The Phase-Transfer Synthesis of Unsymmetrical Dialkyl Sulfides via *O,S*-Dialkyl Dithiocarbonates

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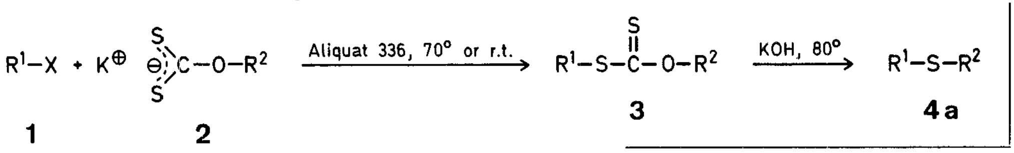
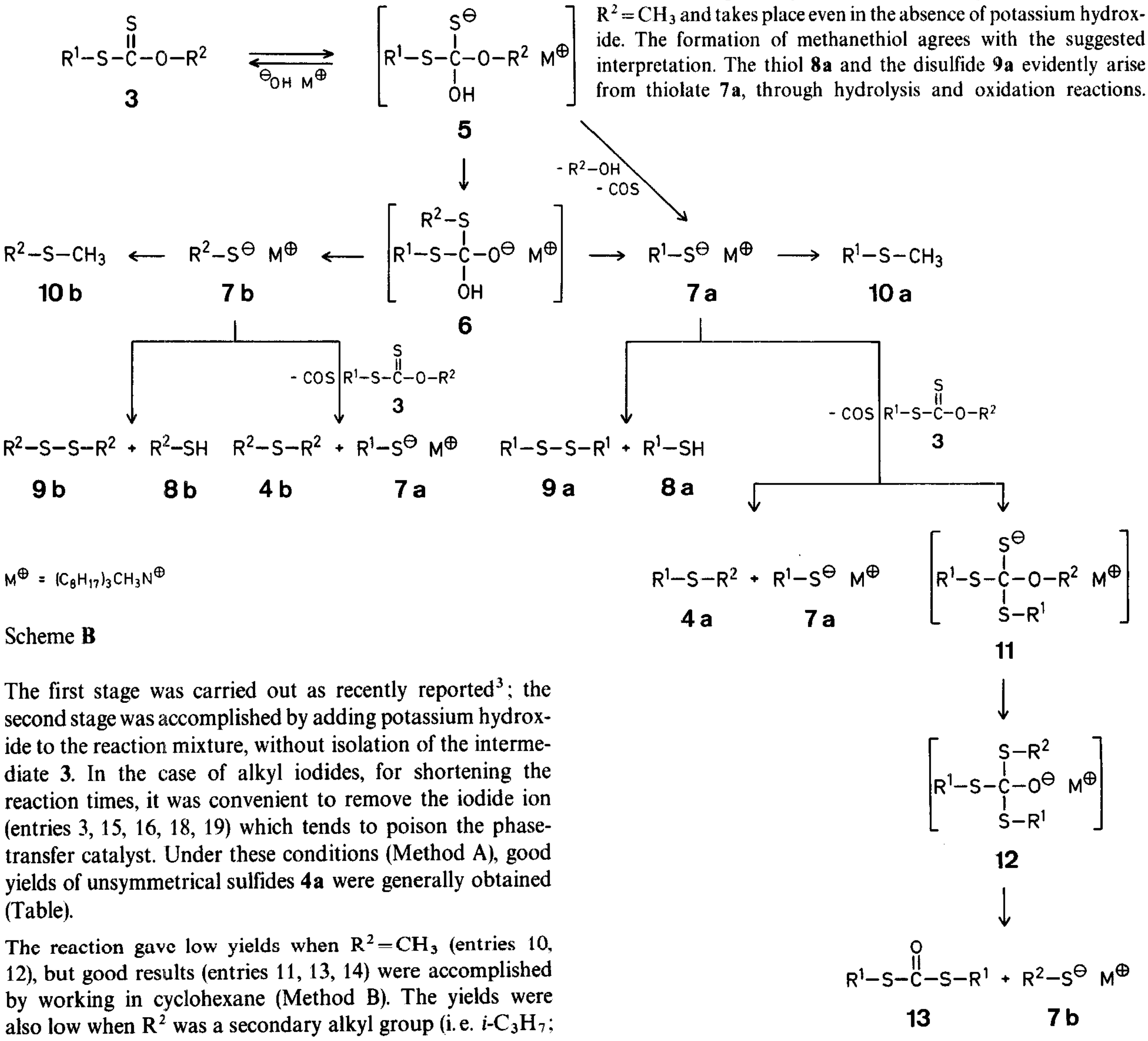
Unsymmetrical dialkyl sulfides are widely synthesized by reactions of alkylating agents with an alkali thiolate under various conditions[1]. To avoid the preliminary preparation and troublesome manipulation of thiols, *O,S*-dialkyl dithiocarbonates are attractive starting compounds, but attempts to utilize these for synthetic purposes have thus far been unsuccessful[2].

In this paper we report a new preparation for sulfides **4a** under phase-transfer conditions as a one-pot synthesis from alkyl halides, methanesulfonates, or *p*-toluenesulfonates **1** and potassium *O*-alkyl dithiocarbonates (**2**) via *O,S*-dialkyl dithiocarbonates **3**, according to Scheme A.



Scheme A



M⊕ = $(C_8H_{17})_3CH_3N^{\oplus}$

Scheme B

The first stage was carried out as recently reported[3]; the second stage was accomplished by adding potassium hydroxide to the reaction mixture, without isolation of the intermediate **3**. In the case of alkyl iodides, for shortening the reaction times, it was convenient to remove the iodide ion (entries 3, 15, 16, 18, 19) which tends to poison the phase-transfer catalyst. Under these conditions (Method A), good yields of unsymmetrical sulfides **4a** were generally obtained (Table).

The reaction gave low yields when $R^2 = CH_3$ (entries 10, 12), but good results (entries 11, 13, 14) were accomplished by working in cyclohexane (Method B). The yields were also low when R^2 was a secondary alkyl group (i.e. i-C_3H_7; entry 21)[4] or when R^1 was a short chain alkyl group (i.e. CH_3, C_2H_5; entries 15, 16, 19); from a synthetic point of view however, the latter limitations can be circumvented by exchanging the positions of R^1 and R^2 in the starting reagents (entries 1–5, 11, 18).

It is noteworthy that as well as sulfides **4a**, a number of by-products are generated in all the reported reactions, but in general, pure **4a** can be obtained by normal work-up procedures. A reasonable pathway which can account for the genesis of the unsymmetrical sulfides **4a** and by-products, is shown in Scheme **B**.

The main reaction involves the initial base-catalyzed hydrolysis of the dithiocarbonate **3** into the thiolate **7a** and subsequent S_N2 displacement reaction of **7a** with unreacted **3** giving the sulfide **4a** together with the restored reagent **7a**, the dithiocarbonate thus functioning both as alkylating agent and source of nucleophile. A competitive reaction of **7a** with **3** can occur to afford *S,S*-dialkyl dithiocarbonate **13** via a nucleophilic attack of the thiolate on the thiocarbonyl group of **3** and subsequent inter- or intramolecular rearrangement of intermediate **11** to **12**. This reaction generally is irrelevant, but predominates when $R^2 = CH_3$ and takes place even in the absence of potassium hydroxide. The formation of methanethiol agrees with the suggested interpretation. The thiol **8a** and the disulfide **9a** evidently arise from thiolate **7a**, through hydrolysis and oxidation reactions.

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The formation of sulfide **10a**, according to results obtained in a control experiment[14], occurs through a demethylation of tricaprylmethylammonium ion by thiolate **7a**. In the case of a short chain radical R^2, since the corresponding low boiling thiol **8a** is easily eliminated, the reaction sequence to sulfide **4a** can be interrupted and, through a preliminary rearrangement of **5** to **6**, the formation of **4b**, **8b**, **9b**, and **10b** can take place, similarly as indicated for **4a**, **8a**, **9a**, and **10a**, respectively.

Despite the complexity of the above pathway, the new method for the synthesis of unsymmetrical sulfides offers the follow advantages: (a) one-pot reaction, (b) thiols are not needed as starting materials, (c) good over-all yields.

All isolated sulfides **4a** were identified by comparison of their b.p., n_D, and N.M.R. data and G.L.C. retention times with those of authentic samples. By-products were identified by G.L.C. (coinjection with authentic samples) and, when their isolation was possible, the assigned structures were confirmed by N.M.R. and I.R. spectra. Potassium *O*-methyl, *O*-ethyl, *O*-*i*-propyl, *O*-octyl, and *O*-decyl dithiocarbonates were prepared by the standard procedure[15] from potassium hydroxide, an excess of the alcohol required and then carbon disulfide. The products were washed several times with dry ether and dried in vacuo.

Ethyl Octyl Sulfide; Typical Procedure:

Method A: Octyl bromide (**1**; $R^1=n\text{-}C_8H_{17}$, X=Br; 9.65 g, 50 mmol), potassium *O*-ethyl dithiocarbonate (**2**; $R^2=C_2H_5$; 8.33 g, 52 mmol), tricaprylmethylammonium chloride (Aliquat 336, Fluka; 1.68 g), and water (50 ml) are mixed and vigorously stirred at 70° for 5 min. G.L.C. analysis of the organic phase (SE 30, 5% over Varaport 30; temperature programmed from 100° to 250°) shows the complete disappearance of **1**. The reaction mixture is cooled to about 50°; then potassium hydroxide pellets (14 g, 250 mmol) are added under vigorous stirring over a period of 2–5 min so that the temperature of the solution does not exceed 80°. This temperature is maintained for another 30 min, until complete disappearance (G.L.C.) of the intermediate *O*-ethyl *S*-octyl dithiocarbonate (**3**; $R^1=n\text{-}C_8H_{17}$, $R^2=C_2H_5$). Petroleum ether (100–150 ml) is added and the organic layer is separated, dried and filtered over a small layer of silica gel, using petroleum ether as eluent. After evaporation of the solvent, G.L.C. analysis of the crude residue shows two major components – *ethyl octyl sulfide* (**4a**; $R^1=n\text{-}C_8H_{17}$, $R^2=C_2H_5$) and *dioctyl disulfide* (**9a**; $R^1=n\text{-}C_8H_{17}$) – and a negligible amount of three minor components – *octanethiol* (**8a**; $R^1=n\text{-}C_8H_{17}$), *methyl octyl sulfide*[12] (**10a**; $R^1=n\text{-}C_8H_{17}$) and S,S-*dioctyl dithiocarbonate* (**13**; $R^1=n\text{-}C_8H_{17}$). Vacuum fractional distillation through a Claisen apparatus of the residue affords *ethyl octyl sulfide* [yield: 7.0 g (80%); b.p. 108°/16 torr; $n_D^{20}=1.4565$; Lit. [6] b.p. 108–110°/14 torr, $n_D^{20}=1.4565$] and *dioctyl disulfide* [yield: 0.8 g (11%); b.p. 170–172°/2 torr, $n_D^{20}=1.4828$; Lit. [13] b.p. 199–200°/10 torr, $n_D^{20}=1.4820$].

By reaction of *O*-ethyl *S*-octyl dithiocarbonate[3] (**3**; $R^1=n\text{-}C_8H_{17}$, $R^2=C_2H_5$; 11.7 g, 50 mmol) with potassium hydroxide (14 g, 250 mmol), Aliquat 336 (1.68 g), and water (50 ml) at 80° for 30 min and subsequent work-up as described above, *ethyl octyl sulfide* and *dioctyl disulfide* are obtained in yields of 84% and 10% respectively. *Octanethiol*, *methyl octyl sulfide*, and S,S-*dioctyl dithiocarbonate* are identified in the crude reaction mixture by G.L.C. analysis. The same products were detected (G.L.C.) in the reactions for entries 2, 3, 4, 5.

When X=J, complete disappearance of **3** was reached after 2 h for entry 2 ($R^2=C_2H_5$), while, even with longer reaction time, it was never reached for entries 15, 16, 18, and 19 ($R^2=n\text{-}C_8H_{17}$, $n\text{-}C_{10}H_{21}$). In these cases, Method A is modified as follows: after the formation of **3**, the aqueous layer is separated and the organic layer is washed with water (2 × 50 ml). After the second separation of the aqueous layer, water (50 ml), Aliquat 336 (1.68 g), and potassium hydroxide (14 g, 50 mmol) are added and the mixture is heated at 80° under vigorous stirring; the reactions are complete after 30 min (entries 3, 15, 16, 18, 19).

When $R^2=CH_3$ in **2**, the crude reaction mixture of entry 10 is fractionated through a Spaltrohr-Column (Fischer) to give: *octanethiol* (**8a**; $R^1=n\text{-}C_8H_{17}$; yield: 5%, b.p. 88–89°/20 torr; Lit. [5] b.p. 88–89°/20 torr) and *methyl octyl sulfide* (**4a**; $R^1=n\text{-}C_8H_{17}$, $R^2=CH_3$; yield: 34%, b.p. 104–105°/20 torr, $n_D^{20}=1.4565$; Lit. [10] b.p. 100.5–102.5/17–18 torr, $n_D^{20}=1.4564$). G.L.C. analysis of the residue of the first distillation shows traces of *dioctyl disulfide* (**9a**; $R^1=n\text{-}C_8H_{17}$) and S,S-*dioctyl dithiocarbonate* (**13**); $R^1=n\text{-}C_8H_{17}$) as a major component. The latter is normally isolated by vacuum distillation: yield: 47%; b.p. 177–178°/0.5 torr; $n_D^{20}=1.4920$.

$C_{17}H_{34}OS_2$	calc.	C 64.09	H 10.76	S 20.13
(318.6)	found	64.15	10.65	20.22

^{1}H-N.M.R. (CCl_4): $\delta=0.7$–1.05 [m, $-(CH_2)_7-C\underline{H}_3$]; 1.05–1.8 [m, $CH_2-(C\underline{H}_2)_6-CH_3$]; 2.92 ppm [t, $C\underline{H}_2-C_7H_{15}\text{-}n$].

I.R. (liquid film): $\nu_{max}=875$, 1465, 1648, 2845, 2915, 2945 cm^{-1}.

It is noteworthy that this reaction is successful even in absence of potassium hydroxide, but a longer reaction time is required (2 h).

In a collateral proof, *O*-methyl *S*-octyl dithiocarbonate[3] (**3**; $R^1=n\text{-}C_8H_{17}$, $R^2=CH_3$; 11.0 g, 50 mmol) is treated with Aliquat 336 (1.68 g) and water (50 ml). The mixture is heated with vigorous stirring at 80°. The complete disappearance of the starting material is noted (G.L.C.) after 2 h. *Octanethiol*, *methyl octyl sulfide*, and S,S-*dioctyl dithiocarbonate* are isolated in yields of 15%, 17%, and 61% respectively. *Methanethiol* and *carbon oxysulfide* are trapped in a Dry Ice/acetone bath and confirmed by mass spectral and N.M.R. analysis; M.S.: $m/e=48$ (M^+, methanethiol), 60 (M^+ carbon oxysulfide);

^{1}H-N.M.R. (CCl_4): $\delta=0.8$–1.2 (m, SH; disappears after addition of D_2O); 1.98–2.15 ppm (m, CH_3).

In entry 12, besides *dodecyl methyl sulfide* (**4a**; $R^1=n\text{-}C_{12}H_{25}$, $R^2=CH_3$), S,S-*didodecyl dithiocarbonate* (**13**; $R^1=n\text{-}C_{12}H_{25}$) was also isolated; yield: 45%, m.p. 30–31° (ethanol).

$C_{25}H_{50}OS_2$	calc.	C 69.70	H 11.70	S 14.89
(430.8)	found	69.58	11.83	14.98

^{1}H-N.M.R. (CCl_4): $\delta=0.7$–1.0 [m, $-(CH_2)_{11}-C\underline{H}_3$]; 1.0–1.8 [m, $CH_2-(C\underline{H}_2)_{10}-CH_3$]; 2.88 ppm [t, $C\underline{H}_2-C_{11}H_{23}\text{-}n$].

I.R. (liquid film): $\nu_{max}=865$, 1460, 1638, 2855, 2925, 2960 cm^{-1}.

When $R^2=n\text{-}C_8H_{17}$ in **2** (entries 15, 16, 17, 18) and $n\text{-}C_{12}H_{25}$ (entries 19, 20), the amount of Aliquat 336 is 0.2 eq. For details, see the footnotes to the Table. When $R^2=i\text{-}C_3H_7$ in **2** (entry 21), under the usual conditions the reaction came to a standstill and afforded O-*isopropyl* S-*octyl dithiocarbonate* (**3**; $R^1=n\text{-}C_8H_{17}$, $R^2=i\text{-}C_3H_7$; yield: 72%; b.p. 126°/0.5 torr; Lit. [3] b.p. 126°/0.5 torr) as major product. However, the complete disappearance of dithiocarbonate is reached after 90 min at 80°, using 1 eq. of Aliquat. In this case the crude reaction mixture is fractionated (Spaltrohr-Column; Fischer) to give *methyl octyl sulfide* (**10a**; $R^1=n\text{-}C_8H_{17}$; yield: 33%, b.p. 104–105°/20 torr, $n_D^{20}=1.4565$) and *isopropyl octyl sulfide* (**4a**; $R^1=n\text{-}C_8H_{17}$, $R^2=i\text{-}C_3H_7$); yield: 25%; b.p. 125–126°/20 torr; $n_D^{20}=1.4552$.

$C_{11}H_{24}S$	calc.	C 70.14	H 12.84	S 17.02
(188.4)	found	70.21	12.73	17.15

^{1}H-N.M.R. (CCl_4): $\delta=0.75$–1.05 [m, $-(CH_2)_7-C\underline{H}_3$]; 1.05–1.65 [m, $-CH_2-(C\underline{H}_2)_6-CH_3$]; 1.22 [d, $CH(C\underline{H}_3)_2$], 2.42 [t, $C\underline{H}_2-C_7H_{15}\text{-}n$]; 2.6–3.1 ppm [hept, $C\underline{H}(CH_3)_2$].

Methyl Octyl Sulfide; Typical Procedure:

Method B: Octyl bromide (**1**; $R^1=n\text{-}C_8H_{17}$, X=Br; 9.65 g, 50 mmol), potassium *O*-methyl dithiocarbonate (**2**; $R^2=CH_3$; 7.60 g, 52 mmol), Aliquat 336 (1.68 g) and water (50 ml) are mixed and vigorously stirred at room temperature for ~25 to 30 min. After the disappearance of **1** (G.L.C.), the mixture is diluted with cyclohexane (50 ml); then potassium hydroxide pellets (14 g, 250 mmol) are added with vigorous stirring and the mixture is heated at 70° for 30 min until the complete disappearance of the intermediate *O*-methyl *S*-octyl dithiocarbonate (**3**; $R^1=n$-

Table. Unsymmetrical Sulfides **4a**

Entry	R^1—X (**1**)	R^2 in **2**	Method	Reaction time [min][a]	Yield[b] [%]	b.p./torr	n_D^{20}	Lit. b.p./torr	Lit. n_D^{20}
1	n-C_8H_{17}—Br	C_2H_5	A	30	80	108°/16	1.4565	108–110°/14[6]	1.4565[6]
2	n-C_8H_{17}—J	C_2H_5	A	120	80				
3			A[c]	30	85				
4	n-C_8H_{17}—OMes	C_2H_5	A	30	80				
5	n-C_8H_{17}—OTos	C_2H_5	A	60	83				
6	n-$C_{10}H_{21}$—Br	C_2H_5	A	30	80	137°/16	1.4592	—[d]	
7	n-$C_{16}H_{33}$—Br	C_2H_5	A	60	73	163°/0.8	1.4640	201–205°/12[7]	—
8	C_6H_5—CH_2—Cl	C_2H_5	A	30	71	103°/16	1.5521	222–223°/759[8]	—
9	n-C_6H_{13}—CH(CH_3)—Br	C_2H_5	A	60	71	100–101°/16	1.4565	92.7–94°/10[9]	1.4564[9]
10	n-C_8H_{17}—Br	CH_3	A[e]	30	34	104–105°/20	1.4565	100.5–102.5/18[10]	1.4564[10]
11			B	30	70	97°/16			
12	n-$C_{12}H_{25}$—Br	CH_3	A	30	45	156°/16	1.4610	163–165°/19[10]	1.4612[11]
13			B	30	73				
14	n-$C_{16}H_{33}$—Br	CH_3	B	30	72	153–154°/0.7	1.4645	210–214°/20–30[12]	1.4642[12]
15	CH_3—J	n-C_8H_{17}	A[c,f]	30	34	97°/16	1.4565	see entry 10	
16	C_2H_5—J	n-C_8H_{17}	A[c,f]	30	47[g]	108°/16	1.4565	see entry 1	
17	n-$C_{10}H_{21}$—Br	n-C_8H_{17}	A[f]	30	86	167–168°/0.7	1.4650	—[h]	
18	i-C_3H_7—J	n-C_8H_{17}	A[c,e,f]	30	60	125°/20	1.4552		
19	C_2H_5—J	n-$C_{10}H_{21}$	A[c,i]	30	37[j]	137°/16	1.4592	see entry 6	
20	n-C_8H_{17}—Br	n-$C_{10}H_{21}$	A[i]	30	85[k]	167–168°/0.7	1.4650		
21	n-C_8H_{17}—Br	i-C_3H_7	A[c,e,l]	90	25[m]	125°/20	1.4552		

[a] Reaction temperature: 80°.

[b] Yield of pure, distilled product.

[c] Procedure modified as indicated in experimental.

[d] $C_{12}H_{26}S$ calc. C 71.21 H 12.95 S 15.85
(202.4) found 71.35 13.08 15.95
^{1}H-N.M.R. (CCl_4): $\delta = 0.75$–1.05 [m, —$(CH_2)_9$—$C\underline{H}_3$] 1.05–1.65 [m, —CH_2—$(C\underline{H}_2)_8$—CH_3 and CH_2—$C\underline{H}_3$]; 2.28–2.70 ppm [m, —$C\underline{H}_2$—C_9H_{19}-n and $C\underline{H}_2$—CH_3].

[e] Isolated by fractional distillation (Spaltrohr-column) of crude residue.

[f] As well as unsymmetrical sulfide **4a**, *dioctyl sulfide* (**4b**; $R^2 = n$-C_8H_{17}) was detected by G.L.C. analysis in entry 17, while it was isolated by fractional distillation in entry 15 (38%), 16 (36%), and 18 (7%); b.p. 143°/0.7 torr; $n_D^{20} = 1.4626$; Lit. [13] b.p. 202°/28 torr, $n_D^{20} = 1.4622$). Moreover 1-octanol (on the reaction mixture before of the filtration through silica gel) and traces of *methyl octyl sulfide* (**10b**; $R^2 = n$-C_8H_{17}) and *dioctyl disulfide* (**9b**; $R^2 = n$-C_8H_{17}) were detected.

[g] Identical with products from entries 1 to 5.

[h] $C_{18}H_{38}S$ calc. C 75.44 H 13.37 S 11.19
(286.6) found 75.59 13.48 11.37
^{1}H-N.M.R. (CCl_4): $\delta = 0.75$–1.05 [m, —$(CH_2)_7$—$C\underline{H}_3$ and —$(CH_2)_9$—$C\underline{H}_3$]; 1.05–1.70 [m, —CH_2—$(C\underline{H}_2)_6$—CH_3 and —CH_2—$(C\underline{H}_2)_8$—CH_3]; 2.43 ppm [t, $C\underline{H}_2$—C_7H_{15}-n and $C\underline{H}_2$—C_9H_{19}-n].

[i] As well as unsymmetrical sulfide **4a**, *didecyl sulfide* (**4b**; $R^2 = n$-$C_{10}H_{21}$) was isolated with a yield of 46% in entry 19 (b.p. 181–182°/0.8 torr, $n_D^{26} = 1.4620$; Lit. [13] b.p. 208–210°/5 torr, $n_D^{26} = 1.4612$), and detected in entry 20 (yield 11%, G.L.C.); moreover *1-decanol* was detected on the reaction mixture before of the filtration through silica gel.

[j] Identical with product from entry 6.

[k] Determined by G.L.C.; the yield of isolated pure product is 70% (cf. entry 17).

[l] Other attempts were made to cleave *O*-isopropyl *S*-octyl dithiocarbonate by increasing the amount of catalyst to 0.5 eq., the reaction time at 80° to 4 h and the reaction temperature to 100°; in the best proof, as well as a large quantity of dithiocarbonate and a certain amount of non identified by-products, isopropyl octyl sulfide was isolated with 18% yield by fractional distillation of the crude residue through a Spaltrohr-Column.

[m] Identical with product from entry 18.

C_8H_{17}, $R^2 = CH_3$). The subsequent work-up is performed as described in Method A. The reaction mixture is distilled in a Claisen flask at 16 torr to give *methyl octyl sulfide* [**4a**; $R^1 = n$-C_8H_{17}, $R^2 = CH_3$; yield: 5.6 g (70%); b.p. 97°/16 torr; $n_D^{20} = 1.4565$]. Then the pressure is lowered to 2 torr and subsequent distillation of the residue gives *dioctyl disulfide* [**9a**; $R^1 = n$-C_8H_{17}; yield: 1.45 g (20%); b.p. 170–172°/2 torr; $n_D^{20} = 1.4828$]. G.L.C. analysis and I.R. spectrum of the residue from distillation, show traces of *S,S-dioctyl dithiocarbonate* (**13**; $R^1 = n$-C_8H_{17}; $\nu_{C=O} = 1648\ cm^{-1}$). Method B failed when R^2 in **2** = C_2H_5, i-C_3H_7, n-C_8H_{17}, n-$C_{12}H_{25}$.

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