

Selective Oxidation of Primary and Secondary Alcohols Using Iminosulfonium Salts

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The oxidation of alcohols to aldehydes or ketones is one of the most widely used reactions in organic synthesis. New developments in the area of the oxidation of alcohols should be designed to effect the selective oxidation of primary and secondary alcohols. Yet, only a few reagents are known for the selective oxidation of primary^{1,2} and secondary³⁻⁶ alcohols. Even these reagents do not show sufficient selectivities or are not readily available. Recently, we have reported the selective oxidation methods for alcohols using diisopropyl sulfide with N-chlorosuccinimide (NCS)⁷ and using potassium ferrate⁸. In the oxidation using diisopropyl sulfide-NCS, primary alcohols were oxidized to aldehyde but secondary alcohols were not oxidized at 0°C, whereas at -78°C, secondary alcohols were oxidized to ketones but primary alcohols were not affected⁷. The remarkable selectivity could not be clearly explained on the basis of the presently known mechanism of related reactions. We further investigated this oxidation reaction using various dialkyl sulfides other than diisopropyl sulfide with NCS and using diisopropyl sulfide and dimethyl sulfide with N-bromosuccinimide (NBS).

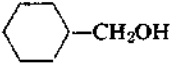
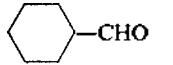
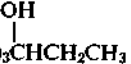
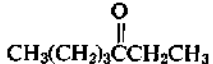

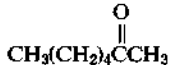
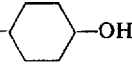
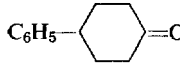
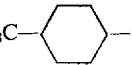
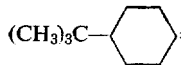
Table 1 summarizes the result for the oxidation of primary and secondary alcohols using dialkyl sulfides with NCS. Di-*s*-butyl sulfide and *t*-butyl methyl sulfide, which have bulky alkyl groups, shows almost same selectivities as diisopropyl sulfide. Thus, dialkyl sulfide-NCS at 0°C oxidizes primary 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. On the other hand, di-*n*-butyl sulfide and methyl *s*-butyl sulfide which have sterically less hindered alkyl groups than diisopropyl sulfide, do not show selectivity although higher yields for the oxidation of primary alcohols are observed at 0°C than at -78°C.

Table 2 shows the results for the oxidation using diisopropyl sulfide and dimethyl sulfide with NBS. Unlike diisopropyl sulfide-NCS system, diisopropyl sulfide-NBS does not show selectivity and oxidizes both primary and secondary alcohols in poor yields. Dimethyl sulfide-NBS is comparable with dimethyl sulfide-NCS⁹ in respect of selectivities and yields. Thus, dimethyl sulfide-NBS oxidizes both primary and secondary alcohols at 0°C and -78°C in good yield.

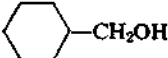
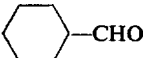
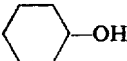
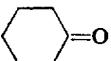
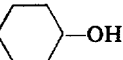
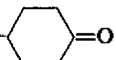
In a typical oxidation, to a stirred solution of 3 mmol of NCS or NBS in 10 ml of methylene chloride is added at 0°C 3.3 mmol of a dialkyl sulfide. The resulting iminosulfonium salt is insoluble in certain cases and appears as a white precipitate. After stirring the solution 30 min at 0°C, a solution of 1 mmol of an alcohol in 1 ml of methylene chloride is added at 0°C. The stirring is continued for 2 h at 0°C, and then a solution of 3 mmol of triethylamine in 0.5 ml methylene chloride is added at 0°C. After stirring the solution at room temperature for 20 min, the organic layer is washed with water, dried (MgSO₄), and analyzed by GLC. The procedure for the oxidation at -78°C is essentially same as that at 0°C. The maximum yield is obtained when the solution of an iminosulfonium salt and an alcohol is stirred for

TABLE 1: Oxidation of Alcohols Using Dialkyl Sulfides with NCS

Alcohols	Aldehydes or ketones	% Yield ^a using di- <i>s</i> -Butyl sulfide		% Yield ^a using <i>t</i> -Butyl methyl sulfide		% Yield ^a using di- <i>n</i> -Butyl sulfide		% Yield ^a using <i>s</i> -Butyl methyl sulfide	
		at 0°C	at -78°C	at 0°C	at -78°C	at 0°C	at -78°C	at 0°C	at -78°C
CH ₃ (CH ₂) ₉ OH	CH ₃ (CH ₂) ₈ CHO	87	3	96	0	89	41	95	45
CH ₃ (CH ₂) ₁₁ OH	CH ₃ (CH ₂) ₁₀ CHO	86	0	85	0	91	41	94	45
		81	0	74	3	88	47	95	50
CH ₃ (CH ₂) ₃ 	CH ₃ (CH ₂) ₃ 	0	87	0	85	89	92	91	95
CH ₃ (CH ₂) ₂ 	CH ₃ (CH ₂) ₂ 	0	88	0	85	75	90	80	93
C ₆ H ₅ - 	C ₆ H ₅ - 	0	82	0	85	82	88	86	92
(CH ₃) ₃ C- 	(CH ₃) ₃ C- 	0	83	0	82	75	89	80	93

^a Determined by GLC analysis on a column of 10 % UCW-982.

TABLE 2: Oxidation of Alcohols Using Diisopropyl Sulfide and Dimethyl Sulfide with NBS

Alcohols	Aldehydes or ketones	% Yield* using diisopropyl sulfide		% Yield* using dimethyl sulfide	
		at 0°C	at -78°C	at 0°C	at -78°C
CH ₃ (CH ₂) ₁₁ OH	CH ₃ (CH ₂) ₁₀ CHO	23	43	87	68
		18	60	83	85
		5	63	78	75
(CH ₃) ₃ C- 	(CH ₃) ₃ C- 	22	77	73	76

* Determined GLC analysis on a column of 10 % UCW-982.

2 h. The temperature control is important for the yield and the selectivity of this oxidation reaction and the reaction temperature should be kept 0°C or -78°C throughout the reaction.

On the basis of the result obtained in the present work, it is apparent that the steric factor, the reaction temperature, and the counteranion of the sulfonium salt are critical for the selectivity. However, the remarkable selectivity shown in the present oxidation process using di-*s*-butyl sulfide or *t*-butyl methyl sulfide with NCS at 0°C or -78°C can not be easily rationalized. Perhaps the iminosulfonium salt and the alkoxy-sulfonium salt might be in equilibrium and the equilibrium constant might be very sensitive to the bulkiness of the dialkyl sulfide, the reaction temperature, and the counteranion of the sulfonium salts.

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1, 1, 3, 3-Tetramethylguanidine. An Efficient and Selective Catalyst for the Benzoylation of Alcohols

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The benzoate group is one of the widely used hydroxy protective groups in organic synthesis.¹ The most commonly used reagent, benzoyl chloride/pyridine, often requires longer reaction times at elevated temperature and may cause side reactions in complex molecules under forcing conditions due to the acidic nature of the reaction medium. In general, benzoylation using benzoic anhydride/pyridine or triethylamine does not proceed to completion, even after prolonged stirring at elevated temperature. Thus, several synthetic methods have been reported in the literature, which proceed under relatively mild conditions.²

In connection with our studies on the use of amidines and related compounds as functional group transfer agents, we have recently reported that the use of 1,1,3,3-tetramethylguanidine (TMG)³ as a catalyst is very effective for the *t*-butyldimethylsilylation of alcohols.⁴ We now wish to report that TMG is an efficient and selective catalyst for the benzoylation of alcohols (eq. 1).

First, the relative rates of benzoylation of phenethyl alcohol using equimolar amounts of TMG and benzoic anhydride at room temperature were examined in several solvents such as methylene chloride, tetrahydrofuran, acetonitrile, and