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Stereoselective Syntheses of *cis*- and *trans*-2-Alkylamino-1,2,3,4-tetrahydro-1-naphthalenols by Acid-catalyzed Ring Opening of 1,2-N-Alkylimino-1,2,3,4-tetrahydronaphthalenes

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5- or 7-Substituted *cis*- and *trans*-2-*tert*-butylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols (*cis*-**29**—*cis*-**32**) and (*trans*-**30**—*trans*-**35**) were synthesized from 1,2-N-*tert*-butylimino derivatives. Acid-catalyzed ring opening of 1,2-alkylimino-1,2,3,4-tetrahydronaphthalene derivatives (**1**—**11**) produced a mixture of *cis*- and *trans*-2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenol derivatives whose ratio was markedly affected by substituents on the benzene ring. Stereoselective ring opening of the aziridines and interconversion of *cis*- and *trans*-2-alkylamino-1-tetralols *via* 1-hydroxysulfonyloxy intermediates were described. The reaction mechanism of acid-catalyzed ring opening of the aziridines and hydrolysis of 2-alkylamino-1-hydroxysulfonyloxy-1,2,3,4-tetrahydronaphthalene derivatives is also discussed.

Keywords——tetrahydronaphthalene; aziridine; ring opening of aziridine; S_{N_1} and S_{N_2} mechanism; *cis*- and *trans*-interconversion; 2-alkylamino-1-tetralol; amino alcohol; substituent effect

Searching for a better bronchodilator in a previous study,[2] we synthesized 5-, 6- and/or 7-substituted 1,2-N-alkylimino-1,2,3,4-tetrahydronaphthalenes. Hydrolytic cleavage of the aziridine ring of methyl 2-benzyloxy-5,6-N-*tert*-butylimino-5,6,7,8-tetrahydro-1-naphthoate with sulfuric or acetic acid gave the 2-*tert*-butylamino-1-hydroxy derivative which was then converted by two steps into *trans*-2-*tert*-butylamino-6-hydroxy-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol, which can be regarded as a conformationally restricted analog of salbutamol. The present paper described a detailed investigation of the stereoselective ring-opening reaction of these aziridines and also interconversion between *cis*- and *trans*-isomers of 2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenols.

Acid-catalyzed Ring Opening of Aziridines

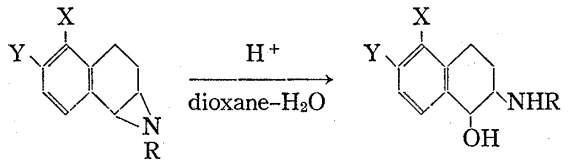
A recent study[3] on the stereochemistry of acid-catalyzed ring opening in *syn*- and *anti*-9,10-imino-1,2,3,4,4a,9,10,10a-(*trans*-4a,10a)-octahydrophenanthrenes, which contain the 1,2-imino-1,2,3,4-tetrahydronaphthalene moiety in their molecules, suggested that the reaction occurred through a benzylic carbonium ion intermediate and involved either the S_{N1} or S_{N2} process. Our previous paper on substituted 1,2-N-alkylimino-1,2,3,4-tetrahydronaphthalenes provided a material useful for studying the substituent effect on this reaction process and mechanism.

Acid-catalyzed ring opening of aziridines (**1**—**11**) carried out in an aqueous dioxane solution containing sulfuric or acetic acid proceeded regioselectively and afforded mixtures of *cis*- and *trans*-2-alkylamino-1-hydroxy derivatives. The ratio of the isomer varied considerably with the substituents on the benzene ring and the reaction condition (Table I). The configuration of each product was determined by its nuclear magnetic resonance (NMR) spectrum (Table IV) as described previously.[4] Table I shows the remarkable influence exerted by the sub-

1) Location: *Juso-honmachi, Yodogawa-ku, Osaka, 532, Japan.*
2) H. Sugihara, K. Ukawa, A. Miyake, and Y. Sanno, *Chem. Pharm. Bull.* (Tokyo), **26**, 394 (1978).
3) W.L. Nelson and B.E. Sherwood, *J. Org. Chem.*, **39**, 66 (1974).
4) H. Sugihara, K. Ukawa, H. Kuriki, M. Nishikawa, and Y. Sanno, *Chem. Pharm. Bull.* (Tokyo), **25**, 2988 (1977).

stituents on the benzene ring upon the stereochemistry of the amino alcohols produced. Electron-withdrawing substituents seem to facilitate the formation of *trans*-isomers. The aziridines bearing a nitro or cyano group at the 5-position (**9** or **5**) gave only *trans*-amino alcohols on hydrolytic ring opening with sulfuric or acetic acid. In contrast, 5,6-dibenzyloxy and 5,6-dimethoxy aziridines (**6** and **7**) produced mainly *cis*-isomer upon the similar treatment. A steric effect of the N-alkyl group on the aziridine ring was also observed and the bulkyl *tert*-butyl group seems to favor backside attack of the water molecule to the aziridine ring. Furthermore, the hydrolytic catalyst used in the reaction also influenced the ratio of *cis*- and *trans*-isomers in the product. Acetic acid depressed the formation of *cis*-isomers compared with sulfuric acid (Table I). The results will be discussed later in more detail.

Table I. Formation of *cis*- and *trans*-2-Alkylamino-1,2,3,4-tetrahydro-1-naphthalenols on Acid-catalyzed Ring Opening of 1,2-Alkylimino-1,2,3,4-tetrahydronaphthalenes (**1**—**11**)

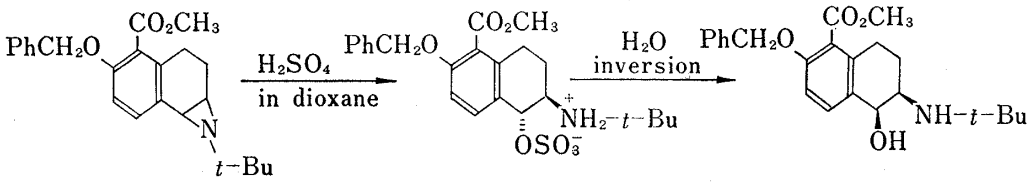


Compd.	Aziridine X	Aziridine Y	Aziridine R	Acid	Reaction temperature[c] (°C)	Time	Ratio of the product (%) *cis*-Isomer	Ratio of the product (%) *trans*-Isomer
1	CO_2CH_3	OCH_2Ph	*t*-Bu	1 equiv. H_2SO_4	RT	3 hr	50	50
				2 equiv. AcOH	80	3 hr	—	100
2	CO_2CH_3	OCH_2Ph	iso-Pr	1 equiv. H_2SO_4	RT	3 hr	60	40
				2 equiv. AcOH	80	3 hr	40	60
3	CO_2CH_3	OCH_2Ph	Et	1 equiv. H_2SO_4	RT	3 hr	70	30
4	CO_2CH_3	OCH_2Ph	Me	1 equiv. H_2SO_4	RT	3 hr	75	25
5	CN	OCH_2Ph	*t*-Bu	Excess H_2SO_4[a]	RT	20 hr	—	100
				2 equiv. AcOH	95	2 hr	—	100
6	OCH_2Ph	OCH_2Ph	*t*-Bu	Excess H_2SO_4[a]	RT	20 hr	100	—
				1 equiv. AcOH	50—60	1 hr	30	70
7	OCH_3	OCH_3	*t*-Bu	Excess H_2SO_4[b]	RT	20 hr	100	—
				1 equiv. AcOH	60	4 hr	—	100
8	CH_3 | NCH_2Ph	OCH_2Ph	*t*-Bu	1 equiv. AcOH	95	5 hr	20	80
9	NO_2	OCH_2Ph	*t*-Bu	Excess H_2SO_4[b]	RT	20 hr	—	100
10	H	NO_2	*t*-Bu	Excess H_2SO_4[b]	70	5 hr	—	100
11	H	H	*t*-Bu	1 equiv. H_2SO_4	RT	3 hr	50	50

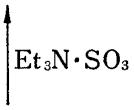
a) 20 equivalent amounts of H_2SO_4.
b) 15 equivalent amounts of H_2SO_4.
c) RT=room temperature.

Ring opening in non-aqueous medium proceeded in a different manner. When methyl 2-benzyloxy-5,6-N-*tert*-butylimino-5,6,7,8-tetrahydro-1-naphthoate (**1**) was treated with an equimolecular amount of sulfuric acid in dioxane, methyl *trans*-2-benzyloxy-6-*tert*-butylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*trans*-**21**) was obtained in a good yield in a configurationally pure form. The structure of *trans*-**21** was confirmed by comparison with an authentic sample prepared from *trans*-amino alcohol (*trans*-**12**) by reaction with the sulfur trioxide-triethylamine adduct. Hydrolysis of *trans*-**21** in aqueous dioxane afforded only *cis*-amino alcohol (*cis*-**12**) involving the inversion at the carbon atom substituted by the hydroxysulfonyloxy group (Chart 1). A similar inversion was accomplished *via* 2-alkylamino-1-chloro-1,2,3,4-tetrahydronaphthalene derivatives (*trans*-**22** and *trans*-**23**), which were readily

prepared by treatment of the aziridines with gaseous hydrogen chloride. Replacement of the 1-chloro group with a hydroxyl group proceeded more easily than hydrolysis of the 1-sulfate ester. This process was especially convenient in the case of the 5-cyano derivative (**5**) (Chart 2). From the NMR spectra of *trans*-**22** and *trans*-**23** in which the proton at –CHCl–CHNHR showed small coupling constants (2Hz), the chloro and alkylamino groups were assigned the *trans*-diaxial conformation as reported for 1,2-dichloro and 1,2-dibromotetralines.[5]



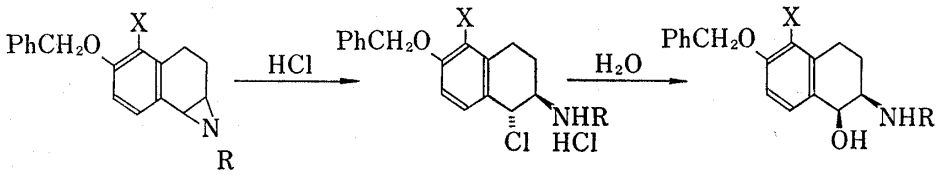
1 *trans*-**21** *cis*-**12**



trans-**12**

Method C

Chart 1



2, 5 *trans*-**22**, *trans*-**23** *cis*-**26**, *cis*-**13**

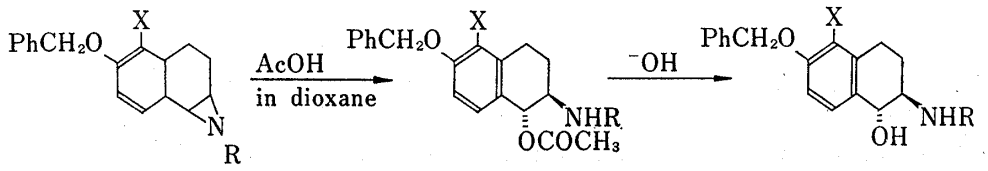
2, *trans*-**22**, *cis*-**26**: X=CO_2CH_3, R=iso-Pr
5, *trans*-**23**, *cis*-**13**: X=CN, R=*tert*-Bu

Ph: phenyl

Method D

Chart 2

Ring opening of aziridines with acetic acid in anhydrous dioxane produced *trans*-1-acetoxy-2-alkylamino-1,2,3,4-tetrahydronaphthalenes exclusively. Subsequent alkaline hydrolysis of the product afforded the *trans*-amino alcohol. The similar methods were successfully used for **2** and **6** (Chart 3). Physical properties of the substituted *cis*- and *trans*-2-*tert*-butyl-



2, 6 *trans*-**24**, *trans*-**25** *trans*-**26**, *trans*-**14**

2, *trans*-**24**, *trans*-**26**: X=CO_2CH_3, R=iso-Pr
6, *trans*-**25**, *trans*-**14**: X=OCH_2Ph, R=*tert*-Bu

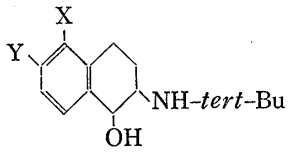
Method E

Chart 3

5) H.R. Buys and C.H. Leeuwestein, *Rec. Trav. Chim.*, **89**, 1089 (1970).

amino-1,2,3,4-tetrahydro-1-naphthalenols prepared by these processes are summarized in Table II.

TABLE II.

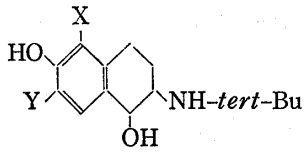


Compd.	X	Y	Salt	Yield (%)	Method[a]	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N
cis-**12**	CO_2CH_3	OCH_2Ph	Base	82	C	104—105	$C_{23}H_{29}NO_4$	72.03 (72.21)	7.62 (7.96)	3.65 (3.67)
cis-**13**	CN	OCH_2Ph	Base	40	D	165—166	$C_{22}H_{26}N_2O_2$	75.40 (75.43)	7.48 (7.24)	7.99 (7.90)
trans-**13**	CN	OCH_2Ph	Base	80	B	120—122	$C_{22}H_{26}N_2O_2$	75.40 (75.22)	7.48 (7.34)	7.99 (8.01)
cis-**14**	OCH_2Ph	OCH_2Ph	Oxalate	54	A	171—173	$C_{30}H_{35}NO_7$	69.08 (68.69)	6.76 (6.75)	2.69 (2.55)
trans-**14**	OCH_2Ph	OCH_2Ph	Oxalate	67	E	213—215	$C_{30}H_{35}NO_7$	69.08 (69.24)	6.76 (6.59)	2.69 (2.48)
cis-**15**	OCH_3	OCH_3	1/2 Fumarate	55	A	218—220	$C_{18}H_{27}NO_5 \cdot 1/2H_2O$	62.40 (62.11)	8.14 (7.78)	4.04 (3.92)
trans-**15**	OCH_3	OCH_3	Fumarate	55	B	216—218	$C_{20}H_{29}NO_7$	60.74 (60.63)	7.39 (7.30)	3.54 (3.82)
cis-**16**	CH_3 N–CH_2Ph	OCH_2Ph	Oxalate	9	B	179—180	$C_{31}H_{38}N_2O_6$	69.21 (69.36)	6.97 (6.83)	5.38 (5.21)
trans-**16**	CH_3 N–CH_2Ph	OCH_2Ph	Oxalate	45	B	189—190	$C_{31}H_{38}N_2O_6$	69.21 (69.08)	6.97 (7.16)	5.38 (5.11)
cis-**17**	H	H	HCl	51	D	263—265	$C_{19}H_{20}ClNO$	65.79 (65.57)	8.67 (8.80)	5.48 (5.42)
trans-**17**	H	H	HCl	56	B	248—250	$C_{19}H_{20}ClNO$	65.79 (65.74)	8.67 (8.37)	5.48 (5.43)
trans-**18**	NO_2	OCH_2Ph	HCl	54	B	255—257	$C_{21}H_{27}ClN_2O_4$	61.98 (61.83)	6.69 (6.53)	6.89 (6.61)
trans-**19**	H	NO_2	HCl	75	B	257—262	$C_{14}H_{21}ClN_2O_3$	55.90 (55.78)	7.04 (7.12)	9.31 (9.02)

a) A: hydrolytic ring opening using sulfuric acid; B: hydrolytic ring opening using acetic acid; C: the method illustrated in Chart 1; D: the method illustrated in Chart 2; E; the method illustrated in Chart 3.

Reduction of *cis*-**12** with lithium aluminum hydride in tetrahydrofuran gave the 5-hydroxymethyl derivative (*cis*-**27**). Similar reduction of *trans*-**13** afforded *trans*-5-aminomethyl-6-benzyloxy-2-*tert*-butylamino-1,2,3,4-tetrahydro-1-naphthalenol (*trans*-**28**). Reduction of *trans*-**13** with diborane in tetrahydrofuran at 50° afforded the debenzylated compound (*trans*-**34**). Removal of the benzyl groups from 5- or 7-substituted *cis*- and *trans*-2-alkylamino-6-benzyloxy-1,2,3,4-tetrahydro-1-naphthalenols was carried out in methanol by catalytic hydrogenation using palladium charcoal at room temperature under an atmospheric pressure. On catalytic hydrogenation of *trans*-**18** and *trans*-**6**-benzyloxy-2-*tert*-butylamino-7-nitro-1,2,3,4-tetrahydro-1-naphthalenol (*trans*-**20**), the nitro group was simultaneously converted into the amino group. Table III shows the 5- or 7-substituted *cis*- and *trans*-2-*tert*-butylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols and their physical properties. Table IV lists the chemical shifts and the coupling constants of the *cis*- and *trans*-isomers.

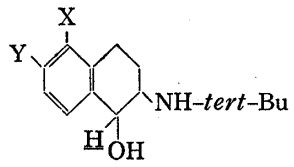
TABLE III.



Compd.	X	Y	Salt	Yield (%)	mp[a] (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N
cis-29	CH_2OH	H	Base	70	163—165	$C_{15}H_{23}NO_3$	67.89 (67.89)	8.74 (8.98)	5.28 (5.15)
cis-30	CN	H	HCl	76	197—199	$C_{15}H_{21}ClN_2O_2 \cdot H_2O$	57.22 (57.28)	7.36 (7.38)	8.90 (8.60)
trans-30	CN	H	HCl	64	190—192	$C_{15}H_{21}ClN_2O_2 \cdot C_2H_5OH$	59.55 (59.12)	7.94 (8.18)	8.17 (8.22)
cis-31	OH	H	1/2 Fumarate	67	186—187	$C_{16}H_{23}NO_5 \cdot 3/2H_2O$	57.12 (57.21)	7.79 (7.65)	4.16 (4.31)
trans-31	OH	H	1/2 Fumarate	71	185—186	$C_{16}H_{23}NO_5 \cdot 3/2H_2O$	57.12 (56.38)	7.79 (7.51)	4.16 (4.38)
cis-32	$NHCH_3$	H	Fumarate	45	195—197	$C_{19}H_{28}N_2O_6$	59.98 (60.13)	7.42 (7.66)	7.69 (7.63)
trans-32	$NHCH_3$	H	1/2 Fumarate	73	205—207	$C_{17}H_{26}N_2O_4$	63.33 (63.30)	8.13 (8.09)	8.69 (8.30)
trans-33	NH_2	H	Fumarate	58	300	$C_{18}H_{26}N_2O_6 \cdot 1/2H_2O$	57.58 (57.82)	7.25 (7.49)	7.46 (7.68)
trans-34	CH_2NH_2	H	2 HCl	63	247—250	$C_{15}H_{26}Cl_2N_2O_2$	53.41 (53.64)	7.77 (7.80)	8.31 (8.24)
trans-35	H	NH_2	Fumarate	73	300	$C_{18}H_{26}N_2O_6$	59.00 (59.09)	7.15 (6.95)	7.64 (7.67)

a) Decomposition.

TABLE IV. NMR Spectral Data of *cis*- and *trans*-2-*tert*-Butylamino-1,2,3,4-tetrahydro-1-naphthalenol Derivatives



X	Y	Salt	Solvent[a]	CH–OH (ppm) ($J_{1,2}$ (H)) *cis*-Isomer	*trans*-Isomer
CO_2CH_3	OCH_2Ph	Base	A	4.33(4)	4.13(9)
CN	OCH_2Ph	Base	A	4.34(4)	4.15(9)
OCH_2Ph	OCH_2Ph	Oxalate	B	4.72(0)	4.60(8)
OCH_3	OCH_3	Fumarate	B	4.68(3)	4.50(8)
CH_3 N–CH_2Ph	OCH_2Ph	Oxalate	B	4.60(3)	4.50(8)
H	H	HCl	B	4.93(3)	4.83(9)
NO_2	OCH_2Ph	HCl	B	—	4.62(8)
H	NO_2	HCl	B	—	4.89(9)
CH_2OH	OH	Base	C	4.25(4)	4.03(7)
CN	OH	HCl	B	4.72(4)	4.66(8)
OH	OH	Fumarate	B	4.68(2)	4.56(8)
$NHCH_3$	OH	Fumarate	B	4.58(3)	4.42(8)
NH_2	OH	Fumarate	B	—	4.40(8)

a) A: in $CDCl_3$ solution; B: in DMSO-d_6–D_2O solution; C: in DMSO-d_6 solution.
Ph: phenyl.

Interconversion of *cis*- and *trans*-Amino Alcohol and Reaction Mechanism

Usually interconversion of diastereomeric amino alcohols is carried out in three steps.[6,7] Amino alcohols are first converted into their N-acyl or N-carbamoyl derivatives. Dehydrating cyclization of the derivatives with thionyl chloride accompanies inversion of the configuration at the carbon atom to which the hydroxy group is bound and forms oxazoline or 2-imino-oxazolidine from N-acyl or N-carbamoyl derivatives, respectively. Hydrolysis of these heterocyclic intermediates gives amino alcohols having the opposite configuration of the starting compounds.

Hydrolytic epimerization of *trans*- into *cis*-isomers of vicinal N-acylamino alcohols on fused rings, *e.g.*, aminotetralols,[8] aminoindanols,[9] and aminobenzocycloheptanols,[10,11] is also assumed to proceed through the similar oxazoline intermediates.

Application of this method of epimerization to our alkylamino tetralols resulted in failure. When *trans*-**12** was reacted with methyl isocyanate, the O-acylated compound resulted instead of the desired N-carbamoyl derivatives. The infrared (IR) spectrum of the crude product showed C=O stretching vibrational absorption at 1760—1720 cm^{-1} attributable to the $O-\overset{O}{\overset{\|}{C}}-N$ group. N-acylation may be inhibited by steric hindrance due to the N-alkyl group and the tetrahydronaphthalene ring on which the alkylamino group is attached. However, we could converted *trans*-isomers into *cis*-isomers by hydrolyzing the O-sulfated derivatives as described above. This method was satisfactorily high yields when the amino group was substituted (*trans*-**12**, *trans*-**26**, *trans*-**36**, and *trans*-**37**) but relatively poor yield in the case of a primary amine (*trans*-**38**) for both sulfation and hydrolysis processes. The sulfation of the derivatives having substituted amino groups with sulfur trioxide-triethylamine gave in good yields the hydroxysulfonyloxy compounds (*trans*-**21**, *trans*-**39**, *trans*-**40**, and *trans*-**41**) retaining the configuration of the starting compounds according to their NMR spectra (coupling constants of $-C\underline{H}OSO_3^-$–CHN^+H_2R– being 9, 9, 8, and 9 Hz). In contrast, the O-sulfated compound could not be obtained in the case of a primary amine (*trans*-**38**). The sulfation of *trans*-**38** with chlorosulfonic acid gave the desired sulfate ester (**42**) but configurationally *cis*-isomer ($J=3$ Hz) which was identical with the authentic sample derived by sulfation of *cis*-**38**. In the treatmnet of the substituted amino alcohol with chlorosulfonic acid, the configuration was retained in the case of the isopropylamino derivative (*trans*-**26**) but partially inverted in the case of the methylamino derivative (*trans*-**37**). The hydrolysis of the *trans*-sulfate esters seemed to be proceeding by S_{N_2} mechanism since *cis*-**12**, *cis*-**26**, *cis*-**36**, and *cis*-**37** were obtained almost quantitatively. Interestingly, *cis*-**42** underwent S_{N_1} hydrolysis retaining its configuration to give *cis*-**38**. Thus configurational inversion was attained as a whole even in this case.

Inversion of the *cis*-isomer to *trans* by a similar method was unsuccessful. Though *cis*-O-sulfate esters (*cis*-**21** and *cis*-**39**) were obtained in yields comparable to those of *trans*-isomer from *cis*-amino alcohols (*cis*-**12** and *cis*-**26**), subsequent hydrolysis gave only the starting materials. When hydrolysis of *cis*-**39** was carried out in $H_2{}^{18}O$, the *cis*-amino alcohol obtained had 98% ^{18}O, according to the mass spectrum. This may indicate that hydrolysis of 2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenol sulfate esters involves elimination of the sulfate group and the formation of carbonium cation as an intermediate, and that subsequent attack of the water molecule forms *cis*-amino alcohols. This suggests that limitation of epimerization described above may be affected by kinetic or thermodynamic control of the step following the production of carbonium cation intermediates. Upon attack of the water molecule, formation of the *cis*-

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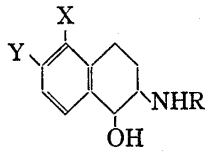
TABLE V. pK_a Values of *cis*- and *trans*-2-Alkylamino-1,2,3,4-tetrahydro-1-naphthalenol Derivatives in 50% Ethanol Solution



X	Y	R	p*K*a value *cis*-Isomer	p*K*a value *trans*-Isomer	Δ p*K*a (*cis-trans*)
CO_2CH_3	OCH_2Ph	*tert*-Bu	9.15	8.8	0.35
CO_2CH_3	OCH_2Ph	iso-Pr	9.20	8.8	0.40
CN	OCH_2Ph	*tert*-Bu	8.95	8.85	0.10
OCH_3	OCH_3	*tert*-Bu	9.40	9.0	0.40
H	H	*tert*-Bu	9.44	9.12	0.32
H	NO_2	*tert*-Bu	—	8.6	—

TABLE VI. σ Values of 5 and/or 6 Substituted 1,2,3,4-Tetrahydronaphthalene Derivatives regarded as *meta* and/or *para* Substituted Benzene Derivatives

Substituent at 6-position	Substituent at 5-position	σ_p[a]	σ_m[a]	σ_{m+p}
$PhCH_2O$	CO_2CH_3	−0.415	+0.315	−0.1
$PhCH_2O$	CN	−0.415	+0.68	+0.265
$PhCH_2O$	NO_2	−0.415	+0.71	+0.295
$PhCH_2O$	$PhCH_2O$	−0.415	+0.15[b]	−0.265
CH_3O	CH_3O	−0.27	+0.115	−0.155
NO_2	H	+0.78	—	+0.78
H	H	—	—	0

a) Substituent constants reported by J. Clark and D. D. Perrin, *Quart. Revs.*, **18**, 295 (1964) were used.
b) σ_m values (OC_2H_5) was used for σ_m value (OCH_2Ph).

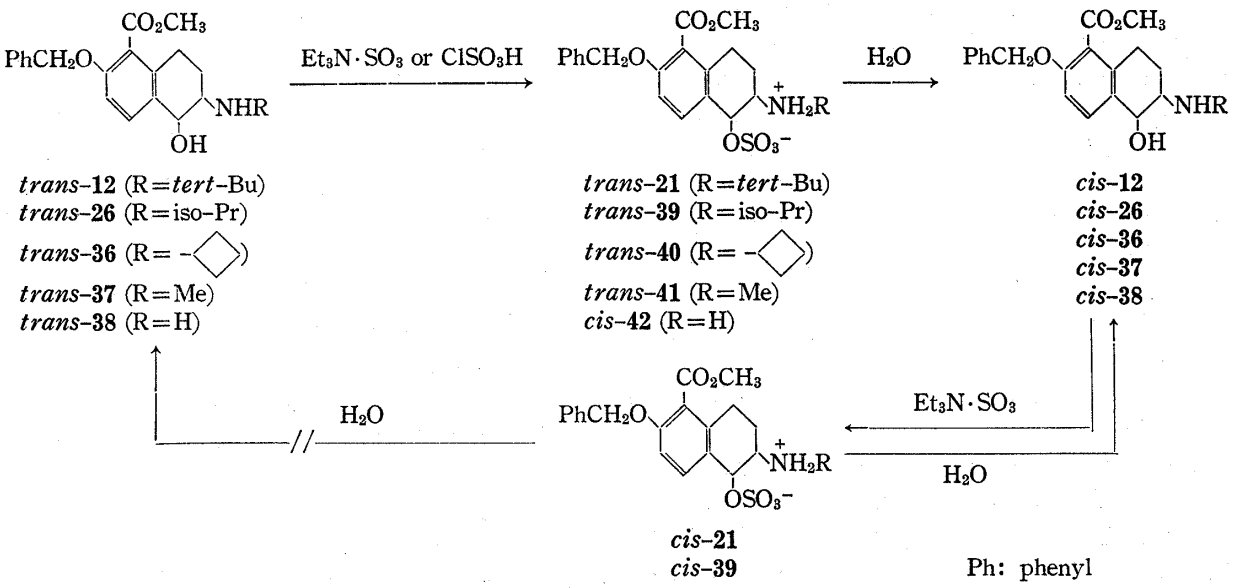
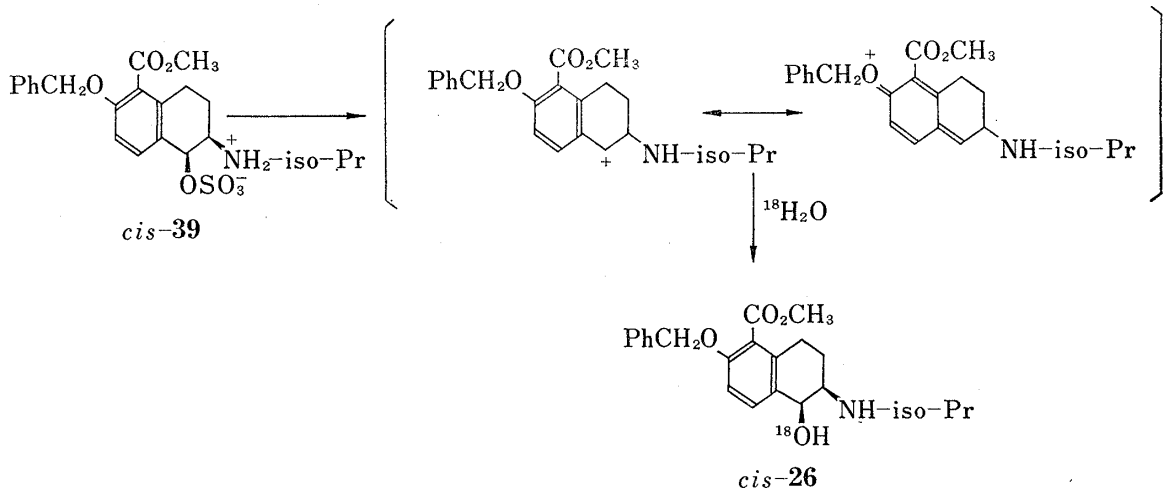


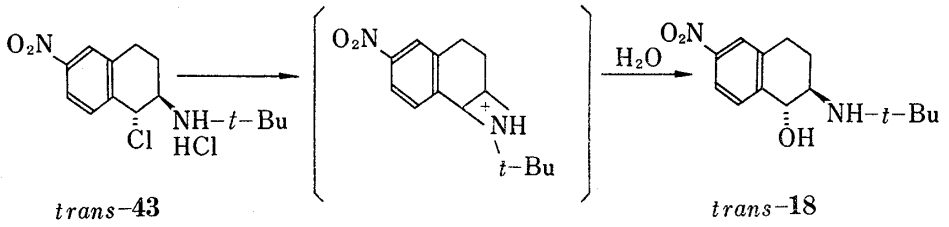
Chart 4

amino alcohol would be favored by an attractive force between the cationic nitrogen atom and the anionic oxygen atom of water. The pK_a values of some *cis*- and *trans*-2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenols measured in 50% ethanolic solutions titrimetrically (Table V) indicate that *cis*-isomers are stronger bases than the corresponding *trans*-isomers. This supports the fact that *cis*-amino alcohols are more thermodynamically stable than the corresponding *trans*-isomers in salt form. Table V also shows the relationship between the substituent on the benzene ring and the pK_a value of the amino alcohol, or ΔpK_a (*cis-trans*); The value may indicate the stability of the end product.



cis-**39** *cis*-**26**

Chart 5



trans-**43** *trans*-**18**

Chart 6

The substituent effect in stereochemistry of hydrolytic ring opening of aziridines (Table I) may be explained similarly. As mentioned before, the reaction would involve either S_{N_1} or S_{N_2} mechanism. The electronic character of the substituent on the benzene ring or the acidity of the catalyst employed may govern the mechanism which affects the stereochemistry of the reaction product. To calculate the electronic effect of the substituent, σ_m and σ_p values were adopted for 5- and 6-substituents in 1,2,3,4-tetrahydronaphthalene derivatives, respectively, since the reactive site is the benzylic carbon atom. These values and their sum (σ_{m+p}) are listed in Table VI. When σ_{m+p} is smaller than -0.15, the ring opening reaction using sulfuric acid seems to involve mainly the S_{N_1} process. On ring opening of 5,6-dibenzyloxy ($\sigma_{m+p}=-0.265$) and 5,6-dimethoxy ($\sigma_{m+p}=-0.155$), derivatives (**5** and **6**) bond fission between the benzylic carbon atom and the nitrogen atom of the aziridine ring may be facilitated by the mesomeric and inductive effect of the 5,6-dibenzyloxy and 5,6-dimethoxy groups. The resulting benzylic carbonium ion may be stabilized by delocalization of the charge over the benzene ring and subsequent attack of the water molecule may proceed under thermodynamic control to afford *cis*-amino alcohols. The difference in the isomer ratio between **6** and **7** on ring opening using acetic acid (Table I) is correlated with the difference of the σ_{m+p} values, which shows that the dibenzyloxy group is much more able to supply electrons to the reactive site than the dimethoxy group. On the other hand, hydrolysis of the aziridines with positive σ_{m+p} values (*e.g.*,

5, **9**, and **10**) would proceed predominantly by the S_{N_2} mechanism owing to their strengthened C-N linkage, and give *trans*-amino alcohols. A typical example is the ring opening of the 6-nitro derivative (**10**, $\sigma_{m+p}=+0.78$) which produced exclusively *trans*-amino alcohol (*trans*-**19**) even in a strong acidic medium. Treatment of **10** with hydrochloric acid at room temperature gave its hydrochloride. On heating **10** at 50° with ethanolic hydrogen chloride in benzene, ring opening occurred to produce *trans*-2-*tert*-butylamino-1-chloro-6-nitro-1,2,3,4-tetrahydronaphthalene (*trans*-**43**), but its hydrolysis gave no *cis*-amino alcohol detectable in the NMR spectrum. The S_{N_2} process involving aziridinium ion[12] as an intermediate seemed to operate in this case. In the case of a compound whose σ_{m+p} value is 0——0.1 (*e.g.*, **11**, **1**, **2**, and **3**), ring opening using sulfuric acid may occur through both S_{N_1} and S_{N_2} mechanisms.

The above evidence clearly shows that the reactivity of the aziridine ring of 1,2-N-alkylimino-1,2,3,4-tetrahydronaphthalene derivatives and epimerization of *cis*- and *trans*-2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenols are greatly affected by the electronic effect of the substituent on the benzene ring.

Experimental[13]

Hydrolytic Ring Opening of 1,2-N-Alkylimino-1,2,3,4-tetrahydronaphthalenes——To a solution of 1,2-N-alkylimino-1,2,3,4-tetrahydronaphthalene (1 mmol) in dioxane (20 ml) and H_2O (10 ml) was added a proper amount of sulfuric or acetic acid. The mixture was stirred until the starting material disappeared on thin-layer chromatography (TLC). The reaction mixture was treated with aqueous Na_2CO_3 solution and extracted with AcOEt or $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The ratio of *cis* and *trans* isomers was determined by NMR data of the crude amino alcohol. Table I lists the conditions used for hydrolysis and the isomer ratios.

Methyl *cis*-2-Denzyloxy-6-*tert*-butylamino-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate (*cis*-12)——To an ice-cooled solution of **1** (2.4 g) in dry dioxane (30 ml), a solution of conc. H_2SO_4 (600 mg) in dry dioxane (5 ml) was added dropwise with stirring. After stirring for another 2 hr, H_2O (100 ml) was added and the mixture was stirred at 85—90° for 15 hr. The cooled reaction mixture was neutralized with 5% Na_2CO_3 solution and extracted with AcOEt. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from benzene–*n*-hexane to give *cis*-**12** (2.06 g, 82%) as colorless prisms. IR ν_{max}^{KBr} cm^{-1}: 3300, 1735, 1595, 1585.

Methyl *trans*-2-Benzyloxy-6-*tert*-butylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*trans*-21)——a) To an ice-cooled solution of methyl 2-benzyloxy-5,6-N-*tert*-butylimino-5,6,7,8-tetrahydro-1-naphthoate (**1**, 365 mg) in dry dioxane (10 ml) was added dropwise a solution of conc. H_2SO_4 (100 mg) in dry dioxane (3 ml). The mixture was stirred at room temperature for 2 hr. The resulting precipitate was collected by filtration, washed with dioxane and dried to give *trans*-**21** (340 mg, 74%) as a white powder, mp 232—234° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 3450, 3000—2500, 1720, 1280, 1215. NMR (DMSO-d_6) δ: 1.35 (9H, s, N-*tert*-Bu), 1.7—3.7 (5H, m), 3.78 (3H, s, CO_2CH_3), 5.14 (2H, s, OCH_2Ph), 5.30 (1H, d, $J=9$ Hz, >C<u>H</u>–OSO_3^-), 7.10 (1H, d, $J=9$ Hz), 7.2—7.4 (5H), 7.62 (1H, d, $J=9$ Hz). MS *m/e*: 365 ($M^+-H_2SO_4$), a spectral pattern very similar to that of **1**. *Anal.* Calcd. for $C_{23}H_{29}NO_7S$: C, 59.59; H, 6.31; N, 3.02. Found: C, 59.38; H, 6.44; N, 2.98.

b) A mixture of *trans*-**12** (200 mg) and sulfur trioxide–triethylamine (300 mg) in benzene (20 ml) was stirred at 80—85° for 5 hr. The resulting precipitate was collected by filtration, washed with a small amount of CH_2Cl_2 and dried to give *trans*-**21** (195 mg, 80%).

Methyl *trans*-2-Benzyloxy-5-chloro-6-isopropylamino-5,6,7,8-tetrahydro-1-naphthoate Hydrochloride (*trans*-22)——To an ice-cooled solution of **2** (1.0 g) in dry ether (50 ml) was introduced gaseous HCl. The reaction mixture was stirred at room temperature for 1 hr. The resulting precipitate was collected by filtration, washed with ether and dried to give *trans*-**22** (1.02 g, 97%) as a white powder, mp 179—183° (dec.). IR ν_{max}^{KBr} cm^{-1}: 3400, 1730, 1720, 1270. NMR (DMSO-d_6) δ: 1.33, 1.36 (6H, d, $J=6$ Hz, N-iso-Pr), 3.82 (3H, s, CO_2CH_3), 5.12 (2H, s, OCH_2Ph), 5.73 (1H, d, $J=3$ Hz, >C<u>H</u>–Cl), 7.08 (1H, d, $J=9$ Hz), 7.2—7.4 (5H), 7.47 (1H, d, $J=9$ Hz). *Anal.* Calcd. for $C_{22}H_{27}Cl_2NO_3$: C, 62.26; H, 6.41; N, 3.30. Found: C, 62.24; H, 6.66; N, 3.19.

12) *a*) N.J. Leonard, E.F. Kiefer, and L.E. Brady, *J. Org. Chem.*, **28**, 2858 (1963); *b*) N.J. Leonard and K. Jann, *J. Am. Chem. Soc.*, **84**, 4806 (1962).

13) All melting points were determined with a Yanagimoto Micro Melting Point apparatus (microscope hot stage) and are uncorrected. IR spectra were measured with a Hitachi Model 215 infrared spectrophotometer. NMR spectra were determined with a Varian Model HA-100 spectrometer using tetramethylsilane as an internal standard. Mass spectra were taken with a JEOL JMS-01SC spectrometer.

***trans*-2-Benzyloxy-6-*tert*-butylamino-5-chloro-5,6,7,8-tetrahydro-1-naphthonitrile Hydrochloride (*trans*-23)**——Similar treatment of **5** with gaseous HCl gave *trans*-**23** in 90% yield. White powder, mp 215—217° (dec.). IR ν_{max}^{KBr} cm^{-1}: 3400, 2220 (CN), 1590, 1580, 1200. NMR (DMSO-d_6) δ: 5.67 (1H, broad d, $J=3$ Hz, >C<u>H</u>–Cl). *Anal.* Calcd. for $C_{22}H_{26}Cl_2N_2O$: C, 65.18; H, 6.47; N, 6.91. Found: C, 65.38; H, 6.29; N, 6.78.

***cis*-2-Benzyloxy-6-*tert*-butylamino-5-hydroxy-5,6,7,8-tetrahydro-1-naphthonitrile (*cis*-13)**——A suspension of *trans*-**23** (640 mg) in H_2O (80 ml) was stirred at 90° for 5 hr. The reaction mixture was treated with 5% $NaHCO_3$ solution and extracted with benzene. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from AcOEt–isopropyl ether to give *cis*-**13** (220 mg, 40%) as colorless needles.

Methyl *trans*-5-Acetoxy-2-benzyloxy-6-isopropylamino-5,6,7,8-tetrahydro-1-naphthoate Acetate (*trans*-24)——A mixture of **2** (12 1mg) and AcOH (2 ml) in dioxane (10 ml) was heated at 60° for 30 min. The reaction mixture was evaporated to dryness *in vacuo*. The residue was recrystallized from ether–*n*-hexane to give *trans*-**24** (139 mg, 86%) as white crystals, mp 106—109°. IR ν_{max}^{KBr} cm^{-1}: 1730. NMR ($CDCl_3$) δ: 1.95 (3H, s, AcO^-), 2.04 (3H, s, CH–OCOC<u>H</u>$_3$), 5.85 (1H, d, $J=5$ Hz, >C<u>H</u>–OAc). *Anal.* Calcd. for $C_{26}H_{33}NO_7$: C, 66.22; H, 7.05; N, 2.97. Found: C, 66.41; H, 6.70; N, 2.85.

Alkaline Hydrolysis of *trans*-24——To a solution of *trans*-**24** (100 mg) in MeOH (5 ml) was added powdered NaOH (50 mg). After stirring at room temperature for 5 hr, the reaction mixture was poured into cold water and extracted with AcOEt. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was recrystallized from AcOEt–*n*-hexane to give *trans*-**26** (55 mg, 76%) which was identified by comparing its NMR spectrum with that of an authentic sample.

***trans*-2-*tert*-Butylamino-5,6-dibenzyloxy-1,2,3,4-tetrahydro-1-naphthalenol Oxalate (*trans*-14)**——A solution of **6** (600 mg) and AcOH (0.5 ml) in dioxane (10 ml) was heated at 60° for 5 hr. The reaction mixture was evaporated to dryness *in vacuo* to give *trans*-1-acetoxy-2-*tert*-butylamino-5,6-dibenzyloxy-1,2,3,4-tetrahydronaphthalene acetate (*trans*-**25**) as a pale brown oil (670 mg); NMR ($CDCl_3$) δ: 1.45 (9H, s, N-*tert*-Bu), 1.97 (3H, s, AcO^-), 2.12 (3H, s, CH–OCOC<u>H</u>$_3$), 5.03 (2H, s, OCH_2Ph), 5.12 (2H, s, OCH_2Ph), 5.97 (1H, d, $J=7$ Hz, >C<u>H</u>–OAc). A solution of *trans*-**25** (670 mg) in MeOH (10 ml) was hydrolyzed with NaOH (300 mg) at room temperature. The reaction mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was dissolved in MeOH and treated with oxalic acid to give *trans*-**14** (507 mg).

***trans*-6-Benzyloxy-2-*tert*-butylamino-7-nitro-1,2,3,4-tetrahydro-1-naphthalenol Oxalate (*trans*-20)**——Hydrolytic ring opening of 6-benzyloxy-1,2-N-*tert*-butylimino-7-nitro-1,2,3,4-tetrahydronaphthalene[2] in dioxane–water containing two equimolecular amounts of AcOH gave *trans*-**20** in 40% yield. Colorless needles recrystallized from MeOH–ether, mp 218—220°. NMR (DMSO-d_6) δ: 4.65 (1H, d, $J=8$ Hz, >C<u>H</u>–OH). *Anal.* Calcd. for $C_{23}H_{28}N_2O_8$: C, 59.99; H, 6.13; N, 6.08. Found: C, 59.75; H, 6.00; N, 6.13.

***cis*-6-Benzyloxy-2-*tert*-butylamino-5-hydroxylmethyl-1,2,3,4-tetrahydro-1-naphthalenol (*cis*-27)**——To a solution of *cis*-**12** (1.04 g) in dry THF (30 ml) was added $LiAlH_4$ (500 mg). The mixture was refluxed with stirring under N_2 stream for 4 hr. After decomposition of the excess $LiAlH_4$ with MeOH and then 20% aqueous NaOH solution, the reaction mixture was extracted with AcOEt. The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from AcOEt–*n*-hexane to afford *cis*-**27** (538 mg, 56%) as white crystals, mp 120—122°. NMR (DMSO-d_6–D_2O) δ: 1.12 (9H, s, N-*tert*-Bu), 4.33 (1H, d, $J=3$ Hz, >C<u>H</u>–OH), 4.58 (2H, s, –C<u>H</u>$_2$OH), 5.06 (2H, s, OCH_2Ph). *Anal.* Calcd. for $C_{22}H_{29}NO_3$: C, 74.33; H, 8.22; N, 3.94. Found: C, 74.53; H, 8.36; N, 3.87.

***trans*-5-Aminomethyl-6-benzyloxy-2-*tert*-butylamino-1,2,3,4-tetrahydro-1-naphthalenol (*trans*-28)**——To a solution of *trans*-**13** (400 mg) in dry THF (30 ml) was added $LiAlH_4$ (500 mg). The mixture was refluxed with stirring under N_2 stream for 3 hr. After decomposition of the excess $LiAlH_4$ with MeOH and then with 20% NaOH solution, the mixture was filtered and the filtrate was extracted with AcOEt. The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from AcOEt-isopropyl ether to give *trans*-**28** (210 mg, 52%) as colorless plates, mp 170—171°. IR ν_{max}^{KBr} cm^{-1}: 3530, 1580, 1485, 1470, 1260, 1080, 1070, 950. NMR ($CDCl_3$) δ: 1.12 (9H, s, N-*tert*-Bu), 3.85 (2H, s, C<u>H</u>$_2$NH$_2$), 4.18 (1H, d, $J=9$ Hz, >C<u>H</u>–OH), 5.06 (2H, s, OCH_2Ph). *Anal.* Calcd. for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.34; H, 8.43; N, 7.79.

Reduction of *trans*-13 with Diborane——To a solution of *trans*-**13** (100 mg) in THF (10 ml) was introduced diborane generated from $NaBH_4$ (200 mg) in diglyme (2 ml) and BF_3 etherate (0.5 ml) in diglyme (3 ml). The reaction mixture was stirred at room temperature for 2 hr and then 50° for 2 hr. After decomposition of excess diborane with EtOH, ethanolic HCl was added to the reaction mixture. The arising precipitate was collected by filtration and recrystallized from EtOH–isopropyl ether to give white crystals (82 mg), which were identified by comparison with *trans*-**34** obtained by debenzylation of *trans*-**28**.

***cis*-2-*tert*-Butylamino-6-hydroxy-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol (*cis*-29)**——A solution of *cis*-**27** (747 mg) in MeOH (30 ml) was hydrogenated with 5% palladium charcoal (50 mg) at room temperature under atmospheric pressure. After hydrogen absorption had ceased, the reaction mixture was evaporated *in vacuo*. The residue was recrystallized from MeOH–AcOEt to afford *cis*-**29** (390 mg, 70%) as white crystals, IR ν_{max}^{KBr} cm^{-1}: 1600 1590, 1260, 1055, 940, 815. NMR (DMSO-d_6) δ: 1.08 (9H, s, N-*tert*-Bu),

1.4—3.1 (4H, m), 4.29 (1H, d, J=4 Hz, >C<u>H</u>–OH), 4.48 (2H, s, C<u>H</u>$_2$OH), 6.59 (1H, d, J=9 Hz), 6.97 (1H, d, J=9 Hz). Similar catalytic hydrogenation of 5- or 7-substituted 6-benzyloxy-2-*tert*-butylamino-1,2,3,4-tetrahydro-1-naphthalenols gave 5- or 7-substituted 2-*tert*-butylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols. Table III gives the yields and physical properties of the amino alcohols obtained.

Methyl *trans*-2-Benzyloxy-6-isopropylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*trans*-39)——a) Treatment of **2** with conc. H_2SO_4 similar to that described in a) for *trans*-**21**, gave *trans*-**39** in 77% yield. White crystals, mp 210—213° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 1735, 1280, 1210. NMR (DMSO-d_6) δ: 5.32 (1H, d, J=9 Hz, >C<u>H</u>–OSO$_3^-$). *Anal.* Calcd. for $C_{22}H_{27}NO_7S$: C, 58.78; H, 6.05; N, 3.12. Found: C, 58.39; H, 6.09; N, 3.06.

b) Treatment of *trans*-**26** with sulfur trioxide-triethylamine similar to that described in b) for *trans*-**21**, afforded *trans*-**39** in 81% yield.

c) To an ice-cooled solution of *trans*-**26** (10.0 g) in CH_2Cl_2 (100 ml) was added chlorosulfonic acid (2 ml) with stirring. The mixture was stirred at room temperature for 10 hr. The arising precipitate was collected by filtration, washed with CH_2Cl_2 and dried to give *trans*-**39** (10.3 g, 86%).

Methyl *trans*-2-Benzyloxy-6-cyclobutylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*trans*-40)——Treatment of methyl *trans*-2-benzyloxy-6-cyclobutylamino-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate[4] with sulfur trioxide-triethylamine similar to that described in b) for *trans*-**21**, afforded *trans*-**40** in 65% yield. White powder, mp 210—213° (decomp. with foaming). IR ν_{max}^{KBr} cm^{-1}: 1735, 1600, 1280, 1270, 1245, 1210. NMR (DMSO-d_6) δ: 5.33 (1H, d, J=8 Hz, >C<u>H</u>–OSO$_3^-$). *Anal.* Calcd. for $C_{23}H_{27}NO_7S$: C, 59.85; H, 5.90; N, 3.04. Found: C, 59.77; H, 5.87; N, 3.07.

Methyl *trans*-2-Benzyloxy-5-hydroxysulfonyloxy-6-methylamino-5,6,7,8-tetrahydro-1-naphthoate (*trans*-41)——Treatment of methyl *trans*-2-benzyloxy-5-hydroxy-6-methylamino-5,6,7,8-tetrahydro-1-naphthoate (*trans*-**37**) [mp 96—97°, NMR ($CDCl_3$) δ: 4.55 (1H, d, J=9 Hz, >C<u>H</u>–OH)] with sulfur trioxide-triethylamine similar to that described in b) for *trans*-**21** afforded *trans*-**41** in 76% yield. White powder, mp 187—189° (dec.). NMR (DMSO-d_6) δ: 5.30 (1H, d, J=9 Hz, >C<u>H</u>OSO$_3^-$). *Anal.* Calcd. for $C_{20}H_{23}NO_7S$: C, 56.99; H, 5.50; N, 3.32. Found: C, 56.75; H, 5.48; N, 3.13.

Sulfation of Methyl *trans*-2-Benzyloxy-5-hydroxy-6-methylamino-5,6,7,8-tetrahydro-1-naphthoate (*trans*-37) with Chlorosulfonic Acid——Treatment of *trans*-**37** with chlorosulfonic acid similar to that described in c) for *trans*-**26** afforded a mixture of methyl *cis*- and *trans*-2-benzyloxy-5-hydroxysulfonyloxy-6-methyl-5,6,7,8-tetrahydro-1-naphthoate in a 1:3 ratio. NMR (DMSO-d_6) δ: 5.30 [d, J=9 Hz, >C<u>H</u>OSO$_3^-$ (*trans*)] and 5.42 [d, J=3 Hz, >C<u>H</u>OSO$_3^-$ (*cis*)].

Methyl *cis*-6-Amino-2-benzyloxy-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*cis*-42)——Treatment of methyl *trans*-6-amino-2-benzyloxy-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate[4] with chlorosulfonic acid as described in c) for *trans*-**39** afforded *cis*-**42** in 70% yield. White powder, mp 222—225° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 1720, 1280, 1265, 1230. NMR (DMSO-d_6) δ: 5.63 (1H, d, J=3 Hz, >C<u>H</u>–OSO$_3^-$). *Anal.* Calcd. for $C_{19}H_{21}NO_7S$: C, 56.01; H, 5.20; N, 3.34. Found: C, 55.73; H, 4.81; N, 3.09.

Formation of *cis*-12, *cis*-26, *cis*-36, *cis*-37 and *cis*-38 on Hydrolysis of *trans*-21, *trans*-39, *trans*-40, *trans*-41 and *cis*-42——A suspension of 1.0 g of the appropriate sulfate ester in dioxane (*ca.* 10 ml) and H_2O (*ca.* 40 ml) was stirred at 80—90° for 8—15 hr. The resulting homogeneous solution was cooled, treated with 5% Na_2CO_3 solution and extracted with AcOEt. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The yields on hydrolysis of *trans*-**21**, *trans*-**39**, *trans*-**40**, *trans*-**41** and *cis*-**42** were 92, 82, 84, 87 and 57%, respectively. The amino alcohols thus obtained were configurationally pure *cis*-isomers according to their NMR spectra. *cis*-**37**: Colorless plates (from AcOEt–isopropyl ether), mp 141—153°. NMR ($CDCl_3$) δ: 2.48 (3H, s, NMe), 4.63 (1H, d, J=3 Hz, >C<u>H</u>OH). *Anal.* Calcd. for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.30; H, 6.76; N, 3.93.

Methyl *cis*-2-Benzyloxy-6-*tert*-butylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*cis*-21)——A mixture of *cis*-**12** (165 mg) and sulfur trioxide-triethylamine (79 mg) in dry benzene (10 ml) was refluxed with stirring for 2 hr. After cooling, the arising precipitates was collected and recrystallized from CH_2Cl_2–benzene to obtain *cis*-**21** (135 mg, 68%) as colorless crystals, mp 220—222° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 1725, 1610, 1270, 1210. NMR (DMSO-d_6) δ: 5.34 (1H, d, J=3 Hz, >C<u>H</u>–OSO$_3^-$). *Anal.* Calcd. for $C_{23}H_{29}NO_7S$: C, 59.60; H, 6.31; N, 3.02. Found: C, 59.60; H, 6.31; N, 2.92.

Methyl *cis*-2-Benzyloxy-6-isopropylamino-5-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (*cis*-39)——A mixture of *cis*-**26** (210 mg) and sulfur trioxide-triethylamine (80 mg) in dry benzene (20 ml) was refluxed with stirring for 2 hr. After cooling, the arising crystals were filtered and washed with benzene and CH_2Cl_2, then dried to obtain *cis*-**39** (178 mg, 70%) as white crystals, mp 206—208° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 1720, 1600, 1280, 1270, 1220. NMR (DMSO-d_6) δ: 5.44 (1H, d, J=3 Hz, >C<u>H</u>–OSO$_3^-$). *Anal.* Calcd. for $C_{22}H_{27}NO_7S$: C, 58.78; H, 6.05; N, 3.12. Found: C, 58.38; H, 6.28; N, 2.89.

Hydrolysis of *cis*-21——A suspension of *cis*-**21** (65 mg) in dioxane (4 ml) and H_2O (10 ml) was heated at 90° for 2.5 hr. The reaction mixture was treated with aqueous Na_2CO_3 solution and extracted with AcOEt. The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4 and evaporated *in vacuo*. The residual oil (45 mg) which was crystallized on standing at room temperature, was consisted of *cis*-**12** (*ca.* 95%) and *trans*-**12** (*ca.* 5%) according to its NMR spectrum.

Hydrolysis of cis-39——A suspension of *cis*-**39** (100 mg) in H_2O (10 ml) and dioxane (2 ml) was heated at 45—50° for 30 min. The reaction mixture was worked up in a manner similar to that described above, yielding crude crystalline solid (91 mg, mp 112—113°) whose NMR spectrum revealed the presence of only *cis*-**26**.

Hydrolysis of *cis*-39 in $H_2{}^{18}O$——A suspension of *cis*-**39** (10 mg) in 0.25 ml of $H_2{}^{18}O$ (99.5% pure, from The Radiochemical Center, Amersham) and dry dioxane (0.1 ml) was heated in a sealed tube at 65° for 8 hr. The reaction mixture was worked up in a manner similar to that described above affording the crude product (6 mg). MS of this material *m/e*: 371 M^+ (^{18}O): 369 M^+ (^{16}O)=40: 1. Mass spectrum of ordinary *cis*-**26** *m/e*: 369 (M^+): 371 or 367 ($M^+ \pm 2$)=50: 1.

***trans*-2-*tert*-Butylamino-1-chloro-6-nitro-1,2,3,4-tetrahydronaphthalene Hydrochloride (*trans*-40)**——A mixture of **10** (108 mg) and ethanolic HCl (4 ml) in benzene (10 ml) was heated at 60—70° for 2 hr. The reaction mixture was evaporated to dryness *in vacuo*. The residue was recrystallized from MeOH–ether to give *trans*-**43** (79 mg, 56%) as colorless needles, mp 168—175° (dec.). IR ν_{max}^{KBr} cm^{-1}: 1590, 1525, 1350, 800, 730. NMR (DMSO-d_6) δ: 1.48 (9H, s, N-*tert*-Bu), 5.73 (1H, d, J=4 Hz, >C<u>H</u>–Cl), 7.0—7.2 (2H), 7.71 (1H, d, J=8 Hz). *Anal.* Calcd. for $C_{14}H_{20}Cl_2N_2O_2$: C, 52.67; H, 6.31; N, 8.78. Found: C, 52.50; H, 6.25; N, 8.96.

Hydrolysis of *trans*-43——A suspension of *trans*-**43** (50 mg) in water (10 ml) was heated at 90° for 15 hr. The reaction mixture was worked up in a manner similar to that described above. The crude amino alcohol containing a small amount of aziridine (**10**) was chromatographed on silica gel using $CHCl_3$–MeOH (10: 3) as an eluant to give amino alcohol (27 mg) which was consisted of only the *trans*-isomer (*trans*-**19**) according to its NMR spectrum.

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