[Chem. Pharm. Bull.
19(10)2154—2160(1971)]

UDC 547.833.3.04 : 547.269.1.04

Studies on Tetrahydroisoquinolines. III.[1] Synthesis of 4-Alkoxy- or Alkyl(phenyl)mercapto-7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolines[2]

BUNSUKE UMEZAWA, OSAMU HOSHINO and YASUHIRO YAMANASHI

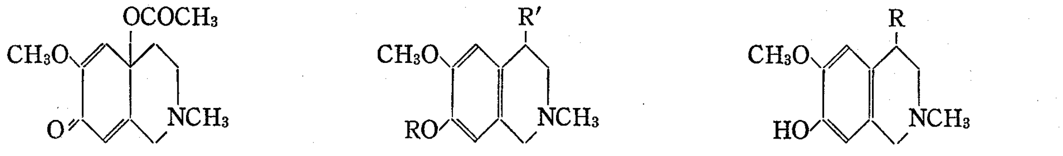
Faculty of Pharmaceutical Sciences, Science University of Tokyo[3]

(Received April 30, 1971)

Treatment of 4,7-diacetate (I) with alcohols or alkyl(phenyl)mercaptans in the presence of base gave the corresponding 4-alkoxy or alkyl(phenyl)mercapto derivatives(VIa—k) in moderate yields. In the case of alcohols, the steric effect of alkyl chains was found to be governing as expected.

Nuclear magnetic resonance spectra of the products were measured and magnetic nonequivalence of isopropoxyl methyl protons due to hindered rotation was observed in the case of 4-isopropoxy compound (VIf).

It has been shown in a previous paper[4] that acid-catalysed reaction of 10-acetoxy-2-methyl-7-oxo-$\Delta^{5,6,8,9}$-hexahydroisoquinoline (*p*-quinol acetate) (I) derived from 7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (II) by means of lead tetraacetate oxidation gives exclusively 4,7-diacetoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (III) and lithium aluminium hydride ($LiAlH_4$) reduction of III followed by methylation with diazomethane affords 4-hydroxy- and 6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline [(IV) and (V)] in approximately 1:1 ratio during the course of studies on its structure elucidation. In the reaction, V must have been formed by replacement of 4-acetoxy group with hydride ion. Then our attention was smoothly focused on reaction of III with other nucleophiles. In general, comparison of nucleophiles having the same attacking atom shows that increased basicity results in increased nucleophilic reactivity. Thus the following series of decreasing reactivity is observed: $C_2H_5O^- > OH^- > C_6H_5O^- > AcO^- > H_2O$. On the other hand, in the comparison of alkoxide and alkylmercaptide ions, the following series of decreasing reactivity is observed: $RS^- > RO^-$.



I

II: R=R'=H
III: R=Ac, R'=OAc
IV: R=CH3, R'=OH
V: R=CH3, R'=H
VII: R=CH3, R'=OCH3
VIII: R=H, R'=OH
XIV: R=CH3, R'=OAc

VIa : R=OCH3
VIb : R=OC2H5
VIc : R=OCH2CH=CH2
VId : R=O-*n*-C3H7
VIe : R=OCH2C6H5
VIf : R=O-iso-C3H7
VIg : R=O-C6H11
VIh : R=SCH3
VIi : R=SC2H5
VIj : R=SCH2C6H5
VIk : R=SC6H5

Chart 1

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[1] Part II: B. Umezawa, O. Hoshino and Y. Yamanashi, *Chem. Pharm. Bull.* (Tokyo), **19**, 2147 (1971).

[2] The preliminary communication of this work appeared in *Tetrahedron Letters*, **1969**, 933, 937.

[3] Location: *12, Ichigayafunagawara-machi, Shinjuku-ku, Tokyo, 162, Japan.*

[4] B. Umezawa, O. Hoshino, Y. Terayama, K. Ohyama, Y. Yamanashi, T. Inoue and T. Toshioka, *Chem. Pharm. Bull.* (Tokyo), **19**, 2138 (1971).

Considering the fact, alcohols or alkylmercaptans were first chosen as typical nucleophiles and employment of base was expected to increase their nucleophilic reactivity. Thereupon, reaction with alcohols or alkyl(phenyl)mercaptans in the presence of base was extensively investigated and the following result was obtained.

Reaction of III in 5% methanolic potassium hydroxide (KOH) solution was carried out under stirring for 45 min at room temperature. Usual treatment of the reaction mixture followed by column chromatographic purification (silicic acid, Mallinckrodt) furnished colorless prisms of VIa, mp 101—104°, in 46% yield. Its nuclear magnetic resonance (NMR) spectrum showed each sharp singlet at τ 6.56 (aliphatic methoxy group at C-4) and τ 6.15 (aromatic methoxy group at C-6), and a triplet (J=5 Hz) at τ 5.66 (C-4 hydrogen). Infrared (IR) spectrum of VIa indicated characteristic band of a hydroxy group at 3500 cm^{-1}. Further, methylation of VIa with diazomethane in methanol (MeOH) afforded 2-methyl-4,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinoline (VII) (oil, 26%, picrate, mp 126—129°).

Thus, from spectral data and elemental analysis, structure of VIa was supposed to be 4,6-dimethoxy-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline, in which a newly formed methoxy group was at 4-position. The assumption would also be supported by the previous result[4] that hydrosis of III in 5% aqueous KOH solution gives 4,7-dihydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (VIII), provided that reaction of III in aqueous solution proceeded through the same reaction pathway as in the case of MeOH.

Therefore, VII was synthesized by an unequivocal route as shown in Chart 2.

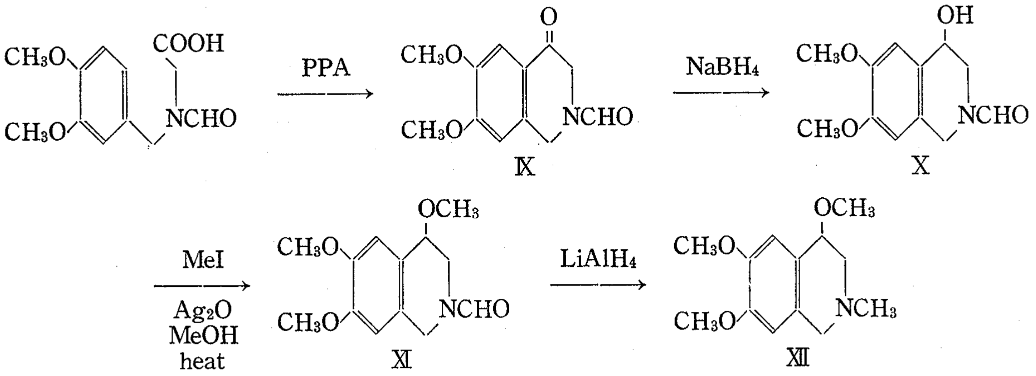

Chart 2

Namely, 6,7-dimethoxy-2-formyl-4-oxo-1,2,3,4-tetrahydroisoquinoline[4] (IX) prepared by cyclization of N-formyl-N-veratrylglycine with polyphosphoric acid was employed as a starting material. Sodium borohydride reduction of IX gave 6,7-dimethoxy-2-formyl-4-hydroxy-1,2,3,4-tetrahydroisoquinoline (X), mp 93—94°, in 46% yield. A methanolic solution of X and methyl iodide in the presence of silver oxide was refluxed under stirring to afford 2-formyl-4,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinoline (XI), mp 125—129°, in 55% yield. Successive LiAlH_4 reduction of XI gave the corresponding 2-methyl-4,6,7-trimethoxy compound (XII) as an oil (picrate, mp 126—127.5°) in 34% yield.

Identity of 4,6,7-trimethoxy compound (VII) from III and the above authentic sample (XII) was secured by comparison of each retention time in gas liquid chromatography (GLC) (free base) and IR spectrum (picrate), and by mixed fusion (picrate), respectively.

The above experiment proved that 4-acetoxy substituent in III was surely replaced by methoxy group. Moreover, the reaction in 50% aqueous MeOH instead of MeOH proceeded smoothly yielding VIa as a sole product in 42% yield. The fact was in well accord with the observation on nucleophilic reactivity as noted above. Thus, analogous reactions of III with other alcohols were performed to give the result shown in Table I.

Then, similar reaction with alkyl(phenyl)mercaptans was undertaken. From the fact that nucleophilic reactivity of alkyl(phenyl)mercaptans [alkyl(phenyl)mercaptide ions] is

Table I. Yield, Reaction Time, Melting Point and Elemental Analysis of VI

Compound	Reaction time (min)	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
VIa	45	46	101—104	$C_{12}H_{17}O_3N$	64.55	7.68	6.27	64.31	7.90	6.04
	90	42	165—166.5	$C_{18}H_{20}O_{10}N_4$[a]	47.79	4.46	12.39	47.56	4.85	11.90
VIb	40	51	163—164.5	$C_{19}H_{22}O_{10}N_4$[a]	48.93	4.75	12.01	49.04	4.97	12.22
VIc	30	53	134—135	$C_{20}H_{22}O_{10}N_4$[a]	50.21	4.64	11.71	49.93	5.08	11.43
VId	30	25	77—80	$C_{14}H_{21}O_3N$	66.90	8.42	5.57	66.79	8.56	5.68
VIe	120	24	153—154	$C_{24}H_{24}O_{10}N_4 \cdot \frac{1}{2}H_2O$[a]	53.63	4.66	10.43	53.93	4.65	10.63
VIf	35	22	93—94	$C_{14}H_{21}O_3N$	66.90	8.42	5.57	66.65	8.54	7.76
VIg	150	13	117—119	$C_{17}H_{25}O_3N$	70.07	8.65	4.81	69.53	8.63	4.68

a) picrate

Table II. Reaction Time, Yield, Melting Point and Elemental Analysis of VI

Compound	Reaction time (hr)	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
VIh	0.50	85	134—135	$C_{12}H_{17}O_2NS \cdot \frac{1}{4}H_2O$	59.02	7.16	5.80	59.34	7.27	6.18
VIi	10.00	76	106.5—107	$C_{13}H_{19}ONS$	61.64	7.56	5.53	62.08	7.21	5.64
VIj	0.25	85	117—118	$C_{18}H_{21}O_2NS$	68.55	6.71	4.44	68.56	6.71	4.42
VIk	17.5	65	137—139	$C_{17}H_{19}O_2NS$	67.76	6.36	4.65	67.50	6.41	4.70

superior to that of alcohols (alkoxide ions), and that the reaction in aqueous MeOH gave the same result as that in MeOH,in the case of alkyl(phenyl)mercaptans, aqueous solution was used without any hesitation. The result was summarized in Table II.

The experiment clearly showed that 4-acetoxy group could be readily substituted by various alkoxy or alkyl(phenyl)mercapto groups and that the reaction was applicable to synthesis of tetrahydroisoquinolines having hetero atoms (oxygen or sulfur) at 4-position.

Yields of 4-alkoxy were generally lower than those of 4-alkylmercapto product. The result was easily explicable by the order of nucleophilic reactivities of alcohols and alkyl(phenyl)mercaptans as noted above. At the mention of alcohols, the finding that the longer the length of alkyl chain, the lower the yield of 4-alkoxy product and that competitive replacement of 4-acetoxy group with alkoxide and hydroxide ion took place in isopropyl- or cyclohexyl alcohol showed that the steric factor was governing in the reaction.

Furthermore this was also exemplified by the result that similar reaction of III with neopentyl- or *tert*-butyl alcohol afforded only the corresponding 4,7-dihydroxy compound (VIII) in each 16% yield.

Inspection of NMR spectral data of products disclosed an interesting fact that in 4-isopropoxy compound (VIf) a triplet (J=6.0 Hz) centered at 8.72 was due to isopropoxyl methyl protons as given in Fig. 1. Such a phenomenon must be ascribable to magnetic nonequivalence of isopropoxyl methyl protons due to hindered rotation. While the similar magnetic nonequivalence of isopropyl[5] or *tert*-butyl[6] methyl protons has been known, the present finding with respect to isopropoxyl methyl protons would be a first one.

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[5] M. Kajtar and L. Radics, *Chem. Commun.*, **1967**, 784, and literature cited therein.

[6] *cf.* H. Kessler, *Angew. Chem. Inter. Ed.*, **9**, 219 (1970) and literature cited therein.

Table III. NMR Spectral Data of VI ($CDCl_3$)

Compound	τ-Values[a]					
	NCH_3	OCH_3	$1\text{-}H_2$[b]	4-H	5-H	8-H
VIa	7.53 (s)	6.12 (s)	6.62, 6.42 (AB q, J=15 Hz)	5.63 (t, J=5 Hz)	3.15 (s)	3.45 (s)
VIb	7.52 (s)	6.11 (s)	6.55 (bs)	5.45 (t, J=5 Hz)	3.08 (s)	3.45 (s)
VIc	7.56 (s)	6.12 (s)	6.64, 6.45 (AB q, J=15 Hz)	5.45 (t, J=5 Hz)	3.09 (s)	3.43 (s)
VId	7.58 (s)	6.16 (s)	6.59 (bs)	5.53 (t, J=5 Hz)	3.12 (s)	3.52 (s)
VIe	7.54 (s)	6.18 (s)	6.64, 6.40 (AB q, J=15 Hz)	5.38 (t, J=5 Hz)	3.19 (s)	3.40 (s)
VIf	7.54 (s)	6.12 (s)	6.52 (bs)	5.43 (t, J=5 Hz)	3.11 (s)	3.47 (s)
VIg	7.54 (s)	6.12 (s)	6.53 (bs)	5.38 (t, J=5 Hz)	3.08 (s)	3.45 (s)
VIh	7.55 (s)	6.11 (s)	6.53 (bs)	5.95 (t, J=5 Hz)	2.92 (s)	3.49 (s)
VIi	7.54 (s)	6.10 (s)	6.60, 6.42 (AB q, J=15 Hz)	5.90 (t, J=6.3 Hz)	2.93 (s)	3.46 (s)
VIj	7.56 (s)	6.19 (s)	6.65, 6.43 (AB q, J=15 Hz)	5.90 (dt)	3.13 (s)	3.48 (s)
VIk	7.57 (s)	6.20 (s)	6.65, 6.32 (AB q, J=15 Hz)	5.49 (t, J=5 Hz)	3.11 (s)	3.44 (s)

a) Following abbreviations were used: s, singlet; bs, broad singlet; t, triplet; dt, defused triplet; AB q, AB quartet.
b) geminal protons at C-1 position

Finally, the reaction pathway on this reaction was infered as follows. When the reaction was assumed to proceed through the same intermediate (XIII) as described in the case of acid-catalysed rearrangement[4] of *p*-quinol acetate (I), the presence of 7-acetoxy group was of great significance. Because hydrolysis of 7-acetoxy group created easily a reactive *p*-quinone methide,[7] *via* the corresponding phenolate ion.

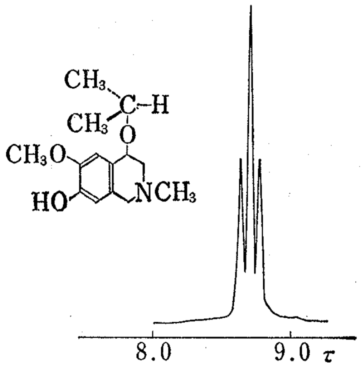

Fig. 1

Therefore, in order to examine whether the assumption was correct or not, the similar treatment of 4-acetoxy-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline[4] (XIV) with 5% methanolic KOH solution was performed to give the corresponding 4-hydroxy compound (IV) as a sole product.

Thus, the finding proved that the presence of 7-acetoxy group was surely prerequisite and supported the assumption that *p*-quinone methide was certainly an intermediate.[8] In consequence, the reaction pathway on formation of 4-alkoxy or alkyl(phenyl)mercapto compounds from III could be visualized as shown in Chart 3.

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[7] *cf.* A.B. Turner, *Quart. Revs.*, **18**, 347 (1964).

[8] While a paper that reflux of an ethanolic solution of 2-benzoyl-4,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinoline gives 2-benzoyl-4-ethoxy-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (formed by replacement of 4-methoxy with ethoxy group) is recently published by B. Jaques, R.H.L. Deeks and P.K.J. Shak (*Chem. Commun.* **1969**, 1283), treatment of III in hot ethyl alcohol (reflux for 2 hr) in our hand showed a quantitative recovery of III. The result supported that hydrolysis of 7-acetoxy group was a crucial step in the reaction.

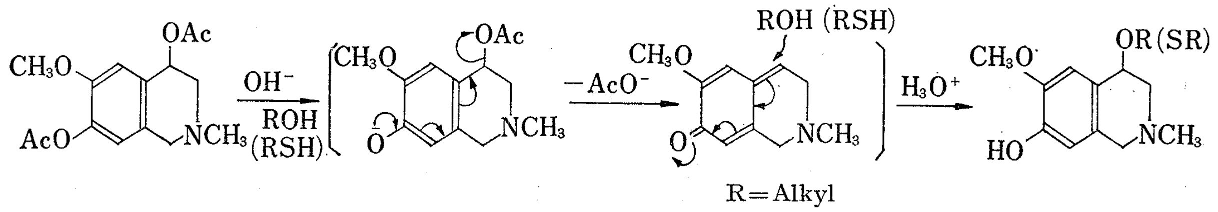

Chart 3

Experimental[9]

General Procedure for the Reaction of I with Alcohols——A solution of I (200 mg) in each 5% KOH–alcohol (3—4 ml) was stirred at room temperature. The solvent was removed under reduced pressure, and H_2O was added to the residue. The resultant solution acidified with 10% HCl and the acidic solution was basified with K_2CO_3 (powder). The product was taken up in $CHCl_3$. The $CHCl_3$ layer was rinsed with brine and dried. Each residue obtained on evaporation of the solvent was subjected to column chromatography.

(1) MeOH: Chromatography of the residue (112 mg) gave an oil (84.5 mg) from an eluate with $CHCl_3$–MeOH (100:2)—(100:4). Treatment of the oil with *n*-hexane yielded colorless prisms of VIa, (70 mg, 46%), mp 101—104° (*n*-hexane); picrate, mp 165—166.5° (iso-PrOH). IR ν_{max}^{KBr} cm^{-1}: 3500 (OH).

(2) 50% Aqueous MeOH: A solution of KOH (150 mg) in 50% aqueous MeOH (3 ml) was employed instead of 5% KOH–MeOH (3 ml). Chromatography of the residue (110 mg) afforded an oil (78 mg) from an eluate with $CHCl_3$–MeOH (100:1). Treatment of the oil with *n*-hexane yielded VIa (63 mg, 42%), mp 100—103° (*n*-hexane). This was identical with a sample obtained above by comparison of IR spectrum and by mixed fusion.

(3) EtOH: Chromatography of the residue (124 mg) gave an oil of VIb (82 mg, 51%) from an eluate with $CHCl_3$–MeOH (100:1)—(100:3); picrate, mp 163—164.5° (iso-PrOH). IR ν_{max}^{KBr} cm^{-1}: 3150 (OH).

(4) Ally Alcohol: 5% KOH–allylalcohol (4 ml) was employed. Chromatography of the residue (120 mg) gave an oil of VIc (90 mg, 53%) from an eluate with $CHCl_3$–MeOH (100:1): picrate, mp 134—135° (iso PrOH). free base: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH).

(5) *n*-Propyl Alcohol: 5% KOH–*n*-PrOH (4 ml) was employed. Chromatography of the residue (122 mg) afforded an oil (77 mg) which was eluted with $CHCl_3$–MeOH (100:1). Treatment of the oil with *n*-hexane furnished colorless prisms of VId, (43 mg, 25%), mp 77—80° (*n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH).

(6) Isopropyl Alcohol: 5% KOH–iso-PrOH (4.0 ml) was employed. Chromatography of the residue (90 mg) gave colorless prisms of VIf [(25 mg, 15%), mp 93—94° (*n*-hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH)] from an eluate with $CHCl_3$–MeOH (100:1), and subsequently a crystalline mass (VIII)(8 mg, 5%) from an eluate with $CHCl_3$–MeOH (100:2). VIII was identical with an authentic specimen by comparison of TLC (*Rf*=0.2).

(7) Cyclohexyl Alcohol: 5% KOH–cyclohexyl alcohol (3 ml) was employed. Chromatography of the residue (102 mg) gave colorless needles of VIg (25 mg, 13%), mp 116—118°, from an eluate with $CHCl_3$–MeOH (100:1), and successively a crystalline mass (VIII),(9 mg, 6%) from an eluate with $CHCl_3$–MeOH (100:2)—(100:5). VIII was identical with an authentic specimen by comparison of TLC (*Rf*=0.2).

Reaction of I with Benzyl Alcohol——A solution of I (200 mg) in 5% KOH–benzyl alcohol (3 ml) was stirred for 2 hr at room temperature. To the reaction mixture H_2O was added and excess of benzyl alcohol was washed with ether. The aqueous solution was acidified with 10% HCl and then the acidic solution was basified with K_2CO_3 (powder). The product was taken up in $CHCl_3$. Usual treatment of the $CHCl_3$ layer gave an oil (152 mg) which was chromatographed to afford an oil of VIe (48 mg, 24%) from an eluate with $CHCl_3$–MeOH (100:1); picrate, mp 153—154° (iso-PrOH).

Reaction of I with Neopentyl Alcohol——A solution of I (200 mg) in 50% aqueous neopentyl alcohol (1.0 ml) containing KOH (200 mg) was stirred for 3 hr at room temperature. The same treatment as noted

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[9] All melting points were uncorrected using a Yanagimoto micro melting point measuring apparatus. All NMR spectra were measured at 100 MHz by a Japan Electron Optics Lab. Model JNR-4H-100 spectrometer in $CDCl_3$ (5—10% solution) using Me_4Si as internal standard. GLC was taken with a Shimadzu GC-1C gas chromatograph (a hydrogen flame ionization detector) with 1.5% SE-30 on Shimalite W (80—100 mesh) as a stationary phase. Thin-layer chromatography (TLC) was run on Silicagel G (Merck) with $CHCl_3$–MeOH (5:1) as developing solvent. IR spectra were measured by a Hitachi Model EPI-S_2. Unless otherwise noted, column chromatography was carried out on silicic acid (Mallinckrodt) and the organic phase was dried over K_2CO_3.

in the case of benzyl alcohol gave colorless prisms of VIII (23 mg, 16%, mp 153—154.5° (decomp.) [lit.[4] mp 153—155°(decomp.)], which was identified with an authentic specimen by comparison of IR spectral datum.

Reaction of I with *tert*-Butyl Alcohol——A solution of (400 mg) in 5% KOH-*tert*-BuOH (8 ml) was stirred for 45 min at room temperature. The same treatment as noted in the case of MeOH afforded colorless prisms of VIII (45 mg, 16%), mp 145—150° (decomp.), which was identical with an authentic specimen by comparison of IR spectral datum.

6,7-Dimethoxy-2-formyl-4-hydroxy-1,2,3,4-tetrahydroisoquinoline (X)——To a stirred solution of 4-oxo compound[4] (IX)(1.6 g) in MeOH (70 ml), $NaBH_4$ (300 mg) was gradually added under ice-cooling. The reaction mixture was allowed to stand for 12 hr at room temperature. To the residue obtained on removal of the solvent, H_2O was added and the product was taken up in $CHCl_3$. The $CHCl_3$ layer was rinsed with brine and dried. Evapolation of the solvent gave an oil (1.5 g), which was subjected to chromatography on neutral Al_2O_3 (Woelm). Elution with $CHCl_3$–MeOH (100:1)—(100:2) afforded an oil (1.2 g), treatment of which with *n*-hexane gave a crystalline mass (X)(750 mg, 47%), mp 90—92°. Recrystallization from CCl_4 gave colorless prisms of X, mp 93—94°. *Anal.* Calcd. for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.37; N, 5.90. Found: C, 63.63; H, 6.48; N, 6.13. IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 1670 (NCHO).

2-Formyl-4,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinoline (XI)——A stirred mixture of 4-hydroxy compound (X)(500 mg), MeI (8 ml) and Ag_2O (800 mg) in MeOH (5 ml) was refluxed. For completion of the reaction, MeI (4 ml) and Ag_2O (400 mg) were added twice to the reaction mixture, and refluxing of the whole was continued for 17.5 hr. After cooling, the precipitate was filtered. Removal of the solvent gave an oil (564 mg), which was chromatographed. Elution with $CHCl_3$–MeOH (100:1) furnished an oil (390 mg), treatment of which with *n*-hexane–iso-PrOH afforded a crystalline mass (XI)(289 mg, 55%), mp 122—124°. Recrystallization from benzene yielded colorless prisms of XI, mp 122—124°. *Anal.* Calcd. for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.35; H, 6.86; N, 5.63. IR ν_{max}^{KBr} cm^{-1}: 1655 (NCHO).

$LiAlH_4$ Reduction of XI to XII——A mixture of (XI)(150 mg) and $LiAlH_4$ (138 mg) in anhydrous ether (15 ml) and anhydrous THF (15 ml) was refluxed for 6 hr. After cooling, wet ether and a small amount of H_2O were carefully added to the reaction mixture. The precipitate was filtered and the filtrate was dried over $MgSO_4$. Removal of the solvent gave an oil (170 mg), which was subjected to chromatography. Elution with $CHCl_3$–MeOH (200:1) afforded an oil of XII (48 mg, 34%), which was converted into its picrate, mp 126—127.5 (MeOH). *Anal.* Calcd. for $C_{19}H_{22}O_{10}N_4$: C, 48.93; H, 4.75; N, 12.01. Found: C, 48.82; H, 4.95; N, 12.19.

2-Methyl-4,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinoline (VII)——A solution of 4-methoxy compound (VIa)(120 mg) and excess of CH_2N_2-ether solution in MeOH (10 ml) was allowed to stand for 1 hr at room temperature. The residue (130 mg) obtained on evaporation of the solvent was chromatographed. Elution with $CHCl_3$–MeOH (200:1) afforded an oil (VII)(33 mg, 26%), which was converted into its picrate, mp 126—129° (MeOH). This was identical with an authentic specimen obtained above by comparison of GLC (free base)($t_R=3.7$ min; column temperature, 170°), IR spectral datum (picrate) and by mixed fusion (picrate), respectively.

Reaction of I with Alkylmercaptans——(1) 20% Aqueous Sodium Methylsulfide: A solution of I (200 mg) in 20% aqueous NaSMe (4 ml) was stirred at room temperature. The reaction mixture was acidified with 10% HCl and excess of MeSH was removed under reduced pressure. Basification of the acidic solution with K_2CO_3 (powser) gave the precipitate which was collected to a crystalline mass (VIh)(142 mg, 85%), mp 129—132°. Recrystallization from *n*-hexane gave colorless prisms of VIh, mp 134—135°.

(2) 50% Aqueous Ethylmercaptan: A solution of I (200 mg), and K_2CO_3 (400 mg) in 50% aqueous EtSH (4 ml) was stirred at room temperature. After removal of excess of EtSH the product was taken up in $CHCl_3$. The $CHCl_3$ layer was rinsed with brine and dried ($MgSO_4$). Removal of the solvent gave an oil (200 mg), treatment of which with *n*-hexane yielded a solid (VIi) (132 mg, 76%), mp 79—90°. Recrystallization from *n*-hexane furnished colorless needless of VIi mp 106—107°.

(3) 10% Aqueous Benzylmercaptan: A solution of I (200 mg) and K_2CO_3 (210 mg) in aqueous benzyl mercaptan (4.5 ml) was stirred at room temerapture. The reaction mixture was acidified with 10% HCl and excess of benzyl mercaptan was washed with ether. The acidic solution was basified with K_2CO_3 (powder) and the product was taken up in $CHCl_3$. Usual work-up of the $CHCl_3$ layer gave an oil (220 mg), treatment of which with *n*-hexane led to a crystalline mass(VIj) (182 mg, 85%), mp 114—117°. Recrystallization from *n*-hexane afforded colorless prisms of VIj, mp 117—118°.

(4) Thiophenol: A solution of I (200 mg), thiophenol (375.5 mg) and KOH (200 mg) in H_2O (4 ml) was stirred at room temperature. The same treatment as noted in the case of benzyl mercaptan furnished a solid (VIk) (198 mg, 65%), mp 129—131.5°, which was recrystallized from *n*-hexane to colorless prisms of VIk, mp 137—139°.

Reaction of XIV with Methanol——A solution of XIV[4] (30 mg) in 5% KOH–MeOH (0.3 ml) was stirred for 30 min at room temperature. The same treatment as noted in the case of MeOH gave a crystalline mass (IV) (23 mg, mp 118—122°), which was recrystallized from *n*-hexane to colorless prisms of IV, mp 126—128° (lit.[4] mp 127—128°). This was identical with an authentic specimen by mixed fusion.

Acknowledgement The authors wish to express their sincere thanks to Dr. I. Iwai of Sankyo Co., Ltd. and Prof. M. Hamana of Kyushu University for their unfailing encouragements. They are indebted to Dr. T. Moroe of Takasaga Perfumery Co., Ltd. for this kind supply of the starting material. Thanks are also due to Dr. Y. Kishida and Dr. H. Mishima of Central Research Laboratories of Sankyo Co., Ltd. for elemental analysis, and to Dr. A. Tahara and Dr. K. Hirao of Rikagaku Kenkyusho (The Institute of Physical and Chemical Research) and to Miss T. Kawana of this Faculty for NMR spectral measurements.