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A NOVEL PROCEDURE FOR DENITROHYDROGENATION BY $Na_2S_2O_4$-Et_3SiH

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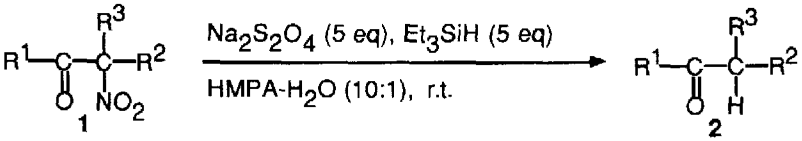
Summary: The nitro group of α-nitro ketones is replaced by hydrogen or deuterium on treatment with $Na_2S_2O_4$-Et_3SiH system in HMPA-H_2O or HMPA-D_2O.

Recently, reductive removal of aliphatic nitro groups has been of interest in organic chemistry, so that many methods have been devised for last ten years. At the present time, the following eight methods are known; CH_3SNa-HMPA,[1] KOH-$HOCH_2CH_2OH$, 140 °C,[2] N-benzyl-1,4-dihydronicotinamide,[3] Bu_3SnH,[4] NaTeH,[5] Pd(0)-HCO_2NH_4,[6] Et_3SiH-Lewis acid,[7] and $LiAlH_4$.[8] As the reaction using Bu_3SnH proceeds under very mild reaction conditions and in a high chemoselective way, Bu_3SnH method is most frequently used in organic synthesis.[8,9] However, tin reagents are highly toxic and create a disposal problem. Sodium dithionite is a powerful, safe, and cheap reducing agent and it is used frequently for the reaction via single electron transfer process. For example, the conversion NAD^+ to NADH[10] or dialkylviologen dication to viologen cation radical[11] is an important reaction of it. If sodium dithionite can be used in the place of Bu_3SnH, the problem related to using tin reagent can be overcome. Sodium dithionite has also been used for reduction of organic functional groups. For example, carbonyl groups or imines are converted into corresponding alcohols[12] or amines[13], respectively. Sodium dithionite is also an effective reagent for reductive cleavage of carbon-bromine[14] or carbon-sulfur[15] bonds. We now report that a new method for reductive removal of aliphatic nitro groups using $Na_2S_2O_4$-Et_3SiH in HMPA-H_2O.

Denitration of variable α-nitro ketones was carried out as a following procedure (Scheme 1). The results are summarized in Table.



Scheme 1

Table. Denitration of α-Nitro Ketones **1**[a)].

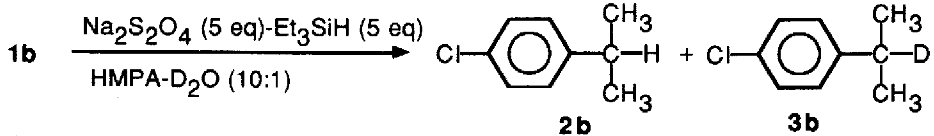
run	compounds	R^1	R^2	R^3	time (h)	**2**; yield (%)[b)]	
1	**1a**	Ph	H	CH_3	3	**2a**	70 (80)[c)]
2	**1b**	p-Cl-C_6H_4	CH_3	CH_3	3	**2b**	86
3	**1c**	Ph	H	$(CH_2)_2C(=O)CH_3$	3	**2c**	70
4	**1d**	m-Cl-C_6H_4	H	$CH(CH_3)CH_2CN$	3	**2d**	67
5	**1e**	m-Cl-C_6H_4	H	$(CH_2)_2CO_2CH_3$	3	**2e**	61
6	**1f**	p-Cl-C_6H_4	H	$(CH_2)_2CH(Br)CH_3$	2	**2f**	68

a) All reactions were carried out under the following reaction conditions; $Na_2S_2O_4$ (5 eq), Et_3SiH (5 eq), HMPA-H_2O (10:1, v/v), 25 °C. b) Isolated yield. c) GLC yield.

The denitration was carried out as following way.; To a mixture of **1a** (1.102 g, 6.15 mmol) and triethylsilane (3.60 g, 31 mmol) in HMPA-H_2O (15 ml, 10:1 v/v) was added sodium dithionite (5.3 g, 30 mmol) at room temperature and the resulting mixture was stirred for 3 h. The reaction mixture was poured into water, then usual work up and purification using column chromatography (silica gel/hexane-ethyl acetate 20:1) gave 577 mg of **2a** (70% yield).

The nitro group was readily replaced by hydrogen under these reaction conditions to give corresponding ketones in good yield. This reaction can be applied to 1,5-diketone synthesis (run 3). The keto, ester, and cyano groups are not affected under this reaction condition (run 3-5). In these cases, the nitro group is removed after it serves as an activating group for carbon-carbon bond formation. Of particular interest is example **1f** which gives the corresponding ketone **2f** in good yield. The survival of the easily reducible bromo moiety demonstrates the mildness of the reagents. However, the nitro group except α-nitro ketones cannot be replaced by hydrogen under these reaction conditions.

Although the precise reaction mechanism is still ambiguous, small amounts of water and 5 eq of Et_3SiH is necessary for the reaction. It is interesting that the nitro group of **1b** was mainly replaced by deuterium to give **3b** when deuterium oxide was used in the place of water (Scheme 2). As H-D exchange of **2b** is not observed under the same reaction conditions, the substitution of the nitro group to deuterium takes place during the denitration process. The reaction should be consisted with more than two reaction pathways because D content of the products was not 100%.



2b **3b**

Scheme 2

83% 17 : 83

In the view of high toxity and environmental pollution problem of tin reagent, this method should be valuable method for denitration of α-nitro ketones. Furthermore, as chemoselective removal of the nitro group of bromo nitro ketone can be achieved, this method may be also superior to tin method at this point. Studies on the mechanism of the reaction will be published in near future.

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