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Regiocontrolled Benzannulation of Diaryl(*gem*-dichlorocyclopropyl)methanols for the Synthesis of Unsymmetrically Substituted α-Arylnaphthalenes: Application to Total Synthesis of Natural Lignan Lactones

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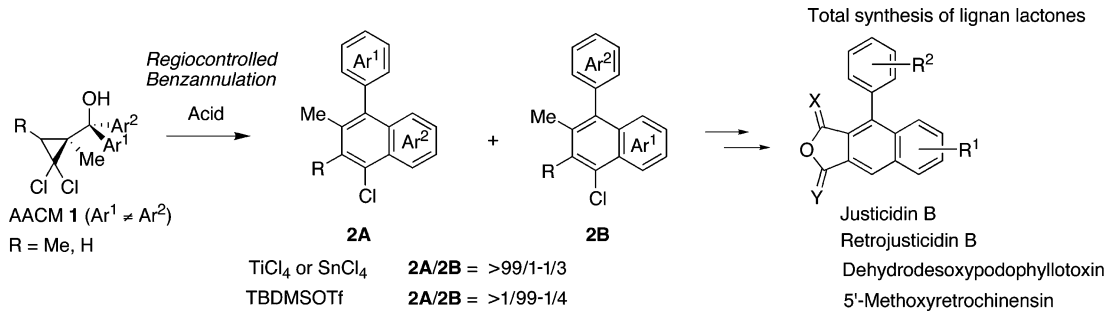

An efficient synthesis of highly substituted α-arylnaphthalene analogues has been developed utilizing Lewis acid-promoted regiocontrolled benzannulation of aryl(aryl′)-2,2-dichlorocyclopropylmethanols (aryl ≠ aryl′; abbreviated as AACMs). Both AACM diastereomers were easily prepared via highly stereoselective addition (>95/5) of ArLi to *gem*-dichlorocyclopropropyl aryl′ ketones. The choice of Lewis acids determined the cyclization regioselectivity of the present benzannulation. $TiCl_4$ and $SnCl_4$ used the chelation pathway, whereas silyl triflates used a nonchelation pathway to give *unsymmetrically* substituted regioisomeric α-arylnaphthalenes in 40−91% yields with moderate to excellent regioselectivity ($TiCl_4$ or $SnCl_4$; >99/1−3/1, TBDMSOTf; >1/99−1/4). Thus, the α-aryl or α-aryl′ moiety (accessory aryl group) was alternatively introduced to α-arylnaphthalenes by choosing either the order of the reaction sequences or the appropriate catalyst. Application of the present method to the total synthesis for *unsymmetrically* substituted natural lignan lactones, justicidin B, retrojusticidin B, dehydrodesoxypodophyllotoxin, and a related analogue, 5′-methoxyretrochinensin, was demonstrated. Lignan retrolactones (retrojusticidin B and 5′-methoxyretrochinensin) were synthesized by the conventional lactonization of the diol precursor, whereas a novel Bu_2SnO-mediated monoacylation method was applied to the synthesis of normal lignan lactones (justicidin B and dehydrodesoxypodophyllotoxin).

Introduction

Highly substituted α-arylnaphthalene analogues are attracting considerable attention due to their widespread distribution in nature and multiple significant biological activities.[1] Several efficient methods for their synthesis have been reported:[2] (a) Michael addition of cyanohydrin with α,β-unsaturated carboxylates, follwed by aldol reaction with aldehyde, and intramolecular Friedel−Crafts cyclization,[2a] (b) sequential Michael addition of 2-(α-lithio)benzonitriles with α,β-unsaturated carboxylates, followed by intramolecular cyclization,[2b] (c) Diels−Alder addition of benzoisofurans to the dienophile,[2c−g] (d) Horner−Wadsworth−Emmons reaction, followed by Claisen condensation,[2h] (e) Pd-catalyzed benzannulation,[2i,j]

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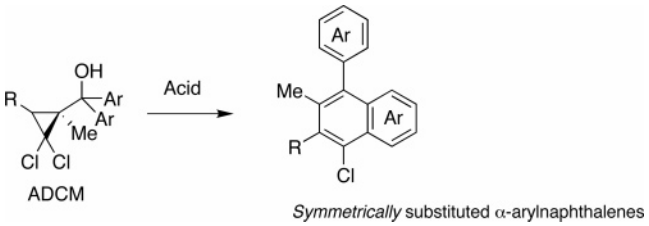
(f) transition-metal-mediated electrocyclization,[2k−m] (g) Pd-catalyzed intramolecular coupling of phenyl 2-bromonaphthoate, followed by asymmetric reduction of lactones,[2n,o] (h) transition metal-catalyzed [2 + 2 + 2] cycloaddition between α,ω-diynes and alkynes or arynes,[2p,q] and (i) others.[2r−u]

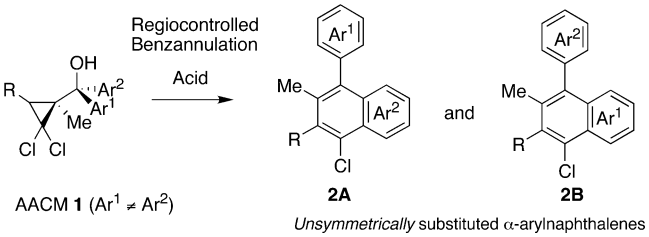
The characteristic features of cyclopropa(e)nes have brought about a number of both unique and useful synthetic reactions.[3] Consistent with our synthetic studies on the transformation of *gem*-dihalocyclopropanes from many-sided cationic,[4a−g] radical,[4h−j] and anionic[4k] type approaches, we previously reported acid-promoted (CF_3CO_2H, BF_3·OEt_2, $TiCl_4$, $SnCl_4$) benzannulation utilizing diaryl(dihalocyclopropyl)methanols (ADCMs), which provide various α-arylnaphthalenes.[4a,d,g] Closely related benzannulation for the synthesis of α-arylnaphthols is also documented.[4b,e] Acid-promoted benzannulation of ADCMs, however, is limited to the synthesis of *symmetrically* substituted α-arylnaphthalenes (Scheme 1).

To overcome this major problem, we focused our attention on a more efficient benzannulation. We disclose herein full details of Lewis acid ($TiCl_4$, $SnCl_4$, *Si*OTf) -promoted *regiocontrolled benzannulation* of aryl(aryl′)-(dihalocyclopropyl)methanols (aryl ≠ aryl′; abbreviated as AACMs) **1**, alternatively producing *unsymmetrically* substituted α-arylnaphthalenes **2A** and **2B** (Scheme 2) (part of this work appeared in a preliminary communication[4f]). Recently, as a notable extension of the present protocol, we achieved the chirality exchange benzannulation from sp^3 central chirality to axial chirality using optically active *ortho*-R^1-substituted AACMs to obtain axially chiral α-arylnaphthalenes with excellent enantioselectivity.[5]

SCHEME 1



SCHEME 2



Unsymmetrically substituted α-arylnaphthalene derivatives are attracting much attentions as a synthetic target, because they served as the basic skeleton of several biologically active lignan-type natural products.[6] Application of the present benzannulation to the total synthesis of three *unsymmetrically* substituted natural lignan lactones, justicidin B,[2a,h,s,6a] retrojusticidin B,[2h,s,6a,d] and dehydrodesoxypodophyllotoxin,[2s,6b] and a related analogue, 5′-methoxyretrochinensin,[2s,6c] was evaluated. The family of these lignans exhibits significant biological activities, for example, inhibitor of HIV-1 reverse transcriptase, and antiviral, antifungal, antitumor, hypolidemic, anti-PAF (platelet activating factor) activities.

Results and Discussion

Benzannulation of 2,2-Dichloro-1-methylcyclopropyl(phenyl)methanols. As a preliminary experiment, we examined benzannulation of *syn* (*erythro*) and *anti* (*threo*) diastereomers of 2,2-dichloro-1-methylcyclopropyl(phenyl)methanol **3**[4d] to check the reactivity (Scheme 3). *syn*-**3** was readily prepared by the reported procedures: (i) stereoselective addition of 2,2-dichloro-1-methylcyclopropanecarbaldehyde with PhMgBr (75% yield, *syn*/*anti* = 7/1) and (ii) Grignard reaction of PhMgBr with 2,2-dichloro-1-methylcyclopropanecarbonyl chloride (98% yield), followed by highly stereoselective $NaBH_4$ reduction

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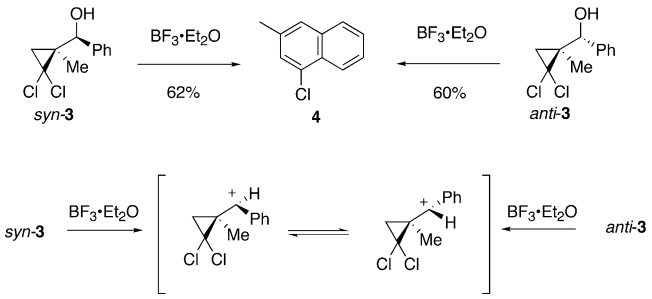
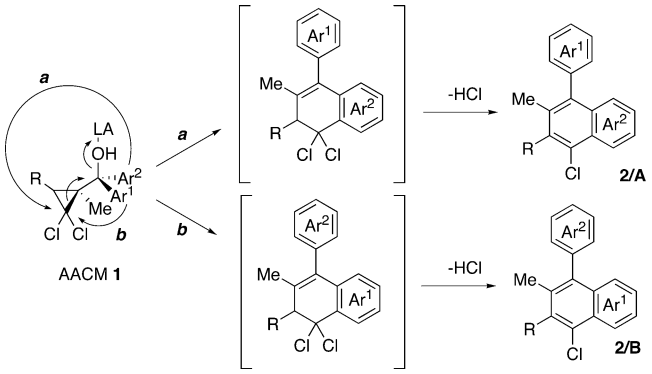
SCHEME 3



SCHEME 4



(65% yield, *syn*/*anti* = 98/2). *anti*-**3** was successfully obtained from *syn*-**3** using the recently reported method (Mukaiyama and co-workers)[7] for the inversion of sterically hindered alcohols in 40% yield (see the Supporting Information).

Each reaction using *syn*-**3** or *anti*-**3** gave 1-chloro-3-methylnaphthalene (**4**) in almost the same yield (ca. 60%). This result indicates that both reactions with BF_3·OEt_2 proceed via the same cationic intermediate through an S_N1'-like mechanism, and are consequently nonregioselective. It is difficult to differentiate two aryl groups during the benzannulation, which was conducted through an SN1′-type pathway. Provided that the conformations of the AACMs **1** are suitably fixed during the ring-opening step, however, the cyclization-orientation would be rationally controlled through path ***a*** or ***b*** (Scheme 4).

Highly Stereoselective Synthesis of AACMs. To investigate the regioselectivity of the benzannulation, C_6D_5-substituted diastereomers of AACMs **1a**−**c** were synthesized via highly stereoselective addition (**1**/**1**′ = > 95/5) of PhLi-d_5 to ketones **6a**−**c**, which were prepared from *gem*-dichlorocyclopropanecarbonyl chlorides **5a**−**c** by the reported procedure[4f] (Scheme 5). By switching these reaction sequences, diastereomeric AACM **1a**′ was similarly synthesized from **6a**′. The relative configuration of **1** or **1**′ was determined based on a previous report:[4d,f] ArLi attacked the less hindered side of the preferential *s-cis* conformer of **6** or **6**′ following the Cram's rule.

Regiocontrolled Benzannulation of AACMs to α-Arylnaphthalenes. Table 1 lists the results of the benzannulation of **1a**−**c** using several Lewis acid reagents. CF_3CO_2H and BF_3·OEt_2 were not effective with regard to regioselectivity (ratio of **A/B** = 2/3 and 1/1, entries 1, 2), the results of which were equivalent to aforementioned reaction of 2,2-dichloro-1-methylcyclopropyl(phenyl)methanol (**3**). On the other hand, $SnCl_4$ and $TiCl_4$ allowed for the regioselective benzannulations to give α-C_6H_5-5,6,7,8-tetradeuterionaphthalenes **2a**−**c/A** as the major products (entries 3−5, 9, 11). Lower temperature (from 0 to −60 °C) enhanced the selectivity (entries 4, 9, 11). In clear contrast, silyl triflates predominantly gave the other regioisomer, α-C_6D_5-naphthalenes **2a**−**c/B**. The reaction of **1a** was superior to that of **1b** in yield and similar with **A/B** regioselectivity (entries 4 and 9, 8 and 10).

These findings ruled out the possibility that the present benzannulation proceeds via the same cationic intermediate and the same transition state. Thus, a chelation mechanism is proposed in the case of MCl_4 (M = Sn, Ti) and a nonchelation mechanism for the case of

SCHEME 5

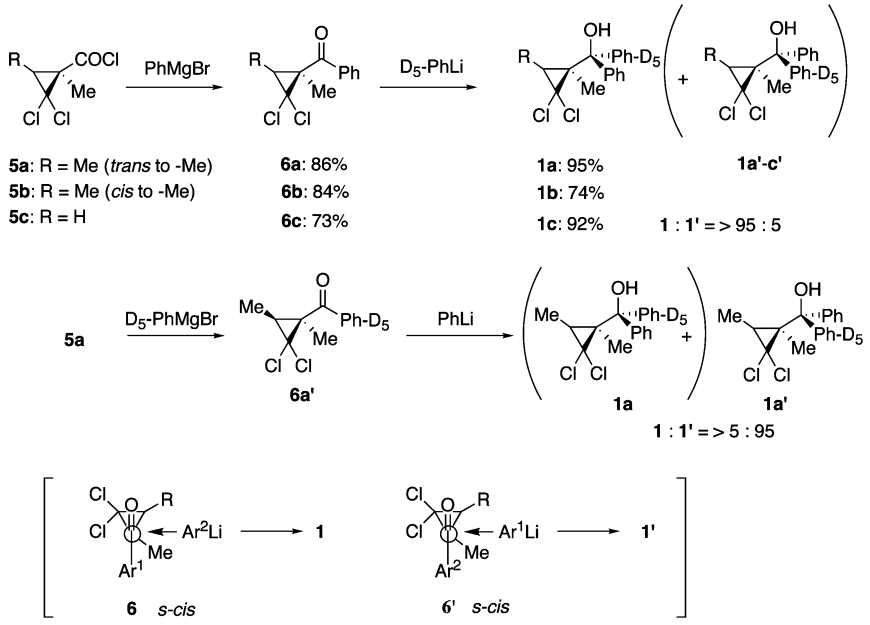
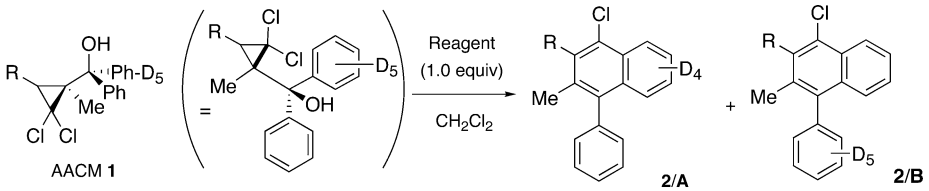


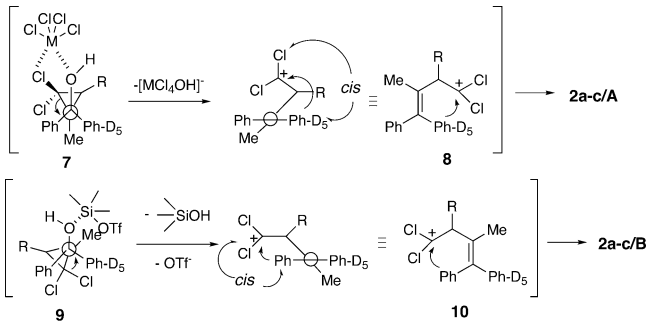
TABLE 1. Regiocontrolled Benzannulation of AACMs 1a−c



Entry	AACM	Reagent	Temp. / ˚C	Product	A/B[a]	Yield /%[b]
1		CF_3CO_2H	0-5	**2a**	2/3	83[c]
2		$BF_3 \cdot OEt_2$	0-5		1/1	94
3	**1a**	$TiCl_4$	0-5		5/1	38
4		$TiCl_4$	-60		92/8	91
5		$SnCl_4$	-60		3/1	90
6		TMSOTf	-60		1/2	35
7		TBDMSOTf	-60		1/6	43
8		TBDMSOTf	-60		1/5	84[d]
9		$TiCl_4$	-60	**2b** (= **2a**)	10/1	46
10	**1b**	TBDMSOTf	-60		1/4	49[d]
11		$TiCl_4$	-60	**2c**	97/3	81
12	**1c**	TBDMSOTf	-60		7/93	51[d]

[a] Determined by ^{1}H NMR. [b] Isolated yield. [c] CF_3CO_2H was used as solvent. [d] Reaction was carried out in toluene.

SCHEME 6



silyl triflates as illustrated in Scheme 6. MCl_4 chelates with the oxygen and chlorine atoms of AACMs **1** to give the rigid intermediate **7**, which in turn eliminates the OH group together with regioselective ring-opening to give cationic intermediate **8**: the *gem*-dichlorocarbenium ion moiety orients itself in the cis position of the D_5Ph group. Finally, Friedel−Crafts type cyclization occurs to give α-C_6H_5-5,6,7,8-tetradeuterionaphthalenes **2a**−**c/A**.

In contrast, silyl triflates coordinate with the oxygen of AACMs **1** to give intermediate **9**, wherein *gem*-dichlorocarbenium ion moiety is located in an *anti*-position to the bulky silyl group bearing the OH group. Then, the elimination of silanols occurs to give the cationic intermediate **10**: the carbocation moiety orients itself in the cis position of the Ph group to give α-C_6D_5-naphthalenes **2a**−**c/B**.

Next, regiocontrolled benzannulation of AACMs **1d**, **1d′**, **1e**, and **1e′** was examined (Table 2). These AACMs were prepared in good yield with stereoselectivity (>95/5) via the aforementioned two alternative methods. Seven crossover experiments demonstrated the usefulness of the present method (entries 1−5, 7, 8). Only one case (entry 6) using **1e** with TBDMSOTf failed to undergo benzannulation and gave an unidentified complex mixture.

Application to Total Synthesis of Natural Lignan Lactones. Encouraged by these successful results, we applied the present method to the total synthesis of three natural arylnaphthalene lignan lactones, justicidin B (**15**)[2a,h,s,6a] retrojusticidin B (**16**),[2h,s,6a,d] and dehydrodesoxypodophyllotoxin (**17**),[2s,6b] and a related synthetic analogue, 5′-methoxyretrochinensin (**18**).[2s,6c] The construction of *unsymmetrically* substituted 4-aryl-2,3-dimethylnaphthalene (lignan) skeletons is the key step.

As shown in Scheme 7, *gem*-dichlorocyclopropanecarbonyl chloride **5a** was converted to AACM **1f** with high regioselectivity by sequential couplings with 3,4-methylenedioxyphenylmagnesium bromide and with 3,4-dimethoxyphenyllithium via intermediary ketone **6f**. In a similar manner, AACM **1g** was prepared from **5a** by successive treatment with 3,4,5-trimethoxyphenyllithium and 3,4-methylenedioxyphenyllithium.

The key regiocontrolled benzannulations of AACMs **1f** and **1g** were successfully performed to afford **2f/A** and **2g/A**, respectively as major products in good yield with highly selectivity (Scheme 8). These reactions were performed using 1.0 equiv of $SnCl_4$ in highly diluted (ca. 0.001 M in 1,2-dichloroethane) in order to circumvent undesirable intermolecular reactions. Unfortunately, the benzannulation of **1f** and **1g** using of $TiCl_4$ gave **2f/A**/**2f/B** and **2g/A**/**2g/B**, respectively, both in ca. 50% total yields with ca. 1:1 regioselectivities.

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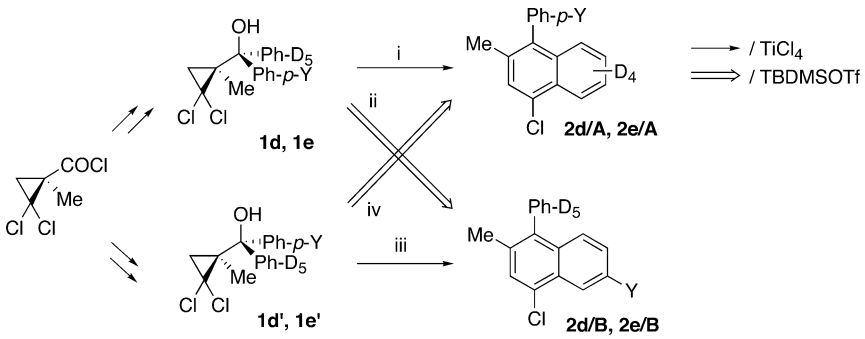
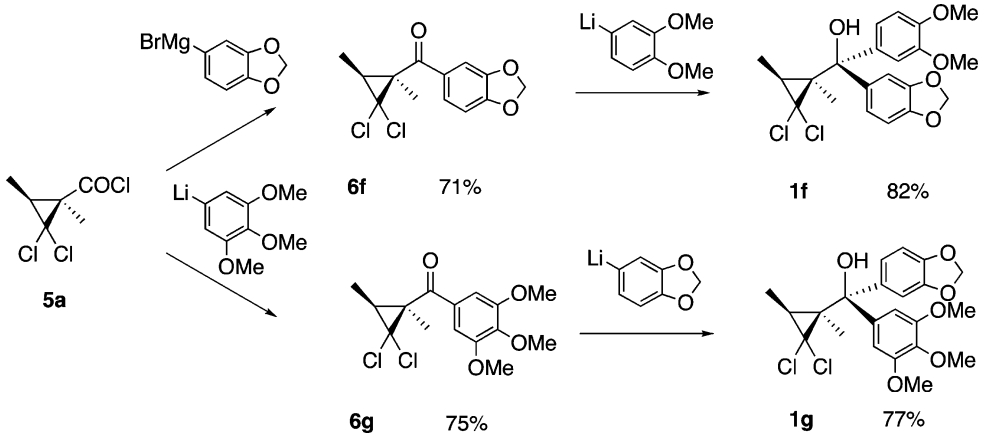
TABLE 2. Regiocontrolled Benzannulation of AACMs 1d, 1e, 1d′, and 1e′[a]



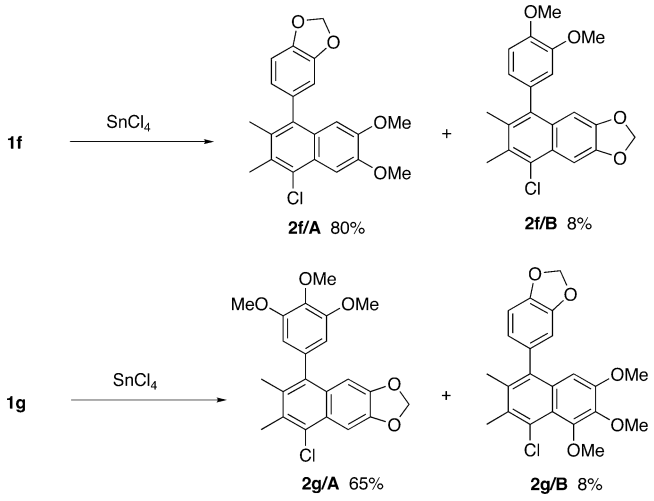
entry	AACM	Y	reagent	major reaction	product	A/B[b]	yield[c] (%)
1	**1d**	Me	$TiCl_4$	i	**2d**	93/7	52
2			TBDMSOTf	ii	**2d**	>1/99	62
3	**1d′**	Me	$TiCl_4$	iii	**2d**	>1/99	40
4			TBDMSOTf	iv	**2d**	96/4	44
5	**1e**	Cl	$TiCl_4$	i	**2e**	95/5	70
6			TBDMSOTf	ii	**2e**		0
7	**1e′**	Cl	$TiCl_4$	iii	**2e**	20/80	68
8			TBDMSOTf	iv	**2e**	>99/1	43

[a] Reaction was carried out at −60 °C. [b] Determined by ^{1}H NMR. [c] Isolated yield.

SCHEME 7



SCHEME 8

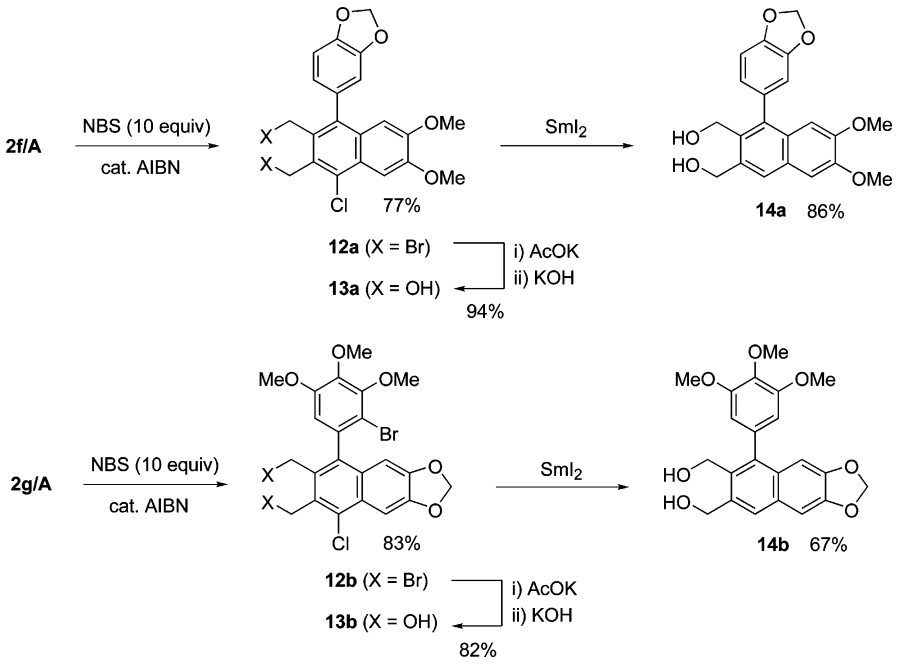


The rational order of the inherent reactivity is 3,4,5-trimethoxyphenyl > 3,4-dimethoxylphenyl > 3,4-methylenedioxyphenyl.[8] Computational calculations also support this view (see the Supporting Information). Nevertheless, "disadvantageous" α-arylnaphthalene **2g/A** was predominantly produced through the present chelation-controlled benzannulation. Namely, the annulation selectivity depends not on the reactivity of aryl group, but on the relative configuration and conformation ($SnCl_4$: chelation-mechanism) of AACM. The nonchelation benzannulation of AACMs **1f** and **1g** using TBDMSOTf, however, failed to proceed and produced unidentified products. A 3,4-di- or 3,4,5-trimethoxy substituent on the benzene ring might interrupt the ideal coordination between TBDMS and OH groups of AACMs **1f** and **1g**.

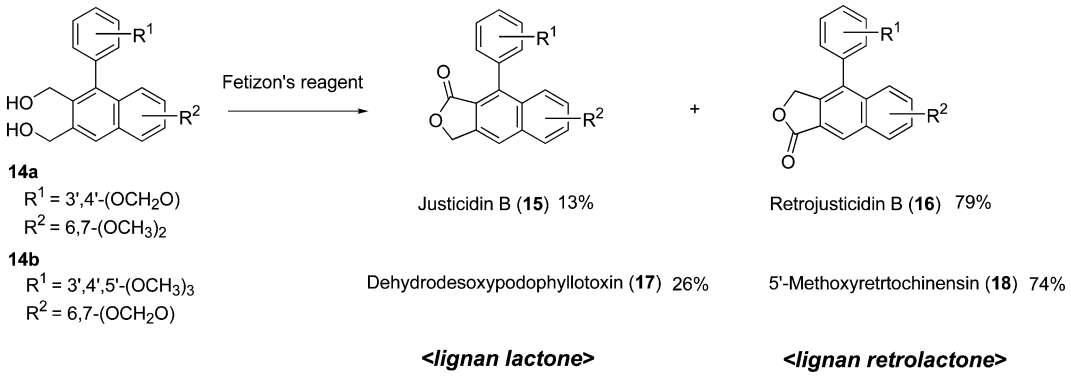
Thus, the basic lignan skeleton framework of the natural lignan lactones **15**, **16**, **17**, and **18** was constructed. Conventional derivatization leading to the corresponding lignan lactones was performed as follows (Schemes 9 and 10). Dibromination of vicinal methyl

(8) Sha and co-workers point out that the Friedel−Crafts reactivity of 3,4-dimethoxylphenyl is higher than that of 3,4-methylenedioxyphenyl during the formation of the cephalotaxane skeleton, due to the favorable planar π-electron overlap of the 3,4-dimethoxy group. Sha, C.-K.; Young, J.-J.; Yeh, C.-P.; Chang, S.-C.; Wang, S.-L. *J. Org. Chem.* **1991**, *56*, 2694.

SCHEME 9



SCHEME 10



groups of naphthalene **2f/A** gave dibromide **12a** using 10 equiv of NBS under optimized conditions. In contrast, using **2g/A** under the same conditions resulted in the formation of tribromide **12b** due to its high reactivity of the 3,4,5-trimethoxyphenyl group. Treatment of **2g/A** with 2.2 equivalent of NBS gave an inseparable 1:1 mixture of tribromide **12b** and the corresponding dibromide in moderate yield (58%). Dibromide **12a** was converted to diol **13a** upon successive treatment with AcOK followed by KOH. Similar procedures using tribromide **12b** gave diol **13b**. All the halogen atoms on the aromatic rings of **13a** and **13b** were smoothly removed by the SmI_2-mediated reduction[9] to give the desired diols **14a** and **14b**, respectively. Finally, oxidation of diol **14a** using Fetizon's reagent (Ag_2CO_3−Celite),[10] followed by separation of the regioisomers gave justicidin B (**15**) (13%) and retrojusticidin B (**16**) (79%), respectively. Similar procedures using **14b** gave dehydrodesoxypodophyllotoxin (**17**) (26%) and its isomeric synthetic analogue 5′-methoxyretrochinensin (**18**) (74%) in quantitative yield.

The aforementioned conventional transformation to the lignan lactones[11] is relatively suitable for the synthesis of retrolactones such as **16** and **18**, however, there remains regioselective synthesis of natural lignan lactones. To this end, we applied the Bu_2SnO-mediated monoacylation (protection) method of vicinal diols with acyl chlorides[12] through the key Sn(IV)−metallacyclic intermediate **19a, b** (Scheme 11). To enhance the regioselectivity for the monoacylation of the less hindered hydroxyl group of the intermediate, we chose bulky pivaloyl chloride. As expected, the pivaloyl group was

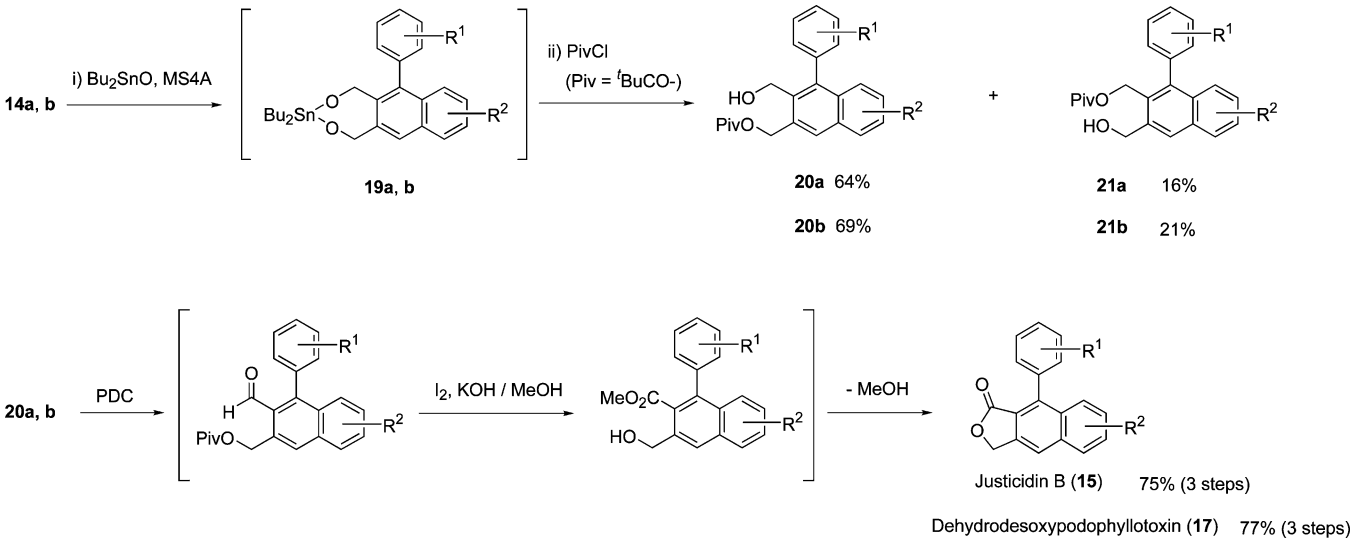
(9) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett*. **1987**, 1485.

(10) (a) Fetizon, M.; Golvier, M. C. R. *Hebd. Seances Acad. Sci.* **1968**, *267*, 900. (b) Fetizon, M.; Golfier, M.; Louis, J. M. *J. Chem. Soc., Chem. Commun*. **1969**, 1102 and 1118. (c) Fetizon, M.; Golfier, M.; Louis, J. M. *Tetrahedron* **1975**, *31*, 171.

(11) (a) Holmes, T. L.; Stevenson, R. *J. Chem. Soc., C* **1971**, 2091. (b) Holmes, T. L.; Stevenson, R. *J. Org. Chem.* **1971**, *36*, 3450. (c) Block, E.; Stevenson, R. *J. Org. Chem.* **1971**, *36*, 3453. (d) Arnold, B. J.; Mellows, S. M.; Sammes. P. G. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1266. (e) Horii, Z.; Tujiuchi, M.; Kanai, K.; Momose, T. *Chem. Pharm. Bull.* **1977**, *25*, 1803.

(12) (a) Shanzer, A. *Tetrahedron Lett.* **1980**, 221. (b) Mukaiyama, T.; Tomioka, I.; Shimizu, M. *Chem. Lett.* **1984**, 49. (c) T. Mukaiyama, Y. Tanabe, M. Shimizu, *Chem. Lett*. **1984,** 401. (d) David, S.; Hanessian, S. *Tetrahedron* **1985**, 41, 643. (e) Aragozzini, F.; Maconi, E.; Potenza, D.; Scolatico, C. *Synthesis*, **1989**, 225.

SCHEME 11



selectively introduced into the outer hydroxyl groups of **14a** and **14b** to give **20a** (64%) and **20b** (69%), respectively, as major products by column chromatographic separation from **21a** and **21b**.

Eventually, PDC oxidation of alcohols **20a** and **20b** gave the corresponding aldehydes, which were treated with I_2−KOH in MeOH[13] to give justicidin B (**15**) (76%) and dehydrodesoxypodophyllotoxin (**17**) (77%), respectively, wherein oxidation to methyl esters, deprotection of the pivaloyl group, and lactonization proceeded successively in a one-pot manner.

Conclusions

We developed regiocontrolled benzannulation of AACMs for the synthesis of "unsymmetrically" substituted α-arylnaphthalenes. The choice of Lewis acids determined the cyclization regioselectivity during the benzannulation: $TiCl_4$ and $SnCl_4$ utilized the chelation pathway, whereas silyl triflates utilized a nonchelation pathway. As a notable application, regioselective total syntheses of three natural lignan lactones, justicidin B, retrojusticidin B, and dehydrodesoxypodophyllotoxin, and a synthetic analogue, 5′-methoxyretrochinensin were performed. The present method is a new avenue for the synthesis of a variety of useful and/or biologically active α-arylnaphthalenes.

Experimental Section

(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](phenyl)-methanol (*syn*-3).** *syn*-**3** was readily prepared by the reported procedures;[4d] (i) stereoselective addition of 2,2-dichloro-1-methylcyclopropanecarbaldehyde with PhMgBr and (ii) condensation of PhMgBr with 2,2-dichloro-1-methylcyclopropanecarbonyl chloride, followed by highly stereoselective $NaBH_4$ reduction.

(*R)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](phenyl)methanol (*anti*-3).** *anti*-**3** was successfully obtained from *syn*-**3** in 40% yield using the reported method.[7] BuLi (1.59 M in hexane, 1.26 mL, 2.0 mmol) was added to a stirred solution of *syn*-**3** (462 mg, 2.0 mmol) in THF (4 mL) at 0−5 °C under an argon atmosphere. After stirring at rt for 1 h, Ph_2PCl (441 mg, 2.0 mmol) in THF (4 mL) was added at 0−5 °C. The reaction mixture was stirred for 1 h at rt, and the solvent was concentrated in vacuo. After the residue was diluted with hexane, the mixture was filtered using Celite to remove LiCl and the resultant solution was concentrated. A mixture of the obtained crude product, benzoic acid (244 mg, 2.0 mmol), and 2,6-dimethyl-1,4-benzoquinone (DMBQ) (272 mg, 2.0 mmol) in CH_2Cl_2 (2 mL) was stirred for 18 h at rt. Water was added to the mixture, which was extracted twice with ether. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2 column chromatography (hexane/ether = 25/1) to give the desired benzoate (309 mg, 46%): colorless crystals; mp 62.0−64.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.42 (d, *Jgem* = 7.57 Hz, 1H), 1.89 (d, *Jgem* = 7.57 Hz, 1H), 6.35 (s, 1H), 7.28−7.44 (m, 3H), 7.47−7.55 (m, 4H), 7.60−7.66 (m, 1H), 8.15−8.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4, 32.1, 34.6, 66.2, 77.2, 126.1, 127.9, 128.5, 128.6, 129.8, 133.4, 137.4, 165.6; IR (KBr) 1723, 764, 731, 711, 698 cm^{-1}. KOH (281 mg, 5.0 mmol) in water (0.5 mL) was added to a stirred solution of benzoate (168 mg, 0.50 mmol) in MeOH (1 mL) at 0−5 °C under argon atmosphere. After the mixture was stirred at rt for 14 h, water was added, and the mixture was extracted twice with ether. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/ether = 5/1) to give the desired product *anti*-**3** (101 mg, 87%): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.44 (d, J_{gem} = 7.22 Hz, 1H), 1.71 (d, J_{gem} = 7.22 Hz, 1H), 4.83 (s, 1H), 7.29−7.34 (m, 1H), 7.37−7.43 (m, 2H), 7.54−7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 31.8, 36.0, 66.5, 75.8, 125.9, 127.6, 128.4, 140.6; IR (neat) 3395, 758, 698 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{12}Cl_2O$ (M+Na$^+$) 253.0163, found 253.0158.

Preparation of AACMs 1. Following the reported procedure,[5] the addition of Ar^{1}MgBr to carbonyl chlorides **5** gave ketones **6**. The addition of Ar^{2}Li to ketones **6** gave AACMs **1**.

(1*R,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropanecarbonyl Chloride (5a).**[4e]

(1*S,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropanecarbonyl Chloride (5b).**[4e]

2,2-Dichloro-1-methylcyclopropanecarbonyl Chloride (5c).[4e,5]

(1*R,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl(phenyl)methanone (6a):** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, *J* = 6.8 Hz, 3H), 1.66 (s, 3H), 1.68 (q, *J* = 6.8 Hz, 1H), 7.51−7.55 (m, 2H), 7.59−7.63 (m, 1H), 7.97−8.00 (m, 2H);

(13) Yamada, S.; Morizono, D.; Yamamoto, K. *Tetrahedron Lett.* **1992**, *33*, 4329.

^{13}C NMR (100 MHz, $CDCl_3$) δ 11.7, 23.2, 35.4, 39.7, 68.2, 128.7, 129.7, 133.5, 134.5, 194.9; IR (neat) 1686, 1451, 1235 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{12}Cl_2O$ (M^+) 242.0265, found 242.0266.

(1*R,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl(pentadeuteriophenyl)methanone (6a′):** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, J = 6.8 Hz, 3H), 1.66 (s, 3H), 1.68 (q, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 23.2, 35.3, 39.6, 68.2, 128.1 (t, J = 24.5 Hz), 129.3 (t, J = 24.5 Hz), 133.0 (t, J = 24.5 Hz), 134.3, 194.8; IR (neat) 1686, 1451, 1235 cm^{-1}; HRMS (EI) calcd for $C_{12}H_7D_5Cl_2O$ (M^+) 247.0574, found 247.0564.

(1*R,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl(phenyl)methanone (6b):** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (d, J = 6.4 Hz, 3H), 1.43 (s, 3H), 2.38 (q, J = 6.4 Hz, 1H), 7.50−7.56 (m, 2H), 7.57−7.64 (m, 1H), 7.92−7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 14.5, 29.1, 41.1, 66.9, 128.6, 129.6, 133.3, 134.8, 196.5; IR (neat) 1686, 1453, 1235 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{12}Cl_2O$ (M+Na^+) 265.0163, found 265.0164.

2,2-Dichloro-1-methylcyclopropyl(phenyl)methanone (6c).[4d,e,5]

2,2-Dichloro-1-methylcyclopropyl(pentadeuteriophenyl)methanone (6c′): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, *Jgem* = 7.4 Hz, 1H), 1.65 (s, 3H), 2.30 (d, *Jgem* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 29.5, 39.7, 62.4, 128.2 (t, J = 24.5 Hz), 129.2 (t, J = 24.5 Hz), 132.9 (t, J = 24.5 Hz), 134.3, 195.4; IR (neat) 3005, 1685, 983, 760, 693 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_5D_5Cl_2O$ (M + Na^+) 256.0315, found 256.0315.

2,2-Dichloro-1-methylcyclopropyl(*p*-tolyl)methanone (6d).[4e]

2,2-Dichloro-1-methylcyclopropyl(4-chlorophenyl)methanone (6e).[4e]

(*S)-[(1*R**,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl](pentadeuteriophenyl)(phenyl)methanol (1a).** BuLi (1.66 M hexane solution, 2.38 mL, 3.95 mmol) was added dropwise to a stirred solution of C_6D_5Br (639 mg, 3.95 mmol) in THF (5 mL) at −60 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Ketone **6a** (800 mg, 3.29 mmol) in THF (4 mL) was added to the mixture at the same temperature. The resulting mixture was allowed to warm to rt during a period of 1 h and was stirred for an additional 5 h at that temperature. The mixture was poured into ice and aqueous sat. NH_4Cl solution (20 mL), and was extracted twice with ether. The combined organic phase was successively washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/ether = 50/1) to give the product **1a** (796 mg, 74%), (**1a/1a′** = >95/5): colorless crystals; mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.52 (q, J = 6.8 Hz, 1H), 1.78 (d, J = 6.8 Hz, 3H), 2.80 (brs, 1H, O*H*), 7.35−7.46 (m, 3H), 7.49−7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 27.8, 36.3, 38.06, 7.94, 83.8, 126.4−127.8 (m, 5*C*D), 127.9, 128.2, 128.9, 144.7, 146.3; IR (KBr) 3557, 3501, 702 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}D_5Cl_2O$ (M + Na^+) 348.0941, found 348.0949.

(*R)-[(1*R**,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl](pentadeuteriophenyl)(phenyl)methanol (1a′).** Following the procedure for the preparation of **1a**, the reaction of **6a′** with C_6H_5Br in the place of C_6D_5Br gave the product **1a′** (72%), (**1a/1a′** = >5/95). **1a′**: colorless crystals; mp 91−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.52 (q, J = 6.8 Hz, 1H), 1.78 (d, J = 6.8 Hz, 3H), 2.80 (brs, 1H, O*H*), 7.20−7.24 (m, 2H), 7.26−7.34 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.1, 27.1, 36.3, 38.1, 73.9, 83.8, 127.1, 127.5, 128.3, 127.3−128.9 (m, 5*C*D), 144.5, 146.5; IR (KBr) 3557, 3501, 702 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}D_5Cl_2O$ (M + Na^+) 348.0941, found 348.0942.

(*S)-[(1*R**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](pentadeuteriophenyl)(phenyl)methanol (1b).** Following the procedure for the preparation of **1a**, the reaction of **6b** with C_6D_5Br gave the product **1b** (74%), (**1b/1b′** = >95/5): colorless crystals; mp 81−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 3H), 1.13 (d, J_{gem} = 6.6 Hz, 3H), 2.69 (q, J_{gem} = 6.6 Hz, 1H), 2.84 (brs, 1H, O*H*), 7.35−7.48 (m, 3H), 7.51−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.2, 17.5, 26.6, 38.2, 72.1, 80.9, 126.5−127.5 (m, 5*C*D), 128.0, 128.2, 129.4, 143.1, 146.4; IR (KBr) 3565, 1335, 706 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}D_5Cl_2O$ (M + Na^+) 348.0941, found 348.0943.

(*S)-[(1*R**)-2,2-Dichloro-1-methylcyclopropyl](pentadeuteriophenyl)(phenyl)methanol (1c).** Following the procedure for the preparation of **1a**, the reaction of **6c** with C_6D_5Br gave **1c** (92%), (**1c/1c′** = >95/5): colorless crystals; mp 66−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.28 (d, J_{gem} = 7.3 Hz, 1H), 2.53 (d, J_{gem} = 7.3 Hz, 1H), 2.81 (brs, 1H, O*H*), 7.32−7.50 (m, 3H), 7.51−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 27.9, 37.4, 67.8, 80.4, 126.8−127.7 (m, 5*C*D), 128.0, 128.2, 129.2, 143.6, 146.4; IR (KBr) 3569, 1688, 754 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{11}D_5Cl_2O$ (M + Na^+) 334.0785, found 334.0783.

(*S)-[(1*R**)-2,2-Dichloro-1-methylcyclopropyl](pentadeuteriophenyl)(*p*-tolyl)methanol (1d).** Following the procedure for the preparation of **1a**, the reaction of **6d** with C_6D_5Br gave **1d** (85%), (**1d/1d′** = >95/5). **1d**: colorless crystals; mp 63−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.27 (d, J_{gem} = 7.3 Hz, 1H), 2.41 (s, 3H), 2.52 (d, J_{gem} = 7.3 Hz, 1H), 2.60−2.85 (br, 1H, O*H*), 7.25 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.4, 27.8, 37.4, 67.8, 80.2, 126.8−127.7 (m, 5*C*D), 128.9, 129.1, 137.8, 140.1, 146.5; IR (KBr) 3570, 1337, 1020, 748 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}D_5Cl_2O$ (M + Na^+) 348.0941, found 348.0947.

(*R)-[(1*R**)-2,2-Dichloro-1-methylcyclopropyl](pentadeuteriophenyl)(*p*-tolyl)methanol (1d′).** Following the procedure for the preparation of **1a**, the reaction of **6a′** with *p*-bromotoluene in the place of C_6D_5Br gave the product **1d′** (79%), (**1d/1d′** = >5/95). **1d′**: colorless crystals; mp 44−49 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.28 (d, J_{gem} = 7.3 Hz, 1H), 2.34 (s, 3H), 2.52 (d, J_{gem} = 7.3 Hz, 1H), 2.72−2.84 (br, 1H, O*H*), 7.05 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 23.4, 27.9, 37.5, 67.8, 80.2, 127.2−129.1 (m, 5*C*D), 127.6, 128.2, 136.9, 143.0, 143.7; IR (KBr) 3580, 1331, 750 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}D_5Cl_2O$ (M + Na^+) 348.0941, found 348.0943.

(*S)-[(1*R**)-2,2-Dichloro-1-methylcyclopropyl](4-chlorophenyl)(pentadeuteriophenyl)methanol (1e).** Following the procedure for the preparation of **1a**, the reaction of **6e** with C_6D_5Br gave **1e** (85%), (**1e/1e′** = >95/5). **1e**: colorless crystals; mp 71−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.30 (d, J_{gem} = 7.3 Hz, 1H), 2.51 (d, J_{gem} = 7.3 Hz, 1H), 2.70−3.00 (br, 1H, O*H*), 7.41 (d, J = 7.3 Hz, 2H), 7.47 (d, J = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 27.9, 37.4, 67.5, 80.0, 126.6−127.7 (m, 5*C*D), 128.4, 130.6, 134.0, 141.7, 145.9; IR (KBr) 3559, 1491, 1093 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{10}D_5Cl_3O$ (M + Na^+) 368.0395, found 368.0397.

(*R)-[(1*R**)-2,2-Dichloro-1-methylcyclopropyl](4-chlorophenyl)(pentadeuteriophenyl)methanol (1e′).** Following the procedure for the preparation of **1a**, the reaction of ketone **6e′** with 1,4-bromochlorobenzene in the place of C_6D_5Br gave the product **1e′** (82%) (**1e/1e′** = >5/95). **1e′**: colorless crystals; mp 98−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.28 (d, J_{gem} = 7.3 Hz, 1H), 2.49 (d, J_{gem} = 7.3 Hz, 1H), 2.78−2.86 (br, 1H, O*H*), 7.11 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 27.7, 37.2, 67.5, 80.0, 127.7, 129.2, 127.9−129.5 (m, 5*C*D), 133.3, 142.4, 145.1; IR (KBr) 3571, 1487, 750 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{10}D_5Cl_3O$ (M + Na^+) 368.0395, found 368.0407.

Regiocontorolled Benzannulation of AACMs 1 to α-Arylnaphthalenes 2.

1-Chloro-5,6,7,8-tetradeuterio-2,3-dimethyl-4-phenylnaphthalene (2a/A) and 1-Chloro-4-(pentadeuteriophenyl)-2,3-dimethylnaphthalene (2a/B) (Method A). A typical procedure: $TiCl_4$ (95 mg, 0.5 mmol) was added to a stirred solution of **1a** (163 mg, 0.5 mmol) in CH_2Cl_2 at −60 °C under an Ar atmosphere, and the mixture was stirred at the same

temperature for 1 h. Aqueous sat. $NaHCO_3$ solution was added to the mixture, which was extracted twice with ether. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane) to give the products **2a/A** and **2a/B** (123 mg, 91%; **A/B** = 92/8). Following the procedure for the preparation of naphthalene **2a**, the reaction using **1b** gave the same products **2a/A** and **2a/B** (49%; **A/B** = 10/1). Following the procedure of method A, the reaction using **1a′** gave the same products **2a/A** and **2a/B** (49%; **A/B** = 1/9).

(**Method B**). A typical procedure: TBDMSOTf (90 mg, 0.34 mmol) was added to a stirred solution of **1a** (100 mg, 0.31 mmol) in toluene (2 mL) at −60 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Aqueous sat. $NaHCO_3$ solution was added to the mixture, which was extracted twice with ether. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was was purified by SiO_2-column chromatography (hexane) to give the products **2a/A** and **2a/B** (84%; **A/B** = 1/5). Following the procedure of method A, the reaction using **1b** gave the same products **2a/A** and **2a/B** (46%; **A/B** = 10/1). Following the procedure of method B, the reaction of **1b** gave the same products **2a/A** and **2a/B** (49%; **A/B** = 1/4). **2a/A**: colorless crystals; mp 103−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.62 (s, 3H), 7.21−7.22 (m, 1H), 7.23−7.25 (m, 1H), 7.42−7.46 (m, 1H), 7.47−7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.01, 18.91, 124.22−126.71 (m, 4*C*D), 127.13, 128.42, 129.39, 130.21, 130.47, 132.37, 133.17, 133.70, 137.42, 140.04; IR (KBr) 1439, 1306, 702 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{11}D_4Cl$ (M^+) 270.1109, found 270.1108. **2a/B**: colorless crystals; mp 102−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.62 (s, 3H), 7.29−7.32 (m, 2H), 7.51−7.52 (m, 1H), 8.34 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 18.9, 124.4, 125.5, 125.9, 126.7, 126.6 (t, J = 24.5 Hz, *C*D), 127.9 (t, J = 24.5 Hz, 2*C*D), 129.8 (t, J = 24.5 Hz, 2*C*D), 129.5, 130.5, 132.5, 133.7, 137.4, 139.8; IR (KBr) 1495, 1323, 760 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{10}D_5Cl$ (M^+) 271.1171, found 271.1174.

4-Chloro-5,6,7,8-tetradeuterio-2-methyl-1-phenylnaphthalene (2c/A) and 4-Chloro-2-methyl-1-(pentadeuteriophenyl)naphthalene (2c/B). Following the procedure of method A, the reaction using **1c** gave the products **2c/A** and **2c/B** (81%, **A/B** = 97/3). Following the procedure of method B, the reaction using **1c** gave the products **2c/A** and **2c/B** (51%, **A/B** = 93/7). **2c/A**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 7.22−7.26 (m, 2H), 7.35−7.55 (m, 3H), 7.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.55, 123.50−127.00 (m, 4*C*D), 127.27, 128.48, 128.54, 129.11, 130.09, 130.79, 133.52, 134.05, 137.56, 139.02; IR (neat) 1587, 1502, 1375, 764 cm^{-1}; HRMS (EI) calcd for $C_{17}H_9D_4Cl$ (M^+) 256.0953, found 256.0958. **2c/B**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 7.33−7.41 (2H, m), 7.47−7.53 (m, 2H), 8.26 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 124.2, 125.8, 126.5, 126.6, 127.0−130.0 (m, 5*C*D), 128.6, 129.2, 130.8, 133.6, 134.1, 137.6, 138.8; IR (neat) 1580, 1375, 764 cm^{-1}; HRMS (EI) calcd for $C_{17}H_8D_5Cl$ (M^+) 257.1015, found 257.1016.

4-Chloro-5,6,7,8-tetradeuterio-2-methyl-1-(*p*-tolyl)naphthalene (2d/A) and 4-Chloro-2,6-dimethyl-1-(pentadeuteriophenyl)naphthalene (2d/B). Following the procedure of method A, the reactions using **1d** gave the products **2d/A** and **2d/B** (52%, **A/B** = 93/7). The reactions of **1d′** gave the products **2d/A** and **2d/B** (40%, **A/B** = 1/99). Following the procedure of method B, the reactions of **1d** gave the products **2d/A** and **2d/B** (62%, **A/B** = 1/99). The reactions of **1d′** gave the products **2d/A** and **2d/B** (44%, **A/B** = 96/4). **2d/A**: a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.46 (s, 3H), 7.13 (d, J = 7.5 Hz, 2H), 7.31 (d, J = 7.5 Hz, 2H), 7.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.58, 21.28, 106.44, 122.00−128.01 (m, 4*C*D), 128.54, 129.17, 129.95, 130.62, 133.61, 134.20, 135.93, 136.85, 137.60; IR (neat) 2361, 1510, 1312, 910 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{11}D_4Cl$ (M^+) 270.1109, found 270.1109. **2d/B**: a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (400 MHz) 2.16 (s, 3H), 2.36 (s, 3H), 7.15 (s, 1H), 7.34 (d, J = 8.9 Hz, 1H), 7.45 (s, 1H), 8.15 (d, J = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 21.8, 124.1, 125.6, 127.5, 127.6, 128.0, 128.5−130.0 (m, *C*D), 130.7, 133.6, 134.3, 136.3, 136.9, 139.0; IR (neat) 1508, 1310, 833 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{10}D_5Cl$ (M^+) 271.1171, found 2701.1168.

4-Chloro-5,6,7,8-tetradeuterio-2-methyl-1-(4-chlorophenyl)naphthalene (2e/A) and 4,6-Dichloro-2-methyl-1-(pentadeuteriophenyl)naphthalene (2e/B). Following the procedure of method A, the reaction using **1e** gave the products **2e/A** and **2e/B** (70%, **A/B** = 20/1), that using **1e′** gave **2e/A** and **2e/B** (68%, **A/B** = 1/4). Following the procedure of method B, the reactions using **1e′** gave the products **2e/A** and **2e/B** (43%, **A/B** = 99/1). **2e/A**: a colorless crystals; mp 49−55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (400 MHz) 2.20 (s, 3H), 7.18 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.52, 122.00−127.00 (m, 4*C*D), 128.52, 128.81, 129.14, 131.21, 131.51, 133.39, 133.61, 133.86, 136.18, 137.43; IR (KBr) 1489, 1310, 1090, 833 cm^{-1}; HRMS (EI) calcd for $C_{17}H_8D_4Cl_2$ (M^+) 290.0563, found 290.0568. **2e/B**: a colorless crystals; mp 48−55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (s, 3H), 7.37 (d, J = 2.0 Hz, 1H), 7.45 (dd, J = 9.5 Hz, J = 2.0 Hz, 1H), 7.52 (s, 1H), 8.20 (d, J = 9.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 123.2, 126.5−130.0 (m, *C*D), 125.4, 126.0, 126.6, 128.8, 130.8, 131.5, 132.8, 134.9, 135.0, 136.9, 138.0; IR (KBr) 1489, 1310, 1090, 833 cm^{-1}; HRMS (EI) calcd for $C_{17}H_8D_4Cl_2$ (M^+) 291.0625, found 291.0621.

Total Synthesis of Natural Lignan Lactone. (1*R,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl(3,4-methylenedioxyphenyl)methanone (6f).** 3,4-Methylenedioxyphenylmagnesium bromide generated from Mg (146 mg, 6.0 mmol) and 1-bromo-3,4-methylenedioxybenzene (1.21 g, 6.0 mmol) in THF (5.0 mL) was added to a stirred solution of carbonyl chloride 5a (1.01 g, 5.0 mmol) in THF (5.0 mL) at 0−5 °C, and the mixture was stirred at the same temperature for 1 h. The mixture was poured into ice and aqueous satd NH_4Cl solution, which was extracted twice with ether. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/ether = 20/1) to give the desired product 6f (1.16 g, 81%): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (d, J = 6.6 Hz, 3H), 1.64 (q, J = 6.6 Hz, 1H), 1.65 (s, 3H), 6.06 (d, J_{gem} = 1.2 Hz, 1H), 6.07 (d, J_{gem} = 1.2 Hz, 1H), 6.07 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 1.7 Hz, 1H), 7.58 (dd, J = 8.3 Hz, J = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.7, 23.5, 35.4, 39.6, 68.3, 68.3, 101.9, 108.1, 109.1, 126.5, 129.3, 148.2, 152.2, 193.1; IR (neat) 2932, 1676, 1605 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{12}Cl_2O_3$ (M^+) 286.0163, found 286.0109.

(1*R,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl(3,4,5-trimethoxyphenyl)methanone (6g).** BuLi (1.59 M in hexane, 0.377 mL, 0.60 mmol) was added dropwise to a stirred solution of 5-bromo-1,2,3-trimethoxybenzene (74 mg, 0.30 mmol) in ether (1.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. The resultant solution was added to a solution of carbonyl chloride **5a** (40 mg, 0.20 mmol) in ether (1.0 mL) at −78 °C and was stirred for 1 h at that same temperature, followed by being allowed to warm to rt. The mixture was poured into ice and aqueous satd NH_4Cl solution (1.0 mL), which was extracted twice with ether. The combined organic phase was successively washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 5/1) to give the desired product **6g** (48 mg, 71%): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (d, J = 6.6 Hz, 3H), 1.68 (q, J = 6.6 Hz, 1H), 1.68 (s, 3H), 3.87 (s, 3H), 3.95 (s, 6H), 7.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 23.6, 35.2, 39.5, 56.2, 61.0, 68.6, 105.2, 107.1, 142.9, 153.0, 193.8; IR (neat) 1678, 1584, 1332 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{18}Cl_2O_4$ (M^+) 332.0582, found 332.0583.

(*R)-[(1*R**,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl]-(3,4-dimethoxyphenyl)(3,4-methylenedioxy)phenylmethanol (1f).** BuLi (1.60 M in hexane, 4.50 mL, 7.20 mmol) was added to a stirred solution of 4-bromo-1,2-dimethoxybenzene (1.56 g, 7.20 mmol) in THF (16 mL) at −78 °C under an Ar atmosphere, which was stirred at the same temperture for 30 min. Ketone **6f** (1.06 g, 4.80 mmol) in THF (8.0 mL) was added to the mixture at the −60 °C and was stirred at the same temperature for 1 h, and then at rt for 30 min. The mixture was poured into ice and aqueous satd NH_4Cl solution, which was extracted twice with ether. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 5/1) to give AACM **1f** (1.14 g, 77%):

1f: colorless amorphous solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.51 (q, J = 6.8 Hz, 1H), 1.76 (d, J = 6.8 Hz, 3H), 2.74 (brs, 1H, O*H*), 3.85 (s, 3H), 3.87 (s, 3H), 6.00 (d, J_{gem} = 1.5 Hz, 1H), 6.10 (d, J_{gem} = 1.5 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 6.59 (dd, J = 1.2 Hz, J = 8.5 Hz, 1H), 6.75 (d, J = 8.5 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.94 (d, J = 1.2 Hz, 1H), 7.04 (dd, J = 2.0 Hz, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.2, 27.1, 36.3, 38.4, 55.8, 73.8, 83.6, 101.2, 107.5, 109.7, 109.8, 111.4, 121.1, 122.2, 138.6, 139.1, 147.1, 147.5, 148.0, 148.2; IR (KBr) 3545, 1491, 1242 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{22}Cl_2O_5$ (M + Na^+) 447.0742, found 447.0741.

(*R)-[(1*R**,3*R**)-2,2-Dichloro-1,3-dimethylcyclopropyl]-(3,4,5-trimethoxyphenyl)(3,4-methylenedioxy)phenylmethanol (1g).** Following the procedure for the preparation of **1g**, the reaction using ketone **6f** (200 mg, 0,60 mmol) with 4-bromo-1,2-methylenedioxybenzene in the place of 4-bromo-1,2-dimethoxybenzene gave AACM **1g** (197 mg, 82%): colorless amorphous solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.56 (q, J = 6.6 Hz, 1H), 1.76 (d, J = 6.6 Hz, 3H), 2.73 (brs, 1H, −OH), 3.86 (s, 6H), 3.92 (s, 3H), 5.96 (d, J = 1.5 Hz, 1H), 5.97 (d, J = 1.5 Hz, 1H), 6.61 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 6.72 (d, J = 8.3 Hz, 1H), 6.77 (s, 2H), 6.81 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.1, 27.1, 36.4, 38.5, 56.3, 60.9, 74.3, 83.9, 101.1, 106.2, 107.1, 108.8, 122.0, 139.9, 140.5, 146.6, 147.2, 152.7; IR (KBr) 3569, 1591, 1487, 1238 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}Cl_2O_5$ (M + Na^+) 477.0848, found 477.0852.

1-Chloro-6,7-dimethoxy-2,3-dimethyl-4-(3,4-methylenedioxyphenyl)naphthalene (2f/A) and 1-Chloro-4-(3,4-dimethoxyphenyl)-2,3-dimethyl-6,7-methylenedioxynaphthalene (2f/B). $SnCl_4$ (460 mg, 1.77 mmol) was added to a stirred solution of **1f** (750 mg, 1.77 mmol) in 1,2-dichloroethane (175 mL) at 0−5 °C, followed by stirring at the same temperature for 2 h. Aqueous satd $NaHCO_3$ solution was added to the mixture, which was extracted twice with ether. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (benzene/hexane = 7/3) to give naphthalene **2f/A** (250 mg, 37%), mixture of **2f/A** and **2f/B** (205 mg, 31%; 8:1), and **2f/B** (35 mg, 5%) following an elute order. **2f/A**: colorless crystals; mp 142−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.56 (s, 3H), 3.73 (s, 3H), 4.04 (s, 3H), 6.05 (d, J_{gem} = 1.2 Hz, 1H), 6.08 (d, J_{gem} = 1.2 Hz, 1H), 6.65−6.75 (m, 3H), 6.94 (d, J = 7.8 Hz, 1H), 7.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 18.8, 55.7, 55.9, 101.1, 103.6, 105.8, 108.4, 110.6, 123.3, 125.2, 128.1, 129.1, 131.2, 132.3, 134.0, 135.7, 146.6, 147.8, 148.9, 149.5; IR (KBr) 3426, 1510, 1256 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{19}ClO_4$ (M^+) 370.0972, found 370.0973. **2f/B**: colorless crystals; mp 174−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.55 (s, 3H), 3.84 (s, 3H), 3.96 (s, 3H), 5.99 (s, 2H), 6.65−6.72 (m, 3H), 6.94 (d, J = 7.8 Hz, 1H), 7.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 18.8, 55.9, 55.9, 101.1, 101.3, 103.3, 111.2, 113.2, 122.2, 126.5, 129.7, 129.7, 131.5, 132.5, 132.9, 136.7, 147.2, 147.7, 148.0, 149.0; IR (KBr) 1516, 1466, 1254, 1032 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{19}ClO_4$ (M^+) 370.0972, found 370.0981.

1-Chloro-2,3-dimethyl-6,7-methylenedioxy-4-(3,4,5-trimethoxyphenyl)naphthalene (2g/A) and 1-Chloro-2,3-dimethyl-4-(3,4-methylenedioxyphenyl)-5,6,7-trimethoxynaphthalene (2g/B). $SnCl_4$ (167 mg, 0.64 mmol) was added to a stirred solution of AACM **1g** (290 mg, 0.64 mmol) in 1,2-dichloroethane (12 mL) under reflux conditions, and the mixture was stirred at the same temperature for 10 min. After the mixture was cooled to rt, an aqueous satd $NaHCO_3$ solution was added, and the mixture was extracted twice with ether. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 7/1) to give the desired products **2g/A** (201 mg, 80%) and **2g/B** (20 mg, 8%). **2g/A**: colorless crystals; mp 224−227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.56 (s, 3H), 3.83 (s, 6H), 3.95 (s, 3H), 6.00 (s, 2H), 6.41 (s, 2H), 6.68 (s, 1H), 7.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 18.8, 56.1, 61.0, 101.2, 101,3, 103.2, 107.0, 126.5, 129.3, 129.8, 131.5, 132.2, 135.9, 136.9, 137.0, 147.3, 147.8, 153.4; IR (KBr) 3424, 1464, 1238, 1121 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{21}ClO_5$ (M^+) 400.1078, found 400.1082. **2g/B**: colorless crystals; mp 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (s, 3H), 2.56 (s, 3H), 3.32 (s, 3H), 3.85 (s, 3H), 4.02 (s, 3H), 6.01 (d, J = 1.5, 1H), 6.02 (d, J = 1.5, 1H), 6.59 (dd, J = 1.7 Hz, J = 7.8 Hz, 1H), 6.68 (d, 1H), 6.85 (d, J = 7.8 Hz, 1H), 7.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 18.4, 18.6, 55.8, 60,8, 60.8, 100.1, 100.8, 107.4, 109.7, 121.5, 123.1, 127.3, 129.8, 132.8, 133.5, 134.4, 137.7, 142.4, 145.6, 146.9, 149.6, 152.8; IR (KBr) 2942, 1613, 1489, 1335 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{21}ClO_5$ (M + Na^+) 423.0975, found 423.0971.

2,3-Bis(bromomethyl)-1-chloro-6,7-dimethoxy-4-(3,4-methylenedioxyphenyl)naphthalene (12a). A mixture of naphthalene **2f/A** (185 mg, 0.50 mmol), *N*-bromosuccinimide (890 mg, 5.0 mmol), and AIBN (4 mg, 0.024 mmol) in benzene (8.0 mL) was refluxed for 1 h. After the mixture was cooled to rt, water was added, and the mixture was extracted twice with EtOAc. The combined organic phase was washed with 1 M HCl, water, and brine, dried (Na_2SO_4), and consentrated. The obtained crude product was purified by SiO_2-column chromatography (benzene) to give dibromide **12a** (202 mg, 77%): amorphous solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 (s, 3H), 4.06 (s, 3H), 4.61 (s, 2H), 5.12 (s, 2H), 6.09 (d, J = 1.3 Hz, 1H), 6.11 (d, J = 1.3 Hz, 1H), 6.68 (s, 1H), 6.82 (d, J = 7.8 Hz, 1H), 6.86 (s, 1H), 6.98 (d, J = 7.8 Hz, 1H), 7.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 30.0, 55.8, 56.1, 101.4, 104.1, 106.3, 108.5, 110.3, 123.3, 127.0, 129.7, 129.9, 130.9, 131.9, 138.7, 147.5, 147.8, 150.6, 151.2; IR (KBr) 1469, 1248, 1112 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}Br_2ClO_4$ (M + Na^+) 548.9080, found 548.9071.

2,3-Bis(bromomethyl)-4-(2-bromo-3,4,5-trimethoxyphenyl)-1-chloro-6,7-methylenedioxynaphthalene (12b). Following the procedure for the preparation of **12a**, the reaction using **2g/A** (50 mg, 0.125 mmol) gave tribromide **12b** (66 mg, 83%): colorless crystals; mp 181−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 3.99 (s, 3H), 4.03 (s, 3H), 4.29 (d, J_{gem} = 10.7 Hz, 1H), 4.71 (d, J_{gem} = 10.7 Hz, 1H), 5.02 (d, J_{gem} = 10.7 Hz, 1H), 5.17 (d, J_{gem} = 9.0 Hz, 1H), 6.07 (d, J = 1.2 Hz, 2H), 6.52 (s, 1H), 6.74 (s, 1H), 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 29.7, 56.3, 61.2, 61.3, 101.9, 102.1, 103.2, 110.3, 110.6, 128.6, 130.3, 130.4, 130.7, 133.0, 133.3, 138.3, 143.1, 149.4, 149.6, 151.5, 153.0; IR (KBr) 1464, 1252, 1107 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}Br_3ClO_5$ (M + Na^+) 656.8291, found 656.8283.

6,7-Dimethoxy-1-chloro-4-(3,4-methylenedioxyphenyl)naphthalene-2,3-diyldimethanol (13a). Dibromide **12a** (240 mg, 0.454 mmol) in DMF (0.6 mL) was added to a stirred mixture of AcOH (82 mg, 1.36 mmol) and K_2CO_3 (188 mg, 1.36 mmol) in DMF (0.6 mL) at rt, followed by being stirred for 2 h. Aqueous KOH (119 mg, 2.1 mmol) solution (1.0 mL) and MeOH (2.0 mL) were successively added to the stirred mixture at rt, followed by being stirred for 2 h. Ice−water was added to the mixture, which was extracted twice with $CHCl_3$. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was

purified by SiO_2-column chromatography (hexane/EtOAc = 1/1) to give the desired product **13a** (172 mg, 94%): colorless crystals; mp 192−196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.93 (brs, 1H, O*H*), 3.20 (brs, 1H, O*H*), 3.74 (s, 3H), 4.05 (s, 3H), 4.65 (s, 2H), 5.18 (s, 2H), 6.04 (d, J_{gem} = 1.1 Hz, 1H), 6.09 (d, J_{gem} = 1.1 Hz, 1H), 6.72 (d, J = 1.7 Hz, 1H), 6.73 (s, 1H) 6.74 (d, J = 1.7 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 7.63 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 56.0, 61.0, 61.3, 101.2, 104.1, 106.3, 108.4, 110.6, 123.4, 126.4, 129.5, 130.7, 132.8, 134.4, 137.6, 147.1, 147.7, 150.0, 150.5; IR (KBr) 3331, 1507, 1262 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{19}ClO_6$ (M + Na^+) 425.0768, found 425.0767.

4-(2-Bromo-3,4,5-trimethoxyphenyl)-1-chloro-6,7-methylenedioxynaphthalene-2,3-diyldimethanol (13b). Following the procedure for the preparation of **13b**, the reaction using tribromide **12b** (450 mg, 0.706 mmol) gave diol **13b** (296 mg, 82%): colorless crystals; mp 169−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.97 (s, 3H), 3.99 (s, 3H), 4.42 (d, J_{gem} = 12.0 Hz, 1H), 4.67 (d, J_{gem} = 12.0 Hz, 1H), 5.02 (d, J_{gem} = 12.8 Hz, 1H), 5.23 (d, J_{gem} = 12.8 Hz, 1H), 6.02 (s, 2H), 6.52 (s, 1H), 6.64 (s, 1H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 60.9, 61.2, 61.3, 61.7, 101.7, 102.2, 103.1, 110.4, 110.7, 128.2, 130.0, 132.1, 133.5, 134.3, 134.7, 137.1, 142.7, 148.8, 149.1, 151.2, 153.0; IR (KBr) 3356, 1462, 1252 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}BrClO_7$ (M + Na^+) 532.9979, found 532.9952.

1-(3,4-Methylenedioxyphenyl)-6,7-dimethoxynaphthalene-2,3-diyldimethanol (14a). Diol **13a** (48 mg, 0.12 mmol) in HMPA (0.79 mL) and THF (1.0 mL) was added to a stirred solution of SmI_2 (0.1 M THF solution, 1.20 mmol, 12.0 mL) at rt, followed by being stirred for 2 h. The mixture was poured into ice and water, which was extracted twice with $CHCl_3$. The combined organic phase washed with water, 10% aqueous KOH solution, 3% aqueous $Na_2S_2O_3$ solution, and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 1/1) to give the desired product **14a** (33 mg, 86%): colorless crystals; mp 181−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 (brs, 1H, O*H*), 3.33 (brs, 1H, O*H*), 3.74 (s, 3H), 3.99 (s, 3H), 4.62 (s, 2H), 4.89 (s, 2H), 6.04 (d, J_{gem} = 1.2 Hz, 1H), 6.09 (d, J_{gem} = 1.2 Hz, 1H), 6.74 (s, 1H), 6.76 (dd, J = 7.8 Hz, 1.7 Hz, 1H), 6.81(d, J = 1.7 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 7.11 (s, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 55.9, 60.7, 65.3, 101.2, 105.9, 106.3, 108.3, 110.7, 123.4, 127.4, 128.6, 128.8, 132.5, 133.2, 135.7, 138.8, 146.9, 147.7, 149.6, 149.7; IR (KBr) 3410, 1508, 1234 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}O_6$ (M + Na^+) 391.1158, found 391.1156.

6,7-Methylenedioxy1-(3,4,5-trimethoxyphenyl)naphthalene-2,3-diyldimethanol (14b). Following the procedure for the preparation of **14a**, the reaction using diol **13b** (56 mg, 0.11 mmol) gave the desired product **14b** (29 mg, 67%): colorless crystals; mp 215−226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (brs, 1H), 2.64 (brs, 1H), 3.82 (s, 6H), 3.94 (s, 3H), 4.63 (s, 2H), 4.92 (s, 2H), 6.01 (s, 2H), 6.51 (s, 2H), 6.78 (s, 1H), 7.12 (s, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.1, 60.7, 61.0, 65.2, 101.2, 103.6, 103.8, 107.3, 128.0, 129.8, 130.0, 133.2, 124.5, 135.9, 137.1, 139.8, 147.8, 148.0, 153.1; IR (KBr) 3355, 1460, 1236 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{22}O_7$ (M + Na^+) 421.1263, found 421.1254.

Justicidin B (15) and Retrojusticidin B (16). A stirred suspension of diol **14a** (115 mg, 0.312 mmol) and Fetizon's reagent (Ag_2CO_3−Celite) (3.12 g) in benzene (50 mL) was refluxed for 1.5 h with azeotropic removal of water using a Dean−Stark apparatus. After cooling to rt, the mixture was concentrated. The obtained crude product was purified by SiO_2-column chromatography ($CHCl_3$/EtOAc = 30/1) to give the desired product **15** (15 mg, 13%) and **16** (90 mg, 79%). **15**: colorless crystals; mp 240−242 °C (lit.[2a] mp 241−243 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H), 4.07 (s, 3H), 5.40 (s, 2H), 6.06 (d, *Jgem* = 1.5 Hz, 1H), 6.11 (d, *Jgem* = 1.5 Hz, 1H), 6.84 (dd, J = 8.1 Hz, J = 1.7 Hz, 1H), 6.86 (d, J = 1.7 Hz, 1H), 6.99 (d, J = 8.1 Hz, 1H), 7.12 (s, 1H), 7.19 (s, 1H), 7.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 56.0, 68.0, 101.2, 105.8, 106.0, 108.2, 110.5, 118.3, 118.5, 123.4, 128.4, 128.8, 133.1, 139.5, 139.6, 147.5, 147.6, 150.0, 151.8; IR (KBr) 1747, 1506 cm^{-1}. ^{1}H and ^{13}C NMR spectral data were identical with those reported.[2s] **16**: colorless crystals; mp 217−219 °C (lit.[6d] mp 218−220 °C);^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 4.08 (s, 3H), 5.22 (s, 2H), 6.08 (d, J_{gem} = 1.2 Hz, 1H), 6.12 (d, J_{gem} = 1.2 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.85 (s, 1H), 7.00 (d, J = 7.6 Hz, 1H), 7.10 (s, 1H), 7.30 (s, 1H), 8.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 56.1, 69.5, 101.4, 104.0, 107.7, 109.0, 109.5, 121.4, 122.7, 124.2, 129.7, 129.9, 131.6, 131.9, 138.0, 147.7, 148.3, 150.1, 152.0, 171.6; IR (KBr) 3470, 1755, 1466 cm^{-1}. ^{1}H and ^{13}C NMR spectral data were identical with those reported.[2s]

Dehydrodesoxypodophyllotoxin (17) and 5′-methoxyretrochinensin (18). Following the procedure for the preparation of **15** and **16**, the reaction of diol **14b** (41 mg, 0.10 mmol) gave the desired product **17** (10 mg, 26%) and **18** (29 mg, 74%). **17**: colorless crystals; mp 268−271 °C (lit.[14] mp 270−272 °C); ^{1}H NMR(400 MHz, $CDCl_3$) 3.84 (s, 6H), 3.97 (s, 3H), 5.38 (s, 2H), 6.09 (s, 2H), 6.55 (s, 2H), 7.12 (s, 1H), 7.21 (s, 1H), 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 56.1, 61.0, 68.0, 101.8, 103.6, 103.7, 107.2, 118.7, 119.1, 130.3, 130.3, 134.6, 137.8, 139.8, 140.4, 148.7, 150.0, 153.0, 169.6; IR (KBr) 3449, 1769, 1464 cm^{-1}. ^{1}H and ^{13}C NMR spectral data were identical with those reported.[2s] **18**: white powder; mp 295−298 °C (lit.[14] mp 283−284 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 6H), 3.96 (s, 3H), 5.22 (s, 2H), 6.10 (s, 2H), 6.54 (s, 2H), 7.11 (s, 1H), 7.32 (s, 1H), 8.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.3, 61.0, 69.4, 101.9, 102.1, 106.2, 121.6, 124.7, 131.2, 133.1, 133.2, 137.9, 138.2, 148.4, 150.5, 153.8, 171.4; IR (KBr) 3470, 1755, 1466 cm^{-1}. ^{1}H and ^{13}C NMR spectral data were identical with those reported.[2s]

3-(2,2-Dimethylpropanoyloxymethyl)-1-(3,4-methylenedioxyphenyl)-6,7-dimethoxynaphthalen-2-ylmethanol (20a) and 2-(2,2-Dimethylpropanoyloxymethyl)-1-(3,4-methylenedioxyphenyl)-6,7-dimethoxynaphthalen-3-ylmethanol (21a). A stirred suspension of diol **14a** (16.0 mg, 0.043 mmol), Bu_2SnO (11 mg) and, molecular sieves 4A (431 mg) in toluene (4.3 mL) was refluxed for 2 h. After cooling to 0−5 °C, and then 2,2-dimethylpropanoyl chloride (5.2 mg, 0.043 mmol) was added. After being stirred for 20 h, the mixture was filtered off using Celite. Being washed with $CHCl_3$, and the organic phase was concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 3/1) to give the desired product **20a** (12.6 mg, 64%) and its isomer **21a** (3.2 mg, 16%). **20a**: colorless crystals; mp 87.5−89.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 9H), 1.93 (brs, 1H, O*H*), 3.75 (s, 3H), 4.01 (s, 3H), 4.60 (s, 2H), 5.44 (s, 2H), 6.07 (d, J_{gem} = 14.1 Hz, 1H), 6.08 (d, J_{gem} = 14.1 Hz, 1H), 6.75 (s, 1H), 6.80 (dd, J = 7.9 Hz, J = 1.7 Hz, 1H), 6.84 (d, J = 1.7 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 7.13 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 38.8, 55.7, 55.9, 59.9, 65.1, 101.2, 105.8, 106.3, 108.3, 110.7, 123.4, 127.7, 128.7, 128.7, 131.0, 132.3, 133.0, 138.8, 146.9, 147.6, 149.7, 149.8, 178.3; IR (KBr) 3484, 1723, 1507 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{28}O_7$ (M+Na^+) 475.1733, found 475.1728. **21a**: colorless crystals; mp 93.0−95.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 9H), 2.00 (brs, 1H, O*H*), 3.76, (s, 3H), 4.01 (s, 3H), 4.88 (s, 2H), 5.00 (d, J_{gem} = 13.8 Hz, 1H), 5.04 (d, J_{gem} = 13.8 Hz, 1H), 6.05 (d, J_{gem} = 12.4 Hz, 1H), 6.06 (d, J_{gem} = 12.4 Hz, 1H), 6.73 (dd, J = 7.9, 1.7 Hz, 1H), 6.76 (d, J = 1.7 Hz, 1H), 6.78 (s, 1H), 6.90 (d, J = 7.9 Hz, 1H), 7.16 (s, 1H), 7.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 38.7, 55.7, 55.9, 62.2, 63.7, 101.2, 105.8, 106.3, 108.2, 110.7, 123.5, 125.9, 127.5, 128.3, 129.4, 132.0, 136.1, 140.7, 147.0, 147.6, 149.6, 150.0, 178.1; IR (KBr) 3434, 1723, 1507 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{28}O_7$ (M + Na^+) 475.1733, found 475.1740.

3-(2,2-Dimethylpropanoyloxymethyl)-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene-2-ylmeth-

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anol (20b) and 2-(2,2-Dimethylpropanoyloxymethyl)-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene-3-ylmethanol (21b). Following the procedure for the preparation of **20a**, the reaction using diol **14b** (14.4 mg, 0.036 mmol) gave the desired product **20b** (12.0 mg, 69%) and **21b** (3.6 mg, 21%). **20b**: colorless crystals; mp 169.0−170.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 9H), 1.93 (brs, 1H, O*H*), 3.84 (s, 6H), 3.95 (s, 3H), 4.60 (s, 2H), 5.43 (s, 2H), 6.01 (s, 2H), 6.54 (s, 2H), 6.77 (s, 1H), 7.13 (s, 1H), 7.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 38.8, 56.2, 60.0, 61.0, 64.9, 101.2, 103.5, 103.8, 107.3, 128.0, 129.9, 130.0, 131.3, 132.7, 134.2, 137.2, 139.8, 147.8, 148.1, 153.1, 178.3; IR (KBr) 3486, 1720, 1464 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{28}O_7$ (M + Na^+) 505.1838, found 505.1832. **21b**: colorless crystals; mp 202.5−203.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 9H), 1.55 (brs, 1H, O*H*), 3.81 (s, 6H), 3.95 (s, 3H), 4.87 (s, 2H), 5.08 (s, 2H), 6.01 (s, 2H), 6.46 (s, 2H), 6.74 (s, 1H), 7.16 (s, 1H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 38.7, 56.1, 61.0, 62.2, 63.4, 101.2, 103.6, 103.8, 107.3, 126.5, 127.4, 129.5, 130.6, 134.0, 136.1, 137.4, 141.4, 148.0, 148.1, 153.1, 178.1; IR (KBr) 3468, 1717, 1462 cm^{-1}; HRMS (EI) calcd for $C_{26}H_{28}O_7$ (M + Na^+) 505.1838, found 505.1818.

Justicidin B (15). PDC (14.7 mg, 0.040 mmol) was added to a stirred solution of monoalcohol **20a** (11.6 mg, 0.026 mmol) in DMF (0.50 mL) at rt, followed by being stirred for 4 h. Water was added to the mixture, which was extracted twice with $CHCl_3$. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. MeOH (1.2 mL), KOH (70 mg, 1.05 mmol), and I_2 (68 mg, 0.53 mmol) were successively added to the crude aldehyde at rt, followed by being stirred for 16 h. 6M-HCl aqueous solution was added to the mixture, which was extracted twice with $CHCl_3$. The combined organic phase was washed with water, aqueous $Na_2S_2O_3$ solution, and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/EtOAc = 3/1) to give the desired product **17** (7.2 mg, 77%).

Dehydrodesoxypodophyllotoxin (17). Following the procedure for the preparation of **15**, the reaction using monoalcohol **20b** (10.2 mg, 0.021 mmol) gave the desired product **17** (6.2 mg, 75%).

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Supporting Information Available: Computational calculation graphics of AACM **1g**. ^{1}H and/or ^{13}C NMR spectral chart for compounds **1**, **2**, **6**, and **12**−**21**. This material is available free of charge via the Internet at http://pubs.acs.org.

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