Studies of Reduction with the Diborane–Transition Metal Salt System

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The reduction of a variety of functional groups with the new diborane–nickelous chloride system was systematically investigated. This system reduced aromatic nitro compounds to the corresponding primary amines under mild conditions in good yields. However, ketone, aldehyde, carboxylic acid, ester, amide and olefin moieties were unaffected by this system. The nitro group in aromatic nitro compounds bearing a ketone, aldehyde, ester, amide or nitrile functionality was selectively reduced with this system to give the corresponding primary amines in good yields.

Keywords——selective reduction; aromatic nitro compound; diborane; nickelous chloride; diborane–transition metal salt system; aromatic primary amine

The selective reduction of nitro compounds bearing other functional groups sensitive to ordinary reducing agents is useful in synthetic chemistry. However, the ordinary reducing agents for a nitro group are not appropriate because of the requirement for acidic or basic medium and their ability to reduce other functional groups.[1] In the previous paper, we reported that aromatic nitro compounds were reduced with the sodium borohydride–nickelous chloride system to give the corresponding amines,[2] but this system reduced nitriles, heterocyclic compounds[3] and olefins[4] as well. As a continuation of this work, the present paper deals with the selective reduction of aromatic nitro compounds with the diborane (B_2H_6)–nickelous chloride $(NiCl_2)$ system.

In general, B_2H_6 hardly reduces aromatic nitro compounds. However, as shown in Table I, the B_2H_6–$NiCl_2$ system reduced nitrobenzene (1) to aniline (2) under mild conditions in good yield.

Similarly, other nitro compounds 3—9 were reduced with this system to give the corresponding amines 10—16 in good yields, as shown in Table II.

As shown in Table III, when the molar ratio of B_2H_6 was decreased, azoxy compounds were obtained as a by-product in these reductions.

In order to investigate the reaction path, nitrosobenzene (17), azoxybenzene (18) and

TABLE I. Reduction of Nitrobenzene (1) with the B_2H_6–Transition Metal Salt System

TMS[a]	TMS[a] (eq mol)	B_2H_6 (eq mol)	Temp.	Time (h)	Product	Yield (%)
$NiCl_2$	1.0	3.0	Room temp.	1	2	97.8
$CoCl_2$	1.0	3.0	Room temp.	1	2	22.1
$CuCl_2$	1.0	3.0	Room temp.	1	2	Trace
$CrCl_3$	1.0	3.0	Room temp.	1	2	Trace

a) TMS = transition metal salt.

TABLE II. Reduction of Aromatic Nitro Compounds with the B_2H_6–$NiCl_2$ System

Compound (No.)		$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Product (No.)		Yield (%)
o-CH_3–C_6H_4–NO_2	(3)	0.5	4.0	o-CH_3–C_6H_4–NH_2	(10)	91.3
m-CH_3–C_6H_4–NO_2	(4)	0.5	4.0	m-CH_3–C_6H_4–NH_2	(11)	94.4
p-CH_3–C_6H_4–NO_2	(5)	0.5	4.0	p-CH_3–C_6H_4–NH_2	(12)	85.0
p-CH_3O–C_6H_4–NO_2	(6)	1.0	4.0	p-CH_3O–C_6H_4–NH_2	(13)	84.3
p-Cl–C_6H_4–NO_2	(7)	0.5	4.0	p-Cl–C_6H_4–NH_2	(14)	92.7
p-HO–C_6H_4–NO_2	(8)	0.5	4.0	p-HO–C_6H_4–NH_2	(15)	83.8
1-Nitronaphthalene	(9)	0.5	4.0	1-Aminonaphthalene	(16)	90.0

TABLE III. Reduction of Nitrobenzene (1) with the B_2H_6–$NiCl_2$ System

1 (eq mol)	$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Solvent	Temp.	Time (h)	Product (No.)	Yield (%)
1.0	0.5	2.0	THF–MeOH	Room temp.	1	2	58.9
						C_6H_5–$\underset{\downarrow}{N}$=N–C_6H_5 (18) O	15.7
1.0	0.5	4.0	THF–MeOH	Room temp.	1	2	78.0
1.0	1.0	3.0	THF–MeOH	Room temp.	1	2	97.8

TABLE IV. Reduction of Compounds 17, 18 and 19 with the B_2H_6–$NiCl_2$ System

Compound (No.)		$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Product	Yield (%)
C_6H_5–$\underset{\downarrow}{N}$=N–C_6H_5 (18) O		0.5	4.0	2	83.3
C_6H_5–N=O	(17)	0.5	4.0	2	76.0
C_6H_5–N=N–C_6H_5	(19)	0.5	4.0	2	86.9

TABLE V. Reduction of Aromatic Hetero Compounds with the B_2H_6–$NiCl_2$ System

Compound	(No.)	$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Product (No.)		Yield (%)
Quinoline	(20)	0.5	4.0	1,2,3,4-Tetrahydroquinoline	(25)	64.3
Quinoline	(20)	4.0	8.0	1,2,3,4-Tetrahydroquinoline	(25)	3.7
Quinaldine	(21)	0.5	4.0	1,2,3,4-Tetrahydroquinaldine	(26)	38.5
Quinaldine	(21)	4.0	8.0	1,2,3,4-Tetrahydroquinaldine	(26)	47.5
Lepidine	(22)	0.5	4.0	Recovery		—
Isoquinoline	(23)	0.5	4.0	1,2,3,4-Tetrahydroisoquinoline	(27)	Trace
Isoquinoline	(23)	4.0	8.0	1,2,3,4-Tetrahydroisoquinoline	(27)	Trace
Acridine	(24)	0.5	4.0	9,10-Dihydroacridine	(28)	45.1

azobenzene (19) were examined with this system; they gave 2 in good yields. The results shown in Tables III and IV indicated that the reduction of nitro compounds proceeded *via* azoxybenzene.

Furthermore, as shown in Table V, heterocyclic compounds 20, 21 and 24 were reduced with this system to give the corresponding reduced products 25,26 and 28. However,·

TABLE VI. Reduction of Nitriles with the B_2H_6–$NiCl_2$ System

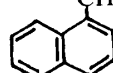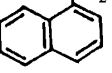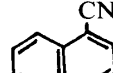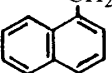| Nitrile	(No.)	$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Product Primary amine	(No.)	Yield (%)	Secondary amine	(No.)	Yield (%)
Ph–CH_2CN	(29)	0.5	4.0	Ph–$CH_2CH_2NH_2$	(33)	31.2	Ph–$(CH_2CH_2)_2NH$	(34)	56.9
Ph–CH_2CN	(29)	1.0	4.0	Ph–$CH_2CH_2NH_2$	(33)	16.5	Ph–$(CH_2CH_2)_2NH$	(34)	58.5
Ph–CH_2CN	(29)	4.0	8.0	Ph–$CH_2CH_2NH_2$	(33)	61.0	—		
Ph–CN	(30)	0.5	4.0	—			Ph–$(CH_2)_2NH$	(35)	83.1
Ph–CN	(30)	4.0	8.0	Ph–CH_2NH_2	(36)	31.8	Ph–$(CH_2)_2NH$	(35)	13.8
naphthyl–CH_2CN	(31)	1.0	4.0	naphthyl–$CH_2CH_2NH_2$	(37)	80.0	—		
naphthyl–CN	(32)	1.0	4.0	naphthyl–CH_2NH_2	(38)	68.7	—		

TABLE VII. Selective Reduction of Nitro Compounds with the B_2H_6–$NiCl_2$ System

Compound (No.)		$NiCl_2$ (eq mol)	B_2H_6 (eq mol)	Product (No.)		Yield (%)
p-CH_3CO–C_6H_4–NO_2	(39)	1.0	4.0	p-CH_3CO–C_6H_4–NH_2	(44)	81.9
p-NC–C_6H_4–NO_2	(40)	2.0	8.0	p-NC–C_6H_4–NH_2	(45)	54.2
p-NC–CH_2–C_6H_4–NO_2	(41)	2.0	8.0	p-NC–CH_2–C_6H_4–NH_2	(46)	68.4
p-CH_3OOC–C_6H_4–NO_2	(42)	1.0	4.0	p-CH_3OOC–C_6H_4–NH_2	(47)	82.2
p-H_2NCO–C_6H_4–NO_2	(43)	2.0	8.0	p-H_2NCO–C_6H_4–NH_2	(48)	54.9

isoquinoline (23) and lepidine (22) were not reduced with this system.

Similarly, the reaction of nitriles 29—32 gave the corresponding primary and secondary amines, as shown in Table VI. In these reductions, the yields of primary amines increased with increasing amount of $NiCl_2$.

Ketone, aldehyde, carboxylic acid, olefin, ester and amide moieties are easily reduced with B_2H_6, but these groups were unaffected in the B_2H_6–$NiCl_2$ system.

Since selectivity for the reduction of any nitro group with the B_2H_6–$NiCl_2$ system was presumed from the above results, we examined the reaction of nitro compounds bearing other functional groups under similar conditions, and obtained the corresponding amines as shown in Table VII. The cyano group (compounds 40 and 41) was unaffected in this system, and thus it can be assumed that the relative reactivity of the nitro group toward this system is higher than that of the cyano group.

The sodium borohydride–transition metal salt system reduces various functional groups. As described above, the selectivity of the B_2H_6–$NiCl_2$ system toward the nitro group is superior to that of other reducing agents, so this system provides a useful synthetic route to aromatic primary amines from various nitro compounds.

Experimental

Commercially available $NiCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $CrCl_3 \cdot 6H_2O$, $CuCl_2 \cdot 2H_2O$, $NaBH_4$ and boron trifluoride etherate were used throughout this work. Melting points were determined on a Yanagimoto micro-melting point apparatus (model MP-S3), and are uncorrected. Infrared (IR) spectra were measured in Nujol mulls or as liquid films with a Nihon Bunko IRA-1 infrared spectrometer, and ultraviolet (UV) spectra were recorded on a JASCO Uvidec-505 spectrometer. Gas chromatography (GC) was done on a Nihon Denshi JGC-20K (SE 30), and chromatography columns of alumina were prepared with Aluminiumoxid 90 (70—230 mesh ASTM, Merck).

The procedure for the reduction of nitrobenzene (1) with the B_2H_6–$NiCl_2$ system will be described in detail as a typical example.

Reduction of Nitro Compounds——A) Compound 1 (1.00 g, 8.1 mmol) and $NiCl_2 \cdot 6H_2O$ (1.93 g, 8.1 mmol) were dissolved in tetrahydrofuran (THF, 30 ml) and methanol (10 ml), and then B_2H_6 (24.3 mmol) was passed into the solution for 1 h with stirring at room temperature. After removal of the solvent under reduced pressure, the black precipitate was dissolved in 10% hydrochloric acid (30 ml). The unreacted compound was extracted with ether, then the aqueous layer was basified by the addition of conc. ammonium hydroxide, and extracted with ether. The extract was dried over anhydrous magnesium sulfate. The ether was evaporated off, and the residue was distilled to give 738 mg (97.8%) of aniline (2), bp 183—184 °C.

The other aromatic nitro compounds 3—9 were reduced similarly; the reaction conditions are listed in Table II. All spectral data for products 10—16 were identical with those for the corresponding authentic samples.

B) Compound 1 (1.00 g, 8.1 mmol) and $NiCl_2 \cdot 6H_2O$ (0.86 g, 4.05 mmol) were dissolved in THF (30 ml) and methanol (5 ml), and then B_2H_6 (16.2 mmol) was passed into the solution for 1 h with stirring at room temperature. After removal of the solvent, 10% hydrochloric acid (30 ml) was added to the reaction mixture till the black precipitate was dissolved, and the mixture was extracted with ether, and dried over anhydrous magnesium sulfate. The ether was evaporated off, and the residue was chromatographed on alumina (column) using benzene as the eluent. The eluate was evaporated, and the resulting residue was recrystallized from 95% ethanol to give 126 mg (15.7%) of azoxybenzene (18) as light yellow needles, mp 35—36.5 °C. This product was identical with an authentic sample on the basis of mixed melting point determination and comparison of IR and UV spectra. The acidic aqueous layer was basified by the addition of conc. ammonium hydroxide, then extracted with ether, and the extract was dried over anhydrous magnesium sulfate. After the ether was evaporated off, the residue was distilled to give 1, 444 mg (58.9%), bp 183—184 °C.

Compounds 17 and 19 were reduced similarly; the results are listed in Table IV.

Reduction of Heterocyclic Compounds——Compound 20 (1.29 g, 10 mmol) and $NiCl_2 \cdot 6H_2O$ (1.19 g, 5 mmol) were dissolved in THF (35 ml) and methanol (5 ml), and then B_2H_6 (40 mmol) was passed into the solution for 1 h with stirring at room temperature. After treatment as described above, the residue was chromatographed on alumina (column) using benzene as the eluent. The eluate was evaporated, and the resulting residue was distilled under reduced pressure to give 830 mg (64.3%) of 1,2,3,4-tetrahydroquinoline (25) as a colorless oil, bp 108—109 °C (7 mmHg) (lit.[5] bp. 251 °C). MS m/e: 133.(M^+), 132 (base peak), 118, 117, 77, 130, 91, 104. The picrate (from ethanol) mp 141—141.5 °C (lit.[5] mp 141.5 °C). This product was identical with an authentic sample on the basis of comparison of IR and UV spectra.

The following products were similarly obtained; the reaction conditions are listed in Table V. 1,2,3,4-Tetrahydroquinaldine (26) (699 mg, 47.5%), bp 105—106 °C (9 mmHg) (lit.[6] bp 115—116 °C (12 mmHg)), the picrate (from ethanol), mp 149.5—150 °C (lit.[6] mp 150 °C). 1,2,3,4-Tetrahydroisoquinoline (27) (trace), bp 232.5—234 °C (lit.[7] bp 234—236 °C), the picrate (from ethanol), mp 196.5—197.5 °C (lit.[8] mp 197—198 °C). 9,10-Dihydroacridine (28) (816 mg, 45.1%) as colorless needles by sublimation, mp 168—169 °C (lit.[9] mp 169 °C). These products were identical with the corresponding authentic samples, based on comparisons of IR and UV spectra.

Reduction of Nitriles——Compound 29 (1.00 g, 8.5 mmol) and $NiCl_2 \cdot 6H_2O$ (1.01 g, 4.25 mmol) were dissolved in THF (30 ml) and methanol (5 ml), and then B_2H_6 (34 mmol) was passed into the solution for 1 h with stirring at room temperature. After removal of the solvent, 10% hydrochloric acid (30 ml) was added, and the precipitate was collected and washed with ether. The precipitate was recrystallized from ethanol to give di-β-phenethylamine hydrochloride as colorless needles, mp 266—269 °C (lit.[10] mp 271 °C). This precipitate was dissolved in water, and the solution was basified by the addition of 10% sodium hydroxide, then extracted with ether. The extract was dried over anhydrous magnesium sulfate. After removal of the ether, the residue was distilled under reduced pressure to give 544 mg (56.9%) of di-β-phenethylamine (34) as a colorless oil, bp 172—173 °C (8 mmHg) (lit.[11] bp 170—175 °C (8 mmHg)). The picrate was obtained as yellow needles (from ethanol), mp 151—152 °C (lit.[12] mp 151—152 °C). The acidic aqueous layer described above was basified by the addition of conc. ammonium hydroxide, and extracted with ether. The extract was dried over anhydrous magnesium sulfate. After the ether was evaporated off, the residue was distilled to give 320 mg (31.2%) of β-phenethylamine (33), bp 196—198 °C. This product was identical with an authentic sample, based on comparisons of IR and UV spectra.

Products 35—38 were similarly obtained, as shown in Table VI. These products were identical with the corresponding authentic samples on the basis of mixed melting point determination and comparisons of IR and UV

spectra.

Reduction of 39——Compound **39** (0.99 g, 6 mmol) and $NiCl_2 \cdot 6H_2O$ (1.43 g, 6 mmol) were dissolved in THF (30 ml) and methanol (5 ml), and then B_2H_6 (24 mmol) was passed through the solution. After treatment as described above, the residue was recrystallized from water to give 660 mg (81.8%) of p-aminoacetophenone (**44**) as yellow needles, mp 105—106 °C (lit.[13] mp 106 °C).

Products **45**—**48** were similarly obtained, as shown in Table VII. Compounds **44**—**48** were identical with the corresponding authentic samples on the basis of mixed melting point determination and comparisons of IR and UV spectra.

Compounds Not Reacting with the B_2H_6–$NiCl_2$ System——The following compounds were not reduced with the B_2H_6–$NiCl_2$ system under conditions similar to those described above. Compound ($NiCl_2 \cdot 6H_2O$ (eq mol), B_2H_6 (eq mol)): benzophenone (1.0, 4.0), 2-octanone (0.5, 4.0), 4-methylacetophenone (0.5, 4.0), 2-ethylhexanal (0.5, 4.0), 4-methylbenzaldehyde (1.0, 4.0), stilbene (1.0, 2.0), 1-dodecene (0.5, 4.0), ethyl cinnamate (1.0, 8.0), ethyl decanoate (0.5, 4.0), benzoic acid (1.0, 4.0), α-phenylacetamide (0.5, 4.0) and phthalide (0.5, 4.0).

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