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Oxidation of Hydroxylamine Derivatives. VI.[1] Anodic Oxidation of *N*-Alkyl-*β*-hydroxyhydroxylamines in Aqueous Buffer Solution

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Anodic oxidation of *N*-alkylhydroxylamines with and without a *β*-hydroxy group was studied by cyclic voltammetry and controlled potential electrolysis in aqueous buffer solution of pH 8.8. The hydroxylamines with a *β*-hydroxy group were oxidized initially to the corresponding nitroxides and gave the final products *via* two routes; i) cleavage of the (*α*)C–(*β*)C bond to give aldehydes and oximes, and ii) disproportionation of the nitroxides to form the nitroso compounds. The hydroxylamines without a *β*-hydroxy group did not undergo cleavage of the (*α*)C–(*β*)C bond and gave nitroso compounds. Substituents on the *α* and *β* carbons affected the product distribution. When a phenyl group or two methyl groups were present on the (*β*)C, or one methyl group was present on both (*α*)C and (*β*)C, (*α*)C–(*β*)C bond cleavage was predominant.

Keywords——*N*-alkyl-*β*-hydroxyhydroxylamine; anodic oxidation; C–C bond fission; C-nitroso compound; aldehyde; oxime; azoxy compound

2-Hydroxyamino-1-phenyl-1-propanols have been reported to be the precursors of *β*-alkanolamine metabolites such as ephedrine and norephedrine, and of arylalkylamines such as amphetamine and phentermine.[2] The oxidation of aliphatic hydroxylamines has been studied fairly well,[3] but little attention has been paid to the oxidation of *N*-alkylhydroxylamines with a hydroxy group on the *β*-carbon. The copper-catalyzed autoxidation of 2-hydroxyamino-1-phenyl-1-propanols to produce benzaldehyde and oximes[2c] is the only study reported so far, but the mechanism and factors affecting the autoxidation were not investigated in detail.

In the present paper we present the results of studies on the anodic oxidation of *N*-alkylhydroxylamines with and without a *β*-hydroxy group (Table I) in buffer solution of pH 8.8, carried out in order to determine whether the hydroxylamines could be an important

TABLE I. $R^1R^2CHCR^3R^4NHOH$

Compd.	R^1	R^2	R^3	R^4
1	C_6H_5	OH	CH_3	CH_3
2	C_6H_5	OH	CH_3	H
3	C_6H_5	OH	H	H
4	CH_3	OH	CH_3	CH_3
5	CH_3	OH	CH_3	H
6	CH_3	OH	H	H
7	H	OH	CH_3	CH_3
8	H	OH	CH_3	H
9	H	OH	H	H
10	C_6H_5	H	CH_3	CH_3
11	H	H	CH_3	CH_3
12	H	H	CH_3	H
13	CH_3	H	H	H

intermediate in the oxidation of the corresponding amines. The oxidation of the hydroxylamines **10**—**13** was studied in order to compare the present results with those from the anodic oxidation in acetonitrile previously studied.[4]

Results and Discussion

Cyclic Voltammetry

The hydroxylamines synthesized were not stable in the buffer solution over pH 9, and did not show a well-defined wave in acidic solution below pH 7. The cyclic voltammetry was thus performed in general in buffer solution of pH 8.8 with a substrate concentration of *ca.* 3 mM at a glassy-carbon electrode. The potentials of the first oxidation wave are shown in Table II. The first waves observed for **4**—**9** and **11**—**13** were ill-defined and were observed only as a shoulder. This can be ascribed to the oxidation of oxalate anion which progressively occurs at a potential of around 1.2 V. When a phenyl group is present on the β-carbon (**1**—**3** and **10**), the potential of the first wave is lower, regardless of the presence or absence of a β-hydroxy group. The value of E_p, however, was not affected significantly by the replacement of α-hydrogen with a methyl group. Steric factor around the α-carbon of hydroxylamines and amines, for example, the presence of a bulky group, or a strongly electron-withdrawing group at the α-carbon in general, make the potential of the first oxidation wave more positive,[4,5] but the effect on the oxidation potential of replacement of α-hydrogen even with two methyl groups was small in the present case (**4**—**9**, **11**—**13**). The *threo*- and *erythro* isomers of compound **2** show the same E_p for the first oxidation. In the case of β-alkanolamines the *threo*- and *erythro* isomers showed essentially the same oxidation potential.[5] Lund *et al.* have also reported that the half-wave potentials of the aliphatic nitro groups of *erythro*- and *threo*-*o*-nitro-α-(1-nitroalkyl)benzylalcohol are not significantly different.[6]

In the oxidation of these *N*-alkyl-β-hydroxyhydroxylamines, the first electron transfer is considered to take place from the hydroxylamino group, probably from the lone pair of the nitrogen, because the pK_a values of these hydroxylamines are about six, no oxidation wave is seen in acidic solution, and the alcohol group is not ionized at all in buffer solution of pH 8.8.

As will be mentioned in the section on controlled potential electrolysis, a phenyl group at the β-carbon makes the cleavage of the (α)C–(β)C bond easier than hydrogen or a methyl group does, and this implies that the rate of the cleavage may be an important factor determining the oxidation potential.

The β-hydroxy group of the hydroxylamines seems to have essentially no effect on the E_p

Table II. Cyclic Voltammetric Data in Buffer Solution of pH 8.8 (pH 10) at 25 °C

Compd.[a]	E_p[b]	Compd.[a]	E_p
1	0.88 (0.30)[c]	**7**	1.10—1.15 (0.33)[c]
2[d]	0.90	**8**	1.10—1.15
threo-**2**[e]	0.90	**9**	1.10—1.20
erythro-**2**	0.90	**10**	0.67 (0.43)[c]
3	0.90	**11**	1.10—1.15 (0.43)[c]
4	1.10—1.15	**12**	1.00—1.10
5	1.05—1.10	**13**	0.98—1.03
6	1.05—1.10		

a) Oxalates of **1**—**13** were used.
b) Peak potential in volts *vs.* SCE.
c) Measured in pH 10.
d) Mixture of *threo*- and *erythro*-isomers.
e) Contains *ca.* 20% *erythro*-isomer.

value at pH 8.8, and this seems contrary to the case of oxidation of β-alkanolamines. The oxidation potentials of the hydroxylamines **1**, **7**, **10** and **11** at pH 10.0, however, show that the β-hydroxy group (**1** and **7**) also makes the E_p value lower than it is for the compounds without the β-hydroxy group (**10** and **11**) (Table II). In this case, the effect of the β-hydroxy group on the E_p value is apparent. The very low values for both groups of compounds may be ascribed to the contribution from the oxidation of the dissociated form of the hydroxylamino group.

Controlled Potential Electrolysis

Controlled potential electrolysis of the hydroxylamines was carried out with a substrate concentration of *ca.* 10 mM in the buffer solution of pH 8.8 using a glassy-carbon plate as an anode under an atmosphere of nitrogen. The results are summarized in Table III. The electrolysis was interrupted when 1 Faraday per mole of the substrate (**3**—**9**) had been passed or after continuing the electrolysis for two hours (**1** and **2**) in order to avoid the influence of autoxidation and secondary reactions of the hydroxylamines and of oxidation products. In the case of *N*-alkyl-β-hydroxyhydroxylamines with a substitutent on the α or β carbon, especially with a phenyl group, products were formed mainly through fission of the (α)C–(β)C

TABLE III. Products from Controlled Potential Electrolysis in Buffer Solution of pH 8.8

Compd.	$E_{app.}$ [a]	F [b]	Products	Yield (%) [c]
1	0.90	1.62	$Me_2C=NOH$	92
			C_6H_5CHO	100
threo-**2** [d]	0.80	1.00	$MeCH=NOH$	91
			C_6H_5CHO	63
erythro-**2**	0.80	1.00	$MeCH=NOH$	88
			C_6H_5CHO	62
3	0.75	1.00	$CH_2=NOH$	92
			C_6H_5CHO	22 [e]
4	0.90	1.00	$Me_2C=NOH$	100
			MeCHO	100
5 [f]	0.85	1.00	$MeCH=NOH$	100
			MeCHO	86
6	0.70	1.00	$CH_2=NOH$	55
			MeCHO	71
			$MeCH(OH)CH_2NO$ (**21**)	35
7	0.88	1.00	$Me_2C=NOH$	100
			HCHO	100
8	0.80	1.00	$MeCH=NOH$	75
			HCHO	67
			$CH_2(OH)CHMeNO$ (**22**)	26
9	0.70	1.00	$CH_2N=OH$	23
			HCHO	28
			$CH_2(OH)CH_2NO$ (**23**)	50
10	0.55	0.59 [g]	$C_6H_5CH_2CMe_2NO$	[h]
11	0.80	1.00	Me_3CNO	[h]
12	0.60	1.00	Me_2CHNO	71
13	0.60	1.00	$Me(CH_2)_2NO$	73

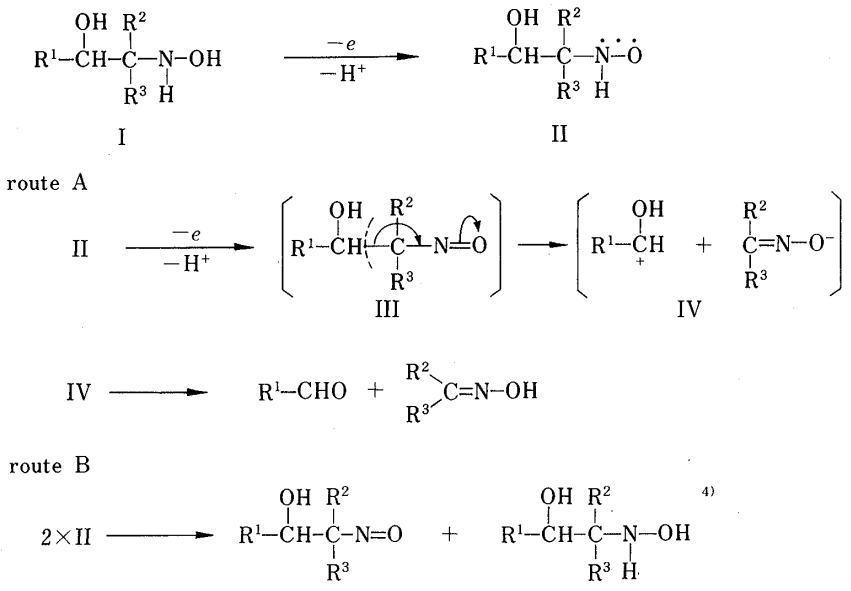
a) Applied potential *vs.* SCE.
b) Faradays (F) passed per mole of the substrate.
c) Current yield %; calculated for $2F\,mol^{-1}$.
d) *threo*-Isomer containing *ca.* 20% *erythro*-isomer.
e) Free benzaldehyde (see the text).
f) Mixture of *threo*- and *erythro*-isomers.
g) Electrolysis did not proceed further.
h) Detected but not determined.

bond, while the hydroxylamines without a β-hydoxy group gave only the corresponding nitroso compounds without (α)C–(β)C bond fission. Thus the α and β substituents affected the rate of the (α)C–(β)C bond fission, and the effect is in the same order, $H < CH_3 < C_6H_5$, as observed in the oxidation of β-alkanolamines.[5] The yields of acetoxime and acetaldoxime from **1** and **2**, respectively, and of benzaldehyde from **1** were nearly quantitative, but the amounts of benzaldehyde from **2** and **3** were less than those of the oximes (estimated by gas liquid chromatography (GLC), though the amount was over 60% from **2**. In the case of **3**, the amount of benzaldehyde was 22%, and a precipitate was formed during the electrolysis. The precipitate was found to be the nitrone formed by the reaction of benzaldehyde with the starting hydroxylamine. The formation of the nitrone, thus, reduced the estimated value of benzaldehyde production. Estimation of the nitrone in the electrolyzed solution was not successful, because of overlap of the absorption with those of other compounds present.

The amounts of acetaldehyde and formaldehyde (estimated by GLC) formed in the oxidation of **4**—**9** were much less than those of the corresponding oximes, and the yields were only trace to a few per cent. This was also ascribed to the formation of nitrones, and the amounts of the aldehydes were estimated from the amounts of the nitrones by the use of the molar absorption coefficient of each nitrone. The nitrones were not isolable from the solution, and the molar absorption coefficients were obtained in the presence of a large excess of the aldehydes over the hydroxylamines in the buffer of pH 8.8.[7]

In the electrolysis of **2**, *threo*- and *erythro* isomers showed essentially the same product distribution. The nitroso compounds obtained in the electrolysis of **6**, **8**, and **9** were assigned as *cis*-dimers based on their ultraviolet (UV) absorption.[8] In the electrolysis of **10**—**13**, the nitroso compounds were the main product and compounds formed through the cleavage of the (α)C–(β)C bond were not detected. During the electrolysis of **12** and **13**, a part of the nitroso compounds reacted with the starting hydroxylamine under the present conditions to give the corresponding azoxy compounds.[9] The amount of the azoxy compounds, however, could not be determined, since the absorption maxima of the azoxy compounds (around 220 nm) merged with the background absorption of the solution. In the anodic oxidation of *N*-alkylhydroxylamines performed in acetonitrile,[4] similar condensation of the nitroso compounds with the hydroxylamines to give the corresponding azoxy compounds was not observed.

Based on the results of the cyclic voltammetry and controlled potential electrolysis, it is suggested that the *N*-alkyl-β-hydroxylamines are oxidized *via* two routes, A and B, as follows.



As mentioned above, both α and β substituents affect the reaction route dramatically after the formation of II. The presence of a β-hydroxy group is necessary for the reaction *via* route A and the relative importance of route A increases in the order of $R^1 = H < CH_3 < C_6H_5$. This order seems to coincide with that of the stability of $R^1\text{–}\overset{+}{C}H(OH)$ in IV, as observed in the anodic oxidation of β-alkanolamines. The importance of route B (**6**, **7**, **8** and **9**) seems to decrease depending on the R of the nitroxide (II), R–N(·)–O, in the order of primary > secondary > tertiary. This may reflect the rates of disproportionation of *N*-alkylnitroxides (II) which decrease in the same order.[10] The results of the present study thus suggest that the hydroxylamino derivatives are not intermediates in the oxidation of the corresponding aliphatic amines insofar as the process proceeds *via* electron transfer.

Experimental

Hydroxylamines——All hydroxylamines used were prepared by the reduction of the corresponding nitro compounds using method A, B or C.

Method A: A nitro compound (0.15 mol) dissolved in 100 ml of 20% (v/v) aq. methanol containing *ca.* 0.4 mol of ammonium chloride was reduced using *ca.* 0.3 mol of zinc powder. The solvent was removed under reduced pressure and excess potassium carbonate was added to the residue. The hydroxylamines were extracted with ether and converted to the corresponding oxalate or hydrochloride.

Method B: A nitro compound (0.06 mol) dissolved in 55 ml of 95% (v/v) aq. ethanol containing a small excess of oxalic acid (0.031 mol) was subjected to the catalytic reduction over 0.3 g of 10% palladium–charcoal at a pressure of 4.2—4.5 kg/cm^2.[11] After completion of the reaction, the solvent was removed and ethanol was added to the residue. The corresponding hydroxylammonium oxalate precipitated.

Method C: A nitro compound dissolved in 3 N HCl containing ethanol was reduced electrochemically using a strirred mercury pool as a cathode at -1.20 V *vs.* SCE.[12] The electrolyte was concentrated under reduced pressure, then neutralized with potassium carbonate and extracted with ether.

In the case of **2**, the mixture of diastereomers was separated into *threo*- and *erythro*-isomer by taking advantage of the lower solubility of the latter in ethanol. The melting point, the results of elemental analysis and the method for preparation of the hydroxylamines, and proton nuclear magnetic resonance (^{1}H-NMR) data for *threo*- and *erythro*-**2** are summarized in Tables IV-1 and IV-2, respectively.

Nitro Compounds——Nitro compounds (starting materials for the hydroxylamines **1**—**4**, **6** and **7**) were prepared according to the method of Hass.[13] The starting materials for **10** and **11** were prepared according to the method of Edwards[14] and Stowell,[15] respectively. Commercially available nitro compounds were used for the synthesis of the hydroxylamines **5**, **8**, **9**, **12** and **13**.

Nitrones——Nitrones were prepared by adding an aldehyde (50 mM) to the buffer solution of pH 8.8 containing a hydroxylamine (5 mM).[7] Nitrones used in the present study were too unstable to be isolable,[7] except for **14**, which was prepared by the reaction of hydroxylamine **3** with benzaldehyde. The apparent UV extinction coefficients of the nitrones were obtained without isolation, on the assumption that all of the added hydroxylamine was converted into the corresponding nitrone, and these values are summarized in Table V. Melting point, spectroscopic data and results of elemental analysis of the nitrone **14**, $C_6H_5\text{–}CH(OH)\text{–}CH_2\text{–}\overset{O}{\overset{\uparrow}{N}}=CH\text{–}C_6H_5$ are as follows. mp 165—166 °C. IR ν_{max}^{Nujol} cm^{-1}: 3250 (OH), 1600 (C=N), 1150 (N→O). ^{1}H-NMR (in DMSO-d_6)[16] δ: 3.80—4.20 (2H, m, $>CH_2$), 5.00—5.40 (1H, m, $>CHOH$), 5.82 (1H, d, J=4.5 Hz, –OH), 7.10—7.60 (8H, m, ArH 5 and 3 protons), 7.76 (1H, s, –N=CH–), 8.10—8.40 (2H, m, *ortho* protons –N=CH–Ar). UV $\lambda_{max}^{dioxane}$ nm (ε) 291 (18000). *Anal.* Calcd for $C_{15}H_{15}NO_2$ (**14**): C, 74.66; H, 6.27; N, 5.81. Found: C, 74.72; H, 6.25; N, 5.98.

Nitroso Compounds——Nitroso compounds, $R^1\text{–}CH(OH)\text{–}CR^2(R^3)\text{–}N=O$ **21** (R^1=Me, $R^2=R^3$=H), **22** ($R^1=R^2$=H, R^3=Me) and **23** ($R^1=R^2=R^3$=H) were prepared according to the method of Emery.[8] The characteristic IR[17] and UV[8] absorptions of the nitroso compounds suggest that these compounds are dimeric *cis*-isomers in the buffer of pH 8.8. The dimeric *cis*-isomers isomerized slowly to the *trans*-isomers on standing in DMSO solution. **21**, mp 81—82 °C, *Anal.* Calcd for $C_3H_7NO_2$: C, 40.44; H, 7.92; N, 15.72. Found: C, 40.11; H, 7.98; N, 15.46. ^{1}H-NMR (in DMSO-d_6) δ: 1.16 (3H, d, J=6.5 Hz, $-CH_3$), 3.75—4.60 (3H, m, $>CH$ and $>CH_2$), 5.25 (1H, br, –OH). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1400 ($\overset{O}{\overset{\diagdown}{>}}N=N\overset{O}{\overset{\diagup}{<}}$). UV $\lambda_{max}^{H_2O(pH\,8.8)}$ nm (ε): 270 (10200). **22**, mp 104—105 °C, *Anal.* Calcd. for $C_3H_7NO_2$: C, 40.44; H, 7.92; N, 15.72. Found: C, 40.16; H, 7.95; N, 15.56. ^{1}H-NMR (in CD_3OD) δ: 1.37 (3H, d, J=6.6 Hz, $-CH_3$), 3.50—4.05 (3H, m, $>CH$ and $>CH_2$), 5.30—5.60 (1H, br, –OH). IR ν_{max}^{KBr} cm^{-1}: 3380 (OH), 1420 ($\overset{O}{\overset{\diagdown}{>}}N=N\overset{O}{\overset{\diagup}{<}}$). UV $\lambda_{max}^{H_2O(pH\,8.8)}$ nm (ε): 270 (9400). **23**, mp 30—31 °C, *Anal.* Calcd for $C_2H_5NO_2$: C, 32.00; H, 6.71; N,

TABLE IV-1. Properties of Hydroxylamines

Compd.	Formula	mp (°C)	Calcd (%)				Found (%)				Method[a]
			C	H	Cl	N	C	H	Cl	N	
1	$C_{22}H_{32}N_2O_8$[b]	195—196	58.40	7.13		6.19	58.17	7.17		6.23	A
1	$C_{10}H_{16}ClNO_2$[c]	170—173	55.17	7.41	16.29	6.43	55.03	7.47	15.99	6.38	A
2[d]	$C_{20}H_{28}N_2O_8$[b]	173—175	56.60	6.65		6.60	55.03	6.65		6.54	A
3	$C_{18}H_{24}N_2O_8$[b]	147—148	54.54	6.10		7.07	54.54	6.21		6.98	B
4	$C_{12}H_{28}N_2O_8$[b]	127—128	43.89	8.59		8.53	43.43	8.78		8.29	B
4	$C_5H_{14}ClNO_2$[c]	125—126	38.59	9.07	22.78	9.00	38.38	9.31	22.76	9.13	A
5[d]	$C_{10}H_{24}N_2O_8$[b]	107—109	40.00	8.05		9.33	39.75	8.24		9.46	B
6	$C_8H_{20}N_2O_8$[b]	111—112	35.29	7.40		10.29	35.38	7.52		10.06	B
7	$C_{10}H_{24}N_2O_8$[b]	158—159	40.00	8.05		9.33	39.71	8.25		9.23	B
7	$C_4H_{12}ClNO_2$[c]	105—106	33.93	8.54	25.04	9.89	33.93	8.75	24.74	9.80	A
8	$C_8H_{20}N_2O_8$[b]	101—102	35.29	7.40		10.29	35.29	7.60		10.08	B
9	$C_6H_{16}N_2O_8$[b]	120—124	29.51	6.60		11.47	29.47	6.70		11.40	B
10	$C_{22}H_{32}N_2O_6 \cdot 1/8\,H_2O$[b]	181—182	62.16	7.59		6.59	62.32	7.68		6.55	C
11	$C_4H_{11}NO$	58—60	(lit.[e] 60—62 °C)								
12	$C_8H_{20}N_2O_6$[b]	131—132	39.99	8.39		11.66	39.74	8.55		6.55	B
13	$C_8H_{20}N_2O_6$	141—142	39.99	8.39		11.66	30.71	8.51		11.61	B

a) See the text.
b) Oxalate.
c) Hydrochloride.
d) Mixture of diastereomers.
e) S. R. Sandler and W. Karo, "Organic Functional Group Preparation," Vol. III, Academic Press, Inc., London, 1972, p. 356.

TABLE IV-2. Properties of *threo*- and *erythro*-**2**

	erythro-**2**[a]	*threo*-**2**[a]
mp (°C)	179—180	188—190
^{1}H-NMR δ (ppm) (in DMSO-d_6)	1.86 (3H, d, J=7.0 Hz, –Me)	1.82 (3H, d, J=7.0 Hz, –Me)
	3.23 (1H, d of q, J=2.7, 7.0 Hz, >CHMe)	3.00—3.30 (1H, m, >CHMe)
	5.06 (1H, d, J=2.7 Hz, >CHOH)	4.56 (1H, d, J=8.0 Hz, >CHOH)
	7.30 (5H, s, ArH)	7.30 (5H, s, ArH)
	8.57 (4H, s, –NHOH, –OH, –COOH)	8.57 (4H, s, –NHOH, –OH, –COOH)

a) Oxalate.

TABLE V. Molar Absorption Coefficients of Nitrones[a]

$$R^1\text{–}CH(OH)\text{–}CR^2R^3\text{–}\overset{\overset{O}{\uparrow}}{N}\text{=}CHR^1$$

Compd.	R^1	R^2	R^3	$\lambda_{max}^{H_2\,(pH\,8.8)}$ (nm)	ε
15	CH_3	CH_3	CH_3	225	7500
16	CH_3	CH_3	H	226	10100
17	CH_3	H	H	225	8500
18	H	CH_3	CH_3	225	7400
19	H	CH_3	H	228	7200
20	H	H	H	229	7100

a) See the text.

18.66. Found: C, 31.39; H, 6.68; N, 18.44. ^{1}H-NMR (in DMSO-d_6) δ: 3.38 (2H, t, J=5.0 Hz, $-CH_2-OH$), 4.49 (2H, t, J=5.0 Hz, $-CH_2-N=O$), 5.15 (1H, t, J=5.0 Hz, –OH). IR ν_{max}^{KBr} cm^{-1}: 3380 (OH), 1405 ($\overset{O}{\diagdown}N=N\overset{O}{\diagup}$). UV $\lambda_{max}^{H_2O(pH\,8.8)}$ nm (ε): 270 (10800).

Oximes——Reagent grade acetaldoxime and acetoxime were used without further purification. Formaldoxime was prepared according to the method of Satake[18] from formaldehyde and hydroxylamine.

Aldehydes——Commercial benzaldehyde and acetaldehyde were purified by distillation prior to use.

Water——Deionized water was purified by distillation.

Apparatus and Procedures——Cyclic Voltammetry: Cyclic voltammetry was performed with a three-electrode system employing a linear scanning unit (Hokuto Denko Co., model HB-101) equipped with a potentiostat (Hokuto Denko Co., model PS-500B). The electrode system consisted of a glassy-carbon indicator, a counter electrode and a saturated calomel electrode (SCE). Measurements were carried out at 25±0.05 °C with a substrate (*ca.* 3 mM) dissolved in deoxygenated buffer solution at a sweep rate of 0.05 V·s^{-1}.

Controlled Potential Electrolysis: Controlled potential electrolyses were carried out with a Hokuto Denko HA 101 or HA 105S potentiostat; the current was recorded on a Toa Dempa EPR 2TB recorder and the quantity of electricity consumed during electrolysis was measured with a Hokuto Denko HF 102 or HF 201 coulombmeter. The anolytes (1×10^{-2} M substrate in Atkins and Pantin buffer, 20 ml or 40 ml, pH 8.8) were electrolyzed under an atmosphere of nitrogen using a glassy-carbon plate electrode (1 cm × 3 cm or 2 cm × 3 cm, respectively) with mechanical stirring and screening from light if necessary (**10** and **11**).

Products Analysis——Products analysis was performed as quickly as possible or after storage of the electrolyzed solution in a refrigerator.

Aldehydes: Benzaldehyde was determined by GLC (with cyclohexanol as an internal standard) using a stainless steel column (2 m × 3 mmϕ) packed with PEG 20M (Nishio Kogyo Co.) and maintained at 120 °C. Acetaldehyde which had reacted with the starting hydroxylamine to give the corresponding nitrone was estimated by measuring the UV absorption of the nitrone. Formaldehyde was estimated by two methods i) by measuring the UV absorption of the corresponding nitrone, ii) by measuring the absorption at 520 nm of formazane dye according to the method of Tanenbaum.[19] There was essentially no difference in the yields of formaldehyde as determined by the two methods.

Oximes: Acetoxime and acetaldoxime were estimated by GLC under the same conditions as used for the determination of benzaldehyde. Formaldoxime was estimated according to the method of Satake[18] by amperometric titration with potassium iodate using a rotating platinum electrode (2000 rpm) at the potential of +0.65 V *vs.* SCE. The three-electrode system, consisting of a rotating platinum indicator electrode, a silver wire (2 mm Φ) counter electrode and an SCE reference electrode, was used in place of the two-electrode system.[18] The titration was performed using an autoburette (Toa Electronics HS 2A), a potentiostat (Hokuto Denko HR 101B) and a rotating electrode system (Hokuto Denko HR 101A) and the titration curve was recorded on an X-Y recorder (Union Giken RA 452).

Nitroso Compounds: Estimation of nitroso dimers was performed on the solution after electrolysis by comparison of UV absorption spectra with those of authentic samples (**21**—**23**) or with those described in the literature[20] (2-methyl-1-nitrosopropane and 2-nitrosopropane). 2-Methyl-2-nitrosopropane was monomeric in the electrolyte and was detected by the appearance of a blue color at 675 nm.[21] 2-Methyl-2-nitroso-1-phenylpropane was extracted from the electrolyte with toluene and the UV absorption spectrum of the nitroso compound in methanol was found to be in accordance with that described in the literature.[21]

Azoxy Compounds: In the electrolysis of **12** and **13**, the formation of the corresponding azoxy compounds was confirmed by comparison of the UV spectra of the solution after electrolysis with those given in the literature.[22]

References and Notes

1) Part V: S. Ozaki and M. Masui, *J. Chem. Soc., Perkin Trans. 2*, **1980**, 1022.
2) *a*) J. Wright, A. K. Cho, and J. Gal., *Life Sci.*, **20**, 467 (1977); *b*) A. K. Cho and J. Wright, *ibid.*, **22**, 363 (1978); *c*) B. Lindeke, A. K. Cho, U. Jonsson, and U. Paulsen, *ibid.*, **23**, 921 (1978).
3) *a*) K. M. Ibne-Rasa and J. O. Edwards, *J. Am. Chem. Soc.*, **84**, 763 (1962); *b*) N. B. Shitova, K. I. Matveev, and M. M. Danilova, *Kinet. Katal.*, **7**, 995 (1966); *c*) W. A. Waters and I.R. Wilson, *J. Chem. Soc.* (*A*), **1966**, 534; *d*) T. D. B. Morgan, G. Stedman, and (in part) M. N. Hughes, *J. Chem. Soc.* (*B*), **1968**, 344; *e*) U. Jonsson, G. Lundkvist, S. O. Eriksson, and B. Lindeke, *J. Pharm. Pharmacol.*, **29**, 358 (1977).
4) H. Sayo, S. Ozaki, and M. Masui, *Chem. Pharm. Bull.*, **21**, 1988 (1973).
5) M. Masui, Y. Kamada, E. Sasaki, and S. Ozaki, *Chem. Pharm. Bull.*, **30**, 1234 (1982).
6) H. Lund and N. H. Nilson, *Acta Chem. Scand., Ser. B*, **30**, 5 (1976).
7) M. Masui and C. Yijima, *J. Chem. Soc.* (*B*), **1966**, 56.
8) T. Emery and J. B. Neilands, *J. Am. Chem. Soc.*, **82**, 4903 (1960).
9) P. E. Iversen, *Chem. Ber.*, **104**, 2195 (1971).
10) D. F. Bowman, J. L. Brokenshire, T. Gillan, and K. U. Ingold, *J. Am. Chem. Soc.*, **93**, 6551 (1971).

11) H. K. Kim, R. E. Bambury, and H. K. Yaktin, *J. Med. Chem.*, **14**, 301 (1971).
12) P. E. Iversen and H. Lund, *Acta Chem. Scand.*, **19**, 2303 (1965).
13) B. M. Vandervirt and H. B. Hass, *Ind. Eng. Chem.*, **32**, 34 (1940).
14) F. H. Marquardt and S. Edwards, *J. Org. Chem.*, **37**, 1861 (1972).
15) J. C. Stowell, *J. Org. Chem.*, **36**, 3055 (1971).
16) Tetramethylsilane (TMS) was used as an internal standard in all ^{1}H-NMR measurements.
17) E. Pretsch, T. Clerc, J. Seibel, and W. Simon, "Tabelen zur Strukturaufklälung organischer Verbindungen mit spektroskopischen Methoden," 2nd Ed., Springer-Verlag, Berlin, 1981. The monograph has been translated into Japanese by K. Nakanishi, M. Kajiwara, and K. Tsutsumi and published by Kodansha, Tokyo, 1982.
18) H. Satake and S. Ikeda, *Nippon Kagaku Zasshi*, **1980**, 717.
19) M. Tanenbaum and C. E. Bricker, *Anal. Chem.*, **23**, 354 (1951).
20) B. G. Gowenlock and J. Trotman, *J. Chem. Soc.*, **1956**, 1670.
21) B. Lindeke, E. Anderson, G. Lundkvist, U. Jonsson, and E. O. Erikson, *Acta Pharm. Suec.*, **12**, 182 (1975).
22) B. W. Langley, B. Lythgoe, and L. S. Rayner, *J. Chem. Soc.*, **1952**, 4191.