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M. M. Lakouraj^a, B. Movassagh^a & Z. Fadaei^b

^a Department of Chemistry, Mazandaran University, Babolsar, 47415, Iran

^b Department of Chemistry, Razi University, Kermanshah, 67149, Iran

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SYNTHESIS OF ORGANIC SULFIDES VIA Zn/AlCl₃ SYSTEM IN AQUEOUS MEDIA

M. M. Lakouraj,^{1,*} B. Movassagh,¹ and Z. Fadaei²

¹Department of Chemistry, Mazandaran University, Babolsar 47415, Iran ²Department of Chemistry, Razi University, Kermanshah 67149, Iran

ABSTRACT

An efficient procedure for preparation of various sulfides has been introduced through a simple reaction of disulfides with suitable alkyl or aryl halides which is promoted by commercial zinc powder in the presence of $AlCl_3$ in aqueous media at 65°C.

Recently, organometallic-type reactions in aqueous media have attracted considerable interest in organic synthesis.¹ If one can perform these reactions in aqueous media just as generally and easily as in organic solvent, such reactions may offer a number of advantage: i) practical convenience and environmental benefits due to the omission of inflammable and anhydrous solvents; ii) protection and deprotection process for certain functional groups can possibly be simplified; iii) water-soluble compounds and substrates bearing active functional groups can be reacted directly without

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^{*}Corresponding author. E-mail: lakouraj@umcc.ac.ir

the need of derivatization; iv) the rate and stereochemical outcomes of the reactions may offer new opportunities in synthesis.

Most commonly, zinc, indium, tin and bismuth or BiCl₃/Al, BiCl₃/Zn and BiCl₃/Fe systems are used.^{1,2} However, the application of aqueous organometallic reactions seems to have been somewhat limited mainly to allylation and propargylation of carbonyl compounds.

Sulfides are useful synthetic reagents and intermediates in organic synthesis. Many methods are known for the formation of sulfides including desulfurization of disulfides, reduction of sulfoxides and sulfones, aryllithium or organocuprate addition to thiocarbonyl compounds;³ the treatment of halides with sodium sulfides,⁴ thiourea;⁵ the use of electrophilic sulfur species;⁶ the use of *bis*(tributyltin)sulfide as a sulfur transfer agent;⁷ treatment of thiols and alkyl halides with DBU.⁸ Under the action of phosphorus(III) compounds disulfides are subjected to partial desulfurization leading to sulfides.⁹ A number of complexes of iron, nickel and other transition metals have been studied rather extensively as reagents for desulfurization of various compounds.¹⁰ But, all methods mentioned above lack in general applicability because of severe reaction conditions and complicated procedures and/or activated reactants are required. The traditional method for preparation of unsymmetrical sulfides and the alkylation of thiols suffer from drawbacks such as foul smelling of thiols and elevated temperature. Recently, montmorillonite-3-aminopropyl triethoxysilane and Ce exchanged zeolite catalyzed synthesis of sulfides has been reported.¹¹ Also, in a more recent study Lu and Zhang reported the formation of benzyl sulfides catalyzed by a Sm/BiCl₃ system in aqueous media, in which disulfides were used as a thiolating source.¹² Disulfides are important reagents in synthetic chemistry, and many methods have been published for synthesis of disulfides.^{9,13} Among them, oxidative coupling of thiols to disulfides is the most important one.¹⁴

In connection with our ongoing work on Zn/AlCl₃ system, we wish to report a convenient route to the preparation of different sulfides through a simple coupling of disulfides with alkyl and aryl halides promoted by cheap and reactive metallic zinc dust in the presence of AlCl₃ in DMF-H₂O-mixed solvent (Scheme 1).

The results are summarized in Table 1. The treatment of symmetrical aryl disulfides with benzyl bromides (Entries 1–7, Table 1) and primary alkyl bromides (Entries 8 and 9, Table 1) affords the corresponding aryl–alkyl

$$RSSR + 2R'X \xrightarrow{Zn/AICl_3} 2RSR'$$

Scheme 1.

SULFIDE SYNTHESIS VIA Zn/AlCl₃ SYSTEM

sulfides in excellent yields. Under the same conditions tertiary alkyl halide (Entry 10, Table 1) does not produce the expected sulfide even after 27 h. This represents the S_N^2 type nucleophilic reaction (Scheme 2). In the case of aryl halides containing strong electron withdrawing substituents (Entries 11–17, Table 1), the reactions proceed more easily to afford diaryl sulfides in good to excellent yields, but simple aryl halides (Entries 18–20, Table 1) and those having electron donating substituents (Entry 21, Table 1) do not react at all. As a result, an S_NAr mechanism is proposed for these halides (Scheme 2). While symmetrical dialkyl disulfides react conveniently with alkyl halides (Entries 24–27, Table 1) to give the corresponding sulfides, the reaction of symmetrical dialkyl disulfides (Entries 22 and 23, Table 1) with aryl halides failed due to fast formation of an unknown complex. Also, under the same conditions, α -cyanothioethers (Entries 28 and 29, Table 1) were easily synthesized in high yields, using chloroacetonitrile as alkyl halide.



Scheme 2.

It is worth mentioning that zinc powder was also examined with different Lewis acids such as BF_3 - Et_2O , $AlCl_3$, $FeCl_3$, and $ZnCl_2$ in different solvents, but the best result was obtained with the $Zn/AlCl_3$ system in DMF-H₂O mixed solvent. The presence of $AlCl_3$ and H_2O is essential in this procedure.

To conclude, this method is attractive since it offers some advantages over earlier reported procedures in that it avoids the need to apply thiol, the manipulation of air-sensitive transition metal complexes, and the use of dry solvent, as well as being carried out under mild conditions.

EXPERIMENTAL

Disulfides were prepared according to the method reported by Rieke et al.¹⁵ Zinc powder and AlCl₃ were purchased from Merck company.

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No.	R	R'X or ArX	Time (h)	Yield ^a (%)	M.P. (°C) (obs.)/M.P. or B.P. (°C/mm) (lit.) ^{ref}
1	Ph	PhCH ₂ Br	13	90	(41.5-42.5)/40-42 ¹²
2	$p-ClC_6H_4$	PhCH ₂ Br	15	90	(53)/53 ¹¹
3	<i>p</i> -MeC ₆ H ₄	PhCH ₂ Br	11	94	$(45-45.5)/45-46^{16}$
4	m-MeC ₆ H ₄	PhCH ₂ Br	12	94	$(30-32)/31^{17}$
5	Ph	$p-NO_2C_6H_4CH_2Br$	12	95	$(79)/79^{18}$
6	<i>p</i> -MeC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄ CH ₂ Br	10.5	93	(94-94.5)/90 ¹⁹
7	<i>p</i> -ClC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄ CH ₂ Br	14	85	$(70-70.5)/66-67^{20}$
8	p-MeC ₆ H ₄	CH ₃ (CH ₂) ₂ CH ₂ Br	17	95 ^b	(80-82/1 mm)/
					$135 - 138 / 15 \mathrm{mm}^{21}$
9	$p-ClC_6H_4$	CH ₃ (CH ₂) ₄ CH ₂ Br	18	100 ^b	(oil)/175–6/12 mm ²²
10	<i>p</i> -MeC ₆ H ₄	Me ₃ CCl	27	0	_
11	Ph	$2,4-(NO_2)_2C_6H_4Cl$	6	95	$(120-121)/120^{23}$
12	$p-ClC_6H_4$	$2,4-(NO_2)_2C_6H_4Cl$	8	85	$(125-126)/123-124^{24}$
13	<i>p</i> -MeC ₆ H ₄	$2,4-(NO_2)_2C_6H_4Cl$	4.5	95	$(102 - 103.5)/102.5 - 104^{25}$
14	<i>m</i> -MeC ₆ H ₄	$2,4-(NO_2)_2C_6H_4Cl$	5.5	75	$(100-101)/100-101.5^{25}$
15	Ph	$2,4-(NO_2)_2C_6H_4F$	3	92	$(120-121)/120^{25}$
16	p-ClC ₆ H ₄	$2,4-(NO_2)_2C_6H_4F$	3.5	92	$(125-126)/124^{25}$
17	<i>m</i> -MeC ₆ H ₄	$2,4-(NO_2)_2C_6H_4F$	2	73	$(100-101)/100-101.5^{25}$
18	Ph	C ₆ H ₅ -F	18	0	_
19	Ph	C ₆ H ₅ -Cl	18	0	_
20	Ph	C ₆ H ₅ -Br	19	0	_
21	Ph	<i>m</i> -MeC ₆ H ₄ Br	17	0	_
22	Cyclohexyl	$2,4-(NO_2)_2C_6H_4Cl$	19	0	_
23	$CH_3(CH_2)_3$	$2,4-(NO_2)_2C_6H_4Cl$	19	0	_
24	$CH_3(CH_2)_3$	CH ₃ (CH ₂) ₂ CH ₂ Br	18	88^{b}	$(oil)/187/5 \mathrm{mm}^{23}$
25	$CH_3(CH_2)_7$	PhCH ₂ Br	19	86	(oil)/175/12 mm ²⁶
26	PhCH ₂	PhCH ₂ Br	21	55 ^b	$(50)/49-51^{23}$
27	$CH_3(CH_2)_3$	PhCH ₂ Br	16	100 ^b	$(oil)/130/5 mm^{27}$
28	Ph	ClCH ₂ CN	3.5	87	(oil)/133–135 ²⁸
29	p-ClC ₆ H ₄	ClCH ₂ CN	6	85	$(89-90)/88-90^{29}$

Table 1. Preparation of Sulfides from Disulfides with Zn/AlCl₃ in DMF/H₂O

^aYields based on pure isolated product.

^bG.C. Yields.

All products were characterized by comparison of their spectral and physical data with those of known samples. IR spectra were obtained using a Shimadzu 470 instrument. ¹H NMR spectra were determined by Jeol JNM-PMX 60 MHz or Bruker 200 MHz NMR spectrometer. Melting points were obtained by a Gallen-Kamp apparatus and were corrected.

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General Procedure for Preparation of Sulfides from Corresponding Diaryl Disulfides (Method A). A mixture of diaryl disulfide (0.5 mmol), zinc powder (130 mg, 2 mmol), aluminum chloride (133 mg, 1 mmol), DMF (10 ml), and water (2.5 ml) was stirred at 65° C for 1 h until the zinc powder disappeared; alkyl halide and/or aryl halide (1.5 mmol) was then added at once to the solution and stirring was continued at that temperature for 2–19 h in air atmosphere. After completion of the reaction, the solution was filtered and washed with diethyl ether. The combined ether/DMF solution was then washed with water and dried over sodium sulfate. The solvent was evaporated in vacuo to give the corresponding sulfide in high yield which recrystallized from ethanol.

General Procedure for Synthesis of Sulfides from Corresponding Dialkyl Disulfides (Method B). A mixture of dialkyl disulfide (0.5 mmol), aryl or alkyl halide (1.5 mmol), zinc powder (130 mg, 2 mmol), aluminum chloride (133 mg, 1 mmol), DMF (10 ml), and water (2.5 ml) was stirred at 65°C for 3.5–19 h in air atmosphere. After completion of the reaction, the solution was filtered and washed with diethyl ether. The combined ether/DMF solution was then washed with water and dried (Na₂SO₄). The solvent was evaporated in vacuo to afford desired sulfide.

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