Convenient Synthesis of Organic Sulfides Using Impregnated Reagents

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We report a convenient procedure for the conversion of primary organic halides into corresponding symmetrical and unsymmetrical sulfides. Our method, which is based on the use of sodium sulfide and sodium hydroxide impregnated on neutral alumina[1,2], offers a simple alternative to conventional phase-transfer procedures[3,4].

Attempted small-scale conversion (0.5 mmol) of 1-bromooctane (**1**, $R^1 = n\text{-}C_8H_{17}$, X = Br) to di-*n*-octyl sulfide (**2**) using solid sodium sulfide in toluene at 90 °C produced a 20% yield after 24 h. In contrast, a similar reaction in which the inorganic salt was first coated on to an alumina support gave a quantitative yield of the organic sulfide in 0.5 h. The convenience associated with the use of sodium sulfide on alumina is exemplified by a preparative scale synthesis of *n*-octyl sulfide. After stirring a toluene solution of 1-bromooctane (20 mmol) with excess sodium sulfide/alumina for 12 h at 90 °C, the spent and unused reagents were removed by simple filtration. Removal of solvent under reduced pressure afforded a 97% yield of di-*n*-octyl sulfide as a colorless liquid which was spectroscopically identical with an authentic sample. Unlike reported phase-transfer syntheses of sulfides, application of sodium sulfide/alumina to secondary alkyl halides gave very poor results.

We have also found that sodium hydroxide on alumina when used in conjunction with organic halides **1** and thiols **3** gives significantly higher yields of unsymmetrical sulfide **4** than use of either pulverized sodium hydroxide or basic alumina. Our results are summarized in the Table.

$$\underset{\mathbf{1}}{R^1\text{–}X} \xrightarrow{Na_2S/Al_2O_3} \underset{\mathbf{2}}{R^1\text{–}S\text{–}R^1}$$

$$\underset{\mathbf{1}}{R^1\text{–}X} + \underset{\mathbf{3}}{R^2\text{–}SH} \xrightarrow{NaOH/Al_2O_3 \text{ or } NaOH \text{ or } Al_2O_3} \underset{\mathbf{4}}{R^1\text{–}S\text{–}R^2}$$

The principal advantages of the procedure described herein over current phase-transfer methods are the low cost and ready availability of alumina, the avoidance of an aqueous phase, and the convenience in product work-up; principal disadvantages are slower reaction rates and the applicability only to primary halides. Nonetheless, this should serve as a valuable alternative procedure, especially for small-scale preparations.

Impregnated Reagents:

Sodium Sulfide/Alumina: A 200-ml round bottomed flask is charged with sodium sulfide nonahydrate (12.0 g, 50 mmol) dissolved in distilled water (20 ml) and neutral alumina (8.6 g; Bio-Rad AG7) is added in one portion. The flask is transferred to a rotary evaporator and water is removed under reduced pressure, keeping the bath temperature below 65 °C. The resulting reagent is then dried (1 h, 110 °C/0.05 torr).

Sodium Hydroxide/Alumina: A procedure similar to the above is used to impregnate sodium hydroxide (6.0 g, 150 mmol) on to neutral alumina (42 g).

Di-*n*-octyl Sulfide (2; $R^1 = n\text{-}C_8H_{17}$):

A 100-ml round bottomed flask is charged with 1-bromooctane (**1**; $R^1 = n\text{-}C_8H_{17}$, X = Br; 3.8 g, 20 mmol) dissolved in dry toluene (50 ml) and sodium sulfide/alumina (15 g). The mixture is stirred for 12 h at 90 °C and the organic sulfide **2** isolated by filtering the mixture, washing spent and unused reagent with toluene (30 ml), and removing the solvent from the combined filtrate under reduced pressure to give di-*n*-octyl sulfide as a colorless liquid; yield: 2.5 g (97%). The I.R. and ^{1}H-N.M.R. spectra were identical with those of an authentic sample.

***n*-Octyl Phenyl Sulfide (4; $R^1 = n\text{-}C_8H_{17}$, $R^2 = C_6H_5$):**

A 100-ml round bottomed flask is charged with 1-bromooctane (0.57 g, 3.0 mmol), thiophenol (**3**; $R^2 = C_6H_5$; 0.33 g, 3.0 mmol) in dry toluene (50 ml) and sodium hydroxide/alumina (6.0 g). The mixture is stirred for 22 h at 90 °C and the product isolated using a work-up identical to that described above for di-*n*-octyl sulfide, affording colorless *n*-octyl phenyl sulfide having I.R. and ^{1}H-N.M.R. spectra identical with those of an authentic sample; yield: 0.64 g (96%).

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[1] For a review on reactions at alumina surfaces see: G. H. Posner, *Angew. Chem.* **90**, 527 (1978); *Angew. Chem. Int. Ed. Engl.* **17**, 487 (1978).

[2] For a review on supported reagents see: A. McKillop, D. W. Young, *Synthesis* **1979**, 401, 481.

[3] D. Landini, F. Rolla, *Synthesis* **1974**, 565.

[4] A. W. Herriott, D. Picker, *Synthesis* **1975**, 447.

Table. Sulfides Prepared using Impregnated Reagents

Substrates R^1–X (**1**)	R^2–SH (**3**)	Reagent	Product	Yield[a] [%]	Reaction conditions (temperature/time)	Purity[b] [%]
n-C_4H_9–Br	—	Na_2S/Al_2O_3	**2a**	98	90 °C/20 h	100
n-C_4H_9–Cl	—	Na_2S/Al_2O_3	**2a**	89	90 °C/20 h	100
n-C_8H_{17}–Br	—	Na_2S/Al_2O_3	**2b**	97	90 °C/12 h	100
n-C_8H_{17}–Cl	—	Na_2S/Al_2O_3	**2b**	80[c]	90 °C/6 h	100
C_2H_5–Br	*n*-C_8H_{17}–SH	$NaOH/Al_2O_3$	**4a**	98	40 °C/20 h	100
n-C_8H_{17}–Br	C_6H_5–SH	$NaOH/Al_2O_3$	**4b**	96	90 °C/20 h	98
n-C_8H_{17}–Br	C_6H_5–SH	pulverized NaOH	**4b**	56	90 °C/22 h	98
n-C_8H_{17}–Cl	C_6H_5–SH	$NaOH/Al_2O_3$	**4b**[d]	38	90 °C/20 h	>95
n-C_8H_{17}–Br	C_6H_5–SH	Al_2O_3 (basic)	**4b**[d]	55	90 °C/22 h	>95

[a] Yield of isolated product unless otherwise stated.
[b] Purity of product determined by G.L.C..
[c] Yield determined by G.L.C. (conditions: OV-17, 160 °C, 6 ft column).
[d] Significant amount of diphenyl disulfide also formed.

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