# AN EFFICIENT AND STEREOSELECTIVE CONVERSION OF LACTONES TO SUBSTITUTED CYCLIC ETHERS

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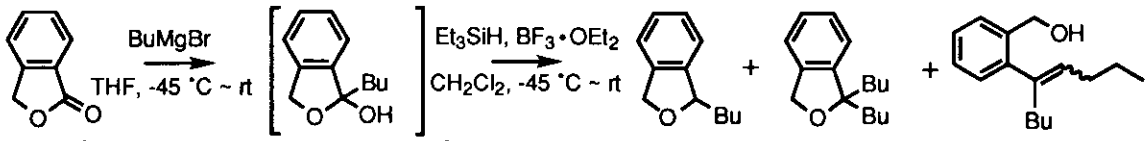
**Abstract-** A general route to substituted cyclic ethers has been described by using nucleophilic addition of Grignard reagents to lactones in the presence of $CeCl_3$ followed by the Lewis acid-induced deoxygenation of the corresponding hemiketals with $Et_3SiH$. Stereoselective reduction of the 5-membered adducts to the disubstituted tetrahydrofurans has been also investigated.

Structurally complex tetrahydrofuran and tetrahydropyran units are often found in many natural products[1] including pheromones,[2] polyether antibiotics,[3] and polyene mycotoxins,[4] and there has been increasing interest in the synthesis of such ring systems.[5] Particularly, since tetrahydrofuran derivatives containing chiral 2,3-disubstituents serve as good templates for the convergent construction of antifungal metabolites,[6] further exploitation of much more convenient stereodefined methods is strongly desired. Although one of the most effective ways to construct these types of compounds is electrophile-induced cyclization[7] of γ, δ-unsaturated alcohols by use of iodine, *N*-bromosuccinimide, mercury(II) acetate, phenylselenenyl chloride, etc., highly stereoselective forms are not readily available.

On the other hand, direct conversion of lactones to cyclic ethers *via* Lewis acid-induced reduction of hemiketal intermediates with $Et_3SiH$ has been studied especially in the carbohydrate area[8] for the synthesis of C-glycosyl compounds, however, little has been known on simpler cyclic systems.[9] The reduction of a hemiketal to a cyclic ether would introduce a new stereogenic center. Thus, in this report we wish to

disclose our results concerning the reactions of Grignard reagents with simple lactones in the presence of $CeCl_3$ followed by the Lewis acid-promoted deoxygenation. Stereoselective conversion of the three types of 5-membered lactones to the disubstituted tetrahydrofurans is also presented.

As shown in Table 1, we initially investigated the nucleophilic attack of butylmagnesium bromide to the lactone (**1**) in THF followed by the one-pot deoxygenation of the corresponding hemiketal intemediate (**2**) in $CH_2Cl_2$ with $Et_3SiH$ in the presence of $BF_3 \cdot OEt_2$[10] after evaporation of the solvent *in vacuo*. Whereas the reaction with Grignard reagent only resulted in the low and non-selective formation of the desired **3** (In this reaction accompanying formation of small amounts of **4** (7%) and **5** (5%) derived from the dialkylation of **1** was also observed.), the reaction in the presence of $CeCl_3$ (1.0 equiv.)[11] afforded **3** as a major product (entry 5). The use of other metal halides such as $MgBr_2$, $SmCl_3$, and $MnCl_2$ (entries 2-4) brought about unsatisfactory results. After detailed investigations the best result was observed under the conditions indicated in entry 6 in 76% isolated yield.




**1** **2** **3** **4** **5**

Table 1. Nucleophilic Addition of Grignard Reagents to **1** Followed by the One-pot Deoxygenation.

| entry | BuMgBr (equiv.) | additive (equiv.) | $Et_3SiH$ (equiv.) | $BF_3 \cdot OEt_2$ (equiv.) | products (%) [a] **3** | **4** | **5** |
|---|---|---|---|---|---|---|---|
| 1 | 1.2 | --- | 10 | 10 | 4 | 7 | 5 |
| 2 | 2.4 | $MgBr_2$ (1.0) | 10 | 10 | | --- [b] | |
| 3 | 2.4 | $SmCl_3$ (1.0) | 10 | 10 | | --- [b] | |
| 4 | 2.4 | $MnCl_2$ (1.0) | 10 | 10 | 5 | trace | trace |
| 5 | 2.4 | $CeCl_3$ (1.0) | 10 | 10 | 34 | 5 | 4 |
| **6** | **2.4** | **$CeCl_3$ (2.5)** | **10** | **10** | **76** | trace | trace |

a) Isolated yield based on the lactone (**1**). b) Grignard addition was not observed. c) Complex mixture.

Next, we examined the reactions with a variety of lactones under similar conditions in the presence of $CeCl_3$. The results are summarized in Table 2. After nucleophilic addition of Grignard reagents to the

lactones (**6**), both reactions in Method A and Method B (entries 1,2) as well as the reactions with a 5-methyl substituent (entries 4,5) smoothly proceeded to give the substituted cyclic ethers (**8**) in moderate to good yields. In addition, it became apparent that the procedure described here was also applicable to the synthesis of 7-membered cyclic ether (**8e**) (entry 8).

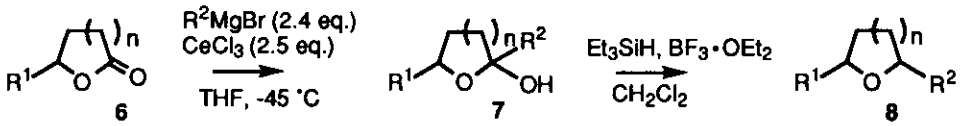



Table 2. Nucleophilic Addition of Grignard Reagents to **6** Followed by the Deoxygenation.

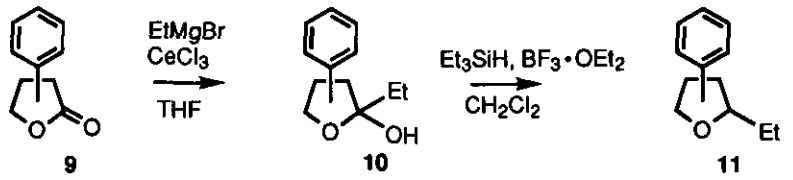
| entry | lactone (6) n | $R^1$ | $R^2$ | $Et_3SiH$ (equiv.) | $BF_3 \cdot OEt_2$ (equiv.) | temp. (°C) | yield of 8 [c] (%) |
|---|---|---|---|---|---|---|---|
| 1 [a] | 1 | H | Ph | 4 | 4 | -45 ~ rt | 50 (**8a**) |
| 2 [b] | 1 | H | Ph | 4 | 4 | -45 | 48 (**8a**) |
| 3 [b] | 1 | H | $C_{11}H_{23}$ | 4 | 4 | -45 ~ rt | 49 (**8b**) |
| 4 [a] | 1 | Me | Ph | 10 | 10 | -45 ~ rt | 75[d] (**8c**) |
| 5 [b] | 1 | Me | Ph | 4 | 4 | -45 | 88[d] (**8c**) |
| 6 [a] | 2 | H | Ph | 10 | 10 | -45 ~ rt | 23 (**8d**) |
| 7 [b] | 2 | H | Ph | 4 | 4 | -45 | 62 (**8d**) |
| 8 [b] | 3 | H | Ph | 4 | 4 | -45 ~ rt | 39 (**8e**) |

a) Method A; the deoxygenation was performed without extraction after evaporation of THF *in vacuo*.

b) Method B; the deoxygenation was performed after extraction with ether.

c) Isolated yield based on the lactone (**6**). d) The ratio of the stereoisomers was not determined.

With the above outcome in hand, we turned our attention to the investigations on the relative stereochemistry of the products derived from the reductive deoxygenation of the 5-membered ring lactones (**9**). As shown in Table 3, in the case of the reaction with 3-phenyllactone (**9a**) the Lewis acid-promoted deoxygenation with $Et_3SiH$ proceeded with complete *trans* diastereoselectivity (100 : 0)[12] at low temperature (entry 2). In contrast, a change of the phenyl group to the 4-position on the lactone ring reversely led to the predominant *cis* selectivity (95 : 5) (entry 3 or 4). However, the reaction employing **9c** with 5-phenyl subsituent did not indicate any diastereoselectivity.




9 10 11

Table 3. Stereoselective Deoxygenation of the Substituted 5-Membered Lactones (**9**).

| entry | lactone **9** [a] | temp. (°C) | yield of **11** [b] (%) | *cis* : *trans* [c] |
|---|---|---|---|---|
| 1 | **9a** | -78 ~ rt | 25 (11a) | 11 : 89 |
| **2** | **9a** | **-78 ~ -60** | **23 (11a)** | **0 : 100** |
| **3** | **9b** | **-78 ~ rt** | **38 (11b)** | **95 : 5** |
| 4 | **9b** | -78 | 44 (11b) | 95 : 5 |
| 5 | **9c** | -78 ~ rt | 53 (11c) | 57 : 43 |
| 6 | **9c** | -78 | 53 (11c) | 60 : 40 |

a) **9a**: 3-phenyl-, **9b**: 4-phenyl-, **9c**: 5-phenyllactone.[13]

b) Isolated yield based on the lactone **9** and not optimized. c) Determined by GC analysis.

Recently Schmitt *et al.* reported the replacement of the hydroxyl group of γ-lactols by the alkyl group of organometallic reagents, where 1,2- and 1,3-induction by a single phenyl substituent leads to *trans* selectivities in the formation of tetrahydrofuran derivatives.[12] They rationalize the observed stereochemical outcome based on the reactivity and stability of the oxocarbenium ion intermediate. In our case, the Felkin-Anh model A derived from the 3-phenyl-substituted lactone (**9a**) is also the thermodynamically preferred conformation rather than B (Figure 1). Since phenyl and ethyl groups on the ring occupy the remotest positions each other owing to the steric repulsion, the attack of $Et_3SiH$ could occur preferentially from the less hindered left-site due to the shielding effect of the ethyl function, leading to the *trans*-selective formation of the product. On the other hand, for the 4-phenyl-substituted lactone (**9b**) the phenyl group strongly hinders the attack from the right-site in the thermodynamically less stable model D. Consequently the reaction also could proceed through the attack to the oxocarbenium ion from the left-site of the more stable model C to give the *cis*-selective product predominantly. In the case of the 5-substituted lactone (**9c**), the phenyl substituent is situated in a rather remote position from the reaction center, expecting no selectivity for the formation of the product.

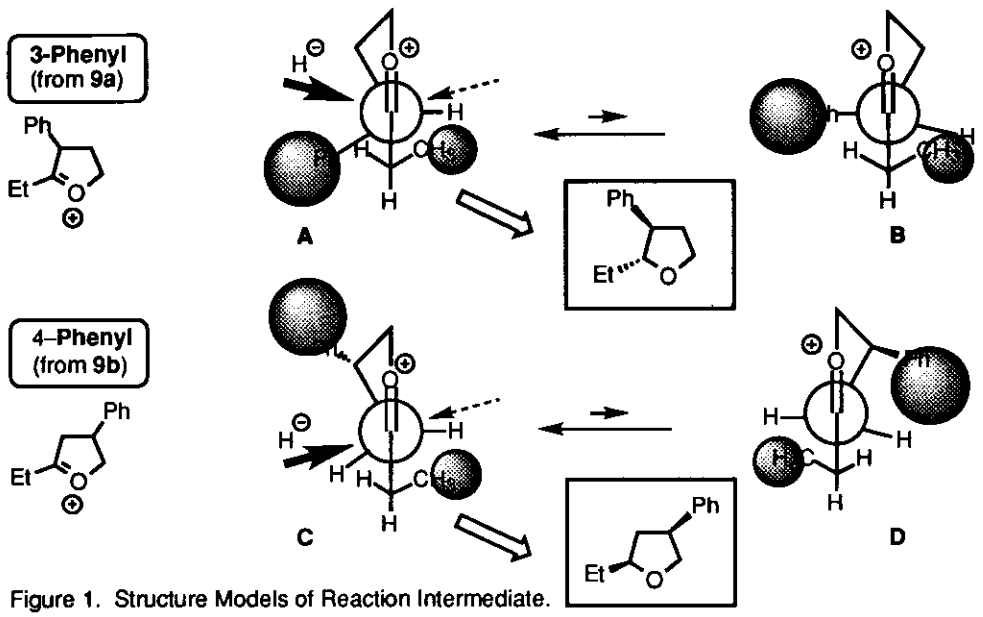



Figure 1. Structure Models of Reaction Intermediate.

In summary, our results demonstrate that the conversion of lactones to cyclic ethers on simpler systems can be achieved in good yield through the nucleophilic addition of Grignard reagents in the presence of $CeCl_3$ followed by the Lewis acid-induced deoxygenation and furthermore an efficient method to control the stereochemistry of the 1,2- and 1,3-positions in the furan rings has been developed. This strategy provides a new synthetic opportunity for the synthesis of biologically active natural products.

## EXPERIMENTAL

Ir spectra were recorded on a JASCO Model A-3 spectrophotometer. $^1H$ NMR and $^{13}C$ NMR spectra were recorded on a JEOL Model EX-90 spectrometer (operated at 90 and 22.4 MHz, respectively) in $CDCl_3$ referenced to internal tetramethylsilane (TMS) at 0.0 ppm. MS spectra were recorded on a GCMS-QP5050 Shimazu, Japan. Reactions were monitored by TLC using 0.25 mm Merck silica gel 60-$F_{254}$ precoated silica gel plates. Column chromatography was performed on Merck silica gel Kieselgel 60 eluting with the indicated solvent system. Yields refer to chromatographically and spectroscopically ($^1H$- and $^{13}C$-NMR) homogeneous materials. All compounds obtained here are well known and fully characterized.

## A TYPICAL PROCEDURE OF METHOD A

**2-Phenyltetrahydrofuran (8a):** Cerium chloride ($CeCl_3 \cdot 7H_2O$) (0.716 g, 2.90 mmol) was quickly and finely ground to a powder and placed in a flask, which was immersed in an oil bath and heated gradually to 135-140 °C with evacuation (*ca.* 1.0 Torr). After maintenance of the cerium chloride for 1 h, a solution of lactone (**6**) (0.1 g, 1.16 mmol) in THF (6 mL) was added and stirred for 1 h under nitrogen at rt. Then, the reaction mixture was cooled to -45 °C and phenylmagnesium bromide (1.2 M in THF, 2.4 mL, 2.88 mmol) was added. After the solution was stirred for 1 h at the same temperature, it was concentrated *in vacuo*. The residue was dissolved in 6 mL of $CH_2Cl_2$ and quickly cooled to -45 °C again.

To this solution was added $Et_3SiH$ (1.316 g, 11.32 mmol) and after the mixture was stirred for 5 min, $BF_3 \cdot OEt_2$ (1.689 g, 11.89 mmol) was slowly added. Then, the reaction flask was gradually warmed to rt for 2 h. It was quenched by the addition of saturated aqueous $NaHCO_3$ (3 mL) and extracted with $CH_2Cl_2$ (3 x 20 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated *in vacuo*. The crude product was purified by using silica gel column chromatography (20:1 hexane-ethyl acetate) to afford 0.085 g (0.574 mmol, 50%) of the furan (**8a**) as a colorless oil: IR(neat)$cm^{-1}$ 2980, 2870, 1070, 760, 700; $^1$H-NMR δ 7.70-7.10 (m, 5H, Ph), 4.88 (t, $J$ = 7.2 Hz, 1H, $CH_2CH$(Ph)O), 4.28-3.75 (m, 2H, $OCH_2CH_2$), 2.48-1.62 (m, 4H, $OCH_2CH_2CH_2CH$(Ph)); $^{13}$C-NMR δ 143.5, 128.3, 127.1, 125.6, 80.6, 68.6, 34.6 26.0; GC-MS m/z 148 (64%, $M^+$), 147 (78), 105 (100), 77 (48) 42 (51). *Anal.* Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.32; H, 8.12.

**A TYPICAL PROCEDURE OF METHOD B**

**2-Phenyltetrahydrofuran (8a):** To a suspension of cerium chloride (0.715 g, 2.90 mmol) prepared by the procedure described above in 4 mL of THF was added a solution of lactone (**6**) (0.101 g, 1.17 mmol) in THF (2 mL) and stirred for 1 h under nitrogen at rt. Then, the reaction mixture was cooled to -45 °C and phenylmagnesium bromide (1.2 M in THF, 2.4 mL, 2.88 mmol) was added. After the solution was stirred for 1 h at the same temperature, it was quenched by the addition of water (3 mL) and filtered through a pad of Celite followed by the extraction with ether (3 x 20 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated *in vacuo* to give an oil of the crude hemiketal. A solution of the above hemiketal in $CH_2Cl_2$ (1 mL) was cooled to -45 °C and $Et_3SiH$ (0.541 g, 4.65 mmol) was added. After the mixture was stirred for 5 min, $BF_3 \cdot OEt_2$ (0.66 g, 4.65 mmol) was slowly added. The solution was further stirred for 2 h at the same temperature and quenched by the addition of saturated aqueous $NaHCO_3$ (3 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 x 20 mL) and the combined organic extracts were dried ($Na_2SO_4$) followed by the concentration *in vacuo*. The residue was chromatographed (20:1 hexane-ethyl acetate) to give 0.083 g (0.56 mmol, 48%) of the furan (**8a**) as a colorless oil.

**2-Butylphthalan (3):** colorless oil; IR(neat)$cm^{-1}$ 2960, 2940, 2870, 1460, 1050, 1030, 760; $^1$H-NMR δ 7.48-7.05 (m, 4H, Ph), 5.36-5.15 (m, 1H, PhC*H*(Bu)O), 5.11 (s, 1H, $PhCH_2O$), 5.09 (s, 1H, $PhCH_2O$), 2.08-1.70 (m, 2H, $CHCH_2CH_2CH_2CH_3$), 1.70-1.16 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.95 (t, $J$ = 6.3 Hz, 3H, $CH_2CH_3$); $^{13}$C-NMR δ 142.4, 139.5, 127.3, 127.2, 121.1, 120.9, 84.0, 72.4, 36.1, 27.4, 22.8 14.1; GC-MS m/z 176 (3%, $M^+$), 119 (100), 91 (39), 65 (14). *Anal.* Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.68; H, 9.29.

**2,2-Dibutylphthalan (4):** colorless oil; IR(neat)$cm^{-1}$ 2900, 2850, 1270, 1130, 1050, 720; $^1$H-NMR δ 7.43-6.93 (m, 4H, Ph), 5.07 (s, 2H, $PhCH_2O$), 2.08-1.03 (m, 12H, $CCH_2CH_2CH_2CH_3$), 0.83 (t, $J$ = 6.0 Hz, 6H, $CH_2CH_3$). *Anal.* Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.81; H, 10.35.

**5-(2'-Hydroxymethylphenyl)-4-nonene (5):** colorless oil; IR(neat)$cm^{-1}$ 3600-3000, 2900, 1450, 1020, 730; $^1$H-NMR δ 7.73-6.90 (m, 4H, Ph), 5.44, 5.33 (2t, $J$ = 7.0, 7.0 Hz, 1H, $CCHCH_2$), 4.68, 4.62 (2s, 2H, $PhCH_2OH$), 2.62-1.98 (m, 5H, $CCHCH_2CH_2$, $PhCCH_2CH_2$, $CH_2OH$), 1.98-0.47 (m, 12H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$). *Anal.* Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.59; H, 10.58.

**2-Undecyltetrahydrofuran (8b):** colorless oil; IR(neat)$cm^{-1}$ 2930, 2850, 1460, 1080; $^1$H-NMR δ

4.11-3.54 (m, 3H, $OCH_2CH_2$, $CH_2CH(C_{11}H_{23})O$), 2.10-1.01 (m, 24H, $OCH_2CH_2CH_2CH(C_{11}H_{23})$, $CH(CH_2)_{10}CH_3$), 0.88 (t, $J$ = 5.4 Hz, 3H, $(CH_2)_{10}CH_3$); $^{13}$C-NMR δ 79.5, 67.6, 35.8, 32.0, 31.5, 29.9, 29.7, 29.4, 26.5, 25.8, 22.8 14.1; GC-MS m/z 226 (0.02%, $M^+$), 225 (0.08), 71 (100), 55 (8.9), 43 (30). *Anal.* Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.29; H, 13.51.

**2-Methyl-5-phenyltetrahydrofuran (8c):** colorless oil; IR(neat)cm$^{-1}$ 2980, 1450, 1080, 1030, 760, 700; $^1$H-NMR δ 7.53-7.09 (m, 5H, Ph), 5.14-4.70 (m, 1H, $CH_2CH(Ph)O$), 4.52-3.93 (m, 1H, $OCH(Me)CH_2$), 2.51-1.43 (m, 4H, $CH(Me)CH_2CH_2CH(Ph)$), 1.34, 1.28 (2d, $J$ = 6.2, 6.2 Hz, 3H, $CHCH_3$); $^{13}$C-NMR δ 128.3, 127.1, 127.0, 125.8, 125.5, 81.0, 80.2, 75.9, 35.6, 34.6, 34.2, 33.1, 21.6, 21.3; GC-MS m/z 162 (75%, $M^+$), 105 (99), 77 (56), 56 (100), 41 (65). *Anal.* Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.66; H, 8.58.

**2-Phenyltetrahydropyran (8d):** colorless oil; IR(neat)cm$^{-1}$ 2950, 2850, 1100, 1060, 1050, 760, 700; $^1$H-NMR δ 7.68-7.10 (m, 5H, Ph), 4.48-3.96 (m, 2H, $OCH_2CH_2$), 3.80-3.36 (m, 1H, $CH_2CH(Ph)O$), 2.10-1.27 (m, 6H, $OCH_2CH_2CH_2CH_2CH(Ph)$); $^{13}$C-NMR δ 143.4, 128.2, 127.2, 125.8, 80.1, 68.9, 34.1, 25.9, 24.0; GC-MS m/z 162 (60%, $M^+$), 161 (54), 105 (100), 77 (53), 41 (51). *Anal.* Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.23; H, 8.81.

**2-Phenyloxepane (8e):** colorless oil; IR(neat)cm$^{-1}$ 2930, 2850, 1450, 1130, 1040, 750, 700; $^1$H-NMR δ 7.49-7.15 (m, 5H, Ph), 4.57 (dd, $J$ = 8.4, 4.1 Hz, 1H,$CH_2CH(Ph)O$), 4.20-3.52 (m, 2H, $OCH_2CH_2$), 2.28-1.36 (m, 8H, $OCH_2CH_2CH_2CH_2CH_2CH(Ph)$); $^{13}$C-NMR δ 144.7, 128.2, 126.8, 125.7, 81.4, 68.7, 37.9, 31.1, 26.8, 25.9; GC-MS m/z 176 (39%, $M^+$), 107 (53), 105 (100), 79 (44), 42 (65). *Anal.* Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.92; H, 9.03.

**2-Ethyl-3-phenyltetrahydrofuran (11a)**[12]**:** colorless oil; IR(neat)cm$^{-1}$ 2840, 1450, 1090, 1060, 1030, 750, 700; $^1$H-NMR (*trans*-**11a**) δ 7.52-7.01 (m, 5H, Ph), 4.01 (t, $J$ = 7.1 Hz, 2H, $CH_2CH_2O$), 3.73 (td, $J$ = 6.1, 7.6 Hz, 1H, $OCH(Et)CH(Ph)$), 2.90 (q, $J$ = 8.4 Hz, 1H, $CH(Et)CH(Ph)CH_2$), 2.36 (dddd, $J$ = 12.5, 8.5, 7.0, 5.0 Hz, 1H, $CH(Ph)CH_2CH_2$), 2.11 (dddd, $J$ = 12.5, 9.0, 8.5, 7.5 Hz, 1H, $CH(Ph)CH_2CH_2$), 1.78-1.36 (m, 2H, $CHCH_2CH_3$), 0.91 (t, $J$ = 7.2 Hz, 3H, $CH_2CH_3$); $^{13}$C-NMR (*trans*-**11a**) δ 142.4, 128.6, 127.7, 126.5, 87.5, 67.5, 50.9, 35.8, 26.9, 10.6; $^{13}$C-NMR (*cis*-**11a**) δ 142.4, 128.6, 128.1, 126.2, 84.5, 66.8, 47.7, 33.5, 24.3, 10.9; GC-MS (*trans*-**11a**) m/z 176 (16%, $M^+$), 118 (100), 117 (95), 91 (33); GC-MS (*cis*-**11a**) m/z 176 (10%, $M^+$), 118 (100), 117 (76), 57 (22).

**2-Ethyl-4-phenyltetrahydrofuran (11b)**[12]**:** colorless oil; IR(neat)cm$^{-1}$ 2850, 1460, 1080, 1050, 1020, 750, 700; $^1$H-NMR (*cis*-**11b**) δ 7.52-7.13 (m, 5H, Ph), 4.34-3.24 (m, 3H, $OCH(Et)CH(Ph)$, $CH(Ph)CH_2O$), 2.62-2.20 (m, 1H, $CH_2CH(Ph)CH_2$), 1.90-1.33 (m, 4H, $CH(Et)CH_2CH(Ph)$, $CHCH_2CH_3$), 0.98 (t, $J$ = 7.2 Hz, 3H, $CH_2CH_3$); $^{13}$C-NMR (*trans*-**11b**) δ 142.8, 128.6, 127.2, 126.5, 80.9, 74.6, 44.7, 39.4, 29.0, 10.4; $^{13}$C-NMR (*cis*-**11b**) δ 142.8, 128.6, 127.2, 126.5, 81.8, 74.2, 45.6, 40.7, 28.6, 10.4; GC-MS (*trans*-**11b**) m/z 176 (12%, $M^+$), 147 (52), 117 (80), 104 (65), 91 (100); GC-MS (*cis*-**11b**) m/z 176 (15%, $M^+$), 147 (74), 117 (98), 104 (59), 91 (100).

**2-Ethyl-5-phenyltetrahydrofuran (11c)**[12]**:** colorless oil; IR(neat)cm$^{-1}$ 2850, 1450, 1080, 1060, 1030, 750, 700; $^1$H-NMR (*trans*-**11c**) δ 7.59-7.12 (m, 5H, Ph), 4.97 (t, $J$ = 7.0 Hz, 1H, $CH_2CH(Ph)O$), 4.29-3.73 (m, 1H, $OCH(Et)CH_2$), 2.52-1.20 (m, 6H, $CH(Et)CH_2CH_2CH(Ph)$, $CHCH_2CH_3$), 0.96 (t, $J$ = 7.3 Hz, 3H, $CH_2CH_3$); $^1$H-NMR (*cis*-**11c**) δ 7.59-7.12 (m, 5H, Ph), 4.86 (t, $J$ = 6.7 Hz,

1H, $CH_2CH$(Ph)O), 4.29-3.73 (m, 1H, OC*H*(Et)$CH_2$), 2.52-1.20 (m, 6H, CH(Et)$CH_2CH_2$CH(Ph), $CHCH_2CH_3$), 0.99 (t, $J$ = 7.1 Hz, 3H, $CH2CH_3$); $^{13}$C-NMR (*trans*-**11c**) δ 144.0, 128.2, 127.1, 125.8, 81.4, 80.2, 35.4, 31.9, 28.9, 10.4; $^{13}$C-NMR (*cis*-**11c**) δ 143.6, 128.2, 127.0, 125.6, 81.3, 80.8, 34.5, 30.9, 28.9, 10.3; GC-MS (*trans*-**11c**) m/z 176 (51%, $M^+$), 147 (100), 129 (50), 105 (59), 91 (91); GC-MS (*cis*-**11c**) m/z 176 (49%, $M^+$), 147 (100), 117 (47), 105 (63), 91 (81).

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## REFERENCES AND NOTES

1. K. Nakanishi, *Nat. Pro. Chem.*, 1974, **1**, 2.
2. K. Mori, *Tetrahedron*, 1989, **45**, 3233.
3. P. A. Bartlett, *Tetrahedron*, 1980, **36**, 2; T. L. B. Boivin, *ibid.*, 1987, **43**, 3309; M. D. Ruff in *'Polyether Antibiotics: Naturally Occurring Acid Ionophors,'* ed. by I. W. Westley, Marcel Dekker, New York, 1982, Vol. 1, chapter 6.
4. For example see: M. Niwa, T. Endo, S. Ogiso, H. Furukawa, and S. Yamamura, *Chem Lett.*, 1981, 1285; S. Rebuffat, D. Davoust, L. Molho, and D. Molho, *Phytochemistry*, 1980, **19**, 1285.
5. E. D. Mihelich, *J. Am. Chem. Soc.*, 1990, **112**, 8995; S. H. Kang, T. S. Hwang, W. J. Kim, and J. K. Lim, *Tetrahedron Lett.*, 1990, **31**, 5917; J.-C. Harmange and Figadère, *Tetrahedron: Asymmetry*, 1993, **4**, 1711; U. Koert, *Synthesis*, 1995, 115.
6. G. V. Sharma and S. R. Vepachedu, *Tetrahedron*, 1991, **47**, 519 and references cited therein; J. Mulzer, L. Kattner, A. R. Schrecker, C. Schröder, J. Buschmann, C. Lehmann, and P. Luger, *J. Am. Chem. Soc.*, 1991, **113**, 4218.
7. G. Cardillo and M. Orena, *Tetrahedron*, 1990, **46**, 3321.
8. M. D. Lewis, J. K. Cha, and Y. Kishi, *J. Am. Chem. Soc.*, 1982, **104**, 4976; G. A. Kraus and M. T. Molina, *J. Org. Chem.*, 1988, **53**, 752; E. Ayadi, S. Czernecki, and J. Xie, *Chem. Commun.*, 1996, 347.
9. G. A. Kraus, M. T. Molina, and J. A. Walling, *J. Org. Chem.*, 1987, **52**, 1273.
10. H. Yoda, T. Nakajima, and K. Takabe, *Synlett*, 1997, 911; H. Yoda, T. Nakajima, and K. Takabe, *Tetrahedron Lett.*, 1996, **37**, 5531; H. Yoda, H. Yamazaki, M. Kawauchi, and K. Takabe, *Tetrahedron: Asymmetry*, 1995, **6**, 2669 and references cited therein.
11. T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiya, *J. Am. Chem. Soc.*, 1989, **111**, 4392.
12. The relative stereochemistry was determined based on the spectral data cited in the following reference; A. Schmitt and H.-U. Reißig, *Chem. Ber.*, 1995, **128**, 871.
13. These substituted lactones were elaborated according to our previous report; H. Yoda, H. Morishita, M. Kudo, T. Katagiri, and K. Takabe, *Chemistry Express*, 1989, **4**, 515.

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