New Birch Type Reduction. Halogen or Halides-Activated Reduction of Disulfides to Thiols with Aluminium in Liquid Ammonia

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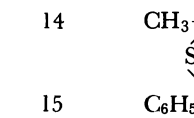
Synopsis. Aromatic and aliphatic disulfides were reduced to the corresponding thiols in high yields by new halogen or halides-activated Birch type reduction with aluminium in liquid ammonia.

In this half century, a great deal of investigations on the Birch type reduction have been reported by many organic and inorganic chemists since the discovery of the reduction with metallic sodium in liquid ammonia by A. J. Birch in 1944.[1] Many improved methods for the Birch reduction have been also developed, for example, use of other metals[2] and amines instead of liquid ammonia,[3] addition of proton sources,[4] and activation of the metals.[5] Recently, Benkeser et al. reported the improved Birch reduction to reveal that a selective reduction of alkynes with metallic calcium in alcohol and amine gave the corresponding alkenes and alkanes in moderate yields.[6] During the course of our investigations on the organic sulfur chemistry in liquid ammonia and amines,[7] we found a new Birch type reduction of disulfides. In this paper, we wish to report this new selective reduction of aromatic and aliphatic disulfides to the corresponding thiols with metallic aluminium, which is activated by halogen or halides in liquid ammonia, as shown in Eq. 1.

$$\underset{\textbf{1a-i}}{\text{R-S-S-R}} \xrightarrow[\text{Activator}]{\text{Al/NH}_3} \underset{\textbf{2a-i}}{2\ \text{R-SH}} \qquad (1)$$

In initial stage of this investigation, to carry out the reaction at ambient temperature, our efforts were centered on activation of the surface of aluminium, e.g., irradiation of supersonic wave and addition of white sand to the reaction system. Ultimately, the best results were obtained when some halogen or halides were added to the reduction system. Thus, a remarkable acceleration of the reduction was observed by employing iodine and sodium chloride as shown in Table 1 (Runs 2 and 3). In the absence of the halogen or halides, the yield of thiol was only 9% (Run 1). Moreover, we also tested other salts as shown in runs 5 to 9. It should be noted that both halogen (I_2) and halides (NaCl, KCl, KI, and NH_4Cl) exhibited comparable effect (Runs 2 to 7). On the other hand, sulfate and nitrate did not affect this reduction at all (Runs 8 and 9). As shown in Run 4 the sufficient reduction of disulfide to thiol was observed even when a catalytic amount of sodium chloride (0.025 mmol) was used. These results suggest that both the halides and halogen play an important role as activator in this reduction. To our knowledge, there has been no report on the halide or halogen-activated Birch reduction although ammonium sulfate have been used as a proton source.[8] The generality of this method was shown in runs 10 to 17. It is noteworthy that bis(4-chlorophenyl) (**1b**) and bis(2-benzothiazolyl) disulfide (**1i**) could be reduced to give the corresponding thiols in good yields (Runs 10 and 17), since the result implies that only the S-S bond, not C-S, C-Cl, and C=C bond, in the disulfide was reduced selectively.

Table 1. Reduction of Disulfides with Aluminium in Liquid Ammonia

Run[a]	Substrate R-SS-R/R		Catalyst	mmol	React. Time/h	Yield of Thiol	% [b,c]
1	C_6H_5-	**1a**	—	—	8	**2a**	9
2	C_6H_5-	**1a**	I_2	0.15	2	**2a**	93
3	C_6H_5-	**1a**	NaCl	0.3	2	**2a**	93
4	C_6H_5-	**1a**	NaCl	0.025	4	**2a**	100 (98)
5	C_6H_5-	**1a**	KI	0.3	2	**2a**	62
6	C_6H_5-	**1a**	KCl	0.3	2	**2a**	100
7	C_6H_5-	**1a**	NH_4Cl	0.3	2	**2a**	98
8	C_6H_5-	**1a**	$(NH_4)_2SO_4$	0.15	2	**2a**	9
9	C_6H_5-	**1a**	NH_4NO_3	0.3	2	**2a**	0
10	4-Cl-C_6H_4-	**1b**	NaCl	0.3	15(min)	**2b**	89 (71)
11	4-CH_3-C_6H_4-	**1c**	NaCl	0.3	1	**2c**	94 (94)
12	4-CH_3O-C_6H_4-	**1d**	NaCl	0.3	2	**2d**	93 (92)
13	4-CH_3CO-C_6H_4-	**1e**	NaCl	0.3	1	**2e**	(32)
14		**1f**	NaCl	0.3	12	**2f**	(54)
15	C_6H_5-CH_2-	**1g**	I_2	0.3	4	**2g**	65 (65)
16	CH_3-$(CH_2)_2$-CH_2-	**1h**	I_2	0.3	6	**2h**	45 (45)
17	2-Benzothiazolyl	**1i**	NaCl	0.3	4	**2i**	68 (68)

a) Substrate: 0.5 mmol, Liquid Ammonia: 10 ml, React. Temp: 25°C, Al: 4 mg atom. b) Yield of thiol by iodometry. c) Isolated yields were shown in parenthesis.

Some aliphatic thiols were also obtained upon treating corresponding aliphatic disulfides such as dibenzyl (**1g**) and dibutyl disulfides (**1h**) with aluminium in liquid ammonia at 25 °C (Runs 15 and 16).

In conclusion, aromatic and aliphatic disulfides were reduced by new Birch type reduction, which was activated by halogen (I_2) and halides (NaCl, KCl, KI, and NH_4Cl), with aluminium to afford the corresponding thiols at ambient temperature in good yields. Although, at present stage, the role of the halogen or halides is not necessarily obvious, further applications of this new method to the reduction of other functional groups are expected.

Experimental

Measurements. All melting points were uncorrected. ^{1}H NMR, IR, and Mass spectra were recorded with HITACHI R-22, HITACHI 295 and HITACHI RMU-6M, respectively. Elemental analyses were determined with YANAGIMOTO MT-3.

Determination of Thiols. The yields of the resulted thiols were determined by the method in the literature.[9]

Materials. Substrates, **1a**, **1b**, **1c**, **1g**, and **1i**, were commercially available and **1d**, **1e**, and **1h** were prepared by the methods in the literature from the corresponding thiols.[10] Bis[4-[1,1-(ethylenedithio)ethyl]phenyl] disulfide (**1f**) was obtained from the corresponding disulfide (**1e**) by the reaction with ethanedithiol in the presence of sodium sulfate and zinc chloride and charaterized as follows. Mp 90 °C; IR (KBr) 2900 and 1480 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.10 (s, 6H, CH_3), 3.39 (s, 8H, 0.8Hz, $-CH_2CH_2-$), 7.38 (d, 4H, 8 Hz, arom) and 7.66 (d, 4H, 8 Hz, arom); Found: C,52.47; H,4.79%. Calcd for $C_{20}H_{22}S_6$: C, 52.82; H, 4.88%.

Reduction of Disulfides to the Corresponding Thiols with Aluminium Activated by Halide in Liquid Ammonia. General Procedure. Disulfide (0.5 mmol), aluminium (grain, 4 mg atom) and sodium chloride (0.3 mmol) were taken into a stainless steel autoclave. After evacuation, liquid ammonia (10 ml) was charged into the autoclave and the mixture was allowed to react with stirring at 25 °C for 1 h. Water (20 ml) was added to the residue obtained after evaporation of ammonia. A part of the solution was provided for the iodometric titration to determine the yields of the resulting thiols. After acidification with hydrochloric acid, the aqueous solution was extracted with chloroform (5 ml×3). Evaporation of the combined chloroform after drying on sodium sulfate gave desired thiol (**2**). The products obtained (**2a—e** and **2g—i**) were identified by comparing the ^{1}H NMR, IR, MS, and elemental analysis with those of the authentic samples which were used for preparation of substrate disulfides.

1-Methyl-1-(4-mercaptophenyl)-1,3-dithiolane (2f): Oil; IR (neat) 2950,2550 and 1500 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.11 (s, 3H, CH_3), 3.23—3.54 (m, 5H, SH and $-CH_2CH_2-$), 7.15 (d, 2H, 9.0 Hz, arom) and 7.58 (d, 2H, 9.0 Hz, arom); MS (70 eV) *m/z* 228 (M^+). Found: C, 53.01; H, 5.46%. Calcd for $C_{10}H_{12}S_3$: C, 52.59; H,5.30%.

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