Boron Trifluoride Monohydrate Catalyzed One-Flask Preparation of Sulfides from Carbonyl Compounds with Thiols and Triethylsilane[1]

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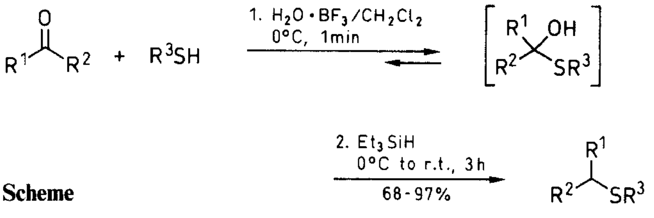
Received 2 August 1991; revised 19 September 1991

Boron trifluoride monohydrate catalyzed thiolation of aldehydes and ketones with thiols and triethylsilane to the corresponding sulfides was carried out in good to excellent yields.

The most common method for the synthesis of sulfides is by the alkylation of thiolate anions with alkyl halides in a typical nucleophilic substitution.[2] Many other synthetically useful methods are also known and the chemistry has been reviewed.[3] More recent methods include reduction of hemithioacetals with reducing agents such as lithium aluminum hydride/aluminum chloride[4] or triethylsilane.[5] Kikugawa[6] has carried out direct reductive thiolation of aldehydes and ketones with thiols to symmetrical and unsymmetrical sulfides using pyridine–borane complex in trifluoroacetic acid medium.

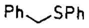
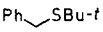
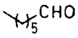
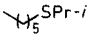
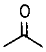
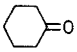
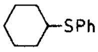
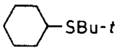
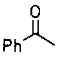
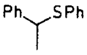
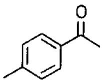
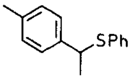
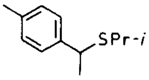
Recently, we have reported boron trifluoride monohydrate catalyzed thioacetalization of carbonyl compounds.[7] Boron trifluoride monohydrate is an inexpensive, non-oxidizing strong acid catalyst comparable in strength to sulfuric acid. We now report that thiols (thiophenol) react with ketones and aldehydes under boron trifluoride monohydrate catalysis to form in situ hemithioacetals which upon treatment with triethylsilane (ionic hydrogenation) then give sulfides in a highly efficient one-pot procedure.

The boron trifluoride monohydrate catalyzed reaction of benzaldehyde with 2-propanethiol and triethylsilane in dichloromethane solution gave benzyl isopropyl sulfide in 97% isolated yield. The reaction was also similarly successful with a wide variety of carbonyl compounds and thiols. Symmetrical and unsymmetrical sulfides were obtained in good to excellent yields (Table 1). The physical data of the sulfides are shown in Table 2.



Scheme

Table 1. Reductive Thiolation of Aldehydes and Ketones

Substrate		Thiol	Product		Yield[a]
PhCHO	**1**	PhSH		**1a**	91
		i-PrSH		**1b**	97
		t-BuSH		**1c**	94
		s-BuSH		**1d**	92
	**2**	*i*-PrSH		**2a**	86
	**3**	*i*-PrSH	*i*-PrSPr-*i*	**3a**	68
	**4**	PhSH		**4a**	76
		t-BuSH		**4b**	78
	**5**	PhSH		**5a**	88
	**6**	PhSH		**6a**	90
		i-PrSH		**6b**	83

[a] Isolated yields.

The mechanism of the reaction is suggested in the Scheme involving the intermediacy of hemithioacetals followed by ionic hydrogenation. An alternative pathway involv-

Table 2. Physical Data of Sulfides Prepared

Compound	^{13}C NMR ($CDCl_3$/TMS)	MS m/z (%)	bp (°C)/Torr or mp (°C) (Lit. data)
1a	39.0, 126.3, 127.1, 128.4, 128.8, 129.8, 136.3, 137.4	200 (M^+, 17.5), 165 (1.0), 121 (1.3), 109 (7.7), 91 (100), 77 (2.4)	41–42 (41–43.5[9])
1b	22.9, 34.0, 34.9, 126.6, 128.2, 128.6, 138.6	166 (M^+, 14.5), 151 (0.7), 123 (3.2), 121 (2.8), 91 (100), 65 (14.3)	71/5 (89–90/14[10])
1c	30.8, 33.3, 42.7, 126.6, 128.3, 128.8, 138.5	180 (M^+, 14.5), 165 (0.5), 124 (29.4), 91 (100), 77 (8.0), 65 (16.0), 57 (100)	75/5 (92–93/14[10])
1d	22.0, 28.2, 36.7, 40.4, 126.8, 128.4, 128.8, 138.6	180 (M^+, 14.7), 137 (3.0), 124 (6.8), 91 (100), 65 (13.9)	88/5 (108–109/15[10])
2a	13.9, 22.5, 23.3, 28.9, 29.0, 29.8, 30.5, 31.7, 34.6	174 (M^+, 22.7), 159 (8.4), 131 (69.1), 97 (23.4), 89 (30.6), 76 (29.5), 55 (84.0), 43 (100)	80/5 (222/760[11])
3a	23.6, 33.4	118 (M^+, 36.3), 103 (45.2), 76 (20.0), 61 (96.3), 43 (100)	176/760 (177/760[11])
4a	25.6, 25.9, 33.2, 46.4, 126.4, 128.6, 131.7, 136.7	192 (M^+, 19.7), 110 (100), 83 (10.7), 65 (11.9), 55 (40.4), 41 (27.4)	142/10 (90–104/0.3[12])
4b	23.9, 25.2, 26.1, 31.3, 41.0, 42.4	172 (M^+, 21.0), 116 (18.3), 83 (35.7), 82 (54.9), 67 (25.4), 57 (100), 41 (61.8)	44/0.1
5a	22.2, 47.7, 126.8, 126.9, 127.1, 128.2, 128.4, 132.2, 135.0, 143.0	214 (M^+, 14.0), 105 (100), 103 (10.3), 79 (15.0), 77 (21.3)	162/15 (163–164/15[13])
6a	21.0, 22.3, 47.5, 126.9, 127.0, 128.6, 129.3, 132.1, 136.6, 140.0	228 (M^+, 4.6), 119 (100), 109 (14.2), 91 (32.0), 77 (13.2), 65 (19.5)	160–167/10
6b	20.9, 22.9, 23.4, 33.9, 42.6, 126.9, 129.0, 136.3, 141.4	194 (M^+, 10.2), 120 (12.7), 119 (100), 91 (29.8), 77 (10.2), 59 (10.0), 41 (15.7)	140–148/10

ing initial reduction of the carbonyl compound to alcohol followed by bimolecular dehydration with thiol is unlikely since very little direct reduction of the carbonyl compound to the corresponding alcohol or ether was observed in our experiments.

In conclusion, we have developed an efficient one-pot procedure for the preparation of sulfides by the boron trifluoride monohydrate catalyzed reductive thiolation of carbonyl compounds using triethylsilane. This procedure was found to be more convenient, inexpensive and easier to handle than that previously reported by Kikugawa[6] employing pyridine–borane complex and trifluoroacetic acid.

Thiolation of Aldehydes and Ketones; General Procedure:

In a typical reaction, aldehyde or ketone (10 mmol) and of thiol (11 mmol) were dissolved in CH_2Cl_2 (10 mL). The mixture was cooled to 0 °C using ice bath and $H_2O \cdot BF_3$[8] (1 mL) was added to the mixture. The reaction mixture was stirred at ice bath temperature for 1 min and Et_3SiH (15 mmol) was added. The solution was stirred for 3 h during which time it warmed up to r.t. The mixture was poured into ice-water (30 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The organic layer was separated and washed with H_2O (2 × 25 mL), 10 % $NaHCO_3$ (3 × 25 mL) and H_2O again (2 × 25 mL) and finally dried ($MgSO_4$). The solvent was removed on rotary evaporator and the sulfide thus obtained was purified by distillation or recrystallization and subjected to NMR and GC-MS analysis.

A slight modification of the above procedure was necessary to obtain good yield for the reaction of heptanal (**2**, Table 1). Heptanal (**2**; 10 mmol), *i*-PrSH (11 mmol) and Et_3SiH (15 mmol) were dissolved in CH_2Cl_2 (10 mL) and the mixture was cooled to ice bath temperature. $H_2O \cdot BF_3$ (1 mL) was added to the mixture and the reaction was stirred for 3 h. The reaction was worked up as above.

Support of our work by the National Science Foundation and National Institutes of Health is gratefully acknowledged.

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