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Efficient Preparation of 3-Alkyl(or Aryl)thio-1(or 2)-propenyl *p*-Tolyl Sulfones

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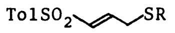
Synopsis. Synthetic routes from 3-chloro-1-propenyl *p*-tolyl sulfone to 3-(*p*-tolylthio)-1(or 2)-propenyl *p*-tolyl sulfone, 3-isopropylthio-1(or 2)-propenyl *p*-tolyl sulfone, and 3-methylthio-2-propenyl *p*-tolyl sulfone were exploited.

In connection with 1,3-bis(methylthio)-2-propenyllithium, an synthetic equivalent of 2-formylethenyl carbanion,[1] our attention was focused on the utilization of 3-alkyl(or aryl)thio-1(or 2)-propenyl *p*-tolyl sulfone (**1** or **2**) as a new type of synthetic reagent.[2] Since these compounds (**1** and **2**) were unknown in the literature,[3] an effective method for the preparation of **1** and **2** first had to be secured in order to accomplish organic syntheses utilizing them. Hence, we chose (*E*)-3-chloro-1-propenyl *p*-tolyl sulfone (**3**)[4] as a starting material.

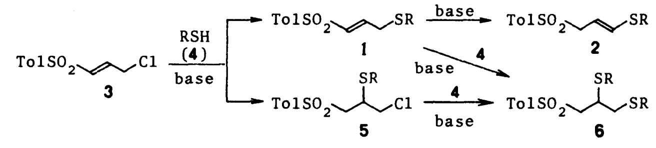

1


2

a: R = Tol b: R = i-Pr c: R = CH_3

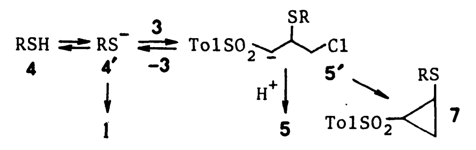
[Tol = p-tolyl]

In the reaction of **3** with a thiolate anion, displacement of chlorine atom by alkyl(or aryl)thio group and the Michael-type addition of a thiol (**4**) to the C–C double bond of **3** are anticipated to take place. Furthermore, migration of the C–C double bond of the displacement product (**1**) must be taken into consideration.[5,6] As is apparent from Table 1, the ratio of the products depended on the employed solvent and reaction time. In the reaction of **3** with **4a** and K_2CO_3 in DMF or CH_3CN, the displacement product (**1a**) was predominantly formed at the first stage, but the proportion of **2a** increased as the reaction proceeded. In contrast, the employment of THF as a solvent afforded **1a** in 90% yield even after a prolonged reaction time. This is probably because the solubility of K_2CO_3 in THF is too low to catalyze the migration of the C–C double in **1a**.



a: R = Tol b: R = i-Pr c: R = CH_3

Scheme 1.



a: R = Tol b: R = i-Pr c: R = CH_3

Scheme 2.

Compared with **4a**, **4b** produced a significant amount of the Michael-type adduct (**5b**) as shown in Table 1. Especially, the yield of **5b** was 70% in the reaction conducted in THF. Scheme 2 shows the whole sequence for the conversion of **3** to **1** and **5**, where a thiolate anion (**4′**) is in equilibrium with **4** and **4′** reacts reversibly with **3** to form the carbanion (**5′**) of **5**. The reaction of **3** with lithium 2-propanethiolate in THF resulted in the exclusive formation of a cyclopropane derivative (**7b**) through an intramolecular cyclization of the intermediary carbanion (**5′b**). This fact suggests that the displacement reaction leading to **1** is relatively slow and **5′** is indeed produced under the present reaction conditions. Since **4b** is a relatively weak acid, the most part of the employed **4b** might remain unchanged to serve as a proton source. The insolubility of K_2CO_3 in THF seems to increase the population of **4b** to cause the rapid protonation of **5′b** resulting in the predominant formation of **5b**. We tried to facilitate the displacement reaction by utilizing of 3-iodo-1-propenyl *p*-tolyl sulfone (**8**). The starting material (**8**) was easily obtained on treatment of **3** with KI in refluxing acetone. In fact, when **8** was subjected to the reaction with **4b** (1.0 mol-equiv) and $NaHCO_3$ (1.0 mol-equiv) in DMF at room temperature, **1b** was cleanly produced in 82% yield.

In the reaction of **3** with **4c**, a commercially available 15% aqueous solution of sodium methanethiolate could be used as a source of methanethiolate

TABLE 1. REACTION OF **3** WITH A THIOL (**4**) AND K_2CO_3[a)]

R (equiv)	K_2CO_3[b)]	Solvent	Time	Yield/%			
				1[c)]	**2**(*Z* : *E*)[d)]	**5**	**6**
Tol (2.0)	2.0	DMF	5 min[e)]	77	—	7	—
Tol (2.0)	4.0	DMF	30 min	—	92 (43 : 57)	—	7
Tol (2.0)	2.0	CH_3CN	30 min	93	—	—	—
Tol (2.0)	2.0	CH_3CN	10 h	—	99 (63 : 37)	—	—
Tol (2.0)	2.0	THF	24 h	90	—	—	—
i-Pr (1.0)	2.0	DMF	20 min	50	10 (60 : 40)	29	—
i-Pr (1.0)	1.5	DMF	72 h	—	64 (54 : 46)	29	—
i-Pr (1.0)	1.2	CH_3CN	48 h	—	38 (63 : 37)	45	2
i-Pr (1.0)	2.0	THF	48 h	9	12 (60 : 40)	70	—

a) At room temperature. b) Mol-equiv to **3**. c) (*E*)-isomer. d) The value in the parenthesis is the ratio of the (*Z*)- and (*E*)-geometrical isomers (by ^{1}H NMR analysis). e) **3** was recovered in 15% yield.

anion to give **2c** as the only isolable product, but its yield was relatively low (72% in DMF, 38% in CH_3CN, and 46% in methanol). Hence, the Schneider's method[7] was applied to the preparation of **1c** or **2c**. Thus, a 1 : 10 mixture of **3** and dimethyl sulfide was stirred at room temperature for 4 d, but no reaction occurred. In contrast, the addition of KI (3 equiv) accelerated the reaction to form a 42 : 58 mixture of **1c** and **2c**. The complete conversion of this mixture to **2c** was readily achieved by treatment with K_2CO_3 in CH_3CN at room temperature. The overall yield of **2c** from **3** was 92%.

Experimental

*Reaction of **3** with* p-*Toluenethiol (**4a**). A Typical Procedure.* To a solution of **4a** (126 mg: 1.01 mmol) in CH_3CN (10 ml) were added K_2CO_3 (137 mg: 1.01 mmol) and **3**[4] (231 mg: 1.00 mmol), and the resulting mixture was stirred at room temperature for 10 h under an atmosphere of nitrogen. Then, saturated aqueous NH_4Cl (30 ml) was added and the mixture was extracted with CH_2Cl_2 (3× 40 ml). The extracts were combined, washed with water, and dried (Na_2SO_4). After evaporating the solvent, the residual yellow solid was subjected to column chromatography on silica gel [hexane–benzene(2:1)] to give 3-(*p*-tolylthio)-2-propenyl *p*-tolyl sulfone (**2a**) (317 mg; 99% yield) as a mixture of two geometrical isomers (*Z*:*E*=63:37). The (*Z*)-isomer was obtained in a pure form by recrystallization from EtOH. (*Z*)-**2a**: colorless crystals; mp 78—79 °C; IR (KBr) 1605, 1595, 1290, 1124 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.29 (3H, s), 2.42 (3H, s), 4.01 (2H, d, *J*=8 Hz), 5.69 (1H, dt, *J*=10, 8 Hz), 6.45 (1H, d, *J*=10 Hz), 7.00 (4H, s), 7.30 (2H, d, *J*=8 Hz), 7.80 (2H, d, *J*=8 Hz). Anal. ($C_{17}H_{18}O_2S_2$) C, H. The (*E*)-isomer of **2a** was isolated by recrystallization of a mixture of two geometrical isomers (*Z*:*E*=43:57) given in the reaction of **3** with **4a** in DMF. (*E*)-**2a**: colorless crystals; mp 109—110 °C (from EtOH); IR (KBr) 1603, 1598, 1302, 1129 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.33 (3H, s), 2.46 (3H, s), 3.78 (2H, d, *J*=7.4 Hz), 5.54 (1H, dt, *J*=15.5, 7.4 Hz), 6.18 (1H, d, *J*=15.5 Hz), 7.0—7.45 (6H, m), 7.72 (2H, d, *J*=7.5 Hz). Anal.($C_{17}H_{18}O_2S_2$) C, H.

1a: colorless crystals; mp 77—78 °C (from EtOH); ^1H NMR ($CDCl_3$) δ=2.25 (3H, s), 2.44 (3H, s), 3.51 (2H, d, *J*=7 Hz), 6.14 (1H, d, *J*=15 Hz), 6.88 (1H, dt, *J*=15, 7 Hz), 6.97 (2H, d, *J*=7 Hz), 7.14 (2H, d, *J*=7 Hz), 7.31 (2H, d, *J*=7.2 Hz), 7.60 (2H, d, *J*=7.2 Hz). Anal.($C_{17}H_{18}O_2S_2$) C, H. **1b**: colorless crystals; mp 36—38 °C; ^1H NMR ($CDCl_3$) δ=1.24 (6H, d, *J*=6.5 Hz), 2.45 (3H, s), 2.72 (1H, septet, *J*=6.5 Hz), 3.23 (2H, d, *J*=6 Hz), 6.35 (1H, d, *J*=14.4 Hz), 6.77 (1H, dt, *J*= 14.4, 6 Hz), 7.30 (2H, d, *J*=8 Hz), and 7.70 (2H, d, *J*=8 Hz). Anal.($C_{13}H_{18}O_2S_2$) C, H. (*E*)-**2b**: colorless crystals; mp 75.5—76.5 °C; ^1H NMR ($CDCl_3$) δ=1.20 (6H, d, *J*=7.2 Hz), 2.40 (3H, s), 3.05 (1H, septet, *J*=7.2 Hz), 3.77 (2H, d, *J*=7.2 Hz), 5.49 (1H, dt, *J*=16.2, 7.2 Hz), 6.09 (1H, d, *J*=16.2 Hz), 7.35 (2H, d, *J*=8.5 Hz), 7.72 (2H, d, *J*=8.5 Hz). Anal.($C_{13}H_{18}O_2S_2$) C, H. (*Z*)-**2b**: colorless crystals; mp 60.5—61.5 °C; ^1H NMR ($CDCl_3$) δ=1.17 (6H, d, *J*=7.0 Hz), 2.44 (3H, s), 2.75 (1H, septet, *J*=7 Hz), 3.80 (2H, d, *J*=7.2 Hz), 5.69 (1H, dt, *J*=11, 7.2 Hz), 6.30 (1H, d, *J*=11 Hz), 7.29 (2H, d, *J*= 7.8 Hz), 7.75 (2H, d, *J*=7.8 Hz). Anal.($C_{13}H_{18}O_2S_2$) C, H.

*Reaction of **3** with Lithium 2-Propanethiolate.* To a solution of 2-propanethiol (421 mg: 5.52 mmol) in THF (5 ml), was added a 1.5 mol/l hexane solution (3.9 ml) of butyllithium (6.0 mmol) under ice-cooling, and the resulting mixture was stirred at room temperature for 1 h. After the addition of **3** (1.28 g: 5.53 mmol), the mixture was further stirred under ice-cooling for 2 h. The aqueous workup and column chromatography on silica gel [benzene–hexane (1:1)] gave **7** (834 mg: 56%) as colorless crystals: mp 58 °C (from benzene–hexane); ^1H NMR ($CDCl_3$) δ=1.20 (3H, d, *J*=6.6 Hz), 1.23 (3H, d, *J*=6.6 Hz), 1.45—1.85 (2H, m), 2.45 (3H, s), 2.40—3.05 (4H, m), 7.29 (2H, d, *J*=7.8 Hz), 7.71 (2H, d, *J*=7.8 Hz). Anal.($C_{13}H_{18}O_2S_2$) C, H.

*Preparation of (*E*)-**1b** via 3-Iodo-1-propenyl* p-*Tolyl Sulfone (**8**).* A mixture of **3** (932 mg: 4.04 mmol) and KI (2.01 g: 12.1 mmol) in acetone (30 ml) was refluxed for 3 h. The aqueous workup gave crude **8** as a pale yellow solid. After a mixture of 2-propanethiol (91 mg: 1.2 mmol) and $NaHCO_3$ (103 mg: 1.22 mmol) in DMF (10 ml) was stirred at room temperature for 30 min, the crude **8** (382 mg: 1.18 mmol) was added and the resulting mixture was further stirred at room temperature for 12 h under an atmosphere of nitrogen. The usual workup followed by column chromatography gave 263 mg (82% yield) of **1b** as colorless crystals.

*Reaction of **3** with Sodium Methanethiolate.* To a solution of **3** (387 mg: 1.68 mmol) in DMF (10 ml), was added a 15% aqueous solution (1.73 g: 4.13 mmol) of sodium methanethiolate (Tokyo Kasei Inc.) under an atmosphere of nitrogen, and the resulting mixture was stirred at room temperature for 3 h. The aqueous workup and the subsequent separation by column chromatography on silica gel [hexane–benzene (1:2)] to afford **2c** (290 mg: 71% yield) as a mixture of two geometrical isomers (*Z*:*E*=27:73). Rechromatography of this mixture and recrystallization gave pure (*Z*)-**2c** and pure (*E*)-**2c**. (*E*)-**2c**: colorless crystals; mp 79—80 °C (from ethanol); ^1H NMR ($CDCl_3$) δ=2.23 (3H, s), 2.46 (3H, s), 3.77 (2H, d, *J*=7.5 Hz), 5.35 (1H, dt, *J*=16, 7.5 Hz), 6.13 (1H, d, *J*=16 Hz), 7.35 (2H, d, *J*=8.5 Hz), and 7.73 (2H, d, *J*=8.5 Hz). Anal.($C_{11}H_{14}O_2S_2$) C, H. (*Z*)-**2c**: a colorless oil; ^1H NMR ($CDCl_3$) δ=2.12 (3H, s), 2.44 (3H, s), 3.94 (2H, d, *J*=7.5 Hz), 5.54 (1H, dt, *J*=7.5 Hz), 6.25 (1H, d, *J*=9 Hz), 7.29 (2H, d, *J*=8.5 Hz), 7.72 (2H, d, *J*=8.5 Hz). Anal.($C_{11}H_{14}O_2S_2$) C, H.

*Reaction of **3** with Dimethyl Sulfide* A mixture of dimethyl sulfide (41.8 g: 0.25 mol), **3** (15.4 g: 0.067 mol), and KI (33.7 g: 0.020 mol) was stirred at room temperature for 7 d. After the addition of water (100 ml), the resulting mixture was extracted with CH_2Cl_2 (3×80 ml). The extracts were combined, washed with saturated aqueous $NaHSO_3$, dried (Na_2SO_4), and evaporated. The residue was dissolved in CH_3CN (50 ml) and K_2CO_3 (929 mg: 6.70 mmol) was added. The mixture was stirred at room temperature for 1 d and water (100 ml) was added. The usual workup followed by column chromatography gave **2c** (14.94 g: 92% yield) (*Z*:*E*=28:72).

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