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1,1-Diphenoxy-2-(phenylsulfonyl)cyclopropane as a Furan Annulating Agent

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Abstract: Reactions of the lithio derivative **2** derived from 1,1-diphenoxy-2-(phenylsulfonyl)cyclopropane (**1**) with both acyl chlorides and acyl imidazoles yielded dihydrofurans **5** which could be transformed to the corresponding furans **6** by treatment with a catalytic amount of *p*-toluenesulfonic acid.
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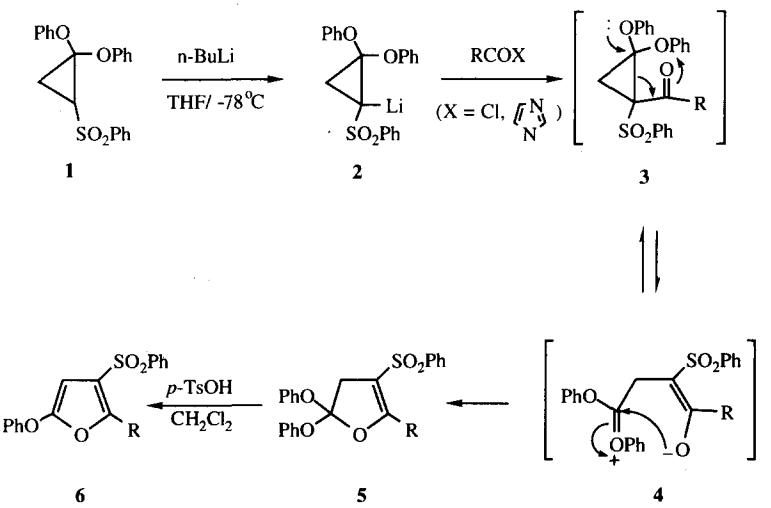
Development of synthetic transformations based on cyclopropane ring-opening reactions has been extensively investigated.[1] Particularly, cyclopropanes containing donor and acceptor functionalities have been often utilized as three-carbon building blocks for the construction of five-membered carbo-[2] and heterocycles.[3] Especially, dihydrofuran and furan derivatives which are found in many biologically active natural products, their syntheses have received considerable attention.[4] Moreover, they are useful synthetic intermediates, and serve as versatile building blocks in organic synthesis.[5] This led us to investigate the possibilities of using 1,1-diphenoxy-2-(phenylsulfonyl)cyclopropane (**1**)[6] as a furan annulation agent.

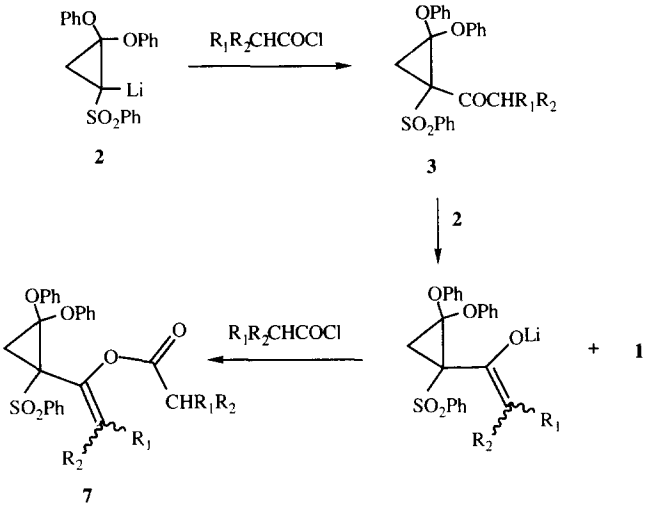
Recently, we have been engaged in the study of the reaction of the lithio derivative **2** derived from vicinally donor-acceptor substituted cyclopropane **1** with various alkylating agents. The results have shown that the cyclopropane **1** can serve as a useful β-lithio acrylate synthon.[7] As an extension of our earlier work, we set out to investigate the acylation reaction of the **2**, expecting to receive highly activated cyclopropanes of type **3**, which would readily undergo ring-opening reaction to zwitterion intermediates of type **4**. Cyclization of **4** would lead to dihydrofurans **5** and finally to substituted furans **6** after elimination of phenol. In this paper, we report a general route for the preparation of **6** by employing the donor-acceptor substituted cyclopropane **1** as illustrated in Scheme I.[8]

Our initial efforts were to examine the reaction of **2** with acyl chlorides. Treatment of **2** with freshly distilled benzoyl chloride (1.2 equiv) in the presence of hexamethylphosphoramide (HMPA) at -78 °C, then slowly warming up to reach room temperature overnight (14 h) followed by workup with water gave a crude product, of which ^{1}H NMR spectrum showed no signals of cyclopropyl protons of **3a**. It revealed only peaks at δ 5.93 ppm as a singlet and at δ 6.83-8.13 ppm as a multiplet due to aromatic protons. Furthermore, the IR spectrum of this product indicated the absence of carbonyl absorption. It was finally confirmed to be a furan derivative **6a** (52% yield, Table 1; entry 1) by a mass spectrum (M^+, 376) and a correct elemental analysis. The formation of the furan **6a** resulted from ring-opening of the initially formed acylated cyclopropane **3a** to a dipolar intermediate of type **4a** (R= Ph), which readily cyclized to a dihydrofuran **5a**. Elimination of phenol from dihydrofuran **5a** to afford substituted furan **6a** was presumably catalyzed by traces of acid during workup. When the reaction mixture was carefully worked up by quenching with a saturated sodium hydrogen carbonate solution, the expected dihydrofuran **5a** could be isolated in good yield. Thus, the reaction of **2** with benzoyl chloride (1.2 equiv) in the presence of HMPA at -78 °C for 1 h provided dihydrofuran **5a** in 70% yield (Table 1, entry 3); a lower yield of **5a** (62%; Table 1, entry 2) was obtained when the reaction was performed at -78 °C (1 h) followed by stirring at 0 °C (1 h). In all cases, no detectable amount of the benzoylated product of type **3a** (R= Ph) could be isolated. Comparable results could be achieved when the reactions were carried out in the absence of HMPA. As shown in Table 1; entry 4, addition of benzoyl chloride (1.1-1.2 equiv) to the THF solution of **2** at -78 °C followed by slowly warmup to room temperature (14 h) gave dihydrofuran **5a** in 79% yield after quenching the reaction mixture with a saturated sodium hydrogen carbonate solution and chromatographic separation.

Scheme I



Scheme II



Having succeeded in preparing the dihydrofuran **5a**, we tried to extend this experiment to other acid chlorides in order to test the generality of the reaction. As expected, the lithio derivative **2** combined with *p*-toluyl chloride furnished **5b** in good yield (79%: Table 1; entry 5). Pivaloyl chloride reacted with **2** in the presence of HMPA at -78 °C (1 h) and at 0 °C (1 h) provided **5c** as the sole product in 70% yield (Table 1; entry 6). The reaction at higher temperature and longer reaction time led to lower yields of the expected **5c** (37-45%) accompanying with **6c** (15-24%: Table 1; entries 7 and 8). We observed that **5c** could be easily converted into furan **6c** quantitatively as we tried to recrystallize it from a mixture of ethyl acetate and hexane. The reaction of **2** with enolized acyl chlorides, e.g. isobutyryl chloride in the presence of HMPA (-78 °C, 1 h and 0 °C, 1 h), on the other hand, afforded a mixture of dihydrofuran **5d** (45%), the recovered starting cyclopropane **1** (15%) and an unexpected product **7a** (12%) (Table 1; entry 9). The formation of compounds of type **7** resulted from deprotonation of the initially formed acylated cyclopropanes of type **3** by **2** giving rise to the corresponding enolate anion, which readily reacted with excess acyl chlorides (Scheme II). This process occurred presumably faster than the ring-opening process leading to the dihydrofurans of type **5**. The results also suggested that the reactivity of the lithio derivative **2** was apparently low. Attempt to react **2** with isobutyryl chloride at -78 °C to room temperature overnight afforded a comparable yield of **5d**. The reaction of **2** with butyryl and valeroyl chlorides afforded similar results (Table 1; entries 10 and 11).

Table 1 Preparation of dihydrofurans **5** by treatment of the lithio derivative **2** with acyl chlorides.

Entry	RCOCl	Conditions	Products	Yields (%)[a]
1	PhCOCl	HMPA/-78 °C to RT, 14 h	**6a**, R = Ph	52%
2	PhCOCl	HMPA/-78 °C, 1 h	**5a**, R = Ph	62%
3	PhCOCl	HMPA/-78 °C, 1 h	**5a**, R = Ph	70%
4	PhCOCl	-78 °C to RT, 14 h	**5a**, R = Ph	79%
5	*p*-TolylCOCl	-78 °C to RT, 14 h	**5a**, R = *p*-Tolyl	79%
6	*t*-BuCOCl	HMPA/-78 °C, 1 h; 0 °C, 1h	**5c**, R = *t*-Bu	70%
7	*t*-BuCOCl	HMPA/-78 °C to RT, 14 h	**5c**, R = *t*-Bu	37%
			6c, R = *t*-Bu	24%
8	*t*-BuCOCl	-78 °C to RT, 14 h	**5c**, R = *t*-Bu	45%
			6c, R = *t*-Bu	15%
9[b]	*i*-PrCOCl	HMPA/-78 °C, 1 h; 0 °C, 1 h	**5d**, = *i*-Pr	45%
			7a, $R_1 = R_2$ = Me	12%
10[b]	*n*-PrCOCl	-78 °C to RT, 14 h	**5e**, R = *n*-Pr	25%
			7b, R_1 = H; R_2 =Et	13%
11[b]	*n*-BuCOCl	-78 °C to RT, 14 h	**5f**, R = *n*-Bu	18%
			6f, R = *n*-Bu	7%
			7c, R_1 = H; R_2 = *n*-Pr	19%

a) Yields of isolated products.

b) The starting cyclopropane could also be isolated (see the experimental part).

Since **2** reacted with enolized acyl chlorides to provide not only the expected dihydrofurans **5,** but also the undesirable products **7**, therefore the reaction with acyl imidazoles were examined. As expected, when **2** was treated with benzoyl imidazole (1.2 equiv) in the absence of HMPA at -78 ° to 0 °C, a good yield of **5a** (90%) was obtained. Enolized isobutyryl imidazole combined with **2** to afford as well the desired product **5d** in 65% yield. It should be noted that better results were obtained and no traces of the by-products of type **7** could be detected. The results with other acyl imidazoles are summarized in Table 2.

Table 2 Preparation of dihydrofurans **5** by treatment of the anion **2** with acyl imidazoles.

Entry	RCOIm	Products 5	Yields (%)[a]
1	PhCOIm	**5a**	90%
2	p-TolylCOIm	**5b**	84%
3	*t*-BuCOIm	**5c**	67%
4	*i*-PrCOIm	**5d**	65%
5	*n*-PrCOIm	**5e**	51%
6	*n*-BuCOIm	**5f**	47%
7	n-C_5H_{11}COIm	**5g**	48%

a) Yields of isolated products.

Substituted furans **6** could be easily prepared from dihydrofurans **5** by treatment with *p*-toluenesulfonic acid in dry dichloromethane at room temperature overnight (12-14 h). Good yields of the desired furans **6** were obtained. The results are listed in Table 3.

Table 3 Preparation of furans **6** from dihydrofurans **5**.

Dihydrofuran 5	Furan 6 (% yield)[a]
5a	**6a,** R = Ph (82%)
5b	**6b,** R = *p*-Tolyl (74%)
5c	**6c,** R = *t*-Butyl (81%)
5d	**6d,** R = *i*-Propyl (79%)
5e	**6e,** R = *n*-Propyl (77%)
5f	**6f,** R = *n*-Butyl (74%)
5g	**6g,** R = *n*-Pentyl (84%)

a) The starting dihydrofurans **5** could be recovered in 10 to 15% yields.

From our above results, it was clearly demonstrated that the lithio derivative **2** derived from 1,1-diphenoxy-2-(phenylsulfonyl)cyclopropane (**1**), which is a vicinally donor-acceptor substituted cyclopropane, could function as a useful three-carbon furan annnulating agent. Thus, a new and versatile method for the synthesis of substituted furans has been achieved.

EXPERIMENTAL SECTION

General: Melting points were determined by an Electrothermal Apparatus and a Buechi 510 Melting Point Apparatus and are uncorrected. ^{1}H NMR spectra were measured with a Varian EM-360L spectrometer using TMS as an internal reference and reported in parts per million (ppm). IR spectra were recorded on a Jasco A-302 Spectrophotometer. Mass spectra were obtained on an INCOS 50 Mass Spectrometer at 70 eV. Elemental analyses were performed by using a Perkin Elmer Elemental Analzer 2400 CHN. Acyl imidazoles were prepared according to the literature procedure[9] and used without further purification.

Reactions of 2 with Acyl imidazoles (*Method A*) and Acyl chlorides (*Method B*)

Preparation of 2,2-Diphenoxy-5-phenyl-4-(phenylsulfonyl)-2,3-dihydrofuran (5a).

General procedure:

Method A: To a cooled (-78 °C) THF (10 ml) solution of 1,1-diphenoxy-2-(phenylsulfonyl)cyclopropane (**1**) (0.36 g, 1 mmol) under an argon atmosphere, was added dropwise *n*-BuLi (1.37 M solution in hexane, 0.91 ml, 1.25 mmol). Stirring was continued under argon at -78 °C for 1 h in order to obtain complete formation of the lithio derivative **2**. A THF solution of freshly prepared benzoyl imidazole (0.22 g, 1.25 mmol) was added. The reaction mixture was kept stirring at -78 °C for 1 h and then at 0 °C for 1 h and quenched with a saturated ammonium chloride solution (5 ml). The mixture was diluted with water (10 ml)and extracted with ethyl acetate (3x20 ml). The combined extract was washed with H_2O (3x10 ml), brine (10 ml) and dried over anhydrous Na_2SO_4. The crude product was purified by radial chromatography (silica gel, 10-20% ethyl acetate in hexane) to give the starting cyclopropane **1** (0.26 g, 8%) and a colorless viscous liquid of **5a** (0.42 g, 90%). ^{1}H NMR (CCl_4): δ 3.5 (*s*, 2H, methylene protons), 6.9-7.8 (*m*, 20H, SO_2*Ph* and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3160, 1590, 1480, 1450, 1300, 1140, 920, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 376 (M^+-94, 39), 283(0.7), 207(25), 191(7), 178(19), 142(10), 125(23), 114(37), 105(46), 94(25), 77(100), 65(22). Anal. Calcd for $C_{28}H_{22}O_5S$: C, 71.47; H, 4.71. Found: C, 71.17; H, 4.83.

Method B: To the THF (10 ml) solution of **2** at -78 °C, freshly distilled benzoyl chloride (0.15 ml, 1.25 mmol) was added and the resulting mixture was slowly warmed up to room temperature overnight (16 h). The mixture was quenched with water (10 ml) and extracted with ethyl acetate (3x20 ml). The combined extract was washed with a saturated $NaHCO_3$ solution (15 ml), water (2x15 ml), brine (15 ml) and dried over anhydrous Na_2SO_4. The organic phase was concentrated to give a crude yellow liquid, which was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to give a colorless liquid of **5a** (0.3710 g, 79%) and the starting cyclopropane **1** (0.0439 g, 12%).

2,2-Diphenoxy-4-(phenylsulfonyl)-5-(*p*-tolyl)-2,3-dihydrofuran (5b).

Method A: Treatment of **2** (1 mmol) with *p*-toluyl imidazole (0.23 g, 1.25 mmol) gave a crude yellow solid. It was purified by radical chromatography (silica gel, 10% ethyl acetate in hexane) to give the starting compound **1** (0.0356 g, 10%) and a solid product of **5b** (0.40 g, 84%; a white solid, mp 97-98 °C, from ethyl acetate in hexane). ^{1}H NMR (CCl_4): δ 2.4 (*s*, 3H, CH_3-Ar), 3.45 (*s*, 2H, CH_2CO), 6.9-7.9 (*m*, 19H, SO_2*Ph* and Ar*H*). IR (nujol): $\sqrt{}_{max}$ 3000, 2590, 1640, 1590, 1450, 1380, 1320, 1300, 1250, 1210, 1160, 1120, 1060, 980, 870, 820, 770, 720, 680 cm^{-1}. MS: m/e (%) relative intensity: 390(M^+-94, 32), 249(0.9), 221(74), 156(19), 141(8), 119(74), 94(40), 77(100), 65(31). Anal. Calcd for $C_{29}H_{24}O_5S$: C, 71.88; H, 4.99. Found: C, 71.63; H, 4.79.

Method B: The lithio derivative **2** (1 mmol) was treated with *p*-toluyl chloride (0.16 ml, 1.25 mmol) to give a crude yellow solid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to afford a solid product of **5b** (0.3818 g, 79%) and the starting compound **1** (0.0198 g, 14%).

5-*t*-Butyl-2,2-diphenoxy-4-(phenylsulfonyl)-2,3-dihydrofuran (5c).

Method A: Treatment of **2** (1 mmol) with pivaloyl imidazole (0.19 g, 1.25 mmol) gave a crude vicous product. It was purified by radial chromatography (silica gel, 10 % ethyl acetate in hexane) to give the starting compound **1** (0.09 g, 27%) and a white solid of **5c** (0.30 g, 67%; mp 74-75 °C, from ethyl acetate in hexane). ^{1}H NMR (CCl_4): δ 1.4 (s, 9H, *t*-butyl group), 3.3 (s, 2H, CH_2CO), 6.8-7.9 (*m*, 15H, SO_2Ph and Ar*H*). IR (nujol): $\sqrt{}_{max}$ 2970, 3060, 1590, 1490, 1450, 1305, 1295, 1250, 1140, 1110, 1060, 920, 750, 720, 680 cm^1. MS: m/e (%) relative intensity 356(M^+-94, 32), 341(37), 309(1.6), 263(9.8), 223(1.1), 203(2.5), 188(1.6), 171(2.6), 141(6), 125(100), 107(5.9), 105(6.6), 97(13.7), 94(17), 77(45), 65(13), 57(8.9), 51(9.8). Anal. Calcd for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.81. Found; C, 69.20; H, 5.82.

Method B: The lithio derivative **2** (1 mmol) was treated with pivaloyl chloride (0.15 ml, 1.25 mmol) to give a crude viscous liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to afford a solid of **5c** (0.1998 g, 45%), furan **6c** (0.0158 g, 15%) and the starting compound **1** (0.1280 g, 35%).

2,2-Diphenoxy-5-isopropyl-4-(phenylsulfonyl)-2,3-dihydrofuran (5d).

Method A: Treatment of **2** (1 mmol) with isobutyryl imidazole (0.16 g, 1.25 mmol) gave a yellow vicous liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to give the starting compound **1** (0.046 g, 13%) and a colorless vicous liquid of **5d** (0.28 g, 65%). ^{1}H NMR (CCl_4): δ 1.1 [d, J = 7 Hz, 6H, $(CH_3)_2$CH)], 3.2 (s, 2H, CH_2CO), 3.6-4.0 (m, 1H, methine proton), 6.8-7.9 (m, 15H, SO_2Ph and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3100, 3000, 1640, 1590, 1490, 1450, 1300, 1250, 1160, 1120, 1050, 980, 920, 760, 720, 680, 600 cm^{-1}. MS: m/e (%) relative intensity 342(M^+-94, 34), 327(13), 295(0.4), 249(28), 217(4), 200(29), 173(9), 143(23), 125(100), 107(55), 94(18), 77(68), 65(18). Anal. Calcd for $C_{25}H_{24}O_5S$: C, 68.78; H 5.54. Found: C, 68.83; H, 5.48.

Method B: **2** (2 mmol) was treated with isobutyryl chloride (0.26 ml, 2.5 mmol) to give a crude yellow liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to afford a colorless liquid of **5d** (0.38 g, 45%), the starting compound **1** (0.11 g, 15%) and compound **7a** (0.13 g, 12%). **7a**: mp 183-185 °C (ethyl acetate in hexane). ^{1}H NMR ($CDCl_3$): δ 0.83-1.66 [m, 12H, $(CH_3)_2$CH and $(CH_3)_2$C=C], 1.93 and 2.76 (each d, J = 7 Hz, 2H, cyclopropyl protons), 2.05-2.6 (m, 1H, CHCO), 6.67-8.20 (m, 15H, Ar*H*). IR (nujol): $\sqrt{}_{max}$ 2950, 1760, 1600, 1500, 1460, 1380, 1320, 1200, 1170, 1120, 980, 950, 760, 690 cm^{-1}. MS: m/e (%) relative intensity: 506 (M^+, 0.11), 277(100), 201(9), 125(8), 77(26).

2,2-Diphenoxy-5-*n*-propyl-4-(phenylsulfonyl)-2,3-dihydrofuran (5e).

Method A: Treatment of **2** (1 mmol) with butyryl imidazole (0.17 g, 1.25 mmol) gave a yellow liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to give the starting compound **1** (0.11 g, 30%) and a colorless viscous liquid of product **5e** (0.22 g, 51%). ^{1}H NMR (CCl_4): δ 0.96 (t, J = 7 Hz, 3H, methyl protons), 1.2-1.9 (m, 2H, $CH_3CH_2CH_2$), 2.7 (t, J = 7 Hz, 2H, $C{=}CCH_2CH_2$), 3.2 (s, 2H, CH_2CO), 6.8-7.9 (m, 15H, SO_2Ph and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3050, 2950, 1640, 1590, 1480, 1440, 1300, 1260, 1120, 1100, 1060, 960, 920, 740, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 342(M^+-94, 6), 316(6), 265(0.1), 249(4), 173(5), 141(10), 125(47), 115(5), 107(32), 94(30),77(100), 65(32), 51(43). Anal. Calcd for $C_{25}H_{24}O_5S$: C, 68.78; H, 5.54. Found: C, 68.87; H, 5.68.

Method B: **2** (1 mmol) was treated with butyryl chloride (0.13 ml, 1.25 mmol) to give a crude yellow liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to afford a colorless liquid of **5e** (0.11 g, 25%), the starting compound **1** (0.0815 g, 22%) and compound **7b** (0.0638 g, 13%; as a liquid).

7b: ^{1}H NMR ($CDCl_3$): δ 0.6 (t, J = 7 Hz, 3H, methyl protons), 0.85 (t, J = 7 Hz, 3H, methyl protons), 1.2-2.7 (m, 8H, methylene protons), 5.0 (t, J = 7 Hz, olefinic protons), 7.0-8.2 (m, 15H, SO_2Ph and Ar*H*). IR (neat): √max 3050, 2950, 1755, 1590, 1480, 1450, 1420, 1310, 1300, 1160, 1120, 1070, 1020, 960, 840, 730, 680 cm^{-1}. MS: m/e (%) relative intensity 506(M^+, 0.1), 413(1), 365(3), 342(10), 295(5), 277(100), 249(4), 225(8), 201(23), 183(24), 171(5), 155(9), 131(18), 125(26), 94(12), 77(68).

5-*n*-Butyl-2,2-diphenoxy-4-(phenylsulfonyl)-2,3-dihydrofuran (5f).

Method A: Treatment of **2** (1 mmol) with *n*-valeroyl imidazole (0.19 g, 1.25 mmol) gave a yellow liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to give the starting compound **1** (0.18 g, 50%) and **5f** as a white solid (0.21 g, 47%; mp 102-103 °C, from ethyl acetate in hexane). ^{1}H NMR (CCl_4): δ 0.7-1.8 (m, 7H, $CH_3CH_2CH_2CH_2$), 2.6-3.0 (m, 2H, CH_2CH_2C=C), 3.2 (s, 2H, CH_2CO), 6.9-7.9 (m, 15H, SO_2Ph and Ar*H*). IR ($CHCl_3$): $\sqrt{}_{max}$ 3050, 2950, 1640, 1595, 1495, 1450, 1300, 1250, 1150, 1110, 1100, 1060, 960, 920 cm^{-1}. MS: m/e (%) relative intensity 356(M^+-94, 49), 313(20), 263(20), 215(8), 203(4), 179(6), 141(12), 125(62), 121(68), 94(44), 85(10), 77(100), 65(35). Anal. Calcd for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.81. Found: C, 69.46; H, 5.75.

Method B: **2** (1 mmol) was treated with *n*-valeroyl chloride (0.15 ml, 1.25 mmol) to give a crude yellow liquid. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to afford a colorless liquid of **5f** (0.0824 g, 18%), furan **6f** (0.02 g, 7%), the starting compound **1** (0.0853 g, 23%) and compound **7c** (0.1018 g, 19%; as a liquid).

7c: ^{1}H NMR ($CDCl_3$): δ 0.4-2.7 (m, 18H, cyclopropyl and alkyl protons), 5.2 (t, J = 7 Hz, 1H, olefinic proton), 6.7-8.2 (m, 15H, SO_2Ph and Ar*H*). IR (neat): √max 3050, 2950, 1760, 1590, 1490, 1450, 1420, 1320, 1300, 1180, 1120, 1080, 1020, 960, 930, 750, 690 cm^{-1}. MS: m/e (%) relative intensity 534 (M^+, 0.1), 441(0.9), 393(2), 357(10), 309(4), 291(100), 263(5), 249(3), 215(20), 197(9), 169(6), 141(6), 125(13), 85(32), 77(48), 57(51).

2,2-Diphenoxy-5-*n*-pentyl-4-(phenylsulfonyl)-2,3-dihydrofuran (5g).

Method A: Treatment of **2** (1 mmol) with caproyl imidazole (0.20 g, 1.25 mmol) gave a crude yellow product. It was purified by radial chromatography (silica gel, 10% ethyl acetate in hexane) to give the starting compound **1** (0.14 g, 38%) and a colorless liquid of **5g** (0.22 g, 48%). ^{1}H NMR (CCl_4): δ 0.7-1.9 (m, 9H, $CH_3CH_2CH_2CH_2CH_2$), 2.76 (m, 2H, CH_2CH_2C=C), 3.23 (s, 2H, CH_2CO), 6.9-7.9 (m, 15H, SO_2Ph and Ar*H*). IR ($CHCl_3$): $\sqrt{}_{max}$ 3050, 2950, 1640, 1595, 1490, 1450, 1300, 1305, 1150, 1100, 1060, 980, 920, cm^{1}. MS: m/e (%) relative intensity 371(M^+-93, 22), 343(0.5), 313(27), 277(9), 249(5), 229(19), 201(2.9), 171(5), 135(57), 125(56), 94(42), 77(100), 65(35). Anal. Calcd for $C_{27}H_{28}O_5S$: C, 69.80; H, 6.07. Found: C, 69.59; H, 6.22.

Preparation of Furans 6 from Dihydrofurans 5.

General procedure: **Preparation of 2-Phenoxy-5-phenyl-4-(phenylsulfonyl)furan (6a).**

Dihydrofuran **5a** (0.739 g, 1.57 mmol) was dissolved in dry CH_2Cl_2 (5 ml). *p* -Toluenesulfonic acid (0.03 g, 0.15 mmol) was added and the resulting mixture was stirred under an argon atmosphere at room

temperature overnight (12 h). It was quenched with a saturated solution of $NaHCO_3$ (15 ml) and the product was extracted with dichloromethane (3x15 ml). The combined extract was washed with H_2O (3x15 ml), brine (10 ml) and dried over anhydrous Na_2SO_4. The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless solid of **6a** (0.4847 g, 82%; m.p. 85-86 °C, from ethyl acetate in hexane). ^1H NMR (CCl_4): δ 6.0 (s, 1H, C=*CH*), 7.0-8.0 (m, 15H, SO_2*Ph* and Ar*H*). IR ($CHCl_3$): $\sqrt{}_{max}$ 3050, 3150, 1610, 1580, 1490, 1450, 1310, 1300, 1240, 1180, 1140, 1100, 1070, 1020, 990, 830, 680 cm^{-1}. MS: m/e (%) relative intensity 376 (M^+, 52), 299(2), 283(1), 207(33), 178(34), 152(3), 142(15), 125(31), 114(71), 105(65), 97(6), 88(8), 77(100), 65(7). Anal. Calcd for $C_{22}H_{16}O_4S$: C, 70.19; H, 4.28. Found: C, 70.01; H, 4.25.

2-Phenoxy-4-(phenylsulfonyl)-5-(*p*-tolyl)furan (6b).

p -Toluenesulfonic acid (0.015 g, 0.08 mmol) was reacted with a solution of **5b** (0.43 g, 0.88 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless semi-solid of **6b** (0.2554 g, 74%). ^1H NMR (CCl_4): δ 2.4 (s, 3H, *CH*$_3$-Ar), 5.9 (s, 1H, C=*CH*), 6.9-8.0 (*m*, 14H, SO_2*Ph* and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3050, 2950, 3150, 1610, 1580, 1490, 1450, 1310, 1300, 1240, 1180, 1140, 1100, 1070, 1020, 990, 820, 760, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 390 (M^+, 0.18), 281(0.13), 207(0.14), 94(100), 65(26). Anal. Calcd for $C_{23}H_{18}O_4S$: C, 70.75; H, 4.65. Found: C, 70.72; H, 4.88.

5-*t*-Butyl-2-phenoxy-4-(phenylsulfonyl)furan (6c).

p-Toluenesulfonic acid (0.019 g, 0.1 mmol) was reacted with a solution of **5c** (0.4508 g, 1 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless liquid of **6c** (0.2890 g, 81%). ^1H NMR (CCl_4): δ 1.4 (s, 9H, *t* -butyl group), 0.7 (s, 1H, C=*CH*), 6.9-8.1 (m, 10H, SO_2*Ph* and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3100, 3000, 1620, 1590, 1540, 1484, 1450, 1310, 1300, 1240, 1180, 1140, 1100, 1020, 990, 820, 750, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 342 (M^+, 6), 341(19), 263(0.08), 247(0.1), 215(0.3), 171(2), 155(2),141(4), 125(30), 107(8), 91(7), 77(100), 65(10), 51(36). Anal. Calcd for $C_{20}H_{20}O_4S$: C, 67.40; H, 5.65. Found: C, 67.72; H, 5.82.

5-Isopropyl-2-phenoxy-4-(phenylsulfonyl)furan (6d).

p-Toluenesulfonic acid (0.009 g, 0.05 mmol) was reacted with a solution of **5d** (0.2117 g, 0.5 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a pale yellow semi-solid of **6d** (0.1347 g, 79%). ^1H NMR (CCl_4): δ 1.25 [d, *J* = 7 Hz, 6H, *(CH$_3$)$_2$*CH], 3.75 [quint., *J* = 7 Hz, 1H, *CH*$(CH_3)_2$], 5.7 (s, 1H, C=*CH*), 6.9-8.1 (m, 10H, SO_2*Ph* and Ar*H*). IR (nujol): $\sqrt{}_{max}$ 3150, 2950, 1630, 1590, 1560, 1480, 1450, 1320, 1300, 1240, 1210, 1180, 1140, 1100, 1080, 1040, 1020, 1060, 980, 890, 820, 760, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 342 (M^+, 9), 327(17), 217(5), 200(32), 185(0.8), 157(3), 141(7),125(51), 115(5), 107(24), 97(8), 77(100), 65(18), 51(23). Anal. Calcd for $C_{19}H_{18}O_4S$: C, 66.64; H, 5.29. Found: C, 66.67; H, 5.24.

2-Phenoxy-4-(phenylsulfonyl)-5-(*n*-propyl)furan (6e).

p-Toluenesulfonic acid (0.0192 g, 0.1 mmol) was reacted with a solution of **5e** (0.5738 g, 1.3 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless semi-solid of **6e** (0.348 g, 77%). ^1H NMR (CCl_4): δ 0.95 (t, *J* = 7 Hz, 3H, *CH$_3$*CH_2), 1.3-2.0 (m, 2H, CH_3*CH$_2$*CH_2), 2.95 (t, *J* = 7 Hz, 2H, CH_2*CH$_2$*C=C), 5.7 (s, 1H, C=*CH*), 6.9-8.2 (m, 10H, -SO_2*Ph* and Ar*H*). IR (nujol): $\sqrt{}_{max}$ 3150, 2900, 2850, 1620, 1590, 1560, 1480, 1460, 1380, 1310, 1300, 1250, 1220, 1180, 1140, 1120, 1100, 1070, 1020, 960, 820, 760, 720, 680 cm^{-1}. MS: m/e (%)

relative intensity 342 (M^+, 8.6), 313(44), 265(0.2), 217(2), 200(2), 171(5), 155(2),125(39), 107(24), 97(6), 95(4), 77(100), 65(11), 51(59). Anal. Calcd for $C_{19}H_{18}O_4S$: C, 66.64; H, 5.29. Found: C, 66.72; H, 5.20.

5-*n*-Butyl-2-phenoxy-4-(phenylsulfonyl)furan (6f).

p-Toluenesulfonic acid (0.015 g, 0.08 mmol) was reacted with a solution of **5f** (0.2117 g, 0.5 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless liquid of **6f** (0.2109 g, 74%). ^1H NMR (CCl_4): δ 0.7-2.0 (m, 7H, butyl protons), 2.9 (br. t, J = 7 Hz, 2H, CH_2CH_2C=C), 5.7 (s, 1H, C=*CH*), 6.9-8.1 (m, 10H, SO_2Ph *and* Ar*H*). IR (neat): $\sqrt{}_{max}$ 3150, 3100, 2950, 2870, 1570, 1480, 1450, 1320, 1300, 1250, 1200, 1140, 1100, 1060, 1040, 1020, 980, 890, 830, 740, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 356 (M^+, 30), 313(61), 279(0.4), 263(1.4), 231(4), 215(12), 187(4),171(8), 155(3), 141(4), 125(51), 121(45), 115(10), 97(9), 93(13), 77(100), 65(15), 51(50). Anal. Calcd for $C_{20}H_{20}O_4S$: C, 67.39; H, 5.65. Found: C, 67.49; H, 5.51.

5-*n*-Pentyl-2-phenoxy-4-(phenylsulfonyl)furan (6g).

p-Toluenesulfonic acid (0.015 g, 0.08 mmol) was reacted with a solution of **5g** (0.3885 g, 0.8 mmol) in dry CH_2Cl_2 (5 ml). The crude product was purified by radial chromatography (silica gel, 5-10% ethyl acetate in hexane) to afford a colorless liquid of **6g** (0.2513 g, 84%). ^1H NMR (CCl_4): δ 0.7-2.0 (m, 9H, pentyl protons), 2.95 (br. t, J = 7 Hz, 2H, CH_2CH_2 C=C), 5.7 (s, 1H, C=*CH*), 6.9-8.1 (m, 10H, SO_2Ph and Ar*H*). IR (neat): $\sqrt{}_{max}$ 3150, 3050, 2950, 1620, 1570, 1480, 1450, 1320, 1300, 1240, 1200, 1140, 1100, 1060, 1020, 980, 950, 830, 740, 720, 680 cm^{-1}. MS: m/e (%) relative intensity 370 (M^+, 15), 313(46), 249(6), 229(22), 171(5), 155(2), 135(65),125(55), 115(10), 107(16), 97(10), 91(13), 77(100), 65(17), 51(53). Anal. Calcd for $C_{21}H_{22}O_4S$: C, 68.08; H, 5.98. Found: C, 68.07; H, 5.52.

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