extracted with ether. The extract was washed with sodium chloride solution, dried over K_2CO_3, and distilled off to give 330 mg of a stereoisomeric mixture of amino ester **12** [ir ($CHCl_3$) 3450, 2900, 2750, 1720, and 1600 cm^{-1}; *m/e* 300 (M^+)], which was used in the following reaction without purification because of difficult crystallization.

(±)-Isodasycarpidone (15) and (±)-Iso-5-epidasycarpidone (16).—A mixture of 300 mg of the amino esters **12**, 1 g of potassium hydroxide, 10 ml of water, and 20 ml of ethanol was refluxed for 5 hr. The resulting mixture was neutralized with concentrated hydrochloric acid and the solvent was evaporated completely to give a residue, which was extracted with dry ethanol. Removal of the extract gave 270 mg of 5-ethyl-4-hydroxycarbonyl-2-(3-indolyl)-1-methylpiperidine (**14**) as a powder, which was treated with polyphosphoric acid (prepared from 2 ml of phosphoric acid and 4 g of phosphorus pentoxide) at 90–95° for 1 hr. To the reaction mixture was added 5 ml of water, and the resulting mixture was basified with ammonia and extracted with ether. The extract was washed with sodium chloride solution, dried over K_2CO_3, and distilled off to give 98 mg of a pale yellow syrup, whose preparative thick layer chromatography (ethyl acetate–benzene–methanol, 2:2:1) on silica gel afforded 16 mg of (±)-isodasycarpdione (**15**) and 9 mg of (±)-iso-3-epidasycarpidone (**16**). Recrystallization of **15** from methanol–ether gave colorless needles: mp 220–221°; ir ($CHCl_3$) 3430, 2900, 2780, and 1645 cm^{-1}; nmr δ ($CDCl_3$) 1.0 (3 H, t, J = 7.0 Hz, CH_2CH_3), 2.25 (3 H, s, NMe), 4.3 (1 H, t, J = 2.5 Hz, β-indolic CHN), 7.0–7.8 (4 H, m, Ar H), 9.7–10.0 (1 H, NH of indole ring, exchanged with D_2O); *m/e* 268 (M^+), 253, 240, 225, 211, 196, and 183.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51; N, 10.44. Found: C, 75.56; H, 7.87; N, 10.70.

Recrystallization of **16** from methanol–ether gave colorless needles: mp 201–202°; ir 3430, 2900, 2780, and 1645 cm^{-1}; nmr δ ($CDCl_3$), 1.1 (3 H, t, J = 7.0 Hz, CH_2CH_3), 2.3 (3 H, s, NMe), 4.35 (1 H, t, J = 2.5 Hz, β-indolic CHN), 7.0–7.8 (4 H, m, Ar H), 10.4–10.8 (1 H, NH of indole ring, exchanged with D_2O); *m/e* 268 (M^+), 253, 240, 225, 211, 196, and 183.

Registry No.—**1**, 18700-27-1; **2**, 19775-50-9; **3**, 18688-38-5; **4**, 19775-51-0; **6**, 28199-31-7; **7**, 28199-32-8; **8**, 28199-33-9; **8** HCl, 28199-34-0; **9**, 28199-35-1; **10**, 28199-36-2; **15**, 28192-70-3; **16**, 28192-71-4.

Acknowledgment.—We thank Professor J. A. Joule, Chemistry Department of Manchester, Manchester M 139 PL, for a gift of natural dasycarpidone and (±)-3-epidasycarpidone and for the data of its ir and nmr spectra. We also thank Dr. L. J. Dolby, department of Chemistry, University of Oregon, Eugene, for a gift of epidasycarpidone. We are grateful to Miss Y. Tadano for nmr spectral determination, Mr. T. Ohuchi for mass spectral measurements, and Miss A. Kawakami and Miss C. Yoshida, Pharmaceutical Institute, Tohoku University, for microanalyses.

Notes

Studies on the Syntheses of Heterocyclic Compounds. CCCXCV. The Synthesis of Homopetaline-Type Compounds

T. KAMETANI* AND K. FUKUMOTO

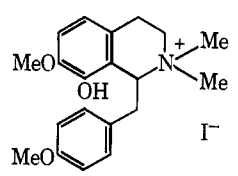
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai, Japan

M. FUJIHARA

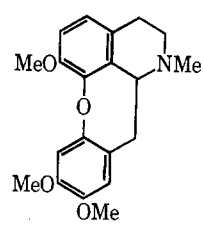
Organic Chemistry Research Laboratory, Tanabe Seiyaku Co. Ltd., Toda, Saitama, Japan

Received September 21, 1970

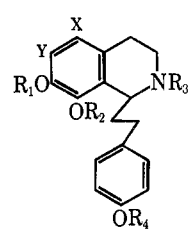
Petaline (**1**)[1,2] and cularine (**2**)[3] are benzylisoquinoline alkaloids having the oxygenated function at the C-7 and C-8 positions on the isoquinoline ring. The former was synthesized by Brossi[4] and the latter by Kametani.[5–7]



1



2



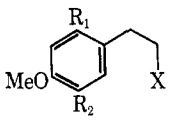
3, $R_1 = R_3 = R_4 = Me$; $R_2 = X = Y = H$
9, $R_1 = R_3 = R_4 = Me$; $R_2 = Y = H$; $X = Br$
13, $R_1 = R_2 = R_3 = R_4 = Me$; $X = H$; $Y = NHCOOEt$
14, $R_1 = R_2 = R_3 = R_4 = Me$; $X = H$; $Y = NH_2$
15, $R_1 = R_2 = R_3 = R_4 = Me$; $X = Y = H$
16, $R_1 = R_3 = Me$; $R_2 = R_4 = X = Y$ H

Several unsuccessful attempts have been made[8,9] to prepare 7,8-dioxygenated isoquinolines by the Bischler–Napieralski or Pictet–Spengler reaction. Therefore, we reinvestigated the synthesis of 7,8-dioxygenated isoquinolines by the above two methods.

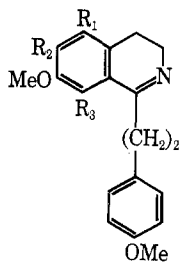
(1) N. J. McCorkindale, D. S. Magrill, M. Martin-Smith, S. J. Smith, and J. B. Stenlake, *Tetrahedron Lett.*, 3841 (1964).
(2) N. J. McCorkindale, A. W. McCulloch, D. S. Magrill, B. Caddy, M. Martin-Smith, S. J. Smith, and J. B. Stenlake, *Tetrahedron*, **25**, 5457 (1969).
(3) R. H. F. Manske, *J. Amer. Chem. Soc.*, **72**, 55 (1950).
(4) G. Grethe, M. Uskoković, and A. Brossi, *Tetrahedron Lett.*, 1599 (1966); *J. Org. Chem.*, **33**, 2500 (1968); *Helv. Chim. Acta*, **53**, 874 (1970).
(5) T. Kametani and K. Fukumoto, *Chem. Ind. (London)*, 291 (1963); *J. Chem. Soc.*, 4289 (1963).
(6) T. Kametani, S. Shibuya, S. Seino, and K. Fukumoto, *Tetrahedron Lett.*, 25 (1964); *J. Chem. Soc.*, 4146 (1964).
(7) T. Kametani and S. Shibuya, *Tetrahedron Lett.*, 1897 (1965); *J. Chem. Soc.*, 5565 (1965).
(8) R. D. Haworth and W. H. Perkin, *ibid.*, **127**, 1448 (1925).
(9) A. R. Battersby, S. Southgate, and J. Staunton, *ibid.*, *C*, 502 (1966).

Homologs of petaline (**1**) have now been synthesized by using bromine or a substituted amino group to block those positions usually involved in the cyclization to isoquinolines.

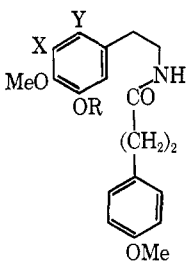
Schotten–Baumann reaction of 5-benzyloxy-2-bromo-4-methoxyphenethylamine (**4**)[10] and 4-methoxyphenylpropionyl chloride (**5**) gave the corresponding amide **6**, which was debenzylated by hydrochloric acid to give the starting phenolic bromo amide **7**. Bischler–Napieralski reaction of amide **7** with phosphoryl chloride in boiling chloroform gave the 3,4-dihydroisoquinoline **8**, whose methiodide was reduced with sodium borohydride to give the 1,2,3,4-tetrahydro-2-methylisoquinoline **9**, which was characterized as its oxalate. Debromination of this bromoisoquinoline (**9**) was achieved by catalytic hydrogenation on Raney nickel to give compound **3**, whose structure was assigned by its nmr spectrum, the C-5 and C-6 protons being shown as a typical AB type of doublets. Thus, we developed a new method for preparing 7,8-dioxygenated isoquinoline derivatives.



4, $R_1 = Br$; $R_2 = OCH_2Ph$; $X = NH_2$
5, $R_1 = R_2 = H$; $X = COCl$



8, $R_1 = Br$; $R_2 = H$; $R_3 = OH$
11, $R_1 = H$; $R_2 = NHCOOEt$; $R_3 = OMe$
12, $R_1 = H$; $R_2 = OMe$; $R_3 = NHCOOEt$



6, $R = CH_2Ph$; $X = H$; $Y = Br$
7, $R = X = H$; $Y = Br$
10, $R = Me$; $X = NHCOOEt$; $Y = H$

The over-all yield of the above sequence was not impressive, and so the following route was examined. Cyclization of the amide **10** gives two types of isoquinolines (**11** and **12**) arising by cyclization ortho and para to a removable group ($NHCO_2Et$ group in **10**).[11] The methiodide of 3,4-dihydroisoquinoline (**11**), prepared in a previous paper,[11] was reduced as usual to the 1,2,3,4-tetrahydro-2-methylisoquinoline **13**. Hydrolysis of the ethoxycarbonylamino group of this compound (**13**) with potassium hydroxide gave the 6-aminoisoquinoline **14**, whose diazonium salt was treated with hypophosphorous acid to give the 7,8-dimethoxyisoquinoline **15**. Demethylation of **15** with 20% hydrochloric acid[12] gave the 8-hydroxy-7-methoxyisoquinoline **3** in addition to 1,2,3,4-tetrahydro-8-hydroxy-1-(4-hydroxyphenethyl)-7-methoxy-2-methylisoquinoline (**16**). The former compound was fully identical with an authentic sample of **3** spectroscopically; the structure **16** was assigned as described in the Experimental Section.

These two routes have been found suitable for the synthesis of 7,8-dioxygenated isoquinolines which are difficult to prepare by the usual methods.

(10) T. Kametani, S. Shibuya, and M. Satoh, *Chem. Pharm. Bull.*, **16**, 953 (1968).

(11) T. Kametani, K. Fukumoto, M. Kawazu, and M. Fujihara, *J. Chem. Soc. C*, 2209 (1970).

Experimental Section[13]

***N*-(5-Benzyloxy-2-bromo-4-methoxyphenethyl)-4-methoxyphenylpropionamide** (**6**).—To a mixture of 5-benzyloxy-2-bromo-4-methoxyphenethylamine (**4**) (prepared from 3.72 g of its hydrochloride by the usual method), 15 ml of 5% sodium hydroxide, and 60 ml of chloroform was added dropwise a solution of 2.4 g of 4-methoxyphenylpropionyl chloride (**5**) in 20 ml of chloroform with stirring at 2–5° during 30 min; stirring was continued at 2–5° for 30 min and then at room temperature for 2 hr. The organic layer was separated, washed with 5% hydrochloric acid and water, dried over Na_2SO_4, and evaporated *in vacuo* to give 3.93 g (81.3%) of the amide **6** as colorless needles (from benzene), mp 164–165°, ir ($CHCl_3$) 3380 and 1650 cm^{-1}.

Anal. Calcd for $C_{26}H_{28}BrNO_4$: C, 62.65; H, 5.67; Br, 16.03; N, 2.95. Found: C, 62.75; H, 5.73; Br, 15.85; N, 2.95.

***N*-(2-Bromo-5-hydroxy-4-methoxyphenethyl)-4-methoxyphenylpropionamide** (**7**).—A mixture of 8.2 g of the above amide (**6**), 300 ml of concentrated hydrochloric acid, 150 ml of ethanol, and 150 ml of acetone was refluxed on a water bath for 1.5 hr, and the excess of reagent and solvents was distilled off to give a residue which was extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to afford 5.65 g (84.8%) of the phenolic amide **7** as pale brown prisms (from benzene): mp 137–138°; ir ($CHCl_3$) 3480, 3400, and 1657 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}BrNO_4$: C, 55.89; H, 5.19; Br, 19.58; N, 3.43. Found: C, 56.08; H, 5.15; Br, 19.32; N, 3.35.

5-Bromo-1,2,3,4-tetrahydro-8-hydroxy-7-methoxy-1-(4-methoxyphenethyl)-2-methylisoquinoline (**9**).—A mixture of 2.7 g of the phenolic amide **7**, 27 ml of phosphoryl chloride, and 50 ml of chloroform was refluxed for 30 min, and an additional 1.4 ml of phosphoryl chloride was then added. The mixture was refluxed for a further 40 min. The excess reagent and chloroform were distilled off *in vacuo*, and the residue was washed with ether, basified with 10% ammonia, and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to leave a pale brown viscous syrup, which was converted into its oxalate by the usual method. The oxalate was washed with ether and basified with 10% ammonia, and the separated oil was extracted with ether. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to give 1.52 g of the 3,4-dihydroisoquinoline **8** as a pale brown syrup, whose methiodide was prepared by the standard method. To a solution of the methiodide in 100 ml of methanol was added 1 g of sodium borohydride in portions with stirring at 0°; stirring was continued at 0° for 2 hr. The mixture was then set aside at room temperature overnight. After evaporation of the solvent at atmospheric pressure, the residue was treated with aqueous ammonium chloride solution and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to leave a pale brown viscous syrup, which was extracted with ether. After removal of an insoluble material, the extract was evaporated *in vacuo* to give 657 mg of a brown syrup, which was purified on thin layer chromatography (silica gel GF 254 nach Stahl, 1 × 200 × 200 mm) using ether to afford 193 mg (7.2%) of the tetrahydroisoquinoline **9** as a pale brown viscous syrup: mass spectrum *m/e* 405 (M^+), 407 ($M^+ + 2$) (isotope ion), 270 (base peak), 272 (isotope ion of *m/e* 270); ir ($CHCl_3$) 3560 cm^{-1}; nmr τ ($CDCl_3$) 7.58 (3 H, s, NMe), 6.23 (3 H, s, OMe), 6.15 (3 H, s, OMe), 5.40 (1 H, broad signal, OH), 3.22

(12) A. Brossi, Symposium Papers of 13th Symposium on the Chemistry of Natural Products, Sapporo, Japan, 1969, p 177.

(13) The ir and uv spectra were taken with Type EPI-3 and EPS-3 Hitachi recording spectrometers, respectively. Mass spectra were measured with a Hitachi RMS-4 mass spectrometer. Nmr spectra were measured with JNM C-60 spectrometer with tetramethylsilane as an internal standard.

(2 H, d, J = 9 Hz, 3′-H and 5′-H), 3.05 (1 H, s, 6-H), and 2.84 (2 H, d, J = 9 Hz, 2′-H and 6′-H). The oxalate formed colorless needles (from ethanol–ether), mp 177–178°.

Anal. Calcd for $C_{20}H_{24}BrNO_3 \cdot C_2H_2O_4$: C, 53.23; H, 5.28; Br, 16.10; N, 2.82. Found: C, 53.05; H, 5.32; Br, 15.86; N, 3.01.

1,2,3,4-Tetrahydro-8-hydroxy-7-methoxy-1-(4-methoxyphenethyl)-2-methylisoquinoline (3).—A solution of 30 mg of the bromoisoquinoline **9** in 40 ml of ethanol was shaken in a current of hydrogen on 10 mg of Raney nickel at room temperature and atmospheric pressure. After absorption of the calculated amount of hydrogen, the catalyst was filtered off and the filtrate was concentrated *in vacuo*. The residue was basified with 10% ammonia and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to give 20 mg (83.3%) of *N*-norhomopetaline (**3**) as a viscous syrup: mass spectrum m/e 327 (M^+); ir ($CHCl_3$) 3520 cm^{-1}; uv (EtOH) 279.5 and 284 nm (log ϵ 3.41 and 3.40); nmr τ ($CDCl_3$) 7.57 (3 H, s, NMe), 6.25 (3 H, s, OMe), 6.16 (3 H, s, OMe), 4.47 (1 H, broad signal, OH), 3.44 (1 H, d, J = 8.5 Hz, 6-H), 3.27 (1 H, d, J = 8.5 Hz, 5-H), 3.23 (2 H, d, J = 9 Hz, 3′H and 5′-H), and 2.86 (2 H, d, J = 9 Hz, 2′-H and 6′-H). The oxalate formed pale brown needles (from methanol–ether), mp 171–172°.

Anal. Calcd for $C_{20}H_{25}NO_3 \cdot C_2H_2O_4 \cdot 0.25H_2O$: C, 62.62; H, 6.45; N, 3.32. Found: C, 62.51; H, 6.36; N, 3.33.

6-Ethoxycarbonylamino-1,2,3,4-tetrahydro-7,8-dimethoxy-1-(4-methoxyphenethyl)-2-methylisoquinoline (13).—A mixture of 2 g of 6-ethoxycarbonylamino-3,4-dihydro-7,8-dimethoxy-1-(4-methoxyphenethyl)isoquinoline[11] (**11**), 1.5 ml of methyl iodide, and 25 ml of methanol was refluxed for 2.5 hr and allowed to stand at room temperature overnight. After evaporation of the solvent *in vacuo*, the residue was washed with ether and taken up in 50 ml of methanol. To this solution was added 1 g of sodium borohydride in small portions at 0° with stirring during 30 min; stirring was continued at 0° for 30 min. After the mixture had been set aside at room temperature overnight, the excess of reagent was decomposed with acetic acid and the solvent was distilled off *in vacuo*. The residue was basified with 10% ammonia and extracted with chloroform. The extract was washed with water, dried over K_2CO_3, and evaporated *in vacuo* to leave 2 g (96.5%) of the tetrahydroisoquinoline **13** as a brown viscous syrup: mass spectrum m/e 428 (M^+); ir ($CHCl_3$ 3410 and 1732 cm^{-1}; uv (EtOH) 279.5 and 286 nm (log ϵ 3.80 and 3.75); nmr τ ($CDCl_3$) 8.67 (3 H, t, J = 7.0 Hz, CH_3CH_2), 7.58 (3 H, s, NMe), 6.27 (3 H, s, OMe), 6.23 (3 H, s, OMe), 6.17 (3 H, s, OMe), 5.76 (2 H, q, J = 7.0 Hz, CH_3CH_2), 3.18 (2 H, d, J = 9.0 Hz, 3′-H and 5′-H), 2.89 (1 H, NH), 2.80 (2 H, d, J = 9.0 Hz, 2′-H and 6′-H), and 2.40 (1 H, s, 5-H). The oxalate was recrystallized from methanol–ether to give colorless needles, mp 159–160°.

Anal. Calcd for $C_{24}H_{32}N_2O_5 \cdot C_2H_2O_4$: C, 60.22; H, 6.61; N, 5.40. Found: C, 60.05; H, 6.91; N, 5.26.

6-Amino-1,2,3,4-tetrahydro-7,8-dimethoxy-1-(4-methoxyphenethyl)-2-methylisoquinoline (14).—A mixture of 480 mg of the 6-ethoxycarbonylaminoisoquinoline **13**, 1.5 g of potassium hydroxide, and 30 ml of methanol was refluxed for 5.5 hr and the solvent was then removed by distillation *in vacuo*. The residue was extracted with chloroform, and the extract was washed with water, dried over K_2CO_3, and evaporated *in vacuo* to give 350 mg (87.5%) of the 6-aminoisoquinoline **14** as a pale brown viscous syrup: mass spectrum m/e 356 (M^+); ir ($CHCl_3$) 3450, 3360, and 1620 cm^{-1}; uv (EtOH) 280.5 and 286.5 nm (log ϵ 3.79 and 3.80); nmr τ ($CDCl_3$) 7.58 (3 H, s, NMe), 6.24 (9 H, s, 3 OMe), 3.75 (1 H, s, 5-H), 3.18 (2 H, d, J = 8.5 Hz, 3′-H and 5′-H), and 2.81 (2 H, d, J = 8.5 Hz, 2′-H and 6′-H). The oxalate gave pale brown needles (from methanol–ether), mp 151–152°.

Anal. Calcd for $C_{21}H_{28}N_2O_3 \cdot C_2H_2O_4 \cdot 0.5H_2O$: C, 60.64; H, 6.86; N, 6.15. Found: C, 61.05; H, 6.90; N, 6.10.

1,2,3,4-Tetrahydro-7,8-dimethoxy-1-(4-methoxyphenethyl)-2-methylisoquinoline (15).—To a solution of 310 mg of the aminoisoquinoline **14** in 8 ml of 1 *N* sulfuric acid was added dropwise 1.2 ml of 10% sodium nitrite with stirring at 0–5° during 15 min; the mixture was stirred at 0° for 1 hr. To this solution was added 0.6 ml of 30% hypophosphorous acid at 0°; the mixture was stirred at 0° for 2 hr, then set aside at room temperature for 2 days, basified with concentrated ammonia, and extracted with chloroform. The extract was washed with water, dried over K_2CO_3, and evaporated *in vacuo* to leave 287 mg of a pale brown viscous syrup, which was subjected to chromatography on 3.0 g of silica gel, eluting with ether to give 166 mg (56.0%) of the 7,8-dimethoxyisoquinoline **15** as a pale brown viscous syrup: mass spectrum m/e 341 (M^+); nmr τ ($CDCl_3$) 7.54 (3 H, s, NMe), 6.28 (3 H, s, OMe), 6.22 (3 H, s, OMe), 6.16 (3 H, s, OMe), 3.20 (2 H, s, 5-H and 6-H), 3.16 (2 H, d, J = 9.0 Hz, 3′-H and 5′-H), and 2.78 (2 H, d, J = 9.0 Hz, 2′-H and 6′-H). The oxalate was recrystallized from methanol–ether to give colorless needles: mp 164–165°; uv (EtOH) (oxalate) 279.5 and 285.5 nm (log ϵ 3.82 and 3.80).

Anal. Calcd for $C_{21}H_{27}NO_3 \cdot C_2H_2O_4$: C, 64.02; H, 6.77; N, 3.25. Found: C, 63.91; H, 6.77; N, 3.26.

Demethylation of 15 (Formation of *N*-Norhomopetaline).—A mixture of 500 mg of the above isoquinoline **15** and 20 ml of 20% hydrochloric acid was heated at 120° for 2 hr and then evaporated *in vacuo* to leave a gum, which was basified with 10% ammonia and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to leave 440 mg of a brown viscous syrup, which was chromatographed on 20 g of silica gel. Evaporation of the first chloroform–methanol (97:3, v/v) eluate *in vacuo* gave 95 mg (19.8%) of *N*-norhomopetaline (**3**) as a pale brown viscous syrup, whose spectroscopic data were superimposable on those of the authentic sample. The oxalate gave pale brown needles (from methanol–ether), mp and mmp 170–171.5°. The second eluate gave 50 mg (10.8%) of the 4′,8-dihydroxyisoquinoline **16** as a red viscous oil: mass spectrum m/e 313 (M^+); ir ($CHCl_3$) 3570 and 3510 cm^{-1}; nmr τ ($CDCl_3$) 7.57 (3 H, s, NMe), 6.18 (3 H, s, OMe), 4.91 (2 H, broad signal, 2 OH), 3.45 (1 H, d, J = 8.0 Hz, 6-H), 3.35 (2 H, d, J = 8.5 Hz, 3′-H and 5′-H), 3.26 (1 H, d, J = 8.0 Hz, 5-H), and 3.01 (2 H, d, J = 8.5 Hz, 2′-H and 6′-H); m/e 192 (base peak) [$M^+ - (CH_2)_2C_6H_4OH$].

Registry No.—**3**, 28116-36-1; **3** oxalate, 28116-37-2; **6**, 28116-38-3; **7**, 28116-39-4; **9**, 28116-40-7; **9** oxalate, 28116-41-8; **13**, 28116-42-9; **13** oxalate, 28201-46-9; **14**, 28116-43-0; **14** oxalate, 28116-44-1; **15**, 28116-45-2; **15** oxalate, 28116-46-3; **16**, 28116-47-4.

Acknowledgment.—We thank Mr. M. Yamazaki and Dr. M. Kawazu, Tanabe Seiyaku Co. Ltd., for their encouragements and Mr. S. Hirata, Miss A. Kawakami, Miss C. Yoshida, Miss R. Kato, Miss T. Yoshida, and Miss Y. Tadano, Pharmaceutical Institute, Tohoku University, for microanalyses and for spectral measurements. We also thank the Analytical Centre of Organic Chemistry Research Laboratory, Tanabe Seiyaku Co. Ltd., for microanalyses and spectral determinations.

Studies on the Syntheses of Heterocyclic Compounds. CCCXCVI.[1] An Alternative Total Synthesis of (±)-Galanthamine

T. KAMETANI,* K. SHISHIDO, E. HAYASHI, C. SEINO, T. KOHNO, S. SHIBUYA, AND K. FUKUMOTO

Pharmaceutical Institute, Tohoku University, Aobayama, Sendai, Japan

Received September 21, 1970

Galanthamine,[2] an *Amaryllidaceae* alkaloid isolated from *Lycoris radiata*, was assigned structure **1** by Barton.[3] A synthesis based on biogenetic lines was also carried out. Recently, some of the present authors reported total syntheses of (±)-galanthamine (**1**) and

(1) Part CCCXCV: T. Kametoni, K. Fukumoto, and M. Fujihara, *J. Org. Chem.*, **36**, 1293 (1971).

(2) W. C. Wildman, *Alkaloids*, **11**, 348 (1968), and references cited therein; T. Kametani, "The Chemistry of the Isoquinoline Alkaloids," Hirokawa Publishing Co., Tokyo, and Elsevier, Amsterdam, 1968, pp 196, 296.

(3) D. H. R. Barton and G. W. Kirby, *J. Chem. Soc.*, 806 (1962).