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# An Efficient Synthesis of 2(5*H*)-Furanone and Furan Derivatives Using 3-(Phenylthio)propenal as a 1,3-Dipolar Synthon

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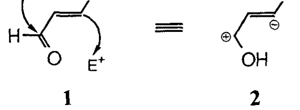
**Various 2(5*H*)-furanone and furan derivatives were synthesized from 3-(phenylthio)propenal by a one-pot process *via* carbonyl addition of a range of organometallic reagents and subsequent sulfide-directed α-lithiation followed by electrophilic trapping. This methodology was successfully applied to the syntheses of *quercus* lactone and 2,5-diarylfuran natural products.**

**Keywords** 2(5*H*)-furanone; furan; lithiation; 3-(phenylthio)propenal; *quercus* lactone; 2,5-diarylfuran

2(5*H*)-Furanone[1] and furan[2] derivatives are well known as components of a large number of biologically important natural products and as useful synthetic intermediates. Many synthetic methods have been developed and used for their construction.[1,2] In this paper, we report a novel and convenient synthesis of 2(5*H*)-furanone and furan derivatives starting from 3-(phenylthio)propenal as a 1,3-dipolar synthon *via* initial 1,2-addition of nucleophiles followed by sulfide-directed α-metalation and electrophilic trapping as shown in Chart 1 and the application of these reactions in the syntheses of naturally occurring lactone and 2,5-diarylfuran derivatives.

The use of a functional vinyl carbanion as a 1,3-dipolar synthon is an attractive and direct route for the construction of the butenolide ring system. During the past decade, (*Z*)-β-bromoacrylic acid,[3] β-(1-pyrrolidinyl)acrylate,[4] and ethyl propiolate[5] as precursors of a 1,3-dipolar synthon have been developed for this purpose. In 1979, Uda and coworkers[6] discoverd the utility of methyl 3-lithio-2-methyl-3-(phenylthio)-2-propenoate generated from methyl 2-methyl-3-(phenylthio)-2-propenoate with lithium diisopropylamide (LDA) at −80 °C as a synthon for butenolide construction. Pioneering work by Oshima,[7] Seebach,[8] and Uda[6] and their co-workers on the carbanions of vinyl sulfides prompted us to examine the synthetic utility of 3-(phenylthio)propenal (**1**) as a 1,3-dipolar synthon (**2**) *via* initial 1,2-addition of organometallic reagents ($R^1$-M) and subsequent sulfide-directed α-lithiation followed by electrophilic trapping ($CO_2$ or $R^2COX$) for providing 2(5*H*)-furanone and furan derivatives (Chart 2). A furan synthesis using ethylene acetal of 3-(phenylthio)propenal was reported by McDougal and Oh recently.[2d)] Iwao and Kuraishi have previously reported[9] the use of 3-(phenylthio)propenal (**1**) as a 1,3-dipolar synthon (**2**) for one-pot 1,4-naphthoquinone synthesis *via* tandem-directed lithiation.



1 2

Chart 1

Although *E*/*Z* mixtures of **1** have been prepared by the nucleophilic addition of thiophenol to propargylaldehyde in 1964[10] or more recently by the oxidation of 3-(phenylthio)-2-propen-1-ol with *tert*-butyl hydroperoxide in the presence of diaryl diselenide,[11] the *E*-isomer of 3-(phenylthio)propenal (**1**)[11] was synthesized in 60% overall yield by applying the Bakuzis procedure[12] which involves the $Et_3N$-catalyzed addition of thiophenol to acrolein, subsequent chlorination with *N*-chlorosuccinimide (NCS), and finally elimination of HCl with $Et_3N$. The *E*-configuration of **1** thus obtained was established by the large vinylic hydrogen coupling constant ($J = 16$ Hz).[9,11]

First, the synthesis of 5-(*n*-butyl)-3-(phenylthio)-2(5*H*)-furanone (**5a**) was carried out under various reaction conditions and the results are summarized in Table I. 3-(Phenylthio)propenal (**1**) was treated with *n*-BuLi (1.2 eq) at −78 °C in tetrahydrofuran (THF) to give the pale yellow allyl alkoxide (**3a**: $R^1 = n$-Bu, M = Li) which, upon sequential treatment at −78 °C with *n*-BuLi (1.2 eq) and $CO_2$ gas, afforded **5a** in 22% yield after acidic work-up (Table I; run 1). In another experiment, after the addition of *n*-BuLi (1.2 eq) for α-lithiation, the reaction mixture was stirred at −78 °C for 30 min and warmed slowly to 0 °C to generate the dianion (**4a**; $R^1 = n$-Bu, M = Li). The resulting light brown solution was again cooled to −78 °C and $CO_2$ gas was passed through the solution to give **5a** in 77% yield (Table I; run 2). When *sec*-BuLi (1.2 eq) was employed for α-lithiation in the above reaction, a higher yield (89%) of **5a** was obtained (Table I; run 3). The above

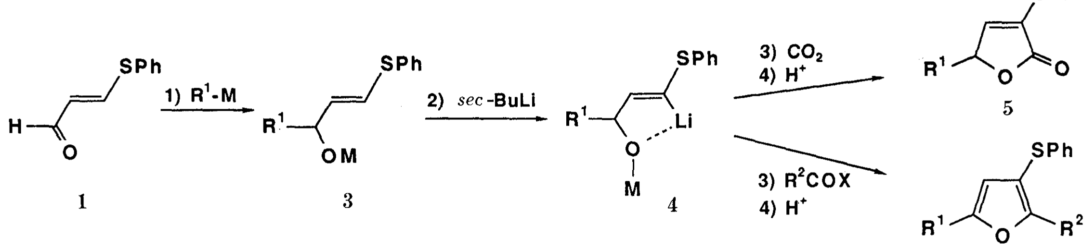


Chart 2

Table I. Synthesis of 3-(Phenylthio)-2(5*H*)-furanones (**5**)

| Run | R$^1$M (eq)[a] | RLi (eq) (Additive) | Condition (°C) | 2(5*H*)-Furanone (**5**) | | |
|---|---|---|---|---|---|---|
| | | | | | R$^1$ | Yield (%) |
| 1 | *n*-BuLi (1.2) | *n*-BuLi (1.2) | −78 | **5a** | *n*-Bu | 22 |
| 2 | *n*-BuLi (1.2) | *n*-BuLi (1.2) | −78→0 | **5a** | *n*-Bu | 77 |
| 3 | *n*-BuLi (1.2) | *sec*-BuLi (1.2) | −78→0 | **5a** | *n*-Bu | 89 |
| 4 | *n*-BuLi (2.2) | — | −78→0 | **5a** | *n*-Bu | 54 |
| 5 | *n*-BuLi (2.2) | (HMPA) (2.0) | −78 | **5a** | *n*-Bu | 53 |
| 6 | *n*-BuLi (2.2) | (TMEDA) (2.0) | −78→0 | **5a** | *n*-Bu | 52 |
| 7 | *sec*-BuLi (1.2) | *sec*-BuLi (1.2) | −78→0 | **5b** | *sec*-Bu | 76 |
| 8 | *tert*-BuLi (1.2) | *sec*-BuLi (1.2) | −78→0 | **5c** | *tert*-Bu | 84 |
| 9 | MeLi (1.2) | *sec*-BuLi (1.2) | −78→0 | **5d** | Me | 85 |
| 10 | MeMgBr (1.2) | *sec*-BuLi (1.2) | −78→0 | **5d** | Me | 20 |
| 11 | MeMgBr (1.3) | *sec*-BuLi (3.9) | −78→0 | **5d** | Me | 65 |
| 12 | EtMgBr (1.3) | *sec*-BuLi (3.9) | −78→0 | **5e** | Et | 61 |
| 13 | PhLi (1.2) | *sec*-BuLi (1.2) | −78→0 | **5f** | Ph | 40 |

*a*) Reagents were injected at −78 °C.

Table II. Physical Properties and Spectral Data of 2(5*H*)-Furanones (**5**)

| Furanone[a] | mp or bp/mmHg (°C) (Recryst. solvent) | MS (*m/z*) (M$^+$) (Formula) | IR (KBr) cm$^{-1}$ $\nu_{CO}$ | UV $\lambda_{max}^{EtOH}$ nm (log ε) | $^1$H-NMR (CDCl$_3$) δ |
|---|---|---|---|---|---|
| **5a** | 150/0.8 | 248<br>($C_{14}H_{16}O_2S$) | 1760[c] | 252 (3.74), 273 (3.66) | 0.76—1.66 (9H, m), 4.66—4.89 (1H, m), 6.50 (1H, d, *J*=2.0), 7.17—7.56 (5H, m) |
| **5b** | Oil | 248<br>($C_{14}H_{16}O_2S$) | 1760[c] | 252 (3.75), 273 (3.66) | 0.79—1.89 (9H, m), 4.56—4.82 (1H, m), 6.43 (1H, d, *J*=2.0), 7.23—7.59 (5H, m) |
| **5c** | 88<br>(*n*-Hexane) | 248<br>($C_{14}H_{16}O_2S$) | 1740 | 252 (3.91), 276 (3.90) | 0.92 (9H, s), 4.46 (1H, d, *J*=2.0), 6.46 (1H, d, *J*=2.0), 7.26—7.56 (5H, m) |
| **5d** | 72[b]<br>(*n*-Hexane) | 206<br>($C_{11}H_{10}O_2S$) | 1740 | 252 (3.76), 273 (3.69) | 1.36 (3H, d, *J*=7.0), 4.89 (1H, dd, *J*=7.0, 2.0), 6.40 (1H, d, *J*=2.0), 7.26—7.59 (5H, m) |
| **5e** | Oil | 220<br>($C_{12}H_{12}O_2S$) | 1755[c] | 252 (3.81), 273 (3.76) | 0.93 (3H, t, *J*=7.2), 1.66 (2H, dq, *J*=6.0, 7.2), 4.88 (1H, td, *J*=6.0, 2.0), 6.54 (1H, d, *J*=2.0), 7.17—7.67 (5H, m) |
| **5f** | 122<br>(Ether) | 268<br>($C_{16}H_{12}O_2S$) | 1750 | 252 (3.86), 275 (3.81) | 5.88 (1H, d, *J*=2.0), 6.58 (1H, d, *J*=2.0), 7.11—7.68 (10H, m) |

*a*) *Anal.* Calcd (Found) for **5a**: C, 67.73 (67.74); H, 6.50 (6.61); S, 12.89 (12.73). **5b**: C, 67.73 (67.86); H, 6.50 (6.62); S, 12.89 (12.96). **5c**: C, 67.73 (67.79); H, 6.50 (6.53); S, 12.89 (12.73). **5d**: C, 64.07 (63.99); H, 4.89 (4.95); S, 15.52 (15.63). **5e**: C, 65.44 (65.46); H, 5.49 (5.68); S, 14.53 (14.20). **5f**: C, 71.63 (71.50); H, 4.51 (4.62); S, 11.93 (11.74). *b*) Lit.[13] bp 160—170 °C/1 mmHg. *c*) Neat.

results clearly indicate that the use of *sec*-BuLi (1.2 eq) and a temperature of 0 °C are most effective for the generation of the dianion species (**4**). The experiment in which 2.2 eq of *n*-BuLi was added at once for 1,2-addition and α-lithiation led to **5a** in lower yield (54%) (Table I; run 4). Under these conditions, we also checked the effect of additives such as hexamethylphosphoric triamide (HMPA) and *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TMEDA), but very similar yields of **5a** were obtained (Table I; runs 5 and 6). Using appropriate alkyllithium reagents for the initial 1,2-addition to the aldehyde functional group in **1**, and sequential treatment with *sec*-BuLi and $CO_2$ gas, led to a variety of 5-substituted-2(5*H*)-furanone derivatives (**5b**, **c**, and **d**) in a one-pot process in high yields (Table I; runs 7, 8, and 9). When phenyllithium was used in this reaction, the expected 5-phenyl-3-(phenylthio)-2-(5*H*)-furanone (**5f**) was isolated in only 40% yield because of its thermal instability to dimerization (see Experimental).[13]

Grignard reagents such as MeMgBr (Table I; runs 10 and 11) and EtMgBr (Table I; run 12) could also be employed for the initial 1,2-addition reaction. However, in these cases, probably as a result of consumption of *sec*-BuLi by metal exchange reaction with the Grignard adduct (**3**; R$^1$ = Me, or Et, M = MgBr), at least 3 eq of *sec*-BuLi had to be used for successful α-lithiation reaction to obtain acceptable yields of the furanone derivatives (**5d**, 65%; **5e**, 61%). The structures of all compounds were established by infrared (IR), proton nuclear magnetic resonance ($^1$H-NMR) and mass spectral (MS) data as summarized in Table II.

When acylating agents were used to quench the dianion (**4**), furan derivatives (**6a**—**i**) were obtained in moderate yields as shown in Table III. Using *N*,*N*-dimethylformamide (DMF) as an acylating agent, 2-substituted-4-(phenylthio)furan derivatives (**6a**—**d**) were obtained in 50 to 71% yields (Table III; runs 1,2,3, and 4). Although *N*,*N*-dimethylamide derivatives (Table III; run 10) were good acylating agents for the dianion (**4**), ester (Table III; run 9), acid chloride (Table III; runs 5, 8, 11, and 12), acyl cyanide (Table III; run 6), and acid anhydride derivatives (Table III; run 7) could also be employed to afford 2,5-disubstituted-3-(phenylthio)furans (**6e**—**i**). Since the phenylthio group can be removed by Raney Ni,[14] this method enables the synthesis of relatively unaccessible 2,5-symmetrically or unsymmetrically substituted furans. Spectral data of the furans are summarized in Table IV.

When (*E*)-3-(phenylthio)-2-propen-1-ol (**7**),[11] which was easily prepared from **1** with $NaBH_4$ in EtOH, was met-

TABLE III. Synthesis of Furans (**6**)

| Run | $R^1M$ (eq)[a] | | $R^2COX$ (eq)[b] | | Furan (**6**) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | $R^1$ | $R^2$ | Yield (%) |
| 1 | *tert*-BuLi | (1.2) | DMF | (2.0) | **6a** | *tert*-Bu | H | 50 |
| 2 | MeLi | (1.2) | DMF | (2.0) | **6b** | Me | H | 71 |
| 3 | PhLi | (1.2) | DMF | (2.0) | **6c** | Ph | H | 53 |
| 4 | *n*-BuLi | (1.2) | DMF | (2.0) | **6d** | *n*-Bu | H | 50 |
| 5 | *tert*-BuLi | (1.2) | $CH_3COCl$ | (2.0) | **6e** | *tert*-Bu | Me | 15 |
| 6 | *tert*-BuLi | (1.2) | $CH_3COCN$ | (2.0) | **6e** | *tert*-Bu | Me | 12 |
| 7 | *tert*-BuLi | (1.2) | $(CH_3CO)_2O$ | (2.0) | **6e** | *tert*-Bu | Me | 35 |
| 8 | *tert*-BuLi | (1.2) | PhCOCl | (2.0) | **6f** | *tert*-Bu | Ph | 54 |
| 9 | MeLi | (1.2) | PhCOOEt | (2.0) | **6g** | Me | Ph | 51 |
| 10 | MeLi | (1.2) | $PhCONMe_2$ | (2.0) | **6g** | Me | Ph | 65 |
| 11 | *tert*-BuLi | (1.2) | 4-MeO-$C_6H_4COCl$ | (2.0) | **6h** | *tert*-Bu | 4-MeO-$C_6H_4$ | 58 |
| 12 | *tert*-BuLi | (1.2) | Furan-2-COCl | (2.0) | **6i** | *tert*-Bu | Furan-2- | 27 |
| 13 | *tert*-BuLi | (1.2) | Furan-2-$CONMe_2$ | (2.0) | **6i** | *tert*-Bu | Furan-2- | 25 |

*a*) Reagents were injected at −78 °C. *b*) *sec*-BuLi (1.2 eq) was used as RLi for α-lithiation before treatment of $R^2COX$.

TABLE IV. Physical Properties and Spectral Data of Furans (**6**)

| Furan[a] | mp or bp/mmHg (°C) (Recryst. solvent) | MS (*m/z*) ($M^+$) (Formula) | UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (log ε) | $^1$H-NMR ($CDCl_3$) δ |
|---|---|---|---|---|
| **6a** | 135/1.5 | 232<br>($C_{14}H_{16}OS$) | 243 (4.00), 255 (s) (3.92) | 1.30 (9H, s), 5.95 (1H, s), 7.13 (5H, s), 7.40 (1H, s) |
| **6b** | Oil | 190<br>($C_{11}H_{10}OS$) | 243 (4.02), 253 (s) (3.96) | 2.27 (3H, s), 5.99 (1H, s), 7.14 (5H, s), 7.40 (1H, s) |
| **6c** | 95<br>(*n*-Hexane) | 252<br>($C_{16}H_{12}OS$) | 247 (s) (4.22), 262 (s) (4.35), 269 (4.37), 273 (4.37), 280 (4.36), 294 (4.14) | 6.66 (1H, s), 7.12—7.73 (10H, m), 7.60 (1H, s) |
| **6d** | Oil | 232<br>($C_{14}H_{16}OS$) | 243 (3.98), 255 (3.90) | 0.77—1.82 (7H, m), 2.60 (2H, t, *J*=7.0), 5.98 (1H, s), 7.17 (5H, s), 7.42 (1H, s) |
| **6e** | Oil | 246<br>($C_{15}H_{18}OS$) | 242 (4.08), 250 (3.99) | 1.30 (9H, s), 2.33 (3H, s), 5.85 (1H, s), 7.06 (5H, s) |
| **6f** | Oil | 308<br>($C_{20}H_{20}OS$) | 248 (4.11), 292 (4.11) | 1.33 (9H, s), 5.97 (1H, s), 7.10—7.50 (8H, m), 7.70—8.00 (2H, m) |
| **6g** | Oil | 266<br>($C_{17}H_{14}OS$) | 248 (4.21), 294 (4.31) | 2.33 (3H, s), 6.01 (1H, s), 7.11—7.32 (8H, m), 7.82—7.98 (2H, m) |
| **6h** | Oil | 338<br>($C_{21}H_{22}O_2S$) | 247 (4.14), 300 (4.29) | 1.33 (9H, s), 3.67 (3H, s), 5.99 (1H, s), 6.76 (2H, d, *J*=16.0), 7.12 (5H, s), 7.83 (2H, d, *J*=16.0) |
| **6i** | Oil | 298<br>($C_{18}H_{18}O_2S$) | 245 (4.11), 294 (s) (4.24), 304 (4.26), 320 (s) (4.06) | 1.33 (9H, s), 5.98 (1H, s), 6.30—6.44 (1H, m), 6.67 (1H, d, *J*=3.0), 7.10—7.40 (6H, m) |

*a*) *Anal.* Calcd (Found) for **6a**: C, 72.39 (71.95); H, 6.94 (6.93); S, 13.80 (14.00). **6b**: C, 76.67 (76.67); H, 5.30 (5.45); S, 12.45 (12.28). **6c**: C, 76.18 (76.16); H, 4.80 (4.93); S, 12.69 (12.58). **6d**: C, 72.39 (72.59); H, 6.94 (7.04); S, 13.80 (14.06). **6e**: C, 73.14 (73.57); H, 7.37 (7.57); S, 12.99 (13.09). **6f**: C, 77.90 (77.87); H, 6.54 (6.61); S, 10.38 (10.53). **6g**: C, 69.46 (69.30); H, 5.30 (5.40); S, 16.83 (16.96). **6h**: C, 74.53 (74.35); H, 6.55 (6.64); S, 9.46 (9.82). **6i**: C, 72.46 (72.38); H, 6.08 (6.30); S, 10.73 (11.08).

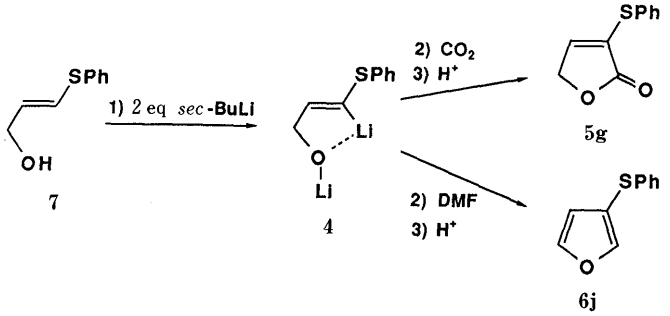


Chart 3

alated with 2.2 eq of *sec*-BuLi followed by treatment with $CO_2$ or DMF, 3-(phenylthio)-2(5*H*)-furanone (**5g**)[13] or 3-(phenylthio)furan (**6j**) were obtained in 50% or 45% yields, respectively (Chart 3).

The utility of this furan synthesis was extended to the preparation of a naturally occurring diphenylfuran. 2,5-Bis-(2′-methoxy-5′-methylphenyl)furan (**11**)[15] is a rare type of compound from *Berberis umbellata* WALL (Berberidaceae), a native of the main Himalayan region. 3-(Phenylthio)-propenal (**1**) was treated with 2-methoxy-5-methylphenyllithium (**8**), which was generated from the corresponding bromide with *n*-BuLi, in THF at −25 °C. *sec*-BuLi was then added and the resulting light brown solution was cooled to −78 °C and treated with 2-methoxy-5-methyl-

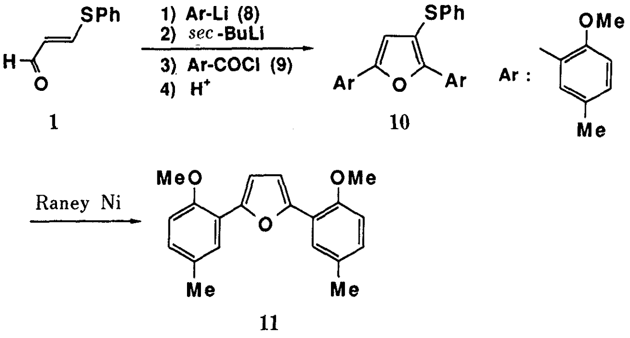
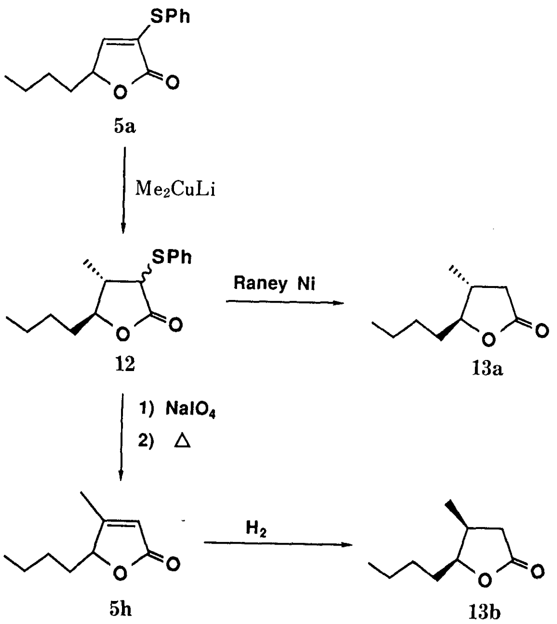


Chart 4



| catalyst | 13a : 13b |
|---|---|
| Pd-C | 44 : 56 |
| Pd-C/HCl | 23 : 77 |
| Rh-Al$_2$O$_3$ | 16 : 84 |

Chart 5

benzoyl chloride (**9**). Normal work-up gave 2,5-diaryl-3-(phenylthio)furan (**10**) in 26% yield. Desulfurization of **10** with Raney Ni afforded the diphenylfuran (**11**) in quantitative yield (Chart 4). Synthetic **11** was shown to be identical with 2,5-bis(2′-methoxy-5′-methylphenyl)furan (**11**) on the basis of the reported[15] melting point and spectroscopic ($^1$H-NMR, IR, and ultraviolet (UV)) comparisons.

Finally, the versatility of 3-(phenylthio)-2(5*H*)-furanones (**5**) as synthetic intermediates was demonstrated in the stereoselective synthesis[16] of *trans-* and *cis-quercus* lactones (**13a** and **13b**) (Chart 5). These lactones have been isolated from alcoholic beverages matured in oak barrels as aging aroma substances.[17,18] The conjugate addition of Me$_2$CuLi[13,19] to the furanone (**5a**) proceeded cleanly to give the lactone (**12**) in 91% yield. Compound **12** was desulfurized by Raney Ni in nearly quantitative yield to afford *trans-quercus* lactone (**13a**). On the other hand, oxidation of **12** with NaIO$_4$ followed by thermolysis[13,18] provided the furanone (**5h**)[18,20] in 86% yield. Catalytic hydrogenation using 10% Pd–C in EtOH–10% HCl (9 : 1)[21] of **5h** proceeded in a quantitive yield to furnish *cis-quercus* lactone (**13b**) as the major stereoisomer (**13b** : **13a** = 77 : 23).[22] When Rh–Al$_2$O$_3$[23] was employed as a catalyst in the above reaction, a higher stereoselectivity was observed (**13b** : **13a** = 84 : 16).[22]

In conclusion, we have shown that 3-(phenylthio)propenal is a useful synthon for the convenient preparation of 2(5*H*)-furanone and furan derivatives. The developed methodology was demonstrated to be applicable for the efficient synthesis of naturally occurring lactones and furan derivatives.

## Experimental

All melting points are uncorrected. The IR spectra were obtained in KBr disk using a JASCO 810 spectrophotometer. The UV spectra were recorded in 95% ethanol on a Hitachi 323 spectrophotometer. The $^1$H-NMR spectra were obtained with JEOL FX 90Q, JEOL JNM-PMX 60, and JEOL JNM GX-400 spectometers using CDCl$_3$ as a solvent and tetramethylsilane as an internal reference. Elemental analyses were performed at the Microanalytical Laboratory of the Center for Instrumental Analysis in Nagasaki University. All solvents used for lithiation reaction were freshly distilled from sodium benzophenone ketyl before use. Chromatography was carried out by flash chromatography on a column of Kieselgel 60 (230—400 mesh).

**3-(Phenylthio)propenal (1)** A solution of Et$_3$N (0.4 ml) in CCl$_4$ (3 ml) was added dropwise to a stirred mixture of thiophenol (12.12 g, 0.11 mol) and acrolein (6.22 g, 0.1 mol) in CCl$_4$ (100 ml) at 0 °C. The cooling bath was removed, and the solution was stirred at room temperature for 2 h. The solvent was evaporated off to leave a viscous oil, which was distilled by bulb-to-bulb distillation to afford 3-(phenylthio)propionaldehyde (14.8 g, 89%, bp 76 °C/0.2 mmHg). IR (neat): 1724 cm$^{-1}$. $^1$H-NMR $\delta$: 2.61—2.85 (2H, m), 3.06—3.32 (2H, m), 7.30 (5H, s), 9.75 (1H, t, $J$ = 1.0 Hz). *N*-Chlorosuccinimide (7.6 g, 57 mmol) was added to a solution of the sulfide (8.7 g, 52 mmol) in benzene (150 ml) at 0 °C, and the suspension was stirred for 1 h at the same temperature and then for an additional 2 h at room temperature. The reaction mixture was cooled with an ice bath, and a solution of Et$_3$N (22 ml) in benzene (60 ml) was added at 0 °C. The solution was stirred at 0 °C for 2 h and at room temperature for 2 h, then washed with water and saturated NH$_4$Cl solution. The organic phase was dried (Na$_2$SO$_4$) and evaporated to give crude 3-(phenylthio)propenal (**1**), which was chromatographed over silica gel with benzene–petroleum ether (1 : 1) to afford **1**[11] (5.7 g, 67%, bp 95 °C/1.2 mmHg). IR (neat): 1675 cm$^{-1}$. $^1$H-NMR $\delta$: 5.98 (1H, dd, $J$ = 9, 16 Hz), 7.47 (5H, s), 7.60 (1H, d, $J$ = 16 Hz), 9.40 (1H, d, $J$ = 9 Hz)

### General Procedure for the Syntheses of 3-(Phenylthio)-2(5*H*)-furanones (5)

**i) Using Lithium Reagents** The following procedure for the synthesis of 5-(*n*-butyl)-3-(phenylthio)-2(5*H*)-furanone (**5a**) using lithium reagents is representative; the other 2(5*H*)-furanones (**5b**, **c**, **d**, and **f**) were obtained similarly.

**5-(*n*-Butyl)-3-(phenylthio)-2(5*H*)-furanone (5a)** A solution of *n*-BuLi (1.18 M in hexane, 1.9 ml, 2.2 mmol) was injected into a stirred solution of 3-(phenylthio)propenal (**1**; 0.33 g, 2.0 mmol) in THF (15 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred for 30 min at the same temperature, and a solution of *sec*-BuLi (0.80 M in cyclohexane, 2.8 ml, 2.2 mmol) was injected. The mixture was stirred for 30 min, and then the dry ice-acetone bath was removed. After being stirred for an additional 15 min, the solution was again cooled to −78 °C and then CO$_2$ gas was passed through it. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with saturated NH$_4$Cl solution, acidified with 10% HCl and evaporated under reduced pressure. The residue was extracted with ether and the ether layer was separated, and washed successively with 5% NaHCO$_3$ solution and brine. The extract was dried (Na$_2$SO$_4$) and evaporated to dryness to give crude **5a** as a viscous oil. This oil was chromatographed over silica gel using benzene as an eluent to give pure **5a** (0.44 g, 89%).

**5-Phenyl-3-(phenylthio)-2(5*H*)-furanone (5f)** The crude **5f** was prepared in 60% yield starting from **1** with phenyllithium under similar reaction conditions to those described above. A pure sample of **5f** (40%, mp 122 °C) was obtained from the crude compound by washing with ether. **5f** was extremely unstable and dimerized during recrystallization to give 2,2′-diphenyl-4,4′-bis(phenylthio)-2,2′,3′,4′,5,5′-hexahydro-2,3′-bifuran-

5,5′-dione, mp 153—154 °C (ether). MS *m*/*z*: 535 $(M-1)^+$. IR: 1770 $cm^{-1}$. UV: 251 (4.13), 279 nm (log ε 4.08). $^1$H-NMR (400 MHz) δ: 3.19 (1H, dd, *J*=7.3, 8.8 Hz), 3.55 (1H, d, *J*=7.3 Hz), 5.18 (1H, d, *J*=7.3 Hz), 6.16 (2H, d, *J*=8.4 Hz), 6.65 (1H, s), 6.85—7.56 (18H, m). *Anal.* Calcd for $C_{32}H_{24}O_4S_2$: C, 71.62; H, 4.51; S, 11.95. Found: C, 71.51; H, 4.69; S, 11.87.

**ii) Using Grignard Reagents** The following procedure for the synthesis of 5-ethyl-3-(phenylthio)-2(5*H*)-furanone (**5e**) using Grignard reagents is representative; the other 2(5*H*)-furanone (**5d**) was obtained similarly.

**5-Ethyl-3-(phenylthio)-2(5*H*)-furanone (5e)** A solution of EtMgBr (0.90 M in THF, 4.0 ml, 3.6 mmol) was injected into a stirred solution of **1** (0.49 g, 3.0 mmol) in THF (30 ml) at −78 °C under a nitrogen atmosphere. After the solution was stirred for 1 h at the same temperature, a solution of *sec*-BuLi (0.74 M in cyclohexane, 14.9 ml, 11.0 mmol) was injected. The mixture was stirred for 1 h, and then the dry ice-acetone bath was removed. After being stirred for 15 min, the solution was again cooled to −78 °C and then $CO_2$ gas was passed through the solution. The reaction mixture was allowed to warm to room temperature and stirred overnight. Standard work-up in a similar manner to that described for **5a** gave **5e** (0.40 g, 61%) after chromatographic purification.

**General Procedure for the Syntheses of 3-(Phenylthio)furans (6)** The following procedure for the synthesis of 2-methyl-4-(phenylthio)furan (**6b**) is representative; the other furans were obtained similarly.

**2-Methyl-4-(phenylthio)furan (6b)** A solution of MeLi (1.08 M in diethylether, 2.8 ml, 3.0 mmol) was injected into a stirred solution of **1** (0.33 g, 2.0 mmol) in THF (15 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred for 30 min at the same temperature, then a solution of *sec*-BuLi (0.71 M in cyclohexane, 3.4 ml, 2.4 mmol) was injected. The mixture was stirred for 30 min, and then the dry ice-acetone bath was removed. After being stirred for an additional 15 min, the solution was again cooled to −78 °C and a solution of DMF (0.29 g, 4.0 mmol) in THF (3 ml) was added. The mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched and acidified with 10% HCl, and evaporated. The residue was extracted with ether and the ether layer was separated, and washed successively with 5% $NaHCO_3$ solution and brine. The extract was dried ($Na_2SO_4$), and evaporated to dryness to give an oil which was purified by chromatography to afford pure **6b** (0.27 g, 71%).

**3-(Phenylthio)-2(5*H*)-furanone (5g)** A solution of *sec*-BuLi (0.64 M in cyclohexane, 10.8 ml, 6.9 mmol) was injected into a stirred solution of 3-(phenylthio)-2-propen-1-ol$^{11)}$ (**7**; 0.50 g, 3.0 mmol), which was prepared by the reduction of **1** with $NaBH_4$ in EtOH, in THF (20 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred for 1 h and then the dry ice-acetone bath was removed. After being stirred for an additional 15 min, the solution was again cooled to −78 °C and $CO_2$ gas was passed through the solution. Then the reaction mixture was allowed to warm to room temperature and stirred overnight. Standard work-up gave crude **5g**, which was recrystallized from ether to afford pure **5g** (0.29 g, 50%, mp 59.5—60.5 °C) (lit.$^{13)}$ mp 57.5—59 °C).

**3-(Phenylthio)furan (6j)** A solution of *sec*-BuLi (0.71 M in cyclohexane, 8.5 ml, 5.0 mmol) was injected into a stirred solution of **7** (0.42 g, 2.5 mmol) in THF (20 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred for 1 h and then the dry ice-acetone bath was removed. After being stirred for an additional 15 min, the solution was again cooled to −78 °C and a solution of DMF (0.37 g, 5.0 mmol) in THF (3 ml) was injected. Then the reaction mixture was allowed to warm to room temperature and stirred overnight. Standard work-up gave **6j** (0.20 g, 45%, oil) after chromatographic purification. MS *m*/*z*: 176 $(M^+)$. UV: 244 (4.00), 255 nm (sh) (log ε 3.92). $^1$H-NMR δ: 6.41 (1H, d, *J*=2.4 Hz), 7.17 (5H, s), 7.42—7.58 (2H, m). *Anal.* Calcd for $C_{10}H_8OS$: C, 68.18; H, 4.58; S, 18.17. Found: C, 68.30; H, 4.73; S, 18.29.

**2,5-Bis(2′-methoxy-5′-methylphenyl)furan (11)** A solution of **1** (0.66 g, 4.0 mmol) in THF (5 ml) was injected at −78 °C into a THF (30 ml) solution of the lithio species (**8**; 5.0 mmol) which was generated *in situ* from 2-methoxy-5-methylphenylbromide with *n*-BuLi at −25 °C. The reaction mixture was warmed to 0 °C for 30 min and then cooled to −78 °C. A solution of *sec*-BuLi (0.71 M in cyclohexane, 7.0 ml, 5.0 mmol) was injected into the solution and the reaction mixture was stirred for 30 min at −78 °C, and then warmed to 0 °C. After being stirred for 30 min at the same temperature, the mixture was cooled to −78 °C. A solution of 2-methoxy-4-methylbenzoyl chloride (**9**; 1.11 g, 6.0 mmol) in THF (5 ml) was added to the mixture. The reaction mixture was stirred for 30 min and then allowed to warm to room temperature and stirred overnight. Standard work-up gave **10** (0.44 g, 26%, mp 138—139 °C) after recrystallization from ether. MS *m*/*z*: 416 $(M^+)$. UV: 240 (sh) (4.31), 252 (sh) (4.24), 277 (4.28), 326 nm (log ε 4.36). $^1$H-NMR δ: 2.30 (3H, s), 2.32 (3H, s), 3.67 (3H, s), 3.84 (3H, s), 6.76—7.32 (11H, m), 7.70 (1H, d, *J*=2.2 Hz). *Anal.* Calcd for $C_{26}H_{24}O_3S$: C, 74.98; H, 5.81; S, 7.68. Found: C, 74.94; H, 5.84; S, 7.62. A solution of **10** (0.44 g) and Raney Ni (1.5 g) in EtOH (30 ml) was refluxed for 2 h. The reaction mixture was filtered, and the filtrate was evaporated under reduced pressure to give a residue, which was recrystallized from MeOH to afford pure **11** quantitatively (mp 114—115 °C) (lit.$^{15)}$ mp 110 °C). MS *m*/*z*: 308 $(M^+)$. IR: 740, 795, 1030, 1145, 1245, 1275, 1510, 1610, 2840, 2920 $cm^{-1}$. UV: 234 (4.20), 246 (sh) (3.99), 254 (sh) (3.79), 294 (4.04), 307 (4.06), 328 (sh) (4.38), 345 (4.58), 363 nm (log ε 4.47). $^1$H-NMR δ: 2.39 (6H, s), 3.92 (6H, s), 6.86 (2H, d, *J*=8.4 Hz), 7.02 (2H, dd, *J*=8.4, 2.3 Hz), 7.02 (2H, s), 7.78 (2H, d, *J*=2.3 Hz). *Anal.* Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.80; H, 6.58.

**(±)-*trans-Quercus* Lactone (13a) and *cis-Quercus* Lactone (13b)** A solution of furanone (**5a**: 0.45 g, 1.8 mmol) in THF (5 ml) was added dropwise to a stirred solution of lithium dimethylcuprate (3.6 mmol)$^{13,19)}$ in THF (30 ml) at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred for 3 h at the same temperature. Then the mixture was quenched with saturated $NH_4Cl$ solution and evaporated. The residue was extracted with ether and the ether layer was washed successively with 10% HCl, 5% $NaHCO_3$ solution and brine, dried ($Na_2SO_4$) and evaporated. The residue was chromatographed over silica gel using benzene as an eluent to afford **12** (0.44 g, 91%) which, without further purification, was used in the subsequent reactions. A solution of **12** (0.44 g, 1.7 mmol) and Raney Ni (1.5 g) in EtOH (30 ml) was refluxed for 1 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to afford **13a**$^{22)}$ in quantitative yield. On the other hand, a solution of **12** (0.26 g, 1.0 mmol) in MeOH (5 ml) was added to a solution of $NaIO_4$ (0.26 g, 1.2 mmol) in water (5 ml) and the reaction mixture was stirred for 24 h at room temperature. The mixture was filtered and the solvent was evaporated off under reduced pressure to give the corresponding sulfoxide which was dissolved in toluene (10 ml). The solution was refluxed for 2 h. The solution was evaporated off under reduced pressure to give a residue, which was chromatographed over silica gel using benzene as an eluent to afford **5h** (0.13 g, 86%, oil, lit.$^{20)}$ bp 70—100 °C/0.15 mmHg).$^{18,20)}$ Catalytic hydrogenations of **5h** were carried out at room temperature under a hydrogen atmosphere by using a balloon under the following conditions: a) a solution of **5h** (0.08 g, 0.5 mmol) in EtOH (10 ml) was hydrogenated over 10% Pd–C (0.08 g) for 12 h; b) a solution of **5h** (0.13 g, 0.84 mmol) in EtOH–10% HCl (9 : 1, 30 ml) was hydrogenated over 10% Pd–C (0.03 g) for 24 h; c) a solution of **5h** (0.06 g, 0.4 mmol) in ethyl acetate (10 ml) was hydrogenated over 5% Rh–$Al_2O_3$ (0.06 g) for 24 h. After standard work-up, mixtures$^{22)}$ of **13b** and **13a** were obtained in quantitative yield with the following ratios: **13b** : **13a** = 56 : 44 from a), 77 : 23 from b), 84 : 16 from c).$^{22)}$

### References and Notes

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