The Reduction of Oximes, Oxime Ethers, and Oxime Esters with Diborane. A Novel Synthesis of Amines

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Oximes and hydroxylamines are reduced by diborane to the corresponding amines in yields of about 70% if reactions are performed at 105–110°. On the other hand, oxime ethers and oxime esters react with diborane already at 25° to give intermediates which on basic or acidic hydrolysis afford the corresponding primary amines and alcohols in yields of 50–90%.

Previously, it was reported that treatment of aldoximes and ketoximes,[1] as well as nitronate salts,[2] with diborane in tetrahydrofuran at 25° afforded the corresponding N-monosubstituted hydroxylamines in very good yield. We are now reporting that oximes were reduced to amines if the reactions were performed at 105–110° in a diglyme–THF solution. A few representative examples are shown in Table I. It is very likely that these reductions proceeded *via* hydroxylamine intermediates because hydroxylamines themselves were reduced in high yields to amines on treatment with diborane at 105–110° (Table I). The

TABLE I

DIBORANE REDUCTION OF OXIMES AND HYDROXYLAMINES TO AMINES

Compound[a]	Amine[b]	Yield, %
1,3-Diphenyl-2-propanone oxime	1,3-Diphenyl-2-propylamine	74.2
Cyclohexanone oxime	Cyclohexylamine[c]	70.5
p-Nitrobenzaldehyde oxime	*p*-Nitrobenzylamine	72.5
Heptanal oxime	*n*-Heptylamine	72.0
N-Cyclohexylhydroxylamine	Cyclohexylamine[c]	84.4
N-Heptylhydroxylamine	*n*-Heptylamine	62.7

[a] Reductions were carried out at 105–110° for 20 hr in a diglyme–THF mixture. [b] These compounds were identified by their physical data which were in agreement with those reported in the literature. [c] Isolated as the oxalate salt, mp 229–230°. *Anal.* Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.84; H, 7.83; N, 7.37.

temperature effect on the course of the reaction was dramatically indicated in the case of 1,3-diphenyl-2-propanone oxime (**1**). While in a temperature range of 25–65°, **1** was recovered unchanged; at 85–90° it was reduced to N-1,3-diphenyl-2-propylhydroxylamine (**2**) in 77% yield, and at 105–110° the amine, 1,3-diphenyl-2-propylamine (**3**) was obtained as the only product in 74% yield (eq 1).

$$(C_6H_5CH_2)_2C{=}NOH \xrightarrow[85\text{–}90^\circ]{B_2H_6} (C_6H_5CH_2)_2CHNHOH$$
1 **2**

$$\mathbf{1} \xrightarrow[105\text{–}110^\circ]{B_2H_6} (C_6H_5CH_2)_2CHNH_2 \quad (1)$$
3

In the case of the oximes of benzophenone (**4**) and dicyclohexyl ketone (**5**), even at reaction temperatures up to 110° the reduction did not proceed beyond the hydroxylamine stage. Previously,[1] compounds **4** and **5** were recovered unchanged when treated with diborane at temperatures as high as 65°.

Oxime Ethers.—While the reduction of oximes to amines by diborane required high temperatures, oxime ethers underwent the reduction already at room temperature (eq 2).

$$\begin{matrix} R' \\ | \\ RC{=}NOR'' \end{matrix} \xrightarrow[25^\circ]{B_2H_6} \begin{matrix} R' \\ | \\ RCHNH_2 \end{matrix} + R''OH \quad (2)$$

R = alkyl or aryl
R′ = alkyl, aryl or H
R″ = alkyl or benzyl

Reactions were carried out mainly with O-methyl oximes because they were obtained directly in high yield on treating aldehydes and ketones with methoxyamine hydrochloride.[3]

These oxime ethers were also prepared by the reaction of potassium oximates with methyl *p*-toluenesulfonate; however, this procedure gave lower yields (eq 3).

$$R_2C{=}NOH \xrightarrow[2.\ p\text{-}CH_3C_6H_4SO_3CH_3]{1.\ K,\ THF,\ \Delta} R_2C{=}NOCH_3 \quad (3)$$

Reaction Conditions.—By employing O-methyl benzaldehyde oxime (**6**) as a model compound, it was found that the following conditions led to optimum yields: (1) during the addition of the borane–THF solution to the oxime ether the reaction temperature had to be kept below 5° to prevent possible fume-offs; (2) a contact time of 1–2 hr at 65° was found to be sufficient to ensure complete reaction; (3) the yield of amine was, over a wide range, independent of the amount of hydride ion per mole of **6**;[4] and (4) basic or acidic hydrolysis of the reaction mixture gave comparable yields of the amine.

Results

As shown by representative examples in Table II, the reduction of oxime ethers gave good to excellent yields of the corresponding amines. The alkoxy portion of the ethers was reduced to the corresponding alcohol. For instance, O-benzylheptanal oxime (**7**) gave benzyl alcohol and heptylamine in yields of 95.2 and 97.8%, respectively.

The reduction of oxime ethers to amines constitutes an attractive route for the conversion of aldehydes and ketones into amines because it can be carried out at

(1) H. Feuer, B. F. Vincent, Jr., and R. S. Bartlett, *J. Org. Chem.*, **30**, 2877 (1965).

(2) H. Feuer, R. S. Bartlett, B. F. Vincent, Jr., and R. S. Anderson, *ibid.* **30**, 2880 (1965).

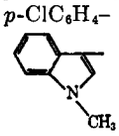
(3) H. M. Fales and T. Luukainen, *Anal. Chem.*, **37**, 955 (1965).

(4) The reduction of **6** with 2.5 and 8.0 equiv of hydride ion gave benzylamine in yields of 91.8 and 91.5%, respectively.

TABLE II

DIBORANE REDUCTION OF OXIME ETHERS TO AMINES[a,b]

$$RCR^1(=NOCH_3) \xrightarrow[2.\ \text{hydrolysis}]{1.\ BH_3,\ THF} RCHR^1(NH_2) + CH_3OH$$

Amine[c] R	Amine[c] R^1	Registry no.	Mp, °C	Bp (mm) or mp, °C	$n^{20}D$	Yield, %
C_6H_5–	H	100-46-9	196–198[c]	73 (14)	1.5410	92.5
p-$(CH_3)_2NC_6H_4$–	H	19293-58-4	203–205[c]	135–136 (15)	1.5761	87.8
p-$NO_2C_6H_4$–	H	7409-30-5	183–185[c]	110–111 (1.25), 39–40	1.5642	81.7
p-ClC_6H_4–	H	104-86-9	207–209[c]	106–108 (15)	1.5579	84.5
	H	19293-60-8	186–187[d]			71.7
C_6H_5–	C_6H_5–	91-00-9	205–206 dec[c]			65.0
p-$CH_3OC_6H_4$–	*p*-$CH_3OC_6H_4$–	19293-62-0	188 dec[e]			70.9
C_6H_5–	$-CH_3$	98-84-0	187–189[c]			51.8
Cyclohexyl–	–Cyclohexyl	19293-63-1	157–158[f]	87–89 (0.6)	1.4951	77.2
$CH_3(CH_2)_6$–	H	111-86-4	120–121[c]	57–58 (15)	1.4251	77.5
C_6H_5–	$-CC_6H_5$(=NOCH$_3$)	19293-64-2	237–240 dec[g]			67.8
C_6H_5–	$-CH_2CC_6H_5$(=NOCH$_3$)	19293-65-3	241–245 dec[g]	145–146 (0.48)	1.5868	89.7

[a] Reactions were carried out for 2 hr at reflux temperature. [b] Hydride ion (2 equiv) per mole of oxime ether was consumed. [c] Melting point of picrate derivative. [d] Isolated and characterized as the phenylthiourea derivative. [e] Isolated and characterized as the picrate derivative. [f] Isolated and characterized as the phenylthiorurea derivative. [g] Melting point of dipicrate derivative.

room temperature, and has been found to be applicable to a wide variety of compounds. As shown in Table II, oxime ethers containing nitro or chloro groups, and dioxime ethers were reduced, respectively, to the corresponding nitro- or chloroamines and diamines in high yields.

Oxime Esters.—The reduction of oxime esters with diborane also led to amines in high yields, and the acyl portion was reduced to the alcohol. Hydride consumption measurements indicated that twice the amount of hydride was consumed in the reduction of an oxime ester as compared to an oxime ether.

For instance, O-(*p*-nitrobenzoyl) cyclohexanone oxime gave 68% cyclohexylamine and 80.6% *p*-nitrobenzyl alcohol (eq 4).[5]

$$RC(=NOCR')=O \xrightarrow[25°]{B_2H_6} RCHNH_2 + R'CH_2OH \qquad (4)$$

R = cyclohexyl–

R′ = CH_3 or *p*-$NO_2C_6H_4$–

Discussion

On the basis of quantitative measurements of hydride consumption and isolation of intermediates which on subsequent hydrolysis gave amines and alcohols, it is proposed that the reduction of oxime ethers with diborane involves essentially three steps (eq 5–7). Although intermediates A, B, and C are presented as monomers they might be polymeric in nature as indicated by the molecular weight determination of the intermediate[6] obtained from **7** and diborane (see Experimental Section).

$$RCH{=}NOR' \longrightarrow \left[\begin{array}{c} H \\ | \\ RC{=}NOR' \\ | \\ H{-}BH_2 \end{array}\right] \longrightarrow \underset{\underset{A}{BH_2}}{RCH_2NOR'} \qquad (5)$$

$$A \xrightarrow{BH_3} \left[\begin{array}{c} H{-}BH_2 \\ \downarrow \\ RCH_2N{-}OR' \\ | \\ BH_2 \end{array}\right] \longrightarrow \underset{\underset{B}{BH_2}}{RCH_2NH} + \underset{C}{R'OBH_2} \qquad (6)$$

$$B + C \xrightarrow[\Delta]{H^+ \text{ or } OH^-} RCH_2NH_2 + R'OH \qquad (7)$$

The reaction sequence is similar to that suggested for the reduction of oximes,[1] except that it differs in the first step, since no acidic hydrogen is present, and it indicates the formation of cleavage products B and C prior to hydrolysis. This is based on the following observations.

The reaction product of diborane with **7** dissolved in pentane was obtained as an opaque viscous liquid after removal of the solvent *in vacuo*. The nmr spectrum of this intermediate confirmed that reduction of the C=N bond had occurred, because the vinyl proton, present in the starting material **7** which appeared as two triplets[7] was absent.

This intermediate still contained active hydride because on hydrolysis, hydrogen was evolved and on work-up benzyl alcohol and heptylamine were obtained in yields of 38 and 42%, respectively.

Step 1 in the reaction is the actual reduction step wherein the double bond becomes saturated. The

(5) After this work was completed A. Hassner and P. Catsoulacos [*Chem. Commun.*, 590 (1967)] reported that treatment of oxime acetates with diborane afforded amines.

(6) The term intermediate applies to a mixture of components.

(7) J. H. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw Hill Book Co., Inc., New York, N. Y., 1959, p 374.

four-centered attack is in agreement with present views of the addition of borane to multiple linkages.[8] In step 2, electrophilic attack of borane on nitrogen is followed by a hydride shift with the resulting cleavage of the N–O bond to give B and C. Evidence that cleavage had occurred was obtained (1) from hydride consumption measurements, which showed that 2 equiv of hydride ion instead of 1 equiv was consumed prior to hydrolysis; (2) from the mass spectrum of the intermediate, which had peaks at *m/e* 233, 127, and 120 (relative intensity 0.88, 1.32, and 36.72, respectively) in agreement with structures A, B, and C, where R = *n*-heptyl and R[1] = benzyl; (3) from the infrared spectrum, which showed bands at 3200 (NH), 2480 (BH), 1605 (BN), and 1170 cm^{-1} (OCH_2);[9] and (4) from the elemental analysis and molecular weight determination, which indicated that the intermediate consisted of a mixture, (see Experimental Section).

Step 3 presents the hydrolysis to the final products. In order to obtain maximum yield of product, it was necessary to reflux basic or acidic solutions of the intermediate.

Experimental Section

Apparatus.—Experiments were performed in the setup described previously.[1]

Reagents.—Diborane was generated as described by Brown[10] and solutions of diborane in THF were prepared and standardized.

Aldehydes and ketones of Eastman White Label grade were distilled or recrystallized prior to use. Hydroxylamine and methoxyamine hydrochloride, Eastman White Label grade, were used as received. Methyl *p*-toluenesulfonate was prepared by the method of Ross, *et al.*[11]

Oximes were prepared by methods described in the literature. Tetrahydrofuran was purified by the method of Feuer and Savides.[12]

Equipment.—All infrared spectra were taken with Perkin-Elmer recording spectrophotometers, Models 21 and 421. Nuclear magnetic resonance spectra were determined on a Varian Model A-60 analytical nmr spectrometer using tetramethylsilane as an internal standard. Gas chromatographic analyses were performed on Aerographs A-700 and A-903 using a 4-ft SF-96 on Chromosorb W column. Mass spectra were obtained with a Hitachi RMU-6A mass spectrometer.

High-Temperature Diborane Reductions. Cyclohexylamine. A. Using Cyclohexanone Oxime.—The following experiment is typical of the procedure employed. To 2.26 g (20.0 mmol) of cyclohexanone oxime dissolved in 50 ml of diglyme at 0° was introduced by means of a hypodermic syringe 91.0 mequiv of hydride ion, at such a rate that the temperature did not exceed 10°. Continuing the reaction for 20 hr at 105–110° and then lowering the temperature to 0° was followed by the addition of 10 ml of 20% potassium hydroxide. (*Caution!* The first few drops of base should be added slowly because a considerable exotherm develops.) Then refluxing the reaction mixture for 1 hr, extracting with pentane for 24 hr, adding the combined extracts to a saturated ethereal oxalic acid solution, cooling, and recrystallizing from ethanol gave 2.72 g (70.5%) of **cyclohexylamine oxalate,** mp 229–230°.

Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.84; H, 7.83; N, 7.37.

B. Using N-Cyclohexylhydroxylamine.[1]—The same procedure as in A was followed. From 0.9445 g (8.20 mmol) of N-cyclohexylhydroxylamine, 50 ml of diglyme, and 75.0 mequiv of hydride ion there was obtained 1.33 g (84.4%) of **cyclohexylamine oxalate,** mp 229–230°.

N-Diphenylmethylhydroxylamine.—The same procedure was followed as in A except that the reaction time was 10 hr and hydrolysis of the reaction mixture was carried out by the addition of 5 ml of water followed by 15 ml of 10% hydrochloric acid.

From 4.0 g (20.3 mmol) of benzophenone oxime, 25 ml of diglyme, and 91.0 mequiv of hydride ion there was obtained 7.5 g (73.1%) of **N-diphenylmethylhydroxylamine oxalate.** The oxalate salt (2.0 g, 4.09 mmol) was neutralized at 25° by adding it to a mixture consisting of 20 g of sodium carbonate, 200 ml of water and 150 ml of ether, and by stirring for 4 hr.

Extracting the aqueous layer with two 200-ml portions of ether, drying the combined extracts (Na_2SO_4), and removing solvent *in vacuo* gave, after sublimation at 50° (0.05 mm), 0.72 g (73.8%) of **N-diphenylmethylhydroxylamine:** mp 80–81°;[13] ir (KBr) 3280 cm^{-1} (NH and OH); nmr ($CDCl_3$) δ 5.20 [s, 1, $(C_6H_5)_2CH$], 5.58 (s, 2, NHOH), and 7.32 (s, 10, aromatic H).

N-Dicyclohexylmethylhydroxylamine.—The same procedure was followed as in the preparation of N-diphenylmethylhydroxylamine except that hydrolysis was carried out with 10 ml of 20% potassium hydroxide.

From 4.0 g (19.15 mmol) of dicyclohexyl ketone oxime, 50 ml of diglyme, and 135.0 mequiv of hydride ion there was obtained after sublimation at 85° (0.05 mm) of 2.95 g (73.0%) of product: mp 93–94°; ir (KBr) 3290 and 3230 cm^{-1} (NHOH); nmr ($CDCl_3$) δ 1.50 [m, 22, $(C_6H_{11})_2CH$], 2.40 (s, 1, CHNHOH), and 5.28 (s, 2, NHOH).

Anal. Calcd for $C_{13}H_{25}NO$: C, 73.88; H, 11.92; N, 6.63. Found: C, 73.66; H, 12.06; N, 6.36.

N-1,3-Diphenyl-2-propylhydroxylamine.—The same procedure was followed as in the preparation of N-diphenylmethylhydroxylamine except that the reaction mixture was refluxed for 20 hr at 85–90° using dioxane as solvent. Also after acidic hydrolysis the reaction mixture was basified to pH 10 at 5° with 20% potassium hydroxide and then extracted with pentane and the extracts added to a saturated ethereal oxalic acid solution.

From 7.0 g (31.0 mmol) of 1,3-diphenyl-2-propanone oxime, 50 ml of dioxane, and 130.0 mequiv of hydride ion there was obtained after sublimation at 70° (0.01 mm) 5.50 g (78.1%) of product: mp 95.5–97°; ir (KBr) 3160 cm^{-1} (NHOH); nmr ($CDCl_3$) δ 2.80 [m, 4, $(C_6H_5CH_2)_2CH$], 3.20 [m, 1, $(C_6H_5CH_2)_2CH$], 6.03 (s, 2, NHOH), and 7.20 (s, 10, aromatic H).

Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.41; H, 7.35; N, 6.17.

Similarly, this compound was obtained in 62% yield when diglyme was substituted for dioxane as the solvent.

Preparation of O-Methyl Oximes. Method A.—The following experiment is typical of the procedure employed. A solution of 5.0 g (0.0313 mol) of N-methylindole-3-carboxaldehyde and 2.7 g (0.0324 mol) of methoxyamine hydrochloride in 100 ml of pyridine and 100 ml of absolute ethanol was refluxed for 24 hr.

Removing solvents *in vacuo*, adding 100 ml of water to the residue, cooling, and recrystallizing from ethanol–water (1:1) gave 5.3 g (89.8%) of **O-methyl N-methylindole-3-carboxaldehyde oxime:** mp 78–80°; ir (KBr) 1618 (C=N) and 1053 cm^{-1} ($NOCH_3$); nmr ($CDCl_3$) δ 3.69 (s, 3, NCH_3), 4.02 (s, 3, $NOCH_3$), 7.30 (m, 4, aromatic H), 8.29 (m, 1, C=CH), and 8.50 (s, 1, HC=N).

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.43; N, 14.88. Found: C, 70.24; H, 6.36; N, 14.79.

O,O′-Dimethyl 1,3-Diphenyl-1,3-propanedione Dioxime.—From 10.0 g (0.0446 mol) of 1,3-diphenyl-1,3-propanedione and 8.35 g (0.10 mol) of methoxyamine hydrochloride there was obtained after recrystallization from ethanol–water (4:1) at −78° 10.5 g (83.4%) of product: mp 58–59°; ir (KBr) 1595 (C=N) and 1048 cm^{-1} ($NOCH_3$); nmr ($CDCl_3$) δ 3.94 [s, 6, $(NOCH_3)_2$], 4.23 (s, 2, $-CH_2-$), and 7.30 (m, 10, aromatic H).

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.45; H, 6.46; N, 10.10.

O-Benzyl Heptanal Oxime.—The same procedure was followed as in method A except that only absolute ethanol was used as solvent.

From 10.0 g (0.0878 mol) of heptanal and 10.8 g (0.0879 mol) of benzyloxyamine[14] there was obtained 17.5 g (91.3%) of

(8) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(9) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy," Academic Press, New York, N. Y., 1963, p 283.

(10) H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **81**, 6428 (1959).

(11) A. T. Ross, H. Gilman, and N. Beaber, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1932, p 146.

(12) H. Feuer and C. Savides, *J. Amer. Chem. Soc.*, **81**, 5826 (1959).

(13) W. Platner and R. Behrend, *Justus Liebigs Ann. Chem.*, **278**, 359 (1893).

(14) B. F. Ludwig, F. Dursch, M. Auerbach, K. Tomeczek, and F. M. Berger, *J. Med. Chem.*, **10**, 556 (1967).

product: bp 100–104° (0.4 mm); n^{20}D 1.5068; ir (neat) 1653 (C=N) and 1026 cm^{-1} ($NOCH_2$); nmr ($CDCl_3$) δ 0.85 (t, 3, CH_2CH_3), 1.21 [m, 8, $(CH_2)_4$], 2.25 (m, 2, CH_2CH_2CH=N), 5.20 (d, 2, $C_6H_5CH_2O$), 6.67 and 7.35 (m, 5, aromatic H).

Anal. Calcd for $C_{14}H_{21}NO$: C, 76.66; H, 9.65; N, 6.39. Found: C, 76.65; H, 9.35; N, 6.31.

O-Methyl 4,4'-Dimethoxybenzophenone Oxime. Method B.—The following experiment is typical of the procedure employed. Into a dry 1-l. three-necked flask equipped with a Hershberg stirrer, condenser provided with a drying tube, and pressure-equalizing addition funnel were placed 20 g (0.0778 mol) of 4,4'-dimethoxybenzophenone oxime and 200 ml of THF. To the stirred solution was added 3.03 g (0.0775 g-atom) of potassium. The reaction mixture was refluxed (*Caution!* Heating must be carried out slowly because of a possible exotherm), and after 3 hr 14.9 g (0.080 mol) of methyl *p*-toluenesulfonate in 100 ml of THF was added dropwise.

Refluxing the reaction mixture an additional 3 hr, filtering, and removing THF *in vacuo* gave after two recrystallizations from ethanol–water (1:1) 12.9 g (61.2%) of product: mp 82–83°; ir (melt) 1612 (C=N) and 1058 cm^{-1} ($NOCH_3$); nmr ($CDCl_3$) δ 3.78 [s, 6, $(OCH_3)_2$], 3.93 (s, 3, $NOCH_3$), and 6.85 and 7.35 (m, 8, aromatic H).

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 71.00; H, 6.43; N, 5.39.

O-Methyl Dicyclohexyl Ketone Oxime.—From 15.0 g (0.0719 mol) of dicyclohexyl ketone oxime, 2.8 g (0.0719 g-atom) of potassium, and 13.4 g (0.0720 mol) of methyl *p*-toluenesulfonate there was obtained 10.7 g (66.8%) of product: bp 76° (0.2 mm); n^{20}D 1.4939; ir (neat) 1620 (C=N) and 1061 cm^{-1} ($NOCH_3$); nmr ($CDCl_3$) δ 1.60 [m, 22, $(C_6H_{11})_2$] and 3.72 (s, 3, $NOCH_3$).

Anal. Calcd for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27. Found: C, 75.34; H, 11.03; N, 6.01.

O-Methyl *p*-Dimethylaminobenzaldehyde Oxime.—From 25.0 g (0.152 mol) of *p*-dimethylaminobenzaldehyde oxime, 6.0 g (0.153 g-atom) of potassium, and 28.4 g (0.153 mol) of methyl *p*-toluenesulfonate there was obtained 17.0 g (62.8%) of product: mp 64–65°; ir (KBr) 1621 (C=N) and 1055 cm^{-1} ($NOCH_3$); nmr (DMSO-d_6) δ 2.90 [s, 6, $(CH_3)_2N$], 3.70 (s, 3, $NOCH_3$), 6.65 and 7.38 (q, 4, aromatic H), and 7.95 (s, 1, HC=N).

Anal. Calcd for $C_{10}H_{14}N_2O$: C, 67.38; H, 7.92; N, 15.72. Found: C, 67.22; H, 7.76; N, 15.44.

Reaction of Diborane with Oxime Ethers.—The following experiment is typical of the procedure employed. To 3.7125 g (27.5 mmol) of O-methyl benzaldehyde oxime dissolved in 20 ml of THF at 0° was introduced by means of a hypodermic syringe 84.4 mequiv of hydride ion at such a rate that the temperature did not exceed 10°. After refluxing the reaction mixture for 2 hr and cooling to 0°, 10 ml of water was added cautiously followed by 10 ml of 20% potassium hydroxide. Refluxing the reaction mixture for 1 hr, extracting with pentane for 24 hr, removing the solvent *in vacuo*, and distilling the remaining liquid gave 2.70 g (92.5%) of **benzylamine**: bp 73° (14 mm); n^{20}D 1.5410;[15] ir (neat) 3390 and 3300 cm^{-1} (NH_2); nmr ($CDCl_3$) δ 1.34 (s, 2, NH_2), 3.73 (s, 2, $C_6H_5CH_2$), and 7.23 (s, 5, aromatic H).

Similarly, treating 3.7125 g (27.5 mmol) of O-methyl benzaldehyde oxime with 84.4 mequiv of hydride ion for 2 hr at reflux, hydrolyzing the reaction mixture at 0° with 5 ml of water and then refluxing for 30 min gave 8.92 mmol of hydrogen. Then removing THF *in vacuo*, adding 20 ml of 20% potassium hydroxide at 0° to the residue, and refluxing for 1 hr gave an additional 16.65 mmol of hydrogen. The total amount of hydrogen evolved was 25.57 mmol of hydrogen, indicating that 2.06 equiv of hydride ion per mole of oximino ether was consumed in the reduction.

Bis(*p*-methoxyphenyl)methylamine.—From 5.43 g (20 mmol) of O-methyl 4,4'-dimethoxybenzophenone oxime and 118 mequiv of hydride ion there was obtained crude product which was converted into the picrate derivative[16] (6.70 g, 70.9%), mp 188° dec.

Anal. Calcd for $C_{21}H_{20}N_4O_9$: C, 53.39; H, 4.27; N, 11.86. Found: C, 53.25; H, 4.58; N, 11.81.

Dicyclohexylmethylamine.—From 12.0 g (53.8 mmol) of O-methyl dicyclohexyl ketone oxime and 254.2 mequiv of hydride ion there was obtained 8.1 g (77.2%) of product: bp 87–89° (0.6 mm); n^{20}D 1.4951. The **phenylthiourea** of dicyclohexylmethylamine was prepared,[16] mp 157–158°.

Anal. Calcd for $C_{20}H_{30}N_2S$: C, 72.69; H, 9.46; N, 8.51; S, 9.40. Found: C, 72.44; H, 9.30; N, 8.40; S, 9.47.

3-Methylamino-1-methylindole.—From 2.17 g (11.5 mmol) of O-methyl N-methylindole-3-carboxaldehyde oxime and 91.0 mequiv of hydride ion there was obtained crude product. It was converted into the **phenylurea derivative,** mp 186–187°, by treatment with phenyl isocyanate.[16]

Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.09; H, 6.13; N, 15.04. Found: C, 72.93; H, 6.24; N, 14.91.

1,3-Diphenyl-1,3-propanediamine.—From 4.23 g (15.0 mmol) of O,O'-dimethyl 1,3-diphenyl-1,3-propanedione dioxime and 97.5 mequiv of hydride ion there was obtained 3.05 g (89.7%) of product: bp 145–146° (0.48 mm); n^{20}D 1.5868.[17] The dipicrate derivative was prepared,[16] mp 241–245° dec.

Anal. Calcd for $C_{27}H_{24}N_8O_{14}$: C, 47.37; H, 3.53; N, 16.37. Found: C, 47.52; H, 3.72; N, 16.32.

Preparation of O-Benzyl Heptanal Oxime–Diborane Adduct (Isolation of Intermediates).—To a mixture of 2.20 g (10 mmol) of analytically pure O-benzyl heptanal oxime and 100 ml of Phillip's pure grade pentane (99 mol % minimum) was introduced at 0° approximately 1428 mmol of gaseous diborane over a 2-hr period. The reaction mixture was held at ambient temperatures for 4 hr. Removing pentane and excess diborane *in vacuo* and heating the residue at 55° (0.5 mm) for 3 days afforded 2.30 g of a viscous opaque liquid: ir (neat) 3200 (NH), 2480 (BH), 1605 (BN), and 1170 cm^{-1} (OCH_2); nmr ($CDCl_3$) δ 0.88 (t, 3, CH_2CH_3), 1.30 [m, 10, $(CH_2)_5$], 2.95 (m, 2, CH_2CH_2N), 3.88 (s, 1, NH), 4.78 (s, 2, $C_6H_5CH_2$), and 7.44 (m, 5, aromatic H); mass spectrum (70 eV) *m/e* (relative intensity) 233 (0.875), 232 (0.435), 149 (10.01), 127 (1.32), 126 (3.93), 120 (36.7), 119 (1.83), 107 (23.6), 106 (50.6), 91 (100.0), 90 (43.6), 79 (26.9), 77 (53.8), 70 (15.3), 65 (21.0), 57 (14.8), 56 (14.8), 55 (19.2), 51 (27.2), 50 (12.6), 43 (18.8), 29 (10.2), 28 (17.9), and 27 (11.1).

Anal. Calcd for $C_{14}H_{24}NOB$ (A): C, 72.12; H, 10.39; N, 6.05; B, 4.64; mol wt, 233.15. Found: C, 67.82, 67.59; H, 9.62, 9.75; N, 4.82, 4.87; B, 5.75, 5.68; mol wt, 266, 267 (in benzene).

Anal. Calcd for $C_7H_{18}NB$ (B): C, 66.15; H, 14.28; N, 11.01; B, 8.56; mol wt, 127.10.

Anal. Calcd for C_7H_9BO (C): C, 70.09; H, 7.56; B, 9.04; mol wt, 119.96.

Refluxing an aliquot (0.3379 g) of the O-benzyl heptanal oxime–diborane adduct with 20% potassium hydroxide evolved 6.15 mmol of hydrogen, and on work-up *n*-heptylamine and benzyl alcohol were obtained in yields of 42 and 38%, respectively.

Reduction of O-(*p*-Nitrobenzoyl) Cyclohexanone Oxime.—The following experiment is typical of the procedure employed to reduce oxime esters. To 2.8021 g (10.7 mmol) of O-(*p*-nitrobenzoyl) cyclohexanone oxime[18] was introduced by means of a hypodermic syringe 84.4 mequiv of hydride ion. Continuing the reaction at ambient temperatures for 20 hr, cooling the reaction mixture to 5°, adding 5 ml of water cautiously, removing excess THF *in vacuo*, refluxing the residue with 20 ml of 10% hydrochloric acid, extracting the reaction mixture with ether for 24 hr, and removing the ether *in vacuo* gave on recrystallization from ethanol–water (1:8) 1.20 g (80.6%) of ***p*-nitrobenzyl alcohol,** mp 92–93°.[19]

Basifying the aqueous layer with 20 ml of 20% potassium hydroxide, extracting with ether for 24 hr, and removing the ether *in vacuo* gave an oil which solidified on standing. The solid was cyclohexylamine carbonate: nmr (DMSO-d_6) δ 1.50 [s, 10, $(CH_2)_5$], 2.85 (m, 1, $CHNH_3$), and 6.15 (s, 3, NH_3). Dissolving the carbonate in hot water, adding a saturated ethanolic picric acid solution, and cooling gave 2.39 g (67.4%) of **cyclohexylamine picrate,** mp 156–157°.[20]

Similarly, treating 2.8021 g (10.7 mmol) of O-(*p*-nitrobenzoyl) cyclohexanone oxime with 84.4 mequiv of hydride ion, continuing the reaction for 20 hr at ambient temperatures, hydrolyzing cautiously at 0° with 5 ml of water and allowing to warm up to room temperature gave 12.84 mmol of hydrogen.

Then removing THF *in vacuo*, adding 20 ml of 10% hydro-

(15) J. W. Bruhl, *Z. Phys. Chem.*, **16**, 216 (1895).

(16) N. D. Cheronis and J. B. Entrikin, "Identification of Organic Compounds," Interscience Publishers, New York, N. Y., 1963.

(17) R. Merten, Belgian Patent 611,643 (1962); *Chem. Abstr.*, **57**, 16573*d* (1963).

(18) L. Gass and F. W. Bope, *J. Amer. Pharm. Assoc., Sci. Educ.*, **48**, 186 (1959).

(19) I. Wender, H. Greenfield, S. Metlin, and M. Orchin, *J. Amer. Chem. Soc.*, **74**, 4079 (1952).

(20) M. Mousseron, R. Jacquier, and H. Christol, *Bull. Soc. Chim. Fr.*, 346 (1957).

chloric acid at 0° to the residue and refluxing for 1 hr gave an additional 20.96 mmol of hydrogen. The total amount of hydrogen evolved was 33.80 mmol, indicating that 4.58 equiv of hydride per mole of oxime ester was consumed in the reduction.

Reduction of O-Acetyl Cyclohexanone Oxime.—From 3.15 g (20.3 mmol) of O-acetyl cyclohexanone oxime[21] and 135.5 mequiv of hydride ion there was obtained 1.2420 g (62.0%) of **cyclohexylamine** and 0.8640 g (94%) of **ethanol** as determined by glpc analysis.

Registry No.—Diborane, 19287-88-8; cyclohexylamine oxalate, 19293-66-4; N-dicyclohexylmethylhydroxylamine, 19293-67-5; N-1,3-diphenyl-2-propylhydroxylamine, 19293-68-6; O-methyl N-methylindole-3-carboxaldehyde oxime, 19293-69-7; O,O′-dimethyl 1,3-diphenyl-1,3-propanedione dioxime, 19293-70-0; O-benzyl heptanal oxime, 19293-71-1; O-methyl 4,4′-dimethoxybenzophenone oxime, 19293-72-2; O-methyl dicyclohexyl ketone oxime, 19293-73-3; O-methyl *p*-dimethylaminobenzaldehyde oxime, 19293-74-4; bis(*p*-methoxyphenyl)methylamine (picrate), 19293-75-5; dicyclohexylmethylamine, 7560-83-0; dicyclohexylmethylamine (phenylthiourea derivative), 19293-50-6; 3-methylamino-1-methylindole (phenylurea derivative), 19293-51-7; 1,3-diphenyl-1,3-propanediamine, 19293-52-8; 1,3-diphenyl-1,3-propanediamine (dipicrate derivative), 19293-53-9.

(21) Z. Czuros, K. Zech, G. Dely, and E. Zuloy, *Acta Chim. Acad. Sci. Hung.*, **1**, 66 (1951).

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Electrochemical Dealkylation of Aliphatic Amines

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The anodic oxidation of tertiary aliphatic amines in nonaqueous systems has been studied, using tri-*n*-propylamine in acetonitrile as a model. The reaction causes dealkylation to produce secondary amine and aldehyde. The reaction product contains unreactive tertiary and secondary amine salts in a 2:1 ratio. When water is rigorously excluded, elemental nitrogen is a major product. The investigation included 12 amines; effect of unsymmetrical substitution on the dealkylation was studied. Solvents used were tetrahydrofuran, dimethyl sulfoxide, water, ethanol–water, methanol, and 1,2-dimethoxyethane.

The electrochemical reactions of aliphatic amines, unlike aromatic amines, have received relatively little attention. Dapo and Mann[1] examined the oxidation of triethylamine in dimethyl sulfoxide and reported an 80% recovery of triethylammonium salt. Russell[2] proposed that, on oxidation in acetonitrile, it undergoes a one-electron reaction to produce the cation radical which was thought to abstract a hydrogen atom from either the solvent or water to form triethylammonium salt and cyanomethylene or hydroxyl radicals.

An examination of the cyclic voltammetric oxidation of a series of aliphatic amines showed that, although the reactions in every case appeared to be irreversible one-step oxidations, substituent inductive effects could be correlated with voltammetric peak potentials for secondary and tertiary amines.[3] This indicates that the primary site of attack is the nitrogen atom and that abstraction of the first electron is the potential-determining step.

In related work, O'Donnell and Mann[4] have studied the anodic oxidation of aliphatic amides and Barnes and Mann[5] have reported on anodic reactions of aliphatic primary amines. Weinberg and Brown[6] and Smith and Mann[7] have examined the anodic methoxylation of tertiary aliphatic amines.

A detailed investigation of the oxidation of amines by chlorine dioxide has been reported by Rosenblatt and coworkers.[8–10] This chemical oxidation causes dealkylation of a tertiary amine to produce secondary amine and the appropriate aldehyde. As a result of kinetics studies involving isotope substitution, it was concluded that the reaction of tertiary amines involves an electron transfer in the rate-determining step.

The same types of products have been obtained on oxidation with N-bromosuccinimide,[11] manganese dioxide,[12] and ozone.[13] In several cases, evidence of the formation of enamines has been found. Leonard and Morrow[14] produced stable cyclic enamines by mercuric acetate oxidation of amines. Buckley, *et al.*,[15] trapped enamines formed from simple amines by reaction with quinones to form stable colored compounds. However, enamines produced from amines with simple straight-chain substituents are insufficiently stable to be isolated. They decompose to the secondary amine and the aldehyde.

The present work has involved examination of the reactions of several tertiary and secondary amines in acetonitrile, dimethyl sulfoxide, tetrahydrofuran, and water. The results indicate that the main reaction, in the presence of at least small amounts of water, involves

(1) R. F. Dapo and C. K. Mann, *Anal. Chem.*, **35**, 677 (1963).
(2) C. P. Russell, *ibid.*, **35**, 1291 (1963).
(3) C. K. Mann, *ibid.*, **36**, 2424 (1964).
(4) J. F. O'Donnell and C. K. Mann, *J. Electroanal. Chem.*, **13**, 157 (1967).
(5) K. K. Barnes and C. K. Mann, *J. Org. Chem.*, **32**, 1474 (1967).
(6) N. L. Weinberg and E. A. Brown, *ibid.*, **31**, 4058 (1966).
(7) P. J. Smith and C. K. Mann, *ibid.*, **33**, 316 (1968).
(8) D. H. Rosenblatt, A. J. Hayes, Jr., B. L. Harrison, R. A. Streaty, and K. A. Moore, *ibid.*, **28**, 2790 (1963).
(9) D. H. Rosenblatt, L. A. Hull, D. C. Deluca, G. T. Davis, R. C. Weglein, and H. K. R. Williams, *J. Amer. Chem. Soc.*, **89**, 1158 (1967).
(10) L. A. Hull, G. T. Davis, D. H. Rosenblatt, H. K. R. Williams, and R. C. Weglein, *ibid.*, **89**, 1163 (1967).
(11) S. Dunstan and H. B. Henbest, *J. Chem. Soc.*, 4905 (1957).
(12) H. B. Henbest and M. J. W. Stratford, *ibid.*, 995 (1966).
(13) H. B. Henbest and M. J. W. Stratford, *ibid.*, 711 (1964).
(14) N. J. Leonard and D. F. Morrow, *J. Amer. Chem. Soc.*, **80**, 371 (1958).
(15) D. Buckley, S. Dunstan, and H. B. Henbest, *J. Chem. Soc.*, 4880 (1957).