evaporated to dryness. The colorless sirup remained was converted to picrylsulfonate. m.p. 161~162° from actone/EtOH. *Anal.* Calcd. for $C_{20}H_{26}O_{15}N_4S_3$: C, 36.48; H, 3.98; N, 8.51. Found; C, 36.73; H, 4.13; N, 8.23.

3,3'-Dibenzenesulfonyloxy-N-phenyldipropylamine (No. 863)——Similarly for Ⅳ (4.1 g.) and benzenesulfonylchloride (7 g.) in pyridine (50 ml). Isolated as free base. m.p. 55.5~56.5° (ether/Petr. ether). *Anal.* Calcd. for $C_{24}H_{27}O_6NS_2$: C, 58.89; H, 5.56; N, 2.86. Found : C, 58.89; H, 5.55; N, 2.91.

3,3'-Di-*p*-toxyloxy-N-phenyldipropylamine (No. 860)——Similarly from Ⅳ (5 g.) *p*-toluenesulfonyl chloride (10 g.) in pyridine (50 ml.). Isolated as hydrochloride. m.p. 107~108° (from acetone/Petr. ether). *Anal.* Calcd. for $C_{26}H_{32}O_6NS_2Cl$: C, 56.37; H, 5.82; N, 2.53. Found : C, 56.81; H, 6.01; N, 2.70.

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Summary

Six new derivatives of sulfonic acid esters of aminoglycols were prepared and tested for their carcinostatic activity against Yoshida sarcoma. All the tested compounds showed strong cytomorphological effects on the tumor cells but not effective in prologation of life span of the tumor bearing animals.

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Yoshio Arata and Tsutomu Ohashi : Constituents of *Rhizoma Nupharis*. XXIII.*1 The Absolute Configuration of Nuphamine.*2

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A new alkaloid, nuphamine,[1,2] $C_{15}H_{23}O_2N$ isolated from the roots of *Nuphar japonicum* DC. has been given the formula (I), in which the remaining unsettled problem was the configuration about the side chain double bond. The present paper deals with the absolute configuration of nuphamine.

The action of thionyl chloride on nuphamine (I) gave a chloro compound (Ⅱ),[2] which, when kept standing in dilute hydrochloric acid, re-formed I. Attempts to direct toward the ring closure of Ⅱ to Ⅲ were unsuccessful recovering only the starting material, but when heated with potassium hydroxide in methanol solution, Ⅱ afforded O-methylnuphamine (Ⅳ) $C_{16}H_{25}O_2N$ (picrolonate : m.p. 178°). These facts suggested that I would be represented by the formula (Ⅶ).

Furthermore, the configuration was studied by the measurement of nuclear magnetic resonance spectra of I, Ⅳ and (−)-anhydronupharamine*4,3 (Ⅵ) derived from (−)-nupharamine (Ⅷ).

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*1 Y. Arata, *et al.* : This Bulletin, **13**, 1247 (1965).

*2 Presented in part the meeting of the Hokuriku Branch of the Pharmaceutical Society of Japan, Kanazawa, June 5th (1965).

*3 Takara-machi 13, Kanazawa (荒田義雄, 大橋 力).

*4 Reduction of Ⅵ gave desoxynupharamine (Ⅴ) derived from Ⅱ.

1) Y. Arata, T. Ohashi : This Bulletin, **13**, 392 (1965).

2) *Idem* : *Ibid.*, **13**, 1247 (1965).

3) *Idem* : Yakugaku Zasshi, **77**, 792 (1957); **79**, 127, 729, 734 (1959).

In system of the type A·CH_2-C(CH_3)=CH-CH_2·B a *trans* relationship between the methyl group and the vinyl proton gives the methyl protons the higher τ value ($\Delta\tau$ 0.06~0.07) as compared with the *cis* isomer. The nuphamine side chain is obviously

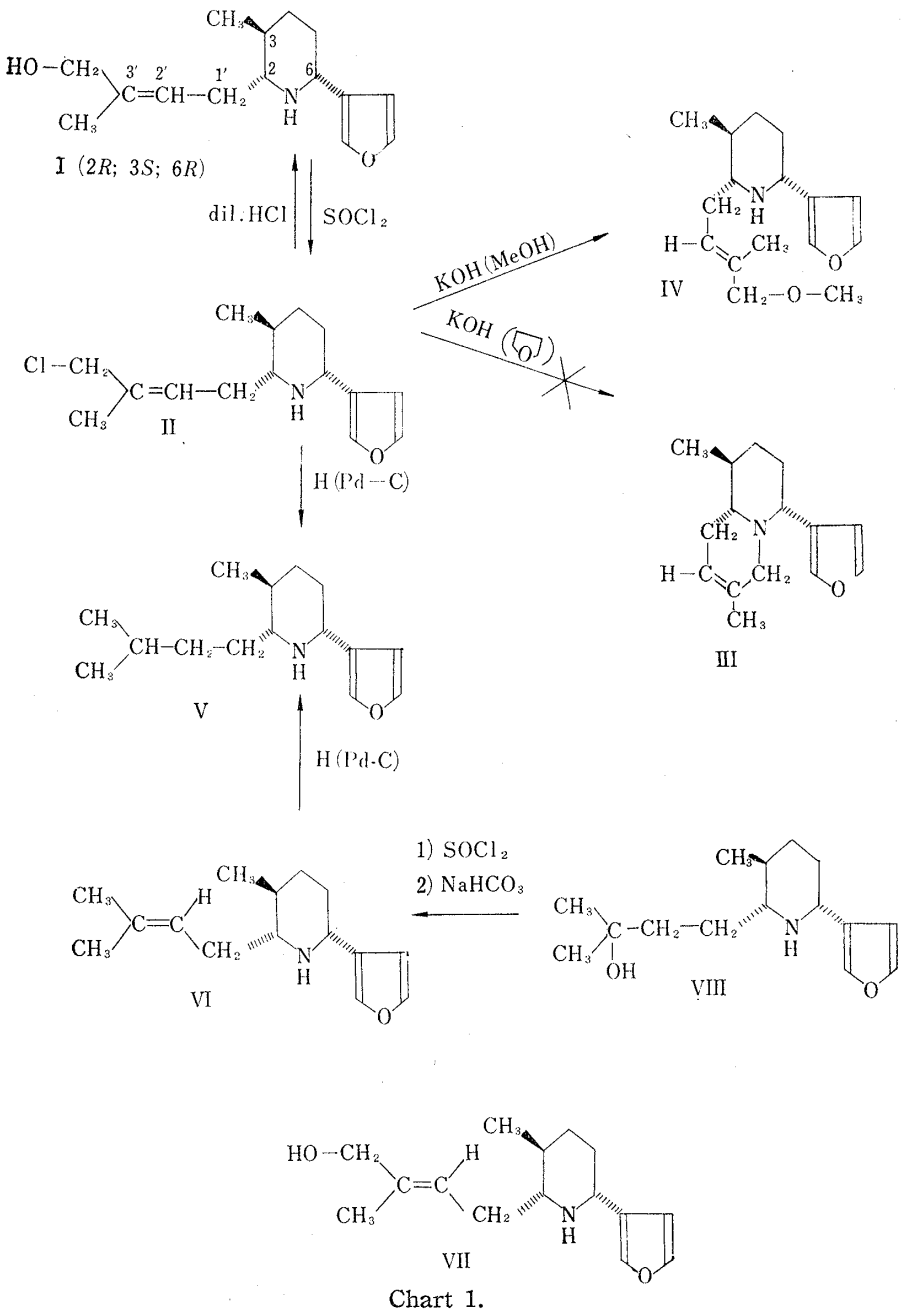
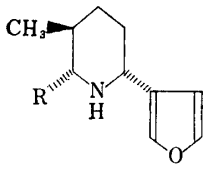


Chart 1.

of this general type with A=OH, B=piperidine ring. The observed values are recorded in Table I. These data are consistent with those already reported[4] and make it certain that the *trans* isomer predominates in nuphamine (I). Consequently, the formula (Ⅶ) would be presented as the absolute configuration of nuphamine.

4) R. B. Bates, *et al.*: J. Am. Chem. Soc., 82, 5749 (1960); Chem. & Ind. (London), **1962**, 1020; J. Org. Chem., 28, 1086 (1963); G. Brieger: Tetrahedron Letters, No. 30, 2123 (1963); T. Sakai, *et al.*: Bull. Chem. Soc. Japan, 38, 384 (1965).

Table I. Nuclear Magnetic Resonance Spectra of Methyl Groups of Type A-CH_2-$C(CH_3)$=CH-CH_2-B



	R	*trans*	*cis*	*Δ*
VI	$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!=\!C\!<\!\begin{matrix}H\\CH_2-\end{matrix}$	τ 8.35	τ 8.28	0.07
I	$\begin{matrix}HO-CH_2\\CH_3\end{matrix}\!\!>\!C\!=\!C\!<\!\begin{matrix}H\\CH_2-\end{matrix}$	τ 8.36	—	
IV	$\begin{matrix}CH_3-O-CH_2\\CH_3\end{matrix}\!\!>\!C\!=\!C\!<\!\begin{matrix}H\\CH_2-\end{matrix}$	τ 8.35 (CH_3-O- τ 6.78)	—	

Spectra were measured in CCl_4 with tetramethylsilan internal reference.

Experimental*5

Preparation of (−)-Nuphamine (I) from Chlorodeoxynuphamine (II)——0.5 g. of nuphamine (I) was dissolved in 20 ml. of $CHCl_3$ and to this 1.5 ml. of $SOCl_2$ was added. After it was kept for 1 hr. at room temperature, 20 ml. of water, 1 g. of $NaHCO_3$ and 30 ml. of ether were added. From the ether soluble extract, colorless liquid (II) of b.p_3 150~160° (bath temperature) was afforded. Yield, 0.4 g. IR spectrum was coincident with that of chlorodeoxynuphamine which was already reported.[2]

0.1 g. of II was dissolved in 5% HCl and it was kept for 7 days at room temperature. After the reaction, $NaHCO_3$ was added to make neutral and extracted with ether. The ether soluble extract gave colorless liquid of b.p_3 160~165° (bath temperature). IR spectrum of the liquid was completely in accordance with that of I.

Picrolonate : Recrystallized from a mixture of EtOH and ether gave yellow needles. By the desiccation at 100° for 7 days, crystalline EtOH was splitted. m.p. 159°. No melting point depression was observed on the admixture of picrolonate of (−)-nuphamine (I).

Attempts to give the Ring Closure of Chlorodeoxynuphamine (II) to III (Preparation of O-Methylnuphamine (IV))——II was dissolved in tetrahydrofuran and it was warmed for several hours with $NaHCO_3$ or Na_2CO_3. The starting material was recovered in all cases.

0.4 g. of II was dissolved in 10 ml. of MeOH and it was heated for 2 hr. with 2.5 ml. of 25% KOH. After the reaction, water was added and extracted with ether, colorless liquid (IV) of b.p_4 120~135° (bath temperature) was afforded. Yield, 0.35 g. IV was purified through picrolonate. IR cm^{-1} : ν_{NH} 3320; 3110, 1500, 1165, 875 (furan), ν_{C-O} 1100 (methoxy) (liq.). NMR : τ 9.08 (CH_3-CH<), τ 8.35 (CH_3-C=), τ 6.78 (CH_3-O-), τ 6.22 (-O-CH_2-C=) (CCl_4 soln.).

Picrolonate : Recrystallized from EtOH to give yellow needles. m.p. 178°. *Anal.* Calcd. for $C_{16}H_{25}O_2N \cdot C_{10}H_8O_5N_4$: C, 59.19; H, 6.31. Found : C, 58.99; H, 6.29.

Anhydronupharamine[3] (VI)——3.5 g. of VII was dissolved in 30 ml. of $CHCl_3$ and kept for 1 hr. at room temperature with 5ml. of $SOCl_2$. After the reaction, the solvent was removed and K_2CO_3 solution was added to make alkaline and extracted with ether. From the ether extract, colorless liquid (VI) of b.p_3 110~115° was afforded. Yield, 3.1 g. NMR : τ 9.09 (CH_3-CH<), τ 8.35, τ 8.28 $\left(\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!=\!C\!<\!\begin{matrix}H\\\end{matrix}\right)$, τ 4.86 $\left(>\!C\!=\!C\!<\!\begin{matrix}H\\CH_2-\end{matrix}\right)$, τ 3.67 (furan β-position), τ 2.73 (furan α-position) (CCl_4 soln.).

Picrolonate : Recrystallization from EtOH, gave yellow prisms, m.p. 203°. No melting point depression was observed by the admixture with picrolonate of (−)-anhydronupharamine.[3]

Perchlorate : Recrystallized from a mixture of AcOEt and petr. ether (1:1) gave colorless needles, m.p. 168°.

*5 IR spectra were measured with a Spectrophotometer, IRDS-402G of Japan Spectroscopic Co., Ltd. and NMR with a Varian A-60, 60 Mc. (room temperature). Melting points were measured with a Yanagimoto, Micro-melting point Apparatus.

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Summary

Judging from the nuclear magnetic resonance spectra of I, Ⅳ and Ⅵ, the formula (Ⅶ) would be presented as the absolute configuration of nuphamine.

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