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Studies of Reduction with the Sodium Borohydride–Transition Metal Boride System. I. Reduction of Nitro and the Other Functional Groups with the Sodium Borohydride–Nickel Boride System

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Aromatic nitro, azoxy, azo and hydrazo compounds were reduced with the sodium borohydride–nickel boride system to the corresponding reduction products under mild conditions.

Keywords——reduction; sodium borohydride; nickel boride; nitrobenzene; azoxy compound; azo compound; hydrazo compound; primary amine; sodium borohydride–nickel boride system

Reduction with sodium borohydride ($NaBH_4$) is greatly accelerated by increasing temperature or by the addition of acidic substances. Particularly, striking is the catalytic effect of certain metal salts, such as nickelous chloride ($NiCl_2$) or cobaltous chloride ($CoCl_2$). The combination of $NaBH_4$ with nickelous,[1] cupric,[2] cobaltous[1] and stannous[3] halides has been employed to reduce nitriles, amides, olefins and nitro compounds. The reaction of $NaBH_4$ with $NiCl_2$ in methanol is exothermic and instantly deposits a black precipitate of nickel boride (Ni_2B)[4,5] while steadily evolving hydrogen. It has been reported that metal borides can be used as catalysts in the reduction of carbonyl compounds[6] and olefins.[7] In addition, it has been reported that alkenes are reduced with P-1 nickel[8] and alkynes can be reduced with $NaBH_4$–Co_2B.[9] In the previous papers, we reported that the $NaBH_4$–transition metal salt system reduces nitro compounds,[10] oximes[11] and heterocyclic compounds.[12] In order to investigate the reducing activity of the $NaBH_4$–Ni_2B system in comparison with the $NaBH_4$–$NiCl_2$ system, the paper deals with the reduction of some functional groups with this system.

As shown in Chart 1, nitrobenzene (1) was reduced with Ni_2B in refluxing methanol to

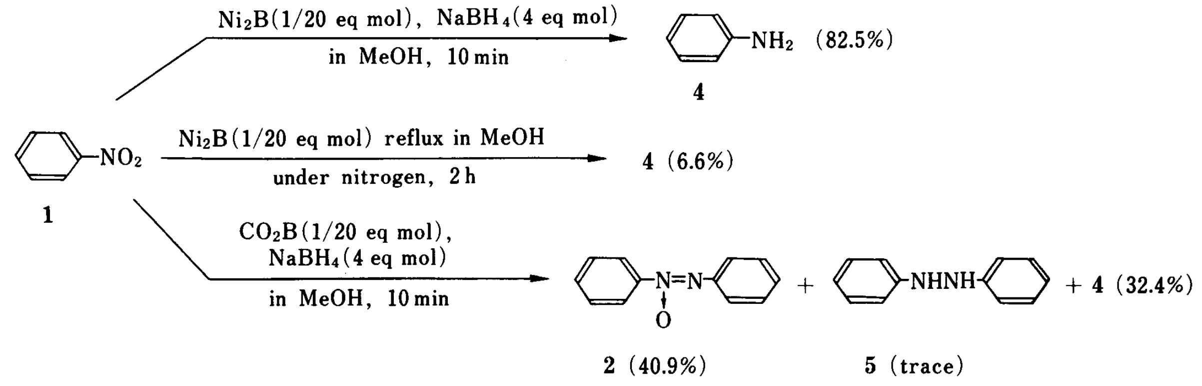
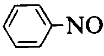
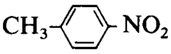
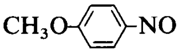
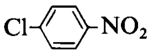


Chart 1

give aniline (**4**) in a low yield. However, the $NaBH_4$–Ni_2B system reduced **1** at room temperature in a good yield, and the reducing reactivity of this system was superior to that of the $NaBH_4$–Co_2B system.

As shown in Table I, on the reduction of nitro compounds with the $NaBH_4$–Ni_2B

TABLE I. Reduction of Nitro Compounds with the $NaBH_4$–Ni_2B System

Nitro compound (No.)	Ni_2B (eq mol)	$NiCl_2$ (eq mol)	$NaBH_4$ (eq mol)	Add. time (min)	Product (No.) Yield (%) Azoxy		Amine	
 (**1**)	1/100		5	35	**2**	89.4		
	1/100		5	18			**4**	75.4
	1/20		4	10			**4**	92.8
	1/100[a]		5	20	**2**	82.7	**4**	12.7
		1/100	4	20	**2**	94.6		
		1/10	4.3	10			**4**	84.9
 (**6**)	1/100		5	30	**9**	82.5	**10**	7.7
	1/100		5	18			**10**	92.2
	1/20		4	8			**10**	88.3
		1/50	4.1	20	**9**	86.9	**10**	8.8
		1/10	4.3	8			**10**	87.0
 (**7**)	1/100		5	30	**11**	81.9	**12**	14.9
	1/20		5	10			**12**	97.8
		1/50	5.1	20	**11**	85.8	**12**	11.0
		1/10	5.3	10			**12**	90.8
 (**8**)	1/100		4	20	**13**	85.7	**14**	9.9
	1/20		4	8	**13**	9.4	**14**	86.5
		1/50	3.1	20	**13**	84.9	**14**	14.1
		1/10	4.3	10			**14**	86.0

[a] Ni_2B was dried over phosphorus pentoxide under vacuum for 24 h.

TABLE II. Reduction of Azoxybenzene Derivatives with the $NaBH_4$–Metal Boride System

Azoxy No.	Ni_2B (eq mol)	Co_2B (eq mol)	$NiCl_2$ (eq mol)	$NaBH_4$ (eq mol)	Add. time (min)	Time (h)	Product (No.) Yield (%) Azo		Hydrazo		Amine	
2	1/100			4	30	0.5			**5**	92.6		
2	1/100			4	30	15	**3**	23.1	**5**	66.7		
2	1/10			2	30	0.5	**3**	35.9	**5**	49.9		
2		1/10		4	30	0	**3**	40.0	**5**	10.8		
2			1/100	3	30	15	**3**	45.7	**5**	12.1	**4**	17.0
2				10	30	0.5[a]	**3**	28.8	**5**	21.5		
2	1				30	0.5[b]	**3**	trace	**5**	14.5	**4**	4.2
9	1/100			3	30	0	**15**	91.5			**10**	7.9
9	1/10			8	40	0	**15**	21.0			**10**	73.9
9			1/50	3	30	2	**15**	87.7	**16**	5.9	**10**	5.8
11	1/100			3	30	4	**17**	55.4			**12**	40.2
11	1/100			7	40	0	**17**	23.5			**12**	73.4
11		1/10		6	30	0	**17**	9.6				
11			1/50	2	30	24	**17**	70.2			**12**	19.9
13	1/100			5	30	24	**18**	90.4	**19**	5.3	**14**	2.9
13	1/10			8	30	0	**18**	20.6	**19**	23.8	**14**	35.6
13			1/50	3	30	24	**18**	78.2	**19**	3.7	**14**	17.8

[a] Reflux. [b] Reflux under nitrogen.

TABLE III. Reduction of Azobenzene (3) with the $NaBH_4$–Metal Boride System

Ni_2B (eq mol)	Co_2B (eq mol)	$NiCl_2$ (eq mol)	$NaBH_4$ (eq mol)	Add. time (min)	Time (min)	Product yield (%)	
						Hydrazobenzene (**5**)	Aniline (**4**)
1/100			4	30	30	81.1	
1/10			2	20	0	89.0	
	1/10		4	30	0	55.4	
		1/10	2	20	0		82.2
1					30[a)]	6.4	57.2
			10	30	30[b)]	4.9	

a) The reaction mixture was refluxed under nitrogen. *b*) The reaction mixture was redflllllluxed.

TABLE IV. Reduction of Other Functional Groups with the $NaBH_4$–Ni_2B System

Compound	Ni_2B (eq mol)	$NiCl_2$ (eq mol)	$NaBH_4$ (eq mol)	Add. time (min)	Product	Yield (%)
Hydrazobenzene	1/10		2	30	Aniline	81.2
Stilbene	1/2		4	30	1,2-Diphenylethane	33.3
Stilbene		1/2	2	30	1,2-Diphenylethane	89.0
Acetophenone oxime	1/20		4	30	1-Phenylethylamine	13.5
Acetophenone oxime		1/10	4	30	1-Phenylethylamine	71.4
Quinoline	1/2		4	30	Recovery	
Quinoline		1/10	10	30	1,2,3,4-Tetrahydroquinoline	83.1
Quinaldine	1/2		4	30	Recovery	
Quinaldine		1/10	4	30	1,2,3,4-Tetrahydroquinaldine	93.8
Isoquinoline	1/2		4	30	Recovery	
Isoquinoline		1/10	10	30	1,2,3,4-Tetrahydroisoquinoline	86.9

system, the corresponding azoxy derivatives (**2**, **9**, **11** and **13**) were obtained as major products when the time of $NaBH_4$ addition was longer than 20 min or 1/100 mol eq of Ni_2B was used. When the time during which $NaBH_4$ was added was less than 10 min or 1/20 mol eq of Ni_2B was used, the corresponding amines (**4**, **10**, **12** and **14**) were obtained in good yields. These results are similar to those obtained with the $NaBH_4$–$NiCl_2$ system.

The similar reaction of azoxybenzene (**2**) gave azobenzene (**3**) and hydrazobenzene (**5**), but the reduction of azoxybenzene derivatives (**9**, **11** and **13**) gave the corresponding azo derivatives (**15**, **17** and **18**) and amines (**10**, **12** and **14**) as major products (Table II). Similarly, azobenzene (**3**) was reduced with this system to give hydrazobenzene (**5**) in good yields, though the reduction of **3** with $NaBH_4$–$NiCl_2$ gave aniline (**4**) (Table III).

As shown in Table IV, the $NaBH_4$–Ni_2B system reduced hydrazobenzene (**5**), stilbene and acetophenone oxime, but did not reduce heterocyclic compounds which were reduced with the $NaBH_4$–$NiCl_2$ system under similar conditions.[12)]

In reduction of the tested functional groups with the $NaBH_4$–Ni_2B system, the time of $NaBH_4$ addition was important factor affecting the yield of the reduction products. Compared with the $NaBH_4$–$NiCl_2$ system, this system exhibited similar reducing reactivity towards nitro and azoxy groups. However, this system gave different results in the reduction of azobenzene (**3**) and did not reduce heterocyclic compounds under similar conditions.

Experimental

Commercially available $NiCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ and $NaBH_4$ 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 JASCO A-100 (Nihon Bunko) infrared spectrometer, and ultraviolet (UV) spectra were recorded on a JASCO Uvidec-505 ultraviolet spectrometer. Gas chromatography was done on a JEOL JGC-20K gas chromatograph. Yields of amines were calculated by gas chromatography on a glass column, packed with SE-30, at 140 °C (column temperature) and 0.8 kg/cm^2 of nitrogen pressure, by comparison with standard amounts of authentic samples.

Ni_2B——Ni_2B was prepared from $NaBH_4$ and $NiCl_2 \cdot 6H_2O$ according to a published procedure.[5]

General Procedure for the Reduction of Nitro Compounds (1, 6, 7 and 8) with the $NaBH_4$–Ni_2B System——A nitro compound (3 mmol) and freshly prepared Ni_2B (molar quantities are shown in Table I) were suspended in methanol (20 ml) and stirred for 10 min. Then, $NaBH_4$ was added to the suspended solution in portions with stirring at 20 °C (the molar ratios of $NaBH_4$ and the addition time are listed in Table I). After the removal of the solvent, the residue was acidified by the addition of 10% hydrochloric acid. The acidic solution was extracted with ether, then the extract was dried over anhydrous magnesium sulfate, and evaporated. The residue was almost completely crystallized in the reaction mixture on cooling. The product was recrystallized from ethanol to give the corresponding azoxy compound (the yield is shown in Table I); azoxybenzene (**2**), mp 35—36.5 °C (lit.[13] mp 35.5—36.5 °C); 4,4′-dimethylazoxybenzene (**9**), yellow needles, mp 69—70°C (lit.[14] mp 69—70 °C). *Anal.* Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.373; H, 6.137; N, 12.466. 4,4′-Dimethoxyazoxybenzene (**11**), yellow needles, mp 118—119 °C (to an anisotropic liquid which becomes clear at 134—135 °C) (lit.[15] mp 119 °C (nematic-liquid transition at 135 °C)). *Anal.* Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85. Found: C, 65.211; H, 5.457; N, 10.912. 4,4′-Dichloroazoxybenzene (**13**), yellow needles, mp 154—155 °C (lit.[16] mp 154—155 °C). *Anal.* Calcd for $C_{12}H_8Cl_2N_2O$: C, 53.95; H, 3.02; N, 10.49. Found: C, 53.936; H, 2.924; N, 10.444. These azoxy compounds were identical with authentic samples on the basis of mixed melting point determination and comparisons of IR and UV spectra. The authentic samples were prepared from the corresponding nitro compounds according to a published procedure.[17] For work-up of the reduction mixture of **1**, the residue described above was directly chromatographed over alumina (column) using petroleum ether as the eluent. The eluate was concentrated and the residue was recrystallized from 90% ethanol to give azobenzene (**3**), mp 66—67 °C (lit.[18] mp 66—67.5 °C). The eluate with benzene was concentrated, and the residue was recrystallized from 95% ethanol to give azoxybenzene (**2**) (the reaction conditions and yields are listed in Table I). The acidic aqueous layer described above was basified by the addition of concentrated 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 the corresponding amines. These amines (**10**, **12** and **14**) were identified by comparison of their IR and UV spectra with those of the corresponding authentic samples, and the results are listed in Table I.

Reduction of Azoxy Compounds (2, 9, 11 and 13) with the $NaBH_4$–Ni_2B System——$NaBH_4$ was added in small protions to a suspension of azoxybenzene (**2**) and Ni_2B in methanol under stirring (in the molar ratios shown in Table II). The reaction was carried out under the reaction conditions of Table II. After treatment as described above, the eluate with petroleum ether–benzene (1 : 2) was concentrated and the resulting residue was recrystallized from 90% ethanol to give azobenzene (**3**), mp 66—67 °C. The acidic aqueous layer was treated as described above, and the residue was recrystallized from ethanol–ether to give hydrazobenzene (**5**), mp 128—131 °C (lit.[19] mp 128—132 °C). The yields of the products are listed in Table II.

The following products were similarly obtained, and the reaction conditions and yields are listed in Table II. The separation of hydrazo compounds and amines of the extract from acidic solution was carried out by alumina (column) chromatography. The eluate with benzene was concentrated and the residue was recrystallized from ethanol–ether to give hydrazo compounds, while the eluate with benzene–chloroform was treated similarly to give the corresponding amines. These products were identified by the mixture melting point test and comparison of the IR and UV spectra with those of authentic samples. 4,4′-Dimethylhydrazobenzene (**16**), mp 129—131 °C (lit.[20] mp 129.5—131 °C); 4,4′-dichlorohydrazobenzene (**18**), mp 127—130 °C (lit.[21] mp 130 °C).

Reduction of Stilbene——$NaBH_4$ (12 mmol) was added in small portions to a suspension of stilbene (3 mmol) and freshly prepared Ni_2B (1.5 mmol) in methanol (20 ml), with stirring over 30 min at room temperature. After treatment as above, the resulting crude product was recrystallized from 95% ethanol to give bibenzyl (33.3%), mp 52.5—53 °C (lit.[22] mp 52.5—53 °C). All spectral data of the product were identical with those of an authentic sample.

Reduction of Acetophenone Oxime——Similar reduction of acetophenone oxime (3 mmol) with Ni_2B (0.15 mmol) and $NaBH_4$ (12 mmol) gave 1-phenylethylamine (13.5%), bp 183 °C (lit.[23] bp 80—81 °C (8 mmHg)), hydrochloride mp 160 °C (from ethanol) (lit.[24] mp 160 °C).

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