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Total synthesis of (±)-sacidumlignans D and A through Ueno–Stork radical cyclization reaction†

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Efficient synthesis of (±)-sacidumlignan D (**4**) has been successfully achieved employing Ueno–Stork radical cyclization of α-bromo acetal **21** as a key step. Two synthetic approaches for the symmetrical diaryl ketone **19** have been discussed in detail. Notably, sacidumlignan A (**1**) can be also efficiently synthesized in only 7 steps with 25% overall yield, where acid triggered tandem reaction starting from analogous Ueno–Stork cyclization product **27** played an important role. Moreover, potentially biomimetic conversion from (±)-sacidumlignan D (**4**) to sacidumlignan A (**1**) could be realized.

Introduction

The plant *Sarcostemma acidum* (Roxb.) grows in and over trees and shrubs near the seashore of Hainan Island of China and is applied in folklore medicine to remedy chronic cough and postnatal hypogalactia.[1] In 2005, investigation into chemical components of the only species of this genus distributed in China by Yue and co-workers resulted in the isolation of four new lignans, namely, sacidumlignans A–D (**1**–**4**) from the ethanolic extract of the whole plant.[2] Sacidumlignan D (**4**) was assigned as a rearranged tetrahydrofuran lignan with an unprecedented skeleton by extensive 2D NMR techniques (Fig. 1). Notably, sacidumlignan A (**1**) possesses the arylnaphthalene backbone, and demonstrates moderate antimicrobial activities against two Gram-positive bacteria *in vitro*. We are interested in the total synthesis of these two natural products, especially their conversion relationship albeit Yue and co-workers did not propose a plausible biogenetic synthetic route.

The first total synthesis of racemic sacidumlignan D (**4**) was completed with a longest linear sequence (LLS) of 14 steps in an overall yield of 2.7% from known bromo-*o*-vanillin by Ramana and co-worker featuring the utilization of reverse Wacker oxidation (Scheme 1a),[3a] and the whole route involved triple adjustment of protecting groups (–OAllyl→–OAc→–OTBS). Subsequently, naturally occurring sacidumlignan D (**4**) was also synthesized by the same group employing an improved 11-step route (17% overall yield) from known compound and the analogous *C–O* bond construction as the key step for the formation of γ-lactol.[3b] Starting from a common γ-lactone intermediate, sacidumlignan A (**1**) was obtained as well in 14 steps with 9.4% overall yield. In our current study, a distinctively different strategy was adopted (Scheme 1b): the Ueno–Stork radical cyclization[4] is responsible for the

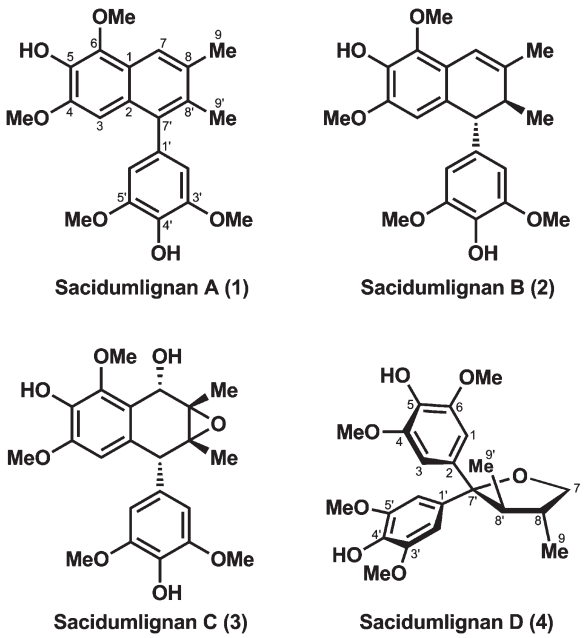

Fig. 1 Structures of sacidumlignans A, B, C and D.

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†Electronic supplementary information (ESI) available: Copies of ^{1}H, ^{13}C NMR, ^{1}H–^{1}H COSY and NOE spectra. CCDC 912716, 912717 and 912718. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ob00053b

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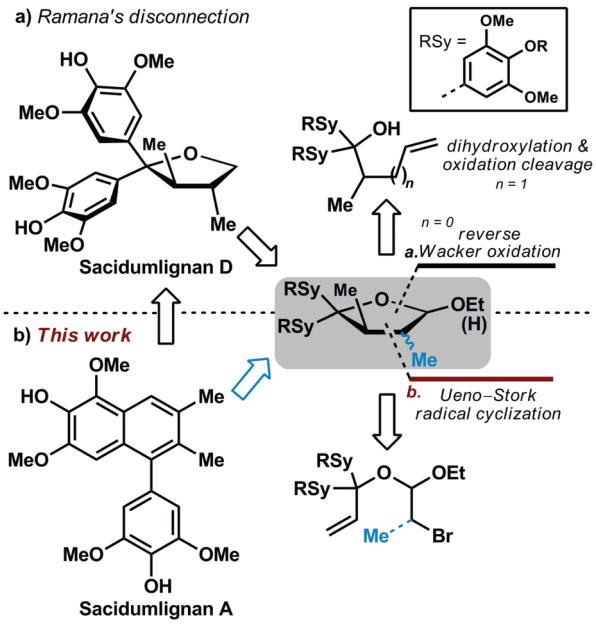


Scheme 1 Retrosynthetic analysis of sacidumlignans D and A.

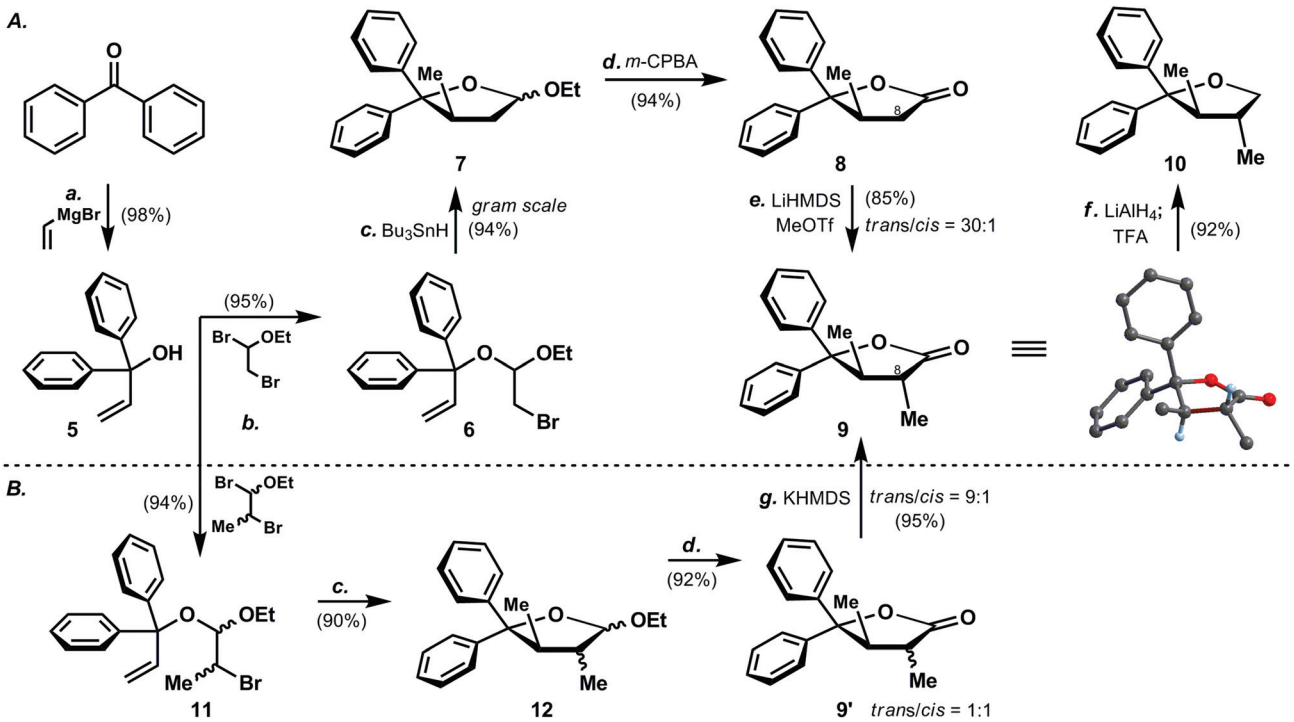
establishment of the key *C–C* bond for the formation of the corresponding acetal. To the best of our knowledge, the application of the Ueno–Stork radical cyclization in the total synthesis of lignans class remains largely unexplored[5] although the great value of this methodology had been proved in the field of natural products synthesis.[6] Herein, we disclose the successful exploit of this strategy, as demonstrated in the efficient synthesis of (±)-sacidumlignan D (**4**) in 9 steps (LLS) from commercially available materials with 24% overall yield and 8 column chromatography manipulation. Moreover, a concise synthesis of sacidumlignan A (**1**) can be achieved (7 steps with 25% overall yield) from analogous Ueno–Stork cyclization product **27**, and a plausible biomimetic conversion relationship between (±)-sacidumlignan D (**4**) and sacidumlignan A (**1**) was also revealed.

Results and discussion

We began by examining the synthesis of model substrate **10** that possesses the skeleton of sacidumlignan D. As shown in Scheme 2A, *gem*-diphenyl allyl alcohol **5** can be readily prepared from benzophenone and vinylmagnesium bromide in almost quantitative yield. The initial access to β-bromo acetal **6** with ethyl vinyl ether and conventional bromination reagents such as NBS proved to be difficult owing to steric hindrance imparted from tertiary allyl alcohol **5**. This problem can be solved through attack of the more reactive 1,2-dibromo-1-ethoxyethane generated *in situ* from Br_2 and ethyl vinyl ether,[7] to **5** promoted by *N*,*N*-dimethylaniline. Thus, the desired **6** was isolated in 95% yield in 10 gram scale, and set the stage for the following Ueno–Stork radical cyclization. We firstly choose our recent developed Ni(0)·2EC·Py[8] [EC = ethyl crotonate, Py = pyridine] catalysis system as a tin-free approach for this key transformation, and disappointedly found that the cyclic acetal **7** was obtained in only 16% yield accompanied by the significant formation of **5** (60–70% yield) resulted from facile β-elimination. Eventually, we turned our attention to classical conditions (Bu_3SnH, AIBN, Δ) for the Ueno–Stork radical cyclization. Thus, subjection of precursor **6** to the above described radical conditions afforded the desired **7** as a mixture of inconsequential diastereomers (d.r. = 1.5 : 1) smoothly in 94% yield in gram scale. Next, γ-lactone **8** could be easily obtained in 94% isolated yield through oxidation of ethyl-protected lactol **7** mediated by an excess of *m*-CPBA and $BF_3{\cdot}Et_2O$.[9] The stereoselective incorporation of the C(8) methyl group could be realized through highly diastereoselective methylation of γ-lactone **8**. Under optimized conditions [LiHMDS (4.0 equiv.), THF, −78 °C, 1.0 h, then MeOTf (2.0 equiv.), −78 °C, 4.0 h], the *trans*-dimethyl γ-lactone **9** (d.r. = 30 : 1, determined by ^1H NMR) was produced in 85% yield, whose stereochemistry assignment was unambiguously confirmed by its single-crystal structure analysis.[10] With **9** in hand, the reduction of lactone with $LiAlH_4$ followed by TFA treatment of the resulting crude diol afforded tetrahydrofuran **10** in 92% overall yield, and therefore the whole route (6 steps, 64% overall yield) established the feasibility for the total synthesis of sacidumlignan D.

Based on the success of synthesizing sacidumlignan D's skeleton, early-stage incorporation of the C(8) methyl group was further investigated in order to extend the application scope of Ueno–Stork cyclization (Scheme 2B). To this end, commercially available ethyl propenyl ether (*E* : *Z* = 1.7 : 1) was utilized to give β-bromo acetal **11** as a mixture of inseparable diastereomers (d.r. = 1.7 : 1) in 94% yield following the similar procedure for **6**. The analogous Ueno–Stork cyclization of **11** proceeded smoothly, a mixture of four diastereomers (d.r. = 2.4 : 1.2 : 2.2 : 1) **12** can be obtained in 90% yield, among which the least polar isomer was carefully separated by column chromatography and its relative stereochemistry had been assigned according to the corresponding NOE spectra.[11] After efficient oxidation of **12** with *m*-CPBA, four diastereomers reduced to a mixture of two inseparable ones **9′** (d.r. = 1 : 1). Since a *trans* relationship of the C(8) and C(8′) methyl groups is desired, the epimerization reaction[12] of **9′** to **9** promoted by a base was next investigated. We screened some bases including DBU, NaOMe, *t*-BuOM (M = Li, K), MHMDS (M = Li, Na, K) in different solvents at variable temperature, and eventually found that excess KHMDS followed by quenching with aq. NH_4Cl is superior for the desired inversion of the C(8) stereogenic center. In addition, the expected *trans*-dimethyl diastereomer could be further enriched through the repeated reaction sequence (reduction to diastereomeric diol and easy separation; oxidation of *cis*-dimethyl diol to the corresponding lactone followed by the second run epimerization to **9**), which provided an alternative to satisfy the need of subsequent synthesis.

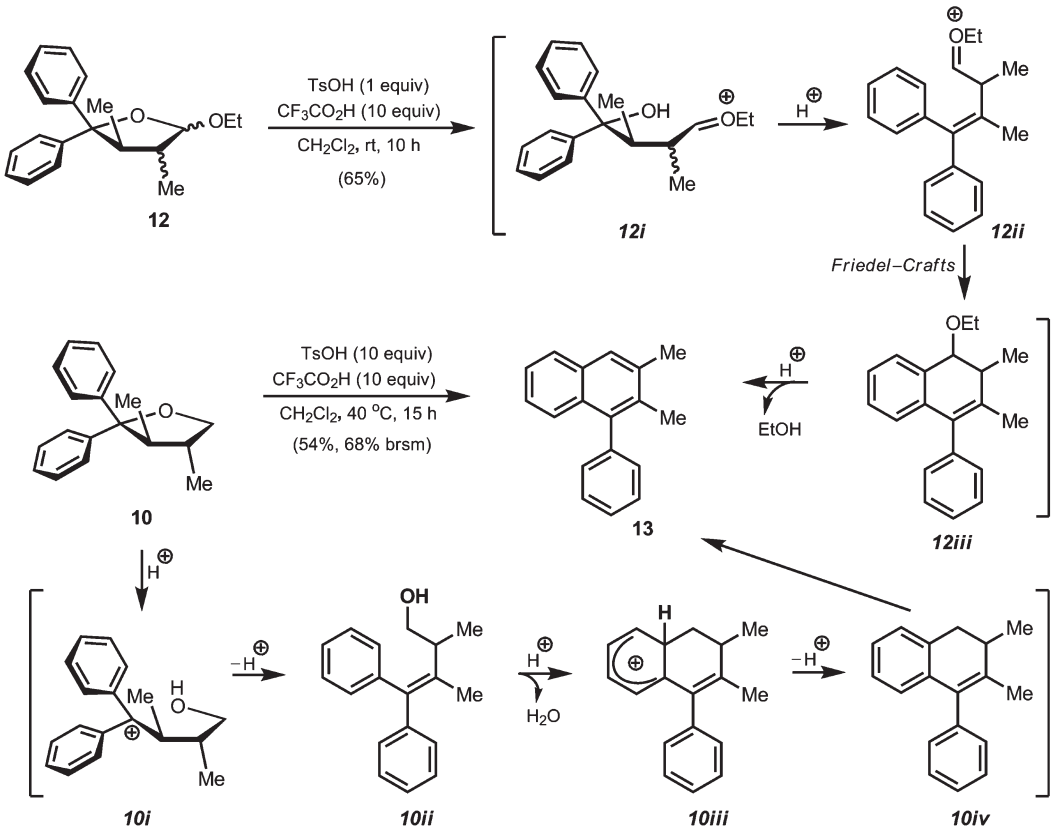
Interestingly, another important value of **12** as a mixture of inconsequential diastereomers had been proved in the direct



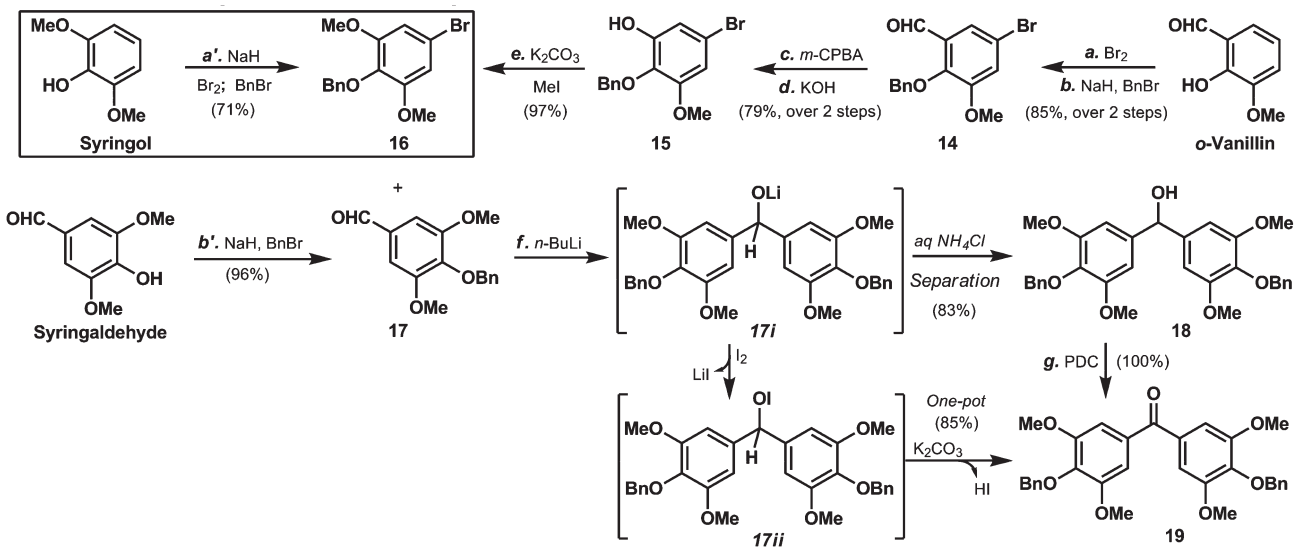
Scheme 2 Model studies for sacidumlignan D. *Reagents and conditions*: (a) vinylmagnesium bromide (1.1 equiv.), THF, 0 °C to rt, 2 h, 98%; (b) Br_2 (15.0 equiv.), ethyl vinyl ether *or* (*E* : *Z* = 1.7 : 1) ethyl propenyl ether (16.0 equiv.), CH_2Cl_2, −78 °C, 15 min, to rt, 15 min; then alcohol **5** (1.0 equiv.), *N*,*N*-dimethylaniline (30.0 equiv.), −78 to 0 °C, 10 h, then rt, 12 h, 95% for **6** *or* 94% (d.r. = 1.7 : 1, determined by ^{1}H NMR) for **11**; (c) Bu_3SnH (10.0 equiv.), AIBN (3.0 equiv.), PhMe, 85 °C, 1.5 h, 94% (d.r. = 1.5 : 1, determined by ^{1}H NMR) for **7** *or* 90% (d.r. = 2.4 : 1.2 : 2.2 : 1, determined by GC-MS) for **12**; (d) *m*-CPBA (3.0 equiv.), $BF_3{\cdot}Et_2O$ (2.0 equiv.), CH_2Cl_2, rt, 15 min, 94% for **8** *or* 92% (*trans*–*cis* = 1 : 1, determined by ^{1}H NMR) for **9'**; (e) LiHMDS (4.0 equiv.), THF, −78 °C, 1 h, then MeOTf (2.0 equiv.), −78 °C, 4 h, 85%; (f) $LiAlH_4$ (2.5 equiv.), THF, 0 °C, 1.0 h; TFA (2.0 equiv.), CH_2Cl_2, 0 °C, 5 min, 92% over 2 steps; (g) KHMDS (4.0 equiv.), PhMe, −15 °C, 12 h then aq. NH_4Cl, 95% (d.r. = 9 : 1, determined by ^{1}H NMR).

access to **13** with sacidumlignan A's skeleton. As shown in Scheme 3, simple exposure of **12** in the solution of CH_2Cl_2 containing TsOH and CF_3CO_2H at room temperature for 10 h, arylnaphthalene **13** could be isolated in 62% yield. This remarkable cascade would be made up of the following sequential transformations: (i) ring-opening of cyclic acetal **12** takes places upon the addition of acid; (ii) The facile dehydration of the resulting tertiary benzyl alcohol **12i** would afford oxonium **12ii**; (iii) the intramolecular Friedel–Crafts reaction of reactive species **12ii** would generate aryldihydronaphthalene **12iii** that converts to more stable arylnaphthalene **13** through the elimination of EtOH molecule. It is noteworthy that a similar transformation is known although the naphthalene derivative was observed as undesired byproduct there.[12a] More importantly, *gem*-diphenyl tetrahydrofuran **10** can also transformed to **13** in 54% (68% brsm) yield under similar acidic conditions,[13] and this interesting cascade shed a light on the plausible chemical correlation between sacidumlignan D and A. The possible reaction mechanism is described in Scheme 3 (bottom), involving a series of transformations *via* intermediacy **10i–10iv**: (i) acid promoted ring-opening of **10** takes places regioselectively followed by β-elimination, affording tetrasubstituted alkene **10ii**; (ii) Friedel–Crafts reaction of **10ii** would generate aryldihydronaphthalene **10iv** that converts to the more stable arylnaphthalene **13** upon aerobic oxidation.

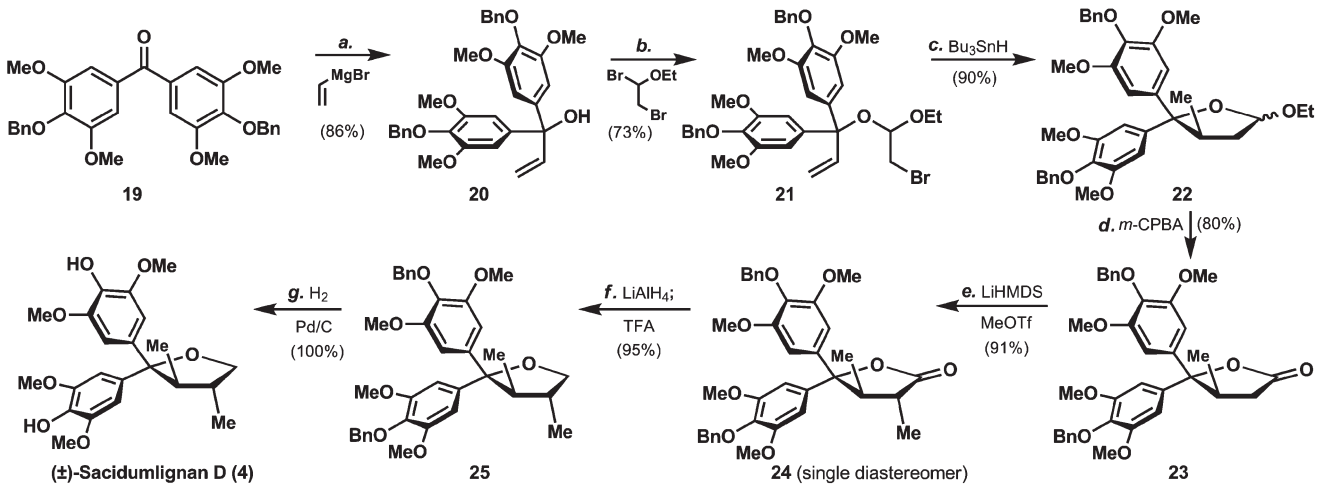
Encouraged by successful model studies, the total synthesis of sacidumlignan D was next pursued. Firstly, we carried out the efficient synthesis of functionalized diaryl ketone **19** (Scheme 4). Starting from *o*-vanillin, the aldehyde **14** could be obtained by regioselective bromination and benzyl protection of free –OH with deca-gram scale. The choice for a benzyl protecting group is important owing to its compatibility with the successive steps that would greatly improve overall synthesis efficiency compared to frequent adjustment of protecting groups in the previous route.[3a] The Dakin oxidation[14] of **14** followed by alkaline hydrolysis afforded phenol **15**. The new generated free –OH was converted its methyl ether **16** in almost quantitative yield after treatment with K_2CO_3 and MeI. The whole route for bromide **16** is efficient with 65% overall yield albeit in 5 steps. The alternative step economic pathway could be realized through the utilization of commercially available syringol, and simple treatment with Br_2 and BnBr under strong base conditions could give bromide **16** in comparable yield as well. Another building block **17** was prepared in only one step from commercially available syringaldehyde in almost quantitative yield. With sufficient amounts of **16** and **17** in hand, the coupling of these two fragments was then investigated. Upon the subjection to aryl lithium, generated *in situ* from bromide **16** with *n*-BuLi at −78 °C, aldehyde **17** could be smoothly transformed into diaryl carbinol **18** in 83% isolated



Scheme 3 Model studies for sacidumlignan A.



Scheme 4 Efficient synthesis of diaryl ketone **19**. *Reagents and conditions*: (a) Br_2 (1.1 equiv.), Na_2CO_3 (1.1 equiv.), $CHCl_3$, 20 °C, 2 d, 87%; (a′) NaH (0.01 equiv.), NBS (1.06 equiv.), CH_2Cl_2–MeOH (125 : 1), −45 °C, 2.5 h, rt, 8 h; NaH (1.1 equiv.), DMF, 0 °C, 8 min, rt, 0.5 h; then *n*-Bu_4NI (0.13 equiv.), BnBr (2.4 equiv.), rt, overnight, 71%; (b) NaH (1.1 equiv.), DMF, 0 °C, 0.5 h; then *n*-Bu_4NI (0.13 equiv.), BnBr (4.8 equiv.), rt, overnight, 97%; (b′) The condition is similar to that given in (b); NaH (1.1 equiv.), DMF, 0 °C, 0.5 h; then *n*-Bu_4NI (0.2 equiv.), BnBr (4.8 equiv.), rt, overnight, 96%; (c) *m*-CPBA (2.0 equiv.), CH_2Cl_2, 0 °C to rt, 2 d; (d) KOH (10% in water), EtOH, rt, 2 h, 79% over 2 steps; (e) K_2CO_3 (1.4 equiv.), DMF, 0 °C, 30 min; then MeI (1.6 equiv.), *n*-Bu_4NI (0.2 equiv.), 0 °C to rt, 10 h, 97%; (f) **16**, *n*-BuLi (1.1 equiv.), THF, −78 °C, 30 min; then aldehyde **17** (1.2 equiv.), −78 °C, 20 min, then to rt, 2 h, quench by aq. NH_4Cl, 83% *or* I_2 (1.6 equiv.), K_2CO_3 (3.0 equiv.), *t*-BuOH, reflux, 10 h, 85%; (g) PDC (1.5 equiv.), CH_2Cl_2, 10 °C, 24 h, 100%.



Scheme 5 Total synthesis of (±)-sacidumlignan D (**4**). *Reagents and conditions*: (a) vinylmagnesium bromide (1.1 equiv.), THF, 0 °C to rt, 2 h, 86%; (b) Br_2 (8.0 equiv.), ethyl vinyl ether (10.0 equiv.), CH_2Cl_2, −78 °C, 40 min; then alcohol **20** (1.0 equiv.), *N*,*N*-dimethylaniline (15.0 equiv.), −78 to 0 °C, 3 h, then 18 °C, 15 h, 73%; (c) *n*-Bu_3SnH (10.0 equiv.), AIBN (3.0 equiv.), PhMe, 85 °C, 1.0 h, 90% (d.r. = 2.3 : 1); (d) *m*-CPBA (2.9 equiv.), $BF_3{\cdot}Et_2O$ (2.0 equiv.), CH_2Cl_2, rt, 10 s, 80%; (e) LiHMDS (4.0 equiv.), THF, −78 °C, 1.0 h, then MeOTf (3.0 equiv.), −78 °C, 4 h, 91%; (f) $LiAlH_4$ (3.0 equiv.), THF, 0 °C, 0.5 h; TFA (2.0 equiv.), CH_2Cl_2, 0 °C, 5 min, 95%; (g) H_2 (1 *atm*), Pd/C (10%, 5.0 equiv.), EtOAc–MeOH (1 : 1), 25 °C, 0.5 h, 100%.

yield after quenching with saturated aqueous NH_4Cl. The next oxidation of **18** with PDC led to the formation of functionalized diaryl ketone **19** in quantitative yield. Furthermore, inspired by Togo's recent cascade protocol,[15] we also investigated the feasibility of access to **19** in one-pot. Indeed, the alkoxide lithium intermediate **17i** could give **17ii** without purification that would deliver to **19** in 85% isolated yield through elimination of HI assisted by K_2CO_3.

With sufficient amounts of diaryl ketone **19** in hand, the total synthesis of sacidumlignan D was then completed (Scheme 5) based on successful experience of model studies. *gem*-Diaryl allyl alcohol **20** can be synthesized from **19** and vinylmagnesium bromide in 86% yield. The access to β-bromo acetal **21** with ethyl vinyl ether under previous optimized conditions proved to be smooth, and the desired Ueno–Stork radical cyclization precursor could be obtained in 75% yield. Again, the classical conditions (Bu_3SnH, AIBN, Δ) allowed the cyclization to proceed smoothly which afforded the cyclic acetal **22** as a mixture of inconsequential separable diastereomers (d.r. = 2.3 : 1) in 90% yield. This cyclization also easily took place under less toxic $(TMS)_3SiH$/AIBN conditions,[16] and the desired **22** could be isolated in 85% yield. Oxidation of cyclic acetal **22** mediated by *m*-CPBA and $BF_3{\cdot}Et_2O$ can provide γ-lactone **23** in 80% isolated yield under carefully controlled conditions due to the highly electron-donating aromatic rings compared to model substrate **7**. Methylation of γ-lactone **23** is highly diastereoselective, and only one diastereomer **24** can be observed under shown condition. With **24** in hand, the reduction of lactone with $LiAlH_4$ followed by TFA treatment afforded benzyl protected sacidumlignan D **25** in 95% overall yield. Eventually, **25** could be transformed to (±)-sacidumlignan D without purification under hydrogenolysis conditions.[17] The NMR spectroscopic data of the synthetic (±)-sacidumlignan D (**4**) agree with those reported for the natural product[2,18] and in the previous racemic synthesis.[3a] The structure assignment of synthetic (±)-sacidumlignan D (**4**) was unambiguously confirmed by its single-crystal structure analysis (Fig. 2).[10] It is noteworthy that the present route (9 steps, 8 column chromatography separation, 24% overall yield) for (±)-sacidumlignan D is superior to the previous racemic one by Ramana and co-workers (14 steps, 2.7% overall yield).[3a]

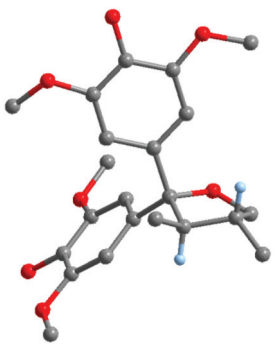
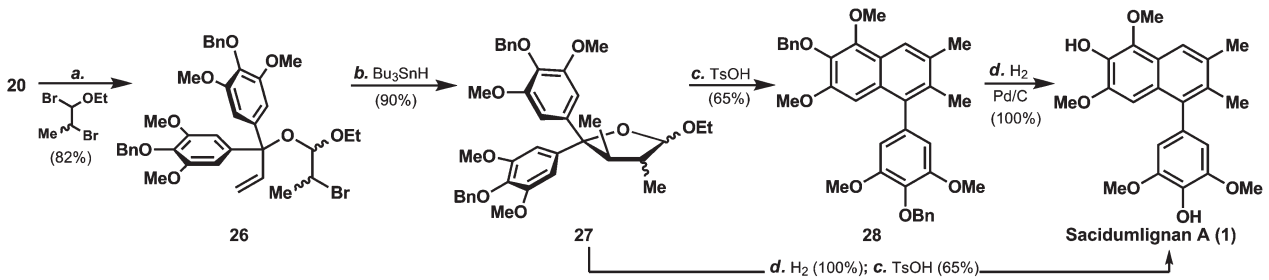


Fig. 2 X-ray crystal structure of (±)-sacidumlignan D (**4**).

Our next focus was the total synthesis of sacidumlignan A (**1**). As shown in Scheme 6, previously synthesized diaryl allyl alcohol **20** and dibromide derived from ethyl propenyl ether were employed to prepare β-bromo acetal **26** as a mixture of inseparable diastereomers (d.r. = 1.7 : 1) in 82% yield following a similar procedure for model substrate **11**. The analogous Ueno–Stork cyclization of **26** proceeded smoothly, providing a mixture of inconsequential diastereomers **27** in 90% yield. The key skeletal rearrangement from cyclic acetal **27** to arylnaphthalene **28** took place at room temperature as expected under acidic conditions, and the desired benzyl protected sacidumlignan A could be obtained in 65% isolated yield.



Scheme 6 A concise total synthesis of sacidumlignan A (**1**). *Reagents and conditions*: (a) Br_2 (10.0 equiv.), ethyl propenyl ether ($E:Z$ = 1.7 : 1, 10.5 equiv.), CH_2Cl_2, −78 °C, 20 min; then alcohol **20** (1.0 equiv.), *N*,*N*-dimethylaniline (20.0 equiv.), −78 °C, 0.5 h, then rt, 5 h, 82% (d.r. = 1.7 : 1); (b) Bu_3SnH (8.0 equiv.), AIBN (3.0 equiv.), PhMe, 85 °C, 1.0 h, 90%; (c) TsOH (1.0 equiv.), CH_2Cl_2, 25 °C, 10 h, 65%; (d) H_2 (1 *atm*), Pd/C (10%, 5.0 equiv.), EtOAc–MeOH (1 : 1), 25 °C, 5 min, 100%.

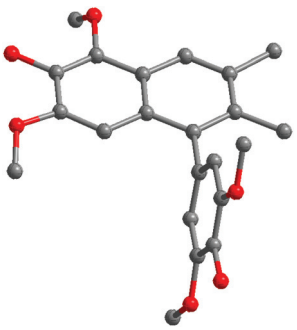
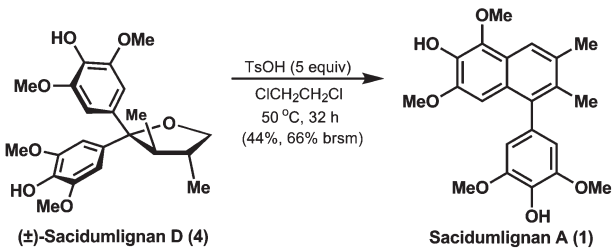


Fig. 3 X-ray crystal structure of sacidumlignan A (**1**).



Scheme 7 Conversion of (±)-sacidumlignan D to sacidumlignan A.

Compared to use of a mixture of two Brønsted acids in the model study (**12**→**13**), only TsOH as milder medium can trigger this cascade reaction, which is attributed to electron-rich aromatic rings in **27** that would make the above mentioned intramolecular Friedel–Crafts reaction proceed much easier. Eventually, **28** could be transformed to sacidumlignan A (**1**) in quantitative yield under similar hydrogenolysis conditions, whose NMR spectroscopic data well agree with those reported for the natural product[2] except for the appearance of phenolic –OH peaks, and in the previous synthesis.[3b,19] The structure assignment of synthetic sacidumlignan A (**1**) was also unambiguously confirmed by its single-crystal structure analysis (Fig. 3).[10] The last two steps of the synthetic sequence could be exchanged, that is, first hydrogenation then tandem cyclization of free phenol intermediate initiated by acid can also afford sacidumlignan A with identical efficiency. Notably, sacidumlignan A can be efficiently accessed (7 steps with 25% overall yield *versus* 14-steps route with 9.4% overall yield from Ramana's synthesis[3b]) employing the present new route.

Interestingly, plausible conversion relationship of (±)-sacidumlignan D (**4**) to A (**1**) has been also disclosed based on the model studies (**10**→**13**, Scheme 3). As shown in Scheme 7, exposure of sacidumlignan D (**4**) in the solution of $ClCH_2CH_2Cl$ containing 5 equivalent of TsOH at 50 °C for 32 h and simple work-up could afforded arylnaphthalene sacidumlignan A (**1**) in 44% yield (66% brsm) along with the recovery of small amounts (*ca.* 33%) of **4**, and therefore chemical correlation of these two natural products was established.

Conclusions

In summary, we have provided an additional example for the synthetic application of Ueno–Stork radical cyclization strategy in lignans class natural products, and achieved total synthesis of (±)-sacidumlignan D (**4**) successfully in 9 steps (LLS) from commercially available materials with 24% overall yield and 8 column chromatography protocols. Employing analogous Ueno–Stork radical cyclization product **27**, sacidumlignan A (**1**) can be also efficiently synthesized in only 7 steps with 25% overall yield, where acid triggered cascade reaction played an important role. More interestingly, facile conversion from (±)-sacidumlignan D (**4**) to sacidumlignan A (**1**) has been observed for the first time, providing an alternative pathway for the access to other arylnaphthalene lignans.

Experimental section

General

For product purification by flash column chromatography, silica gel (200–300 mesh) and petroleum ether (bp. 60–90 °C) are used. All solvents were purified and dried by standard techniques, and distilled prior to use. All organic extracts were dried over Na_2SO_4 or $MgSO_4$, unless otherwise noted. All experiments were conducted under an argon or nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. NMR spectra were measured on 300, 400 and 600 MHz instruments. All ^1H chemical shifts (δ) are relative to residual protic solvent ($CHCl_3$: δ 7.26 ppm; CD_3COCD_3: δ 2.05 ppm), and all ^{13}C

chemical shifts (δ) are relative to the solvent ($CHCl_3$: δ 77.00 ppm; CD_3COCD_3: δ 29.92 ppm). Mass spectra data were measured with ESI or APCI positive ion mode. Infrared spectra were recorded on FT-IR spectrophotometer.

1,1-Diphenylprop-2-en-1-ol (5). To a stirred solution of benzophenone (7.28 g, 20.0 mmol) in anhydrous THF (100 mL) was added vinylmagnesium bromide (0.7 M in THF, 62.8 mL, 44.0 mmol, 1.1 equiv.) dropwise *via* syringe at 0 °C. The resulting mixture was stirred for 0.5 h at this temperature, then warmed to room temperature and further stirred for 2 h. The reaction was carefully quenched by saturated aqueous NH_4Cl (30 mL), and the mixture is concentrated under reduced pressure to remove THF. The resulting mixture was extracted with EtOAc (3 × 60 mL), and the combined organic layers were separated and washed with water (3 × 20 mL) and brine (40 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude allyl alcohol **5** (8.24 g, 98% yield) as a colorless oil could be used directly for the next step without further purification. R_f = 0.42 (petroleum ether–EtOAc = 10 : 1); IR (film): ν_{max} = 3557, 3458, 3059, 3028, 1641, 1599, 1491, 1447, 1325, 1167, 1028, 999, 972, 924, 763, 701, 634, 573 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, J = 8.0 Hz, 4H), 7.30 (t, J = 8.0 Hz, 4H), 7.26–7.21 (m, 2H), 6.49 (dd, J = 17.2 Hz, 10.4 Hz, 1H), 5.30 (d, J = 17.2 Hz, 1H), 5.29 (d, J = 10.4 Hz, 1H), 2.31 (s, 1H, –O*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7 (2C), 143.5, 128.1 (4C), 127.2 (2C), 126.9 (4C), 114.0, 79.4 ppm; HRMS (ESI): m/z calcd for $C_{15}H_{14}ONa^+$ $[M + Na]^+$: 233.0937, found: 233.0936.

(1-(2-Bromo-1-ethoxyethoxy)prop-2-ene-1,1-diyl)dibenzene (6). In a 1 L, round-bottom flask, Br_2 (23.2 mL, 450 mmol, 15 equiv.) was dissolved in dry CH_2Cl_2 (200 mL) and cooled to −78 °C. To the resulting solution was added ethyl vinyl ether (45.5 mL, 480 mmol, 16 equiv.) dropwise over a 30 min period, and the mixture was stirred for 15 min at −78 °C then 10 min at room temperature. This system was cooled to −78 °C again and transferred *via* cannula to another round bottom flask where the solution of allyl alcohol **5** (6.3 g, 30.0 mmol) and *N*,*N*-dimethylaniline (114 mL, 900 mmol, 30 equiv.) in CH_2Cl_2 (400 mL) had been prepared. The resulting mixture was warmed to 0 °C and further stirred for 10 h then 12 h at 25 °C. Eventually, the reaction mixture was carefully quenched by aqueous HCl (1.0 M, 100 mL) and poured into a separatory funnel. The combined organic layers were washed with aqueous HCl (1.0 M, 6 × 40 mL), water (30 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 30 : 1) on silica gel to afford the desired **6** (10.3 g, 95% yield) as a pale yellow oil. R_f = 0.48 (petroleum ether–EtOAc = 60 : 1); IR (film): ν_{max} = 3060, 2977, 2927, 1598, 1491, 1447, 1103, 1016, 764, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.36 (m, 2H), 7.35–7.32 (m, 2H), 7.31–7.28 (m, 4H), 7.27–7.23 (m, 2H), 6.67 (dd, J = 17.2 Hz, 10.8 Hz, 1H), 5.40 (dd, J = 10.8, 1.2 Hz, 1H), 4.92 (dd, J = 17.2, 1.2 Hz, 1H), 4.80 (dd, J = 6.4, 4.4 Hz, 1H), 3.49–3.42 (m, 2H), 3.37–3.30 (m, 2H), 1.06 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 143.2, 140.8, 128.4 (2C), 128.1 (2C), 128.0 (2C), 127.7, 127.6 (2C), 127.2, 118.6, 96.6, 85.3, 59.9, 32.5, 14.9 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}{}^{79}BrO_2Na^+$ $[M + Na]^+$: 383.0617, found: 383.0620.

5-Ethoxy-3-methyl-2,2-diphenyltetrahydrofuran (7). In a 500 mL, two-necked, round-bottom flask, α-bromo acetal **6** (3.0 g, 8.3 mmol) was dissolved in anhydrous toluene (300 mL) followed by the addition of *n*-Bu_3SnH (22.3 mL, 83 mmol, 10 equiv.) and AIBN (4.1 g, 24.9 mmol, 3 equiv.) under argon. The resulting mixture was heated to 85 °C and stirred for 1.5 h. Then reaction mixture was cooled to room temperature and directly concentrated under reduced pressure. The resulting crude residue was dissolved in Et_2O (30 mL) and added saturated aqueous $KF{\cdot}2H_2O$ (30 mL). The mixture was stirred for 2 h and the *n*-Bu_3SnF precipitate was filtered. The filtrate was extracted with Et_2O (2 × 50 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 20 : 1) on silica gel to afford the mixture **7** as two inconsequential diastereoisomers (d.r. = 1 : 1.5, 2.2 g, 94% yield). Colorless oil; R_f = 0.64 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3059, 2973, 2931, 2931, 2901, 1599, 1491, 1448, 1377, 1346, 1185, 1115, 1052, 996, 923, 896, 755, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (t, J = 7.2 Hz, 5H), 7.39 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.2 Hz, 5H), 7.25–7.22 (m, 8H), 7.17–7.13 (m, 5H), 5.43–5.42 (d, J = 4.8 Hz, 1.5H), 5.22 (dd, J = 5.6 Hz, 3.6 Hz, 1H), 4.09–4.02 (m, 1H), 3.71–3.59 (m, 2.5H), 3.48–3.40 (m, 1.5H), 3.36–3.27 (m, 1.5H), 3.10–3.01 (m, 1H), 2.22 (quin, J = 6.8 Hz, 1H), 2.09 (ddd, J = 12.4, 6.4, 1.2 Hz, 1.5H), 1.86 (ddd, J = 12.6, 10.0, 5.2 Hz, 1.5H), 1.75 (ddd, J = 13.0, 6.0, 4.0 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.2 Hz, 4.5H), 0.90 (d, J = 7.2 Hz, 3H), 0.82 (d, J = 7.2 Hz, 4.5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 147.0, 144.1, 144.0, 128.1 (2C), 127.7 (2C), 127.48 (2C), 127.46 (2C), 126.92 (2C), 126.88 (2C), 126.8, 126.7, 126.5 (2C), 126.4, 126.2, 126.1 (2C), 103.3, 102.5, 91.2, 90.6, 64.2, 62.4, 40.8, 40.0, 39.5, 39.4, 17.7, 17.4, 15.5, 14.9 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{22}O_2Na^+$ $[M + Na]^+$: 305.1512, found: 305.1516.

4-Methyl-5,5-diphenyldihydrofuran-2(3*H*)-one (8). To a stirred solution of acetal **7** (1.15 g, 4.0 mmol) in CH_2Cl_2 (30 mL) was added *m*-CPBA (75%, 2.8 g, 12.0 mmol, 3.0 equiv.) at room temperature followed by the addition of $BF_3{\cdot}Et_2O$ (0.9 mL, 7.2 mmol, 2.0 equiv.). After 15 min, the reaction mixture was quenched by saturated aqueous Na_2SO_3 (3 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (4 × 10 mL), water (15 mL) and brine (15 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 3 : 1) on silica gel to afford the desired **8** (947 mg, 94% yield) as a white solid. R_f = 0.44 (petroleum ether–EtOAc = 4 : 1); Mp. 104–106 °C (Hexane); IR (film): ν_{max} = 3061, 2974, 2927, 1783, 1493, 1450, 1219, 1164, 979, 931, 758, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, J = 7.2 Hz, 2H), 7.36 (d, J = 7.2 Hz, 2H), 7.29–7.25 (m, 3H), 7.23–7.22

(m, 3H), 3.42 (ddd, J = 19.2, 12.0, 7.2 Hz, 1H), 2.71 (dd, J = 17.2, 7.2, 1H), 2.32 (dd, J = 17.2, 4.8 Hz, 1H), 0.91 (d, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.7, 140.8, 140.5, 128.6 (2C), 128.2 (2C), 128.1, 127.4, 126.1 (2C), 125.6 (2C), 92.2, 38.1, 37.5, 17.2 ppm; HRMS (ESI): m/z calcd for $C_{17}H_{17}O_2^+$ $[M + H]^+$: 253.1223, found: 253.1224.

(*trans*)-3,4-Dimethyl-5,5-diphenyldihydrofuran-2(3*H*)-one (9). A 25 mL round-bottom flask was charged with HMDS (580 mg, 3.6 mmol, 6.0 equiv.) in anhydrous THF (5.0 mL) and the resulting solution was cooled to −78 °C followed by the addition of *n*-BuLi (1.6 M in THF, 1.5 mL, 2.4 mmol, 1.1 equiv.) dropwise *via* syringe. After 1 h, a solution of γ-lactone **8** (152 mg, 0.6 mmol) in anhydrous THF (5.0 mL) was added dropwise *via* syringe at this temperature and stirring was continued for 1.0 h. Then the resulting enolate was treated with MeOTf (140 μL, 1.2 mmol, 2.0 equiv.) at −78 °C, and the methylation reaction was continued for 4.0 h at the same temperature then quenched by saturated aqueous NH_4Cl (5 mL). The reaction mixture was allowed to warm to room temperature, extracted with EtOAc (3 × 30 mL). The combined organic layers were separated and washed with water (15 mL) and brine (20 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 15 : 1) on silica gel to afford the desired **9** (136 mg, 85% yield, d.r. = 30 : 1) which was dissolved in EtOAc and hexane again. After a few days, white crystals were obtained by slow evaporation of solvent at room temperature and suitable for X-ray analysis of single crystal structure. R_f = 0.54 (petroleum ether–EtOAc = 4 : 1); Mp. 99–101 °C (Hexane); IR (film): ν_{max} = 3060, 2971, 2933, 1775, 1449, 1307, 1231, 1185, 980, 767, 742, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.40–7.33 (m, 3H), 7.32–7.27 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 2.93 (dq, J = 12.0, 6.8 Hz, 1H), 2.37 (dq, J = 12.0, 6.8 Hz, 1H), 1.27 (d, J = 6.8 Hz, 3H), 1.06 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.6, 143.1, 140.1, 128.5 (2C), 128.4, 128.1 (2C), 127.7, 126.9 (2C), 126.7 (2C), 90.6, 46.2, 41.0, 16.1, 13.1 ppm; HRMS (ESI): m/z calcd for $C_{18}H_{19}O_2^+$ $[M + H]^+$: 267.1380, found: 267.1381.

(*trans*)-3,4-Dimethyl-2,2-diphenyltetrahydrofuran (10). To a stirred solution of γ-lactone **9** (48 mg, 0.18 mmol) in anhydrous THF (6 mL) at 0 °C was added $LiAlH_4$ (17 mg, 0.45 mmol, 2.5 equiv.) carefully. The reaction mixture was stirred for 1.0 h at this temperature and quenched carefully by saturated aqueous NH_4Cl (0.5 mL). The resulting precipitate was then filtered with a short plug of Celite and washed with $CHCl_3$ (3 × 5 mL). The filtrate was extracted with $CHCl_3$ (3 × 10 mL). The combined organic layers were washed with water (3 × 3 mL) and brine (4 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude diol could be used directly without further purification. To a solution of the above diol in CH_2Cl_2 (0.8 mL) at 0 °C was added TFA (27 μL, 0.36 mmol, 2.0 equiv.) in one portion. After 5 minutes, the reaction was quenched by saturated aqueous $NaHCO_3$ (2 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 10 : 1) on silica gel to afford 44 mg (92% yield over 2 steps) of the desired **10** as a colorless oil. R_f = 0.84 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3059, 3026, 2962, 2927, 2872, 1598, 1491, 1449, 1044, 754, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, J = 7.6 Hz, 2H), 7.33 (d, J = 7.6 Hz, 2H), 7.27–7.21 (m, 3H), 7.18–7.13 (m, 3H), 4.33 (t, J = 7.6 Hz, 1H), 3.47 (dd, J = 10.4, 8.0 Hz, 1H), 2.45 (dq, J = 10.6, 6.8 Hz, 1H), 2.07–1.95 (m, 1H), 1.00 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.1, 144.9, 128.0 (2C), 127.4 (2C), 127.3 (2C), 127.0, 126.9 (2C), 126.4, 90.5, 73.9, 49.1, 40.5, 15.6, 14.4 ppm; HRMS (ESI): m/z calcd for $C_{18}H_{21}O^+$ $[M + H]^+$: 253.1587, found: 253.1585.

(1-(2-Bromo-1-ethoxypropoxy)-prop-2-ene-1,1-diyl)dibenzene (11). In a 500 mL, round-bottom flask, Br_2 (7.7 mL, 150 mmol, 15 equiv.) was dissolved in dry CH_2Cl_2 (70 mL) and cooled to −78 °C. To the resulting solution was added ethyl propenyl ether (E : Z = 1.7 : 1, 17.6 mL, 160 mmol, 16 equiv.) dropwise over a 30 min period, and the mixture was stirred for 20 min at −78 °C then 10 min at room temperature. This system was cooled to −78 °C again and transferred *via* cannula to another round bottom flask where the solution of allyl alcohol **5** (2.1 g, 10.0 mmol) and *N*,*N*-dimethylaniline (38.2 mL, 300 mmol, 30 equiv.) in CH_2Cl_2 (200 mL) had been prepared. The resulting mixture was warmed to 0 °C and further stirred for 10 h then 10 h at 25 °C. Eventually, the reaction mixture was carefully quenched by aqueous HCl (1.0 M, 60 mL) and poured into a separatory funnel. The combined organic layers were washed with aqueous HCl (1.0 M, 6 × 30 mL), water (30 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 30 : 1) on silica gel to afford the desired **11** (3.52 g, 94% yield, d.r. = 1.7 : 1) as a pale yellow oil. R_f = 0.55 (petroleum ether–EtOAc = 30 : 1); IR (film): ν_{max} = 3060, 2977, 2929, 1634, 1600, 1491, 1447, 1407, 1376, 1201 1098, 1074, 1032, 763, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.35 (m, 11H), 7.33–7.21 (m, 16H), 6.70 (dd, J = 17.2, 10.8 Hz, 1H), 6.63 (dd, J = 17.2, 10.8 Hz, 1.7H), 5.41 (d, J = 10.8 Hz, 1.7H), 5.37 (d, J = 10.8 Hz, 1H), 4.98 (d, J = 17.2 Hz, 1.7H), 4.97 (d, J = 17.2 Hz, 1H), 4.65 (d, J = 3.2 Hz, 1.7H), 4.55 (d, J = 4.8 Hz, 1H), 4.14–4.08 (m, 1H), 4.06–4.00 (m, 1.7H), 3.38–3.29 (m, 2.7H), 3.25–3.14 (m, 2.7H), 1.73 (d, J = 6.8 Hz, 5.1H), 1.72 (d, J = 6.8 Hz, 3H), 1.03 (t, J = 6.8 Hz, 5.1H), 1.01 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.3, 144.1, 143.4, 143.0, 141.2, 140.8, 128.9 (2C), 128.5 (3C), 128.3 (3C), 128.2 (2C), 127.8 (2C), 127.8, 127.7 (2C), 127.6, 127.5 (2C), 127.3, 127.1, 118.7, 118.3, 99.8, 99.7, 85.2, 84.8, 64.1, 61.4, 50.4, 49.4, 20.6, 19.1, 14.95, 14.90 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}{}^{79}BrO_2Na^+$ $[M + Na]^+$: 397.0774, found: 397.0775.

5-Ethoxy-3,4-dimethyl-2,2-diphenyltetrahydrofuran (12). In a 500 mL, two-necked, round-bottom flask, α-bromo acetal **11**

(823 mg, 2.2 mmol) was dissolved in anhydrous toluene (80 mL) followed by the addition of *n*-Bu_3SnH (5.9 mL, 22 mmol, 10 equiv.) and AIBN (1.08 g, 6.6 mmol, 3 equiv.) under argon. The resulting mixture was heated to 85 °C and stirred for 1.5 h. Then reaction mixture was cooled to room temperature and directly concentrated under reduced pressure. The resulting crude residue was dissolved in Et_2O (10 mL) and added saturated aqueous $KF{\cdot}2H_2O$ (10 mL). The mixture was stirred for 2 h and the *n*-Bu_3SnF precipitate was filtered. The filtrate was extracted with Et_2O (2 × 30 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 20 : 1) on silica gel to afford the mixture **12** of 4 diastereoisomers (d.r. = 2.4 : 1.2 : 2.2 : 1 determined by GC-MS, 586 mg, 90% yield) as a colorless oil among which the least polar isomer was isolated and characterized. R_f = 0.50 (petroleum ether–EtOAc = 20 : 1); IR (film): ν_{max} = 3059, 2959, 2929, 2874, 2857, 1597, 1491, 1450, 1379, 1178, 1109, 1052, 1021, 989, 747, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.25–7.21 (m, 3H), 7.17 (d, J = 7.2 Hz, 1H), 7.10 (d, J = 7.2 Hz, 2H), 5.23 (d, J = 4.8 Hz, 1H), 3.61–3.54 (m, 1H), 3.42–3.37 (m, 1H), 2.83–2.78 (m, 1H), 2.02–1.93 (m, 1H), 1.02 (d, J = 6.8 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 0.78 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.1, 144.4, 127.7 (2C), 127.33 (2C), 127.30 (2C), 126.6, 126.53 (2C), 126.47, 104.2, 90.6, 62.1, 45.8, 44.4, 15.8, 14.8, 11.2 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{24}O_2Na^+$ $[M + Na]^+$: 319.1669, found: 319.1679.

(*cis* + *trans*)-3,4-Dimethyl-5,5-diphenyldihydrofuran-2(3*H*)-one (9′). To a stirred solution of the diastereoisomeric mixture **12** (533 mg, 1.8 mmol) in CH_2Cl_2 (15 mL) was added *m*-CPBA (75%, 1.27 g, 5.4 mmol, 3.0 equiv.) at room temperature followed by the addition of $BF_3{\cdot}Et_2O$ (0.45 mL, 3.6 mmol, 2.0 equiv.). After 15 min, the reaction mixture was quenched by saturated aqueous Na_2SO_3 (1 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (4 × 5 mL), water (10 mL) and brine (15 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 6 : 1) on silica gel to afford the desired **9′** (d.r. = 1 : 1, 440 mg, 92% yield) as a white solid. R_f = 0.54 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3061, 2974, 2933, 1776, 1494, 1450, 1334, 1231, 1196, 968, 764, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, J = 7.2 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.37–7.33 (m, 6H), 7.32–7.28 (m, 2H), 7.27–7.21 (m, 5H), 7.21–7.17 (m, 1H), 7.07 (d, J = 8.4 Hz, 2H), 3.38 (quin, J = 6.8 Hz, 1H), 2.91 (dq, J = 12.0, 6.8 Hz, 1H), 2.79 (quin, J = 6.8 Hz, 1H), 2.35 (dq, J = 12.0, 6.8 Hz, 1H), 1.24 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 7.6 Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H), 0.71 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 178.0, 142.9, 142.7, 141.0, 139.9, 128.6 (2C), 128.24 (2C), 128.20 (2C), 128.1, 127.84 (2C), 127.78, 127.5, 127.0, 126.7 (2C), 126.5 (2C), 125.6 (2C), 125.1 (2C), 90.3, 90.2, 46.0, 42.2, 40.8, 40.0, 15.9, 12.9, 11.5, 10.1 ppm; HRMS (APCI): m/z calcd for $C_{18}H_{19}O_2^+$ $[M + H]^+$: 267.1380, found: 267.1391.

2,3-Dimethyl-1-phenylnaphthalene (13). To a stirred solution of the diastereoisomeric mixture **12** (30 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) was added *p*-$TsOH{\cdot}H_2O$ (19 mg, 0.1 mmol, 1.0 equiv.) and CF_3CO_2H (75 μL, 1.0 mmol, 10.0 equiv.) at 25 °C. After 10 h, the reaction mixture was carefully quenched by saturated aqueous $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were washed with water (5 mL) and brine (5 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 100 : 1) on silica gel to afford the desired **13** (15 mg, 65% yield) as a colorless oil. R_f = 0.55 (petroleum ether–EtOAc = 100 : 1); IR (film): ν_{max} = 3056, 2966, 2925, 2872, 1605, 1509, 1456, 1296, 1246, 1184, 1034, 831, 752, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.0 Hz, 1H), 7.66 (s, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.43 (d, J = 7.2 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.30–7.22 (m, 4H), 2.49 (s, 3H), 2.13 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 138.3, 135.4, 133.1, 131.9, 131.7, 130.3 (2C), 128.3 (2C), 127.2, 126.93, 126.86, 126.3, 124.84, 124.79, 21.2, 17.6 ppm; HRMS (APCI): m/z calcd for $C_{18}H_{17}^+$ $[M + H]^+$: 233.1325, found: 233.1323.

(Alternative procedure for **13** from **10**) To a stirred solution of **10** (12 mg, 0.047 mmol) in CH_2Cl_2 (2 mL) was added *p*-$TsOH{\cdot}H_2O$ (91 mg, 0.48 mmol, 10.0 equiv.) and CF_3CO_2H (36 μL, 0.48 mmol, 10.0 equiv.) at room temperature. After stirring for 15 h at 40 °C, the reaction mixture was quenched by saturated aqueous $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were washed with water (5 mL) and brine (5 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 100 : 1) on silica gel to afford the desired **13** (6 mg, 54% yield) as a colorless oil along with the recovery of 2.4 mg (20%) of **10**.

2-(Benzyloxy)-5-bromo-3-methoxybenzaldehyde (14). This bromination reaction was carried out through modified known procedure.[20] In a 500 mL, two-necked, round-bottom flask, *o*-vanillin (16.0 g, 105 mmol) was dissolved in CH_2Cl_2 (220 mL) and cooled to 0 °C. To this stirred solution was added anhydrous Na_2CO_3 (12.4 g, 116 mmol, 1.1 equiv.) portionwise. Then Br_2 (5.9 mL, 114.3 mmol, 1.09 equiv.) was added dropwise to the above mixture with well stirring. After the addition, the reaction mixture was warmed to room temperature and stirred for 2 days. Then the reaction was carefully quenched by saturated aqueous $NaHSO_3$ (30 mL) and the resulting precipitate was removed by filtration. The filtrate was extracted with CH_2Cl_2 (400 mL), and the combined organic layers were washed with water (3 × 40 mL) and brine (30 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the desired bromo-*o*-vanillin (21.0 g, 87% yield) as a yellow solid. R_f = 0.37 (petroleum ether–EtOAc = 8 : 1); Mp. 112–115 °C (Hexane); IR (film): ν_{max} = 2982, 2925, 2877, 2854, 2022, 1653, 1464, 1388, 1274, 1256, 1201, 957, 850, 761, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 11.00 (s, 1H,

–O*H*), 9.86 (s, 1H), 7.31 (d, J = 1.8 Hz, 1H), 7.18 (d, J = 1.8 Hz, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 150.9, 149.3, 126.1, 121.3, 120.8, 111.0, 56.6 ppm; HRMS (ESI): m/z calcd for $C_8H_8{}^{79}BrO_3{}^+$ $[M + H]^+$: 230.9651, found: 230.9653. This resulting material could be used directly without further purification. To the stirred solution of the above bromo-*o*-vanillin (20.0 g, 87 mmol) in DMF (95 mL) was added NaH (60% dispersion in mineral oil, 3.83 g, 95.7 mmol, 1.1 equiv.) portionwise at 0 °C. The resulting mixture was stirred for 0.5 h further followed by the addition of BnBr (50 mL, 410 mmol, 4.8 equiv.) dropwise and *n*-Bu_4NI (4.2 g, 11.4 mmol, 0.13 equiv.). This alkylation reaction was carried out overnight, then quenched by carefully by H_2O (10 mL), diluted with CH_2Cl_2 (800 mL) and poured into a separatory funnel. The combined organic layers were separated and washed with water (6 × 50 mL) and brine (50 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 100 : 1→petroleum ether–EtOAc = 6 : 1) on silica gel to furnish the desired **14** (27.1 g, 97% yield) as a white solid. R_f = 0.73 (petroleum ether–EtOAc = 8 : 1); Mp. 85–87 °C (Hexane); IR (film): ν_{max} = 3073, 3031, 2882, 1683, 1576, 1479, 1375, 1311, 1266, 1234, 1211, 1185, 1076, 957, 844, 737, 700, 581 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.09 (s, 1H), 7.48 (d, J = 2.4 Hz, 1H), 7.39–7.26 (m, 5H), 7.25 (d, J = 2.4 Hz, 1H), 5.16 (s, 2H), 3.94 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.7, 153.9, 150.1, 135.8, 131.1, 128.8 (2C), 128.7 (2C), 121.6, 120.8, 117.1, 76.4, 56.4, 56.4 ppm; HRMS (ESI): m/z calcd for $C_{15}H_{13}{}^{79}BrO_3Na^+$ $[M + Na]^+$: 342.9940, found: 342.9944.

2-(Benzyloxy)-5-bromo-3-methoxyphenol (15). In a 100 mL, two-necked, round-bottom flask, the above benzyl-protected bromo-*o*-vanillin **14** (9.1 g, 28 mmol) was dissolved in CH_2Cl_2 (58 mL) and cooled to 0 °C. To this stirred solution was added *m*-CPBA (75%, 13.0 g, 56.5 mmol, 2.0 equiv.) portionwise. The reaction mixture was then warmed to room temperature and stirred for 2 days. Then the reaction was quenched by saturated aqueous Na_2SO_3 (30 mL) and the stirring was continued for 0.5 h. The mixture was diluted with CH_2Cl_2 (3 × 200 mL), and the combined organic layers were separated and washed with saturated aqueous $NaHCO_3$ (3 × 30 mL), water (30 mL) and brine (50 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure to furnish the desired formate as a colorless oil, which was used directly for the next hydrolysis step without further purification. R_f = 0.56 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3089, 3032, 1744, 1586, 1490, 1449, 1410, 1373, 1202, 1276, 1218, 1113, 1068, 970, 835, 750, 698, 581 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1H, –OC(O)*H*), 7.42–7.31 (m, 5H), 6.99 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 5.02 (s, 2H), 3.90 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 154.4, 143.9, 139.0, 136.7, 128.4 (2C), 128.3 (2C), 128.2, 117.9, 115.8, 114.1, 75.0, 56.4 ppm; HRMS (ESI): m/z calcd for $C_{15}H_{13}{}^{79}BrO_4Na^+$ $[M + Na]^+$: 358.9889, found: 358.9894. Thus, the above crude formate was dissolved in aqueous EtOH (64 mL) and added aqueous KOH (10%, 26 mL) at room temperature. The hydrolysis reaction was continued for 2 h then quenched by aqueous HCl (10%, 30 mL). The resulting mixture was stirred for 0.5 h and poured into a separatory funnel. The aqueous layer was extracted with EtOAc (3 × 150 mL), and the combined organic layers were washed with water (3 × 30 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was carefully purified by flash column chromatography (petroleum ether–EtOAc = 6 : 1) on silica gel to furnish the desired **15** (6.81 g, 79% yield over 2 steps) as a colorless oil. R_f = 0.56 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3031, 2939, 2840, 1592, 1494, 1452, 1325, 1213, 1167, 1107, 973, 838, 754, 730, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.33 (m, 5H), 6.71 (d, J = 2.4 Hz, 1H), 6.62 (d, J = 2.4 Hz, 1H), 5.63 (s, 1H, –O*H*), 5.02 (s, 2H), 3.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 150.3, 136.8, 133.5, 128.71 (2C), 128.65, 128.5 (2C), 116.5, 111.7, 107.8, 75.4, 56.1 ppm; HRMS (APCI): m/z calcd for $C_{14}H_{14}{}^{79}BrO_3{}^+$ $[M + H]^+$: 309.0126, found: 309.0114.

2-(Benzyloxy)-5-bromo-1,3-dimethoxybenzene (16). In a 200 mL, two-necked, round-bottom flask, the above phenol **15** (5.34 g, 17.3 mmol) was dissolved in DMF (65 mL) and cooled to 0 °C. The resulting solution was added K_2CO_3 (3.34 g, 24.3 mmol, 1.4 equiv.) slowly and the mixture was stirred for 0.5 h followed by the addition of MeI (1.7 mL, 27.3 mmol, 1.6 equiv.) dropwise and *n*-Bu_4NI (1.30 g, 3.5 mmol, 0.2 equiv.). This methylation reaction was carried out overnight, and the resulting precipitate was removed by filtration. The cake was washed with Et_2O (3 × 50 mL), and the combined organic layers were washed with water (5 × 30 mL) and brine (40 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 100 : 1→10 : 1) on silica gel to afford the desired **16** (5.43 g, 97% yield) as a white solid. R_f = 0.71 (petroleum ether–EtOAc = 3 : 1); Mp. 55–57 °C (Hexane); IR (film): ν_{max} = 3090, 3030, 2863, 1587, 1495, 1457, 1408, 1378, 1305, 1225, 1184, 1011, 982, 834, 813, 733, 698, 578 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, J = 6.8 Hz, 2H), 7.38–7.29 (m, 3H), 6.72 (s, 2H), 4.99 (s, 2H), 3.81 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 137.5, 136.1, 128.5 (2C), 128.1 (2C), 127.9, 116.2, 109.0 (2C), 75.0 (2C), 56.3 (2C) ppm; HRMS (ESI): calcd for $C_{15}H_{16}{}^{79}BrO_3{}^+$ $[M + H]^+$: 323.0277, found: 323.0280.

(Alternative procedure for **16**)[21] In a 100 mL, two-necked, round-bottom flask, the syringol (3.0 g, 20 mmol) was dissolved in CH_2Cl_2 (50 mL) and MeOH (0.4 mL). The resulting solution was then cooled to −45 °C followed by the addition of NaH (60% dispersion in mineral oil, 10 mg, 0.01 equiv.) portionwise. After 15 min, NBS (3.7 g, 21 mmol, 1.06 equiv.) was added portionwise during a period of 8 min and the bromination reaction mixture was stirred for 2.5 h at −45 °C then 8 h at to room temperature. The reaction was carefully quenched by water (10 mL) and the mixture was extracted with EtOAc (3 × 35 mL), and the combined organic layers were washed with water (3 × 20 mL) and brine (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The

resulting crude residue could be filtered through a short plug of silica gel (elution with petroleum ether–EtOAc), providing the desired 4-bromo-syringol (3.50 g) as a yellow solid which could be used directly for the next step without further purification. The small amount of sample was purified by flash column chromatography (petroleum ether–EtOAc = 10 : 1→petroleum ether–EtOAc = 5 : 1) on silica gel for characterization: R_f = 0.65 (petroleum ether–EtOAc = 4 : 1); Mp. 92–94 °C (Hexane), (lit.[20] mp. 93–100 °C); IR (film): ν_{max} = 3423, 2956, 2925, 2851, 1610, 1504, 1459, 1417, 1359, 1235, 1210, 1114, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.72 (s, 2H), 5.45 (s, 1H), 3.87 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6 (2C), 134.1, 111.1, 108.6 (2C), 56.5 (2C) ppm; HRMS (APCI): *m*/*z* calcd for $C_8H_8O_3{}^{79}Br^+$ $[M - H]^+$: 230.9651, found: 230.9652. The above crude 4-bromo-syringol (3.50 g, 14.9 mmol) was dissolved in DMF (50 mL) then cooled to 0 °C followed by the addition of NaH (60% dispersion in mineral oil, 657 mg, 1.1 equiv.) portionwise during a period of 5 min. After stirring for 8 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 30 min followed by the addition of BnBr (35.9 mL, 24 mmol, 2.4 equiv.) dropwise and *n*-Bu_4NI (717 mg, 1.9 mmol, 0.13 equiv.). This alkylation reaction was carried out overnight, then carefully quenched by H_2O (5 mL) and extracted with Et_2O (3 × 50 mL). The combined organic layers were separated and washed with water (9 × 15 mL) and brine (20 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 100 : 1→petroleum ether–EtOAc = 20 : 1) to afford the desired **16** (4.48 g, 71% yield).

4-(Benzyloxy)-3,5-dimethoxybenzaldehyde (17). To a stirred solution of syringaldehyde (3.64 g, 20 mmol) in DMF (40 mL) was added NaH (60% dispersion in mineral oil, 890 mg, 22.2 mmol, 1.1 equiv.) portionwise at 0 °C. The resulting mixture was stirred for 0.5 h further at room temperature followed by the addition of BnBr (11.5 mL, 96.8 mmol, 4.84 equiv.) dropwise and *n*-Bu_4NI (1.6 g, 4.3 mmol, 0.2 equiv.). This alkylation reaction was carried out overnight, then carefully quenched by H_2O (8 mL), diluted with CH_2Cl_2 (100 mL) and poured into a separatory funnel. The combined organic layers were separated and washed with water (5 × 15 mL) and brine (20 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 100 : 1→petroleum ether–EtOAc = 20 : 1) on silica gel to furnish the desired **17** (5.2 g, 96% yield) as a white solid. R_f = 0.43 (petroleum ether–EtOAc = 3 : 1); Mp. 62–63 °C (Hexane); IR (film): ν_{max} = 2919, 2848, 1689, 1585, 1493, 1458, 1419, 1383, 1324, 1226, 1123, 734, 696, 580 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.84 (s, 1H), 7.47–7.45 (m, 2H), 7.35–7.28 (m, 3H), 7.10 (s, 2H), 5.12 (s, 2H), 3.87 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.0, 153.8 (2C), 142.2, 137.1, 131.8, 128.3 (2C), 128.1 (2C), 127.9, 106.5 (2C), 74.9, 56.1 (2C) ppm; HRMS (ESI): calcd for $C_{16}H_{17}O_4^+$ $[M + H]^+$: 273.1121, found: 273.1125.

Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)methanol (18). In a 100 mL, two-necked, round-bottom flask, the bromide **16** (972 mg, 3 mmol) was dissolved in anhydrous THF (6 mL) and cooled to −78 °C. The resulting solution was treated with *n*-BuLi (1.6 M in THF, 2.06 mL, 3.3 mmol, 1.1 equiv.) dropwise *via* syringe and the mixture was stirred for 0.5 h at this temperature followed by the addition of the solution of aldehyde **17** (980 mg, 3.6 mmol, 1.2 equiv.) in THF (2 mL). The reaction mixture was stirred for 20 min at −78 °C then allowed to warm to room temperature, and stirred further for 2 h. The reaction was carefully quenched by saturated aqueous NH_4Cl (6 mL), and extracted with EtOAc (3 × 30 mL). The combined organic layers were separated and washed with water (3 × 15 mL) and brine (20 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 5 : 1) on silica gel to afford the desired **18** (1.29 g, 83% yield) as a colorless oil. R_f = 0.50 (petroleum ether–EtOAc = 2 : 1); IR (film): ν_{max} = 3488, 3002, 2837, 2023, 1592, 1501, 1460, 1419, 1328, 1233, 1127, 985, 913, 839, 734, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 8.0 Hz, 4H), 7.38–7.27 (m, 6H), 6.58 (s, 4H), 5.66 (s, 1H), 5.03 (s, 4H), 3.79 (s, 12H), 2.76 (brs, 1H, –O*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3 (4C), 139.3 (2C), 137.6 (2C), 135.9 (2C), 128.3 (4C), 128.0 (4C), 127.7 (2C), 103.6 (4C), 76.0, 74.8 (2C), 56.0 (4C) ppm; HRMS (ESI): calcd for $C_{31}H_{32}O_7Na^+$ $[M + Na]^+$: 539.2040, found: 539.2047.

Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)methanone (19). To a stirred solution of diarylcarbinol **18** (1.25 g, 2.4 mmol) in CH_2Cl_2 (8 mL) was added PDC (1.35 g, 3.6 mmol, 1.5 equiv.) portionwise at 0 °C. The resulting mixture was stirred for 24 h further at 10 °C, then filtered and concentrated under reduced pressure to afford the desired **19** (1.24 g, 100% yield) as a white solid. This resulting material could be used directly for the next Grignard addition reaction without further purification. R_f = 0.58 (petroleum ether–EtOAc = 2 : 1); Mp. 84–86 °C (Hexane); IR (film): ν_{max} = 2940, 2838, 2024, 1635, 1576, 1501, 1465, 1412, 1337, 1234, 1176, 1126, 977, 860, 741, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.2 Hz, 4H), 7.38–7.27 (m, 6H), 7.06 (s, 4H), 5.15 (s, 4H), 3.86 (s, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.8, 153.0 (4C), 140.5 (2C), 137.3 (2C), 132.8 (2C), 128.4 (4C), 128.1 (4C), 127.9 (2C), 107.4 (4C), 74.9 (2C), 56.2 (4C) ppm; HRMS (ESI): calcd for $C_{31}H_{31}O_7^+$ $[M + H]^+$: 515.2064, found: 515.2079.

(One-pot procedure for **19**) The bromide **16** (486 mg, 1.5 mmol) was dissolved in anhydrous THF (3 mL) and cooled to −78 °C. The resulting solution was treated with *n*-BuLi (1.6 M in THF, 1.03 mL, 1.65 mmol, 1.1 equiv.) dropwise *via* syringe and the mixture was stirred for 0.5 h at this temperature followed by the addition of the solution of aldehyde **17** (490 mg, 1.8 mmol, 1.2 equiv.) in THF (2 mL). The reaction mixture was stirred for 20 min at −78 °C then allowed to warm to room temperature, and stirred further for 1 h. Then, after the removal of THF, *t*-BuOH (3 mL) was added followed by the addition of I_2 (610 mg, 2.4 mmol, 1.6 equiv.) and K_2CO_3 (620 mg, 4.5 mmol, 3.0 equiv.). The resulting mixture was

stirred for 10 h at refluxing condition. The reaction was then quenched by saturated aqueous Na_2SO_3 (6 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were separated and washed with water (3 × 10 mL) and brine (10 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was carefully purified by flash column chromatography (petroleum ether–EtOAc = 7 : 1→petroleum ether–EtOAc = 5 : 1) on silica gel to afford the desired **19** (656 mg, 85% yield).

1,1-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)prop-2-en-1-ol (20). To a stirred solution of diarylketone **19** (451 mg, 0.88 mmol) in anhydrous THF (3.5 mL) was added vinylmagnesium bromide (0.7 M in THF, 1.4 mL, 0.98 mmol, 1.1 equiv.) dropwise *via* syringe at 0 °C. The resulting mixture was warmed to room temperature and further stirred for 2 h. The reaction was carefully quenched by saturated aqueous NH_4Cl (5 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were separated and washed with water (3 × 5 mL) and brine (10 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 4 : 1) on silica gel to afford the desired **20** (410 mg, 86% yield) as a colorless oil. R_f = 0.48 (petroleum ether–EtOAc = 2 : 1); IR (film): ν_{max} = 3479, 3029, 3001, 2935, 2867, 2837, 1589, 1500, 1456, 1413, 1323, 1236, 1126, 993, 841, 756, 734, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, J = 6.8 Hz, 4H), 7.35–7.27 (m, 6H), 6.58 (s, 4H), 6.42 (dd, J = 17.2 Hz, 10.8 Hz, 1H), 5.34 (d, J = 17.2 Hz, 1H), 5.32 (d, J = 10.8 Hz, 1H), 5.02 (s, 4H), 3.75 (s, 12H), 2.28 (s, 1H, –O*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0 (4C), 143.1, 141.1 (2C), 137.8 (2C), 136.0 (2C), 128.4 (4C), 128.1 (4C), 127.8 (2C), 114.0, 104.4 (4C), 79.6, 74.9 (2C), 56.1 (4C) ppm; HRMS (ESI): calcd for $C_{33}H_{33}O_6^+$ $[M - OH - e]^+$: 525.2272, found: 525.2280.

5,5′-(1-(2-Bromo-1-ethoxyethoxy)prop-2-ene-1,1-diyl)bis-(2-(benzyloxy)-1,3-dimethoxybenzene) (21). In a 50 mL round-bottom flask, Br_2 (0.95 mL, 19.0 mmol, 8 equiv.) was dissolved in anhydrous CH_2Cl_2 (25 mL) and cooled to −78 °C. To the resulting solution was added ethyl vinyl ether (2.3 mL, 23.8 mmol, 10 equiv.) dropwise over a 5 min period, and the mixture was stirred for 40 min at −78 °C. This system was cooled to −78 °C again, and transferred *via* cannula to another round bottom flask where the solution of allyl alcohol **20** (1.29 g, 2.38 mmol) and *N*,*N*-dimethylaniline (4.5 mL, 35.7 mmol, 15 equiv.) in CH_2Cl_2 (20 mL) had been prepared. The resulting mixture was gradually warmed to 0 °C over a 3 h period and further stirred for 15 h at 18 °C. Eventually, the reaction mixture was directly concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 30 : 1→10 : 1) on neutral Al_2O_3 to afford the desired **21** (1.20 g, 73% yield) as a colorless oil. R_f = 0.38 (petroleum ether–EtOAc = 6 : 1); IR (film): ν_{max} = 2972, 2919, 2869, 1585, 1500, 1455, 1413, 1374, 1235, 1124, 734, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.45 (m, 4H), 7.34–7.26 (m, 6H), 6.58 (s, 2H), 6.56 (dd, J = 17.4, 10.4 Hz, 1H), 6.55 (s, 2H), 5.37 (dd, J = 10.4, 1.6 Hz, 1H), 5.06 (s, 2H), 5.03 (s, 2H), 5.02 (dd, J = 17.2, 1.6 Hz, 1H), 4.69 (t, J = 5.6 Hz, 1H), 3.74 (s, 6H), 3.72 (s, 6H), 3.45–3.39 (m, 2H), 3.37–3.31(m, 2H), 1.08 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9 (2C), 152.7 (2C), 140.6, 139.1, 138.2, 137.8, 137.7, 136.1, 136.0, 128.51 (2C), 128.45 (2C), 128.0 (4C), 127.81, 127.76, 118.1, 106.2 (2C), 106.0 (2C), 97.0, 85.6, 74.83, 74.78, 60.8, 56.19 (2C), 56.16 (2C), 32.8, 15.1 ppm; HRMS (APCI): calcd for $C_{37}H_{42}O_8{}^{79}Br^+$ $[M + H]^+$: 693.2058, found: 693.2088.

2,2-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)-5-ethoxy-3-methyltetrahydrofuran (22). In a 250 mL, two-necked, round-bottom flask, α-bromo acetal **21** (623 mg, 0.9 mmol) was dissolved in anhydrous toluene (100 mL) followed by the addition of *n*-Bu_3SnH (2.4 mL, 9 mmol, 10 equiv.) and AIBN (440 mg, 2.7 mmol, 3 equiv.) under argon. The resulting mixture was heated to 85 °C and stirred for 1 h. Then reaction mixture was cooled to room temperature and directly concentrated under reduced pressure. The resulting crude residue was dissolved in Et_2O (10 mL) and added saturated aqueous $KF{\cdot}2H_2O$ (10 mL). The mixture was stirred for 2 h and the *n*-Bu_3SnF precipitate was filtered. The filtrate was extracted with Et_2O (2 × 30 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 15 : 1) on silica gel to afford **22** (560 mg, 90% yield, *more polar isomer*/*less polar isomer* = 2.3 : 1). (*more polar diastereomer*) colorless oil; R_f = 0.40 (petroleum ether–EtOAc = 2 : 1); IR (film): ν_{max} = 3030, 2968, 2935, 2872, 2837, 1588, 1504, 1457, 1412, 1375, 1330, 1238, 1128, 1063, 986, 918, 831, 734, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.43 (m, 4H), 7.35–7.25 (m, 6H), 6.71 (s, 2H), 6.34 (s, 2H), 5.41 (d, J = 4.4 Hz, 1H), 5.04 (s, 2H), 4.99 (s, 2H), 3.79 (s, 6H), 3.77–3.69 (m, 1H), 3.71 (s, 6H), 3.52–3.44 (m, 1H), 3.28–3.19 (m, 1H), 2.11 (dd, J = 12.8, 6.8 Hz, 1H), 1.86 (ddd, J = 12.5, 10.4, 4.8 Hz, 1H), 1.03 (t, J = 6.8 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.8 (2C), 152.6 (2C), 142.9, 139.4, 137.85, 137.83, 135.7, 135.6, 128.5 (2C), 128.4 (2C), 128.02 (2C), 127.99 (2C), 127.73, 127.69, 104.6 (2C), 104.3 (2C), 102.6, 90.8, 74.83, 74.79, 62.5, 56.23, 56.20, 56.08, 56.06, 40.9, 40.2, 17.3, 15.0 ppm; HRMS (APCI): calcd for $C_{37}H_{43}O_8^+$ $[M + H]^+$: 615.2952, found: 615.2946.

5,5-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)-4-methyldihydrofuran-2(3*H*)-one (23). To a stirred solution of acetal **22** (85 mg, 0.16 mmol) in CH_2Cl_2 (4.0 mL) was added *m*-CPBA (95%, 85 mg, 0.47 mmol, 2.9 equiv.) at room temperature followed by the addition of $BF_3{\cdot}Et_2O$ (40.6 μL, 0.32 mmol, 2.0 equiv.). After 10 s, the reaction mixture was quenched by saturated aqueous Na_2SO_3 (10 mL) and extracted with CH_2Cl_2 (30 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (P petroleum ether–EtOAc = 2 : 1) on silica gel to afford the desired **23** (75 mg, 80% yield) as a colorless oil. R_f = 0.31 (petroleum ether–EtOAc = 2 : 1); IR (film): ν_{max} = 2936, 2840, 1785, 1590, 1505, 1458, 1416, 1333, 1243, 1182,

1129, 979, 930, 735, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.46 (t, J = 8.0 Hz, 4H), 7.35–7.27 (m, 6H), 6.70 (s, 2H), 6.45 (s, 2H), 5.02 (s, 2H), 5.00 (s, 2H), 3.82 (s, 6H), 3.75 (s, 6H), 3.35–3.26 (m, 1H), 2.74 (dd, J = 17.2, 7.6 Hz, 1H), 2.33 (dd, J = 17.2, 4.0 Hz, 1H), 0.89 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.6, 153.4 (2C), 153.3 (2C), 138.2, 137.63, 137.60, 137.0, 136.1, 136.0, 128.40 (2C), 128.37 (2C), 128.1 (2C), 128.1 (2C), 127.9, 127.8, 103.9 (2C), 103.0 (2C), 92.3, 74.9, 74.8, 56.4 (2C), 56.2 (2C), 38.4, 37.7, 17.2 ppm; HRMS (ESI): calcd for $C_{35}H_{37}O_8^+$ $[M + H]^+$: 585.2483, found: 585.2496.

(*trans*)-5,5-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)-3,4-dimethyldihydrofuran-2(3*H*)-one (24). A 10 mL, round-bottom flask was charged with LiHMDS (1.0 M in THF, 1.2 mL, 1.2 mmol, 10.0 equiv.) under argon and the resulting solution was cooled to −78 °C. To this precooled base, a solution of γ-lactone **23** (70 mg, 0.12 mmol) in THF (1.0 mL) was added dropwise *via* syringe and stirring was continued for 1.0 h at this temperature. Then resulting enolate was treated with MeOTf (40 μL, 0.36 mmol, 3.0 equiv.) at −78 °C, and the methylation reaction was continued for 1.0 h at the same temperature then quenched by saturated aqueous NH_4Cl (10 mL). The reaction mixture was allowed to warm to room temperature, diluted with CH_2Cl_2 (30 mL) and poured into a separatory funnel. The combined organic layers were separated and washed with water (2 × 5 mL) and brine (10 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 3 : 1) on silica gel to afford 65 mg (91% yield) of the desired **24** as a colorless oil. R_f = 0.47 (petroleum ether–EtOAc = 2 : 1); IR (film): ν_{max} = 2926, 2855, 1773, 1589, 1503, 1456, 1414, 1332, 1243, 1128, 995, 736, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.43 (m, 4H), 7.36–7.27 (m, 6H), 6.65 (s, 2H), 6.24 (s, 2H), 5.04 (s, 2H), 5.01 (s, 2H), 3.81 (s, 6H), 3.70 (s, 6H), 2.89–2.81 (m, 1H), 2.44–2.36 (m, 1H), 1.28 (d, J = 7.2 Hz, 3H), 1.05 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.4, 153.3 (2C), 153.0 (2C), 138.4, 137.6 (2C), 137. 0, 136.3, 135.6, 128.41 (2C), 128.38 (2C), 128.1 (2C), 128.0 (2C), 127.9, 127.8, 104.7 (2C), 104.1 (2C), 90.6, 74.9, 74.8, 56.4 (2C), 56.2 (2C), 46.3, 41.1, 16.2, 13.2 ppm; HRMS (ESI): calcd for $C_{36}H_{39}O_8^+$ $[M + H]^+$: 599.2639, found: 599.2651.

2,2-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)-3,4-dimethyltetrahydrofuran (25). To a stirred solution of γ-lactone **24** (20 mg, 0.033 mmol) in anhydrous THF (1 mL) at 0 °C was added $LiAlH_4$ (3 mg, 0.1 mmol, 3.0 equiv.). The reaction mixture was stirred for 0.5 h at this temperature and quenched carefully by saturated aqueous NH_4Cl (5 mL). The resulting precipitate was then filtered with a short plug of Celite (elution with 10 mL of CH_2Cl_2) and the filtrate was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with water (3 × 5 mL) and brine (5 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude diol could be used directly without further purification. To a stirred solution of the above diol in CH_2Cl_2 (1 mL) at 0 °C was added TFA (5 μL, 0.066 mmol, 2.0 equiv.) in one portion. After 5 minutes, the reaction was quenched by saturated aqueous $NaHCO_3$ (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 2 : 1) on silica gel to afford 19 mg (95% yield over 2 steps) of the desired **25** as a colorless oil. R_f = 0.75 (petroleum ether–EtOAc = 3 : 2); IR (film): ν_{max} = 2956, 2924, 2853, 1586, 1500, 1455, 1410, 1328, 1235, 1126, 1014, 732, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, J = 7.2 Hz, 2H), 7.45 (d, J = 6.8 Hz, 2H), 7.35–7.24 (m, 6H), 6.66 (s, 2H), 6.37 (s, 2H), 5.03 (s, 2H), 4.99 (s, 2H), 4.31 (t, J = 7.6 Hz, 1H), 3.80 (s, 6H), 3.71 (s, 6H), 3.48 (dd, J = 10.0, 8.4 Hz, 1H), 2.42–2.34 (m, 1H), 2.08–1.96 (m, 1H), 1.02 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0 (2C), 152.4 (2C), 142.5, 140.4, 137. 8 (2C), 136.0, 135.4, 128.4 (4C), 128.1 (2C), 128.0 (2C), 127.73, 127.67, 104.8 (2C), 104.5 (2C), 90.7, 74.9, 74.8, 73.8, 56.3 (2C), 56.0 (2C), 49.8, 40.7, 15.7, 14.5 ppm; HRMS (ESI): calcd for $C_{36}H_{41}O_7^+$ $[M + H]^+$: 585.2847, found: 585.2857.

(±)-Sacidumlignan D (4). Benzylated sacidumlignan D **25** (60 mg, 0.107 mmol) was dissolved in a mixture of EtOAc–MeOH (1 : 1, 8 mL) followed by the addition of 10 wt% Pd/C (568 mg, 0.54 mmol, 5.0 equiv.) at 25 °C. The whole system with three-way Teflon stopcock connected to a standard balloon was evacuated and backfilled with H_2, and this protocol was repeated three times. Then the heterogeneous mixture was allowed to stir at 25 °C under a positive pressure of hydrogen. After 0.5 h, the hydrogenation reaction finished, and the reaction mixture was filtered directly though Celite, washed with EtOAc (4 × 5 mL), and concentrated to afford the desired (±)-sacidumlignan D (**4**) (43 mg, 100% yield) as a colorless crystal. R_f = 0.40 (petroleum ether–EtOAc = 1 : 1); Mp. 112–114 °C (EtOAc–*n*-Pentane = 1 : 20); IR (film): ν_{max} = 2956, 2930, 2872, 1611, 1514, 1455, 1418, 1326, 1214, 1114, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.68 (s, 2H), 6.40 (s, 2H), 5.52 (s, 1H, –O*H*), 5.44 (s, 1H, –O*H*), 4.30 (t, J = 7.6 Hz, 1H), 3.87 (s, 6H), 3.80 (s, 6H), 3.46 (dd, J = 10.0, 8.0 Hz, 1H), 2.38 (dq, J = 10.4, 6.8 Hz, 1H), 2.05–1.95 (m, 1H), 1.02 (d, J = 6.4 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H) ppm; ^1H NMR (400 MHz, CD_3COCD_3): δ = 7.16 (s, 1H, –O*H*), 7.05 (s, 1H, –O*H*), 6.78 (s, 2H), 6.53 (s, 2H), 4.26 (t, J = 7.6 Hz, 1H), 3.80 (s, 6H), 3.73 (s, 6H), 3.34 (dd, J = 10.0, 8.0 Hz, 1H), 2.42 (dq, J = 10.0, 6.8 Hz, 1H), 2.04–1.96 (m, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.5 (2C), 146.0 (2C), 138.1, 136.2, 133.9, 133.3, 104.5 (2C), 104.2 (2C), 90.7, 73.7, 56.5, 56.4, 56.2 (2C), 49.6, 40.6, 15.7, 14.5 ppm; ^{13}C/DEPT NMR (100 MHz, CD_3COCD_3): δ = 148.2 (s, 2C), 147.8 (s, 2C), 139.2 (s), 136.9 (s), 136.0 (s), 135.6 (s), 106.2 (d, 2C), 105.8 (d, 2C), 91.3 (s), 74.0 (t), 56.9 (q, 2C), 56.7 (q, 2C), 51.0 (d), 42.1 (d), 16.8 (q), 15.2 (q) ppm; HRMS (ESI): calcd for $C_{22}H_{29}O_7^+$ $[M + H]^+$: 405.1908, found: 405.1914.

5,5′-(1-(2-Bromo-1-ethoxypropoxy)prop-2-ene-1,1-diyl) bis(2-(benzyloxy)-1,3-dimethoxybenzene) (26). In a 50 mL, round-bottom flask, Br_2 (0.24 mL, 4.8 mmol, 10 equiv.) was dissolved

in dry CH_2Cl_2 (15 mL) and cooled to −78 °C. To the resulting solution was added ethyl propenyl ether (*E* : *Z* = 1.7 : 1, 0.49 mL, 5 mmol, 10.5 equiv.) dropwise over a 10 min period, and the mixture was stirred for 20 min at −78 °C. This system was transferred *via* cannula to another round bottom flask where the solution of allyl alcohol **20** (262 mg, 0.48 mmol) and *N*,*N*-dimethylaniline (1.2 mL, 9.6 mmol, 20 equiv.) in CH_2Cl_2 (5 mL) had been prepared. The resulting mixture was further stirred for 0.5 h at −78 °C then 5 h at 25 °C. Eventually, the reaction mixture was carefully quenched by water and poured into a separatory funnel. The organic layers were washed with aqueous HCl (1.0 M, 3 × 10 mL), water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 10 : 1) on silica gel (basified with 1% Et_3N) to afford the desired **26** (278 mg, 82% yield, d.r. = 1.7 : 1) as a colorless oil. R_f = 0.44 (petroleum ether–EtOAc = 4 : 1); IR (film): ν_{max} = 3087, 2935, 2867, 1653, 1582, 1501, 1457, 1413, 1371, 1333, 1238, 1127, 1008, 916, 846, 736, 699 cm^{-1}; (*major isomer*) ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 4H), 7.34–7.24 (m, 6H), 6.60 (s, 2H), 6.59 (s, 2H), 6.53 (dd, *J* = 17.2, 10.8 Hz, 1H), 5.37 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.07 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.06 (s, 2H), 5.04 (s, 2H), 4.49 (d, *J* = 4.0 Hz, 1H), 4.11–4.04 (m, 1H), 3.73 (s, 12H), 3.36–3.27 (m, 1H), 3.26–3.18 (m, 1H), 1.70 (d, *J* = 6.8 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.8 (2C), 152.7 (2C), 140.7, 139.3, 138.3, 137.8, 137.7, 136.1 (2C), 128.5 (2C), 128.4 (2C), 128.0 (4C), 127.77, 127.75, 118.2, 106.5 (2C), 106.1 (2C), 100.1, 85.2, 74.83, 74.76, 63.8, 56.2 (4C), 50.3, 19.8, 15.0 ppm; HRMS (ESI): *m*/*z* calcd for $C_{38}H_{43}O_8{}^{79}BrNa^+$ $[M + Na]^+$: 729.2034, found: 729.2037.

2,2-Bis(4-(benzyloxy)-3,5-dimethoxyphenyl)-5-ethoxy-3,4-dimethyltetrahydrofuran (27). In a 100 mL, two-necked, round-bottom flask, α-bromo acetal **26** (378 mg, 0.55 mmol) was dissolved in anhydrous toluene (50 mL) followed by the addition of *n*-Bu_3SnH (1.5 mL, 4.4 mmol, 8 equiv.) and AIBN (269 mg, 1.65 mmol, 3 equiv.) under argon. The resulting mixture was heated to 85 °C and stirred for 1 h. Then reaction mixture was cooled to room temperature and directly concentrated under reduced pressure. The resulting crude residue was dissolved in Et_2O (5 mL) and added saturated aqueous $KF{\cdot}2H_2O$ (5 mL). The mixture was stirred for 1 h and the *n*-Bu_3SnF precipitate was filtered. The filtrate was extracted with Et_2O (2 × 20 mL), and the combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether→petroleum ether–EtOAc = 6 : 1) on silica gel to afford the mixture **27** of four inconsequential diastereoisomers (309 mg, 90% yield) as a colorless oil among which the less polar component containing two diastereoisomers was isolated and characterized. IR (film): ν_{max} = 2958, 2925, 2855, 1658, 1589, 1501, 1459, 1412, 1376, 1261, 1100, 1024, 800, 697 cm^{-1}; (*major isomer*) ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.43 (m, 4H), 7.36–7.24 (m, 6H), 6.68 (s, 2H), 6.34 (s, 2H), 5.22 (d, *J* = 4.8 Hz, 1H), 5.03 (s, 2H), 4.98 (s, 2H), 3.79 (s, 6H), 3.72–3.65 (m, 1H), 3.69 (s, 6H), 3.48–3.41 (m, 1H), 2.11 (sext, *J* = 6.8 Hz, 1H), 2.02–1.92 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7 (2C), 152.5 (2C), 143.7, 139.8, 137.87, 137.84, 135.54, 135.51, 128.51 (2C), 128.45 (2C), 128.03 (2C), 127.99 (2C), 127.70, 127.66, 105.8, 104.9 (2C), 104.2 (2C), 90.9, 74.9, 74.8, 62.3, 56.4, 56.23, 56.21, 56.0, 46.5, 44.6, 15.8, 14.9, 11.3 ppm; HRMS (ESI): calcd for $C_{38}H_{48}NO_8^+$ $[M + NH_4]^+$: 646.3374, found: 646.3383.

2-(Benzyloxy)-5-(4-(benzyloxy)-3,5-dimethoxyphenyl)-1,3-dimethoxy-6,7-dimethylnaphthalene (28). To a stirred solution of the diastereoisomeric mixture **27** (12 mg, 20 μmol) in CH_2Cl_2 (1 mL) was added *p*-$TsOH{\cdot}H_2O$ (4 mg, 20 μmol, 1.0 equiv.) at 25 °C. After 10 h, the reaction mixture was directly concentrated under reduced pressure, and the resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 6 : 1) on silica gel to afford the desired **28** (7 mg, 65% yield) as a colorless solid. R_f = 0.67 (petroleum ether–EtOAc = 4 : 1); Mp. 122–123 °C (CH_2Cl_2); IR (film): ν_{max} = 3030, 2924, 2852, 1580, 1492, 1460, 1406, 1372, 1337, 1259, 1237, 1126, 1091, 919, 732, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.54 (d, *J* = 7.2 Hz, 4H), 7.39–7.29 (m, 6H), 6.47 (s, 1H), 6.45 (s, 2H), 5.16 (s, 2H), 5.10 (s, 2H), 4.05 (s, 3H), 3.78 (s, 6H), 3.65 (s, 3H), 2.48 (s, 3H), 2.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6 (2C), 152.1, 147.6, 139.2, 137.9, 137.8, 137.3, 136.3, 135.3, 133.2, 133.0, 129.0, 128.6 (2C), 128.29 (2C), 128.25 (2C), 128.0 (2C), 127.9, 127.8, 122.7, 120.8, 107.1 (2C), 101.6, 75.4, 74.9, 61.6, 56.1 (2C), 55.6, 21.2, 17.6 ppm; HRMS (ESI): calcd for $C_{36}H_{36}O_6Na^+$ $[M + Na]^+$: 587.2404, found: 587.2421.

Sacidumlignan A (1). Benzylated sacidumlignan A **28** (6 mg, 10 μmol) was dissolved in a mixture of EtOAc–MeOH (1 : 1, 3 mL) followed by the addition of 10 wt% Pd/C (53 mg, 50 μmol, 5.0 equiv.) at 25 °C. The whole system with three-way Teflon stopcock connected to a standard balloon was evacuated and backfilled with H_2, and this protocol was repeated three times. Then the heterogeneous mixture was allowed to stir at 25 °C under a positive pressure of hydrogen. After 5 min, the hydrogenation reaction finished, and the reaction mixture was filtered directly though Celite, washed with EtOAc (4 × 5 mL), and concentrated to afford the desired sacidumlignan A (**1**) (4 mg, 100% yield) as a colorless crystal. R_f = 0.50 (petroleum ether–EtOAc = 1 : 1); Mp. 149.2–149.5 °C (acetone); IR (film): ν_{max} = 3402, 2935, 2850, 1718, 1673, 1608, 1516, 1457, 1415, 1341, 1212, 1114, 914, 735, 702 cm^{-1}; ^1H NMR (400 MHz, CD_3COCD_3): δ = 7.76 (s, 1H), 7.67 (s, 1H, –O*H*), 7.26 (s, 1H, –O*H*), 6.58 (s, 1H), 6.49 (s, 2H), 3.97 (s, 3H), 3.84 (s, 6H), 3.67 (s, 3H), 2.45 (s, 3H), 2.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 149.2, 149.0 (2C), 140.8, 138.8, 138.2, 135.9, 133.8, 132.0, 131.9, 127.6, 124.1, 120.6, 108.5 (2C), 102.0, 60.8, 56.9 (2C), 56.1, 21.5, 17.7 ppm; HRMS (ESI): calcd for $C_{22}H_{25}O_6^+$ $[M + H]^+$: 385.1646, found: 385.1649.

Conversion of (±)-sacidumlignan D (4) to sacidumlignan A (1). To a stirred solution of (±)-sacidumlignan D (**4**) (12 mg, 30 μmol) in $ClCH_2CH_2Cl$ (1 mL) was added *p*-$TsOH{\cdot}H_2O$

(28 mg, 0.15 mol, 5.0 equiv.) at room temperature. After stirring for 32 h at 50 °C, the reaction mixture was cooled to room temperature and quenched by saturated aqueous $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were washed with water (5 mL) and brine (5 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether–EtOAc = 6 : 1) on silica gel to afford the desired sacidumlignan A (**1**) (5 mg, 44% yield) as a colorless solid and recover 4 mg (33%) of (±)-sacidumlignan D (**4**).

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