JOC The Journal of Organic Chemistry

NOTE

pubs.acs.org/joc

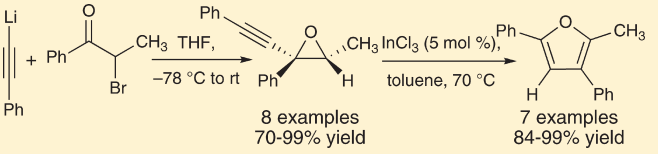
# Synthesis of Substituted Acetylenic Epoxides Followed by Indium-Catalyzed Rearrangement to 2,3,5-Trisubstituted Furans

Jun Yong Kang and Brian T. Connell*

Department of Chemistry, Texas A&M University, P.O. Box 30012, College Station, Texas 77842-3012, United States

Supporting Information

**ABSTRACT:** Syntheses of various aromatic and aliphatic 2,3,5-trisubstituted furans from acetylenic epoxides are described. These epoxides are directly prepared by nucleophilic ring closure of propargylic alkoxides generated by lithium acetylide addition to α-haloketones.




The Feist−Benary synthesis is a classic method for accessing furans, occcuring via a condensation reaction between α-haloketones and β-dicarbonyl compounds.[1] Furans are some of the most-synthesized heterocyclic compounds due to their versatile applications in organic synthesis and numerous appearances in natural products.[2] Since Feist disclosed his synthesis of furans in 1902,[1] many different synthetic methods toward furan synthesis have been reported.

Recent works directly toward furans have featured transition metal-catalyzed reactions and Lewis acid-mediated syntheses. For example, palladium-catalyzed cyclization of acetylenic ketones furnishes substituted furans,[3] platinum-catalyzed cyclization of propargylic oxiranes in aqueous media proceeds successfully to give trisubstituted furans,[4] gold-mediated transformations of alkynylepoxides to furans have been disclosed,[5] and molybdenum-catalyzed cyclization of propagylic oxiranes is well-known.[6] Lewis acid-mediated syntheses, including use of $ZnCl_2$ for cycloisomerization of alkynyl ketones to furans[7] and AgOTf-mediated isomerization of alkynylepoxides,[8] have been reported.

However, transition metal-catalyzed syntheses of furans have suffered from moderate yields for Pd(II)[3] and Pt(II)[4] and limited substrate scope for Au(III)[5] and Mo(V).[6] Some Lewis acid-mediated syntheses of furans exhibit poor functional group tolerance.[8]

We desired an efficient methodology employing mild and atom-economical reaction conditions. Indium attracted our attention both because it is a readily available Lewis acid and is exceptionally stabile to water and air.[9] Indium has been reported to enable allylation of aldehydes as well as aldol and Mannich reactions.[9] In spite of its potential versatile utility, indium-mediated rearrangements and isomerizations have been reported in limited cases, such as the Ferrier rearrangement[10] and the Beckman rearrangement.[11] Herein, we report a mild and efficient furan synthesis under indium catalysis via rearrangement of acetylenic α,β-epoxides that are prepared by treatment of α-haloketones with lithium acetylides.

Acetylenic α,β-epoxides have been prepared by various methods, including Sonogashira cross-coupling[12] of alkynes and vinyl halides and subsequent epoxidation,[13] a cascade reaction of alkynyl halides and disubstituted phenones via α-brominated ketone intermediates,[14] as well as by nucleophilic ring closure of propargylic alcohols derived from α-haloketones and acetylides.[15]

We found the addition of lithium acetylides to α-bromoketones to proceed very efficiently as summarized in Table 1. When lithium phenyl acetylide **1a** was treated with 2-bromopropiophenone (**2a**), phenyl acetylenic α,β-epoxide **3a** was obtained in quantitative yield (Table 1, entry 1). Very good yields are also obtained when β-substituted ketones were employed (Table 1, entries 2 and 3) (89% and 85%, respectively). Treatment of aliphatic ketone **2d** with acetylide **1a** also proceeded well, providing a 90% yield of epoxide **3d**. A somewhat lower yield (70%) of epoxide product **3e** was obtained when an acetylide containing an electron-withdrawing substituent (**1b**) was utilized (Table 1, entry 5). When silyl-protected acetylides **1c** and **1d** were treated with **2a**, epoxides **3f** and **3g** were obtained in 95% and 99% yields, respectively (Table 1, entries 6 and 7). Aliphatic substituted acetylide **1e** yielded **3h** in 96% yield upon treatment with **2a**.

The relative stereochemistry of the epoxides is consistent with Felkin−Anh addition to the ketone, followed by $S_N2$ displacement of the bromide by the neighboring incipient alkoxide.[16,17] Stereochemistry was determined by NOE analysis (see the Supporting Information). It is worth noting that cyclization of a conformationally restricted α-haloketone, 2-bromo-1-indanone, failed to occur. The required backside displacement of the bromide by the neighboring alkoxide could not occur, as nucleophilic attack from the less hindered side of the ketone produces the unreactive *syn*-hydroxybromide (eq 1).

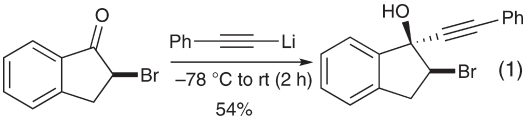
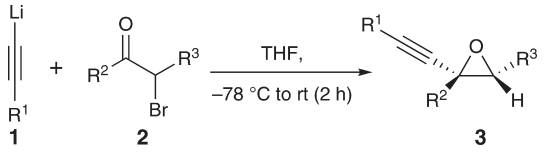



Table 2 summarizes our initial cycloisomerization studies. Palladium,[18] known for cyclization of acetylenic ketones to furans, and platinum,[4] known for cyclization of propargylic oxiranes to furans, were employed under standard reaction

**Received:** January 28, 2011
**Published:** March 09, 2011

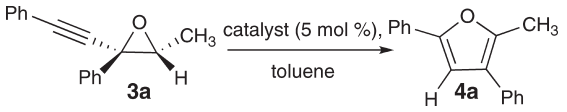
**Table 1. Formation of Epoxides upon Treatment of α-Bromoketones with Lithium Acetylides**[a]




| entry | 1, $R^1$ | | 2, $R^2$ | 2, $R^3$ | | product | yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | Ph | **1a** | Ph | Me | **2a** | **3a** | >99 |
| 2 | Ph | **1a** | Ph | Bn | **2b** | **3b** | 89[c] |
| 3 | Ph | **1a** | Ph | *i*-Pr | **2c** | **3c** | 85[c] |
| 4 | Ph | **1a** | *n*-Pr | Et | **2d** | **3d** | 90[c] |
| 5 | $CO_2Et$ | **1b** | Ph | Me | **2a** | **3e** | 70 |
| 6 | $Si(CH_3)_3$ | **1c** | Ph | Me | **2a** | **3f** | 95 |
| 7 | $Si(CH_2CH_3)_3$ | **1d** | Ph | Me | **2a** | **3g** | 99 |
| 8 | *n*-Pr | **1e** | Ph | Me | **2a** | **3h** | 96 |

[a] Reactions were performed with lithium acetylides **1** (0.35 mmol) and α-haloketones **2** (0.32 mmol) in 1 mL of THF at rt for 2 h and quenched with sat. $NaHCO_3$. [b] Isolated yield after column chromatography. [c] Calculated yield accounting for inseparable impurities. (See the Supporting Information for spectra and details of purity.)

**Table 2. Initial Cycloisomerization Results**[a]




| entry | catalyst | temp, °C | time | yield (%)[b] |
|---|---|---|---|---|
| 1 | $Pd_2(dba)_3$, $PPh_3$ | 100 | 48 h | 16 |
| 2 | $Pt[(C_2H_5)_2S]_2Cl_2$ | 100 | 48 h | 90 |
| 3 | $AuCl_3$ | 100 | 48 h | 70 |
| 4 | CuI | 100 | 48 h | 21 |
| 5 | $InCl_3$ | 100 | 20 min | >99 |
| 6 | $InCl_3$ | 70 | 20 min | >99 |
| 7 | $InCl_3$ | 50 | 1 h | 95 |
| 8 | $InCl_3$ | 40 | 1 h | 10 |

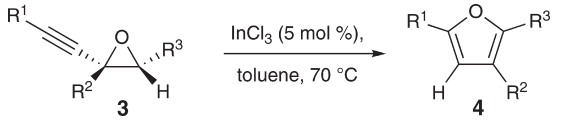
[a] Reactions were performed with acetylenic α,β-epoxides (0.17 mmol) **3a** and catalysts (0.0085 mmol) in 1 mL of toluene and quenched with water. [b] Isolated yield.

conditions (100 °C, 48 h, toluene) but the results showed either low yield (Pd) of products or the necessity for extended reaction times (Pt) (Table 2, entries 1 and 2). Gold and copper catalysts afforded low to moderate yield of the product (Table 2, entries 3 and 4).

Gratifyingly, $InCl_3$-catalyzed cycloisomerization led to furan **4a** in a quantitative yield in only 20 min (Table 2, entry 5). Lowering the temperature to 70 °C maintained the excellent results (Table 2, entry 6). However, when temperature was lowered below 70 °C, the reaction slowed down (Table 2, entries 7 and 8). Toluene is the solvent of choice. Ethereal solvents, including THF and 1,4-dioxane, led to either low yield of products and/or decomposition.

With these reaction conditions in hand, we explored the scope of this reaction with various epoxides and the results are summarized in Table 3. The parent acetylenic α,β-epoxide **3a** underwent

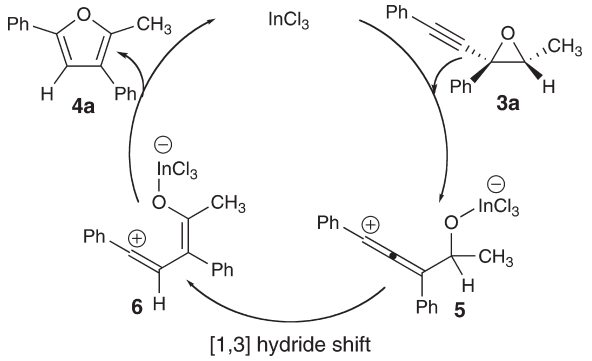
**Table 3. Scope of the Cycloisomerization Reaction**[a]




| entry | 3, $R^1$ | 3, $R^2$ | 3, $R^3$ | | product | yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | Ph | Ph | Me | **3a** | **4a** | >99 |
| 2 | Ph | Ph | Bn | **3b** | **4b** | 84[c] |
| 3 | Ph | Ph | *i*-Pr | **3c** | **4c** | 84[c] |
| 4 | Ph | *n*-Pr | Et | **3d** | **4d** | 95 |
| 5 | $CO_2Et$ | Ph | Me | **3e** | **4e** | 90[c] |
| 6 | $Si(CH_3)_3$ | Ph | Me | **3f** | **4f** | >99 |
| 7 | *n*-Pr | Ph | Me | **3h** | **4h** | >99 |

[a] Reactions were performed with acetylenic α,β-epoxides **3** (0.17 mmol) and $InCl_3$ (0.0085 mmol) in 1 mL of toluene at 70 °C for 20 min then quenched with water. [b] Isolated yield after column chromatography. [c] Calculated yield accounting for inseparable impurities. (See the Supporting Information for spectra and details of purity.)

**Scheme 1. Proposed Mechanistic Cycle for Alkynyl Epoxide Cycloisomerization**




clean reaction to provide the desired product **4a** in quantitative yield after 20 min at 70 °C (Table 3, entry 1). To test the effect of the nature of the β-substituents on epoxides, benzyl and isopropyl β-substituted epoxides (Table 3, entries 2 and 3) were tested with the following reaction conditions: 70 °C, 20 min, toluene. Results indicate that β-substituted epoxides work well, providing 84% yield (Table 3, entries 2 and 3) and indicating that adverse steric interactions appear to be minor in this reaction.

When epoxide **3d** was treated with $InCl_3$ (5 mol %) under standard reaction conditions, the furan **4d** was obtained in 95% yield (Table 3, entry 4). We were also interested in examining the utility of this method with different substitutents on the alkyne. Treatment of alkynyl epoxide **3e**, containing an electron-withdrawing alkynyl ester, under the reaction conditions proceeded well, providing a 90% yield of product **4e** (Table 3, entry 5). Trimethylsilyl-protected alkynyl epoxide **3f** also showed quantitative conversion to furan **4f**. However, it should be noted that the closely related tri*ethyl*silyl-protected alkynyl epoxide unexpectedly decomposed upon exposure to the standard reaction conditions. Aliphatic alkynyl epoxide **3h** also converted to furan **4h** in quantitative yield (Table 3, entry 7).

A proposed mechanistic cycle for the cycloisomerization is shown in Scheme 1. Coordination of indium complex to the


dx.doi.org/10.1021/jo2001353 |*J. Org. Chem.* 2011, 76, 2379–2383

epoxide **3a** is followed by opening of the epoxide to generate zwitterion **5**. An apparent 1,3-hydride shift[19] then generates intermediate benzylic cation/enolate **6**, which undergoes nucleophilic C−O bond formation and loss of $InCl_3$, affording the observed furan product **4a**.

In summary, we have reported a mild, efficient, catalytic cycloisomerization reaction that transforms acetylenic α,β-epoxides to 2,3,5-trisubstituted furans by $InCl_3$ catalysis. The acetylenic α,β-epoxides are prepared by nucleophilic ring closure of propargylic alcohol synthesized by coupling α-haloketones with acetylides. This reaction sequence allows rapid access to valuable, highly substituted furan derivatives.

## EXPERIMENTAL SECTION

**General Information.** All reactions were carried out under an argon atmosphere in oven-dried glassware with magnetic stirring. Dry THF and toluene were obtained by a solvent purification system under argon. All commercially obtained reagents were used as received. Purification of reaction products was carried out by flash column chromatography, using silica gel 60 (230−400 mesh). Analytical thin layer chromatography was performed on 0.25 mm glass-backed silica gel 60-F plates. Visualization was accompanied with UV light and $KMnO_4$ solution. Concentration in vacuo refers to the removal of volatile solvent using a rotary evaporator attached to a dry diaphragm pump (10−15 mmHg) followed by pumping to a constant weight with an oil pump (<300 mTorr). $^1$H NMR spectra are recorded at 300 or 500 MHz and are recorded relative to $CDCl_3$ (δ 7.26) or TMS (δ 0.00). $^1$H NMR coupling constants (*J*) are reported in hertz (Hz) and multiplicities are indicated as follows: s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet). Proton-decoupled $^{13}$C NMR spectra are recorded at 75 or 125 MHz and are reported relative to $CDCl_3$ (δ 77).

**General Procedure (GP1) for Synthesis of Oxiranes: (2*S*,3*R*)-3-Methyl-2-phenyl-2-(phenylethynyl)oxirane (3a).** To a drum vial were added α-haloketone **2a** (0.32 mmol, 68 mg, 1.0 equiv) and THF (1.0 mL). The vial was cooled to −78 °C and followed by addition of (phenylethynyl)lithium **1a** (0.35 mmol, 38 mg, 1.1 equiv), which was prepared from phenyl acetylene (1.0 equiv) and *n*-BuLi (1.01 equiv) in THF at −78 °C. After complete addition of **1a**, the reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was quenched by a saturated aqueous $NaHCO_3$ solution (1.5 mL) and the layers were separated and the aqueous layer was extracted with $Et_2O$. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash chromatography to afford alkynyl oxiranes **3a** as a colorless oil (75 mg, >99% yield). $R_f$ 0.6 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2229, 1317, 938, 867; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.59−7.57 (m, 2H), 7.51−7.49 (m, 2H), 7.48−7.41 (m, 2H), 7.39−7.33 (m, 4H), 3.74(q, *J* = 5.5 Hz, 1H), 1.14(d, *J* = 5.4 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.7, 132.1, 128.7, 128.3, 128.1, 128.0, 127.1, 122.2, 88.92, 82.9, 63.5, 56.2, 13.4; HRMS (ESI) calcd for $C_{17}H_{15}O$ [M + H]$^+$ 235.1123, found 235.1131.

**(2*S*,3*R*)-3-Benzyl-2-phenyl-2-(phenylethynyl)oxirane (3b).** (Phenylethynyl)lithium **1a** (0.35 mmol, 38 mg, 1.1 equiv) and halide **2b** (0.32 mmol, 92 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (96 mg, 99%, ca. 90% pure by $^1$H and $^{13}$C NMR). $R_f$ 0.83 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2226, 1317, 938, 879; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.71−7.67 (m, 2H), 7.55−7.26 (m, 11H), 7.26−7.13 (m, 2H), 3.88 (t, *J* = 6.3 Hz, 1H), 2.79 (dd, *J* = 14.8, 6.1 Hz, 1H), 2.63 (dd, *J* = 14.8, 6.4 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 136.7, 135.5, 132.0, 128.9, 128.8, 128.7, 128.3, 128.3, 127.2, 126.7, 122.1, 88.6, 83.2, 67.5, 56.5, 34.0; HRMS (MALDI) calcd for $C_{23}H_{18}O$ [M + H]$^+$ 311.1436, found 311.1442.

**(2*S*,3*R*)-3-Isopropyl-2-phenyl-2-(phenylethynyl)oxirane (3c).** (Phenylethynyl)lithium **1a** (0.35 mmol, 38 mg, 1.1 equiv) and halide **2c** (0.32 mmol, 77 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (80 mg, 95%, ca. 90% pure by $^1$H and $^{13}$C NMR). $R_f$ 0.76 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2226, 1320, 891, 755; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.60−7.56 (m, 2H), 7.52−7.47 (m, 2H), 7.45−7.31 (m, 6H), 3.27 (d, *J* = 8.3 Hz, 1H), 1.13 (app s, 4H), 0.82 (d, *J* = 6.7 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.9, 132.0, 128.7, 128.3, 128.1, 128.0, 126.9, 122.3, 89.1, 82.9, 73.0, 56.7, 26.8, 19.6, 17.9; HRMS (MALDI) calcd for $C_{19}H_{18}O$ [M + H]$^+$ 263.1436, found 263.1428.

**(2*S*,3*R*)-3-Ethyl-2-(phenylethynyl)-2-propyloxirane (3d).** (Phenylethynyl)lithium **1a** (0.35 mmol, 38 mg, 1.1 equiv) and halide **2d** (0.32 mmol, 62 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1 to afford a colorless oil (68 mg, >99%, ca. 90% pure by $^1$H and $^{13}$C NMR). $R_f$ 0.61 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2226, 1302, 909, 752; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.35−7.32 (m, 3H), 3.24 (t, *J* = 6.58 Hz, 1H), 1.47−1.62 (m, 6H), 1.15−1.01 (m, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 131.9, 128.6, 128.2, 122.4, 89.1, 82.6, 66.5, 55.3, 33.7, 21.5, 19.2, 14.1, 10.5; HRMS (ESI) calcd for $C_{15}H_{18}O$ [M + H]$^+$ 215.1436, found 215.1442.

**Ethyl 3-((2*S*,3*R*)-3-Methyl-2-phenyloxiran-2-yl)propiolate (3e).** (3-Ethoxy-3-oxoprop-1-yn-1-yl)lithium **1b** (0.35 mmol, 36 mg, 1.1 equiv) and halide **2a** (0.32 mmol, 68 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (52 mg, 70%). $R_f$ 0.64 (hexanes:$CH_2Cl_2$ = 2:1); IR (film, cm$^{-1}$) 2235, 1708, 1220, 953, 870; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.45−7.33 (m, 5H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.64 (q, *J* = 5.4 Hz, 1H), 1.28 (t, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 5.4 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.7, 132.1, 128.7, 128.3, 128.1, 128.0, 127.1, 122.2, 88.92, 82.9, 63.5, 56.2, 13.4; HRMS (ESI) calcd for $C_{14}H_{14}O_3$ [M + H]$^+$ 231.1021, found 231.1013.

**Trimethyl(((2*S*,3*R*)-3-methyl-2-phenyloxiran-2-yl)ethynyl)-silane (3f).** ((Trimethylsilyl)ethynyl) lithium **1c** (0.35 mmol, 36 mg, 1.1 equiv) and halide **2a** (0.32 mmol, 68 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (70 mg, 95%). $R_f$ 0.75 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2173, 1249, 938, 844; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.52−7.34 (m, 5H), 3.62 (q, *J* = 5.4 Hz, 1H), 1.07 (d, *J* = 5.4 Hz, 3H), 0.23 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.3, 128.0, 128.0, 127.1, 104.8, 88.1, 63.3, 55.9, 13.2, −0.12; HRMS (ESI) calcd for $C_{14}H_{18}OSi$ [M + H]$^+$ 231.1205, found 231.1213.

**Triethyl(((2*S*,3*R*)-3-methyl-2-phenyloxiran-2-yl)ethynyl)-silane (3g).** ((Triethylsilyl)ethynyl) lithium **1d** (0.35 mmol, 51 mg, 1.1 equiv) and halide **2a** (0.32 mmol, 68 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (86 mg, 99%). $R_f$ 0.70 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, cm$^{-1}$) 2170, 1240, 938, 864; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.52−7.33 (m, 5H), 3.62 (q, *J* = 5.4 Hz, 1H), 1.08 (d, *J* = 5.8 Hz, 3H), 1.03 (t, *J* = 8.3 Hz, 9H), 0.65 (q, *J* = 7.8 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.4, 128.0, 127.9, 127.1, 106.1, 85.8, 63.5, 56.0, 13.1, 7.5, 4.3; HRMS (ESI) calcd for $C_{17}H_{24}OSi$ [M + H]$^+$ 273.1675, found 273.1662.

**(2*S*,3*R*)-3-Methyl-2-(pent-1-yn-1-yl)-2-phenyloxirane (3h).** Pent-1-yn-1-yllithium **1e** (0.35 mmol, 26 mg, 1.1 equiv) and halide **2a** (0.32 mmol, 68 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (1:1) provides a colorless oil (61 mg, 96%). $R_f$ 0.60


dx.doi.org/10.1021/jo2001353 |*J. Org. Chem.* 2011, 76, 2379–2383

(hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 2238, 1448, 867, 752; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.51−7.29 (m, 5H), 3.57(q, $J$ = 5.4 Hz, 1H), 2.24(t, $J$ = 7.1 Hz, 2H), 1.64−1.52 (m, 2H), 1.07 (d, $J$ = 5.4 Hz, 3H), 1.01 (t, $J$ = 7.5 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 136.2, 127.9, 127.8, 127.0, 83.9, 80.1, 63.1, 56.1, 21.9, 20.8, 13.6, 13.3; HRMS (ESI) calcd for $C_{14}H_{16}O$ $[M + H]^+$ 201.1279, found 201.1282.

**(1*R*,2*S*)-2-Bromo-1-(phenylethynyl)-2,3-dihydro-1*H*-inden-1-ol (S1).** (Phenylethynyl)lithium **1a** (0.35 mmol, 38 mg, 1.1 equiv) and 2-bromoindanone (0.32 mmol, 68 mg, 1.0 equiv) were subjected to the reaction conditions described in GP1 for 40 h to afford a colorless oil (60 mg, 60%, ca. 90% by pure by $^1H$ and $^{13}C$ NMR). $R_f$ 0.33 (hexanes:$Et_2O$ = 5:1); IR (film, $cm^{-1}$) 3521, 3052, 2228, 1338, 922, 869; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.77−7.73 (m, 1H), 7.52−7.44 (m, 2H), 7.42−7.29 (m, 6H), 4.84 (t, $J$ = 7.3 Hz, 1H), 3.54−3.39 (m, 2H), 3.08 (s, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 142.1, 140.2, 132.0, 129.9, 128.9, 128.4, 127.9, 124.8, 124.6, 122.0, 88.0, 85.4, 76.1, 60.3, 39.7; HRMS (MALDI) calcd for $C_{17}H_{13}BrO$ $[M + Na]^+$ 335.0048, found 335.0037.

**General Procedure (GP2) for Synthesis of Furans: 2-Methyl-3,5-diphenylfuran (4a).** A drum vial was charged with $InCl_3$ (5 mol %, 0.0085 mmol, 0.05 equiv) in the drybox. To the vial was added a THF (1 mL) solution of oxiranes **3a** (0.17 mmol, 40 mg 1.0 equiv) and the vial was then placed in a 70 °C oil bath for 20 min. After 20 min of stirring at 70 °C the reaction mixture was cooled to room temperature and quenched by addition of water. The layers were separated and the aqueous layer was extracted with $Et_2O$. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash chromatography to afford furan as a colorless oil **4a** (40 mg, >99% yield). $R_f$ 0.83 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3061, 1599, 1495, 1448, 1018; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.76−7.73 (m, 2H), 7.53−7.42 (m, 6H), 7.38−7.27 (m, 2H), 6.85 (s, 1H), 2.58 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 151.6, 147.6, 134.1, 130.8, 128.7, 128.6, 127.5, 127.0, 126.5, 123.4, 123.0, 106.4, 13.2; HRMS (ESI) calcd for $C_{17}H_{14}O$ $[M + Na]^+$:257.0942, found 257.0949.

**2-Benzyl-3,5-diphenylfuran (4b).** Oxirane **3b** (0.17 mmol, 53 mg 1.0 equiv) and $InCl_3$ (0.0085 mmol, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2 to afford a colorless oil (53 mg, ca. 85% pure by $^1H$ and $^{13}C$ NMR). $R_f$ 0.56 (hexanes-$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3064, 1599, 1495, 1448; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.78−7.73 (m, 2H), 7.52−7.27 (m, 13H), 6.89 (s, 1H), 4.27 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 152.5, 149.0, 138.6, 133.8, 130.8, 128.7, 128.7, 128.7, 128.4, 127.8, 127.3, 126.9, 126.5, 125.7, 123.7, 106.7, 33.0; HRMS (MALDI) calcd for $C_{23}H_{18}O$ $[M + H]^+$ 311.1436, found 311.1422.

**2-Isopropyl-3,5-diphenylfuran (4c).** Oxirane **3c** (0.17 mmol, 53 mg 1.0 equiv) and $InCl_3$ (0.0085 mmol, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2 to afford a colorless oil (45 mg, ca. 85% pure by $^1H$ and $^{13}C$ NMR). $R_f$ 0.72 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3058, 1593, 1495; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.79−7.72 (m, 2H), 7.51−7.27 (m, 8H), 6.79 (s, 1H), 3.39−3.29 (m, 1H), 1.43 (d, $J$ = 7.0 Hz, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 156.0, 151.4, 134.4, 131.1, 128.7, 128.6, 128.1, 127.1, 126.6, 126.0, 123.5, 106.7, 26.7, 23.7, 21.9; HRMS (MALDI) calcd for $C_{19}H_{18}O$ $[M + H]^+$ 263.1436, found 263.1448.

**2-Ethyl-5-phenyl-3-propylfuran (4d).** Oxirane **3d** (0.17 mmol, 36 mg 1.0 equiv) and $InCl_3$ (0.0085 mmol, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2. Flash column chromatography on $SiO_2$ eluting with hexanes:$CH_2Cl_2$ (20:1) provides a colorless oil (35 mg, 95%). $R_f$ 0.85 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3061, 1599, 1486, 1456, 1024; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.67−7.65 (m, 2H), 7.41−7.21 (m, 3H), 6.52 (s, 1H), 2.70 (q, $J$ = 7.94 Hz, 2H), 2.39 (t, $J$ = 7.58 Hz, 2H), 1.68−1.56 (m, 2H), 1.31 (t, $J$ = 7.72 Hz, 3H), 1.00 (t, $J$ = 7.42 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 152.6, 151.0, 131.4, 128.6, 126.6, 123.3, 120.5, 107.3, 26.9, 23.9, 19.6, 13.9, 13.5; HRMS (MALDI) calcd for $C_{15}H_{18}O$ $[M + H]^+$ 215.1436, found 215.1444.

**Ethyl 5-Methyl-4-phenylfuran-2-carboxylate (4e).** Oxirane **3e** (0.17 mmol, 40 mg 1.0 equiv) and $InCl_3$ (0.0085 mmol, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2 to afford a colorless oil (40 mg, ca. 90% pure by $^1H$ and $^{13}C$ NMR). $R_f$ 0.15 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3061, 1720, 1619, 1187; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.43−7.38 (m, 5H), 6.26 (s, 1H), 4.31 (q, $J$ = 7.0 Hz, 2H), 2.51 (s, 3H), 1.36 (t, $J$ = 7.45 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 163.4, 130.0, 129.3, 128.8, 128.6, 114.1, 92.9, 61.8, 28.8, 24.4, 14.3; HRMS (ESI) calcd for $C_{14}H_{14}O_3$ 231.1021, found 231.1010.

**Trimethyl(5-methyl-4-phenylfuran-2-yl)silane (4f).** Oxirane **3f** (0.17 mmol, 39 mg 1.0 equiv) and $InCl_3$ (0.0085 mmo0l, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2 to afford a colorless oil (39 mg, >99%). $R_f$ 0.64 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3061, 2176, 1909, 1249, 850; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.48−7.34 (m, 5H), 4.60 (s, 1H), 2.24 (s, 3H), 0.26 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 202.7, 134.6, 128.9, 128.0, 127.9, 101.3, 92.5, 53.7, 25.9, 0.0; HRMS (ESI) calcd for $C_{14}H_{18}OSi$ $[M + Na]^+$ 253.1025, found 253.1014.

**2-Methyl-3-phenyl-5-propylfuran (4h).** Oxirane **3h** (0.17 mmol, 34 mg 1.0 equiv) and $InCl_3$ (0.0085 mmol, 1.9 mg, 0.05 equiv) were subjected to the reaction conditions described in GP2 to afford a colorless oil (34 mg, >99%). $R_f$ 0.88 (hexanes:$CH_2Cl_2$ = 1:1); IR (film, $cm^{-1}$) 3061, 1581, 1495, 1448; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.48−7.26 (m, 5H), 6.18 (s, 1H), 2.62 (t, $J$ = 7.24 Hz, 2H), 2.47 (s, 3H), 1.81−1.69 (m, 2H), 1.06 (t, $J$ = 7.50 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.2, 145.8, 134.7, 128.6, 127.4, 126.1, 121.2, 106.3, 30.1, 21.5, 13.9, 13.1; HRMS (ESI) calcd for $C_{14}H_{16}O$ $[M + H]^+$ 201.1279, found 201.1289.

## ■ ASSOCIATED CONTENT

**Supporting Information.** $^1H$ and $^{13}C$ NMR spectra of new compounds and stereochemical proofs. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

**Corresponding Author**
*E-mail: connell@chem.tamu.edu.

## ■ ACKNOWLEDGMENT

The Robert A. Welch Foundation (A-1623) is acknowledged for support of this research.

## ■ REFERENCES

(1) Feist, F. *Ber. Dtsch. Chem.* **1902**, *35*, 1537–1544.
(2) Meegan, M. J.; Donnelly, D. M. X. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 4, pp 657−712.
(3) Fukuda, Y.; Shiragami, H.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1991**, *56*, 5816–5819.
(4) Yoshida, M.; Al-Amin, M.; Shishido, K. *Synthesis* **2009**, 2454–2466.
(5) Hashmi, A. S. K.; Sinha, P. *Adv. Synth. Catal.* **2004**, *346*, 432–438.
(6) McDonald, F. E.; Schultz, C. C. *J. Am. Chem. Soc.* **1994**, *116*, 9363–9364.
(7) Sniady, A.; Durham, A.; Morreale, M. S.; Wheeler, K. A.; Dembinski, R. *Org. Lett.* **2007**, *9*, 1175–1178.
(8) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 4360–4363.
(9) Loh, T.-P.; Chua, G.-L. *Chem. Commun.* **2006**, 2739–2749.

(10) Boga, S. B.; Kalpattu, K. B. *Tetrahedron Lett.* **2000**, *41*, 1271–1274.
(11) Barman, D. C.; Thakur, A. J.; Prajapati, D.; Sandhu, J. S. *Chem. Lett.* **2000**, *29*, 1196–1197.
(12) Lemay, A. B.; Vulic, K. S.; Ogilvie, W. W. *J. Org. Chem.* **2006**, *71*, 3615–3618.
(13) Cao, G.-A.; Wang, Z.-X.; Tu, Y.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 4425–4428.
(14) Trofimov, A.; Chernyak, N.; Gevorgyan, V. *J. Am. Chem. Soc.* **2008**, *130*, 13538–13539.
(15) (a) Russell, G. A.; Ros, F. *J. Am. Chem. Soc.* **1982**, *104*, 7349–7351. (b) Russell, G. A.; Ros, F. *J. Am. Chem. Soc.* **1985**, *107*, 2506–2511.
(16) Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 146–161.
(17) Mengel, A.; Reiser, O. *Chem. Rev.* **1999**, *99*, 1191–1224.
(18) Sheng, H.; Lin, S.; Huang, Y. *Synthesis* **1987**, 1022–1023.
(19) (a) Pasto, D. J.; Brophy, J. E. *J. Org. Chem.* **1991**, *56*, 4554–4556. (b) Eberle, M. K.; Kahle, G. G. *J. Am. Chem. Soc.* **1977**, *99*, 6038–6042.