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One-Pot Asymmetric Synthesis of 2- and 2,3-Disubstituted Tetrahydrofuran Derivatives

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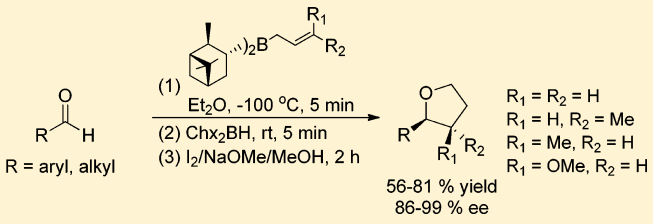
Supporting Information

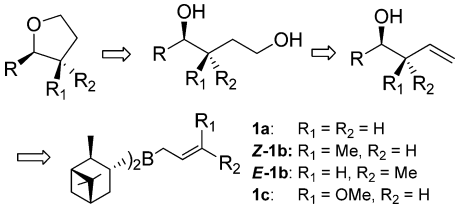
ABSTRACT: A novel and convenient one-pot asymmetric synthesis of 2- and 2,3-disubstituted tetrahydrofurans has been achieved in 56−81% yields and 86−99% ee from aliphatic and aromatic aldehydes via an allyl/crotyl/alkoxyallylboration−hydroboration−iodination−cyclization reaction sequence.



Pinane-based asymmetric allylboration and related reactions[1] are significant C−C bond forming reactions that are used for the stereoselective syntheses of simple and complex molecules.[2] Tandem reactions involving allyl-derived boranes provide a one-pot procedure for the synthesis of either intermediates or end-products. For example, Brown and coworkers reported a tandem allylboration−protection−hydroboration−oxidation−deprotection−cyclization protocol for the synthesis of chiral γ-lactones.[3] Taking advantage of the uniqueness of fluorinated alcohols, this protocol was applied for the preparation of fluorinated γ-lactones, without the need for the protection−deprotection sequence.[4]

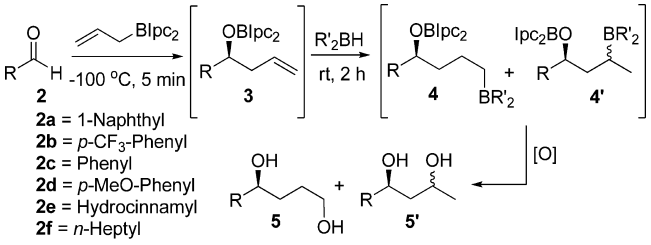
We recently reported the allyboration of imines, followed by hydroboration−oxidation in the same pot, for the preparation of γ-aminobutyric acid derivatives.[5] We also recently described a one-pot synthesis of tetrahydropyrans via an allyl/crotylboration−Prins cyclization.[6] In continuation of our projects on tandem reactions, a simple one-pot synthesis of tetrahydrofurans (THF) involving an intramolecular Mitsunobu reaction of the 1,4-diols obtained via allylboration−oxidation was envisaged (Scheme 1). Substituted THF derivatives are key components of a wide range of biologically active natural products, such as lignans[7] and annonceous acetogenins.[8] Because of this importance, the THF moiety continues to attract the attention of organic chemists. Various methodologies have been described for the synthesis of substituted THF derivatives.[9] Reported herein is a novel, one-pot asymmetric synthesis of chiral THF derivatives in high diastereo- and enantiomeric excesses from aldehydes via a sequential allylboration−hydroboration−iodination−cyclization reaction.

Scheme 1. Retrosynthesis of THF Derivatives via Cyclodehydration



Because of the ease of analysis of the products, we began the project with the allylboration of 1-naphthaldehyde (**2a**) with (−)-*B*-allyldiisopinocampheylborane [(−)-Ipc$_2$BAll, **1a**] in Et$_2$O at −100 °C.[10,11] Analysis of the homoallylic alcohol revealed an ee of 98% (as determined by the ^{1}H NMR of its MTPA ester). The hydroboration of the borinate intermediate **3a** was carried out in the same pot with BH$_3$−SMe$_2$ and was subjected to alkaline H$_2$O$_2$ oxidation.[12] ^{1}H NMR analysis of the crude reaction mixture revealed the formation of a 83:17 mixture of the 1,4- (**5a**) and 1,3-diols (**5′a**) (Scheme 2). HPLC analysis of **5a** on a Chiralcel OD-H column demonstrated that there was a complete transfer of chirality from **1a** to **5a**.

Scheme 2. One-Pot Asymmetric Allylboration−Hydroboration−Oxidation



Screening other hydroborating agents, such as BH$_3$−THF, 9-borabicyclo[3.3.1]nonane (9-BBN), Br$_2$BH−SMe$_2$, and dicyclohexylborane (Chx$_2$BH)[13] revealed the exclusive formation of the 1,4-diol (**5**) with only Chx$_2$BH and 9-BBN (Table 1).

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Table 1. Regioselectivity of Hydroboration of Homoallyl Alcohol Borinate

				diol		
entry	RCHO	R'_2BH	R'_2BH equiv	**5**	yield, %[a]	**5**:**5′**[b]
1	**2a**	BH_3–SMe_2	1.2	**5a**	66	87:13
2	**2a**	BH_3–THF	1.2	**5a**	71	91:9
3	**2a**	Br_2BH–SMe_2	1.2	**5a**	76	93:7
4	**2a**	9-BBN	1.2	**5a**	68	>98:<2
5	**2a**	Chx_2BH	1.2	**5a**	77	>98:<2
6	**2a**	Chx_2BH	1.5	**5a**	81	>98:<2
7	**2a**	Chx_2BH	2.0	**5a**	81	>98:<2
8	**2b**	BH_3–SMe_2	1.2	**5b**	65	83:17
9	**2b**	BH_3-THF	1.2	**5b**	66	88:12
10	**2b**	9-BBN	1.2	**5b**	60	96:4
11	**2b**	Chx_2BH	1.2	**5b**	60	>98:<2
12	**2b**	Chx_2BH	1.5	**5b**	71	>98:<2
13	**2b**	Chx_2BH	2.0	**5b**	71	>98:<2
14	**2c**	Chx_2BH	1.5	**5c**	72	>98:<2
15	**2d**	Chx_2BH	1.5	**5d**	65	>98:<2
16	**2e**	Chx_2BH	1.5	**5e**	67	>98:<2
17	**2f**	Chx_2BH	1.5	**5f**	65	>98:<2

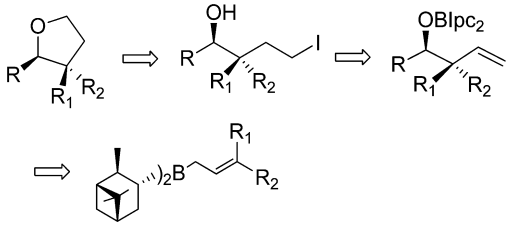
[a]Isolated yield. [b]The ratio of **5**:**5′** was determined by ^1H NMR of the crude reaction mixture.

Increasing the equivalents of Chx_2BH from 1.2 to 1.5 improved the yield of **5** to 81%. Further increasing the amounts of the hydroborating agent did not enhance the yields. We also performed the allylboration–hydroboration–oxidation sequence with *p*-trifluoromethylbenzaldehyde (**2b**); in this case, Chx_2BH gave the best regioselectivity. We therefore chose Chx_2BH for further reactions.

The stage was now set to examine the intramolecular Mitsunobu reaction.[14] Evans and co-workers had reported that the cyclodehydration of (*S*)-phenylethane-1,2-diol with various phosphorus reagents resulted in significant racemization.[15] The application of this method for the synthesis of the THF derivative from 1,4-diol **5a** gave only 33% yield of the desired product, (*S*)-2-(naphthalen-1-yl)tetrahydrofuran (**6a**). Unfortunately, the enantiomeric excess dropped from 98 to 80% for **6a**. Low yields and a significant drop in ee were observed with the chiral 1,4-diols derived from **2b** and **2d** as well.

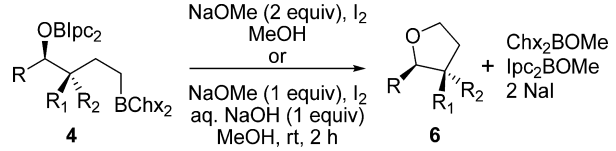
Weissman et al. has described the use of Chx_3P-DIAD as an effective reagent system to achieve high stereoretention for the Mitsunobu cyclodehydration during the preparation of chiral styrene oxide derivatives.[16] The high cost of Chx_3P dissuaded us from using the Weissman protocol, and an intramolecular ether synthesis via the iodination of intermediate **4** appeared attractive (Scheme 3).

Scheme 3. Revised Retrosynthesis of THF Derivatives: Iodination Approach



The allylboration of 1-naphthaldehyde was carried out in Et_2O at −100 °C for 5 min; the reaction mixture was then transferred via cannula to a flask containing Chx_2BH in Et_2O at rt. The solid Chx_2BH was visibly consumed within 5 min, while the ^{11}B NMR spectrum of the intermediate borinate **4a** revealed two broad peaks at δ 52 and 84 ppm (corresponding to a borinate and a trialkylborane, respectively). Iodination of a 1°-carbon attached to boron is reported to be much faster than that of a 2°- or a 3°-carbon.[17] Accordingly, the addition of 1 equiv of methanolic NaOMe to **4a** revealed the disappearence of the trialkylborane (^{11}B NMR peak at δ 84 ppm) and the formation of two different tetracoordinated boron species (^{11}B NMR peaks at δ 8 and 1 ppm).[18] The peak due to the intermediate borinate at δ 52 ppm was still present, though there was a decrease in its size.[19] Iodine was added at this stage and stirred for 2 h, whereafter the ^{11}B NMR spectrum revealed the regeneration of the peak at δ 52 ppm and the disappearance of the peaks due to the "ate" complexes. This could be rationalized by the formation of Chx_2BOMe upon iodination. Workup provided only 10% yield of the corresponding THF derivative **6a** along with the corresponding iodinated product, 4-iodo-1-(naphthalen-1-yl)butan-1-ol, in 61% yield. The above sequence of reactions provided **6a** in 81% yield when 2 equiv of methanolic NaOMe were used. Alternately, a high yield of **6a** can also be achieved by the treatment of **4a** with 1 equiv of methanolic NaOMe and I_2, followed by the addition of 1 equiv of aq NaOH (Scheme 4).

Scheme 4. One-Pot Allylboration–Hydroboration–Iodination–Cyclization



Thus under optimized conditions, a 1 M solution of (−)-*B*-allyldiisopinocampheylborane in pentane (3.1 mL) was added at −100 °C to **2a** (3 mmol) dissolved in dry ether (6 mL), and the mixture was stirred for 5 min. The reaction mixture was added to Chx_2BH (0.8 g, 4.5 mmol) and allowed to warm to room temperature, and then it was stirred for 5 min. Iodine (1.52 g, 6 mmol) was added to the reaction mixture, followed by a 1 M solution of sodium methoxide in methanol (6 mL, 6 mmol). After stirring for 2 h, the crude product was extracted with ether, dried over anhydrous Na_2SO_4, concentrated and purified by flash column chromatography to obtain **6a** in 81% yield and 98% ee. Once the conditions for the one-pot allylboration–hydroboration–iodination–cyclization were optimized, the generality of the reaction was demonstrated with a series of aldehydes possessing varying steric and electronic properties (Table 2). The aldehyde with an electron-withdrawing (*p*-CF_3) group **2b** provided product **6b** in 70% yield and 90% ee, whereas the aldehyde with an electron-donating (*p*-MeO) group **2d** provided the product **6d** in 60% yield and 95% ee. Aliphatic aldehydes **2e** and **2f** formed **6e** and **6f** in 67 and 65% yields, respectively, and 96 and 92% ee, respectively. The ee-values of the THF derivatives were determined by HPLC analysis on a Chiralcel OD-H column and/or by GC analysis on a CP-Chirasil-Dex CB column.

This methodology was then extended to include crotylboration- and methoxyallylboration–hydroboration–iodination–

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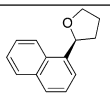
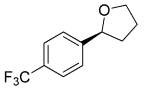
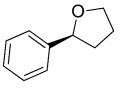
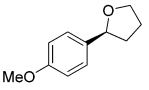
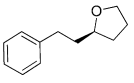
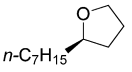
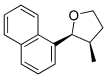
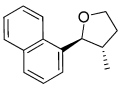
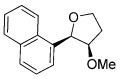
Table 2. One-Pot Allylboration−Hydroboration−Iodination−Cyclization of Aldehydes

Entry	RCHO	R'_2BH	THF derivative	Yield %[a]	ee %	Config.
1	**2a**	**1a**	 **6a**	81	98[b]	*S*
2	**2b**	**1a**	 **6b**	70	90[c]	*S*
3	**2c**	**1a**	 **6c**	74	96[c]	*S*
4	**2d**	**1a**	 **6d**	60	95[c]	*S*
5	**2e**	**1a**	 **6e**	67	96[c]	*R*
6	**2f**	**1a**	 **6f**	65	92[d]	*R*
7	**2a**	***Z*-1b**	 *Cis*-**7a**	63	86[c]	*S, R*
8	**2a**	***E*-1b**	 *trans*-**7a**	66	90[c]	*S, S*
9	**2a**	**1c**	 **8a**	56	99[c]	*S, R*

[a]Isolated overall yield for 4 steps. [b]Determined by HPLC analysis on a Chiralcel OD-H column. [c]Determined by GC analysis on a CP-Chirasil-Dex CB column. [d]On the basis of the ee of the homoallylic alcohol.

cyclization to prepare the corresponding 2,3-disubstituted THF derivative from **2a**. *E*- and *Z*-crotylboration of 1-naphthaldehyde with (*E*)-*B*-crotyldiisopinocampheylborane (*E*-**1b**) and (*Z*)-crotyldiisopinocampheylborane (*Z*-**1b**), followed by hydroboration−iodination−cylization provided the corresponding diastereomerically pure 3-methyl-2-naphthyl-tetrahydrofurans, *trans*-**7a** and *cis*-**7a**, in 90 and 86% ee, respectively. Alkoxyallylboration of 1-naphthaldehyde using *B*-methoxyallyldiisopinocampheyl-borane (**1c**), followed by the hydroboration−iodination−cyclization reaction sequence afforded essentially enantiomerically pure 2-methoxy-3-naphthyltetrahydrofuran (**8a**) in 56% yield, >99% de and 99% ee (Table 2).

In conclusion, an efficient and convenient asymmetric synthesis of 2-substituted and 2,3-disubstituted tetrahydrofurans has been achieved via a novel one-pot allylboration−hydroboration−iodination−cyclization protocol.

EXPERIMENTAL SECTION

General Information. All reactions were performed under inert atmosphere. All solvents for routine isolation of products and chromatography were reagent grade. Reaction flasks were dried in an oven at 110 °C for 12 h. Air- and moisture-sensitive reactions were performed under nitrogen atmosphere. Flash chromatography was performed using silica gel (100−200 mesh) with indicated solvents. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica plates (60F-254) using UV light as visualizing agent. In general, reactions were carried out in dry solvents under nitrogen atmosphere, unless noted otherwise. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded either on a 400 MHz or on a 300 MHz NMR spectrometer. Chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz (Hz), and number of protons. Flash chromatography was performed using silica gel 40−63 μm, 60 Å and hexane−ethyl acetate mixture as eluent.

Procedure of One-Pot Allylboration−Hydroboration−Oxidation Reaction. *Synthesis of 1,4-Diols.* A pentane solution of (−)-*B*-allyldiisopinocampheylborane (1 M, 3.1 mL, 3 mmol) was added at −100 °C to aldehyde (3 mmol) dissolved in dry ether (6 mL) and maintained at −100 °C. After stirring for 5 min, this reaction mixture was added to Chx_2BH (0.8 g, 4.5 mmol) in ether (3 mL), allowed to warm to room temperature, and stirred for 5 min. Reaction was followed by TLC. After completion, the reaction mixture was cooled to 0 °C and quenched by the addition of 3 N aq NaOH solution (2 mL), followed by slow addition of 30% hydrogen peroxide (2 mL), and stirred for 4 h at room temperature. Organic layer was separated, and aqueous layer was extracted with ether (3 × 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified by flash column chromatography.

General Procedure for the Synthesis of THF-Derivative-Cyclodehydration Method. Triisopropylphosphine (0.3 g, 1.87 mmol) was dissolved in anhydrous THF (3 mL) at rt, followed by

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cooling to 5 °C and the addition of diisopropyl azodicarboxylate (0.35 mL, 1.8 mmol). The reaction was warmed to 15 °C. After 10 min, the diol (1.20 mmol) dissolved in THF (3 mL) was added dropwise, followed by warming to 25 °C, and then it was stirred for 6 h. Reaction was followed by TLC. The reaction mixture was quenched by addition of saturated NH_4Cl solution, extracted with ether, dried over Na_2SO_4, and purified using column chromatography.

General Procedure for the Preparation of THF-Derivative: One-Pot Allylboration−Hydroboration−Iodination−Cyclization. Aldehyde (3 mmol) was dissolved in dry ether (6 mL). A 1 M solution of (−)-*B*-allyldiisopinocampheylborane (3.1 mL) in pentane was added at −100 °C and stirred for 5 min. After stirring for 5 min, this reaction mixture was added to Chx_2BH (0.8 g, 4.5 mmol) in ether (3 mL), allowed to warm to room temperature, and stirred for 5 min. Iodine (1.52 g, 6 mmol) was added to the reaction mixture, followed by 1 M solution of sodium methoxide in methanol (6 mL, 6 mmol), and the mixture was stirred for 2 h. Reaction was followed by TLC. The crude product was extracted with ether, dried over anhydrous Na_2SO_4, concentrated, and purified by flash column chromatography.

(*S*)-2-(Naphthalen-1-yl)tetrahydrofuran (6a). **6a** was obtained as pale-yellow liquid in 81% yield (0.481 mg).

Spectral data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.99−7.96 (m, 1H), 7.88−7.85 (m, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H), 7.53−7.43 (m, 3H), 5.65 (t, J = 6.9 Hz, 1H), 4.28−4.20 (m, 1H), 4.07−4.00 (m, 1H), 2.62−2.51 (m, 1H), 2.12−1.86 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.3, 130.4, 128.8, 127.4, 125.8, 125.5, 125.4, 123.4, 121.8, 77.9, 68.8, 33.8, 26.0; HRMS (ESI) $C_{14}H_{14}O$ calc. 198.1045, found 198.1069.

(*S*)-2-(4-(Trifluoromethyl)phenyl)tetrahydrofuran (6b). **6b** was obtained as pale-yellow liquid in 70% yield (0.454 mg).

Spectral data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 4.94 (t, J = 7.2 Hz, 1H), 4.14−3.92 (m, 1H), 3.99−3.92 (m, 1H), 2.42−2.32 (m, 1H), 2.05−1.96 (m, 2H), 1.82−1.70 (m, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ −62.33 (s, 3F); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.8, 125.8, 125.3, 125.2, 80.0, 68.8, 34.7, 25.9; HRMS (ESI) $C_{11}H_{11}F_3O$ calc. 216.0762, found 216.0738.

(*S*)-2-Phenyltetrahydrofuran (6c). **6c** was obtained as colorless liquid in 74% yield (0.328 mg).

Spectral data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2−7.43 (m, 5H), 4.82 (t, J = 7.8 Hz, 1H), 4.08−4.15 (m, 1H), 3.96−3.85 (m, 1H), 2.25−2.36 (m, 1H), 2.06−1.96 (m, 2H), 1.88−1.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.5, 128.4, 127.2, 125.7, 80.8, 68.8, 34.7, 26.1; HRMS (ESI) $C_{10}H_{12}O$ calc. 148.0888, found 148.0899.

(*S*)-2-(4-Methoxyphenyl)tetrahydrofuran (6d). **6d** was obtained as gummy liquid in 60% yield (0.320 mg).

Spectral data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.25 (m, 2H), 6.90−6.86 (m, 2H), 4.83 (t, J = 9.0 Hz, 1H), 4.12−4.05 (m, 1H), 3.95−3.87 (m, 1H), 3.80 (s, 3H), 2.33−2.23 (m, 1H), 2.06−1.96 (m, 2H), 1.88−1.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.8, 135.4, 127.0, 113.7, 80.5, 68.5, 55.3, 34.5, 26.1; HRMS (ESI) $C_{11}H_{14}O_2$ calc. 178.0994, found 178.0982.

(*R*)-2-Phenethyltetrahydrofuran (6e). **6e** was obtained as clear liquid in 67% yield (353 mg).

Spectral data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.05 (m, 5H), 3.94−3.54 (m, 3H), 2.82−2.70 (m, 1H), 2.69−2.61 (m, 1H), 2.04−1.65 (m, 5H), 1.50−1.40 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 128.2, 128.1, 125.5, 78.3, 67.4, 37.2, 32.5, 31.1, 25.5; HRMS (ESI) $C_{12}H_{16}O$ calc. 176.1201 found 176.1235.

(*R*)-2-Heptyltetrahydrofuran (6f). **6f** was obtained as light yellow liquid in 65% yield (0.331 mg).

Spectral data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85−3.54 (m, 3H), 1.95−1.66 (m, 3H), 1.50 (m, 1H), 1.43−1.29 (m, 3H), 1.22 (m, 9H), 0.80 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 79.1, 67.2, 35.5, 31.6, 31.1, 29.5, 29.0, 26.1, 25.4, 22.4, 13.8; HRMS (ESI) $C_{11}H_{22}O$ calc. 170.1671, found 170.1641.

General Procedure for the Preparation of THF-Derivative: One-Pot Crotylboration−Hydroboration−Iodination−Cyclization. A 1 M solution of ^{t}BuOK in THF (2.5 mL, 2.5 mmol) is added to THF (9 mL) and cooled to −78 °C. 2-Butene (5 mmol) was added via cannula, and after 5 min, a 2.5 M solution of *n*-BuLi in hexanes (76.4 mL 2.5 mmol) was added dropwise. The reaction mixure was warmed to −55 °C, stirred there for 45 min, and again cooled to −78 °C. A −78 °C cooled solution of (−)-Ipc_2BOMe (3 mmol) in THF was added dropwise via cannula, and the reaction mixture was stirred for 1 h. $BF_3{\cdot}Et_2O$ (3.6 mmol) was added dropwise, followed by a dropwise addition of the −78 °C cooled solution of aldehyde (2 mmol) in THF (1 mL) via cannula. The reaction mixture was stirred at −78 °C for 3 h. Reaction mixture was warmed to 0 °C, and dicyclohexylborane (7.5 mmol) was added. Reaction mixture was warmed to room temperature and stirred for 5 min. Iodine (1.52 g, 6 mmol) was added to the reaction mixture, followed by a 1 M solution of sodium methoxide in methanol (6 mL, 6 mmol), and the mixture was stirred for 2 h. Reaction was followed by TLC. The crude product was extracted with ether, dried over anhydrous Na_2SO_4, concentrated, and purified by flash column chromatography.

(2*S*,3*R*)-3-Methyl-2-(naphthalen-1-yl)tetrahydrofuran (*cis*-7a). ***cis*-7a** was obtained as pale-brown gummy oil in 63% yield (0.267 mg).

Spectral data: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.81 (m, 2H), 7.77−7.66 (m, 2H), 7.53−7.41 (m, 3H), 5.64 (d, J = 6.0 Hz, 1H), 4.22 (dd, J = 15.3, 7.3 Hz, 1H), 3.99 (td, J = 8.3, 5.8 Hz, 1H), 2.94−2.75 (m, 1H), 2.48−2.22 (m, 1H), 1.85−1.73 (m, 1H), 0.45 (d, J = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 133.4, 130.5,128.9, 127.2, 125.7, 125.5, 125.3, 123.4, 122.9, 80.8, 66.5, 36.7, 34.6, 15.8; HRMS (ESI) $C_{15}H_{16}O$ calc. 212.1201, found 212.1221.

(2*S*,3*S*)-3-Methyl-2-(naphthalen-1-yl)tetrahydrofuran (*trans*-7a). ***trans*-7a** was obtained as yellow gummy oil in 66% yield (0.280 mg).

Spectral data: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 2.2 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.56−7.40 (m, 4H), 5.14 (d, J = 6.4 Hz, 1H), 4.25 (dd, J = 14.1, 8.0 Hz, 1H), 4.12 (dd, J = 14.8, 7.8 Hz, 1H), 2.41 (dq, J = 13.5, 6.8 Hz, 1H), 2.28−2.14 (m, 1H), 1.73 (dt, J = 13.0, 6.7 Hz, 1H), 1.18 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.9, 133.8, 131.1, 128.7, 127.8, 125.7, 125.3, 123.7, 123.3, 85.2, 85.2, 67.7, 41.1, 33.9, 17.7; HRMS (ESI) $C_{15}H_{16}O$ calc. 212.1201, found 212.1231

(2*R*,3*R*)-3-Methoxy-2-(naphthalen-1-yl)tetrahydrofuran (8a). **8a** was obtained as pale-brown gummy solid in 56% yield (0.255 mg).

Spectral data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98−7.97 (m, 1H), 7.90−7.86 (m, 1H), 7.82−7.78 (m, 1H), 7.54−7.47 (m, 2H), 7.53−7.43 (m, 3H), 5.54 (d, J = 3.6 Hz, 1H), 4.35−4.27 (m, 2H), 4.05 (dt, J = 4.8 and 8.7 Hz, 1H), 2.77 (s, 3H), 2.42−2.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.3, 130.4, 128.8, 127.4, 125.8, 125.5, 125.4, 123.4, 121.8, 77.9, 68.8, 33.8, 26.0; HRMS (ESI) $C_{15}H_{16}O_2$ calc. 228.1150, found 228.1170

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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