65; H, 9.85.

**3-Bromo-6-*tert*-butyl-1,2-dimethoxy-4-methylbenzene (11).** To a cooled (0 °C) solution of **10** (22.6 g, 109 mmol) in $CH_2Cl_2$ (300 ml), bromine (5.44 ml, 109 mmol), dissolved in $CH_2Cl_2$ (20 ml), was added slowly. After complete addition stirring was continued for 1 h at room temperature, then water (5 ml) and $K_2SO_3$ (100 mg) were added. After decolorization of the reaction mixture, the aqueous layer was separated and the organic solvent was removed. The remaining oil was crystallized from petroleum ether to yield **11** (23.7 g, 76%) as colorless crystals: mp 52 °C; IR (KBr): $\tilde{\nu}$ 3050, 2980, 2940, 815; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.36 [s, 9H, $C(CH_3)_3$], 2.36 (s, 3H, $ArCH_3$), 3.84 (s, 3H, $OCH_3$), 3.90 ( s, 3H, $OCH_3$), 6.94 (s, 1H, 5-H); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 22.94 ($ArCH_3$), 30.38 [$C(CH_3)_3$], 34.91 [$C(CH_3)_3$], 59.85, 60.27 ($OCH_3$), 117.9, 123.4, 132.6, 142.3, 150.6, 151.3 (Ar-C); MS: *m/z* (%) = 286/288 (54/53) [$M^+$],

271/273 (97/100) [$M^+$ - $CH_3$] 256/258 (24/24) [$M^+$ - $2CH_3$] 192 (25) [271/273 - HBr]; Anal. calcd. for $C_{13}H_{19}BrO_2$ (287.2): C, 54.37; H, 6.67. Found: C, 54.28; H, 6.64.

**2-Bromo-5-*tert*-butyl-3,4-dimethoxybenzoic acid (12).** To **11** (10.0 g, 34.8 mmol), dissolved in glacial acetic acid (180 ml), Co(II)$(OAc)_2 \cdot 4H_2O$ (2.20 g, 7.50 mmol) and 2-butanone (10 ml) were added. Through the preheated (130 °C) reaction mixture oxygen was bubbled for 5 h. Then the mixture was cooled and poured into ice (150 g), filtered and washed with water (300 ml). Drying the residue in a freeze dryer gave crude **12** (10.1 g, 92%), which may be used for the next step without further purification. From ethyl acetate, colorless crystals were obtained: mp 191 °C; IR (KBr): $\tilde{\nu}$ 3300 - 2300, 3050, 2940, 2850, 1670; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.38 [s, 9H, $C(CH_3)_3$], 3.84 (s, 3H, $OCH_3$), 3.98 (s, 3H, $OCH_3$), 7.79 (s, 1H, 6-H); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 30.03 [$C(CH_3)_3$], 35.24 [$C(CH_3)_3$], 59.98, 60.50 ($OCH_3$), 117.5, 126.2, 142.9, 151.5, 157.3, 171.9 (Ar-C), 191.4 (C=O); MS: *m/z* (%) = 316/318 (41/39) [$M^+$], 301/303 (100/97) [$M^+$ - $CH_3$]; Anal. calcd. for $C_{13}H_{17}BrO_4$ (317.2): C, 49.18; H, 5.36. Found: C, 48.96; H, 5.40.

**(3'-*tert*-Butyl-2'-methoxy-5'-methyl-phenyl) 2-bromo-5-*tert*-butyl-3,4-dimethoxybenzoate (13).** A solution of **12** (6.53 g, 20.6 mmol) in $SOCl_2$ (50 ml) was stirred over night at room temperature. The solvent was removed under reduced pressure and the remaining oil was dissolved in dry $CH_2Cl_2$ (50 ml) and added dropwise, under $N_2$, to a suspension of **8** (4.00 g, 20.6 mmol) and NaH (540 mg, 225 mmol) in THF (90 ml), which has already been stirred for 1 h at room temperature. Stirrring was continued for 1 h, then the solvent was evaporated and the residue was purified by filtration through silica gel with petroleum ether / ethyl acetate (10:1) as the eluent. From petroleum ether, **13** was obtained as colorless crystals (7.73 g, 76%): mp 80-83 °C; IR (KBr): $\tilde{\nu}$ 2940, 2850, 1740; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.42 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 2.34 (s, 3H, $ArCH_3$), 3.87 (s, 3H, $OCH_3$), 3.88 (s, 3H, $OCH_3$), 4.02 (s, 3H, $OCH_3$), 6.95 (d, $J$ = 1.5, 1H, 4'-H or 6'-H) , 7.03 (d, $J$ = 1.5, 1H, 4'-H or 6'-H), 7.87 (s, 1H, 6-H); $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 21.03 ($ArCH_3$), 30.02, 30.56 [$C(CH_3)_3$], 35.05, 35.14 [$C(CH_3)_3$], 59.91, 60.41, 61.16 ($OCH_3$), 117.2, 121.9, 125.08, 125.14, 125.9, 132.5, 143.0, 143.6, 143.8, 148.9, 151.5, 156.8 (Ar-C), 164.0 (C=O); MS: *m/z* (%) = 494/492 (3/3) [$M^+$], 301/299 (100/99) [$M^+$ - $(C_6H_2)(OCH_3)(C_4H_9)(CH_3)O^+$]; Anal. calcd. for $C_{25}H_{33}BrO_5$ (493.4): C, 60.85; H, 6.74. Found: C, 60.75; H, 6.57.

**3,8-Di-*tert*-butyl-4,9,10-trimethoxy-1-methyl-dibenzo[b,d]pyran-6-one (14).** In a carefully baked three-necked flask **13** (3.00 g, 6.10 mmol), $Pd(OAc)_2$ (149 mg, 610 µmol), NaOAc (1.00 g, 12.2 mmol) and $PPh_3$ (641 mg, 2.44 mmol) were dissolved under $N_2$ in freshly distilled (over $CaH_2$ and under $N_2$) dimethylacetamide (200 ml). The flask was put into a preheated (140 °C) oilbath and the reaction course was controlled by TLC (petroleum ether / diethyl ether 10:1) every 15 min. After 100 min nearly half conversion and an increased formation of sideproducts was observed. The solvent was removed under reduced pressure and the residue was filtered through silica gel with petroleum ether / diethyl ether (10:1) as the eluent to yield a mixture of **14** and starting material **13**. By crystallization from petroleum ether, **14** (720 mg) was partly separated. Subsequent column chromatography of the mother liquor on silica gel with petroleum ether / diethyl ether (20:1) afforded **14** (175 mg) and recovered **13** (1.43 g, 48%). Recrystallization from petroleum ether gave **14** (817 mg, 32%) as colorless needles: mp 197 °C; IR (KBr): $\tilde{\nu}$ 2965, 2940, 2900, 2840, 1720; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.44 [s, 9H, $C(CH_3)_3$], 1.45 [s, 9H, $C(CH_3)_3$], 2.41 (s, 3H,

$ArCH_3$), 3.49 (s, 3H, 10-$OCH_3$) 4.04 (s, 3H, $OCH_3$), 4.10 (s, 3H, $OCH_3$), 7.06 (s, 1H, 7-H), 8.09 (s, 1H, 2-H); $^{13}C$ NMR (50 MHz, $CDCl_3$): $\delta$ = 23.31 ($ArCH_3$), 30.19, 30.41 [$C(CH_3)_3$], 35.17, 35.44 [$C(CH_3)_3$], 60.55, 60.70, 61.36 ($OCH_3$), 116.3, 118.0, 123.9, 124.7, 128.4, 130.8, 143.4, 144.3, 144.4, 144.8, 149.8, 159.0 (Ar-C), 161.1 (C=O); MS: *m/z* (%) = 412 (100) [$M^+$], 397 (55) [$M^+$ - $CH_3$], 355 (47) [$M^+$ - $C_4H_9$], 340 (23) [355 - $CH_3$]; Anal. calcd. for $C_{25}H_{32}O_5 \cdot 1/2C_6H_{14}$ (455.6): C, 73.81; H, 8.63. Found: C, 73.48; H, 8.34.

***rac*-4,4'-Di-*tert*-butyl-2-hydroxy-6'-hydroxymethyl-3,2',3'-trimethoxy-6-methylbiphenyl (16).** To a cooled (0 °C) solution of **14** (300 mg, 728 µmol) in dry THF (10 ml), $LiAlH_4$ (30.0 mg, 790 µmol) was added under $N_2$. After 2 h of stirring at room temperature, water (2 ml) and 2N HCl (3 ml) were added, the solvent was removed and the aqueous layer was extracted with diethyl ether. The extract was dried ($Na_2SO_4$) and the solvent was evaporated. From petroleum ether, **16** was obtained as colorless crystals (288 mg, 95%): mp 171 °C; IR (KBr): $\tilde{\nu}$ 3490, 3420, 2980, 2930, 2845, 1290, 1220; $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ = 1.42 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 1.92 (s, 3H, $ArCH_3$), 3.54 (s, 3H, 2'-$OCH_3$) 3.83 (s, 3H, $OCH_3$), 3.90 (s, 3H, $OCH_3$), 4.27 (br. s, 2H, $CH_2OH$) 6.80 (s, 1H, 5- or 5'-H), 7.22 (s, 1H, 5- or 5'-H); $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 19.97 ($ArCH_3$), 30.47, 30.82 [$C(CH_3)_3$], 34.94, 35.16 [$C(CH_3)_3$], 60.04, 60.20, 60.72 ($OCH_3$), 64.03 ($CH_2OH$), 120.0, 122.3, 122.8, 127.8, 131.9, 133.8, 142.1, 143.7, 145.1, 146.5, 151.7, 152.8 (Ar-C); MS: *m/z* (%) = 416 (2) [$M^+$], 398 (100) [$M^+$ - $H_2O$ ], 383 (21) [398 - $CH_3$], 327 (20) [383 - $C_4H_8$]; Anal. calcd. for $C_{25}H_{36}O_5$ (416.7): C, 72.08; H, 8.71. Found: C, 71.84; H, 8.42.

**General procedure for analytical ring opening reactions of 14 with *R*- or *S*-15.** To a cooled (0 °C) solution of **15** (20.2 mg, 73.0 µmol) in dry THF (1 ml), 1M $BH_3$·THF solution (100 µl, 100 µmol) was added under $N_2$. Then **14** (10.0 mg, 24.3 µmol), dissolved in dry THF (1 ml), was added dropwise to the reaction mixture which was then stirred for 24 h. If necessary, more $BH_3$·THF solution (50.0 µl, 50.0 µmol) was added, followed by 24 h stirring. Then 2N HCl (2 ml) was added, the solvent was removed *in vacuo* and the aqueous layer was extracted with diethyl ether. The extract was purified by TLC (petroleum ether / diethyl ether 3:4) and analyzed by HPLC.

**Enantioselective ring opening of 14 on a larger scale.** In analogy to the general procedure, *R*-**15** (101 mg, 365 µmol) was dissolved in dry THF (5 ml) and cooled (0 °C). Then a 1M $BH_3$·THF solution (500 µl, 500 µmol) was added and a solution of **14** (50.0 mg, 121 µmol) in dry THF (7 ml) was dropped slowly to the mixture. After 48 h stirring 2N HCl (4 ml) was added, the organic solvent was removed and the aqueous layer was extracted with diethyl ether. Purification of the extract by column chromatography on silica gel with petroleum ether / diethyl ether (1:1) as eluent gave *M*-**16** (34.5 mg, 68%) as an amorphous solid of $[\alpha]_D^{23}$ = -21.8 (*c* = 0.8 in $CHCl_3$). HPLC analysis gave 92:8 e.r.

***rac*-4,4'-Di-*tert*-butyl-6'-hydroxymethyl-2,2',3,3'-tetramethoxy-6-methylbiphenyl (18).** To a solution of **16** (288 mg, 692 µmol) in acetone (10 ml), under $N_2$, $K_2CO_3$ (191 mg, 1.38 mmol) and $Me_2SO_4$ (100 µl, 1.06 mmol) were added. After 3 d of stirring at room temperature conc. aqueous $NH_3$ (2 ml) was added and the solvent was removed under reduced pressure. The aqueous layer was made acidic with 2N HCl and then extracted with diethyl ether. After drying ($Na_2SO_4$) the organic layer and removing the solvent, **18** (270 mg, 93%) was yielded as a colorless solid: mp 150-151 °C (petroleum ether); IR (KBr): $\tilde{\nu}$ 3475, 3410,

2970, 2930, 2840, 1280, 1220; $^1$H NMR (200 MHz, $CDCl_3$): δ = 1.41 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 1.94 (s, 3H, $ArCH_3$), 3.63 (s, 3H, 2- or 2'-$OCH_3$), 3.66 (s, 3H, 2- or 2'-$OCH_3$) 3.85 (s, 6H, 3- and 3'-$OCH_3$), 4.15 (br. s, 2H, $CH_2OH$) 6.95 (s, 1H, 5- or 5'-H), 7.19 (s, 1H, 5- or 5'-H); $^{13}$C NMR (63 MHz, $CDCl_3$): δ = 19.97 ($ArCH_3$), 30.49, 30.65 [$C(CH_3)_3$], 34.98, 35.14 [$C(CH_3)_3$], 59.67, 59.76, 60.00, 60.05 ($OCH_3$), 64.34 ($CH_2OH$), 122.7, 123.3, 128.6, 131.5, 133.8, 142.7, 143.2, 150.4, 150.6, 151.2, 152.2 (Ar-C); MS: *m/z* (%) = 430 (100) [$M^+$], 412 (36) [$M^+$ - $H_2O$], 397 (21) [412 - $CH_3$], 383 (14) [397 - $CH_3$], 341 (39) [397 - $C_4H_8$]; Anal. calcd. for $C_{26}H_{38}O_5$ (430.6): C, 72.53; H, 8.90. Found: C, 72.59; H, 9.19.

***rac*-4,4'-Di-*tert*-butyl-2,2',3,3'-tetramethoxy-6,6'-dimethylbiphenyl (19).** To a solution of **18** (160 mg, 372 μmol) in dry $CH_2Cl_2$ (10 ml), $C_2Br_2Cl_4$ (131 mg, 403 μmol) and $PPh_3$ (106 mg, 404 μmol) were added together. After 2 h stirring at room temperature, the mixture was filtered through silica gel with petroleum ether / diethyl ether (5:1) as the eluent and the solvent was removed. To a solution of the residue in dry diethyl ether (5 ml), $LiAlH_4$ (30.0 mg, 790 μmol) was added and the reaction mixture was stirred for 2 d at room temperature. After addition of water (2 ml) and 2N HCl (3 ml), the mixture was extracted with diethyl ether, the extract was dried ($Na_2SO_4$) and the solvent was removed. The obtained solid was purified by column chromatography on silica gel (petroleum ether / diethylether 5:1). Subsequent recrystallization from petroleum ether afford **19** (128 mg, 83%): mp 160-162 °C; IR (KBr): $\tilde{\nu}$ 2930, 2850, 1290, 1220; $^1$H NMR (250 MHz, $CDCl_3$): δ = 1.41 [s, 18H, $C(CH_3)_3$], 1.93 (s, 6H, $ArCH_3$), 3.63 (s, 6H, 2- and 2'-$OCH_3$), 3.84 (s, 6H, 3- and 3'-$OCH_3$), 6.91 (s, 2H, Ar-H); $^{13}$C NMR (63 MHz, $CDCl_3$): δ = 19.73 ($ArCH_3$), 30.66 [$C(CH_3)_3$], 34.89 [$C(CH_3)_3$], 59.55, 59.80 ($OCH_3$), 122.7, 129.9, 130.7, 141.9, 150.4, 151.0 (Ar-C); MS: *m/z* (%) = 414 (100) [$M^+$], 343 (48) [$M^+$ - $CH_3$ - $C_4H_8$]; Anal. calcd. for $C_{26}H_{38}O_4$ (414.3): C, 75.38; H, 9.17. Found: C, 75.22; H, 9.03.

***rac*-4,4'-Di-*tert*-butyl-2,2',3,3'-tetrahydroxy-6,6'-dimethylbiphenyl (4).** To a cooled (0 °C) solution of **19** (50.0 mg, 121 μmol) in dry $CH_2Cl_2$, a 1M $BBr_3$ solution in $CH_2Cl_2$ (480 μl, 480 μmol) was added under $N_2$. After 2 h of stirring at room temperature, the reaction mixture was quenched with MeOH (2 ml) and the solvent was removed under reduced pressure. Purification of the residue by column chromatography on silica gel with $CH_2Cl_2$ / MeOH (100:1) as the eluent and recrystallization from *n*-hexane gave **4** (41.0 mg, 95%) as colorless fine needles, identical with material obtained above.

**Ring opening of 14 with lithium 1*S*-mentholate.** To a cooled (0 °C) solution of **14** (278 mg, 675 μmol) in dry toluene (10 ml), 0.1M lithium 1*S*-mentholate solution in toluene (14.0 ml, 1.40 mmol) (prepared from 1*S*-menthol with 0.8 eq. of *n*-BuLi) was dropped within 30 min under $N_2$. After additional stirring for 4 h, glacial acetic acid (0.5 ml) was added, the solvent was removed under reduced pressure and a little sample was taken for HPLC analysis. Purification of the residue by column chromatography on silica gel (petroleum ether / diethyl ether 5:1) and recrystallization from petroleum ether gave the chromatographically more rapid **17b** (240 mg, 63%) as colorless needles. Chromatographically less rapid fractions gave a mixture of **17a** and menthol. From this, the excessive menthol was removed *in vacuo* and the residue was crystallized from petroleum ether to yield **17a** (49.0 mg, 13%): *(M,1''S,2''R,5''S)*-menthyl 4,4'-di-*tert*-butyl-2'-hydroxy-2,3,3'-trimethoxy-6'-methyl-1,1'-biphenyl-6-carboxylate (**17a**): mp 137-138 °C; $[\alpha]_D^{23}$ = +35.54 (*c* = 1.1 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{195}$ +6.6, $\Delta\varepsilon_{206}$ -7.47, $\Delta\varepsilon_{221}$ -5.68; IR (KBr): $\tilde{\nu}$ 3430, 2930, 2900, 2840, 1670;

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.65-1.88 (m, 18H, menthyl-H), 1.43 [s, 9H, $C(CH_3)_3$], 1.44 [s, 9H, $C(CH_3)_3$], 1.95 (s, 3H, 6'-$CH_3$), 3.53 (s, 3H, $OCH_3$), 3.82 (s, 3H, $OCH_3$), 3.93 (s, 3H, $OCH_3$), 4.57-4.70 (m, 1H, 1''-H), 4.92 (s, 1H, OH), 6.75 (s, 1H, 5'-H), 7.83 (s, 1H, 5-H). $^{13}$C NMR (63 MHz, $CDCl_3$): δ = 15.79, 20.03, 20.92, 22.01, 22.71, 25.62 (menthyl-C and $CH_3$-6'), 30.26, 31.04 [$C(CH_3)_3$], 31.26, 34.10, 34.87, 35.23, 39.91, 46.62 [menthyl-C and $C(CH_3)_3$], 60.01, 60.22, 60.66 ($OCH_3$), 74.24 (C-1''), 119.2, 123.5, 124.9, 126.1, 130.0, 131.4, 141.1, 143.3, 144.5, 146.2, 151.6, 156.5 (Ar-C), 167.0 (C=O); MS: *m/z* (%) = 568 (16) [$M^+$], 430 (32) [$M^+$ - $C_{10}H_{18}$], 412 (100) [$M^+$ - $C_{10}H_{20}O$], 397 (32) [412 - $CH_3$], 355 (15) [412 - $C_4H_9$]; Anal. calcd. for $C_{35}H_{52}O_6$ (568.8): C, 73.91; H, 9.21. Found: C, 73.59; H, 9.28.

*(P,1''S,2''R,5''S)*-Menthyl 4,4'-di-*tert*-butyl-2'-hydroxy-2,3,3'-trimethoxy-6'-methyl-1,1'-biphenyl-6-carboxylate (**17b**): mp 192 °C; $[\alpha]_D^{23}$ = +23.6 (*c* = 1.1 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{197}$ -12.1, $\Delta\varepsilon_{208}$ +15.9, $\Delta\varepsilon_{225}$ -12.3; IR (KBr): $\tilde{\nu}$ 3360, 2970, 2930, 2840, 1660; $^1$H NMR (250 MHz, $CDCl_3$): δ = 0.63-1.75 (m, 18H, menthyl-H), 1.42 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 1.88 (s, 3H, 6'-$CH_3$), 3.58 (s, 3H, $OCH_3$), 3.85 (s, 3H, $OCH_3$), 3.93 (s, 3H, $OCH_3$), 4.58-4.68 (m, 1H, 1''-H), 5.05 (s, 1H, OH), 6.73 (s, 1H, 5'-H), 7.72 (s, 1H, 5-H); $^{13}$C NMR (63 MHz, $CDCl_3$): δ = 15.96, 19.97, 20.76, 22.06, 22.92, 25.79 (menthyl-C and $CH_3$-6'), 30.26, 30.99 [$C(CH_3)_3$], 31.20, 34.17, 34.85, 35.22, 39.75, 46.59 [menthyl-C and $C(CH_3)_3$], 59.97, 60.18, 60.71 ($OCH_3$), 74.45 (C-1''), 119.5, 123.6, 124.3, 126.9, 129.6, 131.0, 141.4, 143.4, 144.8, 146.6, 151.5, 156.2 (Ar-C), 167.4 (C=O); MS: *m/z* (%) = 568 (18) [$M^+$], 430 (33) [$M^+$ - $C_{10}H_{18}$], 412 (100) [$M^+$ - $C_{10}H_{20}O$], 397 (31) [412 - $CH_3$], 355 (17) [412 - $C_4H_9$]; Anal. calcd. for $C_{35}H_{52}O_6$ (568.8): C, 73.91; H, 9.21. Found: C, 73.82; H, 9.49.

Analogous reaction with 1*R*-menthol gave the enantiomeric esters *ent*-**17a** (chromatographically less rapid) (9.8%) and *ent*-**17b** (more rapid) (65%): *(P,1''R,2''S,5''R)*-menthyl 4,4'-di-*tert*-butyl-2'-hydroxy-2,3,3'-trimethoxy-6'-methyl-1,1'-biphenyl-6-carboxylate (*ent*-**17a**): mp 138-139 °C; $[\alpha]_D^{23}$ = -35.38 (*c* = 0.8 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{198}$ -15.5, $\Delta\varepsilon_{207}$ +6.56, $\Delta\varepsilon_{214}$ +3.90, $\Delta\varepsilon_{254}$ -4.94; *(M,1''R,2''S,5''R)*-menthyl 4,4'-di-*tert*-butyl-2'-hydroxy-2,3,3'-trimethoxy-6'-methyl-1,1'-biphenyl-6-carboxylate (*ent*-**17b**): mp 191-193 °C; $[\alpha]_D^{23}$ = -26.7 (*c* = 1.1 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{196}$ +7.46, $\Delta\varepsilon_{209}$ -8.72.

**(*P*)-4,4'-Di-*tert*-butyl-2-hydroxy-6'-hydroxymethyl-3,2',3'-trimethoxy-6-methylbiphenyl (*P*-16).** To a cooled (0 °C) solution of **17b** (300 mg, 528 μmol) in dry THF (10 ml) $LiAlH_4$ (40.0 mg, 1.05 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C and for 2 h at room temperature. After addition of water (2 ml) and 2N HCl (3 ml), the organic solvent was removed and the aqueous layer was extracted with diethyl ether. The extract was dried ($Na_2SO_4$) and the solvent was evaporated. From the residue menthol was removed by distillation *in vacuo* to get pure *P*-**16** (215 mg, 98%) as an oil: $[\alpha]_D^{23}$ = +25.0 (*c* = 1.0 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{198}$ -21.7, $\Delta\varepsilon_{220}$ +13.1.

Following the above reaction sequence (**16**→**4**) beginning from *P*-**16**, *P*-**18** (97%), *P*-**19** (79%) and *P*-**4** (95%) were obtained: *P*-**18**: mp 163-164 °C; $[\alpha]_D^{23}$ = +46.9 (*c* = 0.8 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{198}$ -9.62, $\Delta\varepsilon_{221}$ +10.1. *P*-**19**: mp 163-164 °C; $[\alpha]_D^{23}$ = +21.9 (*c* = 1.0 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{196}$ -16.5, $\Delta\varepsilon_{209}$ -4.89, $\Delta\varepsilon_{223}$ +19.65, $\Delta\varepsilon_{232}$ -8.34, $\Delta\varepsilon_{242}$ -6.33. *P*-**4**: mp 242-243 °C; $[\alpha]_D^{23}$ = -33.3 (*c* = 0.6 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{203}$ -21.10, $\Delta\varepsilon_{221}$ +4.70, $\Delta\varepsilon_{248}$ +1.86.

In analogy to the above reaction sequence (**17b**→*P*-**4**), but beginning from *ent*-**17b**, *M*-**16** (98%), *M*-**18** (77%), *M*-**19** (77%) and *M*-**4** (95%) were yielded: *M*-**16**: obtained as an oil; $[\alpha]_D^{23}$ = -22.8 (*c* = 0.9 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{198}$ +16.3, $\Delta\varepsilon_{219}$ -10.7. *M*-**18**: mp 163 °C; $[\alpha]_D^{23}$ = -44.9 (*c* = 0.8 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{195}$ -16.9, $\Delta\varepsilon_{221}$ +15.3. *M*-**19**: mp 162-163 °C; $[\alpha]_D^{23}$ = -23.2 (*c* = 0.8 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{194}$ +18.52, $\Delta\varepsilon_{204}$ -1.06, $\Delta\varepsilon_{220}$ -10.50. *M*-**4**: mp 242-244 °C; $[\alpha]_D^{23}$ = +35.5 (*c* = 0.9 in $CHCl_3$); CD (EtOH): $\Delta\varepsilon_{200}$ +24.83, $\Delta\varepsilon_{214}$ -13.93.

**Recycling of 17a to 14.** A solution of **17a** (60.0 mg, 105 µmol) in a mixture of dioxan (5 ml) and 2N NaOH (2 ml) was heated for 8 h (50 °C) under $N_2$. Then the reaction mixture was made acidic with 2N HCl and extracted with diethyl ether. After drying ($NaSO_4$) the organic extract and evaporation of the solvent, the residue was heated (150 °C) under reduced pressure for 6 h. The remaining solid was dissolved in petroleum ether / diethyl ether (5:1) and filtered through silica gel. After removing the solvent under reduced pressure **14** (33.7 mg, 78%) was yielded as a spectroscopically pure solid.

## COMPUTATIONAL

Conformational analyses were performed on Silicon Graphics IRIS 4D, INDIGO (R4000) and Intel P6 (LinuX) workstations using the semiempirical AM1[22] method as implemented in VAMP 5.5/6.0.[23] The rotational strengths were calculated on LinuX workstations with the BDZDO/MCDSPD[24] program package. For CI calculations a basis of 16 x 16 = 256 singly excited configurations plus the ground state were used.

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