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## WITTIG REARRANGEMENT OF ALLYL 2-THIOPHENEMETHYL ETHERS: FACILE SYNTHESIS OF THIOPHENEMETHANOL AND -ETHANOL DERIVATIVES

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**Abstract** – Wittig rearrangement of allyl 2-thiophenemethyl ethers was studied. Deprotonation of allyl 2-thiophenemethyl ethers (**1a-d**) occurred preferentially either the  $\alpha$ - or the  $\alpha'$ -position, depending on three kinds of BuLi. Thiophenemethanol and -ethanol derivatives were obtained as products of [2,3] and [1,2] sigmatropic rearrangements, respectively.

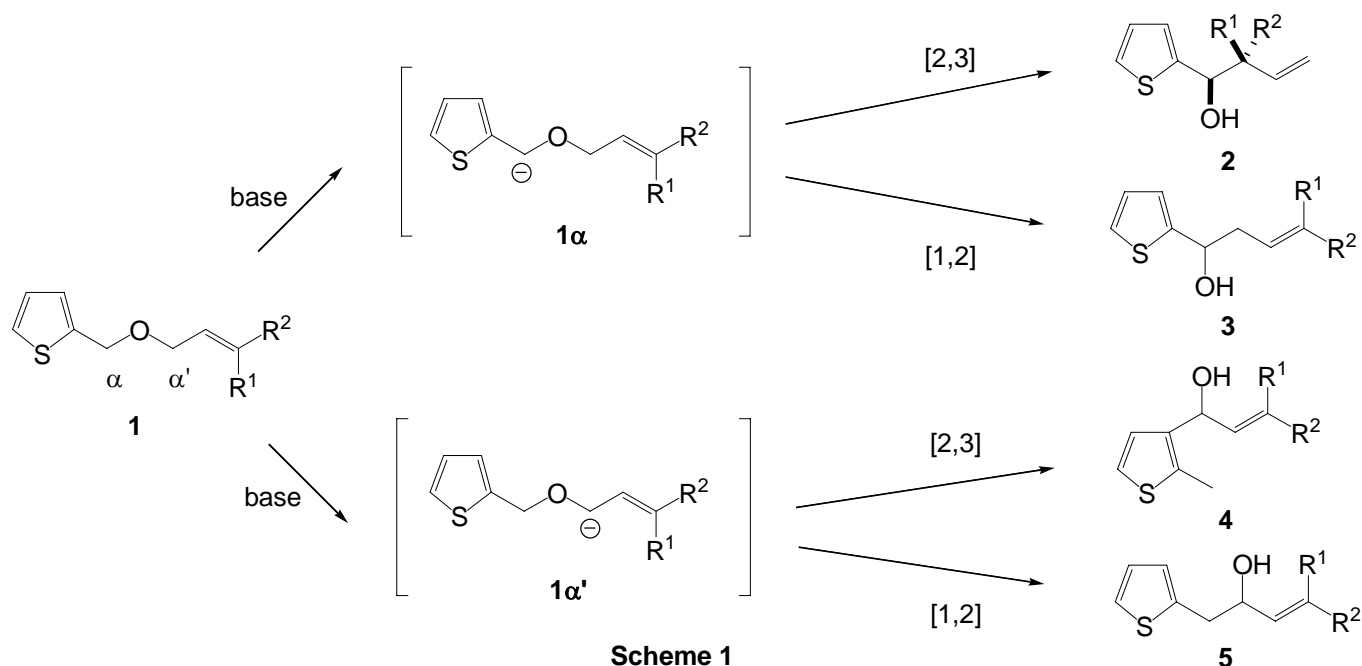
### INTRODUCTION

A variety of naturally occurring thiophene derivatives such as propynylthiophenes and polythiophenes have been isolated from plants and fungi.<sup>1</sup> The polythiophenes show interesting biological activities,<sup>2</sup> for instance  $\alpha$ -terthienyl displays an array of cytotoxic properties which are all light-dependent.<sup>3</sup> Thiophenes are very important because of their role as versatile intermediates for natural product synthesis,<sup>4</sup> essential pharmacore elements for drugs,<sup>5</sup> and functional materials.<sup>6</sup> Numerous efforts have been devoted to the preparation of thiophenes and functionalization of the thiophene ring.<sup>7</sup>

We have found that the Wittig rearrangement of 2- and 3-furylmethyl ethers provides an efficient method for the preparation of 2-furylmethanol derivatives.<sup>8</sup> Recently, we have successfully applied this rearrangement to the stereoselective synthesis of furanocyclic diterpene skeleton<sup>9a</sup> and steroidal side chain.<sup>9b</sup> In this regard, we have been interested in the Wittig rearrangement<sup>10</sup> of thiophenemethyl ethers. Here we report a facile synthesis of thiophenemethanols and thiopheneethanols based on [2,3] and [1,2] Wittig rearrangement of allyl 2-thiophenemethyl ethers.

## RESULTS AND DISCUSSION

2-Thiophenemethyl ethers (**1a-d**) were prepared from by reaction of 2-thiophenemethanol with the corresponding allylic halides in DMF using 1.5 equiv. of NaH. Wittig rearrangement of allyl 2-thiophenemethyl ether (**1**) could lead to both 2,3-rearrangement products (**2** and **4**) and 1,2-rearrangement products (**3** and **5**) *via* anions (**1 $\alpha$**  and **1 $\alpha'$** ) generated by deprotonation (Scheme 1). The Wittig rearrangement of allyl 2-thiophenemethyl ethers (**1a-d**) was investigated under the same condition reported previously,<sup>8b, 11</sup> the results are shown in Table 1.



**Table 1** Wittig rearrangement of 2-thiophenemethyl ethers (**1a-d**)<sup>a</sup>

Substrate	Base <sup>c</sup>	Yield (%)	Product Distribution <sup>b</sup> (%)			
			2	3	4	5
<b>1a</b> R <sup>1</sup> = R <sup>2</sup> = H	<i>n</i> -BuLi	78	7	-	51	42
	<i>s</i> -BuLi	74	-	-	61	39
	<i>t</i> -BuLi	84	44	-	25	31
<b>1b</b> R <sup>1</sup> = H R <sup>2</sup> = CH <sub>3</sub>	<i>n</i> -BuLi	94	17 (47/53) <sup>d</sup>	6	53	24
	<i>s</i> -BuLi	96	18 (56/44) <sup>d</sup>	-	33	49
	<i>t</i> -BuLi	88	68 (47/53) <sup>d</sup>	-	10	22
<b>1c</b> R <sup>1</sup> = CH <sub>3</sub> R <sup>2</sup> = H	<i>n</i> -BuLi	71	14 (100/0) <sup>d</sup>	28	15 (20/80) <sup>e</sup>	43 (33/67) <sup>e</sup>
	<i>s</i> -BuLi	96	-	-	39 (18/82) <sup>e</sup>	61 (51/49) <sup>e</sup>
	<i>t</i> -BuLi	82	52 (100/0) <sup>d</sup>	10	8 (25/75) <sup>e</sup>	30 (66/34) <sup>e</sup>
<b>1d</b> R <sup>1</sup> = R <sup>2</sup> = CH <sub>3</sub>	<i>n</i> -BuLi	82	42	17	-	41
	<i>s</i> -BuLi	73	26	-	-	74
	<i>t</i> -BuLi	82	76	4	-	20

<sup>a</sup> Reactions were carried out with base in THF at -78°C. In case of *n*-BuLi used, reaction was allowed to warm to 0 °C.

<sup>b</sup> Determined by 270 MHz NMR analysis of the crude products. <sup>c</sup> *n*-BuLi (10 equiv.), *s*-BuLi (3 equiv.), and *t*-BuLi (5 equiv.) were employed. <sup>d</sup> In parentheses; the ratio of the *syn* to the *anti* product. <sup>e</sup> In parentheses; the ratio of the (*E*) to the (*Z*) alkene.

Treatment of **1a** with either *n*- or *s*-BuLi brought about selective deprotonation at  $\alpha'$  position to afford both  $\alpha'$ [2,3] product (**4a**), 3-(2-methylthiophenemethyl)vinylcarbinol, and  $\alpha'$ [1,2] product (**5a**), 2-thiophenemethylvinylcarbinol. In contrast, reaction of **1a** with *t*-BuLi underwent deprotonation at  $\alpha$  and  $\alpha'$  positions to give 2-thiophenemethylallylcarbinol [**2a**(=**3a**)], **4a**, and **5a** in a ratio of 44 : 25 : 31, respectively. The similar tendency of product distribution was observed for Wittig rearrangement of (*E*)- and (*Z*)-crotyl ethers (**1b,c**). As expected,  $\alpha$ [2,3] products (**2b,c**) became major isomers when **1b,c** were treated with *t*-BuLi. Remarkable diastereoselectivity was observed with (*Z*)-substrate (**1c**), whereas disappointingly lower stereoselectivity was observed with (*E*)-substrate (**1b**). This findings are in accordance with that most Wittig rearrangement of (*Z*)-crotyl aryl ethers exhibit higher diastereoselectivities.<sup>8b,12</sup>  $\alpha'$ [2,3] And  $\alpha'$ [1,2] products (**4b** and **5b**), obtained from **1b**, have (*E*) geometries at olefins, while the corresponding  $\alpha'$  products (**4c** and **5c**), derived from **1c**, contain mixtures of (*E*) and (*Z*) geometries. The observed partial isomerization can be explained by relaxation of A<sup>1,3</sup> strain in (*Z*)-allylic anion intermediate (**1c $\alpha'$** ). Prenyl ether (**1d**) underwent [2,3] Wittig rearrangement on treatment with either *n*- or *t*-BuLi to give **2d** as a major product in moderate yield. Although  $\alpha'$ [1,2] product (**5d**) was produced from **1d**, none of **4d** was isolated. This observation can be speculated that envelope transition state suffers from steric repulsion between thiophene ring and terminal dimethyl groups.

Thus, we have disclosed Wittig rearrangement of 2-thiophenemethyl ethers leading to thiophenemethanol and -ethanol derivatives. Employing *t*-BuLi reaction of 2-thiophenemethyl ethers preferentially underwent [2,3] Wittig rearrangement of  $\alpha$  anions to give 2-thiophenemethanols, in contrast treatment with *s*-BuLi brought about deprotonation at  $\alpha'$  positions to afford [2,3] and [1,2] rearrangement products, such as 3-thiophenemethanols and 2-thiopheneethanols. Studies on the synthesis of natural product using the Wittig rearrangement of 2-thiophenemethyl ethers are underway.

## EXPERIMENTAL

IR spectra were obtained using a JASCO FT/IR-200 spectrophotometer. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were obtained on a JEOL JNM-LA270 (<sup>1</sup>H-NMR: 270 MHz, <sup>13</sup>C-NMR: 67.8 MHz) instrument for solutions in CDCl<sub>3</sub>, and chemical shifts are reported on the  $\delta$  scale using TMS as an internal standard of  $\delta$  0.00 for <sup>1</sup>H NMR spectra and CDCl<sub>3</sub> as an internal standard of  $\delta$  77.00 for <sup>13</sup>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 thiophenemethanol

To a solution of allylic halide (87.6 mmol) and 2-thiophenemethanol (5 g, 43.8 mmol) in DMF (130 mL)

was added NaH (ca. 60 % purity, 2.63 g, ca. 65.7 mmol) at 0°C and stirring was continued for 30 min at rt. The reaction was carefully quenched with sat. aq. NH<sub>4</sub>Cl solution in ice bath. The reaction mixture was extracted with Et<sub>2</sub>O and CH<sub>2</sub>Cl<sub>2</sub> (v/v, 2:1), and the combined organic layer was washed with brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to give a residue, which was chromatographed on silica gel (100 g, *n*-hexane/Et<sub>2</sub>O=95:5) to afford 2-thiophenemethyl ether as a colorless oil.

**Allyl 2-thiophenemethyl ether (1a)**<sup>13</sup>

87 % yield; bp 65.0 °C (5 mmHg).

**(E)-Crotyl 2-thiophenemethyl ether (1b)**

60 % yield; bp 76.0 °C (5 mmHg). IR 2850, 1670 cm<sup>-1</sup>; <sup>1</sup>H-NMR δ 1.72 (3H, dd, *J*=1.0 and 6.1 Hz, CH<sub>3</sub>), 3.95 (2H, dq, *J*=6.1 and 1.0 Hz, CHCH<sub>2</sub>O), 4.64 (2H, s, thienyl-CH<sub>2</sub>), 5.54-5.80 (2H, m, CH=CH), 6.94-7.00 (2H, m, 3-H and 4-H), 7.24-7.26 (1H, m, 5-H); <sup>13</sup>C-NMR δ 17.7, 66.1, 70.4, 125.6, 126.2, 126.5, 127.2, 130.0, 141.2; MS (EI): 168 (M<sup>+</sup>); HRMS (CI) calcd for C<sub>9</sub>H<sub>12</sub>OS+H: 169.0687. Found: 169.0692. Anal. Calcd for C<sub>9</sub>H<sub>12</sub>OS · 0.1H<sub>2</sub>O: C, 63.57; H, 7.23. Found: C, 63.27; H, 7.19.

**(Z)-Crotyl 2-thiophenemethyl ether (1c)**

52 % yield; bp 75.0 °C (5 mmHg). IR 2860, 1080 cm<sup>-1</sup>; <sup>1</sup>H-NMR δ 1.65 (3H, ddt, *J*=5.8, 0.7 and 1.5 Hz, CH<sub>3</sub>), 4.09 (2H, dq, *J*=5.3 and 0.7 Hz, CHCH<sub>2</sub>O), 4.67 (2H, s, thienyl-CH<sub>2</sub>), 5.54-5.74 (2H, m, CH=CH), 6.96-7.02 (2H, m, 3-H and 4-H), 7.29 (1H, dd, *J*=1.5 and 5.0 Hz, 5-H); <sup>13</sup>C-NMR δ 13.2, 65.0, 66.3, 125.7, 126.3, 126.5, 126.6, 128.3, 141.2; MS (EI): 168 (M<sup>+</sup>); HRMS (EI) calcd for C<sub>9</sub>H<sub>12</sub>OS: 168.0609. Found: 168.0621. Anal. Calcd for C<sub>8</sub>H<sub>10</sub>OS: C, 64.25; H, 7.19. Found: C, 64.40; H, 7.37.

**Prenyl 2-thiophenemethyl ether (1d)**

99 % yield; bp 80.0 °C (5 mmHg). IR 2850, 1670 cm<sup>-1</sup>; <sup>1</sup>H-NMR δ 1.66 and 1.76 (each 3H, each d, *J*=1.5 Hz, (CH<sub>3</sub>)<sub>2</sub>), 4.00 (2H, d, *J*=6.9 Hz, CHCH<sub>2</sub>O), 4.66 (2H, s, thienyl-CH<sub>2</sub>), 5.38 (1H, t septet, *J*=6.9 and 1.5 Hz, C=CH), 6.87-7.01 (2H, m, 3-H and 4-H), 7.26-7.29 (1H, m, 5-H); <sup>13</sup>C-NMR δ 20.0, 25.7, 66.0, 66.1, 120.7, 125.6, 156.2, 126.5, 137.5, 141.4; MS (EI): 182 (M<sup>+</sup>); HRMS (EI) calcd for C<sub>10</sub>H<sub>14</sub>OS: 182.0765. Found: 182.0779. Anal. Calcd for C<sub>10</sub>H<sub>14</sub>OS: C, 65.89; H, 7.74. Found: C, 65.89; H, 7.76.

**General procedure for Wittig rearrangement of 2-thiophenemethyl ether (1a-d)**

To a solution of 2-thiophenemethyl ether (**1a-d**) (1.0 mmol) in THF (10 mL) was added dropwise a base (*n*-BuLi 1.6 M in hexane, 6.25 mL, 10 mmol; *s*-BuLi 1M in cyclohexane, 3.0 mL, 3.0 mmol; *t*-BuLi 1.6 M in pentane, 3.1 mL, 5.0 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<sub>4</sub>Cl solution, and the solvent was removed under vacuum. The residue was extracted with pentane-Et<sub>2</sub>O (1:1, v/v). The extract was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. 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 Table 1. All the rearranged products were isolated by either careful column chromatography or derivatization.

**2-(1'-Hydroxy-3'-buten-1'-yl)thiophene (2a)**<sup>14</sup>

Colorless oil; IR 3480, 2930, 2360, 700  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  2.34 (1H, s, OH), 2.61 (2H, t,  $J=6.3$  Hz, 2'-H<sub>2</sub>), 4.97 (1H, t,  $J=6.3$  Hz, CHOH), 5.22 (2H, m, CH<sub>2</sub>=CH), 5.74-5.91 (1H, m, CH<sub>2</sub>=CH), 6.86-6.97 (2H, m, 3-H and 4-H), 7.23 (1H, dd,  $J=2.1$  and 4.3 Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  43.7, 69.3, 118.7, 123.6, 124.5, 126.6, 133.8, 147.8; MS (EI): 154 (M<sup>+</sup>); HRMS (CI) calcd for C<sub>8</sub>H<sub>10</sub>OS+H: 155.0515. Found; 155.0531.

**3-(1'-Hydroxy-2'-propen-1'-yl)-2-methylthiophene (4a)**

Colorless oil; IR 3340, 2920, 1040  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  2.09 (1H, br s, OH), 2.42 (3H, s, CH<sub>3</sub>), 5.16 (1H, dt,  $J=1.3$  and 10.4 Hz, CHH=CH), 5.24-5.32 (2H, m, CHH=CHCH), 6.03 (1H, ddd,  $J=5.0$ , 10.4 and 17.0 Hz, CH<sub>2</sub>=CH), 6.95 (1H, d,  $J=5.2$  Hz, 4-H), 7.02 (1H, d,  $J=5.2$  Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  12.9, 69.4, 114.5, 121.8, 126.4, 135.1, 138.4, 139.3; MS (EI): 154 (M<sup>+</sup>); HRMS (EI) calcd for C<sub>8</sub>H<sub>10</sub>OS: 154.0452. Found; 154.0427.

**2-(2'-Hydroxy-3'-buten-1'-yl)thiophene (5a)**<sup>15</sup>

Colorless oil; IR 3480, 3080, 2920, 2360  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.85 (1H, br s, OH), 3.00 (1H, dd,  $J=7.6$  and 14.8 Hz, 1'-CHH), 3.1 (1H, dd,  $J=4.9$  and 14.8 Hz, 1'-CHH), 4.36 (1H, brd,  $J=4.9$  Hz, CHOH), 5.17 (1H, dt,  $J=10.4$  and 1.3 Hz, CHH=CH), 5.30 (1H, td,  $J=1.3$  and 17.1 Hz, CHH=CH), 5.94 (1H, ddd,  $J=5.8$ , 10.4 and 17.1 Hz, CH<sub>2</sub>=CH), 6.89-6.98 (2H, m, 3-H and 4-H), 7.17-7.19 (1H, m, 5-H);  $^{13}\text{C-NMR}$   $\delta$  57.8, 73.3, 115.5, 124.3, 126.3, 126.9, 139.5, 139.6; MS (EI): 154 (M<sup>+</sup>); HRMS (EI) calcd for C<sub>8</sub>H<sub>10</sub>OS: 154.0452. Found; 154.0467.

**(1'R\*, 2'R\*)-2-(1'-Hydroxy-2'-methyl-3'-buten-1'-yl)thiophene (2b)**<sup>16</sup>

Colorless oil; IR 3410, 2970, 1640  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.09 (3H, d,  $J=6.9$  Hz, 2'-CH<sub>3</sub>), 2.29 (1H, d,  $J=2.1$  Hz, OH), 2.54 (1H, distorted sextet,  $J=7.8$  Hz, CH<sub>2</sub>=CHCH), 4.66 (1H, dd,  $J=2.1$  and 7.8 Hz, CHOH), 5.20 (1H, dd,  $J=1.3$  and 10.2 Hz, CHH=CH), 5.23 (1H, dd,  $J=1.3$  and 17.3 Hz, CHH=CH), 5.94 (1H, ddd,  $J=7.8$ , 10.2 and 17.3 Hz, CH<sub>2</sub>=CH), 6.95-7.00 (2H, m, 3-H and 4-H), 7.23-7.29 (1H, m, 5-H);  $^{13}\text{C-NMR}$   $\delta$  16.5, 46.7, 73.8, 100.5, 117.3, 124.7, 124.8, 126.4, 140.1; MS (EI): 168 (M<sup>+</sup>); HRMS (EI) calcd for C<sub>9</sub>H<sub>12</sub>OS: 168.0609. Found: 168.0607.

**(E)-2-(1'-Hydroxy-3'-penten-1'-yl)thiophene (3b)**

Colorless oil; IR 3370, 2920, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.64 (3H, dd,  $J=0.8$  and 6.8 Hz, CH<sub>3</sub>), 2.20 (1H, br s, OH), 2.56-2.68 (2H, m, 2'-H<sub>2</sub>), 4.97 (1H, dd,  $J=6.1$  and 7.1 Hz, CHOH), 5.39-5.49 (1H, m, CH<sub>3</sub>-CH=CH-CH<sub>2</sub>), 5.61-5.71 (1H, m, CH<sub>3</sub>-CH=CH-CH<sub>2</sub>), 6.95-6.98 (2H, m, 3-H and 4-H), 7.25 (1H, dd,  $J=1.3$  and 4.5 Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  13.0, 36.9, 69.9, 123.6, 124.5, 125.1, 126.6, 128.0, 148.0; MS (CI): 169 (M+H); HRMS (CI) calcd for C<sub>9</sub>H<sub>12</sub>OS+H: 169.0687. Found: 169.0667.

**(E)-3-(1'-Hydroxy-2'-buten-1'-yl)-2-methylthiophene (4b)**

Colorless oil; IR 3460, 2920, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.75 (3H, dd,  $J=0.7, 6.0$  Hz,  $\text{CH}_3\text{CH}=\text{CH}$ ), 1.89 (1H, br s, OH), 2.42 (3H, s, 2- $\text{CH}_3$ ), 5.21 (1H, d,  $J=2.6$  Hz,  $\text{CHOH}$ ), 5.73-5.68 (2H, m,  $\text{CH}=\text{CHCH}$ ), 6.98-7.03 (2H, m, 4-H and 5-H);  $^{13}\text{C-NMR}$   $\delta$  12.9, 17.6, 69.5, 121.7, 126.3, 126.9, 132.6, 134.5, 139.2; MS (EI): 168 ( $\text{M}^+$ ); HRMS (EI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}$ : 168.0609. Found: 168.0603.

**(E)-2-(2'-Hydroxy-3'-penten-1'-yl)thiophene (5b)**

Colorless oil; IR 3440, 2970, 2930, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.71 (3H, ddd,  $J=0.8, 1.5$  and 6.3 Hz,  $\text{CH}_3$ ), 2.95-3.11 (2H, m, 1'- $\text{H}_2$ ), 4.29 (1H, q,  $J=6.3$  Hz,  $\text{CHOH}$ ), 5.55 (1H, ddd,  $J=1.5, 6.3$  and 15.3 Hz,  $\text{CH}_3\text{CH}=\text{CH}$ ), 5.68-5.80 (1H, m,  $\text{CH}_3\text{CH}=\text{CH}$ ), 6.88 (1H, d,  $J=3.5$  Hz, 3-H), 6.96 (1H, dd,  $J=3.5$  and 5.1 Hz, 4-H), 7.18 (1H, d,  $J=5.1$  Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  17.7, 38.1, 73.2, 124.3, 126.2, 126.9, 127.8, 132.6, 140.0; MS (CI): 169 ( $\text{M}+\text{H}$ ); HRMS (CI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}+\text{H}$ : 169.0687. Found: 169.0715.

**(1'R\*, 2'S\*)-2-(1'-Hydroxy-2'-methyl-3'-buten-1'-yl)thiophene (2c)<sup>16</sup>**

Colorless oil; IR 2980, 1640, 1010  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.08 (3H, d,  $J=6.9$  Hz, 2'- $\text{CH}_3$ ), 2.18 (1H, d,  $J=4.0$  Hz, OH), 2.63 (1H, sextet,  $J=6.8$  Hz,  $\text{CH}_2=\text{CHCH}$ ), 4.83 (1H, dd,  $J=4.0$  and 6.8 Hz,  $\text{CHOH}$ ), 5.06-5.12 (2H, m,  $\text{CH}_2=\text{CH}$ ), 5.73-5.86 (1H, m,  $\text{CH}_2=\text{CH}$ ), 6.93-6.98 (2H, m, 3-H and 4-H), 7.23 (1H, dd,  $J=1.1$  and 5.0 Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  14.7, 45.0, 73.7, 116.0, 124.2, 124.4, 126.4, 139.6, 146.5; MS (EI): 168 ( $\text{M}^+$ ); HRMS (EI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}$ : 168.0609. Found: 168.0605. Anal. calcd for  $\text{C}_9\text{H}_{12}\text{OS}$ : C, 64.25; H, 7.19. Found: C, 64.21; H, 7.21.

**(Z)-2-(1'-Hydroxy-3'-penten-1'-yl)thiophene (3c)**

Colorless oil; IR 2920, 2850, 2460, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.64 (3H, dd,  $J=1.6$  and 6.8 Hz,  $\text{CH}_3$ ), 3.01-3.04 (2H, m, 2'- $\text{H}_2$ ), 4.68 (1H, td,  $J=6.8$  and 8.2 Hz,  $\text{CHOH}$ ), 5.47 (1H, dqt,  $J=10.9, 6.8$  and 1.6 Hz,  $\text{CH}_3\text{CH}=\text{CH}$ ), 5.56-5.68 (1H, m,  $\text{CH}_3\text{CH}=\text{CH}$ ), 6.88 (1H, dd,  $J=1.1$  and 3.5 Hz, 3-H), 6.96 (1H, dd,  $J=3.5$  and 5.1 Hz, 4-H), 7.18 (1H, dd,  $J=1.1$  and 5.1 Hz, 5-H);  $^{13}\text{C-NMR}$   $\delta$  13.3, 37.9, 68.1, 124.3, 126.1, 126.9, 127.4, 131.9, 139.8; MS (CI): 169 ( $\text{M}+\text{H}$ ); HRMS (CI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}+\text{H}$ : 169.0687. Found: 169.0670.

**(Z)-3-(1'-Hydroxy-2'-buten-1'-yl)-2-methylthiophene (4c)**

Colorless oil; IR 3480, 3020, 2920, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.74 (3H, dd,  $J=1.5$  and 6.8 Hz,  $\text{CH}_3\text{CH}$ ), 2.45 (3H, s, 2- $\text{CH}_3$ ), 5.54-5.77 (3H, m,  $\text{CH}_3\text{CH}=\text{CHCH}$ ), 7.05 (2H, s, 4-H and 5-H);  $^{13}\text{C-NMR}$   $\delta$  13.0, 13.2, 64.2, 122.0, 126.0, 126.3, 132.0, 134.5, 139.5; MS (EI): 168 ( $\text{M}^+$ ); HRMS (EI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}$ : 168.0609. Found: 168.0601.

**(Z)-2-(2'-Hydroxy-3'-penten-1'-yl) thiophene (5c)**

Colorless oil; IR 3480, 2920, 1440  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$   $\delta$  1.70 (3H, ddd,  $J=0.6, 0.8$  and 6.6 Hz,  $\text{CH}_3$ ), 2.94-3.10 (2H, m, 1'- $\text{H}_2$ ), 4.28 (1H, q,  $J=6.6$  Hz,  $\text{CHOH}$ ), 5.51-5.60 (1H, m,  $\text{CH}_3\text{CH}=\text{CH}$ ), 5.67-5.77 (1H, m,  $\text{CH}_3\text{CH}=\text{CH}$ ), 6.86-6.88 (1H, m, 3-H), 6.94-6.97 (1H, m, 4-H), 7.18 (1H, dd,  $J=1.2$  and 5.1 Hz, 5-H);

$^{13}\text{C}$ -NMR  $\delta$  17.7, 38.1, 73.2, 124.2, 126.1, 126.8, 127.7, 132.6, 140.0; MS (CI): 169 (M+H); HRMS (CI) calcd for  $\text{C}_9\text{H}_{12}\text{OS}+\text{H}$ : 169.0687. Found: 169.0674.

**2-(2',2'-Dimethyl-1'-hydroxy-3'-buten-1'-yl)thiophene (2d)**<sup>17</sup>

Colorless oil; IR 3460, 2920, 700  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR  $\delta$  1.04 and 1.06 (each 3H, each s, 2'-( $\text{CH}_3$ )<sub>2</sub>), 2.16 (1H, d,  $J=3.5$  Hz, OH), 4.71 (1H, d,  $J=3.5$  Hz,  $\text{CHOH}$ ), 5.12 (1H, dd,  $J=1.3$  and 17.5 Hz,  $\text{CHH}=\text{CH}$ ), 5.18 (1H, dd,  $J=1.3$  and 10.9 Hz,  $\text{CHH}=\text{CH}$ ), 5.97 (1H, dd,  $J=10.9$  and 17.5 Hz,  $\text{CH}_2=\text{CH}$ ), 6.95-6.98 (2H, m, 3-H and 4-H), 7.24 (1H, dd,  $J=1.7$  and 4.8 Hz, 5-H);  $^{13}\text{C}$ -NMR  $\delta$  21.6, 24.1, 42.1, 77.3, 114.1, 124.3, 125.3, 125.9, 144.4, 144.5; MS (CI): 183 (M+H); HRMS (CI) calcd for  $\text{C}_{10}\text{H}_{14}\text{OS}+\text{H}$ : 183.0844. Found: 183.0801.

**2-(1'-Hydroxy-4'-methyl-3'-peneten-1'-yl)thiophene (3d)**

Colorless oil; IR 3380, 2920  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR  $\delta$  1.64 (3H, s,  $\text{CH}_3$ ), 1.73 (3H, d,  $J=1.0$  Hz,  $\text{CH}_3$ ), 2.18 (1H, br s, OH), 2.45-2.65 (2H, m, 2'- $\text{H}_2$ ), 4.93 (1H, t,  $J=6.3$  Hz,  $\text{CHOH}$ ), 5.14-5.21 (1H, m, 3'-H), 6.95-6.97 (2H, m, 3-H and 4-H), 7.23-7.25 (1H, m, 5-H);  $^{13}\text{C}$ -NMR  $\delta$  18.0, 25.9, 38.2, 70.4, 119.1, 123.5, 124.4, 126.5, 136.1, 148.2; MS (EI): 182 ( $\text{M}^+$ ); HRMS (EI) calcd for  $\text{C}_{10}\text{H}_{14}\text{OS}$ : 182.0765. Found: 182.0760.

**2-(2'-Hydroxy-4'-methyl-3'-penten-1'-yl)thiophene (5d)**

Colorless oil; IR 1680, 2920, 3460  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR  $\delta$  1.65 and 1.73 (each 3H, each s, ( $\text{CH}_3$ )<sub>2</sub>), 2.98 (1H, dd,  $J=6.6$  and 14.5 Hz, 1'- $\text{HH}$ ), 3.01 (1H, dd,  $J=8.6$  and 14.5 Hz, 1'- $\text{HH}$ ), 4.55 (1H, dt,  $J=6.6$  and 8.6 Hz,  $\text{CHOH}$ ), 5.24 (1H, d,  $J=8.6$  Hz, 3'-H), 6.86 (1H, dd,  $J=1.1$  and 3.4 Hz, 3-H), 6.95 (1H, dd,  $J=3.4$  and 5.0 Hz, 4-H), 7.17 (1H, dd,  $J=1.1$  and 5.0 Hz, 5-H);  $^{13}\text{C}$ -NMR  $\delta$  18.3, 25.7, 38.2, 69.3, 114.2, 126.0, 126.5, 126.6, 136.3, 140.2; MS (EI) 182( $\text{M}^+$ ); HRMS (EI) calcd for  $\text{C}_{10}\text{H}_{14}\text{OS}$ : 182.0765. Found: 182.0760.

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## REFERENCES AND NOTES

1. a. F. Bohlmann and C. Zdero, *The Chemistry of Heterocyclic Compounds*, Vol. 44, ed. by A. Weissberger and E. C. Taylor, Wiley, New York, 1985, pp. 261-323. b. J. Kagan, *Fortschr. Chem. Org. Naturstoffe*, 1991, **56**, 87.
2. a. R. J. Marles, J. T. Arnason, R. L. Compadre, C. M. Compadre, C. Soucy-Breau, B. Mehta, P. Morand, R. W. Redmond, and J. C. Scaiano, *Recent Advances Phytochem.*, 1991, **25**, 371. b. R. Ebermann, G. Alth, M. Kreitner, and A. Kubin, *J. Photochem. Photobiol., B: Biol.*, 1996, **36**, 95. c. B. Tosi, A. Bonora, G. Dall'Olio, and A. Bruni, *Phytotherapy Res.*, 1991, **5**, 59.
3. a. G. F. Q. Chan, M. Prihoda, G.H.N. Towers, and J. C. Mithell, *Contact Dermatitis*, 1977, **3**, 215.

- b. G. K. Cooper and C. I. Nitsche, *Bioorg. Chem.*, 1985, **13**, 362.
4. a. A. Carpita, A. Lezzi, R. Rossi, F. Marchetti, and S. Merlino, *Tetrahedron*, 1985, **41**, 621. b. C. Rapp, G. Jung, C. Isselhorst-Scharr, and H. Zaehner, *Liebigs Ann. Chem.*, 1988, 1043. c. E. Negishi, C. Xu, Z. Tan, and M. Kotora, *Heterocycles*, 1997, **46**, 209. d. J. Wang, L. H. Pettus, and T. R. R. Pettus, *Tetrahedron Lett.*, 2004, **45**, 1793.
5. a. G. P. Moloney, G. R. Martin, N. Mathews, H. Hobbs, S. Dodsworth, P. Y. Sang, C. Knight, M. Maxwell, and R. C. Glen, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2713. b. D. Tondi, R. A. Powers, E. Caselli, M.-C. Negri, J. Blazquez, M. P. Costi, and B. K. Shoichet, *Chem. Biol.*, 2001, **8**, 593. c. E. Liebana, F. A. Clifton-Hadley, E. Pleydell, B. Abdalhamid, N. D. Hanson, L. Martin, C. Poppe, and R. H. Davies, *Microbial Drug Resistance*, 2004, **10**, 1.
6. a. J. Kowalik and L. M. Tolbert, *Chem. Commun.*, 2000, 877. b. K. Ogura, R. Zhao, M. Jiang, M. Akazome, S. Matsumoto, and K. Yamaguchi, *Tetrahedron Lett.*, 2003, **44**, 3595. c. J. W. Brown, G. J. Lambe, P. J. S. Foot, and J. A. Clipson, *Macromol. Rapid Comm.*, 2004, **25**, 1000.
7. a. D. E. Wolf and K. Folkers, *Org. React.*, 1951, **6**, 410. b. C. W. Bird and G. W. H. Cheeseman, 'Comprehensive Heterocyclic Chemistry,' Vol. 4, ed. by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, pp. 713-934. c. J. Schatz, 'Science of Synthesis,' Vol. 9, ed. by G. Maas, Thieme, Stuttgart, 2001, Chap. 9, 10.
8. a. M. Tsubuki, H. Okita, and T. Honda, *J. Chem. Soc., Chem. Commun.*, 1995, 2135 b. M. Tsubuki, T. Kamata, H. Okita, M. Arai, A. Sigihara, and T. Honda, *Chem. Commun.*, 1999, 2263.
9. a. M. Tsubuki, K. Takahashi, and T. Honda, *J. Org. Chem.*, 2003, **68**, 10183. b. M. Tsubuki, A. Ohinata, T. Tanaka, K. Takahashi, and T. Honda, *Tetrahedron*, 2005, **61**, 1095.
10. For recent reviews, see a. J. A. Marshall, 'Comprehensive Organic Synthesis,' Vol. 3, ed. by B. M. Trost and I. Fleming, Pergamon Press: New York, 1991, pp. 975-1014. b. T. Nakai and K. Mikami, *Org. React.* 1994, **46**, 105. c. K. Tomooka, 'The Chemistry of Organolithium Compounds,' ed. by Z. Rappoport and I. Marek, Wiley, New York, 2004, pp. 749-828.
11. A large excess amount of BuLi was required for the completion of the rearrangement.
12. a. V. Rautenstrauch, *Chem. Commun.*, 1970, 4. b. K. Mikami, Y. Kimura, N. Kishi, and T. Nakai, *J. Org. Chem.*, 1983, **48**, 279.
13. A. V. Anisimov, S. V. Kuznetsova, T. O. Pesina, N. B. Kazennova, and E. A. Viktorova, *Vestnik Moskovskogo Universiteta, Seriya 2: Khimiya*, 1989, **30**, 299 (*Chem. Abstr.*, 1989, **112**, 97835t).
14. Y. Naruta, S. Ushida, and K. Maruyama, *Chemistry Lett.*, 1979, 919.
15. G. T. Gmitter and F. L. Benton, *J. Am. Chem. Soc.*, 1950, **72**, 4586.
16. P. G. M. Wuts and G. R. Callen, *Synth. Commun.*, 1986, **16**, 1833.
17. P. Sinha and S Roy, *Chem. Commun.*, 2001, 1798.