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Selective Reduction of Imines with the Diborane–Methanol System

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The selective reduction of imines with the diborane–methanol system was investigated. This system reduced imines quantitatively, and other functional groups tested were unaffected.

Keywords——imine; diborane; selective reduction; diborane–methanol system; secondary amine; dimethoxyborane

In the previous papers, we reported that quinoline, isoquinoline and quinoxaline derivatives were reduced to the corresponding 1,2,3,4-tetrahydro derivatives by treatment with diborane,[1] and the nitro group in aromatic nitro compounds bearing another functional group was selectively reduced with the diborane–transition metal salt system.[2] As a continuation of that work, the present paper deals with the selective reduction of imines with the diborane–methanol system. As shown in Table I, imines were quantitatively reduced to the corresponding secondary amines with the diborane–methanol system at room temperature.

The reduction of imines with BH_3–tetrahydrofuran proceeds under mild conditions.[3] However, diborane also reduces multiple bonds in organic functional groups containing sulfur, nitrogen, oxygen or carbon, and similar reduction of imines can also be carried out with sodium borohydride. Therefore, diborane would appear to possess limited utility for the reduction of imines unless it can exhibit selective reducing ability toward imines. Thus, in order to examine the reducing ability of the diborane–methanol system, other functional groups were tested under similar conditions. As shown in Table II, the other functional groups listed were not reduced with this system.

TABLE I. Reduction of Imines with the Diborane–Methanol System[a]

Compound[b]	B_2H_6 (mol eq)	Product	Yield (%)
C_6H_5–CH=N–C_6H_5	2.0	C_6H_5–CH_2NH–C_6H_5	96.0
p-CH_3O–C_6H_4–CH=N–C_6H_5	2.0	*p*-CH_3O–C_6H_4–CH_2NH–C_6H_5	95.2
p-CH_3–C_6H_4–CH=N–C_6H_5	2.0	*p*-CH_3–C_6H_4–CH_2NH–C_6H_5	99.8
p-Cl–C_6H_4–CH=N–C_6H_5	2.0	*p*-Cl–C_6H_4–CH_2NH–C_6H_5	93.4
p-HO–C_6H_4–CH=N–C_6H_5	2.0	*p*-HO–C_6H_4–CH_2NH–C_6H_5	93.4
p-CH_3O–C_6H_4–N=CH–C_6H_5	2.0	*p*-CH_3O–C_6H_4–NHCH_2–C_6H_5	93.6
p-CH_3–C_6H_4–N=CH–C_6H_5	2.0	*p*-CH_3–C_6H_4–NHCH_2–C_6H_5	89.7
p-Cl–C_6H_4–N=CH–C_6H_5	2.0	*p*-Cl–C_6H_4–NHCH_2–C_6H_5	91.5
p-HO–C_6H_4–N=CH–C_6H_5	2.0	*p*-HO–C_6H_4–NHCH_2–C_6H_5	98.9
C_6H_5–CH=N–CH_3	2.0	C_6H_5–CH_2NH–CH_3	80.1
$(CH_3)_2$CH–CH=N–C_6H_5	2.0	$(CH_3)_2$CH–CH_2NH–C_6H_5	95.1
C_6H_5–CH=N–C$(CH_3)_3$	2.0	C_6H_5–CH_2NH–C$(CH_3)_3$	87.3

a) Reaction conditions: at room temperature for 30 min in methanol. *b*) Molar quantity = 5 mmol.

TABLE II. Reaction of Various Functional Groups with the Diborane–Methanol System[a)]

Compound	Result	Compound	Result
C_6H_5–COOH	Recovery	$HOCH_2C{\equiv}CCH_2OH$	Recovery
C_6H_5–$COCH_3$	Recovery	C_6H_5–$C(CH_3)$=NOH	Recovery
Cyclohexanone	Recovery	C_6H_5–NO_2	Recovery
C_6H_5–CHO	Recovery	Quinaldine	Recovery
C_6H_5–CH_2CN	Recovery	C_6H_5–CH=N–NH–C_6H_5	Recovery
C_6H_5–$CONH_2$	Recovery	$(CH_3)_2CHCH$=NNH–$C_6H_3(NO_2)_2$(2,4-)	Recovery
$CH_3(CH_2)_{10}COOC_2H_5$	Recovery		C_6H_5–CH_2NHNHCH_2–C_6H_5 (Trace)
CH_2=$CH(CH_2)_9CH_3$	Recovery	C_6H_5–CH=N–N=CH–C_6H_5	
C_6H_5–CH=CH–C_6H_5	Recovery		C_6H_5–CONH–N=CH–C_6H_5 (29.0%)

a) Reaction conditions: at room temperature for 30 min in methanol.

TABLE III. Selective Reduction of Imine Derivatives with the Diborane–Methanol System[a)]

Compound[b)]	Product	Yield (%)
p-HOOC–C_6H_4–CH=N–C_6H_5	*p*-HOOC–C_6H_4–CH_2NH–C_6H_5	99.1
p-CH_3OOC–C_6H_4–CH=N–C_6H_5	*p*-CH_3OOC–C_6H_4–CH_2NH–C_6H_5	99.4
p-NC–C_6H_4–CH=N–C_6H_5	*p*-NC–C_6H_4–CH_2NH–C_6H_5	91.1
p-CH_3CO–C_6H_4–N=CH–C_6H_5	*p*-CH_3CO–C_6H_4–NHCH_2–C_6H_5	92.0
p-CH_3CONH–C_6H_4–N=CH–C_6H_5	*p*-CH_3CONH–C_6H_4–NHCH_2–C_6H_5	99.8
2-C_5H_4N–CH=N–C_6H_5	2-C_5H_4N–CH_2NH–C_6H_5	93.2
C_6H_5–CH=CH–CH=N–C_6H_5	C_6H_5–CH=CH–CH_2NH–C_6H_5	92.1
p-O_2N–C_6H_4–CH=N–C_6H_5	*p*-O_2N–C_6H_4–CH_2NH–C_6H_5	86.2

a) Reaction conditions: at room temperature for 30 min in methanol. *b*) Molar ratio: imine/diborane = 1/2. Molar quantity = 5 mmol.

The reduction of imine derivatives bearing other functional groups was examined under similar conditions to give the corresponding secondary amines in good yields, as shown in Table III. These results show that this system possesses selective reducing ability for the imino group.

It was reported that diborane reacted smoothly with methanol to give dimethoxyborane *via* methoxyborane.[4)] Benzylideneaniline and *p*-cyanobenzylideneaniline were reduced with dimethoxyborane in methanol to give the corresponding secondary amines in good yields (95.0% and 81.4% respectively). Therefore, it is assumed that the actual reductant in the diborane–methanol system is dimethoxyborane, and that dimethoxyborane reacts rapidly with methanol rather than other functional groups (except for imine) to give trimethoxyborane.

It is considered that the diborane–methanol system provides a useful synthetic route under mild conditions for the selective reduction of imine derivatives.

Experimental

Commercially available $NaBH_4$ 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. Aldimines were prepared from purified aldehydes and amines according to a published procedure.[5)] The procedure for the reduction of *N*-benzylideneaniline with the diborane–methanol system is described in detail as a typical example.

Reduction of *N*-Benzylideneaniline——Diborane[6] (10 mmol) was passed into a methanol (30 ml) solution of *N*-benzylideneaniline (0.91 g, 5 mmol) with stirring at room temperature for 30 min. After removal of the methanol, 10% hydrochloric acid (10 ml) was added and the mixture was washed with ether. The aqueous layer was basified with 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 under reduced pressure to give 880 mg (96.0%) of *N*-phenylbenzylamine, bp 180—181 °C (12 mmHg) (lit.[7] bp 144—146 °C (1 mmHg)), mp 36—37 °C (from pet. ether) (lit.[8] mp 36—37.2 °C). This was identical with an authentic sample on the basis of mixed melting point determination and comparison of infrared (IR) and ultraviolet (UV) spectra.

The following products were similarly obtained, and the yields are listed in Tables I and III. All spectral data of products were identical with those of the corresponding authentic samples. The authentic samples were prepared from purified chlorides and amines according to a published procedure.[9] *N*-Phenyl-4-methoxybenzylamine mp 63.5—64.5 °C (from ethanol) (lit.[10] mp 64.5 °C); *N*-phenyl-4-methylbenzylamine mp 47 °C (from pet. ether) (lit.[11] mp 47 °C), hydrochloride mp 190—191 °C (from ethanol) (lit.[11] mp 191 °C); *N*-phenyl-4-chlorobenzylamine bp 178—180 °C (3 mmHg) (lit.[11] bp 333—334 °C), hydrochloride mp 211—212 °C (from ethanol) (lit.[11] mp 211.5—212.5 °C); *N*-phenyl-4-hydroxybenzylamine mp 207—208 °C (from ethanol) (lit.[12] mp 208 °C; *N*-benzyl-*p*-anisidine bp 184—185 °C (5 mmHg) (lit.[13] bp 236—238 °C (32 mmHg)), mp 50 °C (from ligroin) (lit.[14] mp 50—50.5 °C); *N*-benzyl-*p*-toluidine bp 201—203 °C (9 mmHg) (lit.[11] bp 319 °C), hydrochloride mp 180—182 °C (from ethanol) (lit.[11] mp 181—182 °C); *N*-(4-chlorophenyl)benzylamine bp 175—177 °C (3 mmHg) (lit.[15] bp 159 °C (0.7 mmHg)), mp 48—48.5 °C (from pet. ether) (lit.[14] mp 48.5—49 °C); *N*-(4-hydroxyphenyl)benzylamine mp 88—89 °C (from pet. ether) (lit.[16] mp 89 °C); *N*-methylbenzylamine hydrochloride mp 178 °C (from ethanol–ether) (lit.[17] mp 178 °C), picrate mp 118—120 °C (from ethanol) (lit.[18] mp 119—120 °C); *N*-phenylisobutylamine bp 110—112 °C (12 mmHg) (lit.[19] bp 111.5—113.5 °C (11.5 mmHg)), hydrochloride mp 190—191 °C (from benzene) (lit.[20] mp 192 °C); *N*-*tert*-butylbenzylamine hydrochloride mp 244—246 °C (from benzene) (lit.[21] mp 245—247 °C); 4-(anilinomethyl)benzoic acid mp 195—197.5 °C (from methanol–ether). *Anal.* Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.11; H, 5.62; N, 6.17. Methyl 4-(anilinomethyl)benzoate hydrochloride mp 143—145 °C (from methanol). *Anal* Calcd for $C_{15}H_{16}ClNO_2$: C, 64.87; H, 5.81; N, 5.04. Found: C, 65.13; H, 5.76; N, 5.13. 4-(Anilinomethyl)benzonitrile mp 85—87 °C (from ethanol) (lit.[22] mp 86—87 °C); *p*-(benzylamino)acetophenone mp 88—90 °C (from ligroin–ether) (lit.[23] mp 89—90 °C); *N*-(*p*-acetamidophenyl)benzylamine mp 141 °C (from ethanol) (lit.[24] mp 141—142 °C); 2-(anilinomethyl)pyridine mp 50—52 °C (from benzene–pet. ether) (lit.[25] mp 50—53 °C); *N*-cinnamylaniline bp 165—166 °C (10 mmHg) (lit.[26] bp 178 °C (12 mmHg)), hydrochloride mp 183—184 °C (from ethanol) (lit.[26] mp 185 °C); *N*-phenyl-4-nitrobenzylamine mp 67 °C (from ethanol–ether) (lit.[14] mp 67—68 °C).

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