Syntheses of Chlorinated Bisbibenzyls from Bryophytes

Andreas Speicher,* Jürgen Kolz, Rufino Paulino Sambanje

Institut für Organische Chemie, Universität des Saarlandes, PO Box 151150, 66041 Saarbrücken, Germany
Fax +49(681)3022029; E-mail: anspeich@mx.uni-saarland.de

Received 3 June 2002; revised 21 August 2002

Dedicated to Prof. Dr. Dr. h. c. Theophil Eicher on the occasion of his 70th birthday.

Abstract: Chlorinated bisbibenzyls of the isoplagiochin type detected in different bryophyte species were synthesized by an efficient and flexible unit construction system making extensive use of Suzuki and Wittig protocols.

Key words: natural products, total synthesis, cross-coupling, cyclizations, Wittig reactions

An increasing number of halogenated natural products with a broad structural diversity have been detected over the past number of years in marine organisms, bacteria, and fungi. These have been shown to have therapeutic effects.[1–4] Halogenated compounds from higher plants are less numerous although detected in nearly all plant divisions.[5] In contrast, halogen containing compounds are found rarely in bryophytes (mosses) and in fact their presence in this class of compound was not verified until recently.

So, in 1988 15-Methoxyansamitocin P-3 (**1**) was detected in *Isothecium subdiversiforme* and *Thamnobryum sandei* (<50 μg was isolated from 20 kg crude mass)[6] while in 1989 a chlorinated diterpene **2** of the drimane type was found in *Makinoa crispata*,[7] but both compounds were not verified for the corresponding bryophytes because compounds like **1** are typical for microorgansims (*Nocardia sp.*) and chlorohydrins (see in **2**) are mostly artefacts of the isolation procedure.

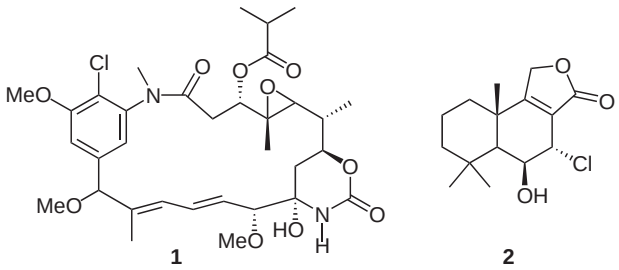


Figure 1

However, in 1997 a monochlorinated bisbibenzyl **3** was found in a *Plagiochila sp.*[8] and similar metabolites named bazzanin A–R (**4**–**21**) bearing 1–8 chlorine substituents were isolated from the liverworts *Bazzania trilobata* and *Lepidozia incurvata* in substantial amounts.[9] These compounds are derived from isoplagiochin C (**25**) or isoplagiochin D (**26**), two known bryophyte constituents[10] which can be decomposed to lunularin (**27**).[11] More recently, three additional but similar compounds **22**–**24** beside **3** were found in *Herbertus sakuraii* and *Mastigophora diclados* (Figure 2).[12]

In preceding papers we reported MALDI-TOF mass spectrometry investigations on crude plant extracts and demonstrated that these chlorinated compounds are not artefacts of an incidental occurrence or of the sample preparation, but should be genuine and produced by the liverwort or an endosymbiotic metabolism.[13,14]

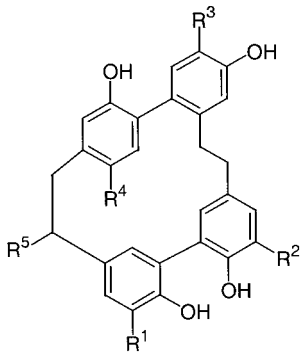
We attempted the total synthesis of these chlorinated bisbibenzyls because of the biological activities of **27** and of some of its derivatives,[15] the effect halogenation had on increasing the activity[5] and also due to their interesting three dimensional structures.

On the basis of our synthetic studies concerning cyclic bisbibenzyls[16] and halogenated lunularins[17] we elaborated a flexible unit construction system where the bisbibenzyl backbone is constructed from polyfunctional aromatic building blocks A–D which were prepared from readily available starting materials **28**–**31** by regioselective chlorination, bromination, iodination, triflation and boronic acid formation as well as protecting procedures (Scheme 1). The biaryl moieties were constructed by regioselective Suzuki protocols[18] and coupled to acyclic bibenzyl and cyclic bisbibenzyls by Wittig and McMurry procedures followed by hydrogenation and deprotection.

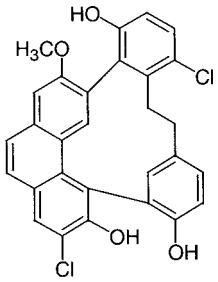
Suitable functionalized aromatic building blocks were obtained as outlined in Scheme 2. Chlorine free building blocks **32**,**33** and **35a** were prepared as previously reported[16] or alternatively (**35b**) from 3-hydroxybenzoic acid (**34**). Mono chlorinated building blocks 'A' (**37**, **38**) were obtained from isovanilline (**30**) by acetylation and chlorination giving **36**, followed by saponification, acetalization and triflate formation yielding **37**. An alternate procedure was starting from 4-hydroxy benzaldehyde (**31a**): chlorination, bromination, methylation and acetalization yielded **38**, from which building block 'B' **39** could be obtained by selective formation of the boronic acid. A mono chlorinated compound 'C' **41** was synthesized from commercially available 2-chloro-3-methylphenol (**40**) by bromination, methylation and selective formation of the boronic acid (Scheme 2).

Synthesis 2002, No. 17, Print: 02 12 2002.
Art Id.1437-210X,E;2002,0,17,2503,2512,ftx,en;T06302SS.pdf.

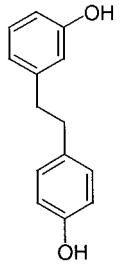
ISSN 0039-7881



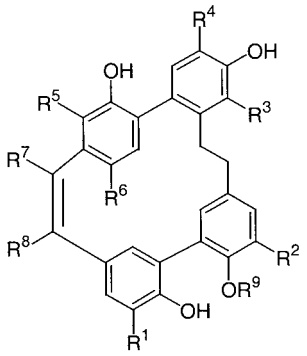
comp.		R^1	R^2	R^3	R^4	R^5
3		H	H	Cl	H	H
13	bazzanin J	Cl	H	Cl	H	H
23		H	Cl	Cl	H	H
24		H	H	Cl	H	Cl
26	isoplagiochin D	H	H	H	H	H



14: bazzanin K



27

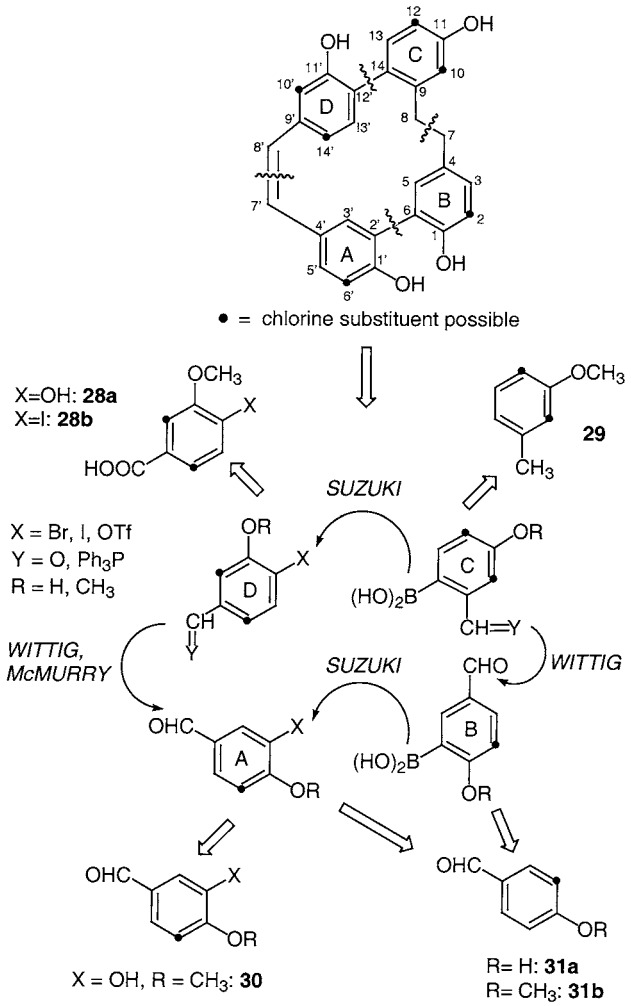


comp.		R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9
4	bazzanin A	Cl	H	H	H	H	H	H	H	H
5	bazzanin B	Cl	H	H	H	H	H	Cl	H	H
6	bazzanin C	Cl	H	H	Cl	H	H	Cl	H	H
7	bazzanin D	Cl	H	H	H	Cl	H	Cl	H	H
8	bazzanin E	Cl	H	H	Cl	Cl	H	Cl	H	H
9	bazzanin F	Cl	H	Cl	H	H	Cl	Cl	H	H
10	bazzanin G	Cl	Cl	Cl	H	Cl	H	Cl	H	H
11	bazzanin H	Cl	H	Cl	H	Cl	Cl	Cl	H	H
12	bazzanin I	Cl	Cl	H	Cl	Cl	Cl	Cl	H	H
15	bazzanin L	H	H	Cl	Cl	Cl	H	H	H	CH_3
16	bazzanin M	H	H	Cl	Cl	Cl	H	H	H	H
17	bazzanin N	H	Cl	Cl	Cl	Cl	H	H	H	H
18	bazzanin O	Cl	H	Cl	Cl	Cl	Cl	H	H	CH_3
19	bazzanin P	Cl	Cl	Cl	Cl	Cl	H	H	H	H
20	bazzanin Q	Cl	Cl	Cl	Cl	Cl	Cl	H	H	H
21	bazzanin R	Cl	Cl	Cl	Cl	Cl	Cl	Cl	Cl	H
22		H	H	H	Cl	H	Cl	H	H	H
25	isoplagiochin C	H	H	H	H	H	H	H	H	H

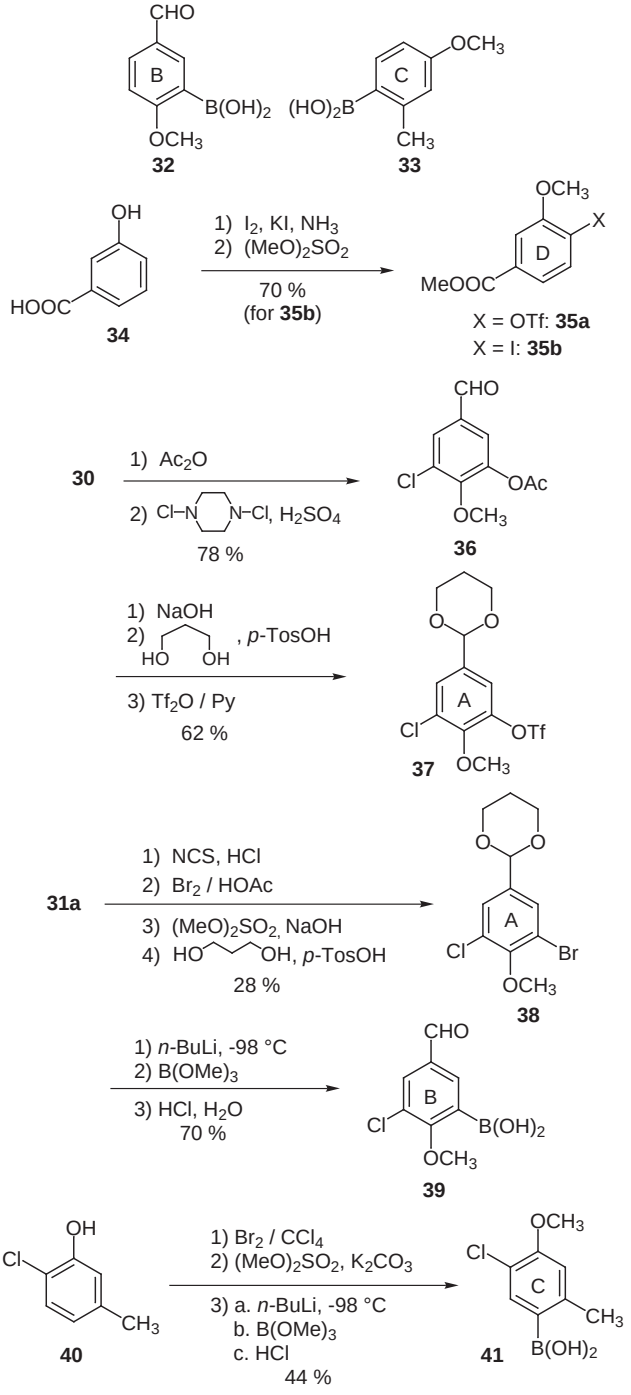
Figure 2 Sources of chlorinated bisbibenzyls: **3**: from *Plagiochila sp.*; **4**–**14**: from *Bazzania trilobata;* **15**–**21**: from *Lepidozia incurvata* **3**,**23**: from *Mastigophora diclados;* **22**–**24**: from *Herbertus sakuraii;* parent substances: isoplagiochin C/D **25**/**26**; lunularin **27**.

Building blocks A/B and C/D (Scheme 3) were prepared using Suzuki protocols as previously reported[17] for **42** and **43** and by regioselective Suzuki-reactions between the boronic acid **32** and the triflate **37** or the bromide **38** yielding a chloro biarylaldehyde **44** ('AB-part'). Also coupling of the iodide **35b** and the boronic acid **41** gave **45**, functionalization of the methyl group yielded a phosphonium salt **46** ('chloro-CD-part').

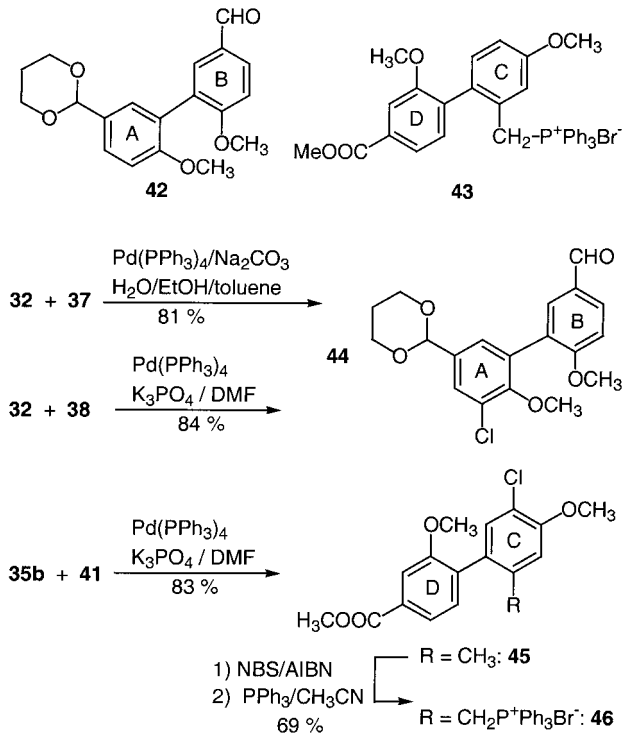
The model syntheses of the chlorinated bisbibenzyls **3**, **4** and **13** were performed as follows (Scheme 4). The biarylaldehydes **42** and **44** ('AB-part') were coupled (Wittig-reaction and hydrogenation) with the phosphonium compounds **43** and **46** ('CD-part') to give the acyclic bibenzyls **47**–**49**. These were further transformed (reduction and hydrolysis) to the hydroxyaldehydes **50**–**52**. The cyclization to the stilbene-like tetramethoxy bisbibenzyls **53**–**55** was achieved by a Wittig protocol via phosphonium salts. The natural products **3** (12-chlorisoplagiochin D) and **13** (bazzanin J) as well as the analogue compound **59** were obtained by hydrogenation of the double bond to give **56**–**58** and subsequent cleavage of the methyl ethers while **4** (bazzanin A) was formed directly from **54**.



Scheme 1 Construction unit system for the synthesis of chlorinated bisbibenzyls.



Scheme 2 Syntheses of functionalized building blocks A–D.



Scheme 3 Syntheses of biaryl parts A/B and C/D.

Further derivatives of the natural compounds, which can be used for biological testing were obtained e.g. by acetylation, **4** was converted to **60**. The cyclization of **51** to form the stilbene bridge could alternatively be performed by a McMurry reaction via the cyclic dialdehyde **61** (Scheme 5).

The crystal structure of **55** is given in Figure 3. The NMR-data of the tetramethylated cyclic compounds like **53**–**58** show the presence of different conformers due to stereogenic axes and planes which is in agreement with the optical rotatory power reported for the isolated natural products. These effects concerning conformational analyses and further NMR experiments are in progress. In addition, the flexible unit construction system is being applied to the synthesis of highly chlorinated bisbibenzyls like bazzanin Q (**20**).

NMR spectra were obtained with a Bruker AM 400 or DRX 500. Chemical shifts (δ) are given in ppm relative to TMS. Mass spectra were recorded on a Finnigan MAT 90 (CI 120 eV, methane; EI 70 eV). Melting points were measured on a Büchi melting point apparatus (Dr. Tottoli). Elemental analyses (C,H,N) were performed with a Leco CHNS-932. FTIR spectra were recorded on a Bio-Rad Excalibur FTS 3000 (data not given in the text). Analytical TLC: Merck aluminium roll 0.2 mm (silica gel 60 HF_{254}); preparative TLC: Macherey-Nagel DC-plates 20 × 20 cm SIL G-200 UV_{254}. Column chromatography (CC): J. T. Baker silica gel 60, 63-200 μm; flash chromatography: Macherey-Nagel silica gel 60, 40–63 μm; Macherey-Nagel Polygoprep 60-50 C18. For catalytic hydrogenations the Parr hydrogenation apparatus was used. Solvents were dried and purified by conventional methods prior to use. All air- or moisture-sensitive reactions were carried out by inert gas techniques under nitrogen or argon.

Methyl 4-iodo-3-methoxybenzoate (35b)[19]

3-Hydroxybenzoic acid (**34**) was iodinated according to Lit.[20] 4-Iodo-3-hydroxybenzoic acid (5.00 g, 18.9 mmol), dimethyl sulfate (8.98 ml, 94.7 mmol) and K_2CO_3 (7.85 g, 56.8 mmol) in acetone (50 mL) were refluxed for 12 h. H_2O (100 mL) was added and the mixture was stirred for 24 h. Acetone was evaporated and the residue extracted with $CHCl_3$ (3 × 50 ml). The organic layers were dried ($MgSO_4$) and evaporated. The product was purified by column chromatography (silica gel, $CHCl_3$) and to give a colorless powder (3.86 g, 70%); mp 44 °C.

^{1}H NMR ($CDCl_3$): δ = 7.84 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.44 (d, *J* = 1.8 Hz, 1 H, Ar-H), 7.36 (dd, J_1 = 8.0 Hz, J_2 = 1.8 Hz, 1 H, Ar-H), 3.93 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3).

^{13}C NMR ($CDCl_3$): δ = 166.5, 158.3, 139.6, 131.7, 123.3, 111.3, 92.7, 56.5, 52.3.

5-Chloro-*O*-acetyl Isovanilline (36)

Isovanilline (**30**) (5.00 g, 32.8 mmol) and Ac_2O (25.0 g, 245 mmol) were refluxed for 1 h. The mixture was cooled, Na_2CO_3 (2 M; 50 mL) was added and the precipitate *O*-acetyl isovanilline was filtered off. An additional portion of *O*-acetyl isovanilline was obtained by extracting the mother liquor with Et_2O (2 × 50 mL), it was then dried ($MgSO_4$) and concentrated to give pure pale yellow crystals (6.29 g, 98%); mp 85 °C. To a soln of *O*-acetyl isovanilline (5.00 g, 25.8 mmol) in H_2SO_4 (80%; 75 mL) below 5 °C was added *N*,*N*'-dichloro piperazine.[21] The mixture was stirred at r.t. for 1 h, poured into ice water and extracted with Et_2O (3 × 50 mL). The organic layers were washed H_2O (20 mL), dil. soln of KI (20 mL), dil. soln of $Na_2S_2O_3$ (20 mL), dil. soln of HOAc (20 mL) and NaOH (2 M; 20 mL), dried and concentrated. The product was purified by column chromatography (silica gel, CH_2Cl_2) to give yellow crystals (4.30 g, 79%); mp 68 °C.

^{1}H NMR ($CDCl_3$): δ = 9.85 (s, 1 H, CHO), 7.71 (d, *J* = 1.8 Hz, 1 H, Ar-H), 7.70 (d, *J* = 1.8 Hz, 1 H, Ar-H), 3.95 (s, 3 H, OCH_3), 2.36 (s, 3 H, CH_3COO).

^{13}C NMR ($CDCl_3$): δ = 189.2 (CHO), 168.7 (CH_3COO), 153.9, 145.5, 132.8, 129.9, 129.7, 123.4, 61.6 (OCH_3), 20.9 (CH_3).

MS (CI): *m*/*z* (%) = 231/229 (35/100; M+1$^+$).

Anal. Calcd for $C_{10}H_9ClO_4$ (228.45): C, 52.53; H, 3.97. Found C, 52.57; H, 3.92.

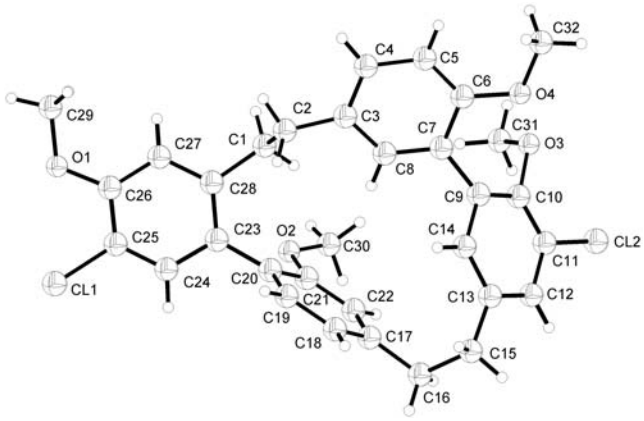
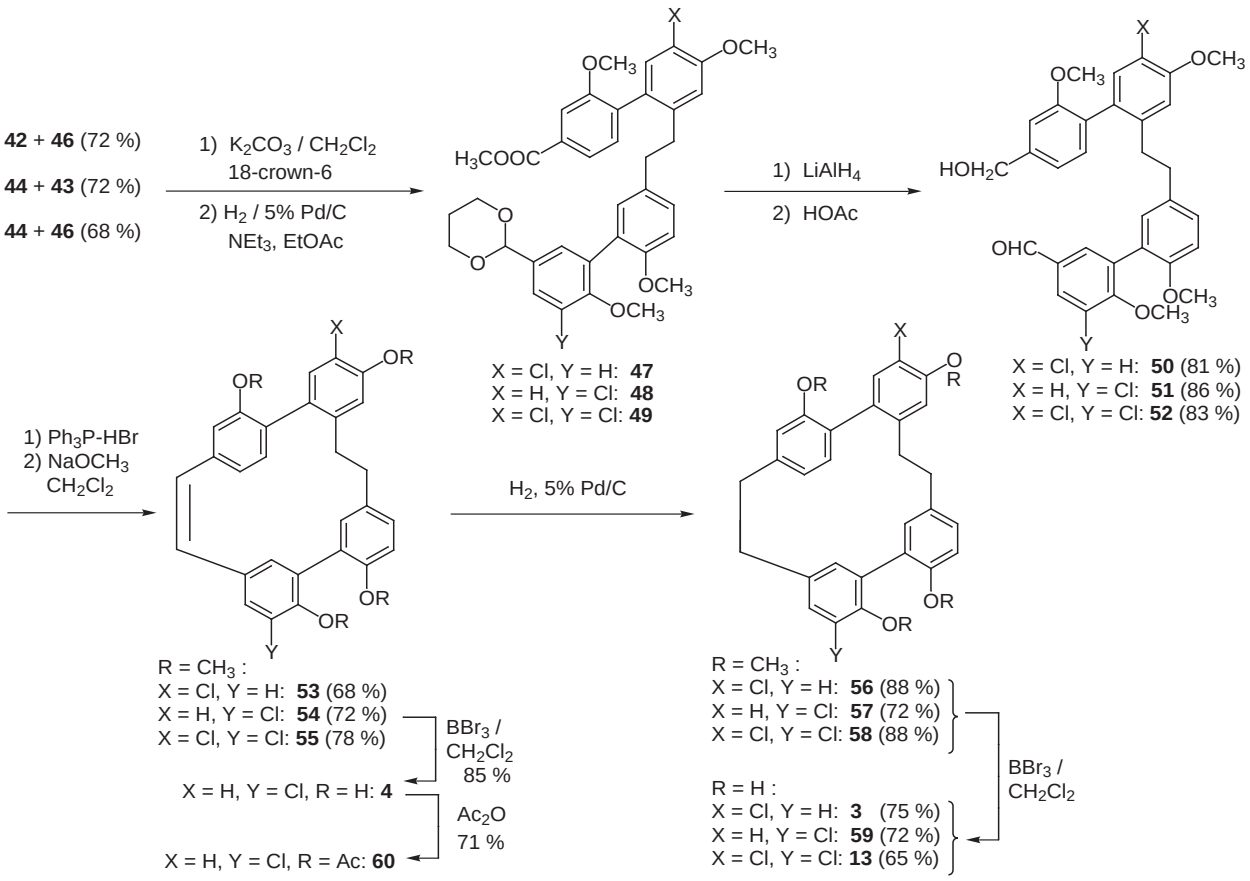


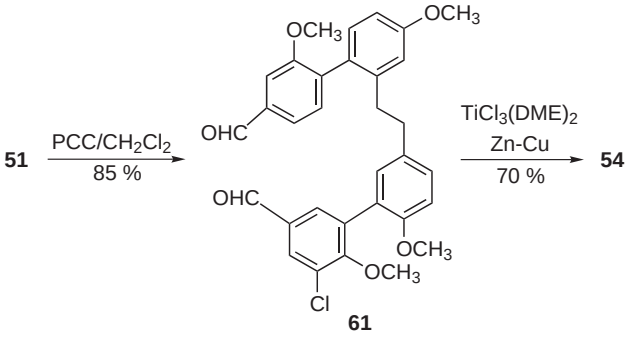
Figure 3 Crystal structure of **55** (ORTEP)

3-Chloro-5-(1,3-dioxan-2-yl)-2-methoxyphenyl Trifluoromethane Sulfonate (37)

Compound **36** (3.00 g, 13.1 mmol) in NaOH (1.25 M, 50 mL) was refluxed for 2 h. The mixture was acidified with concd HCl and 3-chloro-5-hydroxy-4-methoxybenzahldehyde was filtered off, washed and dried in vacuo (P_4O_{10}) to give colorless crystals (2.32 g, 95%); mp 116 °C. The crude aldehyde (1.90 g, 10.2 mmol) in toluene (30 mL) containing 1,3-propanediol (0.82 ml, 0.85 g, 11.3 mmol) and toluene-4-sulfonic acid (50 mg) was refluxed for 24 h (Dean–Stark apparatus), cooled and washed with NaOH (1 M; 20 mL) and sat. NaCl (20 mL), dried ($MgSO_4$) and concentrated to give the intermediate phenolic compound. The product was purified by



Scheme 4 Syntheses of the natural compounds **3**,**4**,**13** and derivatives.



Scheme 5 Cyclization through McMurry protocol to **5**.

column chromatography (silica gel; EtOAc–hexane, 1:1), to give pale yellow crystals (2.39 g, 96%); mp 67 °C.

To this phenolic compound (6.76 g, 27.7 mmol) in CH_2Cl_2 (75 mL) cooled to below 0 °C was added pyridine (4 mL, 3.90 g, 4.98 mmol) followed by trifluoromethane sulfonic acid anhydride (5 ml, 8.30 g, 29.5 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred at 0 °C for 30 min and poured into ice water. The organic layer was separated, washed with sat. $NaHCO_3$ (30 mL), dried ($MgSO_4$) and concentrated. The product was purified by column chromatography (silica gel, CH_2Cl_2) to give a yellow oil (7.10 g, 68%).

^{1}H NMR ($CDCl_3$): δ = 7.15 (d, *J* = 1.8 Hz, 1 H, Ar-H), 7.30 (d, *J* = 1.8 Hz, 1 H, Ar-H), 5.43 (s, 1 H, OCHO), 4.27–4.23 (m, 2 H, OCH_2), 3.98–3.93 (m, 2 H, OCH_2), 3.92 (s, 3 H, OCH_3), 2.23–2.13 (m, 1 H, *H*CH), 1.47–1.42 (m, 1 H, HC*H*).

^{13}C NMR ($CDCl_3$): δ = 148.8, 143.1, 136.1, 130.2, 129.1, 119.0, 117.0 (CF_3), 98.9 (OCHO), 61.6 (OCH_2), 61.1 (OCH_3), 25.7 (HCH).

MS (CI): *m*/*z* (%) = 379/377 (29/100, M + 1$^+$).

2-(3-Bromo-5-chloro-4-methoxyphenyl)-1,3-dioxane (38)
3-Chloro-4-hydroxybenzaldehyde[22]
To 4-hydroxybenzaldehyde (**31a**) (20.0 g, 164 mmol) in $CHCl_3$ (700 mL) at 60 °C was added NCS (21.8 g, 164 mmol) in one portion and the mixture was stirred for 1 h. Concd HCl (3 mL) was added carefully (vigorous reaction) and stirring was continued for 12 h at 60 °C. The solvent was evaporated and the residue recrstallized from H_2O and dried (P_4O_{10}) to give colorless needles (19.5 g, 76%); mp 130 °C.

^{1}H NMR (DMSO-d_6): δ = 9.81 (s, 1 H, CHO), 7.89 (d, *J* = 2.0 Hz, 1 H, Ar-H), 7.74 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 7.16 (d, 1 H, *J* = 8.4 Hz, Ar-H).

^{13}C NMR (DMSO-d_6): δ = 190.2, 158.8, 131.6, 129.9, 129.2, 120.7, 116.8.

3-Bromo-5-chloro-4-hydroxybenzaldehyde[23]
To 3-chloro-4-hydroxybenzaldehyde (10.4 g, 66.4 mmol) in HOAc (100 mL) Br_2 (10.7 g, 66.4 mmol) in HOAc (60 mL) was added dropwise over 30 min at r.t. The soln was heated to 80 °C for 24 h and cooled to r.t. The product was filtered off, washed with ice-water, recrstallized from toluene and washed with petroleum ether to give colorless needles (9.13 g, 60%); mp 154 °C.

^{1}H NMR (DMSO-d_6): δ = 9.80 (s, 1 H, CHO), 8.04 (d, *J* = 1.8 Hz, 1 H, Ar-H), 7.93 (d, *J* = 1.8 Hz, 1 H, Ar-H).

^{13}C NMR (DMSO-d_6): δ = 189.5, 155.2, 133.1, 130.3, 129.8, 122.3, 112.2.

3-Bromo-5-chloro-4-methoxybenzaldehyde
3-Bromo-5-chloro-4-hydroxybenzaldehyde (4.50 g, 19.1 mmol) and NaOH (2 M; 20 mL) were heated to 40 °C for 5 min. The sodium-phenolate was filtered off, dried in vacuo at 40 °C and heated to 100 °C for 10 min together with dimethyl sulfate (10 mL). The mixture was cooled and stirred with H_2O (20 mL) for 15 min. The aqueous layer was separated and the organic layer heated to 100 °C for 15 min with NaOH (2 M; 20 mL). After cooling the product was filtered off and purified through a short pad of silica gel ($CHCl_3$) to give colorless needles (3.81 g, 80%); mp 71 °C

^{1}H NMR ($CDCl_3$): δ = 9.86 (s, 1 H, CHO), 7.98 (d, *J* = 2.0 Hz, 1 H, Ar-H), 7.86 (d, *J* = 2.0 Hz, 1 H, Ar-H), 3.98 (s, 3 H, OCH_3).

^{13}C NMR ($CDCl_3$): δ =& nbsp;188.4, 158.3, 133.8, 133.2, 130.8, 130.4, 119.6, 60.9.

38
3-Bromo-5-chloro-4-methoxy benzaldehyde (2.63 g, 10.5 mmol), 1,3-propanediol (0.88 g, 11.6 mmol) and toluene-4-sulfonic acid (0.10 g) in toluene (50 mL) were heated to reflux for 24 h (Dean–Stark apparatus). The cooled soln was washed with H_2O (2 × 50 mL), sat. NaCl (2 × 50 mL), dried ($MgSO_4$) and concentrated. The oily residue was purified by filtration through a pad of alumina (basic, activity III; cyclohexane–EtOAc, 3: 1), to give yellow crystals (2.50 g, 77%); mp 58 °C.

^{1}H NMR ($CDCl_3$): δ = 7.59 (d, *J* = 2.2 Hz, 1 H, Ar-H), 7.47 (d, *J* = 2.2 Hz, 1 H, Ar-H), 5.40 (s, 1 H, OCHO), 4.26–4.22 (m, 2 H, OCH_2), 3.98–3.92 (m, 2 H, OCH_2), 3.87 (s, 3 H, OCH_3), 2.23–2.14 (m, 1 H, *H*CH), 1.46–1.42 (m, 1 H, HC*H*).

^{13}C NMR ($CDCl_3$): δ = 157.3, 136.7, 129.7, 128.9, 127.5, 118.1, 99.4, 67.3, 60.5, 25.6.

MS (EI): *m*/*z* (%) = 310/305 (7/58, M – 1$^+$).

Anal. Calcd for $C_{11}H_{12}BrClO_3$ (307.57): C, 42.96; H, 3.93. Found C, 43.12; H, 3.88.

(3-Chloro-5-formyl-2-methoxyphenyl)boronic Acid (39)
Compound **38** (1.00 g, 3.26 mmol) in THF– hexane–Et_2O (6:1:1, 80 mL) was cooled to –98 °C and BuLi (1.30 ml, 3.26 mmol, 2.5 M in hexane) was added dropwise. Stirring was continued for 15 min at –98 °C and trimethylborate (1.10 ml, 9.78 mmol) was added in one portion and the mixture was slowly warmed to r.t. over 12 h. H_2O (10 mL) and NaOH (2.5 M; 30 mL) were added and stirring was continued for 1 h. The soln was acidified with concd HCl, the organic solvents were distilled off at reduced pressure and the aqueous layer extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The material thus obtained was added to NaOH (1 M; 100 mL), and the mixture was filtered and acidified with concd HCl (ice-cooling). The product was collected, washed (H_2O) and dried in vacuo ($CaCl_2$) as colorless needles (491 mg, 70%); mp 192 °C.

^{1}H NMR (DMSO-d_6): δ = 9.92 (s, 1 H, CHO), 8.50 [s, 2 H, $B(OH)_2$], 7.94 (d, *J* = 2.0 Hz, 1 H, Ar-H), 7.90 (d, *J* = 2.0 Hz, 1 H, Ar-H), 3.95 (s, 3 H, OCH_3).

^{13}C NMR (DMSO-d_6): δ = 191.0, 162.3, 134.51, 131.7, 131.1, 125.8, 60.3.

MS (EI): *m*/*z* (%) = 216/213 (2/5, M$^+$).

Anal. Calcd for $C_8H_8BClO_4$ (214.41): C, 44.81; H, 3.76. Found C, 44.66; H, 3.78.

(3-Chloro-4-methoxy-6-methylphenyl)boronic acid (41)
4-Bromo-2-chloro-5-methylphenol
To 2-chloro-5-methylphenol (**40**) (20.0 g, 140 mmol) in CCl_4 (200 mL) Br_2 (22.4 g, 140 mmol) in CCl_4 (50 mL) was added dropwise at r.t. The soln was stirred for an additional 24 h, washed with sat.

$NaHSO_3$ (2 × 50 mL), H_2O (3 × 100 ml), dried ($MgSO_4$) and concentrated to give a colorless solid, (27.8 g, 89%); mp 68 °C.

^{1}H NMR ($CDCl_3$): δ = 7.45 (s, 1 H), 6.90 (s, 1 H), 5.43 (s, 1 H), 2.31 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 150.5, 138.4, 131.6, 118.0, 177.8, 114.9, 22.6.

MS (EI): *m*/*z* (%) = 224/219 (8/85%, M^+).

4-Bromo-2-chloro-5-methylanisol

4-Bromo-2-chloro-5-methylphenol (10.0 g, 45.2 mmol), dimethyl sulfate (4.70 ml, 49.7 mmol) and K_2CO_3 (15.6 g, (113 mmol) in acetone (100 mL) were refluxed for 24 h. The mixture was cooled, concentrated and the residue taken up in H_2O (100 mL) and extracted with EtOAc (3 × 75 mL). The combined organic layers were washed with H_2O (2 × 100 mL), NaOH (3.75 M, 2 × 100 mL) and sat. NaCl (2 × 100 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by recrstallization from petroleum ether, or column chromatography (short pad of silica gel, $CHCl_3$) to give colorless needles (8.10 g, 76%); mp 55 °C.

^{1}H NMR (DMSO-d_6): δ = 7.58 (s, 1 H), 7.17 (s, 1 H), 3.85 (s, 3 H, OCH_3), 2.33 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 153.9, 137.5, 131.9, 119.4, 115.1, 113.9, 56.3, 22.3.

41

4-Bromo-2-chloro-5-methylanisol (3.00 g, 12.8 mmol) in THF–hexane–Et_2O (6:1:1, 80 mL) were cooled to –98 °C and BuLi (5.10 ml, 12.8 mmol, 2.5 M in *n*-hexane) was added dropwise. Stirring was continued for 5 min at –98 °C and trimethylborate (4.26 ml, 38.3 mmol) was added in one portion and the mixture was slowly warmed to r.t. over 12 h. H_2O (10 mL) and NaOH (2.5 M, 30 mL) were added and stirring was continued for 1 h. The soln was acidified with concd HCl, the organic solvents were distilled off at reduced pressure and the aqueous layer extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was taken up in NaOH (1 M; 100 mL), filtered and acidified with concd HCl (ice-cooling). The product was collected, washed (H_2O), dried in vacuo ($CaCl_2$) and was isolated as colorless needles (1.12 g, 65%); mp 235 °C.

^{1}H NMR (DMSO-d_6): δ = 7.89 [s, 2 H, $B(OH)_2$], 7.50 (s, 1 H, H-2), 6.90 (s, 1 H, H-5), 3.84 (s, 3 H, OCH_3), 2.44 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 154.8, 143.2, 135.1, 122.7, 117.3, 114.1, 55.8, 22.0.

MS (EI): *m*/*z* (%) = 202/199 (18/76, M^+).

Anal. calcd for $C_8H_{10}BClO_3$ (200.43): C, 47.94; H, 5.03. Found C, 47.76; H, 4.95.

Biarylaldehyde 44

Procedure 1

A soln of the boronic acid **32 (**2.30 g, 12.8 mmol) in EtOH (20 mL) was added to a stirred mixture of the triflate **37** (4.52 g, 12.0 mmol), $Pd(PPh_3)_4$ (0.42 g, 0.36 mmol), toluene (24 mL) and Na_2CO_3 (2 M; 24 mL) and refluxed for 24 h. The slurry was cooled to r.t., H_2O (100 mL) was added and the mixture extracted with Et_2O (3 × 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (alumina, CH_2Cl_2) to give yellow crystals (3.52 g, 81%); mp 128 °C.

Procedure 2

A soln of the boronic acid **32** (2.00 g, 11.1 mmol), bromide **38** (3.08 g, 10.0 mmol), $Pd(PPh_3)_4$ (0.34 g, 0.30 mmol) and K_3PO_4 (3.54 g, 16.7 mmol) in DMF (200 mL) was heated to 80 °C for 24 h. The slurry was cooled to r.t. and filtered after addition of Et_2O (300 mL). The filtrate was washed with H_2O (3 × 200 mL), dried ($MgSO_4$) and concentrated. The crude product was recrstallized from MeOH to give yellow crystals (3.05 g, 84%); mp 132 °C.

^{1}H NMR ($CDCl_3$): δ = 9.90 (s, 1 H, CHO), 7.91 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1 H), 7.77 (d, *J* = 2.2 Hz, 1 H), 7.56 (d, *J* = 1.8 Hz, 1 H), 7.27 (d, *J* = 2.2 Hz, 1 H), 7.07 (d, *J* = 8.4 Hz, 1 H), 5.47 (s, 1 H, OCHO), 4.27–4.23 (m, 2 H), 4.00–3.93 (m, 2 H), 3.84 (s, 3 H, OCH_3), 3.53 (s, 3 H, OCH_3), 2.24–2.15 (m, 1 H), 1.46–1.42 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 190.7, 161.9, 154.4, 135.2, 133.0, 132.6, 131.7, 129.6, 128.1, 127.8, 127.8, 110.8, 100.3, 67.3, 60.8, 56.0, 25.7.

MS (EI): *m*/*z* (%) = 365/361 (8/88, M^+).

Anal. Calcd for $C_{19}H_{19}ClO_5$ (362.1): C, 62.90; H, 5.28. Found C, 62.68; H, 5.35.

Biaryl Ester 45

A soln of the boronic acid **41** (4.00 g, 20.0 mmol), iodide **35b** (5.25 g, 18.0 mmol), $Pd(PPh_3)_4$ (0.67 g, 0.53 mmol) and K_3PO_4 (5.75 g, 27.1 mmol) in DMF (250 mL) was heated to 80 °C for 12 h. The slurry was cooled to r.t., Et_2O (300 mL) was added and the mixture ws filtered. The filtrate was washed with H_2O (5 × 100 mL), dried ($MgSO_4$) and concentrated. The crude product was filtered through a silica gel pad (cyclohexane–EtOAc, 5:1) to give a yellow oil (4.80 g, 83%).

^{1}H NMR ($CDCl_3$): δ = 7.69 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1 H, Ar-H), 7.62 (d, *J* = 1.6 Hz, 1 H, Ar-H), 7.26 (s, 1 H, Ar-H), 7.18 (d, *J* = 7.6 Hz, 1 H, Ar-H), 6.82 (s, 1 H, Ar-H), 3.94 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 2.10 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 166.9, 156.8, 154.3, 136.5, 134.3, 131.2, 131.1, 130.9, 130.8, 122.0, 119.4, 113.7, 111.6, 56.2, 55.7, 52.2, 19.9.

MS (EI): *m*/*z* (%) = 323/320 (8/100%, M^+).

Anal. Calcd for $C_{17}H_{17}ClO_4$ (320.77): C, 63.65; H, 5.34. Found C, 63.51; H, 5.28.

Phosphonium Salt 46

The methylarene **45** (3.00 g, 9.36 mmol), NBS (1.65 g, 9.36 mmol) and a trace of AIBN in CCl_4 (75 mL) were refluxed for 6 h. The mixture was cooled, filtered and concentrated. The residue was taken up in Et_2O (100 mL), washed with sat. $NaHCO_3$ (50 mL) and H_2O (50 mL), dried and concentrated. The crude benzylbromide was refluxed in MeCN (60 mL) together with PPh_3 (2.46 g, 9.36 mmol) for 12 h. The solvent was evaporated and the residue filtered through a silica gel pad ($CHCl_3$ followed by EtOH to elute the product) to give a pale yellow solid (4.27 g, 69%).

^{1}H NMR ($CDCl_3$): δ = 7.76–7.64 (m, 3 H, Ar-H), 7.57–7.39 (m, 15 H, Ar-H), 7.31 (d, *J* = 2.2 Hz, 1 H, Ar-H), 6.54 (d, *J* = 8.0 Hz, 1 H, Ar-H), 5.59 (t, $J_{31P\text{-}1H}$ = 14.3 Hz, 1 H, C*H*HP), 4.83 (t, $J_{31P\text{-}1H}$ = 14.3 Hz, 1 H, CH*H*P), 3.97 (s, 3 H, $COOCH_3$), 3.71 (s, 3 H, OCH_3), 3.60 (s, 3 H, OCH_3).

^{13}C NMR ($CDCl_3$): δ = 166.5 (C=O), 156.1, 154.6, 134.9, 134.8, 134.5, 134.4, 132.4, 132.2, 132.1, 131.3, 131.52, 131.1, 131.0, 130.1, 130.0, 128.6, 128.5, 126.3, 126.2, 122.4, 122.2, 117.9, 117.1, 112.1, 58.3, 57.1, 56.0 (OCH_3), 29.0, 28.5 (CH_2P).

MS (EI): *m*/*z* (%) = 662 (<1, M^+).

Anal. Calcd for $C_{35}H_{31}BrClO_4P$ (661.95): C, 63.51; H, 4.72. Found C, 63.68; H, 5.85.

Bibenzyls 47–49; Wittig-reactions and Hydrogenation

A soln of the aldehyde **42** or **44** (5.00 mmol) and the phosphonium bromide **43** or **46** (5.00 mmol) in CH_2Cl_2 (75 mL) was refluxed for 24 h together with K_2CO_3 (dried, 10.0 mmol) and a trace of 18-

crown-6. The mixture was filtered off, the solid washed with CH_2Cl_2 (25 mL) and the filtrate washed with H_2O (2 × 25 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatograpy (short pad of alumina, CH_2Cl_2) to give colorless crystals; *E/Z* mixture of isomers.

The stilbene (4.00 mmol) in EtOAc (200 mL) was hydrogenated (3.5 bar, 24 h) in the presence of 5% Pd/C (0.50 g) and Et_3N (5 mL). The mixture was filtered and evaporated. The crude product was purified by column chromatography (alumina, CH_2Cl_2) to give colorless crystals.

Bibenzyl 47
Yield: 86%; mp 75 °C.

^{1}H NMR ($CDCl_3$): δ = 7.67 (dd, J_1 = 7.7 Hz, J_2 = 1.6 Hz, 1 H, Ar-H), 7.61 (d, J = 1.6 Hz, 1 H, Ar-H), 7.43 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 7.23 (d, J = 2.2 Hz, 1 H, Ar-H), 7.14 (s, 1 H, Ar-H), 7.14 (d, J = 7.8 Hz, 1 H, Ar-H), 6.92 (d, J = 8.7 Hz, 1 H, Ar-H), 6.87 (d, J = 2.2 Hz, 1 H, Ar-H), 6.79 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.75 (d, J = 8.4 Hz, 1 H, Ar-H), 6.73 (s, 1 H, Ar-H), 5.48 (s, 1 H, OCHO), 4.26–4.22 (m, 2 H), 4.00–3.97 (m, 2 H), 3.94 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3)

3.68 (s, 3 H, OCH_3), 2.64 (br s, 4 H, CH_2CH_2), 2.23–2.17 (m, 1 H), 1.44–1.41 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 166.9, 157.4, 156.7, 155.5, 154.1, 140.1, 134.1, 132.9, 131.4, 131.4, 131.3, 131.1, 130.9, 130.8, 130.7, 130.5, 130.4, 129.1, 128.3, 127.8, 126.2, 121.9, 119.4, 112.9, 111.4, 111.0, 110.7, 101.6, 67.3, 56.1, 55.8, 55.7, 52.2, 36.1, 35.6, 25.8.

MS (EI): *m*/*z* = 635/632 (11/84, M^+).

Anal. Calcd for $C_{36}H_{37}ClO_8$ (633.13): C, 68.29; H, 5.89. Found C, 68.48; H, 5.95.

Bibenzyl 48
Yield: 76%; mp 117 °C.

^{1}H NMR ($CDCl_3$): δ = 7.68 (d, J = 1.3 Hz, 1 H, Ar-H), 7.61 (d, J = 1.8 Hz, 1 H, Ar-H), 7.51 (d, J = 2.2 Hz, 1 H, Ar-H), 7.22–7.12 (not resolved, 2 H, Ar-H), 7.06 (d, J = 9.0 Hz, 1 H, Ar-H), 6.85 (d, J = 9.0 Hz, 1 H, Ar-H), 6.83 (d, J = 2.2 Hz, 1 H, Ar-H), 6.80–6.76 (m, 3 H, Ar-H), 5.46 (s, 1 H, OCHO), 4.26–4.22 (m, 2 H, OCH_2), 4.00–3.97 (m, 2 H, OCH_2), 3.93 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.44 (s, 3 H, OCH_3), 2.66 (br s, 4 H, 2 × CH_2), 2.18 (m, 1 H, HC*H*, dioxane)1.40–1.37 (m, 1 H, *H*CH, dioxane).

^{13}C NMR ($CDCl_3$): δ = 167.0 (CH_3COO), 159.5 (2 signals), 157.0, 155.1, 154.3, 141.5, 135.5, 134.8, 134.0, 133.6, 132.0, 131.1, 131.0, 129.9, 128.7, 128.1, 128.0, 127.2, 123.0, 114.6, 112.0, 111.5, 111.3, 110.9, 100.6 (OCO), 67.4 (2 × OCH_2), 60.6 (OCH_3), 55.8 (OCH_3), 55.7 (OCH_3), 55.2 (OCH_3), 52.2 ($COOCH_3$), 36.0, 35.9, 26.0.

MS (CI): *m*/*z* (%) = 635/632 (8/75, M^+).

Anal. Calcd for $C_{36}H_{37}ClO_8$ (633.13): C, 68.29; H, 5.89. Found C, 68.10; H, 5.83.

Bibenzyl 49
Yield: 86%; mp 105 °C.

^{1}H NMR ($CDCl_3$): δ = 7.67 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1 H), 7.62 (d, J = 1.5 Hz, 1 H), 7.52 (d, J = 2.2 Hz, 1 H,), 7.15 (s, 1 H), 7.145 (s, 1 H), 7.14 (d, J = 7.8 Hz, 1 H), 6.83 (s, 1 H), 6.80 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H), 6.77 (d, J = 8.4 Hz, 1 H), 6.73 (s, 1 H), 5.46 (s, 1 H, OCHO), 4.26–4.23 (m, 2 H), 4.00–3.96 (m, 2 H), 3.94 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.46 (s, 3 H, OCH_3), 2.63 (br s, 4 H, CH_2CH_2), 2.23–2.10 (m, 1 H), 1.46–1.42 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 166.9, 156.8, 155.2, 154.3, 140.0, 134.9, 134.1, 133.8, 133.1, 131.5, 131.2, 130.9, 130.6, 128.8, 128.1, 127.6, 127.3, 126.9, 122.0, 119.7, 113.1, 111.6, 111.0, 100.6, 67.4, 60.6, 56.2, 55.8, 55.7, 52.2, 35.9, 35.7, 25.8.

MS (EI): *m*/*z* (%) = 670/666 (6/26, M^+).

Anal. Calcd for $C_{36}H_{36}Cl_2O_8$ (667.58): C, 64.77; H, 5.44. Found C, 64.64; H, 5.37.

Hydroxyaldehydes 50–52
The methylester **47**, **48** or **49** (3.00 mmol) in Et_2O (40 mL) was added dropwise to a suspension of $LiAlH_4$ (6.00 mmol) in Et_2O (40 mL). The slurry was refluxed for 12 h and then cooled on ice. Ice-cold H_2O (50 mL) was added carefully and the aluminium hydroxide filtered off and washed with EtOAc (50 mL). The organic layer was separated, the aqueous layer extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated. The crude product was taken up in HOAc (32 mL) and H_2O (8 mL) and stirred for 15 h at r.t. The mixture was poured into cold sat. Na_2CO_3 (100 mL), and diluted with sat. NaCl (80 mL). The aqueous layer was extracted with Et_2O (3 × 50 mL), dried ($MgSO_4$) and concentrated. The product was purified by column chromatography (silica gel, EtOAc–$CHCl_3$, 1:3) to give colorless crystals.

Hydroxyaldehyde 50
Yield: (81%); mp 85 °C.

^{1}H NMR ($CDCl_3$): δ = 9.90 (s, 1 H, CHO), 7.85 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1 H, Ar-H), 7.67 (d, J = 2.4 Hz, 1 H, Ar-H), 7.15 (s, 1 H, Ar-H), 7.05 (d, J = 8.5 Hz, 1 H, Ar-H), 6.985 (d, J = 7.9 Hz, 1 H, Ar-H), 6.99 (s, 1 H, Ar-H), 6.91 (dd, J_1 = 8.6 Hz, 1 H, Ar-H), 6.89 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1 H, Ar-H), 6.80 (d, J = 7.9 Hz, 1 H, Ar-H), 6.76–6.74 (m, 2 H, Ar-H), 4.67 (s, 2 H, CH_2OH), 3.86 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 2.67 (br s, 4 H, CH_2CH_2), 1.85 (br s, 1 H, CH_2OH).

^{13}C NMR ($CDCl_3$): δ = 191.2, 162.2, 156.8, 155.3, 153.9, 142.2, 140.3, 133.6, 132.6, 132.2, 132.0, 131.7, 131.4, 131.3, 131.2, 129.5, 129.0, 128.2, 126.2, 119.3, 118.6, 112.8, 110.9, 110.8, 109.1, 65.1, 56.1, 55.9, 55.8, 55.5, 36.2, 35.8.

MS (EI): *m*/*z* (%) = 545/548 (6/18, M – 1^+).

Anal. Calcd for $C_{32}H_{31}ClO_6$ (547.04): C, 70.26; H, 5.71. Found C, 70.35; H, 5.78.

Hydroxyaldehyde 51
Yield: (86%); mp 70 °C.

^{1}H NMR ($CDCl_3$): δ = 9.91 (s, 1 H, CHO), 7.80 (dd, J_1 = 2.2 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 7.70 (d, J = 2.4 Hz, 1 H, Ar-H), 7.10–7.02 (m, 2 H, Ar-H), 6.98 (s, 1 H, Ar-H), 6.95–6.91 (m, 2 H, Ar-H), 6.82 (m, 3 H, Ar-H), 6.75 (d, J = 2.2 Hz, 1 H, Ar-H), 4.66 (s, 2 H, CH_2OH), 3.83 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 2.69 (br s, 4 H, CH_2CH_2), 1.80 (br s, 1 H, CH_2OH).

^{13}C NMR ($CDCl_3$): δ = 191.1 (CHO), 162.3, 159.0, 157.1, 155.3, 141.9, 141.7, 134.5, 132.0, 131.7, 131.7, 131.3, 131.2, 130.7, 130.0, 129.7, 129.0, 126.3, 119.0, 114.5, 114.0, 111.1, 111.0, 110.8, 109.3 65.3 (OCH_2), 56.0, 55.9, 55.5, 55.2 (4 × OCH_3), 36.3, 36.1 (2 × CH_2).

MS (CI): *m*/*z* (%) = 545/548 (10/55, M – 1^+).

Anal. Calcd for $C_{32}H_{31}ClO_6$ (547.04): C, 70.26; H, 5.71. Found C, 70.38; H, 5.66.

Hydroxyaldehyde 52
Yield (83%); mp 88 °C.

^{1}H NMR ($CDCl_3$): δ = 9.90 (s, 1 H, CHO), 7.89 (d, J = 2.2 Hz, 1 H), 7.59 (d, J = 2.2 Hz, 1 H), 7.15 (s, 1 H), 7.02 (d, J = 7.5 Hz, 1 H),

6.99 (br d, 1 H), 6.94 (br dd, 2 H), 6.82 (d, J = 8.4 Hz, 1 H), 6.76 (br d, 1 H), 6.75 (s, 1 H), 4.69 (s, 2 H, CH_2OH), 3.87 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.53(s, 3 H, OCH_3), 2.66 (br s, 4 H, CH_2CH_2), 1.85 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 190.2, 159.1, 156.9, 154.9, 154.0, 142.2, 140.1, 134.3, 133.8, 132.4, 132.3, 131.9, 131.5, 131.0, 130.5, 129.5, 128.9, 128.3, 125.5, 119.6, 118.7, 112.9, 110.9, 109.3, 65.2, 60.8, 56.2, 55.7, 55.5, 36.0, 35.9.

MS (EI): m/z (%) = 584/580 (28/78, M^+).

Anal. Calcd for $C_{32}H_{30}Cl_2O_6$ (581.49): C, 66.10; H, 5.20. Found C, 65.96; H, 5.26.

Stilbene-like Bisbibenzyls 53–55

The benzylalcohol **50**, **51** or **52** (2.50 mmol) and triphenylphosphonium hydrobromide (2.50 mmol) in CH_3CN(80 mL) were refluxed for 24 h. The solvent was evaporated and the residue filtered through a silica gel pad eluting first with $CHCl_3$ for impurities and second with EtOH to obtain the product which after concentration was dissolved in CH_2Cl_2 (600 mL) and added dropwise over 24 h to NaOMe (7.50 mmol) in CH_2Cl_2 (500 mL). After additional stirring for 24 h the mixture was filtered and evaporated. The cyclic product was purified by column chromatography (silica gel, CH_2Cl_2) to give colorless crystals

Bisbibenzyl 53

Yield: (68%); mp 120 °C; mixture of conformers.

^{1}H NMR ($CDCl_3$): δ = 7.22 (m, 2 H, Ar-H), 7.13 (d, J = 7.5 Hz, 1 H, Ar-H), 7.05 (m, 2 H, Ar-H), 6.90–6.82 (m, 4 H, Ar-H), 6.74 (d, J = 8.4 Hz, 1 H, Ar-H), 6.64 (m, 2 H, CH = CH), 6.47 (s, 1 H, Ar-H), 3.95 and 3.84 (2 s, 3 H, OCH_3), 3.81 and 3.80 (2 s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.68 and 3.51 (s, 3 H, OCH_3), 2.90–2.30 (m, 4 H, CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 157.4, 156.8, 156.2, 155.4, 154.2, 142.2, 141.7, 140.5, 139.8, 135.2, 133.7, 135.2, 133.7, 131.9, 131.8, 131.6, 131.3, 131.2, 131.0, 130.4, 130.2, 129.8, 129.7, 128.9, 128.7, 128.3, 127.9, 127.6, 127.5, 127.2, 126.9, 120.9, 120.9, 119.4, 119.3, 112.3, 112.0, 111.6, 110.9, 110.6, 110.6, 110.4, 56.1, 55.9, 55.8, 55.7, 55.6, 55.5, 55.4, 38.1, 37.7, 37.5, 36.8.

MS (EI): m/z (%) = 515/512 (12/100, M^+).

Anal. Calcd for $C_{32}H_{29}ClO_4$ (513.03): C, 74.92; H, 5.70. Found C, 75.01; H, 5.64.

Bisbibenzyl 54

Yield: (72%); mp 86 °C; mixture of conformers.

^{1}H NMR ($CDCl_3$): δ = 7.26–7.24 (m, 2 H, Ar-H), 7.20–7.00 (m, 2 H, Ar-H), 6.88–6.86 (m, 2 H, Ar-H), 6.82–6.78 (m, 2 H, Ar-H), 6.75–6.73 (m, 2 H, Ar-H), 6.72 (d, J_{cis} = 12.0 Hz, 1 H, C*H*=CH), 6.62 (d, J_{cis} = 12.0 Hz, 1 H, CH=C*H*), 6.49 (br d, 1 H, Ar-H), 3.85 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.76 and 3.68 (2 s, 3 H, OCH_3), 3.64 and 3.58 (s, 3 H, OCH_3), 2.79–2.63 (br s, 4 H, CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 159.1, 157.6, 152.9, 149.8, 142.8, 142.0, 137.5, 134.5, 132.1, 131.7, 131.0, 130.2, 129.7, 129.1, 127.5, 127.2, 120.7, 114.6, 114.4, 113.8, 111.5, 111.2, 110.0, 56.7, 56,4, 55.9, 55.6, 55.5, 55.2, 53.4, 53.0, 37.8, 37.4, 36.8, 36.2.

MS (CI): m/z (%) = 513/511 (45/100, M – 1^+).

Anal. Calcd for $C_{32}H_{29}ClO_4$ (513.03): C, 74.92; H, 5.70. Found C, 75.06; H, 5.64.

Bisbibenzyl 55

Yield: (78%); mp 140 °C

^{1}H NMR ($CDCl_3$): δ = 7.26 (m, 1 H, Ar-H), 7.22 (m, 1 H, Ar-H), 7.14 (m, 1 H, Ar-H), 7.06 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.90 (m, 1 H, Ar-H), 6.88 (s, 1 H, Ar-H), 6.86 (s, 1 H, Ar-H), 6.81 (s, 1 H, Ar-H), 6.76 (d, J_{cis} = 12.0 Hz, 1 H, C*H*=CH), 6.74 (d, J = 8.4 Hz, 1 H, Ar-H), 6.55 (d, J_{cis} = 12.0 Hz, 1 H, CH=C*H*), 6.41 (d, J = 2.2 Hz, 1 H, Ar-H), 3.95 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.66 and 3.53 (2 s, 3 H, OCH_3), 3.63 (s, 3 H, OCH_3), 2.85–2.29 (m, 4 H, CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 155.1, 154.3, 153.1, 135.2, 133.5, 132.7, 131.6, 131.1, 130.27, 129.2, 128.2, 127.7, 127.1, 120.9, 119.5, 112.1, 111.6, 110.9, 110.4, 60.7, 56.2, 55.7, 55.5, 37.7, 36.8.

MS (EI): m/z (%) = 550/546 (16/100, M^+).

Anal. calcd for $C_{32}H_{28}Cl_2O_4$ (547.47): C, 70.20; H, 5.15. Found C, 70.31; H, 5.07.

Tetramethoxy Bisbibenzyls 56–58 by Hydrogenation

The dehydrobisbibenzyl **53**, **54** or **55** (1.5 mmol) in EtOAc (150 mL) was hydrogenated (3.5 bar, 24 h) in the presence of 5% Pd/C (250 mg). The mixture was filtered and evaporated. The crude product was purified by column chropmatography (silica gel; $CHCl_3$) to give colorless crystals.

Bisbibenzyl 56

Yield: (88%); mp 145 °C; mixture of conformers.

^{1}H NMR ($CDCl_3$): δ = 7.20–7.13 (m, 2 H, Ar-H), 7.10–6.96 (m, 3 H, Ar-H), 6.90–6.83 (m, 2 H, Ar-H), 6.73 (dd, J_1 = 8.1 Hz, J_2 = 3.6 Hz, 1 H, Ar-H), 6.39–6.20 (m, 3 H, Ar-H), 3.95 (s, 3 H, OCH_3), 3.80–3.45 (s, m, 9 H, 3 × OCH_3), 3.30–3.23 (m, 1 H), 3.10–2.40 (m, 7 H, 2 × CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 157.1, 156.5, 155.3, 154.1, 154.0, 142.6, 142.5, 142.2, 141.7, 135.3, 135.0, 134.3, 134.0, 133.9, 133.8, 132.9, 132.8, 132.2, 132.0, 131.5, 131.2, 130.7, 129.1, 128.2, 127.6, 127.3, 127.2, 127.0, 126.8, 123.3, 120.7, 119.3, 113.9, 112.3, 112.0, 111.2, 111.0, 110.7, 110.4, 110.2, 55.9, 55.8, 55.8, 55.7, 55.6, 55.3, 39.1, 38.8, 38.5, 38.3, 37.6, 36.9, 36.6, 36.0.

MS (EI): m/z (%) = 517/514 (13/100, M^+).

Anal. Calcd for $C_{32}H_{31}ClO_4$ (515.04): C, 74.62; H, 6.07. Found C, 74.56; H, 5.96.

Bisbibenzyl 57

Yield: (72%); mp 140 °C; mixture of conformers.

^{1}H NMR ($CDCl_3$): δ = 7.21–7.15 (m, 2 H, Ar-H), 7.12–6.95 (m, 3 H, Ar-H), 6.88–6.81 (m, 2 H, Ar-H), 6.75 (dd, J_1 = 8.0 Hz, J_2 = 3.2 Hz, 1 H, Ar-H), 6.41–6.23 (m, 3 H, Ar-H), 3.91 (s, 3 H, OCH_3), 3.80–3.45 (s, m, 9 H, OCH_3), 3.28–3.24 (m, 1 H), 3.15–2.30 (m, 7 H, 2 × CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 157.3, 156.7, 155.5, 154.5, 154.1, 142.7, 142.4, 142.2, 141.1, 135.6, 135.0, 134.5, 134.1, 133.7, 133.5, 132.8, 132.6, 132.4, 132.2, 131.4, 131.2, 130.2, 129.4, 128.5, 127.4, 127.3, 127.2, 127.0, 126.5, 123.1, 120.4, 119.5, 113.6, 112.5, 112.3, 111.8, 111.0, 110.5, 110.3, 110.0, 56.0, 55.8, 55.7, 55.6, 55.4, 55.3, 39.1, 38.8, 38.6, 38.3, 37.5, 36.7, 36.5, 36.2.

MS (CI): m/z (%) = 517/514 (21/100, M^+).

Anal. Calcd for $C_{32}H_{31}ClO_4$ (515.04): C, 74.62; H, 6.07. Found C, 74.52; H, 6.12.

Bisbibenzyl 58

Yield: (88%); mp 131 °C; mixture of conformers.

^{1}H NMR (DMSO-d_6): δ = 7.52–7.48 (m, 1 H, Ar-H), 7.27–7.12 (m, 5 H, Ar-H), 6.96 (dd, J_1 = 10.1 Hz, J_2 = 3.1 Hz, 1 H), 6.50–6.45 (m, 1 H, Ar-H), 6.25–6.23 (m, 1 H, Ar-H), 6.15–6.14 (m, 1 H, Ar-H), 3.90 (s, 3 H, OCH_3), 3.67–3.33 (5 s, 9 H, OCH_3), 3.16–2.87 (m, 4 H, CH_2CH_2), 2.49–2.11 (m, 4 H, CH_2CH_2).

^{13}C NMR (DMSO-d_6): δ = 155.0, 154.2, 142.1, 141.6, 136.8, 135.2, 135.0, 133.9, 133.7, 133.2, 132.9, 132.2, 132.0, 131.7, 131.2, 130.8,

129.3, 128.3, 127.9, 127.5, 127.3, 123.2, 120.8, 113.8, 112.4, 112.1, 110.8, 110.1, 110.0, 65.8, 60.6, 56.2, 55.7, 55.3, 38.5, 38.3, 37.6, 36.8, 36.6.

MS (EI): *m*/*z* (%) = 552/548 (25/100, M^+).

Anal. Calcd for $C_{32}H_{30}Cl_2O_4$ (549.49): C, 69.95; H, 5.50. Found C, 70.12; H, 5.57.

Tetrahydroxy Bisbibenzyls 3, 59 and 13 by Cleavage of the Methyl Ethers

To the tetramethylether **56**, **57** or **58** (1.00 mmol) in CH_2Cl_2 (25 mL) was added BBr_3 (1 M; 8.0 mL, 8.00 mmol) at –70 °C. Stirring was continued for 5 h at –70 °C and the mixture was allowed to warm up to r.t. over 24 h. Ice-water (25 mL) was added and the mixture extracted with Et_2O (3 × 25 mL) and the combined organic layers dried ($MgSO_4$) and concentrated. The product was purified by flash chromatography on RP 18 (MeOH–H_2O, 70:30).

12-Chlorisoplagiochin D (3)

Yield: (75%), colorless oil.

^{1}H NMR (CD_3OD): δ = 7.09 (dd, J_1 = 8.1 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 7.05 (s, 1 H, Ar-H), 7.03 (d, *J* = 7.5 Hz, 1 H, Ar-H), 6.95 (dd, J_1 = 8.1 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.88 (s, 1 H, Ar-H), 6.81 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.74 (dd, J_1 = 7.5 Hz, J_2 = 1.4 Hz, 1 H, Ar-H), 6.70 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.65 (d, *J* = 1.3 Hz, 1 H, Ar-H), 6.44 (d, *J* = 2.2 Hz, 1 H, Ar-H), 6.34 (d, *J* = 2.2 Hz, 1 H, Ar-H), 3.05–2.88 (m, 2 H, C*H*$_2$CH$_2$), 2.81–2.75 (m, 2 H, CH$_2$C*H*$_2$), 2.71–2.64 (m, 2 H, C*H*$_2$CH$_2$), 2.51–2.45 (m, 2 H, CH$_2$C*H*$_2$).

^{13}C NMR (CD_3OD): δ = 155.8, 153.6, 152.8, 152.3, 143.9, 143.6, 136.6, 134.9, 134.7, 134.5, 132.9, 132.5, 132.2, 129.9, 128.5, 128.4, 127.0, 126.9, 122.1, 118.3, 118.1, 117.7, 117.4, 116.5, 39.3, 39.2, 38.7, 37.1.

MS (EI): *m*/*z* (%) = 458/461 (2/10, M^+).

Anal. Calcd for $C_{28}H_{23}ClO_4$ (458.94): C, 73.28; H, 5.05. Found C, 73.19; H, 5.12.

The spectroscopic data were coincidental with those reported for the natural compound.[8,12]

6′-Chlorisoplagiochin D (59)

Yield: (72%); colorless oil.

^{1}H NMR (CD_3OD): δ = 7.25 (d, *J* = 2.4 Hz, 1 H, Ar-H), 7.13 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.12 (d, *J* = 2.2 Hz, 1 H, Ar-H), 7.11 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.98 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 6.89 (d, *J* = 2.0 Hz, 1 H, Ar-H), 6.88 (d, *J* = 1.8 Hz, 1 H, Ar-H), 6.87 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1 H, Ar-H), 6.81 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.77 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 6.40 (d, *J* = 1.8 Hz, 1 H, Ar-H), 2.80–2.70 (m, 4 H, CH_2), 2.68–2.60 (m, 4 H, CH_2).

^{13}C NMR (CD_3OD): δ = 157.8, 156.0, 153.3, 152.4, 145.0, 143.5, 136.2, 136.0, 133.7, 132.7, 131.9, 130.5, 131.0, 129.9, 128.9, 128.5, 127.0, 125.0, 123.0, 118.9, 116.9, 116.0, 115.9, 113.0, 39.9, 38.9, 37.1, 36.7.

MS (CI): *m*/*z* (%) = 461/458 (19/38, M^+)

Anal. Calcd for $C_{28}H_{23}ClO_4$ (458.94): C, 73.28; H, 5.05. Found C, 73.18; H, 5.14.

6′,12-Dichlorisoplagiochin D or Bazzanin J (13)

Yield: (65%); colorless oil.

^{1}H NMR ($CDCl_3$): δ = 7.24 (d, *J* = 2.0 Hz, 1 H, Ar-H), 7.23 (s, 1 H, Ar-H), 7.08 (d, *J* = 7.5 Hz, 1 H, Ar-H), 7.05 (s, 1 H, Ar-H), 7.00 (dd, J_1 = 8.2 Hz, J_2 = 2.4 Hz, 1 H, Ar-H), 6.811 (br d, 1 H, Ar-H), 6.810 (d, *J* = 8.2 Hz, 1 H, Ar-H), 6.72 (dd, J_1 = 7.6 Hz, J_2 = 1.5 Hz, 1 H, Ar-H), 6.38 (d, *J* = 2.0 Hz, 1 H, Ar-H), 6.27 (d, *J* = 2.3 Hz, 1 H, Ar-H), 2.78 (m, 8 H).

^{13}C NMR ($CDCl_3$): δ = 153.1, 151.6, 151.1, 145.3, 143.4, 142.8, 135.1, 134.9, 133.6, 133.0, 131.5, 130.7, 128.5, 128.4, 128.3, 125.9, 125.8, 124.4, 122.3, 120.2, 117.9, 117.0, 116.9, 116.4, 37.9, 37.8, 37.6, 35.8.

MS (EI): *m*/*z* (%) = 494/491 (12/50, M^+).

Anal. Calcd for $C_{28}H_{22}Cl_2O_4$ (493.38): C, 68.16; H, 4.49. Found C, 68.08; H, 4.39.

The spectroscopic data were coincidental with those reported for the natural compound.[9]

6′-Chlorisoplagiochin C or Bazzanin A (4)

To the tetramethylether **54** (1.00 g, 1.95 mmol) in CH_2Cl_2 (20 mL) was added BBr_3 (1 M in CH_2Cl_2; 16 mL, 16.0 mmol) at –78 °C. The soln was allowed to come to r.t. over 12 h, poured into ice-water and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL) and the combined organic layers washed with sat. NaCl and dried ($MgSO_4$). After evaporation of the solvent the product was purified by flash chromatography (RP-18; MeOH–H_2O, 75:25), give a mixture of a colorless oil and colorless crystals (755 mg, 85%).

^{1}H NMR (CD_3OD): δ = 7.28 (d, *J* = 2.4 Hz, 1 H, Ar-H), 7.17 (d, *J* = 2.2 Hz, 1 H, Ar-H), 7.13 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.10 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.99 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.83 (d, *J* = 8.4 Hz, 1 H, Ar-H), 6.82 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 6.80 (d, *J* = 2.2 Hz, 1 H, Ar-H), 6.78 (d, *J* = 2.2 Hz, 1 H, Ar-H), 6.76 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 6.67 (d, J_{cis} = 12.0 Hz, 1 H, C*H*=CH), 6.54 (d, *J* = 2.2 Hz, 1 H, Ar-H), 6.51 (d, J_{cis} = 12.0 Hz, 1 H, CH=C*H*), 2.67–2.50 (br s, 4 H, CH_2CH_2).

^{13}C NMR (CD_3OD): δ = 157.8, 157.0, 156.2, 156.0, 144.6, 140.8, 136.8, 134.5, 133.4, 132.6, 131.0, 130.5, 130.2, 130.0, 129.9, 129.6, 129.3, 129.0, 127.7, 123.8, 120.7, 116.6, 115.8, 115.0, 114.9, 113.0, 39.6, 38.6.

MS (CI): *m*/*z* (%) = 458/456 (41/100, M^+).

Anal. Calcd for $C_{28}H_{21}ClO_4$ (456.92): C, 73.60; H, 4.63. Found C, 73.71; H, 5.01.

Tetraacetate 60 of Bazzanin A

Compound (**4**137 mg, 0.30 mmol) of in Ac_2O (5 mL) and pyridine (0.1 mL) were heated to 80 °C for 24 h. HCl (1 M, 20 mL) were added and the mixture extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with NaOH (0.5 M; 2 × 10 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (silica; EtOAc) to give colorless crystals (133 mg, 71%); mp 121 °C.

^{1}H NMR ($CDCl_3$): δ = 7.35 (d, *J* = 2.2 Hz, 1 H, Ar-H), 7.20 (d, *J* = 2.2 Hz, 1 H, Ar-H), 7.19 (m, 2 H, Ar-H), 7.08 (d, *J* = 2.4 Hz, 1 H, Ar-H), 7.10 (d, *J* = 8.4 Hz, 1 H, Ar-H), 6.99 (m, 2 H, Ar-H), 6.95 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.83 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 6.67 (d, *J* = 2.4 Hz, 1 H, Ar-H), 6.59 (d, *J* = 12.4, 1 H, C*H*=CH), 6.48 (s, 1 H, CH=C*H*), 2.32 (s, 3 H, $OCOCH_3$), 2.14 (s, 3 H, $OCOCH_3$), 1.99 (s, 3 H, $OCOCH_3$), 1.79 (s, 3 H, $OCOCH_3$), 2.85–2.68 (br s, 4 H, 2 × HCH).

^{13}C NMR ($CDCl_3$): δ = 159.1, 157.6, 152.9, 149.8, 142.8, 142.0, 137.5, 134.5, 132.1, 131.7, 131.0, 130.2, 129.7, 129.1, 127.5, 127.2, 120.7, 114.6, 114.4, 113.8, 111.5, 111.2, 110.0, 56.7, 55.6, 55.5, 53.4 (4 × OCH_3), 37.4, 36.2 (2 × CH_2).

MS (CI): *m*/*z* (%) = 626/624 (25/65, M^+).

Anal. Calcd for $C_{36}H_{29}ClO_8$ (625.06): C, 69.17; H, 4.68. Found C, 69.27; H, 4.72.

Dialdehyde 61

A slurry of the benzylalcohol **51** (547 mg, 1.00 mmol) and PCC/Al_2O_3 (1.20 equiv) in CH_2Cl_2 (10 mL) was stirred for 24 h at r.t., fil-

tered, washed with CH_2Cl_2 and the CH_2Cl_2 evaporated. The residue was taken up in Et_2O and filtered through a pad of silica gel to give yellow crystals (crude: 463 mg, 85%); mp 80 °C.

^{1}H NMR ($CDCl_3$): δ = 9.98 (s, 1 H, CHO), 9.90 (s, 1 H, CHO), 7.88 (d, *J* = 1.8 Hz, 1 H), 7.56 (d, *J* = 2.2 Hz, 1 H), 7.47 (m, 2 H), 7.07 (dd, J_1 = 8.8 Hz, J_2 = 1.8 Hz, 1 H), 6.92 (dd, J_1 = 11.0 Hz, J_2 = 2.2 Hz, 1 H), 6.82 (m, 4 H), 6.75 (d, *J* = 1.8 Hz, 1 H, Ar-H), 3.82 (s, 3 H,), 3.81 (s, 3 H), 3.72 (s, 3 H), 3.51 (s, 3 H, OCH_3), 2.67 (br s, 4 H, CH_2CH_2).

^{13}C NMR ($CDCl_3$): δ = 191.7, 190.0 (2 × CHO), 159.4, 159.1, 157.7, 154.9, 141.3, 137.5, 137.0, 134.3, 134.0, 132.4, 132.2, 131.0, 130.4, 129.7, 129.4, 125.5, 124.0, 115.0, 114.8, 113.7, 111.3, 111.0, 110.8, 109.3, 60.4, 55.7, 55.6, 55.2 (4 × C–O), 36.5, 36.0.

MS (CI): *m*/*z* (%) = 547/544 (13/65, M^+).

Anal. Calcd for $C_{32}H_{29}ClO_6$ (545.02): C, 70.52; H, 5.36. Found C, 70.68; H, 5.43.

Bazzanin A Tetramethylether 54 via McMurry Reaction[24]

A mixture of $TiCl_3(DME)_2$ (2.10 g, 6.20 mmol) and Zn/Cu couple (1.50 g, 22.9 mmol) in DME (75 mL) was heated to 80 °C for 5 h. The dialdehyde (436 mg, 0.80 mmol) in DME (75 mL) was added dropwise within 6 h. Stirring was continued for 8 h at 80 °C and the mixture cooled, diluted with pentane (300 mL), filtered and concentrated. The product was purified by column (silica gel; pentane–Et_2O, 1:1), to give colorless crystals (285 mg, 70% from **51**); mp 86 °C.

For the spectroscopic data see above.

Acknowledgement

A.S. thanks Prof. Dr. Dr. h. c. T. Eicher for generous support.

References

(1) Naumann, K. *Chem. Unserer Zeit.* **1993**, *27*, 33.
(2) Faulkner, D. J. *Nat. Prod. Rep.* **1992**, *9*, 323.
(3) van Pée, K.-H. *Annu. Rev. Microbiol.* **1996**, *50*, 375.
(4) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, **1983**.
(5) Neidleman, S. L.; Geigert, J. *Biohalogenation: Principles Basic Roles and Applications*; Ellis Horwood: Chichester, **1986**.
(6) Sakai, K.; Ichikawa, T.; Yamada, K.; Yamashita, M.; Tanimoto, M.; Hikita, A.; Ijuin, Y.; Kondo, K. *J. Nat. Prod.* **1988**, *51*, 845.
(7) Hashimoto, T.; Tori, M.; Asakawa, Y. *Phytochemistry* **1989**, *28*, 3377.
(8) Anton, H.; Kraut, L.; Mues, R.; Morales, M. I. *Phytochemistry* **1997**, *46*, 1069.
(9) (a) Martini, U.; Zapp, J.; Becker, H. *Phytochemistry* **1998**, *47*, 89. (b) Schmidt, A. *Dissertation Thesis*; Universität des Saarlandes: Germany, **1996**.
(10) Hashimoto, T.; Kanayama, S.; Kann, Y.; Tori, M.; Asakawa, Y. *Chem. Lett.* **1996**, 741.
(11) Geserü, G. M.; Nogradi, M. *Nat. Prod. Rep.* **1995**, *12*, 69.
(12) Hashimoto, T.; Irita, H.; Takaoka, S.; Tanaka, M.; Asakawa, Y. *Tetrahedron* **2000**, *56*, 3153.
(13) Speicher, A.; Hollemeyer, K.; Heinzle, E. *Rapid Commun. Mass Spectrom.* **2001**, *15*, 124.
(14) Speicher, A.; Hollemeyer, K.; Heinzle, E. *Phytochemistry* **2001**, *57*, 303.
(15) Schultz, T. P.; Cheng, Q.; Boldin, W. D.; Hubbard, T. F.; Jin, J. L.; Fischer, T. H.; Nicholas, D. D. *Phytochemistry* **1991**, *30*, 2939.
(16) Eicher, T.; Fey, S.; Puhl, W.; Büchel, E.; Speicher, A. *Eur. J. Org. Chem.* **1998**, 877.
(17) Speicher, A. *J. Prakt. Chem.* **2000**, *342*, 162.
(18) Speicher, A.; Schulz, T.; Eicher, T. *J. Prakt. Chem.* **1999**, *341*, 605.
(19) Windaus, A.; Schiele, H. *Chem. Ber.* **1923**, *56*, 847.
(20) Corey, E. J.; Myers, A. G. *J. Am. Chem. Soc.* **1985**, *107*, 5574.
(21) John, R.; Lindsay, S.; McKeer, C. L.; Taylor, J. M. *Org. Synth.* **1989**, 67.
(22) Rao, A. V. R.; Chakraborty, T. K.; Reddy, K. L.; Rao, A. S. *Tetrahedron Lett.* **1994**, *28*, 5043.
(23) Cossey, H. D.; Judd, J.; Stephens, F. F. *J. Chem. Soc.* **1965**, 954.
(24) McMurry, J. E.; Matz, J. R.; Kees, K. L.; Bock, P. A. *Tetrahedron Lett.* **1982**, *23*, 1777.