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## PHASE TRANSFER CATALYSIS IN SOLID–LIQUID SYSTEM AS A SELECTIVE METHOD OF MONO-ALKYLATION OF $\alpha$ -SULFONYL THIOESTERS

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### ABSTRACT

$\alpha$ -Phenylsulfonyl methylthioacetate gave monoalkylated products in high yields when treated with alkyl halides in the presence of  $K_2CO_3$  with TEBAC in  $CH_2Cl_2$ , at r.t. The superiority of this method over that in the homogeneous phase is discussed.

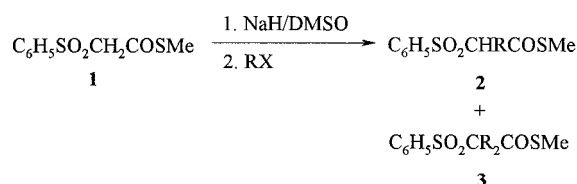
In the course of our investigations on the sulfenylation of  $\alpha$ -sulfonyl thioesters,<sup>1</sup> the synthetic precursors of  $\alpha$ -keto thioesters **1**, we became interested in a facile method of obtaining the starting material— $\alpha$ -alkyl substituted  $\alpha$ -sulfonyl thioacetates.

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This communication reports the alkylation reactions of the  $\alpha$ -phenylsulfonyl thioacetate, showing the superiority of the phase transfer catalytic method over the conventional homogeneous one.

When  $\alpha$ -phenylsulfonyl methyl thioacetate **1** was submitted to reaction with some alkyl halides, using NaH in DMSO as a base, the corresponding monoalkylated products **2a–e** were obtained, which, with exception of benzyl bromide, were accompanied by the corresponding dialkyl derivatives, **3a–c, e** (Scheme 1, Table 1).



*Scheme 1.*

These results differ from those reported for the alkylation of  $\alpha$ -sulfonylacetate,<sup>2,3</sup> for which the monoalkylated derivatives were the only reaction products, but are similar to those for the  $\alpha$ -sulfonyl ketones, which also led to mixtures of mono and dialkyl derivatives.<sup>4</sup> This fact is in accordance with the reduced resonance activation in the thiocarboxylate moiety, which leads to a ketone-like carbonyl group.<sup>5</sup>

However, it was possible to obtain the monoalkylated derivatives as the only reaction product when the alkylation was performed under the phase transfer catalytic conditions.

**Table 1.** Alkylation Reactions of  $\alpha$ -Phenylsulfonyl Methyl Thioacetate **1** by Homogeneous Method<sup>a</sup>

RX		C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CHRCOSMe <b>2</b>		C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CR <sub>2</sub> COSMe <sup>b</sup> <b>3</b>	
		Yield % (GLC)	(isol.)	Yield % (GLC)	
CH <sub>3</sub> I	<b>a</b>	80	—	<b>a</b>	17
C <sub>2</sub> H <sub>5</sub> I	<b>b</b>	82	70	<b>b</b>	14
CH <sub>2</sub> =CHCH <sub>2</sub> Br	<b>c</b>	76	48	<b>c</b>	19
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	<b>d</b>	96	61	<b>d</b>	—
<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	<b>e</b>	71	39	<b>e</b>	12

<sup>a</sup>NaH/DMSO; <sup>b</sup>Identified by GC/MS.



## PHASE TRANSFER CATALYSIS IN SOLID-LIQUID SYSTEM

1485

**Table 2.** Alkylation Reactions of  $\alpha$ -Phenylsulfonyl Methyl Thioacetate **1** by Phase Transfer Catalytic Procedure in Solid-Liquid System<sup>a</sup>

RX	C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CHRCOSMe <b>2</b> Yield % <sup>b</sup>
CH <sub>3</sub> I	<b>a</b> 94
C <sub>2</sub> H <sub>5</sub> I	<b>b</b> 61
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	<b>d</b> 72
<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	<b>e</b> 51

<sup>a</sup>K<sub>2</sub>CO<sub>3</sub>, TEBAC, CH<sub>2</sub>Cl<sub>2</sub>, r.t., 10 h (**2a** and **2b**), 4 h (**2d** and **2e**).

<sup>b</sup>Isolated yield.

Table 2 shows the yields of the monoalkylated products which were obtained when  $\alpha$ -phenylsulfonyl methyl thioacetate **1** was submitted to reaction for 4 or 10 h with some alkyl halides using K<sub>2</sub>CO<sub>3</sub> as a base, TEBAC as a catalyst and dichloromethane as a solvent.

Proof was provided that these alkylations really occur by phase transfer catalysis when the reaction of  $\alpha$ -phenylsulfonyl methyl thioacetate **1** with methyl iodide, in the absence of TEBAC, yielded the corresponding alkylated product **2a** in 19% yield.

Therefore, it may be concluded that the phase transfer catalysis, in the solid-liquid system, is a convenient method of the monoalkylation of  $\alpha$ -phenylsulfonyl thioacetate. Beside the high yields and the absence of dialkylated products, some advantages should be added, such as the use of K<sub>2</sub>CO<sub>3</sub> instead of NaH or KOH, avoiding, respectively, a moisture sensitive or hydrolizing base and using dichloromethane as a solvent instead of DMSO, which is difficult to obtain in an anhydrous state.

## EXPERIMENTAL

Alkylation of  $\alpha$ -Phenylsulfonyl Methyl Thioacetate  
Under Phase Transfer Conditions

## Typical Procedure

To a mixture of thiolester (0.300 g, 1.30 mmol), K<sub>2</sub>CO<sub>3</sub> (0.360 g, 2.60 mmol) and TEBAC (0.030 g, 0.130 mmol) were added 8.0 ml of dichloromethane and methyl iodide (0.08 ml, 1.30 mmol). After stirring, at



r.t. for 4 h, a second portion of catalyst (0.130 mmol) and methyl iodide (1.30 mmol) was added, and the mixture was further stirred at r.t. for 6 h. After this time the reaction mixture was poured into a satd. aqueous solution of ammonium chloride (20 ml), extracted with dichloromethane ( $3 \times 20$  ml), and dried over anhydrous magnesium sulfate. The crude oily product (**2a**, 0.30 g, 94%) showed to be pure on GC analysis.  $^1\text{H NMR}$  ( $\delta$ ,  $\text{CDCl}_3/\text{TMS}$ ): 1.60 (d, 3H,  $J = 7.1$  Hz), 2.30 (s, 3H,  $\text{SCH}_3$ ), 4.18 (q, 1H,  $J = 7.1$  Hz), 7.53–7.88 (m, 5H). Calcd for  $\text{C}_{10}\text{H}_{12}\text{O}_3\text{S}_2$ : C%, 49.16; H%, 4.95. Found: C%, 48.88; H% 4.86.

**$\alpha$ -Ethyl- $\alpha$ -phenylsulfonyl methyl thioacetate (2b):** Prepared as above. The crude oily product was purified by column chromatography on silica gel (hexane:benzene:ethyl acetate, 7:2:1 Yield 61%, v/v/v). m.p. 61.2–62.4°C.  $^1\text{H NMR}$  ( $\delta$ ,  $\text{CDCl}_3/\text{TMS}$ ): 0.98 (t, 3H,  $J = 7.4$  Hz), 1.92–2.12 (m, 2H), 2.32 (s, 3H,  $\text{SCH}_3$ ), 3.99 (dd, 1H,  $J = 10.4$  Hz,  $J' = 4.4$  Hz), 7.51–7.87 (m, 5H). Calcd for  $\text{C}_{11}\text{H}_{14}\text{O}_3\text{S}_2$ : C%, 51.14; H%, 5.46. Found: C%, 51.10; H%, 5.37.

For compound **2d**, a second addition of catalyst and alkylating agent was not necessary, and the reaction time was 4 h. For compound **2e**, a second addition of alkylating agent was not necessary. The crude products were purified by recrystallization from the appropriate solvent.

**$\alpha$ -Benzyl- $\alpha$ -phenylsulfonyl methyl thioacetate (2d):** Yield: 72%, m.p. 81.4–82.7°C (from hexane/chloroform).  $^1\text{H NMR}$  ( $\delta$ ,  $\text{CDCl}_3/\text{TMS}$ ): 2.18 (s, 3H,  $\text{SCH}_3$ ), 3.26 (dd, 1H,  $J = 13.4$  Hz,  $J' = 11.4$  Hz), 3.42 (dd, 1H,  $J = 13.4$  Hz,  $J' = 3.6$  Hz), 4.31 (dd, 1H,  $J = 11.4$  Hz,  $J' = 3.6$  Hz), 7.08–7.22 (m, 5H) 7.55–7.92 (m, 5H). Calcd for  $\text{C}_{16}\text{H}_{16}\text{O}_3\text{S}_2$ : C%, 59.98; H%, 5.03. Found: C%, 60.20; H%, 4.86.

**$\alpha$ -(*p*-Methyl)benzyl- $\alpha$ -phenylsulfonyl methyl thioacetate (2e):** Yield: 51%, m.p. 107.6–108.3°C (from hexane/ethyl acetate).  $^1\text{H NMR}$  ( $\delta$ ,  $\text{CDCl}_3/\text{TMS}$ ): 2.18 (s, 3H,  $\text{SCH}_3$ ), 2.28 (s, 3H), 3.21 (dd, 1H,  $J = 13.5$  Hz,  $J' = 11.2$  Hz), 3.37 (dd, 1H,  $J = 13.5$  Hz,  $J' = 3.6$  Hz), 4.29 (dd, 1H,  $J = 11.2$  Hz,  $J' = 3.6$  Hz), 6.97–7.05 (m, 4H), 7.57–7.91 (m, 5H). Calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_3\text{S}_2$ : C%, 61.05; H%, 5.42. Found: C%, 60.85; H%, 5.17.

### Alkylation in Homogeneous Medium

#### Typical Procedure

A solution of  $\alpha$ -phenylsulfonyl methyl thioacetate (1.00 g, 4.35 mmol) in dry DMSO (6 ml) was added, via syringe, at r.t., to a suspension of NaH (0.20 g, 4.35 mmol), previously washed with dry benzene, in DMSO (2 ml). After stirring for 1 h at r.t., allyl bromide (0.38 ml, 4.35 mmol), dissolved in DMSO (2 ml), was added dropwise via syringe. After stirring for 4 h at r.t.,



## PHASE TRANSFER CATALYSIS IN SOLID-LIQUID SYSTEM

1487

the reaction mixture was poured into satd. aqueous ammonium chloride, (25 ml) and extracted with dichloromethane ( $3 \times 25$  ml). The organic extract was treated with water ( $2 \times 25$  ml) and dried using anhydrous magnesium sulfate. After removal of solvent, the crude solid product was purified by recrystallization from hexane/ethyl acetate. **2c** Yield 48%, m.p. 83.7–84.6°C.  $^1\text{H NMR}$  ( $\delta$ ,  $\text{CDCl}_3/\text{TMS}$ ): 2.30 (s, 3H,  $\text{SCH}_3$ ), 2.71–2.81 (m, 2H), 4.13 (dd, 1H,  $J = 10.1$  Hz,  $J' = 4.8$  Hz), 5.07–5.17 (m, 2H), 5.54–5.74 (m, 1H), 7.53–7.88 (m, 5H). Calcd for  $\text{C}_{12}\text{H}_{14}\text{O}_3\text{S}_2$ : C%, 53.31; H%, 5.22. Found: C%, 53.34; H%, 5.25.

Compounds **2a**, **2b**, **2d** and **2e** were prepared as described above.

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