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Anodic Oxidation of Amines. VII.[1] Oxidation of β-Alkanolamines in Aqueous Buffer of pH 10

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The anodic oxidation of several different types of β-alkanolamines, $R^1R^2C(OH)CR^3R^4NR^5R^6$, was studied by cyclic voltammetry and controlled potential electrolysis in an aqueous carbonate buffer of pH 10 at a glassy carbon electrode. Upon oxidation, both the (α)C–(β)C and the C–N bonds are cleaved. Substituents R^1—R^4 affect the first oxidation potential and product distribution. The relative rates of the bond cleavages were estimated from the oxidation products. It was found that most of the amine cleaves through the (α)C–(β)C bond when at least one of the R groups is phenyl, nearly half cleaves through this bond when R is alkyl, and only about a tenth does so when R^1—R^4 are all hydrogen. The stability of the transient intermediates at the e–c step of the e–c–e process seems to affect the oxidation potentials and to govern the relative rates of the (α)C–(β)C bond cleavage. A scheme for the reaction processes is proposed.

Keywords——β-alkanolamines; anodic oxidation; (α)C–(β)C bond fission; C–N bond fission; carbonate buffer; aldehyde; acetone; glycolaldehyde

In our series of studies on the anodic oxidation of aliphatic amines, the oxidation of ephedrine, as an interesting β-alkanolamine, was studied in an aqueous buffer of pH 10,[1] in which the ordinary oxidative dealkylation of aliphatic amines *via* C–N bond fission was found to be surpassed by carbon(α)-carbon(β) bond fission such as that observed in the oxidation of 1,2-glycols.[2] The anodic oxidation of *N*,*N*-dimethylethanolamine gave *N*-methylethanolamine as a main product at pH 12.[3] The difference in the above results is interesting.

In studies of the chemical oxidation of β-alkanolamines with periodate[4] and lead tetraacetate,[5] the following results have been reported: i) when the amino group is primary or secondary, products are formed primarily *via* (α)C-(β)C bond fission; ii) when the amino group is tertiary, products of both (α)C-(β)C and C–N bond fissions are produced. Details of the reaction processes (the structure of the amines and the relative amounts of the products) have not been reported, however. Mann reported a homolytic cleavage of an (α)C-(β)C bond in the anodic oxidation of phenethylamines having a hydroxy substituent on the side chain in acetonitrile.[6] In order to clarify the oxidation mechanism of β-alkanolamines, we used in the present study several different types of β-alkanolamines: i) those having mono- or diethylamino or methylamino groups (in order to differentiate the reaction pathway by analysis of the products); ii) a series of compounds having phenyl or alkyl groups or hydrogen atoms on either α-C or β-C, keeping the structure around the other vicinal carbon unchanged; iii) compounds having no hydrogen atom on either α-C or β-C; iv) compounds having methoxy and acetoxy groups in place of the hydroxy group (the anodic oxidation was carried out at pH 10 in order to minimize the reactions of aldehydes and amines produced by the electrolysis).

Results

Cyclic Voltammetry

Data obtained by cyclic voltammetry in a carbonate buffer at pH 10 are shown in Table I.

As described previously, the cyclic voltammograms for these amines indicate that the oxidation processes are irreversible. As amines with primary amino groups developed an

Table I. Cyclic Voltammetric Data[a] at pH 10

	Compds.		E_{P^1}	E_{P^2}	E_{P^3}
1	CH_3–CH(OH)–CH($NHMe$)–C_6H_5	(mixture)[b]	0.89	1.51	
2	CH_3–CH(OH)–CH(NMe_2)–C_6H_5	(mixture)[b]	0.78	1.61	
3	C_6H_5–CH(OH)–CH($NHEt$)–H		0.86	1.58	
4	C_6H_5–CH(OH)–CH(NMe_2)–C_6H_5[c]	(±-*erythro*)	0.76	1.65	
		(±-*threo*)	0.78	1.66	
5	C_6H_5–CH(OH)–CH(NMe_2)–CH_3	(±-*erythro*)	0.55	1.57	
6	C_6H_5–CH(OH)–CH($NHMe$)–CH_3	(−-*erythro*)	0.85	1.54	
		(+-*threo*)	0.85	1.53	
7	C_6H_5–CH(OMe)–CH(NMe_2)–CH_3	(±-*erythro*)	0.59	1.46	
8	C_6H_5–CH(OCMe(=O))–CH(NMe_2)–CH_3	(±-*erythro*)	0.76	1.59	
9	H–CH(OH)–CH($NHEt$)–H		1.00	1.53	
10	H–CH(OH)–CH(NEt_2)–H		0.70	1.00	1.38
11	C_2H_5–CH(OH)–CH(NEt_2)–H		0.68	1.00	1.53
12	C_2H_5–CH(OH)–CH(NEt_2)–CH_3	(±-*threo*)	0.66	1.00	1.55
13	$(CH_3)_2$–C(OH)–CH($NHEt$)–H		1.03	1.50	
14	$(CH_3)_2$–C(OH)–CH(NEt_2)–H		0.72	1.00	1.50
15	H–CH(OH)–C(CH_3)$_2$–H($NHEt$)		1.00	1.47	
16	H–CH(OH)–C(CH_3)$_2$–H(NEt_2)		0.80	1.01	1.49

a) Values are V *vs.* SCE at *ca.* 5 mM with a sweep rate of 50 mV s^{-1}.
b) Mixture of ±-*erythro* and ±-*threo* isomers.
c) In 25% ethanol-water.

ill-defined wave above 1.1 V, they were not investigated any further. The presence of *threo*-, *erythro*- stereoisomers must be considered for the amines (**1**), (**2**), (**4**), (**5**), (**6**), (**7**), (**8**), and (**12**). Some of the amines were obtained only as miutures. The oxidation potentials for the stereoisomers were examined on amines (**4**) and (**6**). Although the proton nuclear magnetic resonance (NMR) signals for the vicinal protons are fairly different, especially in (**4**), the values of E_{P^1} are not appreciably different. One difference noticed in the experiment is in the wave form for *threo*-(**6**), which is not as sharp as that for *erythro*-(**6**). Similarity in the electron transfer potentials of the *threo*- and *erythro*-isomers and the *meso*, (±)-isomers has been reported in the reductions of 1,2-nitroalcohols[7] and oxalates,[8] respectively. As the amines have a chain structure and the temperature used is not very low (25°C),[9] rotamers should not be a significant

Table II. Anodic Oxidation Products at pH 10

	Compds. [Number of runs]	E_{app}[a]	n	Products	Yield[b] (%) Mean	(Limit)
1	CH_3–CH(OH)–CH($NHMe$)–C_6H_5 (mixture)[c] [8]	0.91	2.04—2.70	CH_3CHO	43	(10)
				C_6H_5CHO	52	(3)
				NH_2Me	69	(2)
				HCHO	10	(0.4)
				CH_3–CH(OH)–CH(NH_2)–C_6H_5	10	(2)
2	CH_3–CH(OH)–CH(NMe_2)–C_6H_5 (mixture)[c] [5]	0.80	2.83—3.93	CH_3CHO	88	(10)
				C_6H_5CHO	82	(12)
				$NHMe_2$	38	(6)
				HCHO	28	(6)
				CH_3–CH(OH)–CH($NHMe$)–C_6H_5	Trace	
				NH_2Me	33	(7)
				CH_3–CH(OH)–CH(NH_2)–C_6H_5	1.3	(0.6)
3	C_6H_5–CH(OH)–CH($NHEt$)–H [5]	0.76	1.52—2.36	C_6H_5CHO	75	(5)
				HCHO	67	(2)
				NH_2Et	79	(6)
				CH_3CHO	10	(2)
				C_6H_5–CH(OH)–CH(NH_2)–H	1.9	(0.7)
4	C_6H_5–CH(OH)–CH(NMe_2)–C_6H_5 (±-*erythro*) [2]	0.88[d]	2.17—2.56	C_6H_5CHO	174	(3)
				$NHMe_2$	68	(4)
				HCHO	15	(0.3)
				NH_2Me	14	(3)
	(±-*threo*) [2]	0.88[d]	1.75—2.54	C_6H_5CHO	165	(4)
				$NHMe_2$	74	(5)
				HCHO	14	(0.3)
				NH_2Me	14	(3)
5	C_6H_5–CH(OH)–CH(NMe_2)–CH_3 (±-*erythro*) [5]	0.50	1.90—1.93	C_6H_5CHO	91	(0.6)
				CH_3CHO	90	(8)
				$NHMe_2$	91	(2)
				HCHO	6.4	(2)
				C_6H_5–CH(OH)–CH($NHMe$)–CH_3	0.5	(0.1)
6	C_6H_5–CH(OH)–CH($NHMe$)–CH_3 (−-*erythro*) [1]	1.00	2.72	C_6H_5CHO	69	[65][e]
				CH_3CHO	63	[68][e]
				HCHO	10	[12][e]
				NH_2Me	61	[87][e]
	(+-*threo*) [2]	1.00	2.62—2.68	C_6H_5CHO	44	(2)
				CH_3CHO	45	(3)
				HCHO	9	(0.5)
				NH_2Me	48	(3)
7	C_6H_5–CH(OMe)–CH(NMe_2)–CH_3 (±-*erythro*) [5]	0.55	1.65—2.26	C_6H_5CHO	79	(6)
				CH_3CHO	56	(3)
				$NHMe_2$	76	(3)
				CH_3OH	60	(3)
				HCHO	6	(0.4)
				C_6H_5–CH(OMe)–CH($NHMe$)–CH_3	8	(0.7)
				NH_2Me	7	(0.3)

	Compds. [Number of runs]	E_{app}[a]	n	Products	Yield[b] (%) Mean	(Limit)
9	H–CH(OH)–CH(NHEt)–H [5]	1.10	2.19—2.79	HCHO	14	(2)
				NH_2Et	43	(1)
				CH_3CHO	44	(4)
				H–CH(OH)–CH(NH_2)–H	45	(2)
				H–CH(OH)–C(=O)–H[f]		
10	H–CH(OH)–CH(NEt_2)–H [3]	0.75	1.63—1.89	HCHO	5	(0.8)
				$NHEt_2$	20	(2)
				CH_3CHO	72	(2)
				H–CH(OH)–CH(NHEt)–H	73	(1)
				NH_2Et	1.6	(0.4)
11	C_2H_5–CH(OH)–CH(NEt_2)–H [3]	0.72	1.84—2.06	C_2H_5CHO	18	(0.9)
				HCHO	17	(2)
				$NHEt_2$	32	(4)
				CH_3CHO	60	(3)
				C_2H_5–CH(OH)–CH(NHEt)–H	59	(1)
				NH_2Et	3	(2)
12	C_2H_5–CH(OH)–CH(NEt_2)–CH_3 (±-*threo*) [2]	0.72	1.83—2.31	C_2H_5CHO	36	(0.2)
				CH_3CHO	70	(6)
				$NHEt_2$	46	(0.2)
				C_2H_5–CH(OH)–CH(NHEt)–CH_3[f]		
				NH_2Et[f]		
13	$(CH_3)_2$–C(OH)–CH($NHEt$)–H [4]	0.95	2.26—3.02	$(CH_3)_2CO$	43	(5)
				HCHO	18	(2)
				NH_2Et	35	(3)
				CH_3CHO	34	(9)
				$(CH_3)_2$–C(OH)–CH(NH_2)–H	18	(6)
15	H–CH(OH)–C(OH)–$(CH_3)_2$ [3]	0.92	2.19—2.40	HCHO	50	(1)
				$(CH_3)_2CO$	66	(3)
				NH_2Et	44	(2)
				CH_3CHO	26	(3)
				H–CH(OH)–C(OH)–$(CH_3)_2$	14	(0.2)

a) *V vs.* SCE.
b) Mol % of starting material.
c) Mixture of (±)-*erythro* and (±)-*threo* isomers.
d) Contains 50% ethanol.
e) M. Masui, Y. Kamada, and S. Ozaki, *Chem. Pharm. Bull.*, **28**, 1619 (1980).
f) Detected but not determined.

factor in the present experiment. The effect of stereochemistry on the oxidation potential of the amines has therefore not been considered any further. The oxidation potentials E_{pl} are in the same order as those of simple aliphatic amines, that is, primary>secondary>tertiary. Replacement of the hydrogen of the hydroxy group by methyl does not cause an appreciable potential change, although the electron-withdrawing acetyl group does show a significant positive shift (**5**, **7**, and **8**). Except for the above compound, when a phenyl group is present

at the β-carbon, E_{pl} becomes less positive than those of the corresponding simple aliphatic tertiary- and secondary- amines (**3**, **5**, and **6**),[3,10] whereas the steric hindrance of the phenyl group, when it is on the α-carbon, seems to work in the opposite direction for the oxidation of tertiary amines (**2**) and (**4**). The second wave of the alkanolamines corresponds reasonably well to those of their main oxidation products, secondary or primary amines.

Controlled Potential Electrolysis

Controlled potential electrolysis was performed under conditions similar to those described above, but, in general, with about 10 mM amine at the potential around the first oxidation peak. The results are listed in Table II.

Amines and aldehydes are generally labile when they are present in an alkaline solution and change their content with time, but under our experimental conditions, the slow decrease in the amount of the reaction products was found to be less than about 20% after standing for two hours (see experimental section). It may thus be supposed that the estimated values obtained soon after electrolysis are not far from the real values and are therefore adequate for the purpose of this study. The estimated values (Table II) are the means of several runs, and the limits are given in parentheses. Comparison of the estimated values of all products analyzed after the electrolytic oxidation thus indicates the relative rates of the bond cleavages. It is clear from the data that oxidation leads to the cleavage of both C–N and (α)C-(β)C bonds, and that the relative amounts of both cleavages depend mostly on the substituents on the α- and β- carbons, but not on the class of the amino group. The results for the stereoisomers of (**6**) seem to show a difference in the amounts of the products derived from the (α)C-(β)C bond cleavages, but the amounts of the products from the C–N bond cleavages are rather similar. It is thus hard to say whether or not there is a fundamental difference in oxidation path between the stereoisomers. In the case of isoephedrine (**1**), the main products obtained are acetaldehyde and benzaldehyde, derived from (α)C-(β)C bond fission. The amounts of formaldehyde and isonorephedrine produced *via* C–N bond fission are only about 10%, however, and no ketoalcohol from the cleavage of the N-(α)C bond was detected. Methylisoephedrine (**2**), having a tertiary amino group, produces much more acetaldehyde and benzaldehyde than does (**1**), and this result is the opposite of that obtained by chemical oxidations[3] Similar result are also seen in the case of ephedrine[1] and methylephedrine (**5**). The exchange of methyl and phenyl groups at either (α)C or (β)C, therefore, does not seriously affect the results, Amine (**3**), which has no phenyl group on (α)C but has one on (β)C, and amine (**4**), which has two phenyl groups, one each on (α)C and (β)C, show the same trend as amine (**2**). Oxidation of the dimethylamine produced makes the coulometric n values for amine (**2**) larger than the theoretical value of two, yielding a fair amount of methylamine. When both α- and β-carbons are methylene groups (**9** and **10**), C–N bond fission as with a simple aliphatic amine is the main reaction, and much less (α)C-(β)C bond fission occurs. In the oxidation of (**9**), glycolaldehyde[11] was successfully detected by gas liquid chromatography (GLC) as the trimethylsilylated derivative of the dithioacetal.[12] Substitution of an alkyl group (**11**) for hydrogen on the (β)C of amine (**10**) makes the rate of (α)C-(β)C bond fission greater. Further substitution of alkyl (**12**) for hydrogen on the (α)C of (**11**) again increases the relative amount of (α)C-(β)C bond cleavage, but this still does not become the main reaction. Substitution of two methyl groups (**13**) for β-hydrogens of (**9**) also increases the rate of (α)C-(β)C bond fission, and because the total amount of acetone and acetaldehyde is about 80%, the amount of (α)C-N bond fission producing ketoalcohol should be quite small. A similar result was obtained for amine (**15**), which has no hydrogen atom on the α-carbon. Because hydrolysis of the acetoxy derivative (**8**) ocurred in the buffer solution, the controlled potential electrolysis was not examined. Methoxymethylephedrine (**7**) gave a result similar to that of methylephedrine (**5**), but underwent slightly more demethylation. The methoxy group is liberated as methanol. When no current was passed, no methanol was liberated from (**7**) in the system.

The above results indicate that when the substituent on (α)C-(β)C is varied, the rate of

the oxidative (α)C-(β)C bond fission increases in the order H<$-C_2H_5$, $-CH_3$<$-(CH_3)_2$<C_6H_5, and when at least one phenyl group is present on either carbon, the (α)C-(β)C bond fission is the main reaction.

Discussion

As reported in the previous paper,[10] the oxidation is an irreversible two-electron process occurring at the nitrogen atom. The oxidation potential discussed in this paper is only E_{pl}.

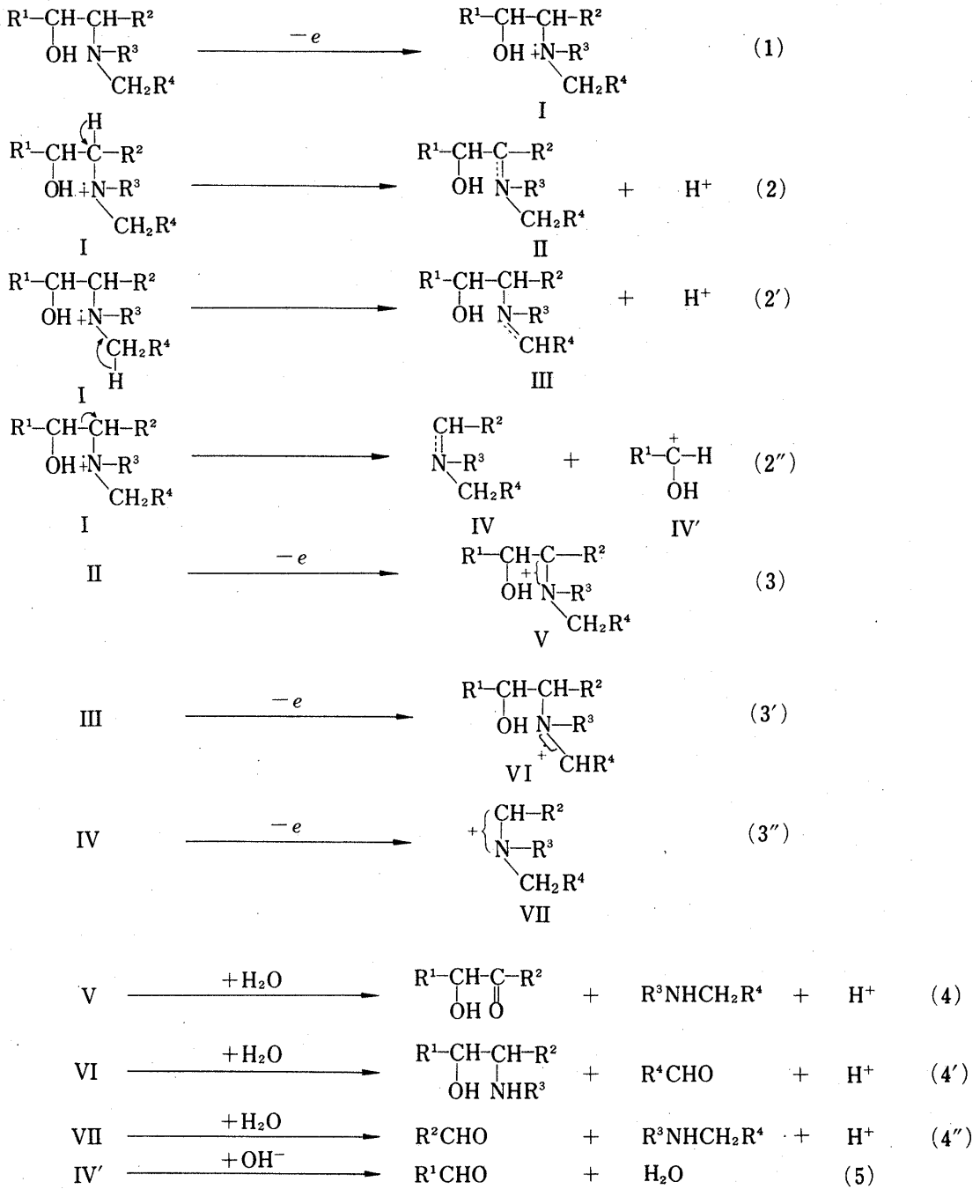

Chart 1

The present results show the effects of a hydroxyl group at the β carbon and of substituents at either the α or the β carbon on the oxidation potentials (Table I) and oxidation products (Table II). To explain the results, we propose the following reaction scheme.

At pH 10, alcoholic hydroxy is not dissociable and thus should have an electron-attracting effect, but the oxidation potentials of the amines, especially of phenethylaminoalcohols (**1**, **3**, **5**, and **6** in Table I), clearly have lower values than those of the corresponding simple aliphatic amines, except for the tertiary amines, in which the steric effect of bulky groups around the α-carbon may inhibit the approach of the nitrogen to the electrode surface (**2** and **4**). When pairs of compounds, (**3**) and (**9**), and (**5**) and (**12**), are compared the order seems to be in accord with the order of stability of the oxycarbocation, R^1–$\dot{C}$H–OH, produced in (1) and (2″). The effect of the substituents at the β-carbon on the acidity of the hydroxyl hydrogen could also have a role in the oxidation, but this effect, if it exists, must be small, as may be seen from the order of oxidation potentials in Table I. The attraction of a proton from the hydroxy group, *via* hydrogen bonding with the base present in the buffer solution, may produce a negative charge on the oxygen, which donates the charge to the amino function through bond or space interaction to make the oxidation potential lower.[1] If the hydroxy group on the benzylposition (**3**—**6**) is sufficiently acidic[13] for hydrogen bonding, the above results could be explained, but the effect is not obvious from the present results. The reason for the lowered potential should thus be explained in terms of the ease of the follow-up chemical reaction (2″). It can be seen from the table that an amine which shows a higher relative amount of (α)C-(β)C bond cleavage tends to have a lower oxidation potential. The small increase in the oxidation potential of (**7**) from that of amine (**5**) may reflect the effect of hydrogen bonding, but the difference seems to be too small to indicate that hydrogen bonding is definitely responsible. As indicated by the production of benzaldehyde and methanol from methoxymethylephedrine (**7**), it is suggested that the attack of a hydroxyl ion or water molecule on the β-carbon assists the process (2″), and if this attack occurs before or at the (α)C-(β)C bond cleavage, the oxidation potential will be higher when the attack is disturbed by a steric effect. This is probably the reason for the relatively high oxidation potentials of amines (**13**) and (**14**). The stabilization effect of the neighboring hetero atom on the aminium radical suggested by Lindsay Smith[14] is not sufficient to explain the present results; other factors, such as those above, appear to affect the oxidation potential-determining step in a complex manner.

The amines used in the present study were selected so as to have groups which make it possible to distinguish the oxidative dealkylation route by means of products analysis. The phenyl group does not necessarily have to be present at the β-carbon for oxidative cleavage of the (α)C-(β)C bond to occur (**1** and **2**). When the applied potential is higher than the oxidation potential for the simple aliphatic amines, the coulometric n value becomes larger and further oxidation of the produced amine occurs. There are some cases where an incorrect conclusion could be reached by looking only at each individual value, but by comparing every value carefully, the relative rates of the reaction routes can be deduced without much difficulty. The aminium radical produced by the first electron transfer from the nitrogen takes one of the three chemical reaction steps (2)—(2″). The more acidic the hydrogen on the α-carbon to the nitrogen or the more stable the oxycarbocation of the β-carbon, the more the reaction will proceed through their liberation from the α-carbon to the nitrogen, leaving the bonding electrons behind. The marked effect of the phenyl group at the α-carbon on the product distribution is rather difficult to understand as above, but this is probably because the stability of the benzylamino radical[3] also contributes to the liberation of the oxycarbocation part of the molecule. The amine with two methyl groups on the same carbon (**13**) shows (α)C-(β)C bond cleavages similar to those seen with a phenyl substituent, although the extent is not as large. Mann[6] suggested homolytic cleavage of a carbon-carbon bond for the anodic oxidation of α-[(dimethylamino)-methyl]-benzylalcohol in acetonitrile, but this scheme is not consistent with our results.

From the results in Table II, excluding (**1**), (**2**), and (**15**), it is obvious that the rate of route (2″) is highly dependent on the substituent on the (β)C and that the order is phenyl>alkyl>hydrogen, which seems to be the order of stability of the oxycarbocation, $R^1R^2\overset{+}{C}(OH)$. To explain the product distribution, it is thus important to consider the stability of transient intermediates in the process, as well as the acidity and number of α protons. The result for the oxidation of amine (**15**) ,which has no hydrogen on the α-carbon, is interesting. In the oxidation of an aliphatic amine, the C–N bond, having no α hydrogen, is not cleaved, but the result for (**15**) is different. This means that the oxidative bond cleavage of (α)C-(β)C, (2″), occurs in advance of that of (α)C–N. In the oxidation of aliphatic amines, the proton alone has been considered to be responsible for carrying the positive charge from the reaction center after the one-electron transfer in the *e-c-e* process, but in the present study it is shown that an oxycarbocation can also play this role in the reaction. A similar chemical reaction step has been observed for the oxidation of hydroxylamine derivatives, where acyl,[15] alkoxycarbonyl,[16] and alkylaminocarbonyl[17] groups act as positive charge carriers.

Experimental

Reagents——Reagent-grade (**10**)·HCl was used without further purification. The commercially available β-alkanolamines (**9**) and (**16**) were converted into the corresponding hydrochloride salts and recrystallized from isopropanol–ether and ethanol–ether, respectively. The other β-alkanolamines were prepared by the method described in the literature. The coupling constants in the H^1 NMR spectra permit assignment of *threo-* and *erythro* isomers except for some amines described later. Isonorephedrine hydrochloride mp 172°C (lit.[18] 170—171°C) and isoephedrine hydrochloride (**1**) mp 194°C (lit.[19] 191—193°C) were obtained as mixtures of (±)-*erythro* and (±)-*threo* isomers. The ratio of stereoisomers was not determined. 1-Phenyl-2-amino-1-ethanol was obtained as the oxalate, mp 249°C (lit[20] 230—231°C) (*Anal.* Calcd for $C_{18}H_{24}N_2O_6$: C, 59.3; H, 6.64; N, 7.69. Found: C, 59.3; H, 6.63; N, 7.87). Compound (**2**) was prepared by methylation of (**1**) by the reported method[21] as a mixture of stereoisomers; (**2**)·HCl, mp 220°C (lit.[22] 220°C). (**3**)·HCl, mp 125—128°C (lit.[23] 130—132°C) (*Anal.* Calcd for $C_{10}H_{16}ClNO$: C, 59.6; H, 8.00; N, 6.94. Found: C, 59.4; H, 8.15; N, 6.89). (±)-*erythro*-(**4**) was prepared by the reaction of commercially available *trans*-stilbene oxide with dimethylamine[24] and showed spectroscopic (IR,[25] NMR[26]) properties in agreement with the assigned structure; δ ($CDCl_3$), 3.13 (1H, d, J 4.2 Hz, $-C\underline{H}(NMe_2)C_6H_5$), 5.20 (1H, d, J 4.2 Hz, $-C\underline{H}(OH)C_6H_5$), (±)-erythro-(4)·HCl mp 268—272°C (*Anal.* Calcd for $C_{16}H_{20}ClNO$: C, 69.18; H, 7.26; N, 5.04; Cl, 12.76. Found: C, 69.08; H, 7.41; N, 5.14; Cl, 12.71). (±)-*threo*-(**4**) was prepared from *cis*-stilbene according to the reported method;[24] the stereochemical assignment rested upon the IR[25] and NMR[26] spectra; δ ($CDCl_3$) 3.58 (1H, d, J 10 Hz, $-C\underline{H}(NMe_2)C_6H_5$), 4.95 (1H, d, J 10 Hz, $-C\underline{H}(OH)C_6H_5$). (±)-*threo*-(**4**)·HCl mp 172—175°C (*Anal.* Calcd for $C_{16}H_{20}ClNO\cdot 1/2H_2O$: C, 67.01; H, 7.38; N, 4.88; Cl, 12.36. Found: C, 67.02; H, 7.34; N, 4.88; Cl, 12.23). Compound (**11**) and (±)-*threo*-(**12**) were prepared by the reaction of diethylamine with 1,2-buteneoxide and *cis*-2,3-penteneoxide,[27,28] respectively (aminolysis of a *cis*-epoxide gives the *threo*-aminoalcohol[27]). (**11**)·HCl, mp 76°C ($C_8H_{20}ClNO\cdot 1/5H_2O$ requires C, 51.9; H, 11.1; N, 7.56; Cl, 19.1. Found: C, 52.0; H, 11.0; N, 7.60; Cl, 19.6). (±)-*threo*-(**12**) IR ν_{max}^{neat} cm^{-1}: 3410 cm^{-1} (OH),[27] bp 30—38°C (6 mmHg) ($C_9H_{21}NO$ requires C, 67.9; H, 13.3; N, 8.80. Found: C, 67.8; H, 13.3; N, 8.58). 1-Amino-2-methyl-2-propanol,[29] (**13**)[30] and (**14**)[31] were prepared by the reaction of isobuteneoxide with ammonia, ethylamine and diethylamine, respectively; 1-amino-2-methyl-2-propanol·HCl, mp 64—67°C (lit.[29] 70—72°C), δ (DMSO-d_6) 1.19 (6H, s, $>CMe_2$), 2.7 (2H, s, $-CH_2-$), 5.0 (1H, br, –OH), 8.05 (3H, br, $-NH_2\cdot HCl$); (**13**)·HCl, mp 154—156°C (lit.[30] 153°); (**14**) as the oxalate, mp 70—72°C (*Anal.* Calcd for $C_{10}H_{21}NO_5$: C, 51.1; H, 9.00; N, 5.95. Found: C, 49.9; H, 9.07; N, 5.93), δ (DMSO-d_6) 1.24 (12H, m, $>CMe_2$ and $2\times -CH_2\underline{Me}$), 3.1 (6H, m, $-CH_2-$), 8.85 (2H, s, $>\overset{+}{N}C_2H_2O_4$).

Compound (**15**) was prepared from 2-amino-2-methyl-1-propanol and ethylbromide by the method of Kremer *et al.*;[32] (**15**)·HCl, mp 127—130°C (lit.[31] 136.5°C), δ (DMSO-d_6) 1.20 (9H, m, $>CMe_2$ and $-CH_2\underline{Me}$), 2.85 (2H, q, $-C\underline{H}_2Me$), 3.42 (2H, s, $-C\underline{H}_2OH$), 5.5 (1H, br, –OH), 8.7 (2H, br, $>NH\cdot HCl$). The commercially available (±)-*erythro*-methylephedrine·HCl (**5**) and (−)-*erythro*-ephedrine·HCl (**6**) were used without further purification. (**5**), δ ($CDCl_3$) 4.84 (1H, d, J 4 Hz, $-C\underline{H}(OH)-$); (**6**), δ ($CDCl_3$) 4.76 (1H, d, J 3.5 Hz, $-C\underline{H}(OH)-$).[33] (+)-*threo*-Ephedrine (**6**) was obtained by the method of Nagai[34] and separated from the other stereoisomer by making use of the difference in solubility in chloroform.[35] mp 180°C (lit.[36] 182.5°C), δ ($CDCl_3$) 4.14 (1H, d, J 8.0 Hz, $>C\underline{H}OH$), (*Anal.* Calcd for $C_{10}H_{16}ClNO$ C, 59.55; H, 8.00; N, 6.94; Cl, 17.58. Found: C, 59.50; H, 8.10; N, 7.11; Cl, 17.60).

(±)-*erythro*-Methoxyephedrine (**7**) and (±)-*erythro*-acetoxymethylephedrine (**8**) were prepared by the reaction of (±)-*erythro*-methylephedrine (**5**) with methyl *p*-toluenesulfonate and acetic acid anhydride, respectively, by the reported methods (±)-*erythro*-(**7**)[37] as the oxalate, mp 160°C ($C_{14}H_{21}NO_5$ requires C,

59.4; H, 7.47; N, 4.94. Found: C, 59.1; H, 7.56; N, 4.95), δ (DMSO-d_6) 1.09 (3H, d, J 7 Hz, >CHMe), 2.5 (1H, m, >CHMe), 2.75 (6H, s, $-NMe_2$), 3.2 (3H, s, -OMe), 4.82 (1H, d, J 2.5 Hz, $>CHC_6H_5$), 7.29 (5H, s, $-C_6H_5$), 8.55 (2H, s, $-C_2H_2O_4$). (±)-*erythro*-(**8**)·HCl,[38] mp 193—199°C ($C_{13}H_{20}ClNO_2$ requires C, 60.5; H, 7.82; N, 5.43. Found: C, 60.3; H, 7.91; N, 5.49), δ (CD_3CN) 1.25 (3H, d, J 6 Hz, >CHMe), 2.19 (3H, s, -OCOMe), 2.7 (6H, d, J 5 Hz, $-NMe_2$), 3.5 (1H, m, $-CHNMe_2$), 6.48 (1H, d, J 3 Hz, >CHOCOMe), 7.3 (5H, s, $-C_6H_5$).

Products Analysis——Products analysis was performed on the electrolysis solution as quickly as possible or after strage of the solution in a refrigerator. The differences between the values obtained from such solutions were not significant.

(a) Amines: Amines were analyzed as their sulfonamides[39] in the same manner as described previously.

(b) Aldehydes: Formaldehyde, acetaldehyde and benzaldehyde were determined by the method described in a previous paper.[1] Propionaldehyde was determined by gas chromatography (GLC) (JEOL JGC-750 20K) using a stainless steel column (2 m × 3 mmϕ) packed with PEG-20M (Nishio Kogyo Co.) and maintained at 60°. When the solution from the electrolysis of (**13**) after the consumption of 1.5 Faradays per mole was left to stand with mechanical stirring for two hours, the amounts of acetone and acetaldehyde fell slowly with time and reached constant values of 85% and 81% of their initial values, respectively.

(c) Other Products: Methanol was determined by GLC using a column packed with Ethofat 60/25 (Shimadzu Co.) and maintained at 75°C. Acetone was identified by a specific drop reaction using salicylaldehyde and sodium hydroxide[40] and determined by GLC using a column packed with Ethofat 60/25 and a column packed with PEG-20M, both maintained at 60°C. Glycolaldehyde was identified as the trimethylsilyl derivative after being converted to diethyldithioacetal[12] by GLC using a glass column packed with Silicone OV-1 (Wako Chemical Co.) and maintained at 190°C. Glycolaldehyde was also identified as its *p*-nitrophenylosazone, *i.e.*, the solution after electrolysis was neutralized with 5 N HCl and concentrated under reduced pressure. The residue was extracted with ethanol, then 300 mg of *p*-nitrophenylhydrazine in 40 ml of 2 N HCl was added to the ethanolic solution and the amorphous product was recrystallized from ethanol–DMF. (*Anal.* Calcd for $C_{14}H_{12}N_6O_4$: C, 51.22; H, 3.68. Found: C, 51.07; H, 3.64).

Electrolysis Procedure: 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 potent ostat (Hokuto Denko Co., Model PS-500B). The electrode system consisted of a glassy-carbon indicator electrode, a glassy-carbon counter electrode, and a saturated calomel electrode (SCE). Measurements were carried out at 25±0.05°C with a substrate concentration of *ca.* 5 mM and a sweep rate of 0.05 V s^{-1}.

Controlled Potential Electrolysis——Controlled potential electrolyses were carried out with a Hokuto Denko HA-101 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 coulombmeter. An H-type electrolysis cell was used; the anode compartment was separated with an agar plugand sintered-glass disk. The anolytes (*ca.* 1×10^{-2} M substrate in 0.1 M carbonate buffer) were electrolyzed using a glassy-carbon electrode with mechanical stirring.

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