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A COMPARATIVE STUDY OF OXIDANTS ON THIOLS[†]

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A recent article described the synthetic utility of sodium chlorite for the conversion of thiols to disulfides.[1] The present work deals with this transformation using hitherto unreported oxidizing agents The study compares reaction times, yields and purity of the products using known oxidants with those of the reagents under investigation. The data presented includes a variety of thiols some of which bear other oxidizable functions. Reagents such as sodium metaperiodate, ammonium persulfate, ceric ammonium nitrate and thionyl chloride so far not studied for this conversion have now been found to furnish high yields of disulfides under simple experimental conditions. The results describe the best conditions which feature short reaction times, quantitative conversion, high purity, process economy and dispensing with the use of solvents. Tetramethylthiuram disulfide and dibenzothiazo-2yldisulfide are well known fungicides and rubber accelerators used extensively in India and the present work allows the choice of the proper oxidant for large scale production. Ammonium persulfate, chlorite and metaperiodate can be advantageously used in place of chlorine gas, hydrogen peroxide/acid or sodium nitrite/hydrochloric acid for the oxidation to the corresponding disulfides. The use of thionyl chloride on thiols in the presence of pyridine has been reported to furnish dithiosulfites;[2] however, our conditions are different as are also the substrates studied for oxidation which makes thionyl chloride the reagent of choice for the oxidation of heterocyclic thiols such as 2-mercaptobenzimidazole, benzoxazole, benzothiazole and similar systems. The results are presented in the Tables. The end products were found to be identical in all respects with authentic samples (Table 3).

$$\underset{\mathbf{1}}{\mathrm{R{-}SH}} \longrightarrow \underset{\mathbf{2}}{\mathrm{R{-}S{-}S{-}R}}$$

R = a) $Me_2NC(=S)$ b) $Et_2NC(=S)$ c) $(CH_2)_5NC(=S)$ d) 2-benzimidazolyl
e) 2-benzothiazolyl f) 2-naphthyl g) phenyl h) 4-tolyl i) 2-aminophenyl
j) 2-carboxyphenyl k) 5-amino-1,3,4-thiadiazoyl l) 4-morpholinyl thiocarbamyl
m) 4-piperidinyl thiocarbamyl n) 4-pyrrolyl thiocarbamyl o) 4-pyrrolidinyl thiocarbamyl
p) 2-benzoxazolyl q) 5-Chlorobenzothiazolyl

EXPERIMENTAL SECTION

Typical Procedure.- To a stirred solution of thiol or dithiocarbamic acid (0.001 m) in THF (5mL) maintained at 10° was introduced an aqueous solution of the oxidant (0.001m, 8mL) in 5 min (thionyl chloride was used as a 5% solution in THF). The product was formed generally in about 20 min. or less (see Tables) as shown by tlc. Dilution with ice water (50 mL) led to the precipitation of the desired disulfide which was collected and dried. It is interesting to note that even aqueous slurries of the substrates were oxidized to the disulfides without any reduction in yield or purity under these conditions.

TABLE 1. Time (min.) and Yields[a] (%) of Disulfides from Oxidation of Thiols

Cmpd	$NaClO_2$	H_2O_2/H^+	$NaNO_2/H^+$	Cl_2	$(NH_4)_2S_2O_8$	$NaIO_4$
2a	(20,93)	(20,86)	(25,80)	(25,87)	(15,85)	(5,85)
2b	(20,92)	(25,85)	(30,85)	(25,85)	(20,87)	(5,90)
2c	(20,90)	(25,70)	(20,75)	(15,80)	(15,85)	(5,89)
2d	(15,95)	(20,87)	(25,85)	(20,85)	(15,90)	(5,95)
2e	(15,97)	(20,87)	(20,85)	(20,90)	(15,95)	(5,94)
2f	(15,96)	(20,87)	(25,90)	(20,80)	(10,85)	(5,90)
2g	(10,96)	(15,80)	(15,92)	(10,90)	(10,95)	(5,97)
2h	(10,96)	(15,85)	(10,90)	(10,85)	(10,87)	(5,95)
2i	(15,92)	(15,80)	(15,85)	(15,80)	(10,85)	(5,92)
2j	(10,86)	(15,75)	(15,70)	(15,75)	(10,72)	(5,85)
2k	(15,90)	(20,83)	(20,80)	(20,75)	(15,85)	(20,73)
2l	(15,94)	(25,87)	(25,82)	(20,83)	(15,89)	(10,92)
2m	(15,93)	(20,86)	(25,80)	(20,85)	(15,90)	(15,90)
2n	(20,96)	(25,80)	(20,85)	(25,80)	(20,90)	(15,85)
2o	(15,93)	(20,85)	(20,80)	(20,80)	(15,85)	(15,89)

a) Crude yields with no trace of starting material.

TABLE 2. Time (min) and Yields[a] (%) of Disulfides from Oxidation of Thiols

Compd	Ferric Chloride	Ceric ammonium nitrate	Thionyl chloride
2d	(b)	(c, 93)	(15, 94)
2e	(b)	(120, 93)	(10, 93)
2f	(5, 90)	(10, 85)	(10, 80)
2g	(5, 97)	(25, 90)	(5, 96)
2h	(5, 94)	(20, 89)	(10, 90)
2i	(5, 92)	(25, 85)	(b)
2j	(10, 85)	(25, 87)	(b)
2k	(5, 73)	(20, 80)	(b)
2p	(b)	(5, 80)	(20, 82)
2q	(b)	(20, 93)	(25, 91)

a) Crude yields with no trace of starting material. b) No reaction. c) Overnight stirring.

TABLE 3. Mps of Compounds **2a-2q**

Cmpd	mp. (°C)	lit mp. (°C)	Cmpd	mp. (°C)	lit mp. (°C)
2a	148	151[3]	**2j**	285-287	289-290[9]
2b	68	70.5[3]	**2k**	235-237	239[10]
2c	88-89	86-87[4]	**2l**	148	149-150[11]
2d	200	198[5]	**2m**	78-80	78[9]
2e	180-181	182-183[6]	**2n**	93	95-96[12]
2f	143	143-144[7]	**2o**	144-146	148[12]
2g	65	61-62[8]	**2p**	113-115	112-113[13]
2h	47	45-46[8]	**2q**	240	238-242[14]
2i	78	79-80[6]			

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SELECTIVE REDUCTION OF α,β-UNSATURATED ALDEHYDES AND KETONES TO ALLYLIC ALCOHOLS WITH DIISOBUTYLALKOXYALANES

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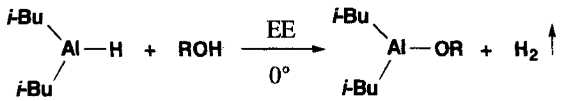
Very recently, we reported that diisobutylchloroalane (DIBAL-Cl) is a highly selective reducing agent for the reduction of enals and enones to the corresponding allylic alcohols,[1] and for the reduction of aldehyde or ketone groups in the presence of many other readily reducible functional groups.[2] We attributed such a high selectivity to the cyclic mechanism in which the β-hydride of the isobutyl group is shifted to the carbonyl carbon of the substrate:[1,2] the reduction is very similar to a Meerwein-Ponndorf-Verley type process.[3] These unique reactions led us to extend our investigation to the alkoxy derivatives of diisobutylaluminum hydride (DIBAL-H) as a reducing agent. In the course of exploring the reducing action of diisobutylalkoxyalanes (DIBAL-OR), we observed that the reagents are much milder than DIBAL-Cl and effectively reduce aldehydes and ketones under mild conditions. Herein we report the application of these newly synthesized reagents, DIBAL-OR, for the selective reduction of α,β-unsaturated aldehydes and ketones to the corresponding allylic alcohols. The reagents are conveniently prepared by a simple reaction between DIBAL-H and the corresponding alcohols in ethyl ether (EE) solution (Eq 1).



$$(i\text{-Bu})_2\text{Al—H} + \text{ROH} \xrightarrow[0^\circ]{\text{EE}} (i\text{-Bu})_2\text{Al—OR} + \text{H}_2\uparrow \qquad (1)$$

R = Et; DIBAL-OEt, R = i-Pr; DIBAL-O^{i}Pr, R = t-Bu; DIBAL-O^{t}Bu

The relative reactivities of DIBAL-OR toward some representative aldehydes and ketones are presented in Table 1. In general, all the alkoxy derivatives examined appear to be much milder than DIBAL-Cl. The relative reactivity of DIBAL-OR is in the order of DIBAL-OEt ≥ DIBAL-O^{i}Pr > DIBAL-O^{t}Bu. Apparently, such a reactivity order arises from the size of the alkoxy substituent. The