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WITTIG REARRANGEMENT OF 3-FURYLMETHYL ETHERS: FACILE SYNTHESIS OF 3-METYL-2-FURYLMETHANOLS AND 3-FURYLETHANOLS

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Abstract – Wittig rearrangement of 3-furylmethyl ethers 1a-i was investigated. Deprotonation of 3-furylmethyl ethers **1a-i** with bases, such as BuLi and LDA, occurred preferentially at the allylic, propargylic, benzylic positions and α-position adjacent to carbonyl group giving the corresponding anions, which underwent 2,3- and 1,2-rearrangements to afford 3-methyl-2-furylmethanols **2a-i** and 3-furylethanols **3a-f,h,i**. Synthesis of naginata ketone and dendrolasin was achieved employing the Wittig rearrangement as a key step.

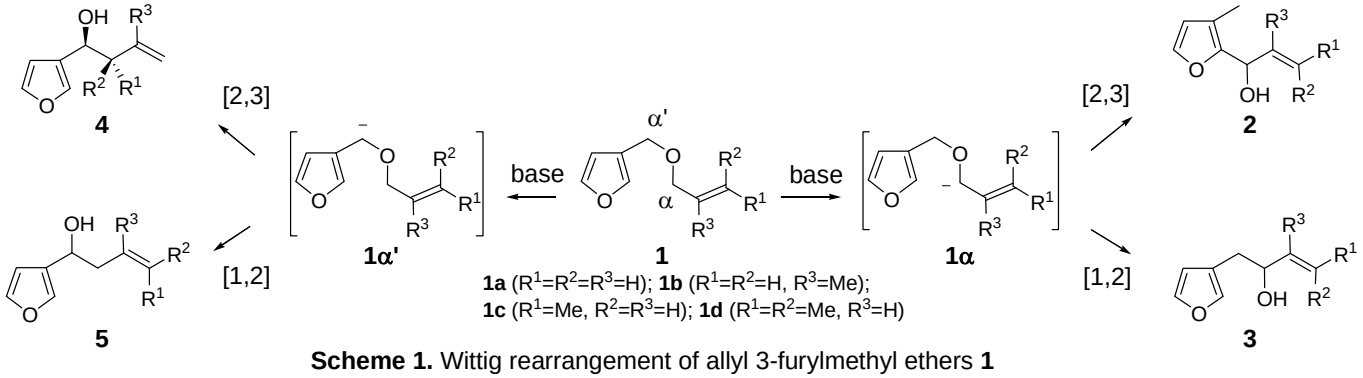
INTRODUCTION

The synthesis of furan derivatives has attracted great interest because of the importance of natural and synthetic furans[1] and the synthetic versatility of furans.[2] Numerous efforts have been devoted to the preparation of furans and functionalization of the furan ring.[3] As a part of our continuing work on the synthesis of biologically active natural compounds using furylmethanols, we were interested in developing a new method for the synthesis of furylmethanols. Previously, we have reported that the Wittig rearrangement of 2- and 3-furylmethyl ethers provides an efficient method for the preparation of 2-furylmethanol derivatives.[4] Recently, we have successfully applied this rearrangement to the stereoselective synthesis of furanocyclic diterpene skeleton,[5a] steroidal side chain,[5b] and OSW-1[5c] and its thiazole analogue.[5d] In the present study we further investigate the Wittig rearrangement of 3-furylmethyl ethers and apply the rearrangement to the synthesis of naturally occurring terpenoids, naginata ketone and dendrolasin.

Dedicated to Dr. Keiichiro Fukumoto, Professor Emeritus of Tohoku University, on the occasion of his 75th birthday.

RESULTS AND DISCUSSION

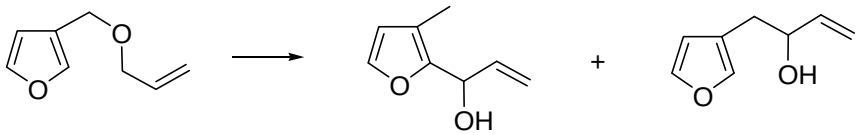
The Wittig rearrangement of allyl 3-furylmethyl ether **1** could theoretically afford both 2,3-rearranged products **2**[6] and **4** and 1,2-rearranged products **3** and **5** depending on the position, either α- or α'-position, of deprotonation (Scheme 1). We first evaluated the relative thermodynamic stabilities of anions **1α** and **1α'** using *ab initio* calculations involving full optimizations with the GAUSSIAN 92 quantum mechanical package.[7] The calculations show that the energy minimums of the **1a-d α** anions were favored by 7.9-17.9 kJ/mol over the energy minimums of the **1a-d α'** anions at the RHF/6-31+G* level. This result suggests that the Wittig rearrangement of allyl 3-furylmethyl ethers **1a-d** would proceed through deprotonation mainly at the α position, yielding **2a-d** and **3a-d**.



Scheme 1. Wittig rearrangement of allyl 3-furylmethyl ethers **1**

With this result in mind, the Wittig rearrangement of allyl 3-furylmethyl ether **1a** was initially studied under standard conditions.[8] Allyl 3-furylmethyl ethers **1a** was prepared in 80% yield from by reaction of 3-furanmethanol with allyl bromide in DMF using 1.8 equiv. of NaH. The results of the rearrangement are shown in Table 1. Reaction of **1a** with base brought about selective deprotonation at the expected α position to give **1α** anion (R^1=R^2=R^3=H), which went through sigmatropic rearrangement to afford α-ethenyl-3-methyl-2-furanmethanol **2a** as a major product, together with α-ethenyl-3-furanethanol **3a**. Treatment of **1a** with 2 equiv. of *n*-BuLi in THF gave 2,3- and 1,2-rearranged products **2a** and **3a** in a ratio of *ca*. 2:1, and there remained 50% of starting material **1a** (entry 1). In contrast, the reaction completed with 5 equiv. of *n*-BuLi (entry 2). The rearrangement proceeded at -30 to -20 °C when *n*-BuLi was employed as a base in THF. A large excess (10 equiv.) of LDA in THF gave a slightly higher ratio (*ca.* 2.6:1) than the ratio obtained by using *n*-BuLi (entry 4), whereas use of TMEDA (12 equiv.) as an additive in pentane-THF (v/v=9:1) resulted in the recovery of starting material again (entry 3). Treatment of **1a** with *s*-BuLi (5 equiv.) in THF at -78 °C produced **2a** and **3a** in a ratio of *ca*. 2.3:1, which is similar to that obtained with LDA (entry 5). Fortunately, reaction of **1a** with *t*-BuLi (4 equiv.) in THF at -78 °C furnished preferentially **2a** (entry 6).

Table 1. Wittig rearrangement of allyl 3-furylmethyl ether **1a**



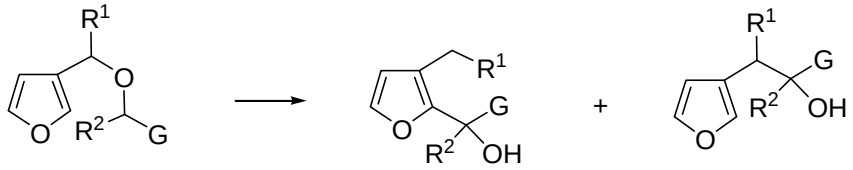
1a **2a** **3a**

Entry	Conditions				Product distribution (%) [a]			
	Base (equiv.)	Solvent	Additive	Temp.	**2a**	**3a**	**1a** [b]	others
1	*n*-BuLi (2 eq)	THF		-78→0°C	34	16	50	
2	*n*-BuLi (5 eq)	THF		-78→0°C	67	33		
3	*n*-BuLi (5 eq)	pentane-THF (v/v=9:1)	TMEDA (12 equiv.)	-78→0°C	35	18	29	18 [c]
4	LDA (10 eq)	THF		-78→0°C	72	28		
5	*s*-BuLi (5 eq)	THF		-78°C	70	30		
6	*t*-BuLi (4 eq)	THF		-78°C	>95	<5		

[a] Determined by 270 MHz NMR analysis of the crude products.
[b] Recovered starting material. [c] Undentified products were formed.

We next examined the Wittig rearrangement of 3-furylmethyl ethers **1b-i** as shown in Table 2. Compounds **1b-i** were prepared by the same method as above **1a**. Reactions of **1b-f,h** were conducted using *n*-BuLi (5 equiv.), *s*-BuLi (5 equiv.), and *t*-BuLi (4 equiv.) as a base in THF. LDA was employed for substrates **1g,i**, and products were isolated as the corresponding methyl esters. Methallyl ether **1b** gave preferentially 2,3-rearranged product **2b**, together with 1,2-rearranged product **3b** (entries 1-3), while crotyl ether **1c** and prenyl ether **1d** produced mainly 1,2-rearranged products **3c,d**, respectively (entries 4-8). The effect of methyl group at the terminal alkene was apparent from the decreased reactivity toward BuLis; starting material **1c,d** were recovered (entries 6 and 7) and reaction of **1d** with *t*-BuLi was sluggish (entry 9). Rising temperature from -78 to 0 °C in the case of entry 9 brought about the formation of complex mixtures. Propargyl ether **1e** gave predominantly **2e** using *s*- and *t*-BuLi (entries 11 and 12), although treatment with *n*-BuLi gave almost equal amounts of **2e** and **3e** (entry 10). Reaction of benzyl ether **1f** with *n*- and *s*-BuLi gave mostly **3f** (entries 13 and 14), whereas reaction with *t*-BuLi afforded **2f** as a major product (entry 15). 3-Furylmethyloxyacetic acid **1g** gave cleanly 2,3-rearranged methyl ester **3g** as a sole product (entry 16), whereas the corresponding propionic acid **1i** gave equal amounts of **2i** and **3i** (entry 20). Compound **1h** gave predominantly 1,2-rearranged product **3h** (entries 17-19), in contrast allyl ether **1a** gave mainly 2,3-rearranged product **2a** (Table 1). The *threo/erythro* stereochemistries were tentatively assigned based on Nakai's observation,[9] in which the ^{1}H NMR signal ascribed to C*H*OH in *threo* isomer is observed further upfield than that of *erythro* isomer. The *threo* isomer, the major product **3h**, shows a triplet due to C*H*OH at δ 4.04 (*J*= 7.1 Hz), while *erythro* isomer presents a distorted triplet due to C*H*OH at δ 4.17 (*J*= 5.9 Hz).

Table 2. Wittig rearrangement of 3-furylmethyl ethers **1b-i** [a]

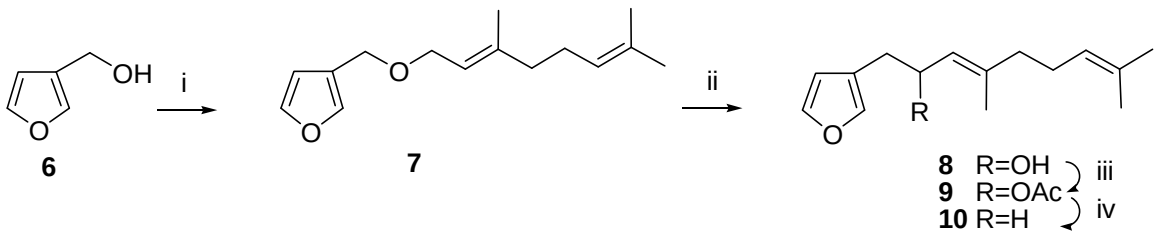


1b-i **2b-i** **3b-i**

Entry	Substrate				Base	Yield (%)	Product distribution (%) [b]	
		G	R^1	R^2			[2,3] product **2**	[1,2] product **3**
1	**1b**	CH_2=C(Me)-	H	H	*n*-BuLi	75	60	40
2					*s*-BuLi	63	64	46
3					*t*-BuLi	68	78	22
4	**1c**	MeCH=CH-	H	H	*n*-BuLi	70	<5	>95
5		(*E*/*Z*=82/18)			*s*-BuLi	66	21	79
6					*t*-BuLi	34 [c]	24	76
7	**1d**	Me_2C=CH-	H	H	*n*-BuLi	48 [c]	<5	>95
8					*s*-BuLi	53	21	79
9					*t*-BuLi	- [d]	-	-
10	**1e**	HC≡CH-	H	H	*n*-BuLi	67	48	52
11					*s*-BuLi	69 [c]	92	8
12					*t*-BuLi	46 [c]	89	11
13	**1f**	Ph	H	H	*n*-BuLi	72	18	82
14					*s*-BuLi	44 [c]	7	93
15					*t*-BuLi	64	64	36
16	**1g**	CO_2H	H	H	LDA	60	100 [e]	0
17	**1h**	CH_2=CH-	Me	H	*n*-BuLi	48	11	89 (80/20) [f]
18					*s*-BuLi	56	14	86 (70/30) [f]
19					*t*-BuLi	60	16	84 (78/22) [f]
20	**1i**	CO_2H	H	Me	LDA [g]	52	49 [e]	51 [e]

[a] Reactions were carried out with base in THF at -78°C. *n*-BuLi (5 equiv.) was employed and the reaction was allowed to warm to 0°C. *s*-BuLi (5 equiv.) was employed. *t*-BuLi (4 equiv.) was employed. LDA (4 equiv.) was employed and the reaction was allowed to warm to 0°C. [b] Determined by 270 MHz NMR analysis of the crude products. [c] Starting material was recovered. [d] Reaction was sluggish. [e] Isolated as the corresponding methyl ester. [f] The ratio of the *threo* to the *erythro* product is given in the parentheses. [g] LDA (10 equiv.) was employed.

We further applied this rearrangement to the synthesis of naturally occurring terpenoids dendrolasin[10] and naginata ketone.[11] The synthesis of dendrolasin was achieved as follows (Scheme 2). Etherification of 3-furanmethanol **6** with geranyl bromide in the presence of NaH gave geranyl ether **7** in 70% yield.

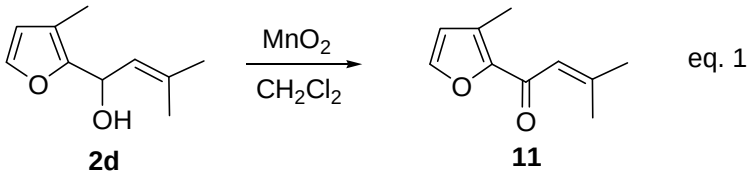


6 **7**

Scheme 2. *Reagents and conditions*: i, geranyl bromide, NaH, DMF, 70%; ii, *s*-BuLi, THF, -78°C, 82%; iii, Ac_2O, pyridine, 91%; iv, Li, $EtNH_2$, 39%

Treatment of **7** with *n*-BuLi (5 equiv.) gave almost starting material together with trace amount of 1,2-rearranged product **8**, indicating lower reactivity of **7** toward BuLis. Next, excess *n*-BuLi (20 equiv.) was used to produce the desired product **8** in 27% yield together with starting material. Treatment of **7** with *t*-BuLi (5 equiv.) in THF at -78 to -25 °C afforded **8** in 51% yield and starting material. Pleasingly, reaction of **7** with *s*-BuLi (5 equiv.) at -78 °C in THF afforded **8** in 82% yield, although the reasons for the improvement of the yield are unclear. Attempts to convert **8** into dendrolasin by deoxygenation under Barton's method[12] were unsuccessful. Thus, alcohol **8** was acetylated to **9** in 91% yield, which was treated with lithium in $EtNH_2$[13] to give dendrolasin **10** in 39% yield. The spectroscopic data obtained were identical with those reported.[10c]

Nginata ketone **11** was also prepared by MnO_2 oxidation of **2d** in poor yield, 11%, due to its high volatility (eq. 1).



2d **11** eq. 1

Thus, we have disclosed the Wittig rearrangement of 3-furylmethyl ethers leading to 3-methyl-2-furylmethanols and 3-furylethanols. Regarding the formation of [1,2] rearranged product, the use of *n*-BuLi is superior to the use of *s*- and *t*-BuLi, whereas the use of *t*-BuLi is suitable for the formation of [2,3] rearranged product rather than the use of *n*- and *s*-BuLi. Synthesis of dendrolasin and naginata ketone has been succeeded in employing the Wittig rearrangement of 3-furylmethyl ethers as a key step.

EXPERIMENTAL

IR spectra were obtained using a JASCO FT/IR-200 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained on a JEOL JNM-LA270 (^{1}H-NMR: 270 MHz, ^{13}C-NMR: 67.8 MHz) instrument for solutions in $CDCl_3$, and chemical shifts are reported on the δ scale using TMS as an internal standard of δ 0.00 for ^{1}H NMR spectra and $CDCl_3$ as an internal standard of δ 77.00 for ^{13}C NMR spectra, respectively. MS spectra were measured with a JEOL JMS-600 spectrometer. Elemental analyses were performed on a Yanaco-MT5.

General procedure for etherification of 3-furanmethanol

To a solution of allylic halide (36.7 mmol) and 3-furanmethanol (2.00 g, 20.4 mmol) in DMF (50 mL) was added NaH (*ca*. 60 % purity, 1.47 g, *ca*. 36.7 mmol) at 0 °C and stirring was continued for 8 h at rt.

The reaction was carefully quenched with sat. aq. NH_4Cl solution in ice bath. The reaction mixture was extracted with Et_2O and CH_2Cl_2 (v/v, 2:1), and the combined organic layers were washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (80 g, *n*-hexane/Et_2O=95:5) to afford 3-furylnmethyl ether as a colorless oil.

Allyl 3-furylmethyl ether (**1a**)

80% yield; bp 70 °C (18 mmHg). IR 2860, 1500 cm^{-1}; ^{1}H-NMR δ 4.00 (2H, dt, *J*= 1.5 and 5.6 Hz), 4.39 (2H, d, *J*= 0.3 Hz), 5.20 (1H, dd, *J*= 1.5 and 10.4 Hz), 5.28 (1H, dd, *J*= 1.5 and 17.3 Hz), 5.93 (1H, ddt, *J*= 1.5, 10.4, and 17.3 Hz), 6.42 (1H, brs), 7.39-7.41 (2H, m); ^{13}C-NMR δ 63.7, 71.3, 110.8, 117.6, 122.7, 135.1, 141.1, 143.7; MS (EI): 138 (M^+); HRMS (EI) calcd for $C_8H_{10}O_2$: 138.0681. Found: 138.0682. Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.29; H, 7.39.

Methallyl 3-furylmethyl ether (**1b**)

88% yield; bp 75 °C (18 mmHg). IR 2850, 1500 cm^{-1}; ^{1}H-NMR δ 1.75 (3H, s), 3.90 (2H, s), 4.36 (2H, s), 4.91 and 4.98 (each 1H, each brs), 6.42 (1H, brs), 7.40 (2H, brd, *J*= 1.8 Hz); ^{13}C-NMR δ 19.4, 63.0, 73.7, 110.2, 112.3, 122.3, 140.5, 142.0, 143.2; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0854. Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.32; H, 7.95.

Crotyl 3-furylmethyl ether (*E*/*Z*=82:18) (1c)

52% yield; bp 50 °C (16 mmHg). IR 2850, 1500 cm^{-1}; ^{1}H-NMR (*E* isomer) δ 1.72 (3H, dd, *J*= 1.2 and 6.1 Hz), 3.92 (2H, dd, *J*= 1.2 and 6.1 Hz), 4.36 (2H, brs), 5.54-5.79 (2H, m), 6.42 (1H, brs), 7.39-7.40 (2H, m); ^{13}C-NMR (*E* isomer) δ 17.6, 62.9, 70.5, 110.3, 123.3, 127.4, 129.5, 140.5, 143.1; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0842. Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.35; H, 7.98.

Prenyl 3-furylmethyl ether (**1d**)

87% yield; bp 90 °C (15 mmHg). IR 2850, 1500 cm^{-1}; ^{1}H-NMR δ 1.66 and 1.75 (each 3H, each brs), 3.97 (2H, d, *J*= 6.7 Hz), 4.37 (2H, s), 5.34-5.40 (1H, m), 6.43 (1H, brs), 7.38-7.41 (2H, m); ^{13}C-NMR δ 18.0, 25.7, 63.1, 66.3, 110.4, 120.9, 122.5, 137.2, 140.6, 143.2; MS (EI): 166 (M^+); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0993. Found: 166.0988. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.36; H, 8.56.

Propargyl 3-furylmethyl ether (**1e**)[14]

76% yield.

Benzyl 3-furylmethyl ether (**1f**)[15]

97% yield.

3-Furylmethoxyacetic acid (**1g**)

85% yield; bp 190 °C (9 mmHg). IR 3450, 3150, 1735 cm^{-1}; ^{1}H-NMR δ 4.13 (2H, s), 4.54 (2H, s), 6.45 (1H, d, *J*= 1.2 Hz), 7.42 (1H, d, J= 1.2 Hz), 7.45 (1H, brs); ^{13}C-NMR δ 64.3, 65.9, 110.3, 120.7, 141.2,

143.6, 175.4; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_7H_8O_4$: 152.0837. Found: 152.0854. Anal. Calcd for $C_7H_8O_4 \cdot 0.2H_2O$: C, 52.73; H, 5.31. Found: C, 52.69; H, 5.27.

Allyl 1-(3-furyl)ethyl ether (**1h**)

68% yield; bp 98 °C (8 mmHg). IR 2860, 1500 cm^{-1}; ^{1}H-NMR δ 1.44 (3H, d, *J*= 6.1 Hz), 3.85 and 3.95 (each 1H, each ddt, *J*=1.2, 5.5, and 12.8 Hz), 4.47 (1H, q, *J*= 6.1 Hz), 5.15 (1H, dq, *J*= 1.2 and 10.4 Hz), 5.25 (1H, dq, *J*= 1.2 and 17.1 Hz), 5.90 (1H, ddt, *J*= 5.5, 10.4, and 17.1 Hz), 6.40 (1H, d, *J*= 1.8 Hz), 7.36 (1H, brs), 7.39 (1H, t, *J*= 1.8 Hz); ^{13}C-NMR δ 22.2, 68.8, 68.9, 108.5, 116.6, 127.5, 135.0,139.4, 143.2; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0839. Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.23; H, 7.83.

2-(3-Furylmethoxy)propionic acid (**1i**)

76% yield; bp 180 °C (5 mmHg). IR 3460, 3150, 1730 cm^{-1}; ^{1}H-NMR δ 1.49 (3H, d, *J*= 7.5 Hz), 4.10 (1H, q, *J*= 7.5 Hz), 4.42 and 4.58 (each 1H, each d, *J*= 12.5 Hz), 6.45 (1H, brs), 7.40 (1H, brs), 7.45 (1H, brs), 9.58 (1H, brs); ^{13}C-NMR δ 18.3, 63.2, 72.9, 110.3, 121.2, 141.0, 143.5, 178.5; MS (EI): 170 (M^+); HRMS (EI) calcd for $C_8H_{10}O_4$: 170.0579. Found: 170.0585. Anal. Calcd for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.24; H, 5.96.

Geranyl 3-furylmethyl ether (**7**)

70% yield; bp 182 °C (6 mmHg). IR 2820, 1060 cm^{-1}; ^{1}H-NMR δ 1.60 and 1.65 (each 3H, each brs), 1.68 (3H, d, *J*= 1.2 Hz), 1.95-2.15 (4H, m), 4.00 (2H, d, *J*= 6.7 Hz), 4.37 (2H, s), 5.09 (1H, tt, *J*= 1.2 and 6.7 Hz), 5.37 (1H, dt, J= 1.2 and 6.7 Hz), 6.42 (1H, d, *J*= 1.8 Hz), 7.39 (2H, brd, *J*= 1.8 Hz); ^{13}C-NMR δ 16.3, 17.5, 25.6, 26.2, 39.5, 62.9, 66.2, 110.3, 120.6, 122.4, 123.9, 131.5, 140.3, 140.5, 143.1; MS (EI): 234 (M^+); HRMS (EI) calcd for $C_{15}H_{22}O_2$: 234.1619. Found: 234.1619. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.63; H, 9.53.

General procedure for Wittig rearrangement of 3-furylmethyl ether

To a solution of 3-furylmethyl ether (**1a-i**, **7**) (1.0 mmol) in THF (10 mL) was added dropwise a base (*n*-BuLi 1.6 M in hexane, 3.12 mL, 5.0 mmol; *s*-BuLi 1 M in cyclohexane, 5.0 mL, 5.0 mmol; *t*-BuLi 1.6 M in pentane, 2.5 mL, 4.0 mmol; LDA 4.0 mmol) at -78 °C under Ar. After stirring for 1 h (the reaction mixture was allowed to warm to 0 °C in the cases of *n*-BuLi), the reaction mixture was quenched with sat. aq. NH_4Cl solution, and the solvent was removed under vacuum. The residue was extracted with pentane-Et_2O (1:1, v/v). The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was chromatographed on silica gel (50 g, *n*-hexane/AcOEt=95:5) to afford rearrangement products, respectively. Yields and the ratio of product distribution are shown in Tables 1 and 2. All the rearranged products were isolated by either careful column chromatography or derivatization.

α-Ethenyl-3-methyl-2-furanmethanol (**2a**)

Colorless oil; IR 3400, 2940, 990 cm^{-1}; ^{1}H-NMR δ 2.06 (3H, s), 5.20-5.23 (1H, m), 5.27 (1H, d, *J*= 12.2 Hz), 5.35 (1H, d, *J*= 17.1 Hz), 6.06-6.18 (1H, m), 6.20 (1H, d, *J*= 1.8 Hz), 7.28 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR δ 9.6, 67.1, 113.2, 115.6, 116.7, 137.1, 141.2, 149.1; MS (EI): 138 (M^+); HRMS (EI) calcd for $C_8H_{10}O_2$: 138.0681. Found; 138.0671.

α-Ethenyl-3-furanethanol (**3a**)

Colorless oil; IR 3380, 2930, 1020 cm^{-1}; ^{1}H-NMR δ 2.63 and 2.71 (each 1H, each dd, *J*= 7.3 and 14.6 Hz), 4.28 (1H, brd, *J*= 5.5 Hz), 5.15 (1H, dt, *J*= 10.4 Hz), 5.28 (2H, d, *J*= 17.1 Hz), 5.93 (1H, ddd, *J*=6.7, 10.4, and 17.1 Hz), 7.31 (1H, brs), 7.38 (1H, d, *J*=1.8 Hz); ^{13}C-NMR δ 32.8, 72.4, 111.5, 115.2, 120.4, 140.1, 140.3, 143.0; MS (EI): 138 (M^+); HRMS (EI) calcd for $C_8H_{10}O_2$: 138.0681. Found; 138.0683.

3-Methyl-α-(1-methylethenyl)-2-furanmethanol (**2b**)

Colorless oil; IR 3410, 2950, 1010 cm^{-1}; ^{1}H-NMR δ 1.69 (3H, s), 2.06 (3H, s), 4.99 (1H, q, *J*=1.2 Hz), 5.14 and 5.18 (each 1H, each s), 6.20 (1H, d, *J*=1.8 Hz), 7.28 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR δ 9.6, 18.9, 69.4, 110.7, 113.1, 117.0, 141.1, 144.6, 148.7; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0844.

α-(1-Methylethenyl)-3-furanethanol (**3b**) [16]

Colorless oil; IR 3450, 2940, 1020 cm^{-1}; ^{1}H-NMR δ 1.79 (3H, s), 2.64 (1H, dd, *J*= 7.9 and 14.6 Hz), 2.73 (1H, dd, *J*= 4.9 and 14.6 Hz), 4.21 (1H, dd, *J*= 4.9 and 7.9 Hz), 4.88 (1H, brs), 4.98 (1H, d, *J*= 1.8 Hz), 6.33 (1H, brs), 7.32 (1H, brs), 7.38 (1H, d, *J*=1.8 Hz); ^{13}C-NMR δ 18.2, 31.3, 75.3, 111.4, 111.5, 121.0, 140.3, 143.1, 146.7; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0831.

3-Methyl-α-1-propenyl-2-furanmethanol (*E*/*Z*=82:18) (**2c**)

Colorless oil; IR 3380, 2920, 1020 cm^{-1}; ^{1}H-NMR (*E* isomer) δ 1.73 (3H, d, *J*= 6.2 Hz), 2.05 (3H, s), 5.17 (1H, d, *J*=6.5 Hz,), 5.74 (1H, dq, *J*=6.2 and 15.3 Hz), 5.83 (1H, dd, *J*= 6.5 and 15.3 Hz), 6.19 (1H, d, *J*=1.8 Hz), 7.27 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR (*E* isomer) δ 9.6, 17.8, 67.0, 113.1, 116.1, 127.8, 130.3, 141.0, 149.8; MS (EI): 152 (M^+); MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0837.

α-1-Propenyl-3-furanethanol (*E*/*Z*=82:18) (**3c**)

Colorless oil; IR 3430, 2860, 960 cm^{-1}; ^{1}H-NMR (*E* isomer) δ 1.70 (3H, d, *J*= 6.1 Hz), 2.60 (1H, dd, *J*= 6.7 and 14.6 Hz), 2.66 (1H, dd, *J*= 6.1 and 14.6 Hz), 4.21 (1H, q, *J*= 6.7 Hz), 5.53 (1H, ddd, *J*= 1.2, 6.7, and 15.3 Hz), 5.70 (1H, dq, *J*= 6.1 and 15.3 Hz), 6.31 (1H, brs), 7.30 (1H, brs), 7.37 (1H, d, *J*=1.8 Hz); ^{13}C-NMR (*E* isomer) δ 17.7, 33.1, 72.4, 111.5, 120.7, 127.3, 133.1, 140.2, 142.9; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0842.

3-Methyl-α-(2-methyl-1-propenyl)-2-furanmethanol (**2d**)

Colorless oil; IR 3360, 2920, 1020 cm^{-1}; ^{1}H-NMR δ 1.73 and 1.75 (each 3H, each brs), 2.05 (3H, s), 5.43 (1H, d, *J*=8.7 Hz,), 5.64 (1H, d, *J*=8.7 Hz), 6.16 (1H, d, *J*=1.6 Hz), 7.27 (1H, d, *J*= 1.6 Hz); ^{13}C-NMR δ 9.6, 18.6, 25.8, 62.8, 113.0, 115.6, 124.1, 135.7, 140.9, 150.4; MS (EI): 166 (M^+); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0993. Found: 166.0991.

α-(2-Methyl-1-propenyl)-3-furanethanol (**3d**)

Colorless oil; IR 3430, 2860, 1020 cm^{-1}; ^{1}H-NMR δ 1.66 and 1.73 (each 3H, each d, *J*= 1.2 Hz), 2.59 (1H, dd, *J*= 5.5 and 14.0 Hz), 2.65 (1H, dd, *J*= 6.7 and 14.0 Hz), 4.50 (1H, dd, *J*= 6.1 and 6.7 Hz), 5.22 (1H, dm, *J*= 8.6 Hz), 6.32 (1H, brs), 7.29 (1H, brs), 7.37 (1H, d, *J*=1.8 Hz); ^{13}C-NMR δ 18.2, 25.7, 33.2, 68.4, 111.5, 120.8, 127.1, 135.8, 140.2, 142.8; MS (EI): 166 (M^+); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0993. Found: 166.0991.

α-Ethynyl-3-methyl-2-furanmethanol (**2e**)

Colorless oil; IR 3290, 2920, 990 cm^{-1}; ^{1}H-NMR δ 2.10 (3H, s), 2.62 (1H, s), 5.47 (1H, brs), 6.21 (1H, d, *J*= 1.6 Hz), 7.31 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR δ 9.7, 56.2, 74.0, 81.1, 113.5, 117.7, 141.7, 146.6; MS (EI): 136 (M^+); HRMS (EI) calcd for $C_8H_8O_2$: 136.0524. Found; 136.0515.

α-Ethynyl-3-furanethanol (**3e**)

Colorless oil; IR 3290, 2950, 2120 cm^{-1}; ^{1}H-NMR δ 2.48 (1H, d, *J*= 2.2 Hz), 2.82 and 2.88 (each 1H, each dd, *J*= 4.2 and 14.6 Hz), 4.51 (1H, t, *J*= 4.2 Hz), 6.40 (1H, brs), 7.38 (2H, brs); ^{13}C-NMR δ 33.2, 61.9, 73.4, 84.2, 111.6, 119.2, 140.7, 142.9; MS (EI): 136 (M^+); HRMS (EI) calcd for $C_8H_8O_2$: 136.0524. Found; 136.0502.

3-Methyl-α-phenyl-2-furanmethanol (**2f**)

Colorless oil; IR 3400, 2920, 1450, 1020 cm^{-1}; ^{1}H-NMR δ 2.00 (3H, s), 5.84 (1H, brs), 6.18 (1H, d, *J*= 1.8 Hz), 7.24-7.42 (6H, m); ^{13}C-NMR δ 9.7, 68.1, 113.2, 116.9, 126.2, 127.6, 128.3, 14.3, 141.4, 149.7; MS (EI): 188 (M^+); HRMS (EI) calcd for $C_{12}H_{12}O_2$: 188.0837. Found; 188.0828.

α-Phenyl-3-furanethanol (**3f**)

Colorless oil; IR 3400, 2920, 1450, 1020 cm^{-1}; ^{1}H-NMR δ 2.83 (2H, d, *J*= 6.6 Hz), 4.79 (1H, t, *J*= 6.6 Hz), 6.20 (1H, brs), 7.23 (1H, brs), 7.23-7.40 (6H, m); ^{13}C-NMR δ 34.9, 74.0, 111.3, 120.7, 125.8, 127.6, 128.3, 140.3, 142.9, 143.7; MS (EI): 188 (M^+); HRMS (EI) calcd for $C_{12}H_{12}O_2$: 188.0837. Found; 188.0818.

Methyl 2-hydroxy-2-(3-methyl-2-furyl)acetate (**2g**)

Colorless oil; IR 3520, 2940, 1740, 1060 cm^{-1}; ^{1}H-NMR δ 2.08 (3H, s), 3.80 (3H, s), 5.21 (1H, d, *J*= 4.9 Hz), 6.22 (1H, d, *J*= 1.8 Hz), 7.28 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR δ 9.5, 53.1, 64.9, 113.2, 118.9, 141.9, 145.7, 172.3; MS (EI): 170 (M^+); HRMS (EI) calcd for $C_8H_{10}O_4$: 170.0579. Found; 170.0590.

α-Ethenyl-3-ethyl-2-furanmethanol (**2h**)

Colorless oil; IR 3430, 2930, 1030 cm^{-1}; ^{1}H-NMR δ 1.16 (3H, t, *J*= 7.2 Hz), 2.47 (2H, q, *J*= 7.2 Hz), 5.20-5.23 (1H, m), 5.25-5.40 (2H, m), 6.05-6.20 (1H, m), 6.26 (1H, d, *J*= 1.8 Hz), 7.28 (1H, d, *J*= 1.8 Hz); ^{13}C-NMR δ 14.1, 17.8, 77.4, 111.9, 115.6, 116.7, 140.9, 141.3, 149.7; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0810.

α-Ethenyl-2-methyl-3-furanethanol (**3h**)

Colorless oil; IR 3410, 2930, 1030 cm^{-1}; ^{1}H-NMR (*threo*) δ 1.21 (3H, d, *J*= 7.1 Hz), 2.78 (1H, quint, *J*= 7.1), 4.04 (1H, t, *J*= 7.1 Hz), 5.10-5.30 (2H, m), 5.75-5.92 (1H, m), 6.34 (1H, brs), 7.31 (1H, brs), 7.39 (1H, brs); ^{13}C-NMR δ 16.9, 36.6, 76.9, 109.9, 116.5, 126.1, 138.8, 139.6, 143.0; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0823.

Methyl 2-hydroxy-2-(3-methyl-2-furyl)propionate (**2i**)

Colorless oil; IR 3520, 2940, 1740, 1060 cm^{-1}; ^{1}H-NMR δ 1.81 (3H, s), 2.05 (3H, s), 3.79 (3H, s), 6.18 (1H, d, *J*= 1.8 Hz), 7.24 (1H, d, J= 1.8 Hz); ^{13}C-NMR δ 10.2, 24.1, 53.2, 72.6, 114.4, 116.7, 140.4, 147.9, 174.9; MS (EI): 184 (M^+); HRMS (EI) calcd for $C_9H_{12}O_4$: 184.0735. Found; 184.0755.

Methyl 3-(3-furyl)-2-hydroxy-2-methylpropionate (**3i**)

Colorless oil; IR 3410, 2920, 1740, 1020 cm^{-1}; ^{1}H-NMR δ 1.47 (3H, s), 2.74 and 2.92 (each 1H, each d, *J*= 14.3 Hz), 3.75 (3H, s), 6.26 (1H, brs), 7.33 (2H, brs); ^{13}C-NMR δ 25.7, 35.8, 52.7, 74.8, 111.8, 118.9, 140.7, 142.7, 176.7; MS (EI): 184 (M^+); HRMS (EI) calcd for $C_9H_{12}O_4$: 184.0735. Found; 184.0755.

(*E*)-α-(2.6-Dimethyl-1,5-heptadienyl)-3-furanethanol (**8**)

Treatment of **7** with *sec*-BuLi afforded the corresponding geraniol **8** in 82% yield. Colorless oil; IR 3450, 2900, 1010 cm^{-1}; ^{1}H-NMR δ 1.60 and 1.68 (each 3H, each brs), 1.64 (3H, d, *J*= 1.2 Hz), 1.95-2.15 (4H, m), 2.59 (1H, dd, *J*= 5.5 and 14.7 Hz), 2.66 (1H, dd, *J*= 6.7 and 14.7 Hz), 4.51 (1H, dq, *J*= 1.8 and 6.7 Hz), 5.00-5.15 (1H, m), 5.22 (1H, dq, *J*= 1.2 and 8.5 Hz), 6.32 (1H, brs), 7.28 (1H, brs), 7.36 (1H, t, *J*=1.8 Hz); ^{13}C-NMR δ 16.6, 17.6, 25.6, 26.3, 33.1, 39.5, 68.4, 111.5, 120.8, 123.8, 126.8, 131.7, 139.0, 140.2, 142.8; MS (EI): 234 (M^+); HRMS (EI) calcd for $C_{15}H_{22}O_2$: 234.1618. Found: 234.1603.

(*E*)-α-(2.6-Dimethyl-1,5-heptadienyl)-3-furanethanol acetate (**9**)

A solution of alcohol **8** (27 mg, 0.115 mmol), Ac_2O (150 mg, 1.47 mmol), and pyridine (200 mg, 2.53 mmol) in CH_2Cl_2 was stirred for 3 h at 0 °C. The reaction mixture was poured into water and the product was extracted with Et_2O-hexane (v/v=1:1). The organic layer was washed successively with saturated aqueous $KHSO_4$, brine, sat. aq. $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by silica gel column chromatography using Et_2O-hexane (v/v=1:49) to give acetate **9** (29 mg) in 91% yield. Colorless oil; IR 2880, 1710, 1020 cm^{-1}; ^{1}H-NMR δ 1.59 and 1.68 (each 3H, each brs), 1.64 (3H, d, *J*= 1.2 Hz), 2.02 (3H, s), 1.95-2.15 (4H, m), 2.62 and 2.76 (each 1H,

each dd, *J*= 6.7 and 14.7 Hz), 5.04 (1H, brt, *J*= 6.7 Hz), 5.13 (1H, dd, *J*= 1.2 and 9.1 Hz), 5.62 (1H, dt, *J*= 6.7 and 9.1 z), 6.28 (1H, d, *J*= 1.2 Hz), 7.23 (1H, brs), 7.33 (1H, t, *J*=1.8 Hz); MS (EI): 216 (M^+-AcOH); HRMS (EI) calcd for $C_{17}H_{24}O_3$ - AcOH: 216.1514. Found: 216.1514.

Dendrolasin (**10**)

To a stirred solution of acetate **9** (18 mg, 0.065 mmol) in $EtNH_2$ (3 mL) was added portionwisely Li metal (9 mg, 1.3 mmol) at 2 °C and the reaction mixture was stirred for 4 h at the same temperature. After filtration of excess Li metal, filtrate was condensed to give a residue, which was purified by silica gel column chromatography using hexane to give dendrolasin **10** (5 mg) in 39% yield. The spectroscopic data obtained were identical with those reported.[10c]

Naginata ketone (**11**)

A mixture of alcohols **2d** and **3d** (231 mg, **2d**/**3d**=21:79, 1.39 mmol), obtained by treatment of **1d** with *s*-BuLi, and MnO_2 (4.8 g, 55.2 mmol) in CH_2Cl_2 (50 mL) was stirred for 8 h at rt. After filtration of inorganic material, filtrate was condensed to give a residue, which was purified by silica gel column chromatography using Et_2O-pentane (v/v=1:49) to give naginata ketone **11** (5.4 mg) in 11% yield based on **2d**. The spectroscopic data obtained were identical with those reported.[11b]

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