32. *Phenolic Alkaloids occurring in* Lycoris radiata.

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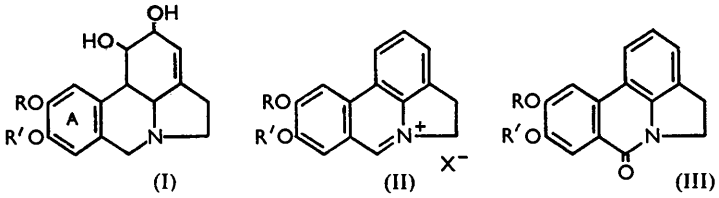
The position of the phenolic hydroxyl group in *pseudo*lycorine (I; R = H, R′ = Me) has been located by degradation of its ethyl ether, and by synthesis of the resulting phenanthridone (III; R = Et, R′ = Me).

Two new phenolic alkaloids, norpluviine and demethylhomolycorine have been isolated from *Lycoris radiata*, and shown to have structures (IV; R = Me, R′ = H) and (V; R = Me, R′ = H), respectively.

Kondo, Tomimura, and Ishiwata [1] reported in 1932 the isolation of a new phenolic base from the bulbs of *Lycoris radiata* and named it *pseudo*lycorine since they presumed that it possessed the same molecular formula as that of lycorine,[2] $C_{16}H_{17}O_4N$. For further characterisation they prepared derivatives such as the hydrochloride, methiodide, and acetate and showed also that the base contained one methoxyl and three hydroxyl groups, but no *N*-methyl group; however, no extensive degradations were undertaken. Nine years later, Professor Kondo generously provided one of us (S. U.) with the original material which made it possible for us to re-investigate this valuable alkaloid. We have found that analytical values of the base and its derivatives are in better agreement with the molecular formula $C_{16}H_{19}O_4N$ than with the previous one. Zinc dust distillation of the base yielded phenanthridine which suggested that the base might belong to the phenanthridine alkaloids, as does lycorine.[3] In order to elucidate the structure, however, it seemed desirable to secure additional quantities of the alkaloid, but no *pseudo*lycorine was ever obtained from extracts of the bulbs of *Lycoris radiata* procured in our vicinity and the problem remained dormant until 1956 when Fales, Giuffrida, and Wildman [4] demonstrated that the *O*-methyl derivative obtained by methylation of *pseudo*lycorine with diazomethane was identical with a new non-phenolic alkaloid occurring in the King Alfred daffodil. They named this new base methyl*pseudo*lycorin and assigned to it the structural formula (I; R = R′ = Me), so that *pseudo*lycorine must be represented by (I; R = H, R′ = Me or *vice versa*).

In order to locate the position of the hydroxyl group, *pseudo*lycorine was ethylated with diazoethane. The resulting *O*-ethyl derivative, when treated with phosphorus oxychloride, gave an anhydro-*O*-ethyl*pseudo*lycorinium salt [5] (II; R = Et; R′ = Me), the sparingly soluble iodide being most conveniently isolated. Oxidation of this salt with alkaline potassium ferricyanide afforded a lactam which was shown to be identical with the synthetic compound (III; R = Et, R′ = Me).



Both the lactam (III; R = Et, R′ = Me) and its isomer (III; R = Me, R′ = Et) were synthesised from the respective *N*-benzoyl dihydroindoles by the method previously used for preparation of the analogous **6** : 7-methylenedioxypyrrolinophenanthridone.[6]

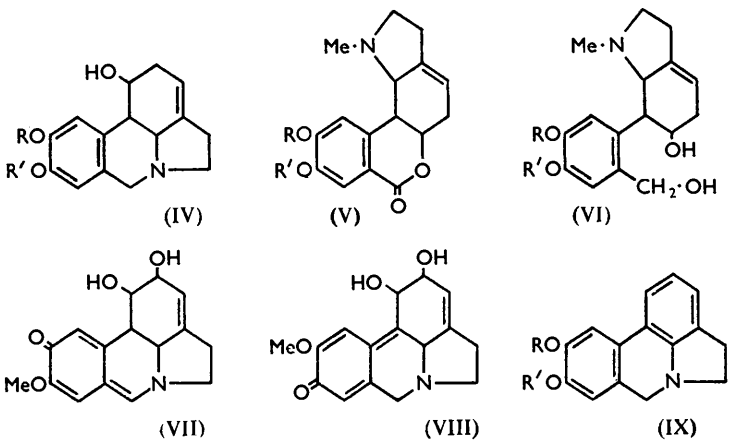
As well as *pseudo*lycorine, two more phenolic alkaloids have recently been isolated from

[1] Kondo, Tomimura, and Ishiwata, *J. Pharm. Soc. Japan*, 1932, **52**, 433.
[2] Kondo and Tomimura, *ibid.*, 1928, **48**, 223.
[3] Kondo and Uyeo, *Ber.*, 1935, **68**, 1756.
[4] Fales, Giuffrida, and Wildman, *J. Amer. Chem. Soc.*, 1956, **78**, 4145.
[5] Cf. Kondo, Takeda, and Kotera, *Ann. Report, Itsuu Lab.*, 1954, **5**, 66.
[6] Humber, Kondo, Kotera, Takagi, Takeda, Taylor, Thomas, Tsuda, Tsukamoto, Uyeo, Yajima, and Yanaihara, *J.*, 1954, 4622.

the same plant, namely norpluviine [7] and demethylhomolycorine. A concentrated methanolic solution of the phenolic fraction deposited crystals of norpluviine on storage for a long time, and the ethyl acetate-soluble fraction of the mother-liquor of norpluviine afforded demethylhomolycorine after chromatography over alumina.

Norpluviine has the formula $C_{15}H_{16}O_2N{\cdot}OMe$. It is soluble in aqueous sodium hydroxide and gives a violet ferric chloride test, indicating its phenolic character. With diazomethane it afforded the non-phenolic pluviine [7] (IV; R = R′ = Me). Norpluviine therefore has structure (IV; R = Me, R′ = H or *vice versa*). The correctness of the first possibility was established by degradation of *O*-ethylnorpluviine to the phenanthridone (III; R = Me, R′ = Et) as follows. *O*-Ethylnorpluviine, heated with acetic anhydride, gave, together with *O*-acetyl-*O*-ethylnorpluviine, an anhydrodehydro-*O*-ethylnorpluviinium salt (II; R = Me, R′ = Et) (pluviine behaved in the same way [7]). This was immediately converted by ferricyanide into the more conveniently identifiable lactam, m. p. 226—228°, identical with the synthetic phenanthridone (III; R = Me, R′ = Et) described above.

The further phenolic alkaloid, demethylhomolycorine, $C_{17}H_{19}O_4N$, was readily soluble in cold aqueous sodium hydroxide and gave a violet colour with ferric chloride. The ultraviolet absorption spectrum exhibited bands which were very similar to those of homolycorine and the infrared spectrum showed absorptions at 3·05 (OH), 5·89 (C=O), and 6·18 μ (aromatic ring) in agreement with expectation. Methylation with diazomethane converted this alkaloid into homolycorine, as shown by a mixed melting point and infrared spectra. While homolycorine contained two methoxyl groups, demethylhomolycorine was shown by analysis to have one, which lead us to propose formula (V; R = Me, R′ = H or *vice versa*) for the latter. A decision in favour of (V; R = Me, R′ = H) was made by the following degradation. Demethylhomolycorine was ethylated, then reduced with lithium aluminium hydride to the diol (VI; R = Me, R′ = Et). This was treated with



toluene-*p*-sulphonyl chloride in pyridine and the product was processed in the manner used for conversion of tetrahydrohomolycorine into pluviine (forthcoming paper). Distillation *in vacuo* of the crude methochloride and purification of the distillate did not lead as expected to ethylnorpluviine, the only isolable product being the phenanthridone (III; R = Me, R′ = Et) formed apparently as a result of aerial oxidation of the intermediate, anhydrodehydro-*O*-ethylnorpluviine (IX; R = Me, R′ = Et). The amount of demethylethylhomolycorine at our disposal precluded a repetition of this experiment, but the isolation of the phenanthridone was sufficient to prove that demethylethylhomolycorine and demethylhomolycorine must be represented by the formulæ (V; R = Me, R′ = Et) and (V; R = Me, R = H), respectively.

[7] Boit, Ehmke, Uyeo, and Yajima, *Chem. Ber.*, 1957, **90**, 363.

It is interesting that *pseudo*lycorine, even in a glass tube, undergoes a colour change first to yellow and finally brown to black. We consider that this may be due to aerial oxidation to a compound having a quinonoid structure (VII) which then undergoes further changes. Since there appears to be no driving force for the formation of a quinone such as (VIII), this ready discoloration of *pseudo*lycorine is in accord with the position assigned to the free hydroxyl group in ring A of the base.

In contrast to *pseudo*lycorine, norpluviine and demethylhomolycorine are stable and do not colour appreciably on long storage.

Experimental

Ultraviolet absorption spectra were determined for 95% ethanol solutions on a Beckman DU spectrometer. Infrared spectra were taken on the Perkin-Elmer Model 21 in Nujol.

pseudo*Lycorine.*—*pseudo*Lycorine crystallised from water as needles, m. p. 247—248° (decomp.), $[\alpha]_D$ −62° (*c* 1·2 in EtOH) (lit.,[1] m. p. 245°) (Found: C, 53·1; H, 7·9; OMe, 8·8. $C_{16}H_{19}O_4N,4H_2O$ requires C, 53·2; H, 7·5; OMe, 8·6%), soluble in hot water, slightly soluble in acetone, chloroform, or methanol and very slightly soluble in ether. A solution of the base in cold aqueous sodium hydroxide deposited the base on addition of ammonium chloride. The alkaloid contains neither a *N*-methyl (Herzig–Meyer) nor a *C*-methyl (Kuhn–Roth) group. For analysis the hydrate was dried *in vacuo* over phosphoric oxide at 100° for 6 hr., after which the anhydrous *form* melted at 240—242° (Found: C, 66·4; H, 6·4; N, 5·1; OMe, 11·2. $C_{16}H_{19}O_4N$ requires C, 66·4; H, 6·6; N, 4·8; OMe, 10·7%). The *hydrochloride* crystallised from methanol as needles, m. p. 266° (decomp.) (lit.,[1] m. p. 261°) (Found: C, 59·0; H, 6·4; N, 4·6. $C_{16}H_{19}O_4N,HCl$ requires C, 59·0; H, 6·1; N, 4·3%). The *methiodide* crystallised from methanol–acetone as prisms, m. p. 250—252° (decomp.) (lit.,[1] 150°) (Found: C, 47·4; H, 5·3; I, 29·4. $C_{16}H_{19}O_4N,CH_3I$ requires C, 47·3; H, 5·1; I, 29·4%).

O-*Acetyl*pseudo*lycorine.*—*pseudo*Lycorine (0·1 g.) and anhydrous sodium acetate (0·1 g.) in acetic anhydride (3 ml.) were heated on a water-bath for 1·5 hr. The mixture was concentrated under reduced pressure, and the residue taken up in water, basified with aqueous ammonia, and extracted with chloroform. The chloroform extract gave on evaporation the *acetate* (70 mg.), plates (from methanol), m. p. 204—205° (lit.,[1] m. p. 98—101°), $[\alpha]_D$ +34·6° (*c* 0·5 in EtOH) (Found: C, 63·9; H, 6·0; Ac, 29·4. $C_{22}H_{25}O_7N$ requires C, 63·6; H, 6·1; Ac, 30·2%), $\lambda_{max.}$ 5·73 and 5·76 μ. The *acetate hydrochloride* was prepared by adding an ethereal solution of dry hydrogen chloride to acetyl*pseudo*lycorine in ether. Recrystallisation from methanol gave needles, m. p. 251° (decomp.) [lit.,[1] 272° (decomp.)] (Found: C, 52·3; H, 6·5. $C_{22}H_{25}O_7N,HCl,3H_2O$ requires C, 52·2; H, 6·4%).

Zinc Dust Distillation of pseudo*lycorine.*—A mixture of *pseudo*lycorine (0·4 g.) and zinc dust (10 g.) was distilled in an atmosphere of hydrogen. The distillate was taken up in ether and extracted with 5% hydrochloric acid. To the acidic aqueous layer was added a saturated solution of mercuric chloride. The resulting precipitate was dissolved in hot water, filtered from insoluble material, and treated with hydrogen sulphide to remove mercury. The clear filtrate was basified, and extracted with ether, which was then evaporated to dryness, and the residue was distilled in a vacuum. The distillate, b. p. 100—115° (bath-temperature)/0·1 mm., which solidified immediately, was converted into its picrate, m. p. 235°, undepressed on admixture with phenanthridine picrate, m. p. 245° (Found: C, 56·1; H, 3·1. Calc. for $C_{13}H_9N,C_6H_3O_7N_3$: C, 55·9; H, 3·0%).

O-*Methyl*pseudo*lycorine.*—To a solution of *pseudo*lycorine (0·1 g.) in ethanol (25 ml.) was added excess of ethereal diazomethane, and the mixture was set aside at room temperature for 10 days. After evaporation, the *ether* (62 mg.) which was insoluble in hot water was crystallised from methanol, to give prisms, m. p. 241° (decomp.), $[\alpha]_D$ −72·5° (*c* 0·4 in MeOH) (lit.,[4] m. p. 234—242°) (Found: C, 67·5; H, 7·1; OMe, 20·3. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0; OMe, 20·5%).

O-*Ethyl*pseudo*lycorine.*—*pseudo*Lycorine (70 mg.) in methanol (15 ml.) was treated with excess of ethereal diazoethane and after 2 days the mixture was concentrated and treated again with additional solution of diazoethane for a further day. After being washed with aqueous sodium hydroxide, the mixture was concentrated to give a residue (45 mg.) which was purified by chromatography in chloroform–ethanol (10 : 1) on alumina. Crystallisation of the eluted material (30 mg.) from methanol gave colourless prisms of the *ether*, m. p. 242° (decomp.), $[\alpha]_D$ −68·6° (*c* 0·35 in EtOH) (Found: C, 68·6; H, 7·2. $C_{18}H_{23}O_4N$ requires C, 68·1; H, 7·3%).

Formation of the Phenanthridone (III; R = Et, R′ = Me).—*O*-Ethyl*pseudo*lycorine (20 mg.) and phosphorus oxychloride (0·5 ml.) were heated on a water-bath for 1 hr. Ice-water (2 ml.) was added to the mixture and the solution saturated with potassium iodide to precipitate anhydro-*O*-ethyl*pseudo*lycorinium iodide. This salt (16 mg.), potassium ferricyanide (25 mg.), and potassium hydroxide (25 mg.) in 50% ethanol (2 ml.) were heated on a water-bath. Crystals began to separate in 10 min. and the reaction was complete in 1 hr. The precipitate was extracted with chloroform, and the chloroform extract washed with dilute hydrochloric acid and water, dried, and evaporated to give a residue (3 mg.) which was purified by sublimation at 160—190° (bath-temperature)/0·1 mm., followed by crystallisation from methanol; it then had m. p. 175—177°, undepressed upon admixture with synthetic 6-ethoxy-7-methoxypyrrolino-(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone (III; R = Et, R′ = Me) as described below. The ultraviolet and infrared spectra of both the natural and the synthetic product were identical.

4-*Ethoxy*-5-*methoxy*-2-*nitrobenzoic Acid.*—*O*-Ethylvanillic acid (7·5 g.) was nitrated with nitric acid (32 ml.; *d* 1·52) with stirring for 1 hr. at 20—30°. The mixture was poured into ice-water, and the yellow precipitate collected and extracted with saturated sodium hydrogen carbonate solution. The insoluble material (2 g.) was filtered off and the clear solution when acidified with hydrochloric acid gave crude 4-*ethoxy*-5-*methoxy*-2-*nitrobenzoic acid* (5·2 g.) which crystallised from methanol as pale yellow needles, m. p. 172—174° (Found: C, 50·0; H, 4·6; N, 5·6. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6; N, 5·8%). The insoluble material mentioned above, 1-*ethoxy*-2-*methoxy*-3 : 5-*dinitrobenzene*, crystallised from ethanol in yellow leaflets, m. p. 143—145° (Found: C, 45·0; H, 4·1; N, 11·2. $C_9H_{10}O_6N_2$ requires C, 44·6; H, 4·2; N, 11·6%).

1-(4-*Ethoxy*-5-*methoxy*-2-*nitrobenzoyl*)-2 : 3-*dihydroindole.*—To a stirred solution of 2 : 3-dihydroindole (0·75 g.) and pyridine (5 ml.) in chloroform (15 ml.) was added dropwise a solution of 4-ethoxy-5-methoxy-2-nitrobenzoyl chloride (from 1·7 g. of acid and excess of thionyl chloride) in chloroform (10 ml.) during 30 min. and the mixture refluxed on a water-bath for 2 hr. Next morning the chloroform solution was washed successively with 5% hydrochloric acid, 5% sodium hydroxide solution, and water, dried, and evaporated to a solid (1·7 g.) which on crystallisation from methanol gave the pure *nitro-amide* as pale yellow needles, m. p. 167—168° (Found: C, 63·4; H, 5·6; N, 8·1. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·3; N, 8·2%).

1-(2-*Amino*-4-*ethoxy*-5-*methoxybenzoyl*)-2 : 3-*dihydroindole.*—The nitro-amide (1·65 g.) obtained as above was reduced catalytically in ethyl acetate (30 ml.) in the presence of palladium–carbon (0·6 g.; 1 : 5). The mixture was filtered and evaporated to dryness and the residue dissolved in 5% hydrochloric acid, washed with ether, basified with sodium carbonate solution, and extracted with chloroform. Removal of the chloroform gave a solid (1·3 g.) which crystallised from ethanol to give the *amino-amide* as prisms, m. p. 137—138° (Found: C, 69·1; H, 6·3; N, 9·1. $C_{18}H_{20}O_3N_2$ requires C, 69·2; H, 6·5; N, 9·0%).

Pschorr Cyclisation of the Amino-amide.—The amino-amide (0·5 g.) was diazotised in 5% sulphuric acid (35 ml.) and methanol (10 ml.) with 5% sodium nitrite solution (10 ml.) at 0—5° and the whole kept for 1 hr. at room temperature. The temperature was then raised to 75—80° for 2 hr., and finally to 100° for 1 hr., an oil separating which was extracted with chloroform after cooling. The chloroform extract was washed with 5% sodium hydroxide solution, then with water, dried, and evaporated to an oil (0·42 g.) which was chromatographed over alumina. Elution with chloroform gave 1-(4-*ethoxy*-3-*methoxybenzoyl*)*indole* which on crystallisation from ethanol formed prisms, m. p. 113—114°, $\lambda_{max.}$ 250 and 305 mμ (log ε 4·31 and 4·13) (Found: C, 73·2; H, 5·8; N, 4·7. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%). Hydrolysis of this product in 5% sodium hydroxide solution afforded indole (identified as its picrate, m. p. and mixed m. p. 159—160°) and *O*-ethylvanillic acid, m. p. and mixed m. p. 193—194°. Further elution with the same solvent gave 6-*ethoxy*-7-*methoxypyrrolino*(3′ : 2′ : 1′-1 : 10*a* : 10)*phenanthridone* (40 mg.). After crystallisation from methanol, followed by sublimation in a vacuum and recrystallisation from methanol, it formed needles and had m. p. 176—177°, $\lambda_{max.}$ 250, 271, 325, and 340 mμ (log ε 4·58, 4·35, 3·81, and 3·88) (Found: C, 72·9; H, 5·9; N, 4·9. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%).

5-*Ethoxy*-4-*methoxy*-2-*nitrobenzaldehyde.*—6-Nitro*iso*vanillin (5 g.) in 10% sodium hydroxide solution (25 ml.) was ethylated with diethyl sulphate (6 g.) with stirring on a water-bath for 3 hr. After cooling, the precipitate (5·6 g.) was collected and crystallised from ethanol; the *aldehyde* had m. p. 160—161° (Found: C, 53·2; H, 4·8. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9%).

5-*Ethoxy*-4-*methoxy*-2-*nitrobenzoic Acid.*—To a stirred mixture of the above nitro-aldehyde (5·2 g.) in benzene (70 ml.) with sodium hydroxide (4 g.) in water (60 ml.) was added dropwise

an aqueous solution (200 ml.) of potassium permanganate (3 g.) at 70—80°. After the oxidising agent had been consumed, the mixture was filtered hot. The aqueous layer was acidified with hydrochloric acid, and the pale yellow *acid* (4·3 g.) which separated collected and crystallised from ethanol as yellow prisms, m. p. 215—216° (Found: C, 49·5; H, 4·4; N, 5·6. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6; N, 5·8%).

1-(5-*Ethoxy*-4-*methoxy*-2-*nitrobenzoyl*)-2 : 3-*dihydroindole*.—To a stirred solution of dihydroindole (1·1 g.) in pyridine (6 ml.) and chloroform (50 ml.) was added dropwise (30 min.) a solution of 5-ethoxy-4-methoxy-2-nitrobenzoyl chloride (from 2·6 g. of acid and excess of thionyl chloride) in chloroform (15 ml.). After a further 2 hours' refluxing and cooling, the chloroform solution was washed with 5% hydrochloric acid, then with 5% aqueous sodium hydroxide and water, and dried. Evaporation of the chloroform gave a solid *derivative* (2·95 g.) which crystallised from methanol as pale yellow needles, m. p. 176—177° (Found: C, 63·4; H, 5·5; N, 8·2. $C_{18}H_{18}O_5N_2$ requires C, 63·2; H, 5·3; N, 8·2%).

1-(2-*Amino*-5-*ethoxy*-4-*methoxybenzoyl*)-2 : 3-*dihydroindole*.—The preceding nitro-amide (1·3 g.) was reduced in chloroform with hydrogen in the presence of palladium–carbon and, after working up, 1-(2-*amino*-5-*ethoxy*-4-*methoxybenzoyl*)-2 : 3-*dihydroindole* (1·15 g.) was obtained. Crystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 100—101° (Found: C, 68·9; H, 6·5; N, 9·1. $C_{18}H_{20}O_3N_2$ requires C, 69·2; H, 6·5; N, 9·0%).

Pschorr Cyclisation of the Preceding Amino-amide.—The amino-amide (0·5 g.) obtained above was diazotised in 5% sulphuric acid (30 ml.). On working up as described above, two products were isolated after chromatography over alumina. The first eluate (190 mg.) gave 1-(3-*ethoxy*-4-*methoxybenzoyl*)*indole*, needles, m. p. 122—123° (from ethanol), $\lambda_{max.}$ 250 and 305 mμ (log ε 4·37 and 4·15) (Found: C, 72·9; H, 5·9; N, 4·8. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%); the second (40 mg.) afforded 7-*ethoxy*-6-*methoxypyrrolino*(3′ : 2′ : 1′-1 : 10*a* : 10)-*phenanthridone* which on sublimation at 180—210° (bath-temperature)/0·1 mm. and crystallisation from methanol formed needles, m. p. 229—230°, $\lambda_{max.}$ 250, 271, 325, and 340 mμ (log ε 4·63, 4·48, 3·91, and 3·98) (Found: C, 73·0; H, 5·9; N, 4·6. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%).

Norpluviine.—The crude alkaloids extracted from the bulbs of *Lycoris radiata* were dissolved in chloroform and extracted with 2% aqueous sodium hydroxide. The aqueous layer was made ammoniacal by the addition of ammonium carbonate and extracted with chloroform. After evaporation of the chloroform, the residue was triturated with a little methanol and kept at room temperature for a week or longer, a solid *alkaloid* being precipitated which was collected and crystallised from water or ethanol to give needles or prisms, m. p. 274—275° (decomp.), $[\alpha]_D$ −160° (*c* 0·15 in MeOH) (Found: C, 70·2; H, 6·8; N, 5·4; OMe, 11·7. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0; N, 5·1; OMe, 11·4%).

O-*Methylnorpluviine*.—Norpluviine (60 mg.) in methanol (25 ml.) was treated with excess of an ethereal solution of diazomethane for 2 days. The mixture was then concentrated and an additional fresh diazomethane solution was added. After 24 hr., the mixture was evaporated, and the residue redissolved in chloroform, washed with aqueous sodium hydroxide, dried, and filtered through alumina. The filtrate gave on evaporation a solid which when crystallised from ethanol formed prisms and had m. p. 225—226°, undepressed on admixture with pluviine, $[\alpha]_D$ −181° (*c* 0·3 in EtOH) (Found: C, 70·9; H, 7·3. Calc. for $C_{17}H_{21}O_3N$: C, 71·0; H, 7·4%). The infrared spectrum was identical with that of pluviine.

O-*Ethylnorpluviine*.—Norpluviine (100 mg.) in methanol (30 ml.) was ethylated with diazoethane in the usual way; the resulting O-*ethyl derivative* crystallised from acetone as prisms, m. p. 148—149°, $[\alpha]_D$ −186° (*c* 0·28 in EtOH) (Found: C, 71·5; H, 7·7; N, 4·7; OMe + OEt, 25·3. $C_{18}H_{23}O_3N$ requires C, 71·7; H, 7·7; N, 4·7; OMe + OEt, 25·2%).

O-*Acetyl*-O-*ethylnorpluviine*.—*O*-Ethylpluviine (50 mg.) in acetic anhydride (2 ml.) was heated on a water-bath for 3 hr. Excess of acetic anhydride was removed by distillation under reduced pressure and the residue dissolved in 5% hydrochloric acid. The solution was basified with aqueous ammonia and extracted with ether, a small amount of insoluble material (5 mg.) remaining. The ethereal extract afforded *O*-acetyl-*O*-ethylnorpluviine (40 mg.) which crystallised from ether as needles, m. p. 185—186°, $[\alpha]_D$ −133° (*c* 0·3 in EtOH) (Found: C, 69·6; H, 7·3; N, 4·3. $C_{20}H_{25}O_4N$ requires C, 70·0; H, 7·3; N, 4·1%).

Formation of an Anhydrodehydro-O-*ethylnorpluviinium Salt and its Oxidation*.—*O*-Acetyl-*O*-ethylnorpluviine (55 mg.) in acetic anhydride (2 ml.) was heated at 130—140° for 3 hr. After evaporation of the excess of acetic anhydride in a vacuum, water was added, the mixture

basified with aqueous ammonia, and the precipitate extracted with chloroform. The chloroform was evaporated to dryness and the residue extracted with ether to remove unchanged acetylethylnorpluviine (11 mg.). The insoluble material (15 mg.) which remained undissolved in ether was oxidised in aqueous ethanol (10 ml.) with potassium ferricyanide (50 mg.) at water-bath temperature for 3 hr. After cooling, the mixture was extracted with chloroform, and the chloroform extract dried and concentrated to an oil which was distilled at 180—220° (bath-temperature)/0·1 mm. The distillate was crystallised from ethanol to give needles, m. p. 226—228°, identical with 7-ethoxy-6-methoxypyrrolino(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone as shown by its mixed m. p. and infrared spectrum.

Demethylhomolycorine.—The mother-liquor (30 g.) from *Lycoris radiata*, from which the norpluviine had been obtained above, was extracted with ethyl acetate (100 ml.) on a water-bath, and the extract after concentration to 50 ml. was chromatographed over alumina. The ethyl acetate eluate gave on concentration a residue (2·5 g.) which was triturated with ethyl acetate, yielding *demethylhomolycorine* as colourless needles (300 mg.). Further elution with acetone, chloroform, and ethanol gave no crystalline compound. Demethylhomolycorine crystallised from ethyl acetate or hot water as needles, m. p. 213—214°, $[\alpha]_D$ +96·4° (*c* 0·28 in $CHCl_3$), $\lambda_{max.}$ 229, 269, and 307 mμ (log ε 4·32, 3·88, and 3·73), 3·05 μ (OH), 5·88 μ (C=O) (Found: C, 67·8; H, 6·2; N, 4·6; OMe, 10·5. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·7; OMe, 10·3%).

Demethyl-O-methylhomolycorine.—Demethylhomolycorine (100 mg.) in methanol (15 ml.) was methylated with ethereal diazomethane, furnishing homolycorine (95 mg.), m. p. and mixed m. p. 174—175° (from methanol), $[\alpha]_D$ +94·1° (*c* 0·51 in chloroform), $\lambda_{max.}$ 225, 269, and 303 mμ (log ε 4·36, 3·97, and 3·79), 5·82 μ (C=O) (Found: C, 68·2; H, 6·6; N, 4·4. Calc. for $C_{18}H_{21}O_4N$: C, 68·6; H, 6·7; N, 4·4%).

Demethyl-O-ethylhomolycorine.—Demethylhomolycorine (0·2 g.) in methanol (10 ml.) with diazoethane afforded the *ethyl derivative* (0·17 g.) as needles (from ethyl acetate–ether), m. p. 203—204°, $[\alpha]_D$ +95·2° (*c* 0·2 in $CHCl_3$) (Found: C, 68·8; H, 6·9; N, 4·3. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·0; N, 4·3%).

Demethyl-O-ethyltetrahydrohomolycorine.—Demethyl-*O*-ethylhomolycorine (0·3 g.) in tetrahydrofuran (8 ml.) was heated on a water-bath with lithium aluminium hydride (0·2 g.) for 4 hr. After cooling, excess of lithium aluminium hydride was destroyed by the addition of a few drops of water, and the precipitate was filtered off and washed with tetrahydrofuran. The filtrate and washings were combined and evaporated to dryness and the residual *diol* (0·28 g.) crystallised from acetone, to give colourless prisms, m. p. 195—196° (Found: C, 68·1; H, 7·9; N, 4·3. $C_{19}H_{27}O_4N$ requires C, 68·4; H, 8·2; N, 4·2%).

Conversion of Demethyl-O-ethyltetrahydrohomolycorine into 7-Ethoxy-6-methoxypyrrolino-(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone.—The above product (0·2 g.) and toluene-*p*-sulphonyl chloride (0·18 g.) in pyridine (10 ml.) was set aside overnight at room temperature and then heated on a water-bath for 1 hr. Pyridine was removed in a vacuum, and the residue taken up in water (10 ml.) and washed with ether. The aqueous layer was filtered through Amberlite IRA-400 ion-exchange resin, and the filtrate evaporated to dryness, taken up again in water, neutralised with hydrochloric acid, evaporated to dryness, and distilled [180—240° (bath)/0·01 mm.]. The distillate (20 mg.) was chromatographed in chloroform over alumina, and the first eluate was redistilled to give a product which after crystallisation from ethanol melted at 94—96°, $\lambda_{max.}$ 273, and 344 mμ (log ε 4·56 and 4·07). Although the amount of the product was insufficient for analysis, it appeared to be anhydrodehydro-*O*-ethylnorpluviine (IX; R = Me, R′ = Et) on the ground that its spectrum was very similar to that of anhydrodehydropluviine (IX; R = R′ = Me). The second eluate afforded 7-ethoxy-6-methoxypyrrolino(3′ : 2′ : 1′-1 : 10a : 10)phenanthridone which had m. p. and mixed m. p. 226—228° after sublimation at 180—210° (bath)/0·01 mm. followed by crystallisation from methnol. The ultraviolet and infrared spectra were also identical with those of an authentic sample described above.

We are grateful to Professor H. Kondo for a generous supply of *pseudo*lycorine which made this work possible, Dr. W. I. Taylor for reading the manuscript, and Messrs. Ikemoto and Takagishi, who were students of this school, for technical assistance in synthesising the phenanthridones.

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[*Received, August 11th*, 1958.]