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First Total Synthesis of Dermocanarin 2

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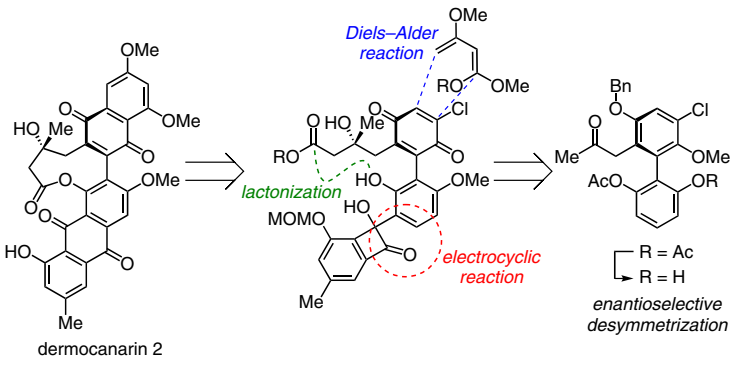

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Abstract The first total synthesis of dermocanarin 2 is described. The synthesis features the construction of the anthraquinone and naphthoquinone frameworks through annulation reactions onto an axially chiral biphenyl intermediate, obtained by an enzyme-catalyzed enantioselective desymmetrization of a σ-symmetric precursor, followed by a stereoselective aldol reaction to construct the stereogenic center in the side chain.

Key words axial chirality, biphenyls, enzymes, desymmetrizations, annulations, total synthesis

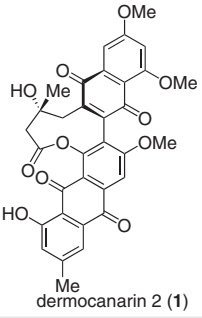
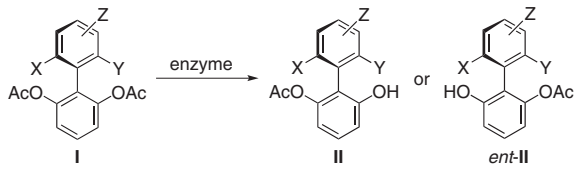


Figure 1 Structure of dermocanarin 2 (**1**)

Axially chiral biaryls are structural motifs abundant in natural products.[1] Such structures arise from diverse aromatic precursors produced by various biosynthetic routes, including polyketide and shikimate pathways, primarily through oxidative coupling. Consequently, many natural biaryls are composed of multiply functionalized polyaromatic derivatives, rather than simple monocyclic aromatic derivatives, and they are exceedingly congested around the biaryl axis; as a result, they present formidable challenges as target compounds in organic synthesis.[2]

In this communication, we describe the first total synthesis of dermocanarin 2 (**1**; Figure 1),[3a,b] a pigment isolated from an Australian toadstool, *Dermocybe canaria*, and one of ten analogues isolated from the related species.[3] The structure features anthraquinone and naphthoquinone moieties interconnected by a σ-bond and bridged by a nine-membered lactone structure. Hindered rotation of the C(sp^2)–C(sp^2) bond between the quinone moieties imparts axial chirality, and a stereogenic center is present in the lactone portion.

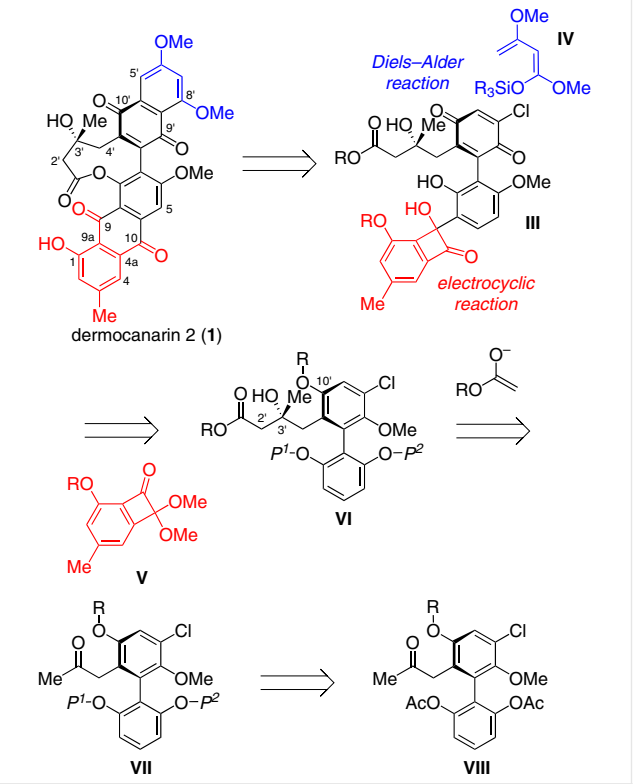
We previously reported a simple and highly enantioselective synthesis of axially chiral biaryls through an enzyme-catalyzed desymmetrization (Scheme 1).[4] A feature of this method is that the operation responsible for enantioselection is executed by using an achiral biaryl precursor. This leads to a reduction in the difficulties associated with synthesis of sterically congested biaryl derivatives. Furthermore, the enzymatic process is compatible with a broad range of biaryls **I**. We expected that the monoacetate **II** would permit multidirectional elaboration through exploitation of well-discriminated functionalities to give a biaryl structure composed of the highly oxygen-functionalized polycyclic chromophores present in dermocanarin 2 (**1**).[5]



Scheme 1 Desymmetrization approach to axially chiral biaryls by enzyme-catalyzed hydrolysis

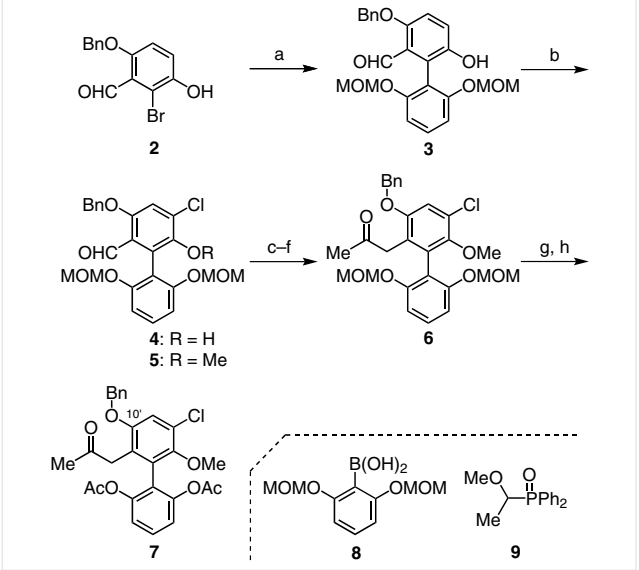
Our retrosynthetic analysis of dermocanarin 2 (**1**) is shown in Scheme 2.[6] On the assumption that the lactone bridge could be formed in the final stage of the synthesis, dermocanarin 2 (**1**) was traced back to the stereodefined biphenyl **VI** with a β-hydroxybutenoic acid side chain, as a key intermediate. We surmised that the anthraquinone moiety might be constructed through sequential electrocyclic reactions using benzocyclobutene **V** as the building block corresponding to the C1–C4, C4a, C9a, C9, C10, and C3-Me atoms (shown in red in Scheme 2).[5,7] The naphthoquinone moiety should be accessible through selective oxidation of one of the aromatic rings (the upper portion of **VI**) followed by a Diels–Alder reaction with siloxydiene **IV**, with the chloro substituent controlling the regiochemical course of the reaction.[8] Disconnection of the C2′–C3′ linkage leads to the ketone **VII** and an acetate-derived enolate as the precursors. We hoped that the axial chirality of the biphenyl would induce diastereodifferentiation of the π-faces of the carbonyl group in an aldol reaction with a suitable choice of the phenol-protecting groups P^1 and P^2. Biphenyl ketone **VII**, in which the two phenolic groups are differentiated by protection, should be accessible enantioselectively from the corresponding diacetate **VIII** through the enzyme-catalyzed desymmetrization described above.

The synthesis began with the preparation of the biphenyl diacetate **7**, the substrate for the enzymatic desymmetrization (Scheme 3). We selected a benzyl protecting group



Scheme 2 Retrosynthetic analysis of dermocanarin 2

for the C10′ phenol, as this should have been capable of selective detachment at a later stage to permit selective oxidation of the aromatic ring (Scheme 2, **VI**→**III**). Suzuki–Miyaura coupling of aryl bromide **2**[9,10] with boronic acid **8**[4a] proceeded in high yield under the standard conditions [10 mol% $Pd(PPh_3)_4$, K_3PO_4, DME, H_2O, reflux].[11] The resulting biphenyl **3** was selectively chlorinated at the *ortho* position of the free phenol by treatment with NCS and NaH (THF, –10 °C),[12] to give chloride **4**. After methylation of the hydroxy group (MeI, K_2CO_3, DMF), aldehyde **5** was converted into the methyl ketone **6** by alkoxyethylenation with the phosphine oxide **9**.[13] Finally, cleavage of the methoxymethyl groups (6 M aq HCl, phloroglucinol, THF),[14] followed by acetylation, gave the desired σ-symmetric biphenyl diacetate **7**.

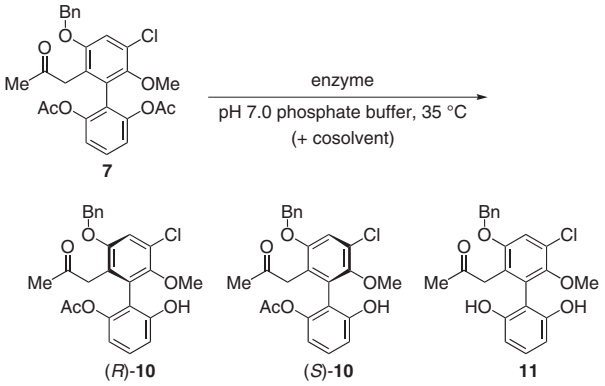


Scheme 3 Synthesis of diacetate **7**. *Reaction conditions*: (a) **8**, $Pd(PPh_3)_4$ (10 mol%), K_3PO_4, DME, H_2O, reflux, 20 h (84%); (b) NCS, NaH, THF, –10 °C, 10 min; (c) MeI, K_2CO_3, DMF, r.t., 2 h (**5**: 92% from **3**); (d) **9**, LDA, THF, –78 °C, 15 min; (e) NaH, THF, r.t., 12 h; (f) TsOH, acetone, H_2O, 0 °C, 5 h (82% from **5**); (g) 6 M aq HCl, phloroglucinol, THF, r.t., 15 h; (h) Ac_2O, DMAP, py, 0 °C, 2.5 h (92% from **6**).

We screened various enzymes for the enantioselective desymmetrization by treating diacetate **7** with a fixed weight of the appropriate enzyme in pH 7 phosphate buffer (0.1 M) at 35 °C (Table 1). Among the commercially available enzymes that we tested,[15] porcine pancreas lipase (PPL; Sigma, Type II) and *Rhizopus oryzae* lipase (ROL; Amano, lipase F-AP15) brought about the desired reaction (entries 1 and 2). Although the yields of monoacetate **10** were far from satisfactory due to competing overhydrolysis of **10** to the diol **11**, the product **10** obtained by the reaction with PPL was enantiomeric with that obtained by the reaction with ROL, and their enantiomeric purities were both fairly high. Fortunately, the use of an organic cosolvent in the reaction with ROL effected an improvement in enantioselec-

tivity, as well as suppressing the overhydrolysis (entries 5–8).[16] $(i\text{-Pr})_2O$ was the best cosolvent, and gave (*R*)-(+)-**10** in 83% yield and in an enantiomerically pure form (entry 6). Further optimization proved that the catalyst load could be reduced to 30 wt% on the substrate in a gram-scale reaction (entry 9). The absolute stereochemistry of **10** was determined by X-ray crystal structure analysis.[17]

Table 1 Optimization of Conditions of the Desymmetrization of **7**[a]

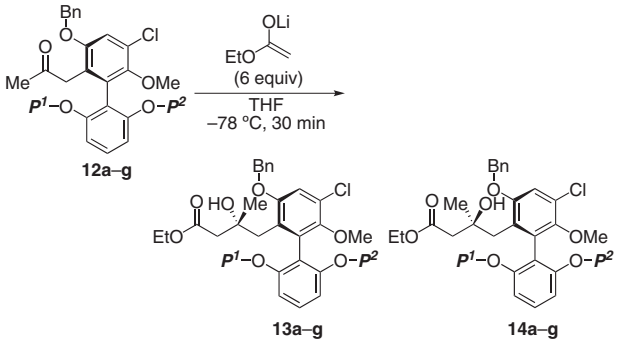


Entry	Enzyme	Cosolvent	Time (d)	Yield (%)		
				7	**10** (ee[b])	**11**
1	PPL	–	3	69	13 (92, *S*)	11
2	ROL	–	3	47	30 (96, *R*)	18
3	PPL	heptane	3	90	3 (70, *S*)	1
4	PPL	$(i\text{-Pr})_2O$	3	81	9 (62, *S*)	2
5	ROL	heptane	1	6	67 (>99, *R*)	19
6	ROL	$(i\text{-Pr})_2O$	1	5	83 (>99, *R*)	11
7	ROL	Et_2O	3	17	66 (>99, *R*)	15
8	ROL	CH_2Cl_2	3	59	39 (N.D.)	2
9[c]	ROL	$(i\text{-Pr})_2O$	1	5	84 (>99, *R*)	11

[a] The reaction was performed in a test tube (ϕ = 24 nm) by using **7** (20 mg), enzyme (20 mg), solvent (4.2 mL of phosphate buffer for entries 1 and 2; 2.8 mL of phosphate buffer + 1.4 mL of organic cosolvent for entries 3–8).
[b] Determined by chiral HPLC analyses [CHIRALPAK® IA (Daicel), 0.46 × 25 cm, 85:15 hexane–*i*-PrOH (1.0 mL/min), 20 °C, λ = 254 nm]; t_R = 11.5 min for (*R*)-**10**, 7.2 min for (*S*)-**10**.
[c] The reaction was performed in a 1 L round-bottomed flask by using **7** (4.34 g), ROL (1.29 g, 30 wt%), phosphate buffer (290 mL), and $(i\text{-Pr})_2O$ (145 mL) at r.t. (24–26 °C).

With axially chiral biphenyl (*R*)-**10** in hand, our next task was the stereocontrolled construction of the stereogenic center at C3′. To this end, we first examined the addition of ethyl acetate-derived lithium enolate to the racemic biphenyl ketones **12a–d** (Table 2, entries 1–4), in which one of the enantiotopic phenol groups was protected as a methoxymethyl ether (P^1), which has potent metal-ion coordinating ability, and the other phenol was protected as a methyl ether or as one of a series of silyl ethers with various steric demands (P^2). We expected that the difference in properties of the protecting groups would permit effective diastereofacial differentiation in enolate addition. However, the results proved disappointing, and the stereoselectivities were very low in all four cases. We then attempted to execute the reaction without protecting one of the phenol groups (P^1 = H; entries 5–7). To our delight, the reactions of racemic **12e–g** proceeded in very high selectivities, regardless of the nature of the phenol-protecting group P^2, to give *tert*-alcohols (R^*,aS^*)-**13e–g** as the major isomers.

Table 2 Diastereoselective Aldol Reaction



Entry	Substrate	P^1	P^2	Yield (%)	dr[a] (**13**/**14**)
1	**12a**	MOM	Me	95	56:44
2	**12b**	MOM	TBDMS	96	68:32
3	**12c**	MOM	TBDPS	96	65:35
4	**12d**	MOM	TIPS	99	67:33
5	**12e**	H	Me	94	97:3
6	**12f**	H	MOM	98	97:3
7	**12g**	H	TBDPS	92	97:3

[a] Determined by ^1H NMR (400 MHz).

The proposed stereochemical course of the reaction is shown in Figure 2. As a result of restricted rotation about the biphenyl linkage and the presence of the five sp^2 carbon atoms, the nine-membered lithium chelate adopts the conformation shown.[18] The enolate preferentially attacks the bottom face of the carbonyl, because the trajectory to the upper face is hindered by the C10′ benzyloxy substituent. Results for the comparative reactions of biphenyl ketones

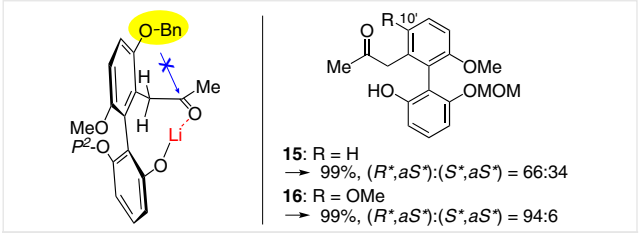
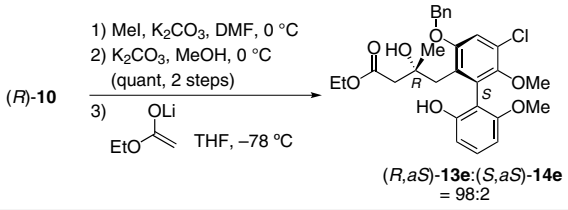


Figure 2 Proposed stereochemical course of the aldol addition

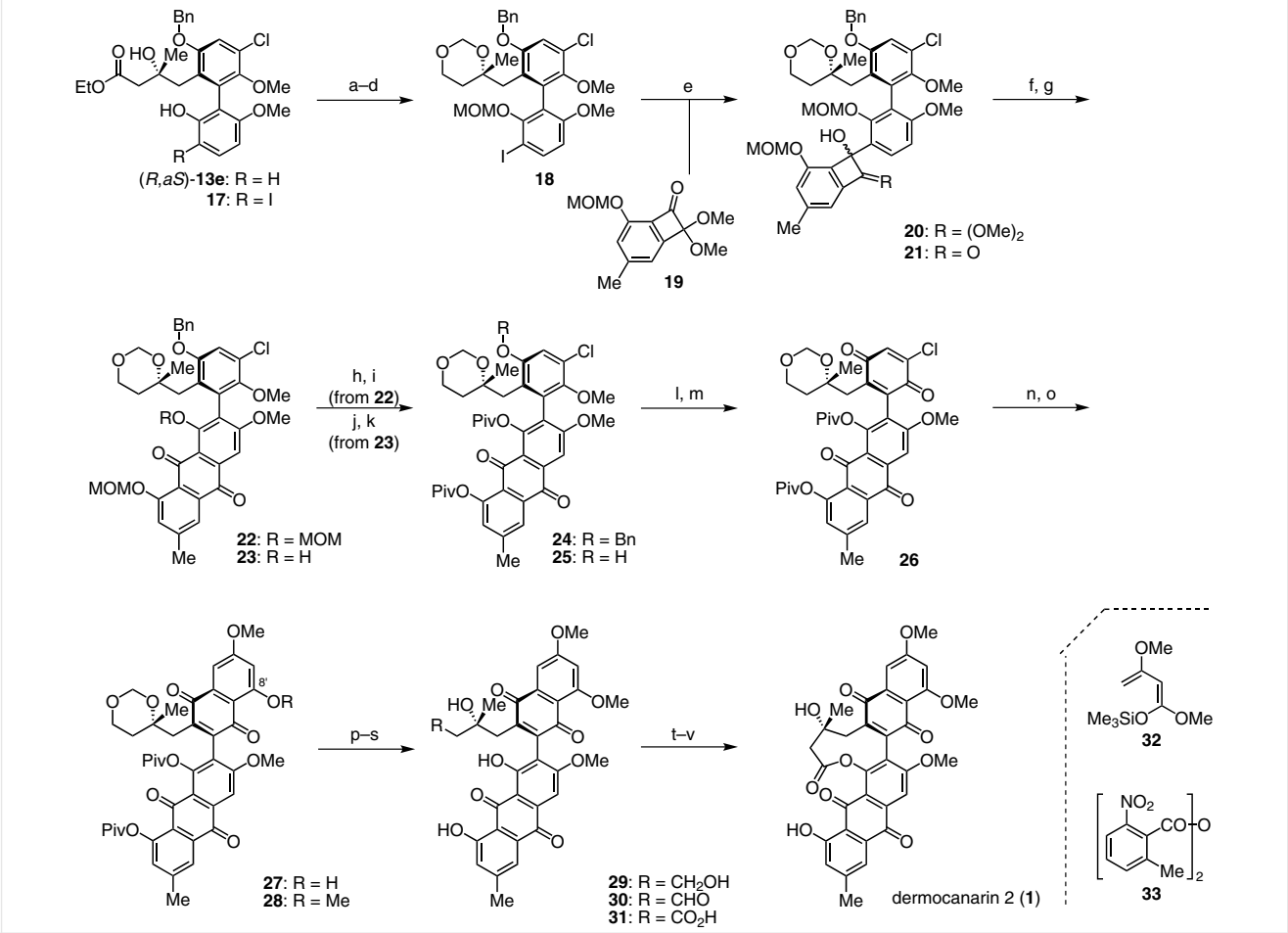


Scheme 4 Synthesis of (*R*,*aS*)-**13e**

15 and **16** under similar conditions supported this hypothesis. The reaction of **15** showed a significant decrease in selectivity [(*R**,*aS**)/(*S**,*aS**) = 66:34], whereas a high selectivity was observed in the reaction of **16**, with a methoxy group in the relevant position [(*R**,*aS**)/(*S**,*aS**) = 94:6].

We then prepared (*R*,*aS*)-**13e**, the planned key intermediate, in an enantiomerically pure form (>99% ee)[19] starting from (*R*)-**10** in three steps: methyl etherification of the phenol, deacetylation, and aldol addition (Scheme 4).

The total synthesis of dermocanarin 2 (**1**) was completed by construction of the anthraquinone and the naphthoquinone moieties, with a final lactonization, as shown in Scheme 5.



Scheme 5 Completion of the total synthesis of **1**. *Reagents and conditions:* (a) I_2, AgO_2CCF_3, $CHCl_3$, –20 °C, 5 min (**17**: 88%); (b) $LiAlH_4$, Et_2O, –20 to 0 °C, 50 min (85%); (c) $(MeO)_2CH_2$, (±)-CSA, CH_2Cl_2, reflux, 3.5 h; (d) MOMCl, DIPEA, CH_2Cl_2, 0 °C, 1.5 h (88%, 2 steps); (e) *i*-PrMgCl·LiCl, THF, –40 °C, then **19**, –40 to 0 °C, 28 h (85%, dr = 1.4:1); (f) pyridinium *p*-toluenesulfonate, acetone, H_2O, r.t., 30 h (**21**: 87%, dr = 1.4:1); (g) BHT, 1,2-dichlorobenzene, 165 °C, 1 h, then air, 3 h (**22**: 70%, **23**: 11%); (h) 6 M aq HCl, r.t., 5 h; (i) PivCl, DMAP, Et_3N, CH_2Cl_2, 0 °C, 1 h (89%, 2 steps); (j) 6 M aq HCl, r.t., 2.5 h; (k) PivCl, DMAP, Et_3N, CH_2Cl_2, 0 °C, 1 h (85%, 2 steps); (l) H_2, Pd/C, EtOAc, r.t., 40 min (**25**: 88%); (m) CAN/SiO_2, CH_2Cl_2, H_2O, 0 °C, 10 min; (n) **32**, toluene, r.t., 1.5 h, then SiO_2, r.t., 12 h; (o) K_2CO_3, EtOH, 0 °C, 1.5 h (72%, 3 steps); (p) MeI, K_2CO_3, DMF, 0 °C, 5 h (**28**: 82%); (q) 1 M aq NaOH, MeOH, 0 °C, 34 h (94%); (r) $(F_3CCO)_2O$, AcOH, r.t., 2 h (82%); (s) K_2CO_3, MeOH, 0 °C, 5 h (99%); (t) IBX, DMSO, r.t., 2.5 h (**30**: 93%); (u) $NaClO_2$, NaH_2PO_4, 2-methylbut-2-ene, *t*-BuOH, H_2O, r.t., 15 min; (v) **33**, DMAP, CH_2Cl_2, 0 °C, 15 min (70%, 2 steps). BHT = 2,6-di-*tert*-butyl-4-methylphenol; IBX = 2-iodoxybenzoic acid.

To construct the anthraquinone, the biphenyl ester (*R*,*aS*)-**13e** was first converted into the iodide **18** (Scheme 5). Selective iodination at the position *ortho* to the unprotected phenol was effected by the treatment with I_2 and AgO_2CCF_3 ($CHCl_3$, –20 °C).[20] Reduction of the ester moiety with $LiAlH_4$ (Et_2O, –20 to 0 °C) proceeded cleanly without affecting the iodine substituent. The resulting 1,3-diol moiety was protected as the methylene acetal [$(MeO)_2CH_2$, CSA, CH_2Cl_2, reflux], and the phenol was protected as the methoxymethyl ether (MOMCl, DIPEA, CH_2Cl_2, 0 °C) to give iodide **18** in 88% yield. Treatment of iodide **18** with *i*-PrMgCl·LiCl[21] in THF at –40 °C, followed by addition of the benzocyclobutenone **19**[22] gave the adduct **20** as a mixture of diastereomers (dr = 1.4:1) which was then converted into ketone **21** by acid hydrolysis of the dimethyl acetal moiety (pyridinium *p*-toluenesulfonate, acetone, H_2O).

On heating at 165 °C in 1,2-dichlorobenzene in the presence of 2,6-di-*tert*-butyl-4-methylphenol,[23] ketone **21** underwent a sequential electroreversion/electrocyclization to give a dihydroanthraquinone, which, on exposure to air, gave anthraquinone **22** in 70% yield, along with the byproduct **23** (11%), formed by detachment of one of the MOM groups. Anthraquinones **22** and **23** were individually converted into pivaloate **24**. Importantly, this procedure for construction of the anthraquinone, despite requiring a high temperature, preserved the stereochemical integrity of (*R*,*aS*)-**13e**.

After removal of the benzyl group from **24** (H_2, Pd/C, EtOAc), the resulting phenol was cleanly oxidized by ceric ammonium nitrate impregnated silica gel (CH_2Cl_2, H_2O, 0 °C) to give the benzoquinone **26**.[24,25] Diels–Alder reaction of **26** with the siloxy diene **32**[8] proceeded smoothly at room temperature in toluene to give the naphthoquinone **27** in 72% yield after conversion of the silyl acetal moiety into a carbonyl group during workup on silica gel, followed by aromatization with K_2CO_3 in ethanol. Subsequent methylation of the C8′ phenol (MeI, K_2CO_3, DMF, 0 °C) led to the completion of the naphthoquinone structure of dermocanarin 2.

We then proceeded to the final lactonization stage. Cleavage of the two pivaloyl groups by alkaline hydrolysis (1 M aq NaOH, MeOH, 0 °C) and liberation of the 1,3-diol in the side chain in high yield by sequential treatment with $(F_3CCO)_2O$ in AcOH and with K_2CO_3 and MeOH (0 °C)[26] gave the tetraol **29**. This was oxidized with 2-iodoxybenzoic acid in DMSO[27] to give the corresponding aldehyde **30**, which was further oxidized with $NaClO_2$ (NaH_2PO_4, 2-methylbut-2-ene, *t*-BuOH, H_2O)[28] to give the trihydroxy acid **31**. Lactonization of **31** was cleanly promoted by the Shiina method using 2-methyl-6-nitrobenzoic anhydride (**33**; DMAP, CH_2Cl_2, 0 °C)[29] to give dermocanarin 2 (**1**) in 70% yield from aldehyde **30**.[30] The spectroscopic data, including the ^1H NMR, ^{13}C NMR, IR, and CD spectra, were in accordance with those reported for natural dermocanarin 2.[30]

In summary, we have accomplished the first total synthesis of dermocanarin 2. The present approach using an axially chiral biphenyl obtained by enzyme-catalyzed desymmetrization of a σ-symmetric precursor as a versatile platform for multidirectional elaboration should find widespread application in syntheses of axially chiral natural products composed of multiply functionalized polyaromatic derivatives that are sterically congested around the axial linkage.

Acknowledgment

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561417.

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(9) Aryl bromide **2** was prepared from the known phenol **34** (see ref. 10), as shown in Scheme 6:
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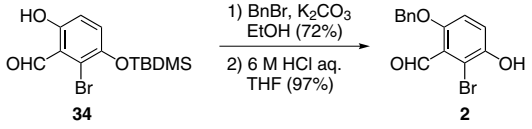

Scheme 6 Synthesis of aryl bromide **2**

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(15) In addition to ROL and PPL, we tested *Pseudomonas fluorescence* lipase (Amano, lipase AK), pig liver esterase (Sigma), *Pseudomonas cepacia* lipase (Amano, lipase PS), *Candida rugosa* lipase (Amano, lipase AY), *Aspergillus niger* lipase (Amano, lipase AS), *Candida antarctica* lipase (Roche Diagnostics, Chirazyme L-2), *Mucor javanicus* lipase (Amano, Lipase M), *Burkholderia cepacia* lipase (Amano, Lipase PS), *Penicillium camembertii* lipase (Amano, Lipase G), and a lipase from *Alcaligenes* sp. (Meito).
(16) Heptane, $(i\text{-Pr})_2O$, Et_2O, CH_2Cl_2, toluene, acetone, DMSO, THF, 1,4-dioxane, MeCN, and *t*-BuOH were tested.
(17) CCDC 1445353 (**10**), 1445412 [(*R**,*aR**)-**35**], 1445413 [(*S**,*aR**)-**36**], 1445869 (**17**), and 1445886 (**18**) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures. Two of these structures are shown in Figure 3.

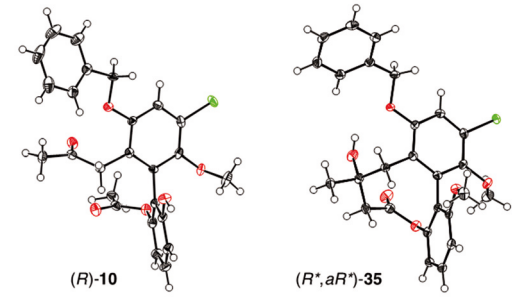
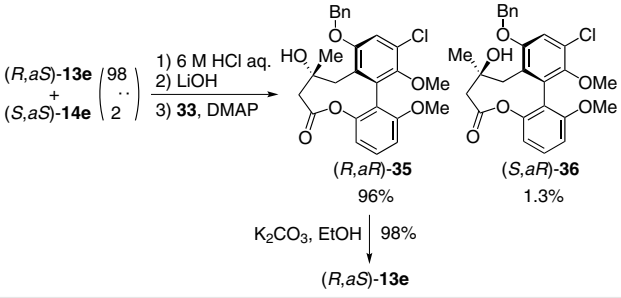


Figure 3 X-ray crystal structures of (*R*)-**10** and (*R**,*aR**)-**35**

(18) The lithium chelate in Figure 2 was drawn on the basis of the DFT-optimized geometries of the model compounds. See the Supporting Information.
(19) Although direct separation of diastereomers (*R*,*aS*)-**13e** and (*S*,*aS*)-**14e** was difficult, conversion into the corresponding lactones **35** and **36**, accomplished quantitatively by Shiina lactonization (Scheme 7), permitted easy separation by silica-gel chromatography. Transesterification of lactone **35** with EtOH and K_2CO_3 regenerated (*R*,*aS*)-**13e** in a diastereomerically pure form. Furthermore, the stereochemistry at C3′ could be determined by means of an X-ray crystal structure analysis of (±)-**35**. A racemic sample of **35** gave a single crystal (colorless plate), suitable for X-ray crystal structure analysis, on crystallization from hexane–CH_2Cl_2, whereas optically pure **35** and **13e** did not.



Scheme 7 Separation of (*R*,*aS*)-**13e**

(20) Janssen, D. E.; Wilson, C. V. *Org. Synth. Coll. Vol. IV 1963*, 547.
(21) Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333.
(22) For the synthesis of ketone **19**, see the Supporting Information; see also: (a) Hamura, T.; Hosoya, T.; Yamaguchi, H.; Kuriyama, Y.; Tanabe, M.; Miyamoto, M.; Yasui, Y.; Matsumoto, T.; Suzuki, K. *Helv. Chim. Acta* **2002**, *85*, 3589. (b) Tsujiyama, S.; Suzuki, K. *Org. Synth.* **2007**, *84*, 272.
(23) The reaction in the absence of BHT was less successful, giving anthraquinone **22** and **23** in 54% and 5% yields, respectively, together with many unidentified byproducts.
(24) Ali, M. H.; Niedbalski, M.; Bohnert, G.; Bryant, D. *Synth. Commun.* **2006**, *36*, 1751.
(25) Attempts to oxidize of **24** and model compounds **37a**–**c** (Figure 4) under various conditions led to intractable mixtures of products, whereas the reaction of **38** with CAN/SiO_2 in wet CH_2Cl_2 gave the corresponding benzoquinone in 99% yield.

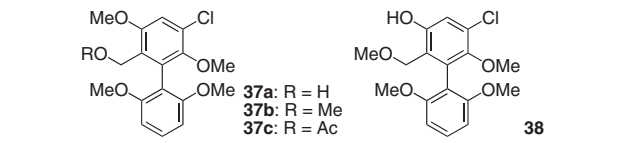


Figure 4 Structures of model compounds for oxidation

(26) Gras, J.-L.; Pellissier, H.; Nouguier, R. *J. Org. Chem.* **1989**, *54*, 5675.
(27) (a) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019. (b) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.
(28) (a) Lindgren, B. O.; Nilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888. (b) Kraus, G. A.; Taschner, M. J. *J. Org. Chem.* **1980**, *45*, 1175. (c) Kraus, G. A.; Roth, B. *J. Org. Chem.* **1980**, *45*, 4825.
(29) (a) Shiina, I. *Chem. Rev.* **2007**, *107*, 239. (b) Shiina, I. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 196.
(30) **Dermocanarin 2 (1); Experimental Procedure for the Final Synthetic Step**
$NaH_2PO_4{\cdot}2H_2O$ (32.7 mg, 210 μmol) and $NaClO_2$ (13.0 mg, 175 μmol) were added to a solution of aldehyde **30** (23.7 mg, 39.4 μmol) and 2-methylbut-2-ene (167 mg, 2.38 mmol) in *t*-BuOH (4.0 mL) and H_2O (1.0 mL) at r.t., and the mixture was stirred for 15 min. The mixture was then poured into brine at 0 °C, and the

products were extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was dissolved in CH_2Cl_2 (6.0 mL) and added to a solution of 2-methyl-6-nitrobenzoic anhydride (**33**; 29.1 mg, 84.6 µmol) and DMAP (19.8 mg, 162 µmol) in CH_2Cl_2 (1.0 mL) at 0 °C. The mixture was then stirred for 15 min before the reaction was stopped by adding 0.1 M phosphate buffer (pH 7). The products were extracted with CH_2Cl_2, and the combined organic extracts were washed sequentially with 1 M aq HCl, brine, sat. aq $NaHCO_3$, and brine, then dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by preparative TLC [$CHCl_3$–MeOH (95:5)] to give dermocanarin 2 (**1**) as a yellow solid; yield: 16.6 mg (70%, 2 steps). Reprecipitation from hexane–CH_2Cl_2 followed by crystallization (EtOH, –20 °C) gave a yellow powder; mp 227–230 °C (dec.); R_f = 0.63 ($CHCl_3$–MeOH, 95:5); $[\alpha]_D^{22}$ +2.1 × 10^2 (*c* 0.50, $CHCl_3$); IR (ATR): 3505, 1774, 1657, 1632, 1582 cm^{-1}; HRMS (ESI-TOF): *m*/*z* calcd $[M + H]^+$ for $C_{33}H_{27}O_{11}$: 599.1553; found: 599.1563.

The ^1H NMR (Table 3) and ^{13}C NMR data (Table 4) for synthetic and natural dermocanarin 2 (**1**) are listed.

Table 3 ^1H NMR (400 MHz, $CDCl_3$) of Dermocanarin 2 (**1**)

	Synthetic	Reported[3b]
2-H	7.12 (s)	7.12 (br s)
4-H	7.64 (s)	7.64 (br s)
5-H	7.83 (s)	7.83 (s)
3-Me	2.47 (s)	2.47 (s)
6-OMe	3.99 (s)	3.98 (s)
1-OH	12.39 (s)	12.38 (s)
2′-H_A	2.51 (d, *J* = 13.2 Hz)	2.47 (d, *J* = 13.2 Hz)
2′-H_B	2.72 (d, *J* = 13.2 Hz)	2.71 (d, *J* = 13.2 Hz)
4′-H_A	1.98 (d, *J* = 13.5 Hz)	1.97 (d, *J* = 13.9 Hz)
4′-H_B	3.36 (d, *J* = 13.5 Hz)	3.36 (br d, *J* = 13.9 Hz)
5′-H	7.32 (d, *J* = 2.4 Hz)	7.32 (d, *J* = 2.4 Hz)
7′-H	6.75 (d, *J* = 2.4 Hz)	6.75 (d, *J* = 2.4 Hz)
3′-Me	1.40 (s)	1.39 (s)
3′-OH	3.05 (s)	3.03 (s)
6′-OMe	3.97 (s)	3.96 (s)
8′-OMe	3.92 (s)	3.92 (s)

Table 4 ^{13}C NMR (100 MHz, $CDCl_3$) of Dermocanarin 2 (**1**)

	Synthetic	Reported[3b]		Synthetic	Reported[3b]
C-1	162.6	162.6	C-2′	44.1	44.1
C-2	125.1	125.1	C-3′	71.3	71.3
C-3	148.2	148.2	C-4′	40.6	40.6
C-4	120.8	120.9	C-4a′	143.3	143.3
C-4a	132.2	132.2	C-5′	104.2	104.2
C-5	107.0	107.0	C-6′	162.1	162.2
C-6	161.7	161.7	C-7′	104.5	104.6
C-7	125.5	125.5	C-8′	164.8	164.8
C-8	151.1	151.2	C-8a′	114.2	114.3
C-8a	118.1	118.1	C-9′	178.8	178.8
C-9	186.4	186.4	C-9a′	142.9	142.9
C-9a	114.1	114.1	C-10′	185.7	185.7
C-10	181.6	181.6	C-10a′	135.8	135.8
C-10a	137.2	137.2	3′-Me	33.9	33.9
3-Me	22.1	22.1	6′-OMe	56.4	56.5
6-OMe	57.0	57.0	8′-OMe	56.0	56.0
C-1′	166.6	166.6			