

A New Use of the Tetrahydrofuran/Powdered Potassium Hydroxide System: Convenient α -Sulfonylation of Ketones and Preparation of Dialkyl Polysulfides

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α -Sulfonylated ketones are useful intermediates in organic syntheses¹. These compounds are generally obtained from lithium enolates or 1-alkenyl trimethylsilyl ethers and organic disulfides^{1,2,3}, sulfonyl chlorides^{1,4}, or *S*-phenyl thio-sulfonates². Further methods for the synthesis of α -sulfonylated ketones are the reaction of sulfonyl chlorides with 1,3,2-dioxaphospholes⁵ or α -diazoketones⁶, and the reactions of α -haloketones with thiolate ion⁷ or sulfonyl chlorides/zinc⁸. Some β -oxoketones are mono- or bis-sulfonylated by various benzenesulfenamides and sulfenimides⁹.

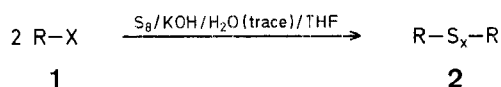
α -(Phenylthio)-ketones are also prepared from α -hydroxy-dithioacetals³¹.

We have previously described a simple procedure for the sulfonylation of aliphatic and aromatic nitriles, using potassium hydroxide suspended in tetrahydrofuran and either diphenyl disulfide¹⁰ or elemental sulfur plus an alkyl halide¹¹. The latter method avoids the use of aliphatic disulfides which are generally of low efficiency.

We report here an easy preparation of α -ketocarbanions in a two-phase system at room temperature. These carbanions are sulfonylated *in situ* by diphenyl disulfide or dimethyl tetrasulfide to give α -ketosulfides or α -ketodithioacetals. Dimethyl disulfide is an inefficient reagent under these conditions.

Preparation of Dialkyl Polysulfides

A new synthesis of dialkyl tri- and tetrasulfides (**2**, R₂S_n, n = 3, 4) was carried out by alkylating *in situ* generated potassium polysulfide (K₂S_n). The procedure consists of adding elemental sulfur to a suspension of potassium hydroxide in tetrahydrofuran containing a small quantity of water or a phase-transfer catalyst, and then adding the alkyl halide (**1**). Usually, a mixture of dialkyl polysulfides is formed, the composition depending on the reaction conditions. The dialkyl trisulfide or tetrasulfide is generally the main product and can be isolated by bulb-to-bulb distillation.



This method for the synthesis of tri- and tetrasulfides was found to be more convenient than known methods which involve alkylation of isolated alkali metal polysulfides^{12,13}, reaction of mercaptans with sulfur chlorides^{12,14,15,16}, or amine-catalyzed reaction of mercaptans with sulfur¹⁷. Some tri- and tetrasulfides have also been prepared by treatment of sodium *S*-alkyl thiosulfates with alkali metal sulfides^{18,19,20} or of alkyl alkoxy-carbonyl disulfides with potassium *t*-butoxide^{21,22}. Numerous dialkyl disulfides have been obtained from alkyl halides and sulfur in an alkaline medium²³.

α -Sulfonylation of Ketones

The primary α -oxocarbanions generated from methyl ketones (**3**, R¹ = H) are *gem*-bis-sulfonylated by diphenyl disulfide and dimethyl tetrasulfide to give α -oxodithioacetals (**4**) whereas the secondary α -oxocarbanions generated from alkyl ketones (**3**, R¹ = alkyl, aryl) are mono-sulfonylated to give α -alkylthio- or α -arylthio ketones (**5**). Symmetrical dialkyl ketones (**6**) are α,α' -bis-sulfonylated or α,α,α' -tris-sulfonylated to give products **7** or **8**, respectively.

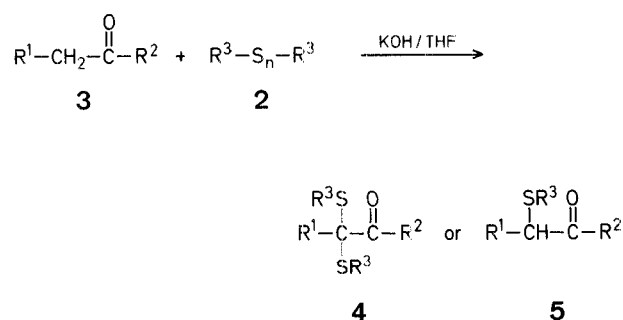



Table 1. Dialkyl Polysulfides (**2**) from Sulfur and Alkyl Halides (**1**) (at room temperature)

1	Catalyst	Reaction time [h]	2	Yield ^a [%]	b.p. [°C]/torr or m.p. [°C]		¹ H-N.M.R. (CDCl ₃ /TMS) δ [ppm] ^c
					found ^b	reported	
H ₃ C-J	H ₂ O	2	H ₃ C-S ₄ -C-H ₃	60	70°/0.07	59°/1 ¹²	2.62 (s, CH ₃) ²⁴
C ₂ H ₅ -J	H ₂ O	2	C ₂ H ₅ -S ₄ -C ₂ H ₅	30 ^d	70°/0.07	43-45°/0.1 ¹³ 58-68°/0.1 ¹⁴	2.97 (q, CH ₂) ²⁵
<i>i</i> -C ₃ H ₇ -Br	(C ₂ H ₅) ₄ N [⊕] Cl [⊖]	3	<i>i</i> -C ₃ H ₇ -S ₃ -C ₃ H ₇ - <i>i</i>	50	50°/0.07	86-90°/8 ¹⁵ 56°/2 ²¹	3.22 (m, CH) ¹⁷
H ₂ C=CH-CH ₂ -Cl	H ₂ O	2	H ₂ C=CH-CH ₂ -S ₃ -CH ₂ -CH=CH ₂	30 ^e	50°/0.07	66-67°/0.0008 ¹⁹	3.51 (d, CH ₂ -S) ²⁵
Br-(CH ₂) ₃ -Br	H ₂ O	2		30	46°	44° ²⁰	3.13 (t, CH ₂ -S) ²⁰

^a The yields, based on sulfur, are given for distilled products (purity according to ¹H-N.M.R. analysis) or recrystallized 1,2,3-trithiane (from ethanol).

^b Bulb-to-bulb distillation (bath temperature).

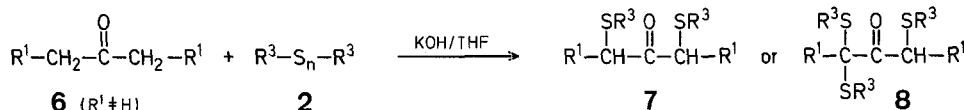
^c Only the protons next to sulfur are significant. They are in good agreement with the literature values.

^d (C₂H₅)₂S₃ is also isolated; yield: 15%; b.p. 60°C/0.07 torr (Ref. ¹², b.p. 82.5°C/11 torr; Ref. ¹⁸, b.p. 40°C/0.07 torr; Ref. ¹⁹, b.p. 80°C/11 torr; Ref. ²¹, b.p. 60-61°C/3 torr.

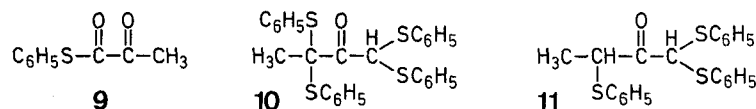
^e ¹H-N.M.R. (CDCl₃/TMS): δ = 2.89 ppm (q, CH₂)²⁵.

^f (H₂C=CH-CH₂)₂S₄ is also isolated; yield: 10%; b.p. 90°C/0.07 torr.

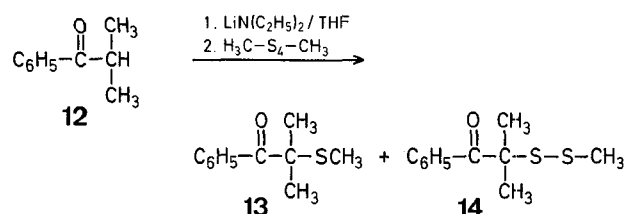
^g ¹H-N.M.R. (CDCl₃/TMS): δ = 3.59 ppm (d, CH₂-S)²⁵.



The reaction of acetone (**3a**) with diphenyl disulfide under the general conditions affords the expected product **4a** (80%) along with a small amount of *S*-phenyl 2-oxopropoanethioate (**9**, 10%). Butanone (**3d**) reacts with diphenyl disulfide to give a mixture of mono- (**5d**; 10%), bis- (**4d**; 30%), tris- (**11**; 10%), and tetrakis-sulfenylation product (**10**; 20%).



2-Methyl-1-phenyl-1-propanone (**12**) is not deprotonated by potassium hydroxide. Its carbanion may, however, be obtained using lithium diethylamide at -70°C; subsequent addition of dimethyl tetrasulfide gives 2-methyl-2-methylthio-1-phenyl-1-propanone (**13**; 65%) and methyl 2-benzoyl-2-propyl disulfide (**14**; 5%). Compound **14** may also be prepared from **12** using excess sulfur and methyl iodide.



Dialkyl Polysulfides (**2**); General Procedure:

Powdered sulfur (2.56 g, 10 mmol) is added to a vigorously stirred suspension of finely powdered potassium hydroxide (10 g) in tetrahydrofuran (140 ml, containing 0.2% water). Stirring is continued for 5 min. A brown coloration is observed which disappears upon addition of a solution of the alkyl halide **1** (80 mmol) in tetrahydrofuran (40 ml, containing 0.2% water). The mixture is stirred at room temperature for 2 h, and then filtered. The solvent is distilled

off and ether (50 ml) is added to the residue. This solution is washed with 0.02 normal hydrochloric acid (20 ml), dried with sodium sulfate, and evaporated. The residue is fractionated by evaporative bulb-to-bulb distillation under reduced pressure. A small amount of polysulfide R₂S₃ or R₂S₄ is disproportionated during the distillation^{18,24}.

Diisopropyl trisulfide is prepared following the above procedure with the modification that dry tetrahydrofuran is used as solvent and tetraethylammonium chloride (0.7 g) as catalyst in place of water.

α -Alkylsulfenylation and α -Arylsulfenylation of Ketones **3** and **6** in a Heterogeneous System; General Procedure:


To a vigorously stirred suspension of powdered potassium hydroxide (3 g) in tetrahydrofuran (60 ml) are added the ketone **3** or **6** (10 mmol) and, after 5 min, a solution of diphenyl disulfide or dimethyl tetrasulfide (amount, see Table 2) in tetrahydrofuran (20 ml). Stirring is continued at room temperature for the time given in Table 2. The mixture is then filtered and the solvent distilled off. The residue is poured into 0.02 normal hydrochloric acid (50 ml) and the mixture extracted with ether (3 × 20 ml). The extract is dried with sodium sulfate and the solvent evaporated. Products **4c**, **5i**, **7a**, **7c**, and **8d** are purified by recrystallization (for solvent, see Table 2). In all other cases, the residual oil is fractionated by bulb-to-bulb distillation in vacuo. The collected fractions are purified by another distillation in the case of products **4d**, **4e**, **5e**, **5f**, and **5h** and by recrystallization in the case of the other products. Ketones **5d** and **8a** cannot be sufficiently purified by distillation.

α -Alkylsulfenylation of Ketones **3h** and **12** in a Homogeneous System:

Activated lithium diethylamide is prepared by the procedure of Ref.³⁷.

Method A, using Dimethyl Tetrasulfide: A mixture of diethylamine (2.7 g, 37 mmol), hexamethylphosphoric triamide (10 ml), an-

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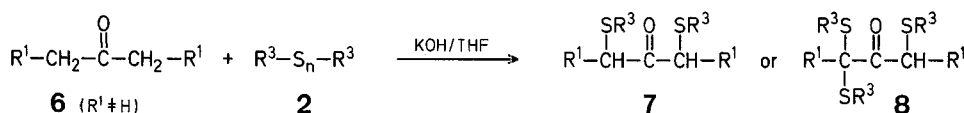
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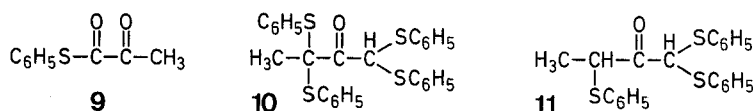
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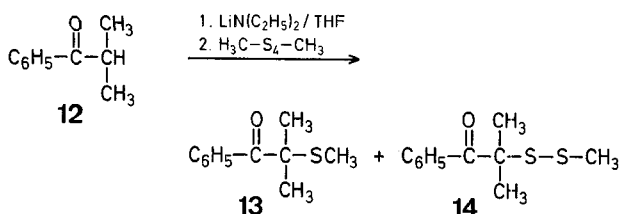
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Method A, using Dimethyl Tetrasulfide: A mixture of diethylamine (2.7 g, 37 mmol), hexamethylphosphoric triamide (10 ml), an-

is maintained at 20–25 °C and dry tetrahydrofuran (8 ml) is added to the dark-red solution. The mixture is then cooled to –70 °C and a solution of the ketone **12** (17 mmol) in dry tetrahydrofuran (10 ml) is added dropwise within 10 min. The mixture is allowed to warm to 0 °C within 1 h and then, powdered sulfur (1.09 g, 0.004 mol) and, after 5 min, a solution of methyl iodide (8.5 g, 60 mmol) in tetrahydrofuran (20 ml) are added. The mixture is stirred for 4 h at room temperature, and worked up as described above. Products **13** and **14** are purified by bulb-to-bulb distillation in vacuo.

2-Methyl-2-methylthio-1-phenyl-1-propanone (13); yield: 0.33 g (10%); b.p. 70 °C/0.05 torr (Ref.³⁶, b.p. 71–73 °C/0.05 torr).

¹H-N.M.R. (CDCl₃/TMS): δ = 1.54 (s, 6H); 1.98 (s, 3H); 7.25–8.15 ppm (m, 5H_{arom}).

2-Benzoyl-2-propyl Methyl Disulfide (14); yield: 1.55 g (40%); b.p. 100 °C/0.05 torr.

C ₁₁ H ₁₄ OS ₂	calc.	C 58.36	H 6.24	S 28.32
(226.4)	found	58.29	6.37	28.57

¹H-N.M.R. (CDCl₃/TMS): δ = 1.64 (s, 6H); 2.26 (s, 3H); 7.4–8.1 ppm (m, 5H_{arom}).

This work was supported by the D.G.R.S.T.

Received: January 31, 1980
(Revised form: March 24, 1980)

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