

Selective Oxidation of Primary and Secondary Alcohols using Di-isopropyl Sulphide–*N*-Chlorosuccinimide

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Di-isopropyl sulphide in combination with *N*-chlorosuccinimide at 0 °C oxidizes primary alcohols to aldehydes but does not oxidize secondary alcohols, whereas at –78 °C, the same reagent mixture oxidizes secondary alcohols to ketones but does not affect primary alcohols.

There are many reagents available for the oxidation of primary or secondary alcohols to aldehydes or ketones, respectively. However, only a few of those reagents can selectively oxidize primary^{1,2} or secondary alcohols.^{3–6} Unfortunately, these selective oxidizing agents do not show sufficient selectivities or are not readily available.

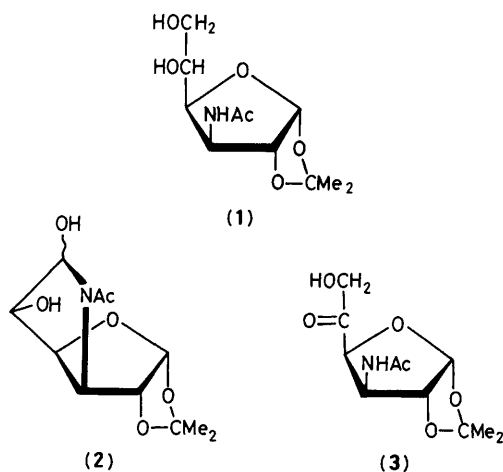
Herein we report a new process for the selective oxidation of primary and secondary alcohols. We speculated that di-isopropyl sulphide and *N*-chlorosuccinimide (NCS) might preferentially oxidize primary rather than secondary alcohols

since di-isopropyl sulphide has bulkier alkyl groups than dimethyl sulphide which in combination with NCS is known to oxidize both primary and secondary alcohols.⁷ Indeed, oxidation of decan-1-ol using di-isopropyl sulphide–NCS at 0 °C afforded decanal in 90% yield, whereas heptan-3-ol was not oxidized at all under the same conditions and was recovered in 90% yield. However, unexpected results were obtained when oxidations were carried out at –78 °C. Thus, the oxidation of secondary alcohols using di-isopropyl sulphide–NCS at –78 °C gave the corresponding ketones in high

Table 1

Alcohol ^a	Aldehyde or ketone	% Yield ^{b,c} using di-isopropyl sulphide		% Yield ^b using di-n-butyl sulphide	
		at 0 °C	at -78 °C	at 0 °C	at -78 °C
Decan-1-ol	Decanal	90	0(92)	89	41
Dodecan-1-ol	Dodecanal	88	0(95)	91	41
Cyclohexylmethanol	Cyclohexanecarbaldehyde	84	0(95)	88	47
Heptan-2-ol	Heptan-2-one	0(91)	88	75	90
Heptan-3-ol	Heptan-3-one	0(90)	88	89	92
4-Phenylcyclohexanol	4-Phenylcyclohexanone	0(95)	83	82	88
4-t-Butylcyclohexanol	4-t-Butylcyclohexanone	0(95)	83	75	89
Cinnamyl alcohol	Cinnamaldehyde	72	100	79	100
4-Phenylbut-3-en-2-ol	4-Phenylbut-3-en-2-one	65	75	68	80
Benzyl alcohol	Benzaldehyde	96	98	93	98
1-Phenylethyl alcohol	Acetophenone	78	85	80	88
(1)	(2)	70 ^d	0(85)		
(1)	(3) ^e	0(85)	65 ^d		

^a The reaction was conducted as described in the text for oxidation of decan-1-ol. ^b Determined by g.l.c. analysis on a column of 10% UCW-982. ^c The values in parentheses refer to the recovered isolated yields of starting alcohols. ^d Isolated yields of purified products. ^e (3): syrup; ¹H n.m.r. (CDCl₃): δ 1.32 (s, 3H), 1.52 (s, 3H), 2.09 (s, 3H), 4.35 (m, 1H), 4.64 (s, 2H), 4.83–4.62 (m, 2H), 5.92 (d, J 3.7 Hz, 1H); satisfactory i.r. and analytical data were obtained.



yield, but primary alcohols were not oxidized at -78 °C. Allylic or benzylic alcohols were oxidized to the corresponding aldehydes or ketones both at 0 and -78 °C although slightly higher yields were observed at -78 °C.

Di-*s*-butyl sulphide, methyl *t*-butyl sulphide, or methyl phenyl sulphide with NCS showed almost the same selectivity as di-isopropyl sulphide in the oxidation of primary and secondary alcohols. On the other hand, di-*n*-butyl sulphide and methyl *s*-butyl sulphide, which have sterically less hindered alkyl groups than di-isopropyl sulphide, did not show selectivity. Reaction mixtures were carefully analysed for by-products since the methylthiomethyl ether of the starting alcohol is known to be the undesired product in the oxidation of alcohols by dimethyl sulphide-NCS. In the present oxidation, only oxidation products and unreacted alcohols were detected or isolated. The di-isopropyl sulphide-NCS system also showed notable selectivities in the oxidation of (1) which contains both primary and secondary hydroxy groups. Thus, oxidation of diol (1) at 0 °C afforded compound (2)⁸ in 70% yield, whereas ketoalcohol (3) was obtained in 65% yield at -78 °C. Some selected experimental results are summarized in Table 1.

In a typical oxidation, to a stirred solution of 3 mmol of NCS in 10 ml of methylene dichloride was added at 0 °C, 3.3 mmol of di-isopropyl sulphide under nitrogen. After stirring the solution for 30 min at 0 °C, a solution of 1 mmol of decan-1-ol in 1 ml of methylene dichloride was added dropwise at 0 °C. The stirring was continued for 2 h at 0 °C, and then a solution of 3 mmol of triethylamine in 0.5 ml of methylene dichloride was added dropwise at 0 °C. The cooling bath was removed and after stirring for 20 min, 20 ml of diethyl ether was added. The organic layer was washed with 5 ml of 1% aqueous hydrochloric acid and with water, dried over MgSO₄, and analysed by g.l.c. The procedure for the oxidation at -78 °C was essentially the same as that at 0 °C. When oxidations with di-isopropyl sulphide were carried out at -24 or -50 °C, the selectivities and yields decreased.

Although it is apparent that the steric factors and the reaction temperature are critical for the selectivity, the exact reason for the selectivity shown in the present oxidation process at 0 and -78 °C is unclear as yet. Perhaps the stability of the alkoxy-sulphonium salt formed from di-isopropyl sulphide-NCS might somehow be related to the selectivity.

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