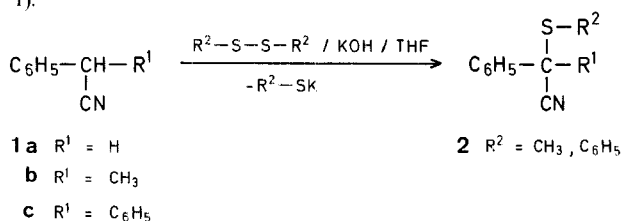


A Convenient Method for the Sulfenylation of Nitriles

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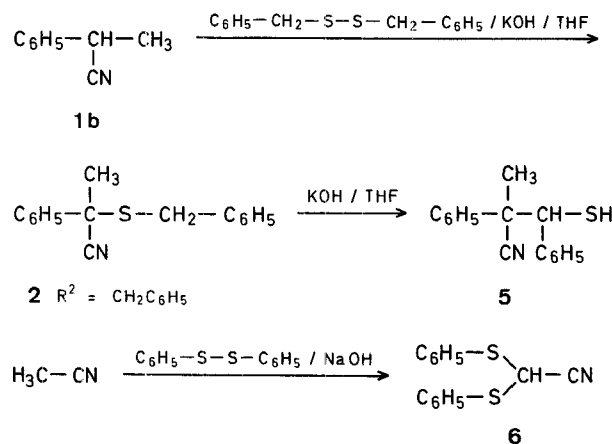
There are many reports on the α -sulfenylation of ketones^{1,4} or nitriles^{2,3} with lithium amide at -78° and diphenyl disulfide or dimethyl disulfide^{1,2}, benzenesulfonyl chloride³ or phenyl benzenethiosulfonate⁴. We wish to describe an easier method for α -sulfenylation of nitriles in a two phase system (solid-liquid) without a catalyst. We have previously described the utilisation of anhydrous potassium hydroxide and carbon tetrachloride for chlorination of nitriles in the α -position⁵. This method is modified as follows: the carbanions, generated by using anhydrous potassium hydroxide or sodium hydroxide in tetrahydrofuran, are reacted with a disulfide at room temperature and good yields of the appropriate α -cyanosulfide are obtained generally (Table 1).



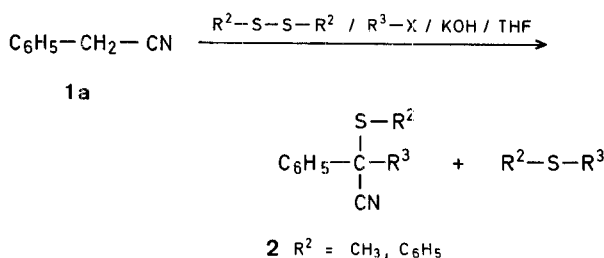
However, this sulfenylation of diphenylacetoneitrile (**1c**) gives only poor yields of the corresponding **2** (Table 1). Better results are obtained by reacting **1c** with sodium hydride and phenylthiosuccinimide^{6,7} or methylthiosuccinimide⁷ (yields 50–70 %).

The sulfenylation of **1b** by dibenzyl disulfide gives the thiol **5** (two diastereoisomers) which results from a Stevens rearrangement of the carbanion provided by the intermediate sulfide **2** ($\text{R}^2 = \text{CH}_2\text{C}_6\text{H}_5$). Biellmann and Schmitt⁸ reported another example of the same rearrangement with the carbanion of dibenzyl sulfide.

Bis-sulfenylation of acetonitrile occurs when the reaction is carried out in tetrahydrofuran/hexamethylphosphoric triamide mixture¹ as shown below.



The sulfides **2** ($\text{R}^3 = \text{alkyl}$) may be prepared easily in a one-step procedure, starting from **1a**, by reaction with potassium hydroxide, a disulfide, and excess of alkyl halide R^3-X .



The sulfenylation of the succinonitrile **3** ($\text{R} = \text{CH}_3$) is very difficult, because the elimination of cyanide ion leads to a cinnamionitrile⁹. However, the reaction of the succinonitrile **3** ($\text{R} = \text{H}$) with dimethyl disulfide and methyl iodide gives only the sulfide **4**.

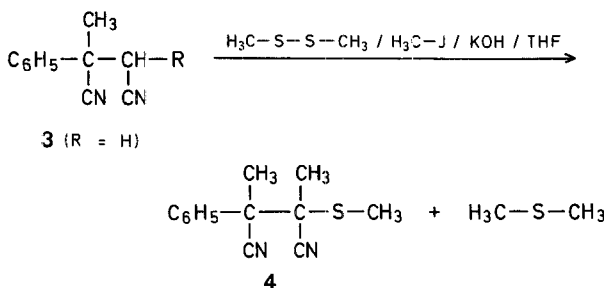


Table 1. Sulfenylation Reactions

Starting material	Product type	R ¹	R ²	R ³	Reaction time	Yield [%]	m.p. (solvent)	Molecular formula ^a
1a	2	H	C ₆ H ₅	—	2.5 h	98	50° (C ₂ H ₅ OH) ^b	C ₁₄ H ₁₁ NS (225.3)
1b	2	CH ₃	C ₆ H ₅	—	2.5 h	90	40–41° (C ₂ H ₅ OH) ^c	C ₁₅ H ₁₃ NS (239.3)
1b	2	CH ₃	CH ₃	—	6 h	98	oil	C ₁₀ H ₁₁ NS (177.3)
1c	2	C ₆ H ₅	C ₆ H ₅	—	5 h	35	73–74° (CH ₃ OH) ^c	C ₂₀ H ₁₅ NS (301.4)
1c	2	C ₆ H ₅	CH ₃	—	18 h	8	53–54° (cyclohexane)	C ₁₅ H ₁₃ NS (239.3)
1a	2	—	C ₆ H ₅	CH ₃	5 h	95	40–41° (C ₂ H ₅ OH) ^c	C ₁₅ H ₁₃ NS (239.3)
1a	2	—	C ₆ H ₅	C ₂ H ₅	5 h	98	oil ^c	C ₁₆ H ₁₅ NS (253.3)
1a	2	—	C ₆ H ₅	<i>n</i> -C ₃ H ₇	5 h	98	oil	C ₁₇ H ₁₇ NS (267.3)
1a	2	—	C ₆ H ₅	H ₂ C=CH-CH ₂	5 h	98	oil	C ₁₇ H ₁₅ NS (265.3)
1a	2	—	CH ₃	CH ₃	18 h	50 ^d	oil	C ₁₀ H ₁₁ NS (177.3)
3 (R = H)	4	—	—	—	30 h	90	oil ^c	C ₁₃ H ₁₄ N ₂ S (230.3)
CH ₃ CN	6	—	—	—	24 h	81	oil	C ₁₄ H ₁₁ NS ₂ (257.4)

^a All products gave satisfactory microanalyses (C $\pm 0.24\%$, H $\pm 0.37\%$, N $\pm 0.34\%$).

^b Lit.¹⁰ m.p. 49.5–50.5°.

^c Reported in Lit.³ but no m.p. is given.

^d **1b** is also formed in 50 % yield.

^e Mixture of two diastereoisomers.

Table 2. $^1\text{H-N.M.R.}$ Data for Sulfides **2** (CDCl_3 solutions)

R^1	R^2	δ [ppm]
H	C_6H_5	4.37 (s, 1 H, CH); 7.30 (m, 10 H_{arom})
CH_3	C_6H_5	1.94 (s, 3 H, CH_3); 7.20–7.50 (m, 10 H_{arom})
CH_3	CH_3	1.94 (s, 3 H, CH_3); 2.05 (s, 3 H, CH_3); 7.20–7.50 (m, 5 H_{arom})
C_6H_5	C_6H_5	7.20–7.60 (m, 15 H_{arom})
C_6H_5	CH_3	2.11 (s, 3 H, CH_3); 7.30–7.70 (m, 10 H_{arom})
C_2H_5	C_6H_5	1.00 (t, 3 H, CH_3); 2.26 (q, 2 H, CH_2); 7.40 (m, 10 H_{arom})
$n\text{-C}_3\text{H}_7$	C_6H_5	0.88 (t, 3 H, CH_3); 1.44 (m, 2 H, CH_2); 2.17 (m, 2 H, CH_2); 7.20 (m, 10 H_{arom})
$\text{H}_2\text{C}=\text{CH}-\text{CH}_2$	C_6H_5	2.93 (d, 2 H, CH_2); 5.16 (m, 2 H, $\text{H}_2\text{C}=\text{CH}$); 5.68 (m, 1 H, $-\text{CH}-$); 7.30 (m, 10 H_{arom})

These results show that the system anhydrous potassium hydroxide/tetrahydrofuran is a powerful agent for the generation of carbanions.

All reactions are carried out under nitrogen at room temperature.

Preparation of 2-Phenyl-2-phenylthiopropenenitrile (2; $\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{C}_6\text{H}_5$) from 2-Phenylpropanenitrile (1b):

To a suspension of powdered potassium hydroxide (1 g) in anhydrous tetrahydrofuran (20 ml) are added **1b** (0.65 g, 5 mmol) and diphenyl disulfide (1.1 g, 5 mmol). The suspension is stirred for 2.5 h. After evaporation of the tetrahydrofuran and addition of water acidified with 2 normal hydrochloric acid, the sulfide **2** and the thiophenol are extracted with ether. The ethereal extract is dried over sodium sulfate, then evaporated. Thiophenol and sulfide **2** are separated from the residue by fractional distillation through a Vigreux column.

For the preparations of **2** ($\text{R}^1 = \text{R}^2 = \text{CH}_3$) and **2** ($\text{R}^1 = \text{C}_6\text{H}_5$, $\text{R}^2 = \text{CH}_3$), two equivalents of dimethyl disulfide are used with one equivalent of the corresponding acetonitrile **1**.

Preparation of 2-Phenyl-2-phenylthiopentanenitrile (2; $\text{R}^1 = \text{C}_3\text{H}_7$, $\text{R}^2 = \text{C}_6\text{H}_5$) from Phenylacetonitrile (1a):

To a suspension of powdered potassium hydroxide (2 g) in anhydrous tetrahydrofuran (70 ml) are added **1a** (1.17 g, 10 mmol), propyl bromide (2.46 g, 20 mmol), and diphenyl disulfide (2.18 g, 10 mmol). The suspension is stirred for 5 h. The reaction mixture is concentrated under reduced pressure, poured into 2 normal hydrochloric acid (30 ml), and then extracted with ether. The extract is dried and concentrated. Fractional distillation through a Vigreux column gives the sulfide **2**; the phenyl propyl sulfide is collected as the first fraction.

Preparation of 2-Cyano-1,2-diphenylpropanethiol (5):

A suspension of powdered potassium hydroxide (2 g) in tetrahydrofuran (40 ml) is mixed with **1b** (1.3 g, 10 mmol) and dibenzyl disulfide (2.46 g, 10 mmol), then stirred for 48 h. The precipitate is filtered, dissolved in 1 normal hydrochloric acid, and extracted with ether. The ether is removed and the residue, purified by evaporative bulb-to-bulb short path distillation, gives the diastereoisomer **5a**; yield: 0.43 g (17%); m.p. 72–73° (from cyclohexane). $^1\text{H-N.M.R.}$ (CDCl_3): $\delta = 1.88$ (s, 3 H, CH_3); 2.18 (d, 1 H); 4.16 (d, 1 H, $\text{CH}-\text{SH}$, $J_{\text{CH}-\text{SH}} = 7.5$ Hz); 7.30 ppm (m, 10 H_{arom}).

The tetrahydrofuran solution is concentrated, poured into 1 normal hydrochloric acid and then extracted with ether. The ether is removed; the distillation of the residue gives the diastereoisomer **5b**; yield: 0.77 g (31%); m.p. 110–112° (from cyclohexane).

$^1\text{H-N.M.R.}$ (CDCl_3): $\delta = 1.56$ (s, 3 H, CH_3); 1.93 (d, 1 H); 4.15 (d, 1 H, $\text{CH}-\text{SH}$, $J_{\text{CH}-\text{SH}} = 5.5$ Hz); 7.70 ppm (m, 10 H_{arom}).

Preparation of Bis[phenylthio]acetonitrile (6):

Powdered sodium hydroxide (2 g), acetonitrile (5 g), diphenyl disulfide (4.36 g) in tetrahydrofuran (30 ml) and hexamethylphosphoric triamide (20 ml) are stirred for 24 h. After removal of the tetrahydrofuran 1 normal hydrochloric acid is added to the residue. The compound **6** is extracted with ether and purified by distillation under reduced pressure; yield: 2.1 g (81%); b.p. 150°/0.06 torr. $^1\text{H-N.M.R.}$ (CDCl_3): $\delta = 4.80$ (s, 1 H, CH); 7.50 ppm (m, 10 H_{arom}).

Sulfenylation of Succinonitrile 3 ($\text{R} = \text{H}$):

To a suspension of powdered potassium hydroxide (5 g) in tetrahydrofuran (40 ml) are added the succinonitrile **3** ($\text{R} = \text{H}$; 3.8 g, 22 mmol) and methyl iodide (9.5 g, 67 mmol). Then, dimethyl disulfide (16 g, 170 mmol) in tetrahydrofuran (35 ml) is slowly added to the well-stirred suspension. After 30 h, the tetrahydrofuran is removed on a rotary evaporator. The residue is acidified with 2 normal hydrochloric acid and extracted with ether. The ethereal solution is washed with sodium thiosulfate. The solvent is removed and the sulfide **4** is purified by distillation (200°/0.07 torr) under reduced pressure; yield: 4.6 g (90%); ratio **4a**:**4b** = 3:7.

The diastereoisomer **4a** crystallises; m.p. 103° (ethanol).

$^1\text{H-N.M.R.}$ (CDCl_3): $\delta = 1.61$ (s, 3 H, CH_3); 2.05 (s, 3 H, CH_3); 2.21 (s, 3 H, CH_3); 7.40–7.80 ppm (m, 5 H_{arom}).

Diastereoisomer **4b**; oil.

$^1\text{H-N.M.R.}$ (CDCl_3): $\delta = 1.81$ (s, 3 H, CH_3); 1.92 (s, 3 H, CH_3); 2.05 (s, 3 H, CH_3); 7.40–7.80 ppm (m, 5 H_{arom}).

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