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Syntheses of 1,2-N-Alkylimino-1,2,3,4-tetrahydronaphthalene Derivatives and Preparation of Ring Closed Analog of Salbutamol as a New β-Adrenoceptor Agent

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A method for preparing 5-substituted 2-tertiary-alkylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols was described. The method involves the preparation of 1-alkylamino-2-hydroxy-1,2,3,4-tetrahydronaphthalenes from 2-bromo-1-hydroxy derivatives *via* 1,2-epoxides followed by the transposition of 1-alkylamino and 2-hydroxy groups *via* the ring closure to 1,2-aziridines. Formation of the epoxides and aziridines and the reaction of epoxides with amines were examined in detail. The ring-opening reaction of epoxides was regioselective and the attacking position of a nucleophile was not affected by the electronic effects of substituents on the benzene ring. Cyclization into aziridine rings was best accomplished by the Wenker method using a sulfur trioxide-triethylamine adduct as the sulfating agent. Using our process, *trans*-2-*tert*-butylamino-6-hydroxy-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol (**70**) was synthesized as conformationally fixed analog of salbutamol.

Keywords——aziridine; tetrahydronaphthalene; β_2-stimulant; epoxide; 2-alkylamino-1-tetralol; Wenker method

Subclassification of β-adrenoceptors into β_1- and β_2-types, proposed by Lands and his associates,[2] has been supported by recent findings of agonists or antagonists having selectivity for β_1- or β_2-type adrenoceptors. Study of the structure activity relationship shows that the presence of a lipophilic bulky group attached to the amino group in the catecholamine molecule seems to be one of the important factors in selectivity for the β_2-adrenoceptor.[3] In previous papers,[4–6] we reported several methods for synthesizing 5-substituted 2-alkylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols which possess potent β_2-stimulating activity *in vitro*. The methods involved reductive alkylation of 2-amino-1,2,3,4-tetrahydro-1-naphthalenols or 2-amino-3,4-dihydro-1(2*H*)-naphthalenones with ketones or aldehydes using lithium cyanoborohydride as a reducing agent. However, a tertiary alkyl substituent was unable to be introduced to the amino group by this method. This paper reports the synthesis of 5-substituted 2-*tert*-butylamino-6-hydroxy-1,2,3,4-tetrahydro-1-naphthalenols which are expected to have an increased selectivity for the β_2-adrenoceptor.

1) Location: *Juso-honmachi, Yodogawa-ku, Osaka 532, Japan.*
2) *a*) A.M. Lands, A. Arnold, J.P. McAuliff, F.P. Luduena, and T.G. Brown, Jr., *Nature* (London), **214**, 597 (1967); *b*) A.M. Lands, F.P. Luduena, and H.J. Buzzo, *Life Sci.*, **6**, 2241 (1967).
3) R.T. Brittain, D. Jack, and A.C. Ritchie, *Adv. Drug Res.*, **5**, 197 (1970).
4) *a*) M. Nishikawa, M. Kanno, H. Kuriki, H. Sigihara, M. Motohashi, K. Itoh, O. Miyashita, Y. Oka, and Y. Sanno, *Life Sci.*, **16**, 305 (1975); *b*) Y. Oka, M. Motohashi, H. Sugihara, O. Miyashita, K. Itoh, M. Nishikawa, and S. Yurugi, *Chem. Pharm. Bull.* (Tokyo), **25**, 632 (1977); *c*) K. Itoh, M. Motohashi, H. Kuriki, H. Sugihara, N. Inatomi, M. Nishikawa, and Y. Oka, *Chem. Pharm. Bull.* (Tokyo), **25**, 3289 (1977).
5) H. Sugihara, K. Ukawa, H. Kuriki, M. Nishikawa, and Y. Sanno, *Chem. Pharm. Bull.* (Tokyo), **25**, 2988 (1977).
6) *a*) A. Miyake, N. Tada, H. Kuriki, Y. Oka, and M. Nishikawa, *Chem. Pharm. Bull.* (Tokyo), **25**, 3066 (1977); *b*) A. Miyake, K. Itoh, H. Kuriki, Y. Oka, and M. Nishikawa, *ibid.*, **25**, 3289 (1977).

We examined a synthetic route of 2-*tert*-butylamino derivatives from the 1,2-epoxide of a tetraline. Conventional reduction of various substituted 3,4-dihydro-1(2*H*)-naphthalenones[4–8] with sodium borohydride gave 1,2,3,4-tetrahydro-1-naphthalenols (**1**—**8**) in 75—95% yields (Table I). Dehydration of **1**—**8** with potassium bisulfate in benzene afforded the corresponding 1,2-dihydro-naphthalenes (**9**—**16**) in good yields (Table II). But an attempt at direct epoxidation of 7,8-dimethoxy-1,2-dihydronaphthalene (**13**) with *m*-chloroperbenzoic acid resulted in cleavage of the epoxide ring to give the 1-*m*-chlorobenzoyloxy-2-hydroxy derivative. *trans*-α-Bromohydrin is considered preferable for the formation of epoxide.

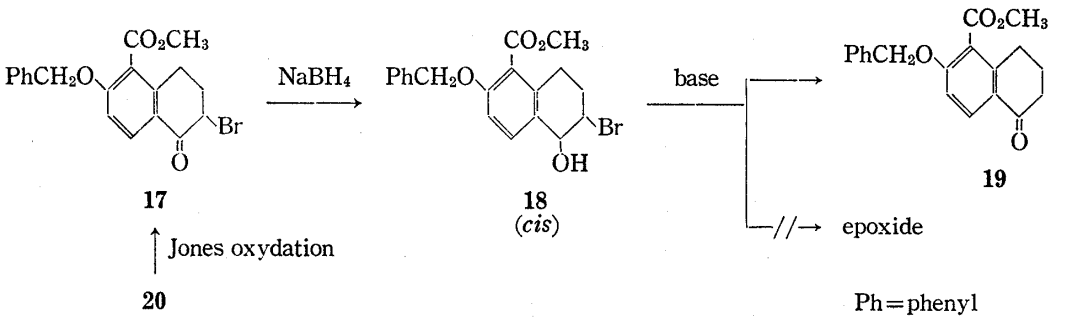
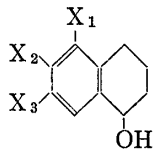


Chart 1

Table I. 1,2,3,4-Tetrahydro-1-naphthalenols (**1**—**8**)

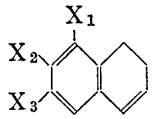


Compound	X_1	X_2	X_3	Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. (Found) C	H	N
1	CO_2CH_3	OCH_2Ph	H	95[a]	Oil		$C_{19}H_{20}O_4$	73.06 (72.82)	6.45 (6.31)	
2	CN	OCH_2Ph	H	75[a]	123—124	Benzene–*n*-hexane	$C_{18}H_{17}NO_2$	77.39 (77.09)	6.13 (6.24)	5.01 (4.71)
3	H	NO_2	H	80[b]	Oil		$C_{10}H_{11}NO_3$	62.01 (62.39)	5.74 (5.59)	7.25 (7.01)
4	OCH_2Ph	OCH_2Ph	H	83[c]	84— 86	Benzene–petr. ether	$C_{24}H_{24}O_3$	79.97 (79.60)	6.71 (6.70)	
5	OCH_3	OCH_3	H	95[d]	74— 76	Benzene–petr. ether	$C_{12}H_{16}O_3$	69.21 (69.13)	7.74 (7.62)	
6	NO_2	OCH_2Ph	H	95[e]	73— 75	Benzene–ether	$C_{17}H_{17}NO_4$	68.21 (68.33)	5.73 (5.75)	4.68 (4.42)
7	CH_3 | $N-CH_2Ph$	OCH_2Ph	H	83[e]	Oil		$C_{25}H_{27}NO_2$	80.36 (80.41)	7.29 (7.05)	3.75 (3.63)
8	H	OCH_2Ph	NO_2	93[e]	123—124	Benzene	$C_{17}H_{17}NO_4$	68.21 (68.44)	5.73 (5.51)	4.68 (4.65)

The starting 3,4-dihydro-1(2*H*)-naphthalenones were prepared by the method reported following literature; *a*) lit. 5, *b*) lit. 7, *c*) lit. 4, *d*) lit. 8, *e*) lit. 6.

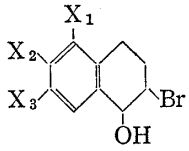
7) M. Tomita, S. Minami, and S. Ueo, *J. Chem. Soc.*, **1969**, 183.
8) W.K. Sprenger, J.G. Cannon, and B.K. Barman, *J. Med. Chem.*, **12**, 487 (1969).

Table II. 1,2-Dihydronaphthalenes (**9**—**16**)

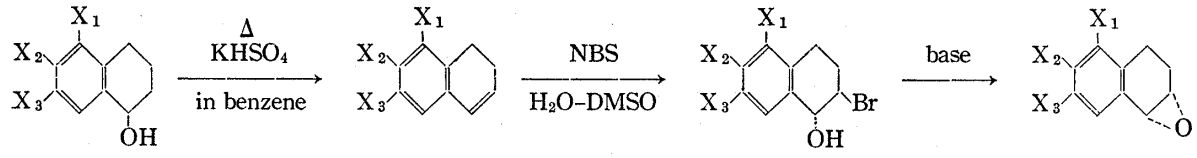


Compd.	X_1	X_2	X_3	Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. (Found) C	H	N
9	CO_2CH_3	OCH_2Ph	H	78	100—101	MeOH	$C_{19}H_{18}O_3$	77.53 (77.34)	6.16 (6.01)	
10	CN	OCH_2Ph	H	70	90—100	EtOH	$C_{18}H_{15}NO$	82.73 (82.53)	5.79 (5.84)	5.36 (4.97)
11	H	NO_2	H	88	47— 48	*n*-Hexane	$C_{10}H_9NO_2$	68.56 (68.64)	5.18 (4.97)	8.00 (8.07)
12	OCH_2Ph	OCH_2Ph	H	90	67— 69	MeOH	$C_{24}H_{22}O_2$	84.17 (83.81)	6.47 (6.46)	
13	OCH_3	OCH_3	H	99	38— 39	Benzene–petr. ether	$C_{12}H_{14}O_2$	75.76 (75.51)	7.42 (7.25)	
14	NO_2	OCH_2Ph	H	80	79— 81	Benzene–petr. ether	$C_{17}H_{15}NO_3$	72.58 (72.75)	5.37 (5.43)	4.98 (4.73)
15	CH_3 | $N-CH_2Ph$	OCH_2Ph	H	66	Oil		$C_{25}H_{25}NO$	84.47 (84.36)	7.09 (7.14)	3.94 (3.68)
16	H	OCH_2Ph	NO_2	87	121—122	MeOH–acetone	$C_{17}H_{15}NO_3$	72.58 (72.30)	5.37 (5.40)	4.98 (4.88)

Table III. *trans*-2-Bromo-1,2,3,4-tetrahydro-1-naphthalenols (**20**—**27**)



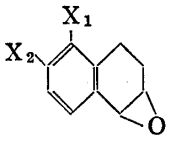
Compd.	X_1	X_2	X_3	Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. (Found) C	H	N
20	CO_2CH_3	OCH_2Ph	H	83	124—125	Benzene–*n*-hexane	$C_{19}H_{19}BrO_4$	58.32 (58.24)	4.89 (4.59)	
21	CN	OCH_2Ph	H	74	123—124	Benzene–*n*-hexane	$C_{18}H_{16}BrNO_2$	60.35 (60.65)	4.50 (4.21)	3.91 (3.73)
22	H	NO_2	H	94	146—148	MeOH	$C_{10}H_{10}BrNO_3$	44.14 (44.19)	3.70 (3.64)	5.15 (5.03)
23	OCH_2Ph	OCH_2Ph	H	69	90— 93	Ether–petr. ether	$C_{24}H_{23}BrO_3$	65.61 (65.80)	5.28 (5.30)	
24	OCH_3	OCH_3	H	66	98—101	Ether–petr. ether	$C_{12}H_{15}BrO_3$	50.18 (50.04)	5.26 (5.22)	
25	NO_2	OCH_2Ph	H	85	103—105	MeOH	$C_{17}H_{16}BrNO_4$	53.98 (53.71)	4.26 (4.38)	3.70 (3.56)
26	CH_3 | $N-CH_2Ph$	OCH_2Ph	H	96	Oil		$C_{25}H_{26}BrNO_2$	66.37 (66.11)	5.79 (5.60)	3.10 (3.34)
27	H	OCH_2Ph	NO_2	75	Oil		$C_{17}H_{16}BrNO_4$	53.98 (53.76)	4.26 (4.02)	3.70 (3.62)



1—8 (Table I) **9—16** (Table II) **20—27** (*trans*) (Table III) **28—30** (Table IV)

Chart 2

TABLE IV. 1,2-Epoxy-1,2,3,4-tetrahydronaphthalenes (**28—30**)



Compd.	X_1	X_2	Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. (Found) C	H	N
28	CO_2CH_3	OCH_2Ph	83	135—136	Benzene–*n*-hexane	$C_{19}H_{18}O_4$	73.53 (73.47)	5.85 (5.89)	
29	CN	OCH_2Ph	84	158—159	Benzene–*n*-hexane	$C_{18}H_{15}NO_2$	77.96 (77.58)	5.45 (5.46)	5.05 (4.83)
30	H	NO_2	98	42	Ether–*n*-hexane	$C_{10}H_9NO_3$	62.82 (62.97)	4.75 (4.82)	7.33 (7.33)

According to the method of Dalton *et al.*,[9] the *trans*-bromohydrin (**20**) was prepared in good yield by treating the corresponding dihydronaphthalene (**9**) with N-bromosuccinimide in dimethylsulfoxide containing a small amount of water. The structure of **20** was confirmed as followed. Jones oxidation of **20** gave **17** in 86% yield, and a doublet peak at 4.69 ppm due to >CHOH in the nuclear magnetic resonance (NMR) spectrum of **20** indicated a *trans* (J=7 Hz) configuration. But treatment of 1,2-bromohydrin (**18**), obtained from its keto derivative (**17**) by sodium borohydride reduction, with a base gave only **19** (Chart 1). The NMR spectrum of **18** showed that the adjacent hydroxy and bromo groups were *cis* (J=2 Hz). Dehydrohalogenation of **20—22** with powdered sodium hydroxide in benzene gave the *cis* epoxides[10] (**28—30**) as stable crystals (Table IV).

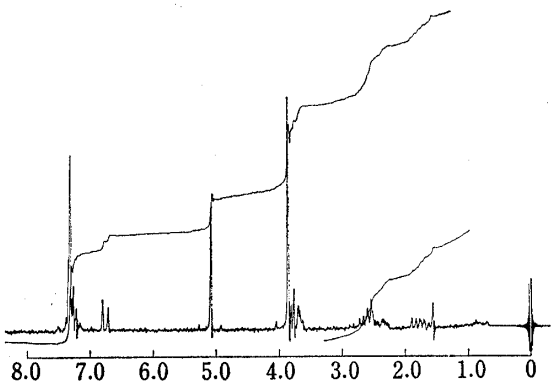


Fig. 1. NMR Spectrum of the Epoxide **38** in $CDCl_3$ (100 MHz)

Then, we treated the epoxides (**28—30**) or their precursors, *trans*-2-bromo-1,2,3,4-tetrahydro-1-naphthalenols (**20—27**), with some amines (*tert*-butylamine, isopropylamine, ethyl-

9) D.R. Dalton, V.P. Dutta, and D.C. Jones, *J. Am. Chem. Soc.*, **90**, 5498 (1968).
10) A. Rosowsky, "Chemistry of Heterocyclic Compounds," Vol. 19, part 1, ed. by A. Weissberger, John Wiley and Sons, Inc., New York, N.Y., 1964, p. 94.

amine, methylamine, and phenethylamine) and obtained amino alcohols[11,12] (**31**—**47**). Amino alcohol **32** obtained by the reaction of **28** with isopropylamine, differed from both *cis*- and *trans*-1-hydroxy-2-isopropylamino derivatives (**48** and **49**) obtained in the previous study[5] and its NMR spectrum showed no characteristic doublet due to a proton (Ph–CHOH) in the 4—5 ppm range indicating that the ring-opening took place at C_1 to give 1-amino-2-alcohol derivative in this reaction. Reaction of the epoxides with amines proceeded rapidly in a protic solvent. In contrast, in an aprotic solvent, the reaction retarded: the reaction of **28** with methylamine in aqueous methanol proceeded at room temperature for 10 hr to give the amino alcohol (**34**) in 86% yield. On the other hand, the reaction with dry methylamine in anhydrous acetonitile in a sealed tube at 70° for 10 hr resulted in recovery (40%) of the starting material and 45% yield of the ring-opening product (**34**). These results, *i.e.*, selective ring opening of the benzylic C–O bond together with the solvent dependency of reactivity, shows that the reaction proceeds through S_{N1} type process. Therefore, the amino alcohol obtained may be a stereochemical mixture. The configuration was ascribed to be *trans* on the basis of the results that the amino alcohol (**31**—**47**) could be converted into aziridines as described subsequently and the NMR spectrum of **33** showed a doublet peak (J=8 Hz) of the benzylic proton (Ph–CHNHEt–CHOH) at 3.51 ppm. Nucleophilic ring-opening position of stylene oxide is reportedly affected by both electronic effect of the substituent of the benzene ring and steric hindrance around the epoxy group.[13] Thus, we examined the possibility of S_{N2} type reaction by using 1,2-epoxy-6-nitro-1,2,3,4-tetrahydronaphthalene (**30**) which bears a strong electron-withdrawing group at the *p*-position. The reaction of **30** with *tert*-butylamine was retarded and gave 1-*tert*-butylamino-6-nitro-1,2,3,4-tetrahydro-2-naphthalenol (**36**, 60%) as the main product and a little (1.5%) *trans*-2-*tert*-butylamino-6-nitro-1,2,3,4-tetrahydro-1-naphthalenol (**50**), whose structure was assigned on the basis of the result of its NMR spectrum [4.89 ppm (1H, doublet, J=9 Hz, Ph–CHOH–)]. The reaction of *p*-nitrostylene oxide derivatives with amine (*tert*-butylamine or isopropylamine) has been reported to give only 2-alkylamino-1-phenylethanol derivatives.[14] These results show that in the case of 1,2-epoxy-1,2,3,4-tetrahydronaphthalenes, in contrast to stylene oxides,[13,14] the attack-

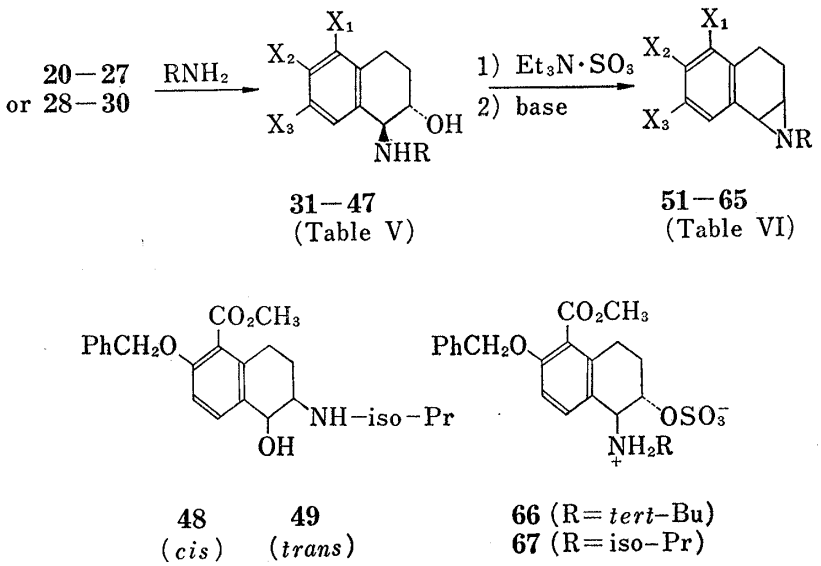
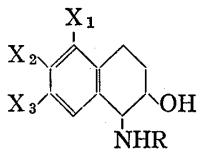


Chart 3

11) F. Straus and A. Rohrbacher, *Chem. Ber.*, **54**, 40 (1921).
12) J.V. Braun and K. Weissbach, *Chem. Ber.*, **63**, 3052 (1930).
13) R.E. Parker and N.S. Isaacs, *Chem. Rev.*, **59**, 737 (1959).
14) S.J. Pasaribu and L.R. Williams, *Aust. J. Chem.*, **28**, 1023 (1975).

ing position of the nucleophile is at benzylic position independently of the substituent on the benzene ring (regioselective).

TABLE V. *trans*-1-Alkylamino-1,2,3,4-tetrahydro-1-naphthalenols (**31**—**47**)



Compd.	X_1	X_2	X_3	R	Salt	Yield[a] (%)	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N
31	CO_2CH_3	OCH_2Ph	H	*t*-Bu	HCl	85	235—236	$C_{23}H_{30}ClNO_4$	65.78 (65.52)	7.20 (7.21)	3.34 (3.39)
32	CO_2CH_3	OCH_2Ph	H	iso-Pr	Base	80	123—125	$C_{22}H_{27}NO_4$	71.75 (71.43)	7.37 (7.33)	3.79 (3.67)
33	CO_2CH_3	OCH_2Ph	H	Et	HCl	73	162—164	$C_{21}H_{26}ClNO_4$	64.36 (64.43)	6.69 (6.60)	3.57 (3.41)
34	CO_2CH_3	OCH_2Ph	H	Me	HCl	86	217—219	$C_{20}H_{24}ClNO_4$	63.57 (63.52)	6.40 (6.39)	3.71 (3.98)
35	CN	OCH_2Ph	H	*t*-Bu	Base	61	115—116	$C_{22}H_{26}N_2O_2$	75.40 (75.55)	7.48 (7.54)	7.99 (7.94)
36	H	NO_2	H	*t*-Bu	HCl	60	230—235	$C_{14}H_{21}ClN_2O_3$	55.90 (55.91)	7.04 (6.99)	9.31 (9.40)
37[b]	H	H	H	*t*-Bu	Base	60	106—108	$C_{14}H_{21}NO$	76.60 (76.52)	9.65 (9.43)	6.39 (6.51)
38	OCH_2Ph	OCH_2Ph	H	*t*-Bu	HCl	37	203—204	$C_{28}H_{34}ClNO_3$	71.85 (71.77)	7.32 (7.39)	2.99 (3.00)
39	OCH_2Ph	OCH_2Ph	H		Fumalate	49	153—155	$C_{29}H_{31}NO_5$	73.24 (73.39)	7.00 (6.81)	2.95 (2.84)
40	OCH_3	OCH_3	H	*t*-Bu	HCl	57	209—210	$C_{16}H_{26}ClNO_3$	60.85 (61.07)	8.30 (8.28)	4.44 (4.34)
41	OCH_3	OCH_3	H	iso-Pr	HCl	57	195—198	$C_{15}H_{24}ClNO_3$	59.69 (59.29)	8.02 (8.01)	4.64 (4.48)
42	OCH_3	OCH_3	H		HCl	21	206—208	$C_{18}H_{28}ClNO_3$	63.23 (63.01)	8.26 (8.30)	4.10 (4.07)
43	OCH_3	OCH_2	H	CH_2-CH_2Ph	HCl	32	223—225	$C_{20}H_{26}ClNO_3$	66.01 (65.88)	7.20 (7.30)	3.85 (3.86)
44	NO_2	OCH_2Ph	H	*t*-Bu	HCl	84	245—248	$C_{21}H_{27}ClN_2O_4$	61.98 (61.81)	6.69 (6.66)	6.89 (6.64)
45	CH_3 | $N-CH_2Ph$ | CH_3	OCH_2Ph	H	*t*-Bu	Oxalate	56	186—188	$C_{31}H_{38}N_2O_6$	69.21 (69.33)	6.97 (6.95)	5.38 (5.08)
46	CH_3 | $N-CH_2Ph$ | CH_3	OCH_2Ph	H	iso-Pr	Oxalate	85	156—157	$C_{30}H_{36}N_2O_6$	68.75 (68.44)	6.77 (6.89)	5.53 (5.60)
47	H	OCH_2Ph	NO_2	*t*-Bu	Oxalate	74	208—210	$C_{23}H_{28}N_2O_8$	59.99 (59.62)	6.13 (5.87)	6.08 (5.94)

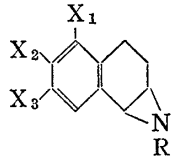
a) **31**—**37** and **38**—**47** were prepared from their corresponding epoxide and bromohydrine derivatives, respectively.
b) The precursor (epoxide) of **37** was prepared according to the method described by Straus and Rohrbacher.[11]

Thus to synthesize 2-alkylamino-1,2,3,4-tetrahydro-1-naphthalenols from **31**—**47**, the alkylamino and hydroxy groups must be transposed. This was achieved by hydrolytic cleavage of aziridine (**51**) prepared from **31**. Aziridine derivatives are usually prepared from β-amino alcohols by the Gabriel or Wenker methods.[15] Recently, an improved Gabriel method

15) P.E. Fanta, "Chemistry of Heterocyclic Compounds," Vol. 19, part 1, ed. by A. Weissberger, John Wiley and Sons, Inc., New York, N.Y., 1964, p. 524.

using triphenylphosphine dibromide has been reported by Okada *et al.*[16] We examined a synthetic method of aziridines from the 1-alkylamino-1,2,3,4-tetrahydro-2-naphthalenol (**31**—**47**) and obtained good result by the Wenker method using a sulfur trioxide-triethyl-

Table VI. 1,2-Alkylimino-1,2,3,4-tetrahydronaphthalenes (**51**—**65**)



Compd.	X_1	X_2	X_3	R	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N
51	CO_2CH_3	OCH_2Ph	H	*t*-Bu	91	78— 80	$C_{23}H_{27}NO_3$	75.59 (75.31)	7.45 (7.59)	3.83 (3.58)
52	CO_2CH_3	OCH_2Ph	H	iso-Pr	52	103	$C_{22}H_{25}NO_3$	75.18 (75.32)	7.17 (7.29)	3.99 (3.81)
53	CO_2CH_3	OCH_2Ph	H	Et	23	Oil	$C_{21}H_{23}NO_3$	MS *m/e*: 337 (M^+)		
54	CO_2CH_3	OCH_2Ph	H	Me	8	Oil	$C_{20}H_{21}NO_3$	MS *m/e*: 323 (M^+)		
55	CN	OCH_2Ph	H	*t*-Bu	85	114—115	$C_{22}H_{24}N_2O$	79.48 (79.63)	7.28 (6.90)	8.43 (8.27)
56	H	NO_2	H	*t*-Bu	83	70— 75	$C_{14}H_{18}N_2O_2$	68.27 (68.32)	7.37 (7.17)	11.37 (11.40)
57	H	H	H	*t*-Bu	75	Oil	$C_{14}H_{19}N$	MS *m/e*: 201 (M^+)		
58	OCH_2Ph	OCH_2Ph	H	*t*-Bu	81	Oil	$C_{28}H_{31}NO_2$	MS *m/e*: 413 (M^+)		
59	OCH_3	OCH_3	H	*t*-Bu	49	Oil	$C_{16}H_{23}NO_2$	MS *m/e*: 261 (M^+)		
60	OCH_3	OCH_3	H	iso-Pr	37	Oil	$C_{15}H_{21}NO_2$	MS *m/e*: 247 (M^+)		
61	OCH_3	OCH_3	H	*cyclo*-Hex	60	Oil	$C_{18}H_{25}NO_2$	MS *m/e*: 287 (M^+)		
62	NO_2	OCH_2Ph	H	*t*-Bu	81	115—117	$C_{21}H_{24}N_2O_3$	71.57 (71.36)	6.86 (6.67)	7.95 (7.77)
63	CH_3 | $N-CH_2Ph$	OCH_2Ph	H	*t*-Bu	73	Oil	$C_{29}H_{34}N_2O$	MS *m/e*: 426 (M^+)		
64	CH_3 | $N-CH_2Ph$	OCH_2Ph	H	iso-Pr	70	Oil	$C_{28}H_{32}N_2O$	MS *m/e*: 412 (M^+)		
65	H	OCH_2Ph	NO_2	*t*-Bu	75	Oil	$C_{21}H_{24}N_2O_3$	MS *m/e*: 352 (M^+)		

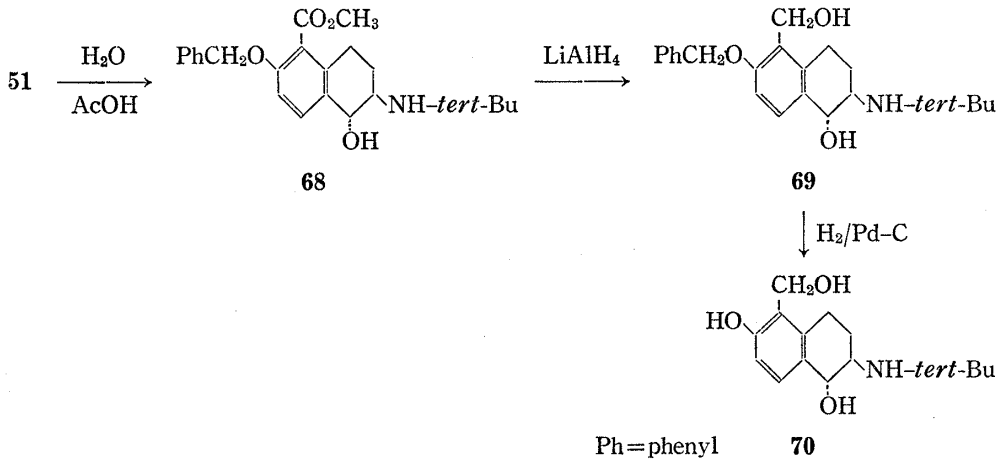


Chart 4

16) I. Okada, K. Ichimura, and R. Sudo, *Bull. Chem. Soc. Japan*, **43**, 1185 (1970).

amine adduct, a mild sulfating agent.[17] The reaction of **31** with a sulfur trioxide-triethylamine adduct in boiling benzene was carried out under monitoring with thin-layer chromatography (TLC). The starting amino alcohol (**31**) disappeared within 4—6 hr and an only spot presumably due to the sulfate ester appeared. On treatment of the reaction mixture with a base, 1,2-N-*tert*-butylimino derivative (**51**) was isolated in 91% yield as crystals (mp 78—80°). The structure of **51** was confirmed by elementary analysis and spectroscopy. Its infrared (IR) spectrum shows neither the NH nor OH stretching band (3500—3000 cm^{-1}). The NMR spectrum (Fig. 2) had a multiplet at 2—3 ppm assignable to the aziridine ring. Table VI lists the 1,2-N-alkylimino-1,2,3,4-tetrahydronaphthalenes (**51—65**) prepared by the Wenker method. Their yields were largely affected by steric bulkiness of the alkylamino groups; bulky *tert*-butylamino derivatives gave about 80—90% yields of aziridines, isopropylamino derivatives about 50%, the ethylamino derivative (**33**) 25% and the methylamino derivative (**34**) 8%. High yields with bulky alkylamino derivatives may be due to the lower chance of sulfation of the alkylamino group in the initial step and an increased population of the *trans*-diaxial conformation of nucleophilic amino and leaving sulfate groups in an activated state. The yield with the isopropylamino derivative (**32**) was improved from 50 to 75% by using chlorosulfonic acid. 2-Hydroxysulfonyloxy compounds **66** and **67** were isolated as reaction intermediates on sulfation of **31** with sulfur trioxide-triethylamine or of **32** with chlorosulfonic acid, respectively.

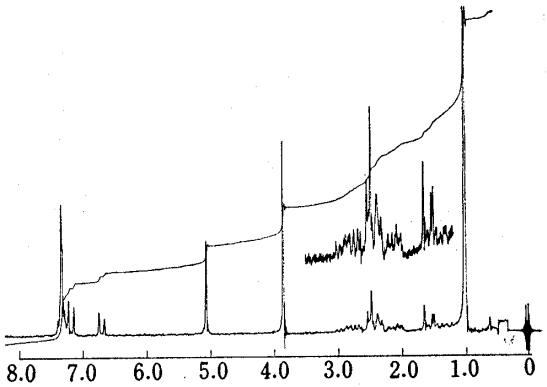


Fig. 2. NMR Spectrum of the Aziridine **51** in $CDCl_3$ (100 MHz).

Hydrolytic cleavage of the aziridine ring in **51** with acid afforded the 2-*tert*-butylamino-1-hydroxy derivative (**68**). The use of sulfuric acid as a catalyst of the hydrolysis gave a mixture of two products. The NMR spectrum of this crude hydrochloride showed two peaks at 4.67 ppm (doublet, $J=9$ Hz) and 4.79 ppm (doublet, $J=3$ Hz) in a 1:1 ratio assignable to the benzylic protons (Ph–CHOH–CHNH–*t*–Bu) of *trans*- and *cis*-amino alcohols, respectively. On the other hand, the use of acetic acid afforded the *trans*-amino alcohol, exclusively. The methoxycarbonyl group of **68** (*trans*-isomer) was reduced to a hydroxymethyl group with lithium aluminum hydride to afford **69**. Removal of the benzyl group by catalytic hydrogenation using 5% palladium charcoal afforded *trans*-2-*tert*-butylamino-6-hydroxy-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol (**70**) as a fixed analog of salbutamol.

The β_2-stimulating activity of **70** was evaluated *in vitro* using guinea-pig tracheal strips. In the case of straight-chain related analogs, *tert*-butyl substitution of the side-chain amino group caused more potency and selectivity for the tracheal muscle.[3,18] But in our 1,2,3,4-tetrahydronaphthalene system, **70** showed less β_2-stimulating activity than the corresponding isopropylamino derivative reported in the previous paper.[5]

Experimental[19]

Methyl *cis*-2-Benzyloxy-6-bromo-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate (**18**)——To a solution of methyl 2-benzyloxy-6-bromo-5-oxo-5,6,7,8-tetrahydro-1-naphthoate (**17**, 3.5 g) in isopropanol (30 ml) and

17) W.B. Hardy and M. Scalera, *J. Am. Chem. Soc.*, **74**, 5212 (1952).
18) C. Kaiser, D.F. Colera, M.S. Schwartz, E. Garvey, and J.R. Wardell, Jr., *J. Med. Chem.*, **17**, 49 (1974).
19) 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 (MS) were taken with a JEOL JMS-01SC spectrometer.

THF (10 ml), was added $NaBH_4$ (350 mg) at room temperature with stirring. After stirring for another 2 hr, the reaction mixture was poured into water. The resulting precipitate was collected by filtration, washed with water and recrystallized from MeOH to give **18** (3.0 g, 86%) as colorless needles, mp 128—129°. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1730 (CO_2CH_3). NMR (DMSO-d_6–D_2O) δ: 2.1—2.4 (2H, m, $-CH_2-$), 2.6—2.9 (2H, m, $-CH_2-$), 3.82 (3H, s, CO_2CH_3), 4.5—4.7 (1H, m, >C<u>H</u>–Br), 4.68 (1H, d, J=2 Hz, >C<u>H</u>–OH), 5.04 (2H, s, OCH_2Ph), 7.04 (1H, d, J=8 Hz, 3-H), 7.2—7.35 (6H, m). *Anal.* Calcd. for $C_{19}H_{19}BrO_4$: C, 58.32; H, 4.89. Found: C, 58.30; H, 4.85.

Reaction of 18 with Base——A mixture of **18** (200 mg), anhydrous K_2CO_3 (600 mg) and triethylamine (2 ml) in benzene (10 ml) was refluxed for 2 hr. After removal of insoluble materials by filtration, the filtrate was evaporated to dryness *in vacuo* to give methyl 2-benzyloxy-5-oxo-5,6,7,8-tetrahydro-1-naphthoate (**19**), (103 mg, 65%) which was identified by comparing its IR spectrum with that of the authentic sample.[2]

1,2,3,4-Tetrahydro-1-naphthalenols (1—8)——To an ice-cooled solution of 3,4-dihydro-1(2*H*)-naphthalenone (10 g) in MeOH (100 ml) was added $NaBH_4$ (*ca.* 1.0 g) in small portions with stirring for 1 hr, the reaction mixture was concentrated to *ca.* 20 ml *in vacuo*, poured into ice-water and extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4 and evaporated to dryness *in vacuo* to give **1—8** (Table I).

Methyl 2-Benzyloxy-7,8-dihydro-1-naphthoate (9)——A mixture of **1** (10 g) and potassium bisulfate (1.0 g) in benzene (100 ml) was refluxed for 2 hr under continuous removal of water. The cooled reaction mixture was washed with water, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from MeOH to give **9** as colorless needles. IR ν_{max}^{KBr} cm^{-1}: 1720 (CO_2CH_3), 1480, 1270, 1238, 1135, 1065, 825, 730. NMR ($CDCl_3$) δ: 2.2—2.5 (2H, br, $-CH_2-$), 2.5—3.0 (2H, m, $-CH_2-$), 3.90 (CO_2CH_3), 5.10 (2H, s, OCH_2Ph), 5.75 (1H, m, 7-H), 6.40 (1H, d, J=9 Hz, 8-H), 6.70 (1H, d, J=9 Hz), 6.90 (1H, d, J=9 Hz), 7.2—7.5 (5H). Similar dehydration of **2—8** gave **10—16** (Table II).

Methyl *trans*-2-Benzyloxy-6-bromo-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate (20)——To a solution of **9** (10 g) in DMSO (100 ml) and water (5 ml) was added N-bromosuccinimide (7.0 g) with stirring at 15—20°. After stirring for 1 hr, the reaction mixture was poured into ice-water. The resulting precipitate was collected by filtration, washed with water and recrystallized from benzene–*n*-hexane to give **20** as colorless needles. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1725 (CO_2CH_3), 1285, 1265, 1140, 1090, 985, 820, 735. NMR ($CDCl_3$) δ: 2.0—2.5 (2H, br, $-CH_2-$), 2.6—2.9 (2H, broad t, $-CH_2-$), 3.90 (3H, s, CO_2CH_3), 4.05—4.30 (1H, m >C<u>H</u>–Br), 4.70 (1H, d, J=7 Hz, >C<u>H</u>–OH), 5.00 (2H, s, OCH_2Ph), 6.75 (1H, d, J=8 Hz, 3-H), 7.1—7.5 (6H). Similar reactions of **10—16** gave **21—27** (Table III).

Jones Oxidation of 20——To a solution of **20** (200 mg) in acetone (15 ml) was added Jones reagent (0.3 ml) at room temperature. The reaction mixture was stirred for 30 min. After addition of MeOH (1 ml), the mixture was filtered and the filtrate was evaporated to dryness *in vacuo*. The solution of the residue in benzene was washed with water, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from ether–*n*-hexane to give methyl 2-benzyloxy-6-bromo-5-oxo-5,6,7,8-tetrahydro-1-naphthoate (**17**, 168 mg, 85%), which was identified by comparing its IR spectrum with that of an authentic sample.[5]

Methyl 2-Benzyloxy-5,6-epoxy-5,6,7,8-tetrahydro-1-naphthoate (28)——A mixture of **20** (10 g) and powdered NaOH (8 g) in benzene (100 ml) was stirred at room temperature for 5 hr, then filtered. The filtrate was washed with aqueous $NaHCO_3$, dried over anhydrous K_2CO_3 and evaporated to dryness *in vacuo*. The residue was recrystallized from benzene–*n*-hexane to give **28** as colorless plates. IR ν_{max}^{KBr} cm^{-1}: 1725 (CO_2CH_3), 1275, 1240, 1160, 825, 740. Similar treatment of **21** and **22** gave **29** and **30**, respectively (Table IV).

Methyl *trans*-2-Benzyloxy-5-tert-butylamino-6-hydroxy-5,6,7,8-tetrahydro-1-naphthoate (31)——a) A mixture of **20** (1.0 g) and *tert*-butylamine (2 ml) in MeOH (10 ml) was heated at 60—65° for 15 hr, then evaporated to dryness *in vacuo*. The solution of residue in AcOEt was washed with water, dried over Na_2SO_4 and concentrated to *ca.* 20 ml. The residual solution was treated with ethanolic HCl and the resulting precipitate, collected by filtration, was recrystallized from MeOH–ether to give **31** (863 mg, 60%) as the hydrochloride. IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 3000—2000, 1730 (CO_2CH_3), 1600, 1590, 1275, 1140. NMR (DMSO-d_6) δ: 1.47 (9H, s, N-*t*-Bu), 3.80 (3H, s, CO_2CH_3), 4.2—4.4 (2H, br, $-C\underline{H}NHR-C\underline{H}OH-$), 5.17 (2H, s, OCH_2Ph), 7.04 (1H, d, J=9 Hz), 7.2—7.4 (6H). Free base (oil). IR ν_{max}^{Film} cm^{-1}: 3550—3300 (OH, NH), 1720 (CO_2CH_3). NMR ($CDCl_3$) δ: 1.15 (9H, s, N-*t*-Bu), 1.5—2.0 (2H, m, $-CH_2-$), 2.2—2.4 (2H, m, $-CH_2-$), 3.5—3.7 (2H, m, $-C\underline{H}NHR-C\underline{H}OH-$), 3.81 (3H, s, CO_2CH_3), 5.01 (2H, s, OCH_2Ph), 6.72 (1H, d, J=8 Hz), 7.1—7.4 (6H). b) A mixture of **28** (1.0 g) and *tert*-butylamine (2 ml) in MeOH (10 ml) was heated at 60—65° for 15 hr, then worked up in a manner similar to that described in a. Yield 1.147 g (85%). c) A mixture of **28** (1.0 g) and *tert*-butylamine (2 ml) in MeOH (10 ml) and water (2 ml) was stirred at room temperature for 10 days, then worked up in a similar manner. Yield 743 mg (55%). Compounds **32—35** and **37** were prepared from their corresponding epoxides using methods similar to that described in b. Compounds **38—47** were prepared from **23—27** as described in a. Table V lists the *trans*-1-alkylamino-1,2,3,4-tetrahydro-2-naphthalenols obtained and their physical properties.

Reaction of 1,2-Epoxy-6-nitro-1,2,3,4-tetrahydronaphthalene (30) with *tert*-Butylamine——A mixture of **30** (2.0 g) and *tert*-butylamine (5 ml) in MeOH (5 ml) was refluxed for 20 hr, then evaporated to dryness *in vacuo*. The residue was purified by column chromatography on silica gel using $CHCl_3$–MeOH (5:1) as

an eluant. The first eluate was evaporated to dryness *in vacuo*. The residue was dissolved in EtOH and treated with ethanolic HCl. The hydrochloride separated was collected by filtration and recrystallized from EtOH to give **36** (1.9 g, 60%) as colorless prisms. IR ν_{max}^{KBr} cm^{-1}: 1585, 1530, 1200, 1100, 1060. NMR (DMSO-d_6-D_2O) δ: 1.59 (9H, s, N-*t*-Bu), 1.6—3.0 (4H, m), 4.3—4.6 (2H, m, -CHNR-CHOH-), 7.59 (1H, d, J=9 Hz), 7.9—8.1 (2H, m). Similarly, the second eluate gave *trans*-2-*tert*-butylamino-6-nitro-1,2,3,4-tetrahydro-1-naphthalenol hydrochloride (**50**, 48 mg, 1.5%) as colorless prisms (from EtOH–ether), mp 257—262° (dec.). IR ν_{max}^{KBr} cm^{-1}: 1580, 1530, 1345, 1200, 1060. NMR (DMSO-d_6-D_2O) δ: 1.58 (9H, s, N-*t*-Bu), 2.0—3.6 (5H, m), 4.89 (1H, d, J=9 Hz, >CHOH), 7.96 (1H, d, J=9 Hz), 8.1—8.4 (2H). *Anal.* Calcd. for $C_{14}H_{21}ClN_2O_3$: C, 55.90; H, 7.04; N, 9.31. Found: C, 55.78; H, 7.12; N, 9.02.

Formation of Aziridines from *trans*-1-Alkylamino-1,2,3,4-tetrahydro-2-naphthalenols——a) To a mixture of **31** hydrochloride (322 mg) in benzene (20 ml) was added thionyl chloride (100 mg). The resulting homogeneous solution was heated at 60—65° for 1 hr and evaporated to dryness *in vacuo*. The residue was dissolved in CH_3CN (10 ml). Triethylamine (500 mg) was added to the solution which was heated at 60—65° for 1 hr, and then evaporated to dryness *in vacuo*. The residue was purified by column chromatography on silica gel using benzene as an eluant to give **51** (34 mg, 12%) as colorless needles (ether–petr. ether). IR ν_{max}^{KBr} cm^{-1}: 2950, 1720 (CO_2CH_3), 1590, 1260, 1140, 800, 740, 730. MS *m/e*: 365 (M^+), 350 (M^+-CH_3), 334 (M^+-OCH_3), 308 (M^+-t-Bu), 276, 274.

b) To an ice-cooled solution of triphenylphosphine (491 mg) in dry CH_3CN (10 ml) was added dropwise a solution of Br_2 (300 mg) in dry CH_3CN (2 ml). To the resulting mixture was added **35** (600 mg). After stirring for 15 min, a solution of triethylamine (400 mg) in dry CH_3CN (4 ml) was added. The reaction mixture was stirred at room temperature overnight, and then 5% Na_2CO_3 solution was added. The benzene extract of the mixture was washed with water, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. Chromatographic separation of the residue over silica gel using $CHCl_3$ as an eluant gave the starting material (220 mg, 37%) and **55** (230 mg, 41%) as colorless plates (from benzene–*n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 2950, 2230 (CN), 1590, 1485, 1450, 1285, 1220, 1100, 1090, 1070, 805, 745, 695. MS *m/e*: 332 (M^+).

c) A mixture of **31** (10.0 g) and sulfur trioxide-triethylamine adduct (14 g) in benzene (500 ml) was refluxed with stirring for 5 hr. Powdered NaOH (10 g) was added to the mixture. After heating at 85° with stirring for 4 hr, the reaction mixture was filtered. The filtrate was evaporated to dryness *in vacuo*. The residue was recrystallized from ether–petr. ether to give **51** as colorless needles. Compounds **52**—**65** were prepared from **32**—**38**, **40**—**42** or **44**—**47** using methods similar to that described in c (Table VI).

Methyl *trans*-2-Benzyloxy-5-*tert*-butylamino-6-hydroxysulfonyloxy-5,6,7,8-tetrahydro-1-naphthoate (66)——A mixture of **31** (1.1 g) and sulfur trioxide-triethylamine adduct (410 mg) in benzene (50 ml) was refluxed for 5 hr. The cooled reaction mixture was filtered. The residue on the filter was washed with CH_2Cl_2 and dried to give **66** (1.2 g, 90%) as a white powder, mp 225—227° (decomp. with foaming). IR ν_{max}^{KBr} cm^{-1}: 3500—3400, 3100—2500, 1730 (CO_2CH_3), 1610, 1600, 1280—1270, 1225, 1175. NMR (DMSO-d_6) δ: 1.47 (9H, s, N-*t*-Bu), 2.0—2.3 (2H, br, $-CH_2-$), 2.5—2.8 (2H, br, $-CH_2-$), 4.83 (3H, s, CO_2CH_3), 4.73 (2H, br, $-CH\overset{+}{N}H_2R-CHOSO_3^-$), 5.20 (2H, s, OCH_2Ph), 7.11 (1H, d, J=9 Hz), 7.2—7.5 (6H). *Anal.* Calcd. for $C_{23}H_{29}NO_7S$: C, 59.59; H, 6.31; N, 3.02. Found: C, 59.28; H, 6.31; N, 2.79.

Methyl *trans*-2-Benzyloxy-6-hydroxysulfonyloxy-5-isopropylamino-5,6,7,8-tetrahydro-1-naphthoate (67)——To an ice-cooled solution of **32** (10 g) in CH_2Cl_2 (100 ml) was added dropwise chlorosulfonic acid (2.0 ml) with stirring. The reaction mixture was stirred for a further 4 hr under ice-cooling. The resulting precipitate was collected by filtration, washed with CH_2Cl_2 and dried to give **67** (10.3 g, 86%) as a white powder, mp 243—245° (dec. with foaming). IR ν_{max}^{KBr} cm^{-1}: 3500—3400, 3000—2500, 1730, 1600, 1280—1270, 1215, 1030, 970, 835, 700. NMR (DMSO-d_6) δ: 1.26—1.28 (6H, d, J=7 Hz, N-iso-Pr), 1.8—2.2 (2H, m, $-CH_2-$), 2.5—2.8 (2H, m, $-CH_2-$), 3.80 (3H, s, CO_2CH_3), 4.5 (1H, br), 4.75 (1H, br), 5.10 (2H, s, OCH_2Ph), 7.10 (1H, d, J=9 Hz), 7.2—7.5 (6H). *Anal.* Calcd. for $C_{22}H_{27}NO_7S$: C, 58.78; H, 6.05; N, 3.12. Found: C, 58.58; H, 5.97; N, 3.14.

Methyl *trans*-2-Benzyloxy-6-*tert*-butylamino-5-hydroxy-5,6,7,8-tetrahydro-1-naphthoate (68)——To a solution of **51** (8.7 g) in dioxane (250 ml) and water (90 ml) was added AcOH (2.0 g), and the mixture was stirred at 80° for 3 hr then evaporated to dryness *in vacuo*. The residue was dissolved in AcOEt and treated with ethanolic HCl. The resulting precipitate was collected by filtration and recrystallized from MeOH–AcOEt to give **68** hydrochloride (6.4 g, 63%), as colorless needles, mp 240—242° (dec.). IR ν_{max}^{KBr} cm^{-1}: 1720 (CO_2CH_3), 1275, 1135, 1060, 1020, 805, 755, 700. NMR (DMSO-d_6-D_2O) δ: 1.40 (9H, s, N-*t*-Bu), 2.0—2.3 (2H, br, $-CH_2-$), 2.6—3.5 (3H, br), 3.86 (3H, s, CO_2CH_3), 4.63 (1H, d, J=8 Hz, >CH-OH), 5.14 (2H, s, OCH_2Ph), 7.05 (1H, d, J=8 Hz), 7.2—7.5 (5H), 7.56 (1H, d, J=8 Hz). *Anal.* Calcd. for $C_{23}H_{30}ClNO_4 \cdot 1/2H_2O$: C, 64.40; H, 7.28; N, 3.27. Found: C, 64.25; H, 7.18; N, 3.14. Free base: Colorless needles (from benzene–*n*-hexane), mp 92—93°. IR ν_{max}^{KBr} cm^{-1}: 3400, 3320, 1720, 1595, 1585, 1270, 1205, 820. NMR ($CDCl_3$) δ: 1.10 (9H, s, N-*t*-Bu), 3.82 (3H, s, CO_2CH_3), 4.10 (1H, d, J=9 Hz, >CH-OH), 5.04 (2H, s, OCH_2Ph). *Anal.* Calcd. for $C_{23}H_{29}NO_4$: C, 72.03; H, 7.62; N, 3.65. Found: C, 72.01; H, 7.60; N, 3.66.

***trans*-6-Benzyloxy-2-*tert*-butylamino-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol (69)**——To a suspension of $LiAlH_4$ (1.0 g) in THF (50 ml) was added dropwise a solution of **68** (3.0 g) in THF (10 ml). The mixture was refluxed with stirring for 5 hr. After decomposition of excess $LiAlH_4$ with MeOH, the

mixture was treated with a saturated NaCl solution and AcOEt. The organic layer was separated, washed with a saturated NaCl solution, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was recrystallized from AcOEt, yielding **69** (2.096 g, 73%) as colorless prisms, mp 143—144°. IR ν_{max}^{KBr} cm^{-1}: 1595, 1580, 1260, 1245, 1080, 1010. NMR (DMSO-d_6) δ: 1.06 (9H, s, N-*t*-Bu), 4.08 (1H, d, J=7 Hz, >C<u>H</u>–OH), 5.06 (2H, s, OCH_2Ph). *Anal.* Calcd. for $C_{22}H_{29}NO_3 \cdot 1/3H_2O$: C, 73.10; H, 8.27; N, 3.88. Found: C, 73.17; H, 8.33; N, 3.64.

***trans*-2-*tert*-Butylamino-6-hydroxy-5-hydroxymethyl-1,2,3,4-tetrahydro-1-naphthalenol (70)**——A mixture of **69** (355 mg) in MeOH (30 ml) was hydrogenated over 5% Pd-C (20 mg) under atmospheric pressure at room temperature. After hydrogen uptake had ceased (40 min), the catalyst was filtered off and the filtrate was evaporated to dryness *in vacuo*. The residue was recrystallized from MeOH–AcOEt to give **70** (197 mg, 75%) as white crystals, mp 197—204° (dec.). IR ν_{max}^{KBr} cm^{-1}: 3300—2500, 1610, 1590, 1060, 1005, 970, 865, 820, 800. NMR (DMSO-d_6) δ: 1.06 (9H, s, N-*t*-Bu), 1.3—1.6 (1H, m), 1.8—2.2 (1H, m), 2.6—2.9 (2H, m), 3.16 (3/2H, s, $1/2CH_3OH$), 4.03 (1H, d, J=7 Hz, >C<u>H</u>–OH), 4.49 (2H, s, $C\underline{H}_2OH$), 6.61 (1H, d, J=8 Hz), 7.12 (1H, d, J=8 Hz). MS *m/e*: 265 (M^+), 250 (M^+-CH_3), 232. *Anal.* Calcd. for $C_{15}H_{23}NO_3 \cdot 1/2CH_3OH$: C, 66.17; H, 8.96; N, 4.98. Found: C, 66.19; H, 9.07; N, 4.85. **70** Sulfate. Colorless prisms (from MeOH–AcOEt), mp 220—225° (dec.). NMR (DMSO-d_6–D_2O) δ: 1.37 (9H, s, N-*t*-Bu), 4.5 (3H, broad s, $C\underline{H}_2OH$, >C<u>H</u>–OH), 6.74 (1H, d, J=8 Hz), 7.26 (1H, d, J=8 Hz). *Anal.* Calcd. for $C_{15}H_{25}NO_7S$: C, 49.57; H, 6.93; N, 3.85. Found: C, 49.21; H, 7.08; N, 3.77.

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