# Enantiocontrolled Synthesis of Burseran, Brassilignan, Dehydroxycubebin, and Other Tetrahydrofuran Lignans in Both Enantiomeric Forms. Application of Intermolecular Nitrile Oxide Cycloadditions and Lipase Mediated Kinetic Resolutions

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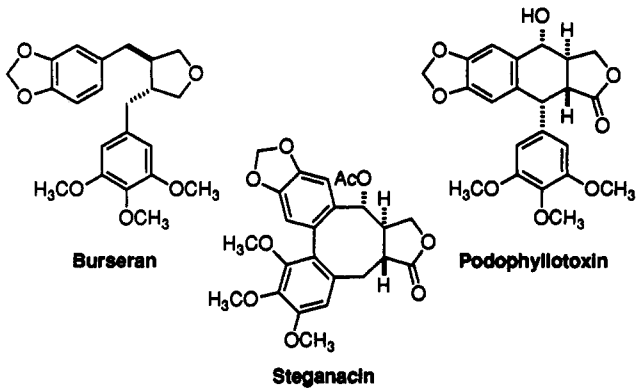
Several natural and unnatural tetrahydrofuran lignans have been synthesized by a convergent approach. Our methodology utilizes a nitrile oxide cycloaddition to dihydrofuran 8 and an enzymatic resolution of alcohols 11 by lipase PS. The lipase-mediated kinetic resolution of alcohols 11 furnished both enantiomers of the lignan precursors 12 and 14 in high optical purity (>99% ee). This is followed by a $S_N2$ displacement of tosylates 15 and 18 by $\alpha$-lithiobenzyl phenyl sulfides. In this manner, both enantiomers of 3,4-dibenzyltetrahydrofuran (**17a, 20a**), 3,4-bis(3-methoxybenzyl)-tetrahydrofuran (**17b, 20b**), brassilignan (**17c, 20c**), dehydroxycubebin (**17d, 20d**), and burseran (**17e, 20e**) were synthesized in overall yields of 6-16%.

## Introduction

Lignan natural products have been of interest because of their wide spread occurrence, varied biological activity, and use in folk medicine.[1] Several members of this family of natural products and their analogs have been shown to possess potent antitumor properties. One class of antitumor agents, called the *spindle poisons*, are compounds whose mode of action is prevention of the normal function of the mitotic spindle. Natural products colchicine, podophyllotoxin, steganacin,[2] and tetrahydrofuran lignans burseran and dehydroxycubebin[3] are a few examples of spindle poisons (Scheme I). These compounds interact with the tubulin-microtubule system, the precursors for spindle formation.[4] Most of the drugs which interfere with the tubulin-microtubule system interact with tubulin by binding it at different regions. The binding site known as the *colchicine site* has been shown to recognize a number of natural and unnatural products that contain two aromatic rings connected by a variety of structural elements and is a potential target site for the rational design of new antitubulin agents.[4,5] Therefore, a general methodology for the preparation of analogs which have potential for binding at the *colchicine site* for structure-activity studies is very attractive. Besides their antitumor activity,[3a] the tetrahydrofuran lignans also exhibit platelet-activating-factor antagonism[6] and diuretic[7] properties.

**Scheme I**




Several routes for the synthesis of both racemic and chiral tetrahydrofuran lignan natural products have been reported in the literature, and the majority of these procedures use Michael additions, dehydration of substituted 1,4-diols, or alkylation methodologies.[8-11] We were interested in developing a convergent route to these lignans from readily available starting materials with the added flexibility of control over the relative and absolute stereochemistry and the nature of the aryl substituent.[12] Another attractive feature we incorporated into our approach was the application of an enzymatic method for the introduction of optical activity. This chiral induction was planned near the end of the synthetic sequence and therefore would require limited handling of chiral materials. Hence, the methodology would be amenable for the preparation of analogs for structure-activity studies.

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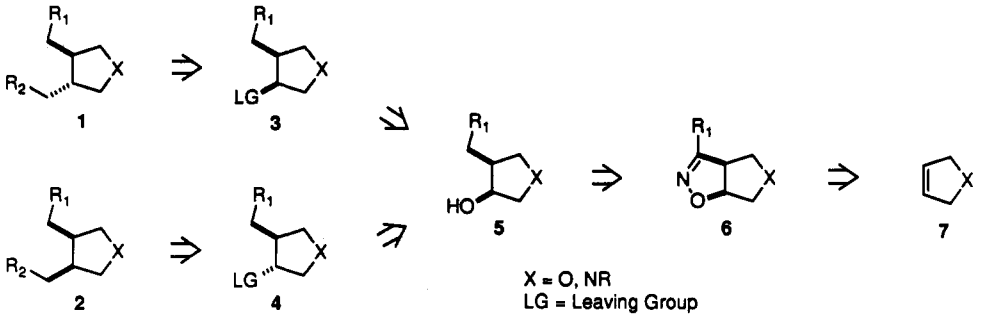
(8) Synthesis of burseran: (a) Trumbull, E. R.; Cole, J. R. *J. Pharm. Sci.* **1969**, *58*, 176. (b) Tomioka, K.; Ishiguro, T.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 652. (c) Tomioka, K.; Ishiguro, T.; Mizuguchi, H.; Koga, K. *Koen Voshishu-Tennen Yuki Kagobutsu Toronkai, 22nd* **1979**, 315. (d) Tomioka, K.; Koga, K. *Heterocycles* **1979**, *12*, 1523. (e) Tomioka, K.; Ishiguro, T.; Koga, K. *Chem. Pharm. Bull.* **1985**, *33*, 4333. (f) Rehnberg, N.; Magnusson, G. *Tetrahedron Lett.* **1988**, *29*, 3599. (g) Magnusson, H. G.; Rehnberg, P. N. PCT Int. Appl. WO 89 00, 160, 1989. (h) Rehnberg, N.; Magnusson, G. *J. Org. Chem.* **1990**, *55*, 4340. (i) Sibi, M. P.; Gaboury, J. A. *Synlett* **1992**, 83. (j) Hanessian, S.; Leger, R. *Synlett* **1992**, 402. (k) Morimoto, T.; Chiba, M.; Achiwa, K. *Heterocycles* **1992**, *33*, 435. (l) Belletire, J. L.; Fry, D. F.; Fremont, S. L. *J. Nat. Prod.* **1992**, *55*, 184.

(9) Synthesis of dehydroxycubebin: (a) Ishiguro, T. *J. Pharm. Soc., Jpn.* **1936**, *56*, 444; *Chem. Zentr.* **1936**, *II*, 2926. (b) Haworth, R. D.; Wilson, L. *J. Chem. Soc.* **1950**, 71. (c) Reference 8f-j.

0022-3263/93/1958-2173$04.00/0 

**Scheme II**




Our convergent approach to natural and unnatural tetrahydrofuran lignans (Scheme II) starts with a nitrile oxide cycloaddition to a five-membered heterocycle (**7** to **6**). The key steps in this approach are an enzyme-mediated resolution of alcohols **5** and nucleophilic displacements of **3**. The conversion of **3** to **1** can be accomplished by $S_N2$ displacement, thus establishing the trans stereochemistry of the final natural products. On the other hand, similar nucleophilic displacements of **4** could provide access to products **2** wherein the aryl substituents have a cis relationship. In this manner, one can envision the synthesis of a variety of lignans depending on the nature of the heterocycle, the nitrile oxide, or the nucleophile. In this work, we report the synthesis of several tetrahydrofuran lignan natural products **1** in both enantiomeric forms in high optical purity along with several unnatural compounds also in enantiomerically pure form.

## Results and Discussion

**Nitrile Oxide Cycloadditions.** Inter- and intramolecular nitrile oxide cycloadditions have found extensive applications in organic synthesis.[13] Dihydroisoxazolines are the product formed from a nitrile oxide cycloaddition to an alkene, and they serve as a β-hydroxy carbonyl equivalent.[14] Our experiments began with the functionalization of commercially available 2,5-dihydrofuran (**8**). The cycloaddition of nitrile oxides to **8** has been reported in the literature.[15] Aryl nitrile oxides generated in situ reacts with 2,5-dihydrofuran producing dihydroisoxazolines **9** (Scheme III) in moderate to good yields (Table I). Two methods were used for generating the nitrile oxides.

**Scheme III**

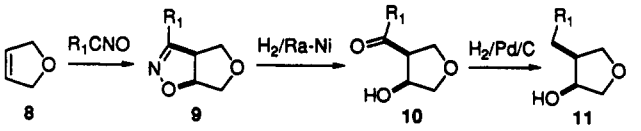



**Table I. Preparation of Starting Material for Lipase Resolution**

| | | yields (%) | | |
|---|---|---|---|---|
| entry | $R_1$ | 9 | 10 | 11 |
| a | phenyl | 84 | 84 | 92 |
| b | 3-methoxyphenyl | 62 | 94 | 88 |
| c | 3,4-dimethoxyphenyl | 58 | 92 | 90 |
| d | 3,4-(methylenedioxy)phenyl | 78 | 91 | 92 |

The first method consisted of dehydrohalogenation of a hydroximinoyl chloride by triethylamine for in situ generation of the nitrile oxide, and this was used for the preparation of compounds **9a** and **9d**.[16] For the synthesis of compounds **9b** and **9c**, the hydroximinoyl chlorides could not be prepared in a clean fashion; therefore, they were generated in situ from the corresponding oxime, NCS, catalytic pyridine, and concomitant addition of triethylamine to give the nitrile oxide[17] needed for the cycloaddition reaction.

Release of the β-hydroxy carbonyl unit was the next step in the sequence.[18] Excellent yields of the β-hydroxy carbonyls **10** were obtained by using $H_2$/Raney-Ni and 10 equiv boric acid. In these experiments, a large excess of boric acid was necessary to control epimerization of the cis isomer **10** to the trans isomer. As reported by Curran,[19] boric acid complexes and stabilizes the intermediate hydroxyimine. As a consequence, the imine ene–amine isomerization becomes less likely and thus prevents erosion of the stereochemical integrity. The amount of trans isomer produced in our reactions using the conditions discussed earlier ranged from 0 to 5%. The stereochemistry of the products was established by analysis of the $^{13}C$ NMR chemical shifts of carbons in positions 3 and 4.[20] Using a literature procedure for reductive deoxygenation of benzyl ketones,[21] the pure cis isomers **10** were converted to the fully reduced compounds **11** using $H_2$ and 10% Pd/C as the catalyst.

(10) Synthesis of brassilignan: (a) Haworth, R. D.; Woodcock, D. *J. Chem. Soc.* **1939**, 1054. (b) Haworth, R. D.; Woodcock, D. *J. Chem. Soc.* **1939**, 1237. (c) Reference 9b. (d) Schrecker, A. W.; Hartwell, J. L. *J. Am. Chem. Soc.* **1955**, *77*, 432. (e) Bakke, J. E.; Klosterman, H. J. *Proc. North Dakota Acad. Sci.* **1956**, *10*, 18. (f) Schrecker, A. W. *J. Am. Chem. Soc.* **1957**, *79*, 3823. (g) Row, L. R.; Srinivasulu, C. Smith, M.; Rao, G. S. R. S. *Tetrahedron* **1966**, *22*, 2899. (h) Row, L. R.; Satyanarayana, P.; Rao, G. S. R. S. *Tetrahedron* **1967**, *23*, 1915. (i) Cambie, R. C.; Clark, G. R.; Craw, P. A.; Jones, T. C.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem.* **1985**, *38*, 1631. (j) Buckleton, J. S.; Cambie, R. C.; Clark, G. R.; Craw, P. A.; Rickard, C. E. F.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem.* **1988**, *41*, 305. (k) Hirano, T.; Oka, K.; Naitoh, T.; Hosaka, K.; Mitsuhashi, H. *Res. Commun. Chem. Pathol. Pharmacol.* **1989**, *64*(2), 227. (l) Brown, E.; Daugan, A. *Tetrahedron* **1989**, *45*, 141. (m) Oka, K.; Hirano, T.; Naito, T.; Hosaka, K. Jp. Patent 01,228,928, 1989. (n) Okaki, T.; Hirano, T.; Naito, T.; Hosaka, K. Jp. Patent 02,101,011, 1990.

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**Scheme IV**

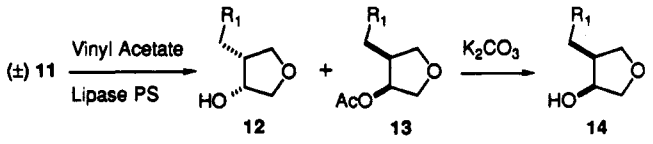



**Table II. Lipase Resolution of Racemic Alcohols 11**

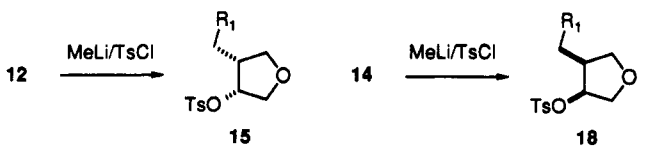
| entry | $R_1$ | conversn 13[a] | enantiomeric excess (%) 12 | 14 |
|---|---|---|---|---|
| a | phenyl | 51 | >99 | >99 |
| b | 3-methoxyphenyl | 52 | >99 | >99 |
| c | 3,4-dimethoxyphenyl | 50 | >99 | >99 |
| d | 3,4-(methylenedioxy)phenyl | 50 | >99 | >99 |

[a] Conversion was determined by $^1$H NMR integration (±2%).

**Enzymatic Resolutions.** The next step in our synthetic strategy involved preparation of both antipodes of the alcohols 11. To achieve this goal we investigated the utility of enzyme-mediated resolution experiments. The synthesis of optically active compounds has been enhanced greatly by using enzymes in organic solvents. The utility of lipases in the resolution of racemates has been well documented.[22] The enzyme of choice for our resolution experiments was lipase PS. This choice was based on literature precedents wherein the successful application of lipase PS in the kinetic resolution of cyclopentanols,[23] hydroxytetrahydrofurans,[24] and others[25] has been reported. In our experiments (Scheme IV), lipase PS accomplished the kinetic resolution in high enantiomeric excesses for several substrates (Table II). The experiment consisted of mixing the racemic alcohols 11 with lipase and excess vinyl acetate (irreversible acyl donor and solvent) and then stopping the reaction near 50% conversion to acetates 13. Reactions were monitored by periodic sampling of the mixture and analyzing by $^1$H NMR to determine the conversions. The acetates 13 were hydrolyzed with $K_2CO_3$ to alcohols 14 without loss of optical purity. Enantiomeric excesses of the alcohols were determined by conversion of 12 and 14 to their corresponding Mosher esters[26] and further analysis by $^1$H NMR integration. The excellent enantiomeric excesses (>99%) for 12 and 14 indicate the high degree of kinetic resolution for these substrates. The absolute stereochemistries of the product alcohols could not be determined at this stage, and this was established by conversion of these compounds to natural products of known absolute stereochemistry (vide infra).

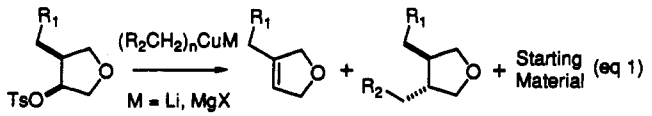
**Nucleophilic Displacements.** Tosylation of the optically active alcohols 12 and 14 proceeded smoothly (Scheme V). Methyllithium was a more efficient base

**Scheme V**




compared to pyridine for this task because it gave higher yields of tosylates 15 and 18 (73–90% yield) and reaction times were drastically reduced. The ensuing step was the introduction of the other benzyl substituent by a nucleophilic displacement of the secondary tosylate. Two objectives could be accomplished by these displacements: introduction of the desired benzyl unit and inversion of stereochemistry establishing the required trans configurations in the natural products.

Initially, we examined a variety of both lower and higher order copper reagents[27] for the introduction of the second benzyl substituent. The preparation of the copper lithium reagents were problematic because of the difficulty in obtaining benzyllithium compounds[28] cleanly. On the other hand, benzyl Grignard reagents[29] are more readily available then benzyllithiums. When benzyl Grignard reagents were used in combination with copper salts,[30] the tosylates did undergo displacements, although these experiments were uniformly disappointing. The results of these experiments were the formation of substitution products in low yields (<20%) along with moderate amounts of elimination products and unreacted starting material (eq 1). The next reagent tried was α-lithiobenzyl




diphenyl dithioacetals which gave no displacement products, and only starting material was recovered presumably because of the bulk of the nucleophile.

A two-step sequence was successful for the introduction of the second benzylic substituent (Scheme VI). Thus, treatment of the tosylates 15 and 18 with 4 equiv of the α-lithiobenzyl phenylsulfide[31] at 0 °C, warming to room temperature, and stirring for 17 h produced 16 and 19 as a mixture of diastereomers (diastereomeric at the C–S

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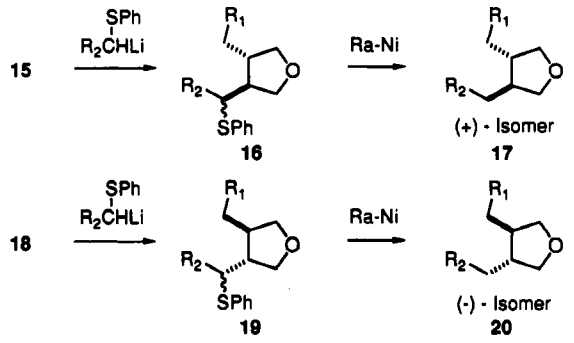
(31) The benzyllithiums were prepared from the corresponding benzyl sulfides by treatment with n-BuLi at 0 °C; see: Krief, A.; Kenda, B.; Barbeaux, P. *Tetrahedron Lett.* **1991**, *32*, 2509 and references cited therein. For the preparation of the benzyl sulfides see: (a) Pelter, A.; Ward, R. S.; Pritchard, M. C. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1615. (b) Mori, K.; Takaishi, H. *Tetrahedron* **1989**, *45*, 1639. For examples of nucleophilic displacements and conjugate additions with benzyllithiums see: (a) Hodges, P. J.; Procter, G. *Tetrahedron Lett.* **1985**, *26*, 4111. (b) Takaki, K.; Yasumura, M.; Tamura, T.; Negoro, K. *J. Org. Chem.* **1987**, *52*, 1256. (c) Mori, K.; Takaishi, H. *Tetrahedron* **1989**, *45*, 1639. (d) Pelter, A.; Ward, R. S.; Pritchard, M. C. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1615. (e) Yanagida, M.; Hashimoto, K.; Ishida, M.; Shinozaki, H.; Shirahama, H. *Tetrahedron Lett.* **1989**, *29*, 3799.

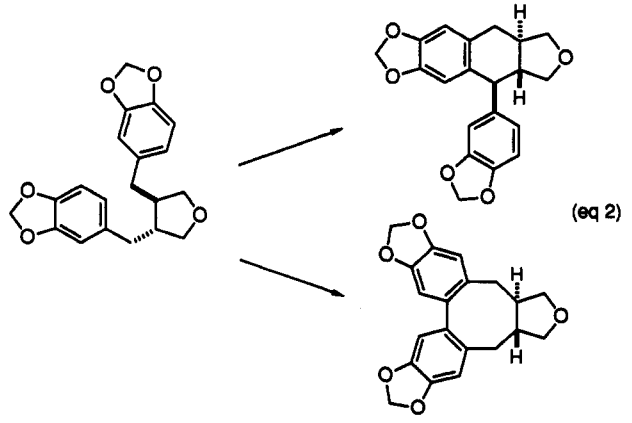
**Scheme VI**




bond) in moderate yields (46–73%). The byproducts from this reaction were alcohols **12** and **14**, obtained in 20–30% yields arising from the cleavage of the sulfur-oxygen bond in **15** and **18** during the displacement reaction. The stereochemistry of the displacement reactions was established by desulfurization of **16** and **19** and comparison of spectral data of the products **17** and **20** with those reported in the literature.[8-10] In this manner, natural products [burseran (**17e** and **20e**) and brassilignan (**17c** and **20c**)] and unnatural products [dehydroxycubebin (**17d** and **20d**), 3,4-dibenzyltetrahydrofuran (**17a** and **20a**), and 3,4-bis-(3-methoxybenzyl)tetrahydrofuran (**17b** and **20b**)] were readily obtained in both enantiomeric forms and high optical purity (Table III).

The conversion of the (+)-alcohol **12d** to (+)-burseran **17e** thus establishes the absolute stereochemistry of the product obtained from the lipase-mediated kinetic resolutions as 3*R*,4*R*.[32] Similarly, the absolute configuration of alcohols **12c**, **14c**, and **14d** were established by conversion to products **17c**, **20c**, **20d**, and **20e** of known configurations. In the case of alcohols **12a,b** and **14a,b** where the lignans prepared from these precursors were not known, the absolute stereochemistry was assigned by correlation with alcohols **12c,d** and **14c,d**.

The synthesis of burseran, brassilignan, and dehydroxycubebin also constitutes a formal total synthesis of aryltetralins and dibenzocyclooctadienes based on literature procedures for selective conversion of tetrahydrofuran lignans to compounds of this type[33] (eq 2).




(eq 2)

## Conclusions

In conclusion, we have shown that 2,5-dihydrofuran is a good precursor for the tetrahydrofuran class of lignan natural products. The ready availability of a variety of aryl nitrile oxides and aryl phenyl sulfides coupled with enzymatic resolutions makes the present methodology well suited for the synthesis of a variety of both natural and unnatural lignan natural products. The extension of the present methodology for the preparation of lignan analogs such as aza derivatives is underway. Further transformations of the tetrahydrofuran lignans to lignans with the butyrolactone skeleton are also being pursued.

## Experimental Section

**General.** Dihydrofuran was purchased from Aldrich Chemical Co. (Milwaukee, WI) and was distilled before use. Lipase PS was donated by Amano Co. Benzyl phenyl sulfide was purchased from Pfaltz and Bauer, Inc. 3-Methoxybenzyl phenyl sulfide, 3,4-dimethoxybenzyl phenyl sulfide, 3,4,5-trimethoxybenzyl phenyl sulfide, and 3,4-(methylenedioxy)benzyl phenyl sulfide were prepared according to the literature procedures listed in ref 31. Oximes and hydroximinoyl chlorides were synthesized from the corresponding aldehydes.[34] $CHCl_3$ and $CH_2Cl_2$ were distilled from calcium hydride, and THF was distilled from sodium benzophenone/ketyl prior to use. All other solvents and reagents were purified by standard techniques. Thin-layer chromatographic analyses were performed on silica gel Whatmann-60F glass plates, and components were visualized by illumination with UV light or by staining with phosphomolybdic acid. Flash chromatography[35] was performed using E. Merck silica gel (230–400 mesh). Melting points were determined using a Thomas Hoover capillary melting point apparatus and are uncorrected. All glassware was oven/and or flame dried, assembled hot, and cooled under a stream of dry nitrogen or argon before use. Reactions with air-sensitive materials were carried out by standard syringe techniques. IR spectra were recorded on a Mattson 2220 FT-IR spectrometer. $^1H$ NMR was recorded on JEOL GSX-400 (400 MHz) and JEOL GSX-270 (270 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm) downfield from TMS using residual $CHCl_3$ (7.27 ppm) as an internal standard. $^{13}C$ NMR was recorded on JEOL-GSX-400 (100 MHz) and JEOL GSX-270 (65 MHz) spectrometers using broad-band proton decoupling. Chemical shifts are reported in parts per million (ppm) downfield from TMS using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard. Rotations were determined on a JASCO-DIP-370 polarimeter. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, Desert Analytics, Tucson, AZ, or M-H-W Laboratories, Phoenix, AZ.

**Nitrile Oxide Cycloadditions (Method A).** 2,5-Dihydrofuran (8) (20 mmol) was mixed with benzylhydroximinoyl chloride or [3,4-(methylenedioxy)benzyl]hydroximinoyl chloride (30 mmol) in 20 mL of dry $Et_2O$. $Et_3N$ (30 mmol) dissolved in 5 mL of ether was added to the mixture over 3 h by use of a syringe pump. The reaction mixture was stirred at room temperature for an additional 15 h. $H_2O$ (50 mL) was added followed by extraction with $CH_2Cl_2$ (3 × 25 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The products were purified by flash column chromatography using silica gel.

**3a,4,6,6a-Tetrahydro-3-phenylfuro[3,4-*d*]isoxazole (9a):** yield 84%; mp 64 °C; IR ($CHCl_3$) 1597, 1568, 1500, 1447, 1354, 1091 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) δ 7.63 (m, 2 H), 7.40 (m, 3 H), 5.35 (dd, *J* = 4.03, 9.16 Hz, 1 H), 4.28 (m, 2 H), 4.12 (m, 1 H), 3.85 (dd, *J* = 6.96, 9.16 Hz, 1 H), 3.76 (dd, *J* = 3.85, 10.81 Hz, 1 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) δ 156.5, 129.9, 128.7, 128.4, 126.7, 86.1, 76.2, 71.6, 53.6. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.20; H, 6.21; N, 7.26.

**3a,4,6,6a-Tetrahydro-3-[3,4-(methylenedioxy)phenyl]furo[3,4-*d*]isoxazole (9d):** yield 78%, mp 143–144 °C; IR ($CHCl_3$) 1611, 1580, 1505, 1453, 1256, 1041 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 1.61 Hz, 1 H), 6.98 (dd, *J* = 1.61, 8.06 Hz, 1 H), 6.81 (d, *J* = 8.05 Hz, 1 H), 6.00 (s, 2 H), 5.34 (dd, *J* = 3.76,

(32) The assigned absolute stereochemistry is consistent with the stereochemistry observed for other lipase PS resolved hydroxytetrahydrofurans; see ref 24.

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(34) Liu, K.-C.; Shelton, B. R.; Howe, R. K. *J. Org. Chem.* **1980**, *45*, 3916.

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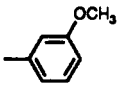
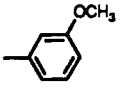
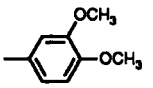
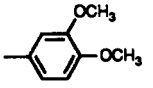
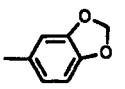
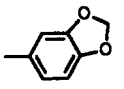
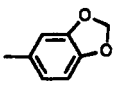
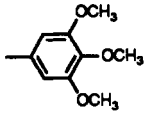
**Table III. Natural and Unnatural Tetrahydrofuran Lignans**

| compds | $R_1$ | $R_2$ | overall yields[a] 17 | 20 |
|---|---|---|---|---|
| a, 3,4-dibenzyltetrahydrofuran |  |  | 16 | 14 |
| b, 3,4-bis(3-methoxybenzyl)tetrahydrofuran |  |  | 8 | 7 |
| c, brassilignan |  |  | 6 | 6 |
| d, dehydroxycubebin |  |  | 14 | 12 |
| e, burseran |  |  | 10 | 10 |

[a] Overall yields are computed on the basis of 50% as the theoretical maximum value for the production of each enantiomer in the lipase resolution.

9.13 Hz, 1 H), 4.29 (d, $J$ = 10.75 Hz, 1 H), 4.22 (m, 1 H), 4.14 (appr dd, $J$ = 1.61, 2.15, 9.4 Hz, 1 H), 3.85 (dd, $J$ = 6.99, 9.14 Hz, 1 H), 3.76 (dd, $J$ = 3.76, 10.75 Hz, 1 H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 156.8, 149.9, 148.9, 123.3, 122.0, 108.9, 107.4, 102.1, 86.7, 77.0, 72.5, 54.6. Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.52; H, 4.68; N, 5.92.

**Nitrile Oxide Cycloadditions (Method B).** NCS (19.8 mmol) and pyridine (1.2 mmol) were mixed with 20 mL of $CHCl_3$. 3-Methoxybenzaldehyde oxime or 3,4-dimethoxybenzaldehyde oxime (20 mmol) dissolved in 20 mL of $CHCl_3$ was added to the mixture and allowed to stir at rt for 30 min. 2,5-Dihydrofuran (99 mmol) was then added to the oxime mixture. This was followed by addition of $Et_3N$ (21 mmol) dissolved in 10 mL of $CHCl_3$ over 4 h by use of a syringe pump. The reaction was stirred an additional 15 h. The mixture was washed with 2 M HCl (1 × 15 mL) and saturated $NaHCO_3$ (1 × 15 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The products were purified by flash column chromatography using silica gel.

**3a,4,6,6a-Tetrahydro-3-(3-methoxyphenyl)furo[3,4-*d*]isoxazole (9b)**: yield 62%; mp 69–70 °C; IR ($CHCl_3$) 1605, 1573, 1467, 1347, 1089 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.25 (m, 2 H), 7.11 (m, 1 H), 6.95 (m, 1 H), 5.34 (dd, $J$ = 3.85, 9.34 Hz, 1 H), 4.26 (m, 2 H), 4.13 (m, 1 H), 3.84 (m, 1 H), 3.81 (s, 3 H), 3.74 (dd, $J$ = 3.66, 10.63 Hz, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 159.7, 156.5, 129.8, 129.3, 119.2, 116.1, 111.6, 86.2, 76.2, 71.7, 55.2, 53.7. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.87; H, 6.25; N, 6.25.

**3a,4,6,6a-Tetrahydro-3-(3,4-dimethoxyphenyl)furo[3,4-*d*]isoxazole (9c)**: yield 58%; mp 144 °C; IR ($CHCl_3$) 1603, 1571, 1514, 1467, 1262, 1026 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.37 (d, $J$ = 1.83 Hz, 1 H), 6.94 (dd, $J$ = 1.83, 8.42 Hz, 1 H), 6.83 (d, $J$ = 8.43 Hz, 1 H), 5.34 (dd, $J$ = 4.03, 9.16 Hz, 1 H), 4.27 (m, 2 H), 4.15 (m, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.84 (m, 1 H), 3.75 (dd, $J$ = 4.03, 10.63 Hz, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 156.3, 150.7, 149.2, 121.3, 119.9, 110.5, 109.2, 86.0, 76.3, 71.8, 55.8, 53.8. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.65; H, 6.20; N, 5.62.

**Reductive Cleavage of Dihydroisoxazolines.** Dihydroisoxazoline **9** (10 mmol) was dissolved in 25 mL of MeOH/$H_2O$ (5:1), and boric acid (100 mmol) was added. A spatula tip of W-2 Ra-Ni was then added, and the reaction vessel was covered with a balloon filled with $H_2$. The reaction vessel and contents were evacuated and filled with $H_2$. This procedure was repeated three times, and the reaction was allowed to proceed under a $H_2$ atmosphere. The reaction was followed by TLC. After consumption of starting material, the mixture was filtered through Celite and the plug washed with MeOH. The solvent was removed under reduced pressure. $H_2O$ (25 mL) was added followed by extraction with EtOAc (3 × 40 mL). The combined organic layers were washed with 5% $NaHCO_3$ solution (2 × 20 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The cis and trans isomers could be separated by recrystallization with $CH_2Cl_2$ and hexane to give pure cis compound.

**(3*RS*,4*RS*)-*cis*-4-Benzoyl-3-hydroxytetrahydrofuran (10a)**: yield 84%; mp 71–72 °C; IR ($CHCl_3$) 3456, 1667, 1598, 1449, 1070 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.98 (m, 2 H), 7.63 (m, 1 H), 7.51 (m, 2 H), 4.78 (m, 1 H), 4.22 (m, 2 H), 4.03 (m, 3 H), 3.51 (bs, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 198.4, 136.8, 133.5, 128.6, 128.0, 75.9, 73.4, 68.2, 51.3. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.97; H, 6.17.

**(3*RS*,4*RS*)-*cis*-3-Hydroxy-4-(3-methoxybenzoyl)tetrahydrofuran (10b)**: yield 94%; mp 92–93 °C; IR ($CHCl_3$) 3464, 1668, 1598, 1430, 1261 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.50 (m, 2 H), 7.38 (t, $J$ = 7.88 Hz, 1 H), 7.12 (dd, $J$ = 2.01, 8.24 Hz, 1 H), 4.73 (bs, 1 H), 4.24 (t, $J$ = 8.61 Hz, 1 H), 4.10 (t, $J$ = 8.24 Hz, 1 H), 4.04–3.85 (m, 3 H), 3.83 (s, 3 H), 3.63 (bs, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 198.4, 159.9, 138.2, 129.7, 120.7, 120.0, 112.5, 76.0, 73.6, 68.4, 55.3, 51.4. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.15; H, 6.47.

**(3*RS*,4*RS*)-*cis*-4-(3,4-Dimethoxybenzoyl)-3-hydroxytetrahydrofuran (10c)**: yield 92%; mp 105–106 °C; IR ($CHCl_3$) 3450, 1660, 1596, 1516, 1421, 1204 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.56 (d, $J$ = 8.42 Hz, 1 H), 7.47 (s, 1 H), 6.86 (d, $J$ = 8.43 Hz, 1 H), 4.69 (bs, 1 H), 4.12 (m, 2 H), 3.99–3.74 (m, 2 H), 3.90 (s, 3 H), 3.87 (s, 3 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 197.4, 153.9, 149.1, 130.0, 123.0, 110.0, 75.9, 73.6, 68.7, 55.9, 55.8, 50.4. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.97; H, 6.35.

**(3*RS*,4*RS*)-*cis*-3-Hydroxy-4-[3,4-(methylenedioxy)benzoyl]tetrahydrofuran (10d)**: yield 91%; mp 112–114 °C; IR ($CHCl_3$), 3462, 1663, 1605, 1489, 1445, 1256 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.59 (d, $J$ = 8.06 Hz, 1 H), 7.45 (s, 1 H), 6.90 (d, $J$ = 8.06 Hz, 1 H), 6.08 (s, 2 H), 4.73 (d, $J$ = 1.61 Hz, 1 H), 4.19 (appr dd, $J$ = 1.61, 2.69, 9.13 Hz, 2 H), 3.95 (m, 2 H), 3.71 (d, $J$ = 3.22 Hz, 1 H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 152.4, 148.4, 131.6, 124.7, 107.9, 107.7, 101.9, 75.9, 73.5, 68.8, 50.5. Anal. Calcd for $C_{12}H_{12}O_5$: C, 61.02; H, 5.12. Found: C, 61.12; H, 5.24.

**Deoxygenation of Ketones.** Ketone **10** (1 mmol) and 10% Pd/C (25 mg) were mixed with 4 mL of EtOH and 10 drops of concd $H_2SO_4$. The reaction was covered with a balloon filled with $H_2$. The reaction vessel and contents were evacuated and filled with $H_2$. This procedure was repeated three times, and the reaction was allowed to proceed under a $H_2$ atmosphere. The mixture was stirred overnight at rt and then filtered through a plug of Celite which was then washed with MeOH. The solvent was removed under reduced pressure. $H_2O$ (3 mL) was added followed by extraction with EtOAc (3 × 10 mL). The combined organic layers were washed with 5% $NaHCO_3$ solution (2 × 3

mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The products were purified by flash column chromatography using silica gel.

**(3*RS*,4*RS*)-*cis*-4-Benzyl-3-hydroxytetrahydrofuran (11a)**: yield 92%; IR ($CHCl_3$) 3620, 3434, 1604, 1495, 1455, 1212, 1051 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.24 (m, 5 H), 4.18 (t, $J$ = 3.85 Hz, 1 H), 3.89 (m, 2 H), 3.77 (dd, $J$ = 1.10, 9.89 Hz, 1 H), 3.62 (dd, $J$ = 8.06, 10.25 Hz, 1 H), 2.91 (dd, $J$ = 8.06, 13.92 Hz, 1 H), 2.68 (dd, $J$ = 7.51, 13.74 Hz, 1 H), 2.57 (bs, 1 H), 2.41 (m, 1 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 140.4, 128.4, 126.0, 76.1, 72.2, 71.0, 46.4, 31.7. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.91; H, 7.87.

**(3*RS*,4*RS*)-*cis*-3-Hydroxy-4-(3-methoxybenzyl)tetrahydrofuran (11b)**: yield 88%; IR ($CHCl_3$) 3618, 3441, 1731, 1610, 1491, 1259, 1044 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.22 (t, $J$ = 8.20 Hz, 1 H), 6.79 (m, 3 H), 4.23 (t, $J$ = 3.85 Hz, 1 H), 3.93 (m, 2 H), 3.80 (s, 3 H), 3.79 (m, 1 H), 3.65 (dd, $J$ = 8.06, 10.26 Hz, 1 H), 2.92 (dd, $J$ = 8.06, 13.93 Hz, 1 H), 2.69 (dd, $J$ = 7.33, 13.92 Hz, 1 H), 2.45 (m, 1 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 159.7, 142.0, 129.5, 120.9, 114.4, 111.3, 76.1, 72.3, 71.0, 55.0, 46.3, 31.8. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.01; H, 7.74. Found: C, 69.13; H, 7.72.

**(3*RS*,4*RS*)-*cis*-4-(3,4-Dimethoxybenzyl)-3-hydroxytetrahydrofuran (11c)**: yield 90%; IR ($CHCl_3$) 3619, 3435, 1591, 1513, 1465, 1258, 1029 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 6.77 (d, $J$ = 2.57 Hz, 3 H), 4.22 (t, $J$ = 3.85 Hz, 1 H), 3.96–3.79 (m, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.63 (dd, $J$ = 8.06, 10.26 Hz, 1 H), 2.87 (dd, $J$ = 8.43, 13.92 Hz, 1 H), 2.66 (dd, $J$ = 7.15, 13.74 Hz, 1 H), 2.44 (m, 1 H), 2.04 (bs, 1 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 148.9, 147.4, 133.0, 120.3, 111.9, 111.4, 76.2, 72.4, 71.1, 55.9, 55.8, 46.6, 31.3. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.31; H, 7.46.

**(3*RS*,4*RS*)-*cis*-3-Hydroxy-4-[3,4-(methylenedioxy)benzyl]-tetrahydrofuran (11d)**: yield 92%; mp 66–67 °C; IR ($CHCl_3$) 3620, 3440, 1491, 1444, 1249, 1041 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 6.75–6.65 (m, 3 H), 5.92 (s, 2 H), 4.22 (t, $J$ = 3.67 Hz, 1 H), 3.95–3.88 (m, 2 H), 3.81 (d, $J$ = 10.99 Hz, 1 H), 3.62 (dd, $J$ = 8.06, 10.26 Hz, 1 H), 2.85 (dd, $J$ = 8.79, 13.92 Hz, 1 H), 2.63 (dd, $J$ = 7.33, 13.92, Hz, 1 H), 2.44–2.36 (m, 1 H), 2.19 (bs, 1 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 147.7, 145.8, 134.2, 121.3, 109.0, 108.2, 100.8, 76.2, 72.3, 71.0, 46.7, 31.5. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.60; H, 6.33.

**Lipase Resolutions.** Racemic alcohol 11 (4.8 mmol) was mixed with 10 mL of vinyl acetate. Lipase PS (0.10 g) was added to the mixture and stirred vigorously with a magnetic stir bar. The reaction was monitored by NMR and stopped after the desired conversion was reached. On the average, our reactions reached ~50% conversion in approximately 13 h. The reaction mixture was filtered through a plug of Celite and the plug washed with $CH_2Cl_2$. The solvent was removed, and the products were purified by flash column chromatography using silica gel.

**(3*R*,4*R*)-4-Benzyl-3-hydroxytetrahydrofuran (12a)**: yield 51%; mp 63–64 °C; $[\alpha]^{27}_D$ +18.0 ($c$ = 1.43, $CH_2Cl_2$); IR and NMR were identical to **11a**. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.88; H, 7.66.

**(3*R*,4*R*)-3-Hydroxy-4-(3-methoxybenzyl)tetrahydrofuran (12b)**: yield 43%; $[\alpha]^{27}_D$ +14.1 ($c$ = 1.265, $CH_2Cl_2$); IR and NMR were identical to **11b**. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.01; H, 7.74. Found: C, 69.18; H, 7.88.

**(3*R*,4*R*)-4-(3,3-Dimethoxybenzyl)-3-hydroxytetrahydrofuran (12c)**: yield 43%; $[\alpha]^{27}_D$ +11.9 ($c$ = 0.94, $CH_2Cl_2$): IR and NMR were identical to **11c**. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.34; H, 7.62.

**(3*R*,4*R*)-3-Hydroxy-4-[3,4-(methylenedioxy)benzyl]tetrahydrofuran (12d)**: yield 51%; mp 92–93 °C; $[\alpha]^{27}_D$ +15.7 ($c$ = 1.29, $CH_2Cl_2$); IR and NMR were identical to **11d**. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.95; H, 6.28.

**(3*S*,4*S*)-3-Acetoxy-4-benzyltetrahydrofuran (13a)**: yield 41%; $[\alpha]^{27}_D$ –53.6 ($c$ = 1.54, $CH_2Cl_2$); IR ($CHCl_3$) 1728, 1496, 1464, 1374, 1264, 1057 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.28–7.10 (m, 5 H), 5.17 (m, 1 H), 4.00 (dd, $J$ = 4.03, 10.62 Hz, 1 H), 3.89 (t, $J$ = 7.70 Hz, 1 H), 3.79 (dd, $J$ = 1.47, 10.63 Hz, 1 H), 3.61 (dd, $J$ = 8.24, 9.71 Hz, 1 H), 2.85 (dd, $J$ = 6.41, 13.38 Hz, 1 H), 2.67–2.52 (m, 2 H), 2.09 (s, 3 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 170.5, 139.7, 128.5, 128.3, 126.2, 75.0, 74.0, 71.6, 44.8, 31.9, 20.9. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.72; H, 7.45.

**(3*S*,4*S*)-3-Acetoxy-4-(3-methoxybenzyl)tetrahydrofuran (13b)**: yield 43%; $[\alpha]^{27}_D$ –46.4° ($c$ = 1.915, $CH_2Cl_2$); IR ($CHCl_3$) 1737, 1603, 1491, 1264, 1046 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.19 (t, $J$ = 7.88 Hz, 1 H), 6.73 (m, 3 H), 5.21 (m, 1 H), 4.03 (dd, $J$ = 4.03, 10.62 Hz, 1 H), 3.93 (t, $J$ = 7.88 Hz, 1 H), 3.83 (dd, $J$ = 1.10, 10.63 Hz, 1 H), 3.78 (s, 3 H), 3.63 (dd, $J$ = 8.24, 9.71 Hz, 1 H), 2.84 (m, 1 H), 2.61 (m, 2 H), 2.13 (s, 3 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 170.4, 159.7, 141.3, 129.5, 120.6, 114.2, 111.4, 75.0, 74.0, 71.5, 55.0, 44.7, 31.9, 20.9. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.33; H, 7.09.

**(3*S*,4*S*)-3-Acetoxy-4-(3,4-dimethoxybenzyl)tetrahydrofuran (13c)**: yield 43%; $[\alpha]^{27}_D$ –42.7° ($c$ = 2.00, $CH_2Cl_2$); IR ($CHCl_3$) 1736, 1592, 1514, 1261, 1028 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 6.75 (m, 1 H), 6.66 (m, 2 H), 5.21 (m, 1 H), 4.02 (dd, $J$ = 4.03, 10.63 Hz, 1 H), 3.93–3.76 (m, 2 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.61 (dd, $J$ = 8.06, 9.53 Hz, 1 H), 2.82 (m, 1 H), 2.57 (m, 2 H), 2.11 (s, 3 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 170.4, 148.9, 147.5, 132.3, 120.2, 111.6, 111.3, 75.0, 73.9, 71.5, 55.7, 55.6, 45.0, 31.4, 20.9. Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 63.98; H, 6.95.

**(3*S*,4*S*)-3-Acetoxy-4-[3,4-(methylenedioxy)benzyl]tetrahydrofuran (13d)**: yield 47%; $[\alpha]^{27}_D$ –41.0 ($c$ = 1.665, $CH_2Cl_2$); IR ($CHCl_3$) 1731, 1503, 1491, 1254, 1041 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 6.70 (d, $J$ = 7.69 Hz, 1 H), 6.59 (m, 2 H), 5.90 (s, 2 H), 5.19 (m, 1 H), 4.02 (dd, $J$ = 4.40, 10.63 Hz, 1 H), 3.90 (appr. t, $J$ = 7.33, 8.06 Hz, 1 H), 3.81 (dd, $J$ = 1.28, 10.81 Hz, 1 H), 3.60 (dd, $J$ = 8.06, 9.89 Hz, 1 H), 2.75 (dd, $J$ = 6.60, 12.46 Hz, 1 H), 2.54 (m, 2 H), 2.11 (s, 3 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 170.5, 147.7, 145.9, 133.4, 121.1, 108.6, 108.2, 100.8, 75.0, 74.0, 71.5, 45.0, 31.6, 20.9. Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.66; H, 6.22.

**Hydrolysis of Acetates.** Acetate 13 (2 mmol) was dissolved in 5 mL of MeOH and 0.5 mL of $H_2O$. $K_2CO_3$ (6 mmol) was then added to the reaction mixture, and the reaction was followed by TLC (reaction takes place in less than 1 h). Then methanol was removed under reduced pressure, and the residue was treated with 2 M HCl (5 mL). The mixture was then extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic layers were washed with 5% $NaHCO_3$ solution (1 × 7 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed.

**(3*S*,4*S*)-4-Benzyl-3-hydroxytetrahydrofuran (14a)**: yield 94%; mp 60–61 °C; $[\alpha]^{27}_D$ –16.6 ($c$ = 1.555, $CH_2Cl_2$); IR and NMR were identical to **11a**. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.96; H, 7.88.

**(3*S*,4*S*)-3-Hydroxy-4-(3-methoxybenzyl)tetrahydrofuran (14b)**: yield 87%; $[\alpha]^{27}_D$ –13.1 ($c$ = 1.40, $CH_2Cl_2$); IR and NMR were identical to **11b**. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.01; H, 7.74. Found: C, 68.80; H, 7.76.

**(3*S*,4*S*)-4-(3,4-Dimethoxybenzyl)-3-hydroxytetrahydrofuran (14c)**: yield 89%; $[\alpha]^{27}_D$ –11.1 ($c$ = 1.11, $CH_2Cl_2$); IR and NMR were identical to **11c**. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.33; H, 7.69.

**(3*S*,4*S*)-3-Hydroxy-4-[3,4-(methylenedioxy)benzyl]tetrahydrofuran (14d)**: yield 96%; mp 89–90 °C; $[\alpha]^{27}_D$ –14.5 ($c$ = 1.205, $CH_2Cl_2$); IR and NMR were identical to **11d**. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.24; H, 6.08.

**Tosylation of Optically Active Alcohols.** Alcohol 12 or 14 (1 mmol) was dissolved in 2 mL of THF, the reaction mixture cooled to –78 °C, and MeLi (1.1 mmol) added. The reaction was stirred for 30 min. While the reaction mixture was still at –78 °C, TsCl (1.1 mmol) dissolved in 0.5 mL of THF was added. The reaction mixture was allowed to warm to rt and stirred for 3 h. The reaction was quenched with saturated $NH_4Cl$ solution (5 mL) and extracted with $CH_2Cl_2$ (3 × 7 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The products were purified by flash column chromatography using silica gel followed by recrystallization with $Et_2O$.

**(3*R*,4*R*)-4-Benzyl-3-(toluenesulfonyl)tetrahydrofuran (15a)**: yield 79%; mp 80 °C; $[\alpha]^{27}_D$ +26.4° ($c$ = 1.07, $CH_2Cl_2$); IR ($CHCl_3$) 1600, 1496, 1455, 1368, 1176 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.06 Hz, 2 H), 7.37 (d, $J$ = 8.79 Hz,

2 H), 7.24 (m, 3 H), 7.10 (m, 2 H), 5.04 (m, 1 H), 3.93 (d, $J$ = 2.56 Hz, 2 H), 3.87 (t, $J$ = 7.88 Hz, 1 H), 3.62 (dd, $J$ = 8.06, 10.26 Hz, 1 H), 2.85 (dd, $J$ = 5.86, 13.56 Hz, 1 H), 2.67 (dd, $J$ = 8.43, 13.92 Hz, 1 H), 2.57 (m, 1 H), 2.47 (s, 3 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 145.0, 139.2, 133.9, 129.9, 128.6, 128.3, 127.7, 126.3, 82.4, 73.3, 71.3, 45.5, 31.7, 21.6. Anal. Calcd for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06. Found: C, 64.98; H, 6.17.

**(3*R*,4*R*)-4-(3-Methoxybenzyl)-3-(toluenesulfonyl)tetrahydrofuran (15b)**: yield 82%; mp 56–57 °C; $[\alpha]^{27}_D$ +20.0° ($c$ = 1.05, $CH_2Cl_2$); IR ($CHCl_3$) 1601, 1492, 1369, 1261, 1176 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.43 Hz, 2 H), 7.35 (d, $J$ = 8.06 Hz, 2 H), 7.17 (m, 1 H), 6.73 (m, 3 H), 5.05 (m, 1 H), 3.90 (m, 3 H), 3.80 (s, 3 H), 3.61 (dd, $J$ = 8.25, 10.08 Hz, 1 H), 2.83 (dd, $J$ = 5.86, 13.56 Hz, 1 H), 2.65 (dd, $J$ = 8.42, 13.56 Hz, 1 H), 2.57 (m, 1 H), 2.46 (s, 3 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 159.7, 145.0, 140.9, 133.8, 129.9, 129.5, 127.7, 120.6, 114.1, 111.7, 82.4, 73.2, 71.2, 55.1, 45.3, 31.7, 21.6. Anal. Calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.12. Found: C, 63.15; H, 6.23.

**(3*R*,4*R*)-4-(3,4-Dimethoxybenzyl)-3-(toluenesulfonyl)tetrahydrofuran (15c)**: yield 77%; mp 88–89 °C; $[\alpha]^{27}_D$ +18.8° ($c$ = 1.095, $CH_2Cl_2$); IR ($CHCl_3$) 1598, 1525, 1465, 1368, 1262, 1177 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.42 Hz, 2 H), 7.35 (d, $J$ = 8.06 Hz, 2 H), 6.69 (m, 3 H), 5.06 (m, 1 H), 4.06–3.82 (m, 3 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.61 (dd, $J$ = 8.24, 10.08 Hz, 1 H), 2.83 (dd, $J$ = 6.23, 13.56 Hz, 1 H), 2.67–2.53 (m, 2 H), 2.47 (s, 3 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 148.9, 147.5, 144.9, 133.9, 131.8, 129.9, 127.6, 120.2, 111.8, 111.4, 82.4, 73.1, 71.2, 55.8, 45.7, 31.2, 21.6. Anal. Calcd for $C_{20}H_{24}O_6S$: C, 61.21; H, 6.16. Found: C, 61.18; H, 6.39.

**(3*R*,4*R*)-4-[3,4-(Methylenedioxy)benzyl]-3-(toluenesulfonyl)tetrahydrofuran (15d)**: yield 90%; mp 73–74 °C; $[\alpha]^{27}_D$ +25.3° ($c$ = 1.42, $CH_2Cl_2$); IR ($CHCl_3$) 1599, 1491, 1444, 1368, 1249, 1177 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 8.42 Hz, 2 H), 7.35 (d, $J$ = 8.43 Hz, 2 H), 6.67 (d, $J$ = 7.69 Hz, 1 H), 6.53 (m, 2 H), 5.92 (s, 2 H), 5.01 (m, 1 H), 3.91 (d, $J$ = 2.57 Hz, 2 H), 3.86 (t, $J$ = 7.88 Hz, 1 H), 3.58 (dd, $J$ = 8.24, 10.08 Hz, 1 H), 2.75 (dd, $J$ = 5.86, 13.55 Hz, 1 H), 2.62–2.48 (m, 2 H), 2.46 (s, 3 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 147.7, 146.0, 145.0, 133.8, 129.9, 127.7, 121.2, 108.7, 108.2, 100.8, 82.3, 73.3, 71.2, 45.6, 31.4, 21.6. Anal. Calcd for $C_{19}H_{20}O_6S$: C, 60.63; H, 5.36. Found: C, 60.96; H, 5.47.

**(3*S*,4*S*)-4-Benzyl-3-(toluenesulfonyl)tetrahydrofuran (18a)**: yield 83%; mp 78–79 °C; $[\alpha]^{27}_D$ –26.9° ($c$ = 1.03, $CH_2Cl_2$); IR and NMR identical to **15a**. Anal. Calcd for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06. Found: C, 65.36; H, 6.12.

**(3*S*,4*S*)-4-(3-Methoxybenzyl)-3-(toluenesulfonyl)tetrahydrofuran (18b)**: yield 77%; mp 53 °C; $[\alpha]^{27}_D$ –19.8° ($c$ = 0.975, $CH_2Cl_2$); IR and NMR identical to **15b**. Anal. Calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.12. Found: C, 63.14; H, 6.00.

**(3*S*,4*S*)-4-(3,4-Dimethoxybenzyl)-3-(toluenesulfonyl)tetrahydrofuran (18c)**: yield 73%; mp 91–92 °C; $[\alpha]^{27}_D$ –19.7° ($c$ = 1.085, $CH_2Cl_2$); IR and NMR identical to **15c**. Anal. Calcd for $C_{20}H_{24}O_6S$: C, 61.21; H, 6.16. Found: C, 61.36; H, 6.06.

**(3*S*,4*S*)-4-[3,4-(Methylenedioxy)benzyl]-3-(toluenesulfonyl)tetrahydrofuran (18d)**: yield 83%; mp 72–73 °C; $[\alpha]^{27}_D$ –26.1° ($c$ = 1.38, $CH_2Cl_2$); IR and NMR identical to **15d**. Anal. Calcd for $C_{19}H_{20}O_6S$: C, 60.63; H, 5.36. Found: C, 61.03; H, 5.66.

**Displacement of Tosylates by Benzyllithiums.** Benzyl phenyl sulfide (0.2 mmol) was dissolved in 5 mL of THF and cooled to 0 °C. n-BuLi (0.2 mmol) was added dropwise over ~5 min, and then the mixture was stirred at 0 °C for 30 min. Tosylate **15** or **18** dissolved in 1.25 mL of THF was added to the reaction mixture. The mixture was stirred at 0 °C for 1–2 h, and then the cooling bath was removed and the mixture stirred at rt for 17 h. The reaction was quenched with saturated $NH_4Cl$ solution (5 mL) and product extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and solvent was removed. The products were purified by flash column chromatography using silica gel.

**(3*S*,4*S*)-4-Benzyl-3-[phenyl(phenylthio)methyl]tetrahydrofuran (16a)**: yield 69%; IR ($CHCl_3$) 1603, 1583, 1495, 1480, 1453, 1439, 1083 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.34–7.14 (m, 28 H), 6.82 (dd, $J$ = 1.46, 2.20, 7.33 Hz, 2 H), 4.19 (dd, $J$ = 7.15, 9.35 Hz, 1 H), 4.07 (m, 2 H), 3.98 (d, $J$ = 10.62 Hz, 1 H), 3.79 (m, 3 H), 3.54 (m, 3 H), 2.77 (m, 1 H), 2.67 (dd, $J$ = 10.26, 12.82 Hz, 1 H), 2.55–2.19 (m, 5 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 141.5, 141.1, 140.4, 140.2, 134.5, 134.4, 132.8, 132.5, 129.0, 128.6, 128.5, 128.3, 127.2, 126.2, 126.0, 77.2, 76.3, 73.1, 72.6, 71.6, 58.3, 57.8, 50.7, 50.4, 46.0, 45.8, 40.8, 40.1. Anal. Calcd for $C_{24}H_{24}OS$: C, 79.96; H, 6.71. Found: C, 80.10; H, 6.90.

**(3*S*,4*S*)-4-(3-Methoxybenzyl)-3-[(3-methoxyphenyl)(phenylthio)methyl]tetrahydrofuran (16b)**: yield 61%; IR ($CHCl_3$) 1600, 1584, 1489, 1467, 1439,, 1263, 1044 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.18 (m, 16 H), 6.75 (m, 8 H), 6.46 (d, $J$ = 7.33 Hz, 1 H), 6.36 (m, 1 H), 4.17 (dd, $J$ = 7.15, 9.34 Hz, 1 H), 4.04 (m, 1 H), 3.94 (d, $J$ = 10.63 Hz, 1 H), 3.83 (s, 3 H), 3.74 (s, 6 H), 3.72 (s, 3 H), 3.81–3.70 (m, 3 H), 3.54 (m, 3 H), 3.10 (dd, $J$ = 4.58, 13.00 Hz, 1 H), 2.76 (m, 1 H), 2.63 (dd, $J$ = 10.26, 12.82 Hz, 1 H), 2.52.–2.22 (m, 5 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 159.8, 159.6, 159.5, 143.2, 142.7, 142.0, 141.8, 134.6, 134.5, 132.7, 132.3, 129.5, 129.3, 128.7, 127.3, 127.2, 121.3, 121.0, 120.7, 114.7, 114.2, 113.9, 113.8, 112.8, 112.7, 111.6, 111.5, 77.3, 77.2, 73.1, 72.5, 71.6, 58.2, 57.7, 55.2, 50.7, 50.3, 45.9, 45.7, 40.8, 40.3. Anal. Calcd for $C_{26}H_{28}O_3S$: C, 74.25; H, 6.71. Found: C, 74.15; H, 6.63.

**(3*S*,4*S*)-4-(3,4-Dimethoxybenzyl)-3-[(3,4-dimethoxyphenyl)(phenylthio)methyl]tetrahydrofuran (16c)**: yield 52%; IR ($CHCl_3$) 1606, 1591, 1513, 1465, 1259, 1141, 1028 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.17 (appr. d, $J$ = 4.39 Hz, 10 H), 6.95–6.61 (m, 10 H), 6.43 (dd, $J$ = 1.83, 8.06 Hz, 1 H), 6.27 (d, $J$ = 1.83 Hz, 1 H), 4.17 (dd, $J$ = 7.15, 9.35 Hz, 1 H), 4.04 (m, 2 H), 3.93–3.72 (m, 28 H), 3.65–3.44 (m, 3 H), 3.06 (dd, $J$ = 4.58, 13.01 Hz, 1 H), 2.75 (m, 1 H), 2.61 (dd, $J$ = 10.08, 13.01 Hz, 1 H), 2.53–2.27 (m, 4 H), 2.16 (m, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 148.9, 148.8, 148.7, 148.1, 147.6, 147.4, 134.4, 134.1, 133.6, 133.1, 132.9, 132.8, 132.6, 128.6, 127.3, 127.2, 123.4, 120.8, 120.5, 120.4, 112.3, 111.9, 111.3, 111.1, 110.7, 110.6, 77.2, 73.0, 72.5, 71.6, 58.2, 57.7, 55.8, 55.7, 55.6, 50.6, 50.3, 46.1, 45.9, 40.3, 40.3. Anal. Calcd for $C_{28}H_{32}O_5S$: C, 69.97; H, 6.71. Found: C, 70.09; H, 6.63.

**(3*S*,4*S*)-4-[3,4-(Methylenedioxy)benzyl]-3-[[3,4-(methylenedioxy)phenyl](phenylthio)methyl]tetrahydrofuran (16d)**: yield 65%; IR ($CHCl_3$) 1521, 1503, 1443, 1248, 1041 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.20 (s, 4 H), 7.18 (s, 6 H), 6.78–6.73 (m, 3 H), 6.70–6.60 (m, 3 H), 6.54–6.49 (m, 3 H), 6.34 (m, 3 H), 5.95 (s, 2 H), 5.94 (s, 2 H), 5.93 (s, 2 H), 5.91 (s, 2 H), 4.15 (dd, $J$ = 7.33, 9.53 Hz, 1 H), 4.02 (m, 2 H), 3.90–3.72 (m, 4 H), 3.58–3.43 (m, 3 H), 3.01 (appr. dd, $J$ = 4.40, 5.13, 12.83 Hz, 1 H), 2.75–2.65 (m, 1 H), 2.56 (dd, $J$ = 10.26, 13.19 Hz, 1 H), 2.47–2.23 (m, 4 H), 2.18–2.10 (m, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 147.8, 147.7, 147.6, 146.6, 145.8, 135.5, 135.0, 134.5, 134.4, 134.2, 133.9, 132.6, 132.5, 132.3, 128.9, 128.7, 127.2, 127.2, 121.8, 121.7, 121.5, 109.3, 108.9, 108.2, 108.1, 108.0, 107.6, 107.5, 101.0, 100.8, 77.2, 76.8, 73.0, 72.5, 71.6, 58.2, 57.7, 50.5, 50.4, 46.0, 45.8, 40.5, 39.9. Anal. Calcd for $C_{26}H_{24}O_5S$: C, 69.62; H, 5.39. Found: C, 69.64; H, 5.56.

**(3*S*,4*S*)-3-[[3,4-(Methylenedioxy)phenyl](phenylthio)methyl]-4-(3,4,5-trimethoxybenzyl)tetrahydrofuran (16e)**: yield 46%; IR ($CHCl_3$) 1591, 1504, 1490, 1247, 1129, 1041 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.19 (d, $J$ = 5.49 Hz, 10 H), 6.69 (m, 4 H), 6.32 (m, 6 H), 5.95 (s, 2 H), 5.90 (s, 2 H), 4.15 (m, 1 H), 4.05 (dd, $J$ = 5.32, 9.35 Hz, 1 H), 3.95 (d, $J$ = 10.62 Hz, 1 H), 3.86–3.75 (m, 22 H), 3.55 (m, 3 H), 3.05 (dd, $J$ = 4.77, 12.83 Hz, 1 H), 2.70 (m, 1 H), 2.58 (m, 1 H), 2.46–2.27 (m, 4 H), 2.17 (m, 1 H); $^{13}$C NMR (65 MHz, $CDCl_3$) $\delta$ 152.9, 147.6, 145.8, 137.1, 136.6, 134.3, 134.2, 134.1, 133.8, 133.3, 132.8, 128.7, 127.5, 127.4, 121.7, 121.4, 109.2, 108.8, 108.2, 107.9, 105.3, 100.9, 76.3, 73.0, 72.3, 71.7, 60.9, 58.8, 58.5, 56.1, 50.4, 50.1, 46.0, 40.5, 40.1. Anal. Calcd for $C_{28}H_{30}O_6S$: C, 68.0; H, 6.11. Found: C, 67.62; H, 6.32.

**(3*R*,4*R*)-4-Benzyl-3-[phenyl(phenylthio)methyl]tetrahydrofuran (19a)**: yield 73%; IR and NMR identical to **16a**. Anal. Calcd for $C_{24}H_{24}OS$: C, 79.96; H, 6.71. Found: C, 80.14; H, 7.00.

**(3*R*,4*R*)-4-(3-Methoxybenzyl)-3-[(3-methoxyphenyl)(phenylthio)methyl]tetrahydrofuran (19b)**: yield 54%; IR and NMR identical to **16b**. Anal. Calcd for $C_{26}H_{28}O_3S$: C, 74.25; H, 6.71. Found: C, 74.12; H, 6.46.

**(3*R*,4*R*)-4-(3,4-Dimethoxybenzyl)-3-[(3,4-dimethoxyphenyl)(phenylthio)methyl]tetrahydrofuran (19c)**: yield 54%; IR and NMR identical to **16c**. Anal. Calcd for $C_{28}H_{32}O_5S$: C, 69.97; H, 6.71. Found: C, 70.19; H, 7.01.

**(3*R*,4*R*)-4-[3,4-(Methylenedioxy)benzyl]-3-[[3,4-(methylenedioxy)phenyl](phenylthio)methyl]tetrahydrofuran (19d)**: yield 60%; IR and NMR identical to **16d**. Anal. Calcd for $C_{26}H_{24}O_5S$: C, 69.62; H, 5.39. Found: C, 69.85; H, 5.81.

**(3*R*,4*R*)-3-[[3,4-(Methylenedioxy)phenyl](phenylthio)-methyl]-4-(3,4,5-trimethoxybenzyl)tetrahydrofuran (19e)**: yield 56%; IR and NMR identical to **16e**. Anal. Calcd for $C_{28}H_{30}O_6S$: C, 68.0; H, 6.11. Found: C, 67.82; H, 6.01.

**Cleavage of Phenyl Sulfides to Lignans.** The diastereomeric mixture of sulfide **16** or **19** (0.1 mmol) was dissolved in 5 mL of EtOH. A spatula tip of W-2 Ra-Ni was then added and the reaction refluxed for 20 h. The reaction mixture was filtered through a pad of Celite, and the plug was washed repeatedly with $CH_2Cl_2$. The products were purified by flash column chromatography using silica gel.

**(3*S*,4*S*)-3,4-Dibenzyltetrahydrofuran (17a)**: yield 87%; mp 63–64 °C; $[\alpha]^{27}_D$ +32.1 (*c* = 0.92, $CHCl_3$); IR ($CHCl_3$) 1604, 1494, 1454, 1079, 1047 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.21 (m, 6 H), 7.08 (m, 4 H), 3.87 (dd, *J* = 6.78, 8.62 Hz, 2 H), 3.50 (dd, *J* = 6.23, 8.79 Hz, 2 H), 2.68 (dd, *J* = 5.86, 13.56 Hz, 2 H), 2.55 (dd, *J* = 8.43, 13.56 Hz, 2 H), 2.21 (m, 2 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 140.4, 128.7, 128.4, 126.1, 73.3, 46.6, 39.3. Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.76; H, 8.18.

**(3*S*,4*S*)-3,4-Bis(3-methoxybenzyl)tetrahydrofuran (17b)**: yield 72%; $[\alpha]^{27}_D$ +40.5 (*c* = 0.57, $CHCl_3$); IR ($CHCl_3$) 1601, 1491, 1454, 1266, 1154, 1045 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.20 (t, *J* = 7.88 Hz, 2 H), 6.73 (m, 6 H), 3.92 (dd, *J* = 6.60, 8.80 Hz, 2 H), 3.79 (s, 6 H), 3.53 (dd, *J* = 6.23, 8.79 Hz, 2 H), 2.68 (dd, *J* = 5.86, 13.56 Hz, 2 H), 2.56 (dd, *J* = 8.24, 13.37 Hz, 2 H), 2.24 (m, 2 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 159.7, 142.0, 129.4, 121.1, 114.5, 111.4, 73.3, 55.1, 46.5, 39.4. Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.04; H, 8.06.

**(3*S*,4*S*)-3,4-Bis(3,4-dimethoxybenzyl)tetrahydrofuran (brassilignan) (17c)**: yield 75%; mp 117–118 °C; $[\alpha]^{27}_D$ +41.3 (*c* = 0.88, $CHCl_3$); IR and NMR identical to reported spectra.[10]

**(3*S*,4*S*)-3,4-Bis[3,4-(methylenedioxy)benzyl]tetrahydrofuran (dehydroxycubebin) (17d)**: yield 72%; $[\alpha]^{27}_D$ +54.7 (*c* = 0.565, $CHCl_3$); IR ($CHCl_3$) 1503, 1490, 1443, 1249, 1041 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 6.71 (d, *J* = 8.06 Hz, 2 H), 6.56 (s, 2 H), 6.53 (d, *J* = 4.17 Hz, 2 H), 5.93 (s, 4 H), 3.90 (dd, *J* = 6.60, 8.80 Hz, 2 H), 3.51 (dd, *J* = 5.87, 8.80 Hz, 2 H), 2.59 (dd, *J* = 6.60, 13.92 Hz, 2 H), 2.50 (dd, *J* = 8.06, 13.92 Hz, 2 H), 2.15 (heptet, 2 H); $^{13}C$ NMR (65 MHz, $CDCl_3$) $\delta$ 147.6, 145.8, 134.1, 121.5, 108.9, 108.1, 100.9, 73.2, 46.5, 39.2. Anal. Calcd for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.46; H, 6.12.

**(3*S*,4*S*)-4-[3,4-(Methylenedioxy)benzyl]-3-(3,4,5-trimethoxybenzyl)tetrahydrofuran (burseran) (17e)**: yield 71%; $[\alpha]^{27}_D$ +43.7 (*c* = 1.03, $CHCl_3$); IR and NMR identical to reported spectra.[8]

**(3*R*,4*R*)-3,4-Dibenzyltetrahydrofuran (20a)**: yield 91%; mp 64–65 °C; $[\alpha]^{27}_D$ −31.0 (*c* = 1.245, $CHCl_3$); IR and NMR identical to **17a**. Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.29; H, 8.01.

**(3*R*,4*R*)-3,4-Bis(3-methoxybenzyl)tetrahydrofuran (20b)**: yield 82%; $[\alpha]^{27}_D$ −38.0 (*c* = 1.305, $CHCl_3$); IR and NMR identical to **17b**. Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.02; H, 8.19.

**(3*R*,4*R*)-3,4-Bis(3,4-dimethoxybenzyl)tetrahydrofuran (brassilignan) (20c)**: yield 77%; mp 113 °C; $[\alpha]^{27}_D$ −37.9 (*c* = 0.90, $CHCl_3$); IR and NMR identical to reported spectra.[10]

**(3*R*,4*R*)-3,4-Bis[3,4-(methylenedioxy)benzyl]tetrahydrofuran (dehydroxycubebin) (20d)**: yield 80%; $[\alpha]^{27}_D$ −48.8 (*c* = 1.04, $CHCl_3$); IR and NMR identical to reported spectra.[9]

**(3*R*,4*R*)-4-[3,4-(Methylenedioxy)benzyl]-3-(3,4,5-trimethoxybenzyl)tetrahydrofuran (burseran) (20e)**: yield 74%; $[\alpha]^{27}_D$ −37.8 (*c* = 0.87, $CHCl_3$); IR and NMR identical to reported spectra.[8]

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