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Solid Supported Reagents and Reactions. Part 21.[1] Rapid and Clean Synthesis of Thiols from Halides Using Polymer-supported Hydrosulfide†‡

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A variety of thiols are prepared from corresponding halides using polymer-supported hydrosulfide in excellent yields. Isolation of pure products by simple filtration and evaporation is an important feature of this method.

Thiols are important not only for their use in the synthesis of organosulfur compounds but also for their roles in cell biochemistry. Therefore, many synthetic methods have been developed.[2,3] Although direct preparations of thiols from alkyl halides and metal sulfides would be straightforward, direct methods give only a moderate yield of thiols accompanying a considerable amount of dialkyl sulfide.[2] Therefore, indirect methods involving thiourea,[2] xanthate[2] and thioacetate[2] are commonly utilized for the synthesis of thiols and other new indirect methods have been reported.[4–9] These indirect methods usually give around 80% yield and no dialkyl sulfides or other undesired by-products; however, intermediates have to be transformed to thiols by hydrolysis with base[5–9] or by reduction with lithium aluminium hydride.[10,11] Recently thiols have been prepared in quantitative yield from the corresponding thioacetates *via* Pd-catalyzed methanolysis with borohydride exchange resin under mild and neutral conditions.[2]

$$\mathrm{R{-}X} + \textcircled{P}^{+}\,\bar{\mathrm{S}}\mathrm{H} \xrightarrow[\text{15 min}]{\text{MeCN, 25 °C}} \mathrm{R{-}SH} + \textcircled{P}^{+}\,\bar{\mathrm{X}}$$

	R	X
a	$Me[CH_2]_2CH_2$	Br
b	$Me[CH_2]_2CH_2$	I (carried out at 0 °C)
c	Me_3C	Br
d	Me_3C	Cl
e	$PhCH_2$	Cl
f	$4\text{-}ClC_6H_4CH_2$	Cl
g	$2,4\text{-}ClC_6H_3CH_2$	Cl
h	$4\text{-}NO_2C_6H_4CH_2$	Br
i	$C_6H_4\text{-}1,2\text{-}[CH_2]_2$	Br_2

Scheme 1

We now report on an exceedingly simple method for the direct synthesis of thiols from halides using hydrosulfide exchange resin (Scheme 1). It is important to note that this method produces thiols in excellent yields (93–98%) without any trace of dialkyl sulfides.[3]

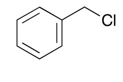
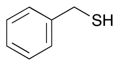
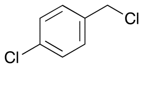
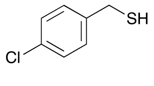
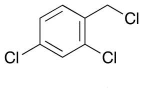
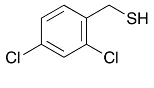
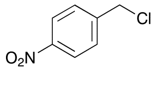
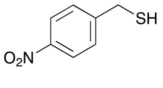
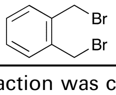
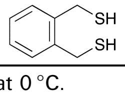
The synthesis of thiols from alkyl halides and NaSH always results in the formation of dialkyl sulfides[12] because any alkyl thiols formed initially further react with excess alkyl halides. However, Tulsion A-77-supported hydrosulfide has more nucleophilic character than NaSH and therefore alkyl halides react with hydrosulfide exchange resin much faster than NaSH giving corresponding thiols within a very short time (15 min) at 25 °C. Thus the formation of dialkyl sulfides as by-products is avoided. Tertiary alkyl halides (entries **c** and **d** in Table 1) are also smoothly converted into corresponding thiols at 25 °C. These reactions not only proceed with unique chemoselectivity but also give excellent yields of thiols compared to those prepared by indirect methods.[4–9] The isolation of pure products by simple filtration and evaporation is an important feature of this method. The recovered resin can be recycled in the process after regeneration by treatment with dilute HCl.

Experimental

All reactions were conducted in oven-dried flasks. Solvents were distilled before use. All chemicals were of analytical grade. Reactions were monitored by TLC. The strongly anionic exchange resin, Tulsion A-27 (Cl^-) was procured from Thermax Chemicals, Pune.

Preparation of Hydrosulfide Exchange Resin.—To a solution of NaSH (50 mmol) in MeOH (50 ml), Tulsion A-27 (chloride form) (10 g) was added and the mixture was shaken for 1 h. The resin was filtered off and washed with distilled water until it was free from Cl^- and excess NaSH. The resin was then washed with methanol, diethyl ether and dried under vacuum at 50 °C for 2 h. The capacity

Table 1 Synthesis of thiols from halides at 25 °C

Entry	Halide	Product	Yield (%)	mp/bp (Torr) (Lit.) (°C)
a	$Me[CH_2]_2CH_2Br$	$Me[CH_2]_2CH_2SH$	98	97 (760 mm) [96–97 (760 mm)][13]
b	$Me[CH_2]_2CH_2I$	$Me[CH_2]_2CH_2SH$[a]	93	97 (760 mm) [96–97 (760 mm)][13]
c	Me_3CBr	Me_3CSH	96	63 (760 mm) [61.60 (700.8 mm)][14]
d	Me_3CCl	Me_3CSH	95	63 (760 mm) [61.60 (700.8 mm)][14]
e			98	194 (760 mm) [192–194 (760 mm)][11]
f			93	103 (12 mm) [105 (10 mm)][15]
g			97	121 (14 mm) [123–125 (10 mm)][15]
h			97	58 [58][16]
i			96	43 [44][17]

[a]The reaction was carried out at 0 °C.

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*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

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of hydrosulfide exchange resin was found to be 2 mmol g^{-1} of dry resin.

General Procedure for the Synthesis of Thiols from Halides.—A mixture of halide (10 mmol) in acetonitrile (20 ml) and hydrosulfide exchange resin (5 g for monohalides and 10 g for dihalides) was shaken for 15 min at 25 °C. The reaction was monitored by TLC. The resin was filtered off and washed with ether (3 × 10 ml). Removal of the solvent under reduced pressure gave thiols in excellent yields.

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