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THE CHEMOSPECIFIC REDUCTION OF ALDEHYDE AND KETONE WITH SODIUM BOROHYDRIDE IN THE PRESENCE OF THIOL

Yuji Maki* and Katsuo Kikuchi
(Department of Chemistry, Yamagata University, Yamagata 990)
Hiroshi Sugiyama* and Shuichi Seto
(Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Sendai 980, Japan)

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Under usual conditions sodium borohydride cannot reduce aldehyde and ketone selectively. However, the recent excellent studies by Murahashi et al[1] and by Gribble and Ferguson[2] have shown that boracyclononane ate complex and triacetoxyborohydride can reduce aldehyde and ketone selectively. Their selectivity can be attributable to their decreased reducing capability. As we have shown before, sodium borohydride in the presence of thiol is a much stronger reducing agent than sodium borohydride alone and reduces ester,[3] amide,[4] and nitro groups.[5] In this communication, it will be shown that selected thiols decreased the reducing capability of sodium borohydride and sodium borohydride-thiol complexes reduced aldehyde and ketone selectively.

The general procedure of this reduction is as follows. A mixture of sodium borohydride and thiol in dry tetrahydrofuran was refluxed for 2 - 3 hours and then cooled. An equimolar mixture of aldehyde and ketone was added to the above suspension and stirred. After appropriate time, the reaction mixture was treated with water and then with ether. The products and their ratio were examined by G.C.-M.S. and G.L.C.

As shown in the Table, when this reduction was applied to a mixture of benzaldehyde (I) and acetophenone (II), in the case of ethyl mercaptan the shorter reaction time was, the better the reaction selectivity was. In the case of o-tolyl mercaptan, the larger an amount of carbonyl compounds relative to the reducing agent was, the better a result was, and when a molar ratio of carbonyl compounds to sodium borohydride was 7.2/3, a reasonable result was given (100% of benzyl alcohol (III) and 9% of α-phenethyl alcohol (IV)). In the case of t-butyl mercaptan, however, even with the excess reducing agent relatively short reaction time gave an excellent product ratio ((III) 93% and (IV) 5%), and long reaction time gave an unsatisfied result ((III) 100% and (IV) 86%). The reaction with cyclohexyl mercaptan showed the same tendency. The optimum reaction time with both of these thiols was 30 minutes under the present conditions. When this reaction was extended to aliphatic carbonyl compounds, the reduction with t-butyl mercaptan gave 94% yield of 1-nonanol and only 6% yield of 2-nonanol from an equimolar mixture of nonanal and 2-nonanone.

In spite of the stronger reducing capability of this system with thiophenol than with ethyl mercaptan in general,[4,5] camphor and fenchone were more easily reduced by this system with ethyl mercaptan than with thiophenol. Therefore, this reduction with sodium borohydride-thiol complex could be controlled by the steric factor of thiol.

Table. Sodium borohydride reduction of aldehyde and ketone in the presence of thiol.

Aldehyde and ketone (mmole)	Thiol	Reaction time	Product (% yield)
(I) (0.75), (II) (0.75)	EtSH	10 min.	(III) (93), (IV) (14)
(I) (0.75), (II) (0.75)	EtSH	30 min.	(III) (100), (IV) (37)
(I) (0.75), (II) (0.75)	EtSH	2 hr.	(III) (100), (IV) (42)
(I) (0.75), (II) (0.75)	o-TolSH	30 min.	(III) (100), (IV) (60)
(I) (1.5), (II) (1.5)	o-TolSH	10 min.	(III) (100), (IV) (49)
(I) (3.0), (II) (3.0)	o-TolSH	10 min.	(III) (100), (IV) (14)
(I) (3.8), (II) (3.8)	o-TolSH	10 min.	(III) (100), (IV) (9)
(I) (0.75), (II) (0.75)	t-BuSH	10 min.	(III) (75), (IV) (2)
(I) (0.75), (II) (0.75)	t-BuSH	30 min.	(III) (93), (IV) (3)
(I) (0.75), (II) (0.75)	t-BuSH	2 hr.	(III) (100), (IV) (86)
(I) (0.75), (II) (0.75)	CyclohexSH	10 min.	(III) (69), (IV) (3)
(I) (0.75), (II) (0.75)	CyclohexSH	30 min.	(III) (90), (IV) (5)
nonanal (1.5), 2-nonanone (1.5)	t-BuSH	10 min.	1-nonanol (87), 2-nonanol (5)
nonanal (1.5), 2-nonanone (1.5)	t-BuSH	30 min.	1-nonanol (94), 2-nonanol (6)

For each reaction 3 mmol of $NaBH_4$ and 9 mmol of thiol were used. EtSH=ethyl mercaptan, t-BuSH=t-butyl mercaptan, o-TolSH=o-tolyl mercaptan, CyclohexSH=cyclohexyl mercaptan.

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