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Studies on the Chemical Constituents of Rutaceous Plants. XXXVI.[1] Synthesis of Ethyl Isodecarine

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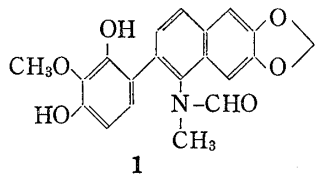
Ethyl isodecarine (3) was synthesized by Pschorr reaction of (E)-styrene carboxylic acid (13).

The structure of decarine (2) was established by chemical evidence that ethyl isodecarine (3) is not identical with the sample of ethyl decarine (15).

Keywords——ethyl isodecarine; benzo[*c*]phenanthridine; synthesis; dihydroisoquinoline; Pschorr reaction

In the course of studies on the chemical constituents of *Rutaceous* plants, we[3] isolated a new phenolic amide alkaloid (1) from the bark of *Xanthoxylum arnottianum* Maxim. (Japanese name: Iwa-zansho) and designated it as "Iwamide." Its structure[4] was established by chemical correlation with decarine (2), a tertiary phenolic benzo[*c*]phenanthridine alkaloid, which naturally occurred in the same plant.



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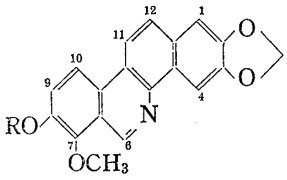

2: R=H
16: R=CH_3

Chart 1

In 1974, Cavé *et al.*[5] showed the presence of the methoxy group at the C_7 position in decarine (2) by observation of nuclear Overhauser effect (NOE) between the methoxy group and the C_6 imine proton. But, there lacks any chemical proof supporting this spectrological result. Furthermore, we need a derivative of the positional isomer on the methoxy and the hydroxy groups of decarine (2) in connection with our another work on developing the use of a lanthanide shift reagent to determine the functional group at the C_7 position of the fully aromatized benzo[*c*]phenanthridine alkaloid. Therefore, we have prepared ethyl isodecarine (3) in which an ethoxy and a methoxy group are located at C_7 and C_8, respectively. We utilized the reaction sequence developed by Abramovitch[6] and Dyke[7] for the present purpose.

1) Part XXXV: H. Ishii, T. Ishikawa, K. Hosoya, and N. Takao, *Chem. Pharm. Bull.* (Tokyo), **26**, 166 (1978).
2) Location: *1–33, Yayoi-cho, Chiba, 280, Japan.*
3) H. Ishii, T. Ishikawa, and J. Haginiwa, *Yakugaku Zasshi*, **97**, 890 (1977).
4) T. Ishikawa and H. Ishii, *Heterocycles*, **5**, 275 (1976).
5) J. Vaquette, J.-L. Pousset, R.-R. Paris, and A. Cavé, *Phytochemistry*, **13**, 1257 (1974).
6) R.A. Abramovitch and G. Terzakian, *Can. J. Chem.*, **41**, 2265 (1963).
7) S.F. Dyke, M. Sainsbury, and B.J. Moon, *Tetrahedron*, **24**, 1467 (1968); M. Sainsbury, S.F. Dyke, and B.J. Moon, *J. Chem. Soc.* (*C*), **1970**, 1797; W.J. Gensler, S.F. Lawless, A.L. Bluhm, and H. Dertouzos, *J. Org. Chem.*, **40**, 733 (1975).

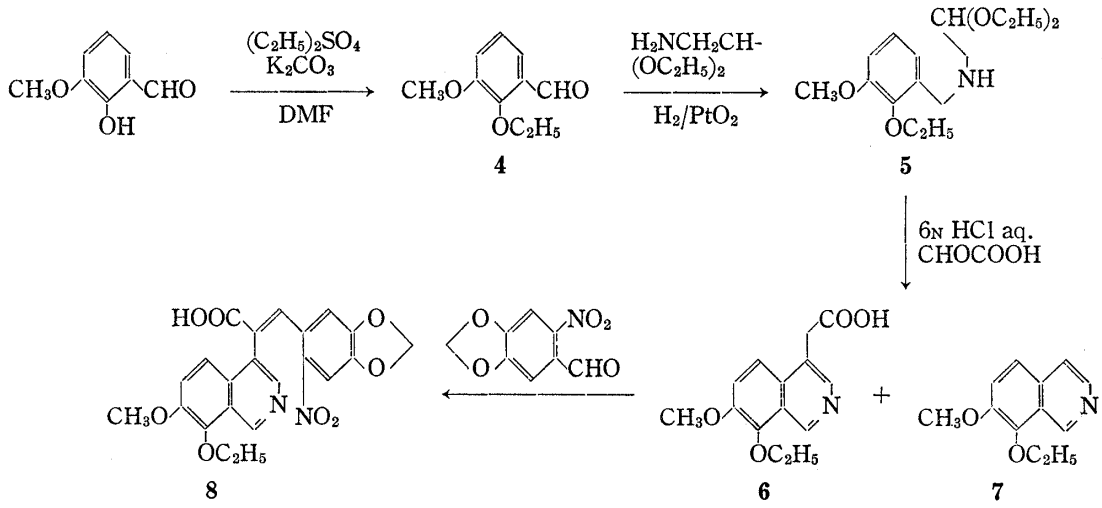

Chart 2

The starting 2-ethoxy-3-methoxybenzaldehyde[8,9] (**4**) was prepared by treatment of *o*-vanillin with diethyl sulfate in dimethylformamide[10] in good yield. Catalytic reduction of the aldehyde (**4**) in the presence of diethyl aminoacetal gave 2-ethoxy-3-methoxybenzylaminoacetaldehyde diethylacetal (**5**) as an oily substance in 95.1% yield. Treatment of the aminoacetal (**5**) with 6N hydrochloric acid followed by addition of glyoxylic acid afforded 8-ethoxy-7-methoxy-4-isoquinolineacetic acid (**6**) hydrochloride in 84.7% yield with a small amount of 8-ethoxy-7-methoxyisoquinoline (**7**) as a by-product. Condensation of the acid (**6**) with 6-nitropiperonal[11] yielded the (E)-styrene carboxylic acid (**8**), mp 245—248° (dec.), in 71.2% yield as a sole product. The (E)-configuration of this acid (**8**) was supported from the results obtained on the following decarboxylation reaction.

At this stage of our experiments, we planned to attempt the photo-Pschorr reaction. Decarboxylation of the (E)-styrene carboxylic acid (**8**) with copper chromite[12] in quinoline under the relatively mild condition gave a mixture of the (Z)-styrene (**9**), mp 195—196.5°, and the (E)-styrene (**10**), mp 239—240°, in 32.2% and 26.4% yields, respectively. But the same reaction under the relatively strong condition gave a trace amount of the (Z)-styrene (**9**), the (E)-styrene (**10**) in 29.0% yield and the third product (**11**) as yellow needles, mp 202—204°, in 8.8% yield. The configurations of these styrenes (**9** and **10**) were assignable by the facts that, in the nuclear magnetic resonance (NMR) spectra, the coupling constant of the olefinic proton in the (Z)-styrene (**9**) is 11.0 Hz, but that in the (E)-styrene (**10**) 16.0 Hz. The formation of a large amount of the styrene having the (Z)-form under the mild condition indicates that the configuration of the original styrene carboxylic acid (**8**) should have the (E)-form. This observation is consistent with the reported deduction[6] in the synthesis of a simple benzo[*c*]phenanthridine.

8) *a*) W. Davies and L. Rubenstein, *J. Chem. Soc.*, **123**, 2839 (1923). *b*) R. Delaby, G. Tsatsas, and M.C. Jendrot, *Bull. Soc. Chim. France*, **1956**, 1830 [*C.A.*, **51**, 7318*g* (1957)].

9) The reported method[8] for ethylation of *o*-vanillin required a long reaction time (19—43 hr) and gave relatively bad yield (23—73%). Therefore, we examined the reaction condition precisely and succeeded in shortening the reaction time (3.5 hr) and increasing the yield (89.0%).

10) We also used dimethylsulfoxide (DMSO) as solvent. In this case, the yield is almost quantitative but a small amount of 3-methoxy-2-methylthiomethoxybenzaldehyde was formed. [(3-MeO) (2-CH_3SCH_2O)-Ph(CHO): Colourless oil, bp 90—95° (1 mmHg). *Anal.* Calcd. for $C_{10}H_{12}O_3S$: C, 56.58; H, 5.70. Found: C, 57.49; H, 5.78. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1685 (C=O). NMR (CCl_4) δ: 2.13 (3H, s, SCH_3), 3.84 (3H, s, OCH_3), 5.24 (2H, s, OCH_2S), 6.92—7.20 (2H, m, arom. H), 7.24—7.48 (1H, m, C_6–H), 10.28 (1H, s, CHO). MS *m/e*: 212 (M^+, 25.9%), 150 (base peak), 61 ($CH_3SCH_2^+$, 83.8%)].

11) J.B. Ekeley and M.S. Klemme, *J. Am. Chem. Soc.*, **50**, 2711 (1928).

12) W.A. Lazier and H.R. Arnold, "Org. Synth.," Coll. Vol. 2, 1943, p. 142.

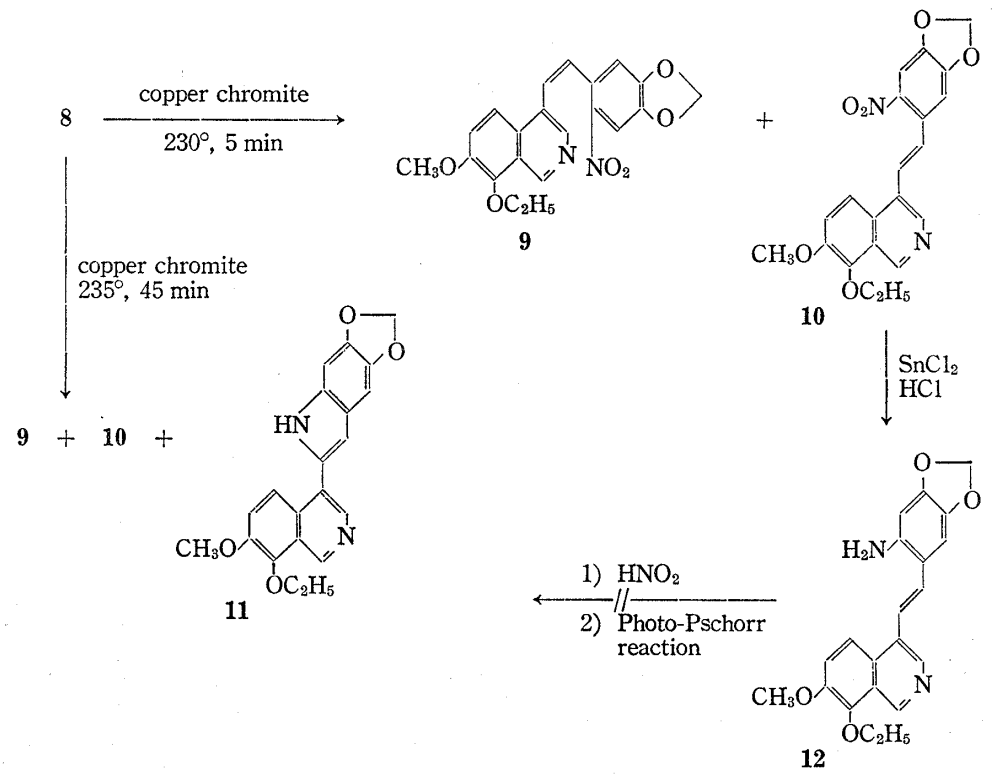

Chart 3

The empirical formula of the third product (**11**) was fixed to $C_{21}H_{18}N_2O_4$ on the basis of the elemental analysis and the mass spectrum. The NMR spectrum of it shows the presence of a methoxy, an ethoxy, a methylenedioxy and an NH group in its molecule and also shows five 1H singlets and one pair of AB type signals in the aromatic region. These evidences suggested that the third product (**11**) is 8-ethoxy-7-methoxy-4-(5,6-methylenedioxyindol-2-yl)-isoquinoline. This is the first case that the indolic product was obtained by decarboxylation of a styrene carboxylic acid which is an intermediate in Pschorr reaction, although formation of coumarin derivatives[13] was reported, as far as we know. Reduction of the (E)-styrene (**10**) with stannous chloride gave the (E)-amino styrene (**12**), mp 177—179°, in 64.8% yield,

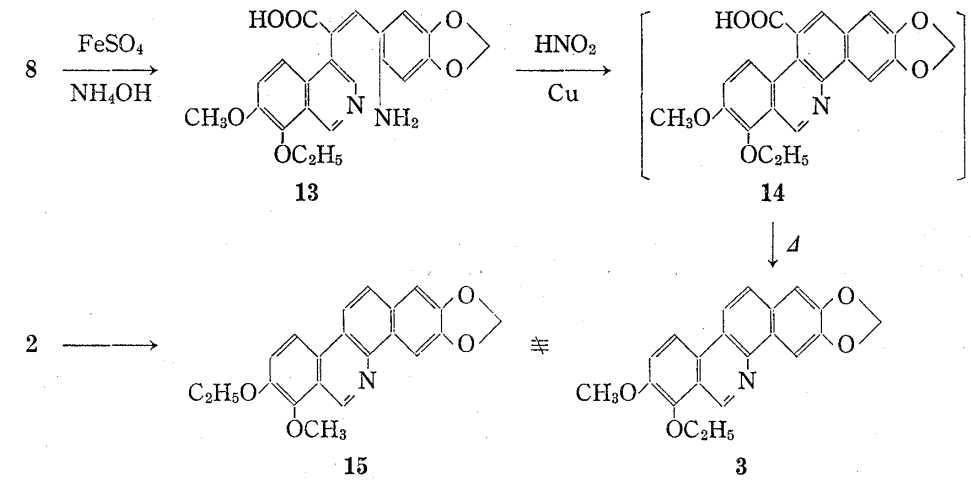

Chart 4

13) N. Oda, *Yakugaku Zasshi*, **82**, 1185 (1962).

but the subsequent diazotization followed by photo-Pschorr cyclization[14] did not give any isolable product.

On the other hand, reduction of the (E)-styrene carboxylic acid (**8**) with ferrous sulfate in a basic medium gave an amino acid (**13**), mp 230° (dec.), in 93.2% yield. Purification of this was so hard that the crude material was used in the following step. Diazotization of the amino acid (**13**) followed by Pschorr reaction afforded the ring-closure product (**14**), which was decarboxylated thermally to give ethyl isodecarine (**3**), mp 185.5—186.5°, in 32.1% yield. We confirmed that this material (**3**) was undoubtedly different from ethyl decarine (**15**) which was obtained by ethylation of decarine (**2**). As it is known that methylation of decarine[5,15] (**2**) gave the known norchelerythrine (**16**), this result becomes the chemical evidence for the structure of decarine (**2**). Now a pair of isomers on the substituents located at the C_7 and C_8 positions is available to our work on a lanthanide shift reagent. The results[16] on this matter will be published elsewhere in the near future.

Experimental[17]

2-Ethoxy-3-methoxybenzaldehyde (**4**)——A mixture of *o*-vanillin (2.0137 g), Et_2SO_4 (1.92 ml), and anhydr. K_2CO_3 (2.0030 g) in DMF (20 ml) was stirred at room temperature for 2 hr and then at 50—55° for 1.5 hr. The mixture was poured into a large quantity of water and extracted with ether. The ethereal solution was washed with 5% NaOH aq., dried over anhydr. K_2CO_3, and evaporated to dryness. Distillation of the residue at 112.5—113° (3 mmHg) gave colourless oil (2.1217 g) [lit.[8a] bp 140° (18 mmHg)]. IR ν_{max}^{neat} cm^{-1}: 1685 (C=O).

2-Ethoxy-3-methoxybenzylaminoacetaldehyde Diethylacetal (**5**)——A mixed solution of the above aldehyde (**4**) (4.9956 g) and aminoacetal (11.1012 g) in abs. EtOH (50 ml) was hydrogenated over PtO_2 (100.4 mg) at atmospheric pressure and room temperature. After the catalyst was filtered off, the filtrate was evaporated to dryness *in vacuo*. Distillation of the residue at 147° (2 mmHg) gave colourless oil (7.8439 g). IR ν_{max}^{neat} cm^{-1}: 3370 (NH). NMR (CCl_4) δ: 1.14 (6H, t, J=7.0 Hz, $OCH_2C\underline{H}_3\times 2$), 1.34 (3H, t, J=7.0 Hz, $ArOCH_2C\underline{H}_3$), 1.34 (1H, s, NH, exchangeable with D_2O), 2.57 (2H, d, J=6.0 Hz, $NC\underline{H}_2CH$), 3.46 and 3.53 (each 2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 3.68 (2H, s, $ArCH_2N$), 3.79 (3H, s, OCH_3), 3.99 (2H, q, J=7.0 Hz, $ArOC\underline{H}_2CH_3$), 4.45 (1H, t, J=6.0 Hz, $CH_2C\underline{H}$(O)–O), 6.60—6.90 (3H, m, arom. H). MS *m/e*: 297 (M^+, 0.66%), 165 (M^+-132, 100%).

8-Ethoxy-7-methoxy-4-isoquinolineacetic Acid (**6**) **Hydrochloride**——A solution of the aminoacetal (**5**) (505.0 mg) in 6 N HCl aq. (10 ml) was stirred at room temperature for 24 hr under argon. After the reaction solution was heated at 95° for 10 min, glyoxylic acid (212.5 mg) in 2 N HCl aq. (0.5 ml) was added. The mixture was heated for 1 hr at 95° under argon and then evaporated to dryness *in vacuo*. The residue (548.7 mg) was dissolved in distilled water (100 ml) and adjusted to pH 7 with NaOH aq. The solution was adsorbed to an ion exchange column (Amberlite CG-400: 10 g). The adsorbed resin was washed with distilled water and then eluted with 0.01 N HCl aq. The eluant was evaporated to dryness *in vacuo*. Recrystallization of the residue from EtOH–ether gave yellow needles (428.4 mg), mp 176.5—177° (dec.). *Anal.* Calcd. for $C_{14}H_{15}NO_4\cdot HCl$: C, 56.47; H, 5.42; N, 4.70. Found: C, 56.39; H, 5.39; N, 4.68. IR ν_{max}^{Nujol} cm^{-1}: 2500 ($=\overset{|}{N}{}^+H$), 1710 (C=O). NMR (D_2O)[18] δ: 1.47 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 4.11 (3H, s, OCH_3), 4.34 (2H, s, $ArCH_2CO$), 4.36 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.96 (1H, d, J=9.5 Hz, C_6–H), 8.07 (1H, d, J=9.5 Hz, C_5–H), 8.36 (1H, s, C_3–H), 9.53 (1H, s, C_1–H).

14) T. Kametani and K. Fukumoto, *Accounts of Chem. Research*, **5**, 212 (1972); T. Kametani, R. Charubala, M. Ihara, M. Koizumi, K. Takahashi, and K. Fukumoto, *J. Chem. Soc. (C)*, **1971**, 3315.
15) H. Ishii, T. Ishikawa, S.-T. Lu, and I.-S. Chen, *Yakugaku Zasshi*, **96**, 1458 (1976).
16) H. Ishii, T. Ishikawa, Y.-I. Ichikawa, and H. Ohida, in preparation.
17) All melting points were measured on a micro-melting hot-stage (Yanagimoto) and are uncorrected. Infrared (IR) and ultraviolet (UV) spectra were obtained with Hitachi EPI-G3 and Hitachi EPS-3T spectrometers, respectively. NMR spectra were obtained with JEOL JNM-MH-100 using tetramethylsilane as internal reference and the abbreviations of singlet, doublet, triplet, quartet, and multiplet were represented as s, d, t, q, and m, respectively. Mass spectra were measured with Hitachi RMU-6E spectrometer at 70 eV of chamber voltage on direct inlet system. For TLC and preparative thin-layer chromatography (TLC), Kieselgel GF_{254} nach Stahl (Merck) was used. For column chromatography SILICIC ACID, 100 mesh, Mallinckrodt Chemical Works, was used.
18) As internal reference is used 3-(trimethylsilyl)propanesulfonic acid, sodium salt (DSS).

8-Ethoxy-7-methoxyisoquinoline (7)——The initial aqueous elution on the ion exchange resin column in the above experiment and washings of the adsorbed column were gathered. The solution was made alkaline with NaOH aq. and extracted with ether. The ethereal solution was dried over anhydr. K_2CO_3 and evaporated. Distillation of the residue at 120° (1 mmHg) gave colourless oil (43.4 mg). NMR (CCl_4) δ: 1.47 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 3.94 (3H, s, OCH_3), 4.24 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.24—7.56 (3H, m, arom. H), 8.28 (1H, dif. d, J=7.0 Hz, C_3–H), 9.38 (1H, br. s, C_1–H). Picrate, mp 205—216°, which was recrystallized from MeOH–$CHCl_3$.

(E)-8-Ethoxy-7-methoxy-α-(6-nitropiperonylidene)-4-isoquinolineacetic Acid (8)——A mixture of the acid (6) hydrochloride (501.0 mg), 6-nitropiperonal[11] (496.7 mg), AcONa (145.0 mg), Ac_2O (7.5 ml), and Et_3N (5 ml) was stirred at 95—98° for 30 min and then poured into hot water (25 ml). After stirring at 100° for 10 min, the mixture was allowed to stand in a refrigerator for 24 hr. The precipitate was collected by filtration and recrystallized from MeOH–$CHCl_3$ to give yellow prisms (525.3 mg), mp 245—248° (dec.). *Anal.* Calcd. for $C_{22}H_{18}N_2O_8 \cdot 1/4H_2O$: C, 59.66; H, 4.21; N, 6.33. Found: C, 59.65; H, 4.12; N, 6.31. IR ν_{max}^{Nujol} cm^{-1}: 1685 (C=O), 1510, 1330 (NO_2). NMR (CF_3COOH) δ: 1.56 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 4.16 (3H, s, OCH_3), 4.64 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.01 (2H, s, OCH_2O), 6.41 (1H, s, vinyl H), 7.66 (1H, s, $C_{2'}$–H), 7.94 (1H, d, J=9.0 Hz, C_6–H), 8.12 (1H, d, J=9.0 Hz, C_5–H), 8.28 (1H, br. s, C_3–H), 8.86 (1H, s, $C_{5'}$–H), 9.74 (1H, br. s, C_1–H).

Decarboxylation of the (E)-Styrene Carboxylic Acid (8) a) Under the Mild Condition——To a solution of the (E)-styrene carboxylic acid (8) (500.2 mg) in quinoline (5 ml) was added copper chromite[12] (52.0 mg). The mixture was heated at 230° for 5 min under argon. After the catalyst was filtered off, quinoline as solvent was removed off by steam-distillation. The filtrate was evaporated to dryness *in vacuo*. The residue was dissolved in $CHCl_3$ and chromatographed on SiO_2.

(Z)-8-Ethoxy-7-methoxy-4-(4,5-methylenedioxy-2-nitrostyryl)isoquinoline (9)——First eluant with $CHCl_3$ gave slightly yellow plates (144.9 mg), mp 195—196.5°, which were recrystallized from $CHCl_3$–ether. *Anal.* Calcd. for $C_{21}H_{18}N_2O_6$: C, 63.95; H, 4.60; N, 7.10. Found: C, 63.91; H, 4.63; N, 7.06. IR ν_{max}^{Nujol} cm^{-1}: 1505, 1330 (NO_2). NMR ($CDCl_3$) δ: 1.45 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 3.98 (3H, s, OCH_3), 4.30 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 5.90 (2H, s, OCH_2O), 6.28 (1H, s, $C_{6'}$–H), 7.04 (1H, d, J=11.0 Hz, vinyl H), 7.22 (1H, d, J=11.0 Hz, vinyl H), 7.46 (1H, d, J=9.0 Hz, C_6–H), 7.52 (1H, s, $C_{3'}$–H), 7.72 (1H, d, J=9.0 Hz, C_5–H), 8.04 (1H, br. s, C_3–H), 9.38 (1H, br. s, C_1–H).

(E)-8-Ethoxy-7-methoxy-4-(4,5-methylenedioxy-2-nitrostyryl)isoquinoline (10)——Second eluant with $CHCl_3$ gave orange needles (118.6 mg), mp 239—240°, which were recrystallized from $CHCl_3$–MeOH. *Anal.* Calcd. for $C_{21}H_{18}N_2O_6$: C, 63.95; H, 4.60; N, 7.10. Found: C, 63.58; H, 4.60; N, 7.04. IR ν_{max}^{Nujol} cm^{-1}: 1510, 1305 (NO_2). NMR (CF_3COOH) δ: 1.56 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 4.18 (3H, s, OCH_3), 4.63 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.18 (2H, s, OCH_2O), 7.26 (1H, s, $C_{6'}$–H), 7.50 (1H, d, J=16.0 Hz, vinyl H), 7.72 (1H, s, $C_{3'}$–H), 7.93 (1H, d, J=16.0 Hz, vinyl H), 8.12 (1H, d, J=9.5 Hz, C_6–H), 8.32 (1H, d, J=9.5 Hz, C_5–H), 8.48 (1H, d, J=6.0 Hz, C_3–H), 9.62 (1H, d, J=7.0 Hz, C_1–H).

b) Under the Strong Condition——The mixture of the (E)-styrene carboxylic acid (8) (1.5004 g) and copper chromite[12] (151.4 mg) in quinoline (15 ml) was heated at 235° for 45 min under argon. Treatment of the reaction mixture by the same procedure described in the preceding item gave a mixture which showed three spots on TLC. This mixture was columnchromatographed on SiO_2 using $CHCl_3$ as solvent.

First eluant shows the spot corresponding to that of the (Z)-isomer (9) on TLC but the amount of it was negligible.

Second eluant gave (E)-8-ethoxy-7-methoxy-4-(4,5-methylenedioxy-2-nitrostyryl)isoquinoline (10) (391.1 mg) as orange needles, mp 238—240°.

8-Ethoxy-7-methoxy-4-(5,6-methylenedioxyindol-2-yl)isoquinoline (11)——Third eluant gave yellow needles (109.6 mg), mp 202—204°, which were recrystallized from $CHCl_3$–MeOH. *Anal.* Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.00; N, 7.73. Found: C, 69.65; H, 4.97; N, 7.68. NMR ($CDCl_3$) δ: 1.48 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 3.96 (3H, s, OCH_3), 4.28 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 5.94 (2H, s, OCH_2O), 6.69[19] (1H, d, J=2.3 Hz, $C_{3'}$–H), 6.92 and 7.04 (each 1H, s, $C_{4'}$ and $C_{7'}$–H), 7.44 (1H, d, J=9.3 Hz, C_6–H), 8.03 (1H, d, J=9.3 Hz, C_5–H), 8.46 (1H, s, C_3–H), 8.90 (1H, br. s, NH, exchangeable with D_2O), 9.44 (1H, s, C_1–H). MS *m/e*: 362 (M^+, 100%).

(E)-8-Ethoxy-7-methoxy-4-(2-amino-4,5-methylenedioxystyryl)isoquinoline (12)——To a suspension of the (E)-styrene (10) (98.9 mg) in ether (1.5 ml) was added a solution of $SnCl_2 \cdot 2H_2O$ (864.3 mg) in conc. HCl (0.9 ml). The mixture was heated at 60°, and the same amount of $SnCl_2 \cdot 2H_2O$ (864.2 mg) in conc. HCl (0.9 ml) was added after 35 min. The mixture was kept at 60° for further 3 hr and poured into ice-water. The aqueous solution was made alkaline and carefully extracted with AcOEt. The organic layer was dried over anhydr. K_2CO_3 and evaporated to dryness *in vacuo*. Recrystallization of the residue from MeOH–$CHCl_3$ gave fine orange needles (59.2 mg), mp 177—179°. *Anal.* Calcd. for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.07; H, 5.62; N, 7.63. IR ν_{max}^{Nujol} cm^{-1}: 3380, 3450 (NH_2). NMR (DMSO-d_6) δ: 1.38 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 3.96 (3H, s, OCH_3), 4.21 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 5.84 (2H, s, OCH_2O), 6.31 (1H, s,

19) This signal changed into singlet after addition of D_2O.

$C_{3'}$–H), 7.28 (1H, s, $C_{6'}$–H), 7.44 (2H, s, vinyl H), 7.65 (1H, d, J=10.0 Hz, C_6–H), 8.12 (1H, d, J=10.0 Hz, C_5–H), 8.73 (1H, s, C_3–H), 9.22 (1H, s, C_1–H). MS *m/e*: 364 (M^+, 100%).

Photo-Pschorr Reaction——A solution of $NaNO_2$ (10.4 mg) in water (0.2 ml) was added dropwise at 0° to a solution of the (E)-amino styrene (**12**) (54.6 mg) in 1 N H_2SO_4 aq. (7.6 ml) containing AcOH (0.5ml). After stirring at 0—3° for 1 hr, the mixture was diluted with water to 50 ml. The solution was irradiated with a Hanovia 450 W mercury lamp (Pyrex filter at 5—10° for 8 hr), made alkaline with NH_4OH aq., and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated to dryness *in vacuo*. All trials to obtain the pure product from the residue[20] showing more than seven spots on TLC were failed.

(E)-8-ethoxy-7-methoxy-α-(6-aminopiperonylidene)-4-isoquinolineacetic Acid (**13**)——A hot aqueous solution of $FeSO_4 \cdot 7H_2O$ (26.880 g in 94 ml) was added to a solution of the (E)-styrene carboxylic acid (**8**) (4.7035 g) in conc. NH_4OH (140 ml) at 80° with vigorous stirring and kept to stir at the same temperature for 10 min. After the hot solution was filtered off, the filtrate was acidified with AcOH and kept to stand for 24 hr in a refrigerator. The yellow crystalline solid (4.0820 g), mp 230° (dec.), was collected by filtration. IR ν_{max}^{KBr} cm^{-1}: 3400, 3470 (NH_2). This crude material was used to the following experiment.

7-Ethoxy-8-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridine[Ethyl Isodecarine] (**3**)——An aqueous solution of $NaNO_2$ (1.2654 g in 100 ml) was added dropwise at 0° to a cooled suspension of the amino acid (**13**) (4.9536 g) in 2 N HCl aq. (300 ml). The mixture was stirred at 0° for 30 min. After excess of nitrous acid was decomposed with urea (374 mg), copper powder (4.6755 g) was added to the mixture. The mixture was kept to stir at room temperature for 5 hr. The precipitate was collected by filtration and dissolved in quinoline (40 ml). After addition of copper powder (700 mg), the solution was heated at 250° for 25 min with stirring, steam-distilled to remove quinoline, and extracted with $CHCl_3$. The chloroform solution was washed with 5% NaOH aq., dried over anhydr. K_2CO_3, and evaporated to dryness *in vacuo*. Purification of the residue by column chromatography on SiO_2 (Kieselgel 60, Merck 100 g) using a mixed solvent [benzene–AcOEt (50: 1 v/v)] as eluant gave colourless needles (1.3512 g), mp 185.5—186.5°, which were recrystallized from $CHCl_3$–MeOH. *Anal.* Calcd. for $C_{21}H_{17}NO_4$: C, 72.61; H, 4.93; N, 4.03. Found: C, 72.24; H, 4.86; N, 4.00. IR ν_{max}^{Nujol} cm^{-1}: 1600, 1585 (C=C). NMR ($CDCl_3$) δ: 1.51 (3H, t, J=7.0 Hz, $CH_2\underline{CH_3}$), 3.99 (3H, s, OCH_3), 4.32 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 6.06 (2H, s, OCH_2O), 7.19 (1H, s, C_1–H), 7.50 (1H, d, J=9.0 Hz, C_9–H), 7.75 (1H, d, J=9.0 Hz, C_{12}–H), 8.25 (2H, d, J=9.0 Hz, C_{10} and C_{11}–H), 8.64 (1H, s, C_4–H), 9.69 (1H, s, C_6–H). MS *m/e*: 347 (M^+, 100%).

Ethyl Decarine (**15**)——A solution of diazoethane in ether [prepared from nitrosoethylurea (4 g)] was added to a solution of decarine[3,15] (**2**) (30 mg) in abs. EtOH (30 ml). After kept to stand at room temperature for 2 hr, the mixture was evaporated to dryness *in vacuo*. Recrystallization of the residue from $CHCl_3$–EtOH gave colourless fine needles (24.9 mg), mp 197—199°. *Anal.* Calcd. for $C_{21}H_{17}NO_4 \cdot 1/5CHCl_3$: C, 68.59; H, 4.67; N, 3.77. Found: C, 68.62; H, 4.69; N, 3.68. IR ν_{max}^{Nujol} cm^{-1}: 1605, 1590 (C=C). UV λ_{max}^{EtOH} nm (log ε): 243 (4.57), 257 (4.56), 277 (4.70), 324 (4.19), 364 (3.47) sh, 386 (3.40). NMR ($CDCl_3$) δ: 1.51 (3H, t, J=7.0 Hz, $CH_2\underline{CH_3}$), 4.15 (3H, s, OCH_3), 4.23 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 6.09 (2H, s, OCH_2O), 7.25 (1H, s, C_1–H), 7.52 (1H, d, J=9.0 Hz, C_9–H), 7.81 (1H, d, J=9.0 Hz, C_{12}–H), 8.25 (1H, d, J=9.0 Hz, C_{10}–H), 8.28 (1H, d, J=9.0 Hz, C_{11}–H), 8.66 (1H, s, C_4–H), 9.71 (1H, s, C_6–H).

20) TLC of this residue did not show the spot corresponding to ethyl isodecarine (**3**).