[Chem. Pharm. Bull. 18(9)1850—1855(1970)]
UDC 547.833.04.07 : 547.94.07 : 582.682.04

Synthesis of Aminoisoquinolines and Related Compounds. X.[1) A Modified Synthesis of *dl*-Cularine

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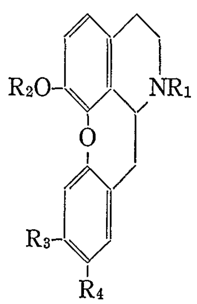
(Received March 17, 1970)

The Bischler–Napieralski reaction of the phenethylamides (VIIa and VIIb) gave respectively the 6-ethoxycarbamido-3,4-dihydroisoquinolines, formed by the cyclization at the position *para* to the ethoxycarbamido group, and both 3,4-dihydroisoquinolines were converted to the 6-aminoisoquinolines (Xa and Xb). Each 7,8-disubstituted isoquinolines (XIIa and XIIb), prepared by deamination reaction of Xa and Xb, were submitted to the Ullmann reaction to give respectively 6-methoxy-1-methyl-1,2,3,12,12a-pentahydrobenzoxepino[2,3,4-*i*,*j*]isoquinoline (XIII) and *dl*-cularine (Ia).

Cularine (Ia), cularimine (Ib), cularicine (Ic), and cularidine (Id) were isolated from the genera *Corydalis* and *Dicentra* by R.H.F. Manske[3) and two (Ia and Ib) of these four cularine type alkaloids were synthesized by Kametani and his co-workers.[4)



Ia : $R_1=R_2=Me$, $R_3=R_4=OMe$
Ib : $R_1=H$, $R_2=Me$, $R_3=R_4=OMe$
Ic : $R_1=Me$, $R_2=H$, $R_3+R_4=OCH_2O$
Id : $R_1=Me$, $R_2=H$, $R_3=R_4=OMe$
XIII: $R_1=R_2=Me$, $R_3=R_4=H$

Chart 1

On the other hand, Iida and his co-workers[5) also reported the synthesis of cularine type compounds by the intramolecular Ullmann reaction of appropriate isoquinolines. But there is no works on the intramolecular Ullmann reaction fo 7,8-disubstituted isoquinolines, which can not be synthesized by the usual Bischler–Napieralski reaction.[6)

In the present investigation, the authors wish to report the synthesis of *dl*-cularine (Ia) by the intramolecular Ullmann reaction of the 7,8-disubstituted isoquinoline (XIIb).

It is known that the ethoxycarbamido group is a good substituent for accelerating the Bischler–Napieralski reaction of β-phenethylamide and the ring-closure occurs selectively at the position *para* to the ethoxycarbamido group.[7) This group is easily hydrolyzed to an amino group, which is successively deaminated by the diazotization step following by reduction.

In order to examine the synthetic path of a model compound (XIII), the experiments described bellow were undertaken.

1) Part IX: S. Ishiwata and K. Itakura, *Chem. Pharm. Bull.* (Tokyo), **18**, 1846 (1970).
2) Location: *No. 600, Kashiwagi-4-chome, Shinjuku-ku, Tokyo.*
3) R.H.F. Manske, *J. Am. Chem. Soc.*, **72**, 55 (1950); *idem*, *Can. J. Chem.*, **43**, 989 (1965); **44**, 561 (1966).
4) *a*) T. Kametani and K. Fukumoto, *J. Chem. Soc.*, **1963**, 4289; *b*) T. Kametani, S. Shibuya, S. Seino, and K. Fukumoto, *J. Chem. Soc.*, **1964**, 4146.
5) *a*) H. Iida, T. Kikuchi, K. Sakurai, and T. Watanabe, *Yakugaku Zasshi*, **89**, 645 (1969); *b*) H. Iida, T. Kikuchi, S. Tanaka, and M. Shinbo, *Yakugaku Zasshi*, **89**, 1169 (1969).
6) W.M. Whaley and T.R. Govindachari, *Org. Reactions*, **VI**, 80 (1951).
7) S. Ishiwata and K. Itakura, *Chem. Pharm. Bull.* (Tokyo), **16**, 778 (1968); **17**, 2256 (1969).

Nitration of 3-bromo-4-methoxyphenethylamine (II)[8] with 70% nitric acid afforded 5-nitrophenethylamine (III), which was condensed with 2-benzyloxyphenylacetyl chloride (IVa) under the Schotten–Baumann reaction conditions to give the phenethylamide (Va), whose reduction with iron powder and glacial acetic acid yielded the amino substituted amide (VIa). This amino compound (VIa) was converted to the ethoxycarbamido derivative (VIIa) with ethyl chloroformate in the presence of pyridine in a tetrahydrofurane solution.

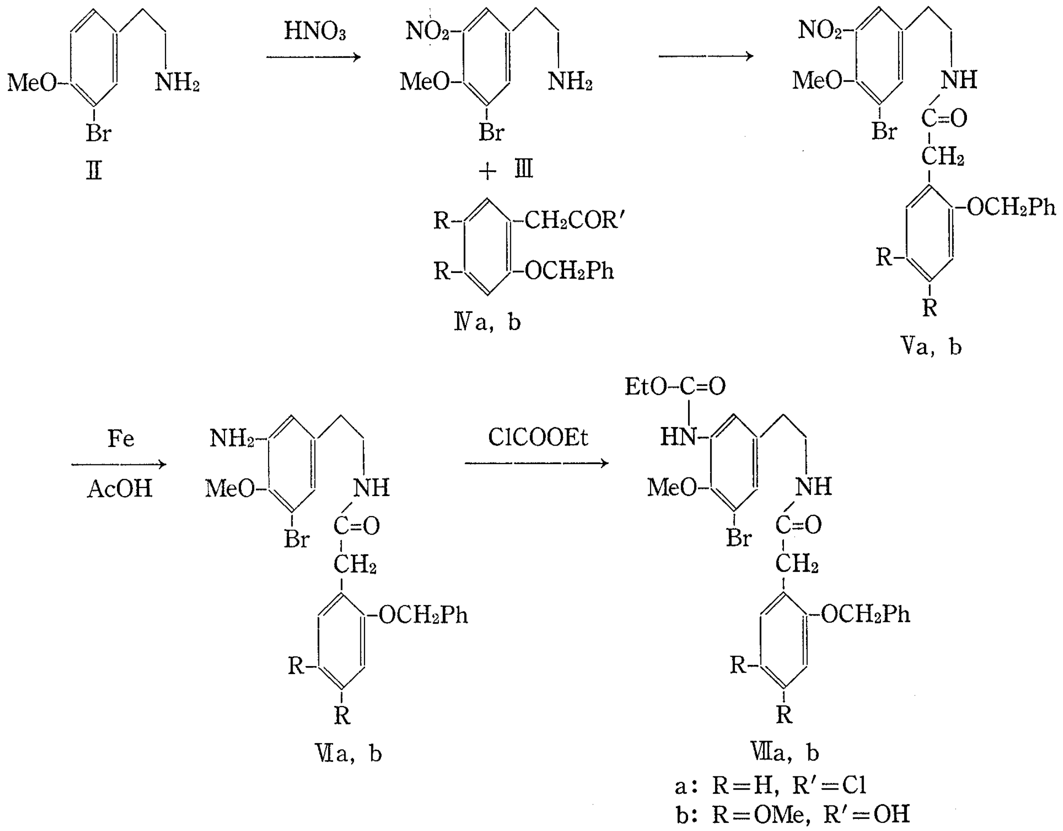


Chart 2

The amide (VIIa) was submitted to the Bischler–Napieralski reaction to give 1-(2-benzyloxybenzyl)-8-bromo-6-ethoxycarbamido-7-methoxy-3,4-dihydroisoquinoline, formed by the ring-closure at the position *para* to the ethoxycabamido group. This result was proved by the following facts.

The methiodide (VIIIa), prepared from the 3,4-dihydroisoquinoline with methyl iodide, was reduced with sodium borohydride in a methanol solution to the N-methyl compound (IXa), whose nuclear magnetic resonance (NMR) spectrum showed the benzenoid proton (C_5-H) resonance at 2.17 τ as a singlet. The chemical shift of the benzenoid proton adjacent to the ethoxycarbamido group is known to be a lower field than that of general benzenoid protons.[9]

IXa was hydrolyzed with 10% ethanolic solution of potassium hydroxide to afforde the 6-aminoisoquinoline (Xa), which was deaminated with 50% hypophosphorous acid solution after diazotization step to the 8-bromo-7-methoxyisoquinoline (XIa). XIa was debenzylated to the phenolic isoquinoline (XIIa) with 50% ethanolic solution of 35% hydrochloric acid.

This phenolic isoquinoline was submitted to the Ullmann reaction by using cupric oxide in the presence of pyridine and anhydrous potassium carbonate at 160° for 6 hours to furnish

8) S. Ishiwata, *Yakugaku Zasshi*, **51**, 755 (1931).
9) S. Ishiwata and K. Itakura, *Chem. Pharm. Bull.* (Tokyo), **17**, 2261 (1969).

a biphenyletherlinkage (XIII). The produced basic compound showed one spot on thin-layer chromatogram of silica gel and negative Beilstein reaction.

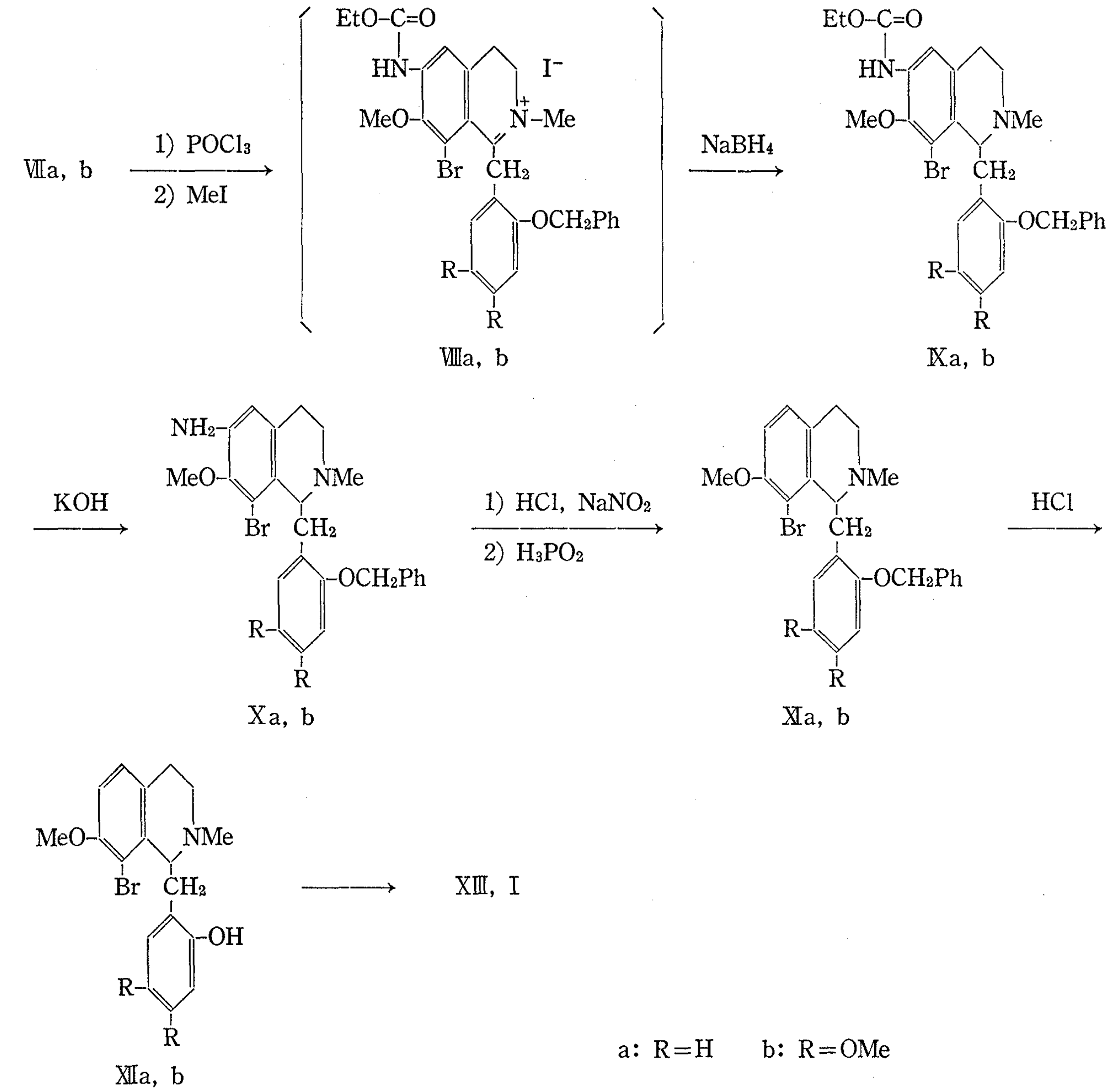


Chart 3

XIII was characterized as its picrate and in its NMR spectrum, the chemical shift of C-12a proton was 5.45 τ as a quartet, which was characteristic of cularine type compounds.[5,10]

These facts revealed that the Ullmann reaction product of XIIa was 6-methoxy-1,2,3,12,12*a*-pentahydrobenzoxepino[2,3,4-*i,j*]isoquinoline (XIII).

In the same way, a total synthesis of *dl*-cularine was attempted.

Since the chlorination of IVb with thionyl chloride did not give the corresponding acid chloride, condensation of the amine (III) and IVb was reformed in the presence of dicyclohexylcarbodiimide (DCC)[11] to yield the nitrophenethylamide (Vb).

The Ullmann reaction of the phenolic isoquinoline (XIIb), prepared from Vb by the same method as described for XIIa, gave *dl*-cularine, melted at 135°,[12] whose infrared (IR) and NMR spectra were superimposable with those of natural cularine.

10) N.S. Bhacca, J.C. Craig, R.H.F. Manske, S.K. Roy, M. Shamma, and W.A. Slusarchyk, *Tetrahedron*, **22**, 1467 (1967).
11) M. Tomita, K. Fujitani, and Y. Aoyagi, *Chem. Pharm. Bull.* (Tokyo), **16**, 62 (1968).
12) Our sample was recrystallized from *n*-hexane. On the other hand, Kametani reported the melting point at 114° (from ether) for *dl*-cularine in the reference 2.

On the above these facts, it was indicated that the ethoxycarbomido group was a good substituent for the synthesis of 7,8-disubstituted isoquinolines (XIIa and XIIb), which were able to convert to cularine type compounds (Ia and XIII).

Further works are in progress on the synthesis of another cularine type alkaloids.

Experimental[14]

3-Bromo-4-methoxy-5-nitro-β-phenethylamine (III)——3-Bromo-4-methoxy-β-phenethylamine (II, 10 g) was added dropwise to 90 ml of 70% HNO_3 with stirring at 20—25° and the stirring was continued for 2 hr at 25°. The reaction mixture was poured into ice-water and the resultant precipitates were collected by filtration. The amine was characterized as its hydrochloride, which was recrystallized from EtOH to yield pale yellow needles, mp 193—194° (decomp.). *Anal.* Calcd. for $C_9H_{11}O_3N_2Br \cdot HCl$: C, 34.65; H, 3.85. Found: C, 34.61; H, 3.96. Yield: 6 g.

N-(3-Bromo-4-methoxy-5-nitrophenethyl)-2-(2-benzyloxyphenyl)acetamide (Va)——To a well stirred mixture of 5 g of the amine (III), 50 ml of ether, and 100 ml of 5% aq.NaOH, was added dropwise a solution of 5 g of IVa in 50 ml of dry ether with chilling. After 1 hr stirring, the ethereal solution was washed with 3% aq. HCl and water, dried over K_2CO_3, and evaporated to yield 4.5 g of a pale yellow solid. Recrystallization of the product from benzene gave colorless prisms, mp 86—87°. *Anal.* Calcd. for $C_{24}H_{23}O_5N_2Br$: C, 57.75; H, 4.61; N, 5.61. Found: C, 57.69; H, 4.68; N, 5.31. IR cm^{-1} (KBr): ν_{NH} 3260, $\nu_{C=O}$ 1660, NO_2 1535 and 1365. NMR: 2.65 (5H, s, $PhC\underline{H}_2$), 4.18 (1H, broad, $N\underline{H}$), 4.97 (2H, s, $PhC\underline{H}_2$), 6.08 (3H, s, $O-C\underline{H}_3$).

N-(3-Amino-5-bromo-4-methoxyphenethyl)-2-(2-benzyloxyphenyl)acetamide (VIa)——A mixture of 13 g of Va, 12 g of Fe powder, and 130 ml of AcOH was heated on a water bath for 2 hr. The reaction mixture was basified with conc. NH_4OH and the product was extracted with $CHCl_3$. The extract was washed with water, dried over K_2CO_3, and evaporated to give the desired amino compound (10 g) as a viscous oil, which was characterized as its Hydrochloride. Recrystallization of the hydrochloride from EtOH-ether gave colorless powder, mp 156—157°. *Anal.* Calcd. for $C_{24}H_{25}O_3N_2Br \cdot HCl$: C, 57.17; H, 4.95; N, 5.55. Found: C, 56.71; H, 2.56; N, 5.32.

N-(3-Bromo-5-ethoxycarbamide-4-methoxyphenethyl)-2-(2-benzyloxyphenyl)acetamide (VIIa)——To a stirred mixture of 10 g of VIa, 3.8 g of pyridine, and 100 ml of THF, was added 5 g of ClCOOEt dropwise and the mixture was stirred further for 1.5 hr. Evaporation of the solvent afforded a yellow residue, which was taken up in $CHCl_3$ and the extract was washed with successively water, 3% aq. HCl, and water, dried over K_2CO_3, and evaporated. Recrystallization of the amide from benzene-*n*-hexane yielded 7.6 g of colorless needles, mp 79—80°. *Anal.* Calcd. for $C_{27}H_{29}O_5N_2Br$: C, 59.89; H, 5.36; N, 5.18. Found: C, 60.07; H, 5.47; N, 5.37. IR cm^{-1} ($CHCl_3$): ν_{NH} 3390, $\tau_{C=O}$ 1738 (urethane), 1670 (amide). NMR: 2.18 (1H, d, $J=2$ cps, $C_6-\underline{H}$), 2.65—3.20 (10H, aromatic $\underline{H}$), 4.25 (1H, broad, amide $N\underline{H}$), 6.20 (3H, s, $O-C\underline{H}_3$).

The Bischler-Napieralski Reaction of the Amide (VIIa)——A mixture of 5.8 g of VIIa, 28 ml of $POCl_3$, and 28 ml of anhyd. benzene was refluxed for 2 hr. The solvent and the reagent were evaporated and the resultant residue was taken up in $CHCl_3$. The extract was shaken with 10% NH_4OH, washed with water, and dried over K_2CO_3. After evaporation of the solvent, the residue was heated with 20 g of MeI in 50 ml of MeOH for 2 hr under N_2 atmosphere. The solvent and an excess of MeI was evaporated and the residue was washed with ether. To a solution of the crude methiodide in 60 ml of MeOH was added 1 g of $NaBH_4$ portionwise and the stirring was continued for 1 hr at room temperature. After the mixture was acidified with AcOH, the solvent was evaporated and the residue was basified with 10% NH_4OH, and the product was taken up in $CHCl_3$. The extract was washed with water, dried over K_2CO_3, and evaporated to yield 3.5 g of IXa. Recrystallization of IXa from hexane gave colorless prisms, mp 115—116°. *Anal.* Calcd. for $C_{28}H_{31}O_4N_2Br$: C, 62.34; H, 5.75; N, 5.19. Found: C, 62.09; H, 5.76; N, 5.27. IR cm^{-1} ($CHCl_3$): ν_{NH} 3370, $\nu_{C=O}$ 1730. NMR: 2.17 (1H, s, $C_5-\underline{H}$), 4.95 (2H, s, $PhC\underline{H}_2$), 6.23 (3H, s, $O-C\underline{H}_3$), 7.69 (3H, s, $N-C\underline{H}_3$).

6-Amino-1-(2-benzyloxybenzyl)-8-bromo-1,2,3,4-tetrahydro-7-methoxy-2-methylisoquinoline (Xa)——A mixture of 3.5 g of IXa, 6 g of KOH, 6 ml of water, and 48 ml of EtOH was refluxed for 2 hr. Evaporation of the solvent gave a brown residue, which was treated by the usual method. This product was purified by chromatography on alumina to yield 1.7 g of a pale yellow oil, which was used for the next step without further purification. IR cm^{-1} ($CHCl_3$): ν_{NH_2} 3360, 3450. NMR: 2.50—3.20 (9H, aromatic $\underline{H}$), 3.55 (1H, s, $C_5-\underline{H}$), 4.90 (2H, s, $PhC\underline{H}_2$), 6.25 (3H, s, $O-C\underline{H}_3$), 7.70 (3H, s, $N-C\underline{H}_3$).

1-(2-Benzyloxybenzyl)-8-bromo-1,2,3,4-tetrahydro-7-methoxy-2-methylisoquinoline (XIa)——To a well stirred mixture of 3 g of Xa, 6 ml of conc. HCl, and 12 ml of water was added dropwise a solution of 0.5 g of $NaNO_2$ in 4 ml of water over period of 30 min at 0—5°.

14) All melting points were not corrected. NMR spectra were measured in deuteriochloroform by JNM-4H spectrophtometer at 100 Mc and tetramethylsilane was used as internal standard and chemical shift was reported as τ value.

After stirring for an additional 30 min at 0—5°, 76 ml of 50% hypophosphorous acid was added dropwise to the diazonium solution for 15 min and the reaction mixture was kept in an ice box for 20 hr.

The reaction mixture was basified with conc.NH_4OH and the product was extracted with $CHCl_3$, and the extract was washed with water, dried over K_2CO_3, and evaporated. The resultant residue was subjected to alumina chromatography eluted with benzene, yielding 1.2 g of XIa, which was recrystallized from benzene–*n*-hexane as colorless prisms, mp 102—103°. *Anal.* Calcd. for $C_{25}H_{26}O_2NBr$: C, 66.37; H, 5.78; N, 3.04. Found: C, 66.87; H, 5.97; N, 2.90. NMR: 2.60—3.40 (11H, aromatic $\underline{H}$), 4.95 (2H, s, $PhC\underline{H}_2$), 6.20 (3H, s, $O{-}C\underline{H}_3$), 7.75 (3H, s, $N{-}C\underline{H}_3$).

8-Bromo-1,2,3,4-tetrahydro-1-(2-hydroxybenzyl)-7-methoxy-2-methylisoquinoline (XIIa)——A solution of 1.2 g of XIa in 20 ml of EtOH–conc. HCl (1:1) was refluxed for 2 hr. After evaporation of the solvent, the residue was basified with 10% NH_4OH and the product was extracted with $CHCl_3$, and the extract was washed with water, and dried over K_2CO_3. Evaporation of the solvent gave the phenolic isoquinoline, which was recrystallized from EtOH as colorless plates, mp 145—146°. *Anal.* Calcd. for $C_{18}H_{20}O_2NBr$: C, 59.68; H, 5.56; N, 3.87. Found: C, 59.45; H, 5.58; N, 3.90. IR cm^{-1} ($CHCl_3$): chelated OH 2400—2600. NMR: 2.60—3.30 (6H, aromatic $\underline{H}$), 6.10 (3H, s, $O{-}C\underline{H}_3$), 7.52 (3H, s, $N{-}C\underline{H}_3$).

The Ullmann Reaction of 8-Bromo-1-(2-hydroxybenzyl)isoquinoline (XIIa)——To a stirred mixture of 165 mg of XIIa and 200 mg of K_2CO_3 in 6 ml of anhyd. pyridine was added 80 mg of CuO at 120° under N_2 atmosphere and the reaction mixture was heated for 6 hr at 150—160°. After cooling, the mixture was taken up in $CHCl_3$ and the extract was filtered off and the filtrate was washed with water and dried over K_2CO_3. Evaporation of the solvent gave a reddish brown residue, which was purified by chromatography on silica gel eluted with $CHCl_3$–MeOH (50:1) to yield 80 mg of XIII as a pale yellow viscous oil. Picrate: Recrystallized from EtOH, as yellow needles, mp 212—214° (decomp.). *Anal.* Calcd. for $C_{18}H_{19}O_2N \cdot C_6H_3O_7N_3$: C, 56.47; H, 4.35; N, 10.97. Found: C, 56.90; H, 4.23; N, 10.91. NMR: 2.65—3.25 (6H, aromatic $\underline{H}$), 5.45 (1H, q, $C_{12a}{-}\underline{H}$), 6.19 (3H, s, $O{-}C\underline{H}_3$), 7.38 (3H, s, $N{-}C\underline{H}_3$).

N-(3-Bromo-4-methoxy-5-nitrophenethyl)-2-(2-benzyloxy-4,5-dimethoxyphenyl)acetamide (Vb)——A mixture of 3.1 g of III, 2.2 g of 2-benzyloxy-4,5-dimethoxyphenylacetic acid (IVb)[15] and 1.5 g of DCC in 40 ml of anhyd. CH_2Cl_2 was stirred for 3 hr at room temperature. Precipitated N,N'-dicyclohexylurea was filtered off and the filtrate was washed with successively 3% aq. HCl, 5% aq. $NaHCO_3$, and water and dried over K_2CO_3. The solvent was evaporated to leave 3 g of a white solid, which was recrystallized from $CHCl_3$–ether as colorless needles, mp 124—125°. *Anal.* Calcd. for $C_{26}H_{27}O_7N_2Br$: C, 55.81; H, 4.83; N, 5.00. Found: C, 56.30; H, 5.04; N, 5.21. IR cm^{-1} ($CHCl_3$): $\nu_{C=O}$ 1663, NO_2 (1525 and 1355). NMR: 2.45—2.60 (7H, aromatic $\underline{H}$), 3.25 (1H, s, $C_6{-}\underline{H}$), 3.41 (1H, s, $C_3{-}\underline{H}$), 4.10 (1H, broad, $N\underline{H}$), 5.04 (2H, s, $PhC\underline{H}_2$), 6.09, 6.18, and 6.21 (9H, s, $3 \times O{-}C\underline{H}_3$).

N-(3-Amino-5-bromo-4-methoxyphenethyl)-2-(2-benzyloxy-4,5-dimethoxyphenyl)acetamide (VIb)——Prepared from Vb (3 g) and Fe powder (3 g) in AcOH (40 ml) by the same method as described for VIa. Recrystallization of VIb from EtOH gave 2.5 g of colorless prisms, mp 119—120°. *Anal.* Calcd. for $C_{26}H_{29}O_5N_2Br$: C, 58.97; H, 5.48; N, 5.29. Found: C, 58.55; H, 5.61; N, 5.43. IR cm^{-1} ($CHCl_3$): $\nu_{C=O}$ 1655. NMR: 2.65 (5H, $\underline{Ph}CH_2$), 3.24—3.75 (4H, aromatic $\underline{H}$), 4.20 (1H, broad, $N\underline{H}$), 5.05 (2H, s, $PhC\underline{H}_2$), 6.20, 6.22, and 6.30 (9H, s, $3 \times O{-}C\underline{H}_3$).

N-(3-Bromo-5-ethoxycarbamido-4-methoxyphenethyl)-2-(2-benzyloxy-4,5-dimethoxyphenyl)acetamide (VIIb)——Prepared from VIb (2.1 g) and ClCOOEt (1 g) in the same way as described for VIIa, giving 2 g of white powder, which was recrystallized from benzene–*n*-hexane to afford amorphous powder, mp 110—115°. *Anal.* Calcd. for $C_{29}H_{33}O_7N_2Br$: C, 57.90; H, 5.49; N, 4.76. Found: C, 58.06; H, 5.73; N, 4.79. IR cm^{-1}: ($CHCl_3$): ν_{NH} 3400 (amide and urethane), $\nu_{C=O}$ 1730 (urethane), 1658 (amide). NMR: 2.70 (5H, s, $\underline{Ph}CH_2$), 4.20 (1H, broad, $N\underline{H}$ (amide)), 5.05 (2H, s, $PhC\underline{H}_2$), 6.21, 6.24, and 6.26 (9H, s, $3 \times O{-}C\underline{H}_3$).

1-(2-Benzyloxy-4,5-dimethoxybenzyl)-8-bromo-6-ethoxycarbamido-1,2,3,4-tetrahydro-7-methoxy-2-methylisoquinoline (IXb)——The methiodide (VIIIb), prepared from the product of the Bischler–Napieralski reaction of VIIb (1.9 g) and MeI (10 g), was reduced with $NaBH_4$ (0.8 g) as described for IXa to yield 1 g of a white solid, whose recrystallization from benzene–hexane gave colorless needles, mp 141—142°. *Anal.* Calcd. for $C_{30}H_{35}O_6N_2Br$: C, 60.10; H, 5.84; N, 4.67. Found: C, 59.88; H, 5.93; N, 4.77. IR cm^{-1} ($CHCl_3$): ν_{NH} 3390, $\nu_{C=O}$ 1730. NMR: 2.15 (1H, s, $C_5{-}\underline{H}$), 3.17 (1H, s, $C_6{-}\underline{H}$), 3.47 (1H, s, $C_3{-}\underline{H}$), 5.00 (2H, s, $PhC\underline{H}_2$), 6.23 (6H, s, $2 \times O{-}C\underline{H}_3$), 6.25 (3H, s, $O{-}C\underline{H}_3$), 7.67 (3H, s, $N{-}C\underline{H}_3$).

6-Amino-1-(2-benzyloxy-4,5-dimethoxybenzyl)-8-bromo-7-methoxy-1,2,3,4-tetrahydro-2-methylisoquinoline (Xb)——Prepared from IXb (0.9 g), KOH (3 g), water (3 ml) and EtOH (24 ml) in the same way as described for Xa, yielding 0.61 g of a brown oil, which was purified by chromatography on alumina to give a pale yellow oily product. The product was used for the next step without further purification. IR cm^{-1} ($CHCl_3$): ν_{NH_2} 3360, 3470.

1-(2-Benzyloxy-4,5-dimethoxybenzyl)-8-bromo-1,2,3,4-tetrahydro-7-methoxy-2-methylisoquinoline (XIb)——Prepared from Xb (0.61 g), $NaNO_2$ (90 mg), and 50% hypophosphorous acid (15 ml) by the same method as described for XIa, giving 0.36 g of a white powder, which was recrystallized from benzene as colorless

15) A. H. Jackton and J. A. Martin, *J. Chem. Soc.* (*C*), **1966**, 2222.

amorphous solid, mp 95—102°. *Anal.* Calcd. for $C_{27}H_{30}O_4NBr$: C, 63.28; H, 5.86; N, 2.73. Found: C, 63.33; H, 6.20; N, 2.47. NMR: 6.18, 6.23, and 6.25 (9H, s, $3\times O-C\underline{H}_3$), 7.63 (3H, s, $N-C\underline{H}_3$).

8-Bromo-1,2,3,4-tetrahydro-1-(2-hydroxy-4,5-dimethoxybenzyl)-7-methoxy-2-methylisoquinoline (XIIb) ——Debenzylation of XIb (0.33 g) by the usual method gave 0.21 g of a pale yellow solid, which was recrystallized from EtOH as colorless plates, mp 139—140°. *Anal.* Calcd. for $C_{20}H_{24}O_4NBr$: C, 56.87; H, 5.69; N, 3.31. Found: C, 57.17; H, 5.84; N, 3.18. IR cm^{-1} ($CHCl_3$): chelated OH 2400—2600. NMR: 2.85—3.45 (4H, aromatic $\underline{H}$), 6.15, 6.22, and 6.29 (9H, s, $3\times O-C\underline{H}_3$), 7.54 (3H, s, $N-C\underline{H}_3$).

***dl*-Cularine (I)**——To a solution of 70 mg of XIIb and 150 mg of K_2CO_3 in anhyd. pyridine (3 ml) was added 60 mg of CuO with stirring at 120° under N_2 atmosphere. After the heating was continued for 4 hr at 150—160°, the reactant was treated in the same way as described for XIII to yield 42 mg of a pale yellow solid, which was recrystallized from *n*-hexane as pale yellow cubes, mp 134—135°. IR (in $CHCl_3$) and NMR (in $CDCl_3$) spectra of this compound were completely identical with those of the natural product. NMR: 3.05—3.50 (4H, aromatic $\underline{H}$), 5.56 (1H, q, $C_{12a}-\underline{H}$), 6.17, 6.20, and 6.25 (9H, s, $3\times O-C\underline{H}_3$), 7.44 (3H, s, $N-C\underline{H}_3$).

Acknowledgement The authors express their deep gratitude to Dr. R.H.F. Manske for gift of natural cularine. Thanks are also due to the members of Mycroanalyses Laboratory of this college for elemental analyses and Miss K. Kiyonaga for measurement of NMR spectra.