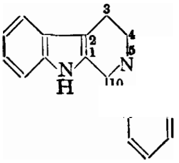
## 369. *The Constitution of Yohimbine and Related Alkaloids. Part III. The Structure of Sempervirine and Some Further Observations on the Structure of Ketoyobyrine.*

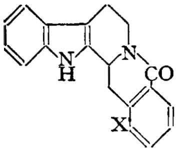
By G. A. Swan.

A compound having the structure (I) assigned to sempervirine by Prelog *et al.* is synthesised; it differs from the alkaloid in both physical and chemical properties. Both the ketoyobyrine and the synthetic product previously (this vol., p. 110) held to be identical with it are now considered to be mixtures.

Goutarel, Janot, and Prelog (*Experientia*, 1948, **4**, 24) and Prelog (*Helv. Chim. Acta*, 1948, **31**, 588) recently suggested structure (I) for sempervirine, one of the alkaloids of *Gelsemium sempervirens*. As (II) and (III) have already been synthesised (*J.*, 1946, 618; this vol., p. 110; Schlittler and Allemann, *Helv. Chim. Acta*, 1948, **31**, 128), further work has been directed towards the synthesis of 3 : 4-*dihydro*-7 : 8-*benzindolo*(2′ : 3′-1 : 2)*pyridocoline* (I).



(I.) Double bond at $C_{(9)}$—$C_{(10)}$.
(III.) As formula.
(VIII.) Double bond at $C_{(3)}$—$C_{(4)}$.



(II.) X = H; double bond at $C_{(9)}$—$C_{(10)}$.
(X.) X = Me; double bond at $C_{(9)}$—$C_{(10)}$.
(XI.) X = Me; double bond at $C_{(3)}$—$C_{(4)}$.
(XII.) X = Me; double bonds at $C_{(3)}$—$C_{(4)}$ and $C_{(9)}$—$C_{(10)}$.

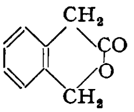
The oxidative ring-fission of cyclic ketones by Caro's acid, previously studied by Baeyer and Villiger (*Ber.*, 1899, **32**, 3625; 1900, **33**, 858), Robinson and Smith (*J.*, 1937, 371), and others, has now been extended to indan-2-one which furnished iso*chroman*-3-*one* (IV) in good yield. This lactone with tryptamine yielded a neutral product which appears to be 3-(2′-o-*hydroxymethyl*-

*phenylacetamidoethyl)indole* (V; R = $CH_2$·OH), which was also obtained by reduction of (V; R = $CO_2Me$) with lithium aluminium hydride but which could not be cyclised to (I).

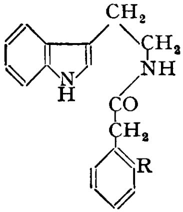
Attention was therefore directed to the synthesis of 3-(2′-*o*-methoxymethylphenylacetamidoethyl)indole (V; R = $CH_2$·OMe). *iso*Chroman-3-one with methyl sulphate and 50% potassium hydroxide solution gave *methyl* o-*methoxymethylphenylacetate* (VI; R = OMe), which was hydrolysed by alkali to the *acid* (VI; R = OH). Treatment with thionyl chloride then furnished the *chloride* (VI; R = Cl), which condensed with tryptamine to give a gum, presumably (V; R = $CH_2$·OMe); with phosphoryl chloride this furnished a small yield of a base, m. p. 214—215°; analysis, agreeing with $C_{19}H_{18}ON_2$ or $C_{20}H_{20}ON_2$, and the ultra-violet absorption spectrum, which shows considerable resemblance to that of harmaline (Pruckner and Witkop, *Annalen*, 1943, **554**, 127) suggest that this compound is (VII; R = H) or (VII; R = Me). The amounts obtained have, so far, been too small for attempts at cyclisation to (I).

Synthesis of (I) in good yield was finally realised by reducing (II) with lithium aluminium hydride. The reduction of amides to amines by this reagent was first described by Ehrlich (*J. Amer. Chem. Soc.*, 1948, **70**, 2286), and the reduction of (±)-oxysparteine to (±)-sparteine has been recorded by Clemo, Raper, and Short (*Nature*, 1948, **162**, 296). (I) separates from aqueous alcohol in golden-yellow leaflets, m. p. 210—215° (decomp.), darkening at 190°, and undoubtedly differs from sempervirine, m. p. 228° (from chloroform) or 258° (from aqueous alcohol). The intense blue-violet fluorescence of salts of the latter is here quite absent, although solutions of the base show a faint greenish fluorescence under ultra-violet irradiation. The ultra-violet absorption of the synthetic compound differs from that recorded by Prelog (*loc. cit.*) for sempervirine; and, although there is some difference in the spectra in neutral and alkaline solutions, this change is not so great as in the case of the alkaloid, and, in particular, there is no strong band at λ *ca.* 2900.

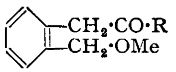
The p*K* for (I) could not be determined by electrometric titration of its hydrochloride with sodium hydroxide as, even in water containing 20% of alcohol, precipitation occurred after only a drop or two of alkali had been added. However, it is evident that this is a very much weaker base than sempervirine, for which Prelog quotes p*K* ~10·6 in water.



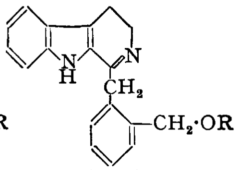
(IV.)



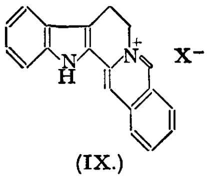
(V.)



(VI.)



(VII.)



(IX.)

Hydrogenation of (I) in the presence of Adams's catalyst in glacial acetic acid, gave (III), identical with the product obtained previously (Part I); the new method is far superior and may be of value in further work in this field, *e.g.*, for synthesis of deoxyyohimbol (Witkop, *Annalen*, 1943, **554**, 83). Moreover, (III) can be further hydrogenated in presence of platinic oxide in acetic acid containing a drop of concentrated sulphuric acid (cf. Kindler and Kwok, *Annalen*, 1943, **554**, 9, and Witkop, *J. Amer. Chem. Soc.*, 1948, **70**, 2617). The absorption of a further 3 moles of hydrogen seems to indicate hydrogenation of the benzene ring of the tetrahydro*iso*quinoline part of the molecule, and further work along these lines is planned.

In alcohol, in the presence of palladised charcoal, no hydrogenation of (I) occurred, but reduction by hydriodic acid gave (III). Forsyth, Marrian, and Stevens (*J.*, 1945, 579) recovered sempervirine as its hydriodide after boiling it for 30 hours with hydriodic acid (*d* 1·7) and red phosphorus, whilst, on hydrogenation, 3 moles of hydrogen were absorbed over palladium and 5 moles in all over Adams's catalyst. Even if Prelog's suggested structure were modified to (VIII), it is difficult to see how this could accommodate these results.

The structure of sempervirine has also been investigated in another manner. If Prelog's structure were correct, one might expect to be able to oxidise the alkaloid with iodine to 3 : 4-*dihydro*-7 : 8-*benzindolo*(2′ : 3′-1 : 2)*pyridocolinium iodide* (IX; X = I) (cf. the oxidation of tetrahydropalmatine to palmatine iodide; Haworth, Koepfli, and Perkin, *J.*, 1927, 548). Accordingly, compounds (I), (III), and sempervirine were each treated with iodine and potassium acetate in alcoholic solution. From (I) and (III), a product, apparently (IX; X = I), crystallising in golden-yellow needles, was obtained. However, from the alkaloid, sempervirine hydriodide was recovered; again, even if structure (VIII) were correct, one might have expected oxidation with iodine to occur. The iodide (IX; X = I) is a very sparingly soluble compound, but silver chloride in aqueous alcohol gave the more soluble corresponding *chloride* (IX; X = Cl); on hydrogenation over Adams's catalyst in glacial acetic acid this absorbed 2 moles of hydrogen with the formation of (III) (as the hydrochloride) but in alcohol containing slightly more than 1 mole of sodium hydroxide only 1 mole of hydrogen was absorbed, with the formation of (I).

The absorption spectra suggest that the action of light on a solution of (I) involves oxidation to a product such as (IX; probably X is OH).

*Ketoyobyrine.* The properties of a substance formulated as (XI) (Part II; this vol., p. 110) agree with those described for ketoyobyrine, and were unchanged after crystallisation first from glacial acetic acid and then three times from alcohol. There seemed every reason to believe that this product and ketoyobyrine were both homogeneous and were identical, and it was tentatively suggested that they had structure (XI). This has now been shown to be untenable, as the reduction, by lithium aluminium hydride, of the analogous product of the action of Raney nickel on (II) gives mainly (I), together with a red compound in amount too small to allow of further investigation. Moreover, Woodward and Witkop (*J. Amer. Chem. Soc.*, 1948, **70**, 2409) have shown that on heating ketoyobyrine with palladium at 280°, 1 mole of hydrogen is evolved, with the formation of (XII), a yellowish-green compound of very low solubility, whose solutions exhibit a powerful fluorescence similar to that of ketoyobyrine. Also Schlittler and Speitel indicated that they experienced difficulty in establishing the identity of synthetic (X) (*Helv. Chim. Acta*, 1948, **31**, 1199) with ketoyobyrine (even after chromatography, there was still some difference in the colour of the products). The synthesis of (X) has also been recorded by Julian, Karpel, Magnani, and Meyer (*J. Amer. Chem. Soc.*, 1948, **70**, 2834), and Raymond-Hamet (*Compt. rend.*, 1948, **226**, 137) has put forward the structure (X) for ketoyobyrine on the grounds of similarity in the ultra-violet absorption spectrum to that of ruteacarpine.

In the light of the above work, it is now suggested that in the form usually obtained, ketoyobyrine is not homogeneous, but consists essentially of (X), contaminated by traces of (XII). The Raney-nickel treatment no doubt dehydrogenates a small amount of (X) to (XII), and hence the product appears to be identical with ketoyobyrine. In support of this, it has been shown that a mixture of (II) (10 parts) with its palladium-dehydrogenation product (1 part), on recrystallisation from alcohol, gives a product indistinguishable from ketoyobyrine in its colour and fluorescence and in the fading of its solution in light. The change observed when dilute solutions of ketoyobyrine are kept in light must, presumably, be due to reduction of the trace of (XII) to (X) at the expense of the solvent.

## EXPERIMENTAL.

Phosphoryl chloride and thionyl chloride were distilled from quinoline before use. Tetrahydrofuran was kept for 1 week over potassium hydroxide, heated under reflux over sodium wire, and distilled.

iso*Chroman-3-one* (IV).—Powdered potassium persulphate (85·7 g.) was gradually added to a stirred mixture of sulphuric acid (121 c.c., *d* 1·8) and water (41 c.c.), followed by absolute alcohol (170 c.c.), the temperature being maintained below 15° throughout. Then, during 1 hour, a solution of indan-2-one (Read and Hurst, *J.*, 1922, **121**, 2550) (20·6 g.) in absolute alcohol (170 c.c.) was added at $-2°$ to $+3°$. The mixture was stirred for a further 30 minutes at *ca.* $+3°$ and then for $1\frac{1}{2}$ hours during which the temperature was allowed to rise slowly to 18°. Water (1 l.) was added, the product extracted with chloroform, the extract washed with sodium hydrogen carbonate solution, and dried ($Na_2SO_4$); the solvent was removed and the residual oil stirred with light petroleum (b. p. 40—60°), whereupon it rapidly crystallised. The resulting solid (21 g.) was collected, washed with light petroleum (b. p. 40—60°), and recrystallised from light petroleum (b. p. 80—100°), affording iso*chroman-3-one* as colourless leaflets, m. p. 82—83°, b. p. 130°/1 mm. (Found : C, 72·9; H, 5·65. $C_9H_8O_2$ requires C, 73·0; H, 5·4%).

3-(2'-o-*Hydroxymethylphenylacetamidoethyl)indole* (V; R = $CH_2$·OH).—(*a*) The lactone (0·3 g.) and tryptamine (0·32 g.) were heated for 1 hour at 180—190°. After cooling, the *product* was stirred with benzene, filtered off, and recrystallised from methanol (charcoal), affording colourless plates or prisms (0·3 g.), m. p. 163—164° (after drying at 140°/1 mm.) (Found : C, 74·35; H, 6·5; N, 8·85. $C_{19}H_{20}O_2N_2$ requires C, 74·0; H, 6·5; N, 9·1%). (*b*) The lactone (0·16 g.) and tryptamine (0·18 g.) were heated under reflux in dry benzene (5 c.c.) for 6 hours. After cooling, the product (0·24 g.) was collected and crystallised as in (*a*). (*c*) The ester-amide (V; R = $CO_2Me$) (0·1 g.) in dry benzene (1 c.c.) was treated with lithium aluminium hydride (Finholt, Bond, and Schlesinger, *J. Amer. Chem. Soc.*, 1947, **69**, 1199) (30 mg.) in ether (0·7 c.c.). After being heated under reflux for 3 hours, the solution was cooled, treated with water and dilute hydrochloric acid, and extracted with chloroform. The extract was washed with dilute sodium hydroxide solution and dried ($K_2CO_3$), the chloroform removed, and the residue recrystallised from methanol, affording the product (70 mg.) as colourless plates, m. p. 163—164°, not depressed by admixture with that obtained in (*a*).

*Attempted Cyclisation of the Above Amide.*—The amide (50 mg.) was heated under reflux for 1 hour, in an atmosphere of nitrogen, with phosphoryl chloride (1 c.c.), the latter removed by distillation (water-bath; reduced pressure), and the residue treated with dilute hydrochloric acid and extracted with chloroform. The acid layer was filtered, basified (40% NaOH), and extracted with chloroform, the extract dried

($K_2CO_3$), and the solvent removed. The residue was negligible. A similar result was obtained after boiling for 4½ hours with phosphoryl chloride.

o-*Methoxymethylphenylacetic Acid* (VI; R = OH).—A solution of potassium hydroxide (4 g.) in water (4 c.c.) was prepared. The above lactone (3 g.) was dissolved in one third of this, and the resulting solution stirred vigorously with water-cooling. Purified methyl sulphate (2 c.c.) was added gradually during 5 minutes; then the remainder of the potassium hydroxide solution and further methyl sulphate (4 c.c.) were added gradually and simultaneously during 20 minutes. After being stirred for a further 1 hour, the mixture was heated under reflux for 1 hour with 30% aqueous sodium hydroxide (6 c.c.) and methanol (20 c.c.). The bulk of the methanol was removed by distillation (water-bath), and the residue dissolved in water, cooled, extracted with ether, acidified (hydrochloric acid), and again extracted with ether. Evaporation of the latter extract after drying ($Na_2SO_4$) gave an oil (2 g.), which soon solidified. Recrystallised from light petroleum (b. p. 40—60°), this afforded the *acid* (1·5 g.) as colourless prisms or needles, m. p. 53—54° (Found: C, 67·0; H, 6·75. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%). Acidification of the remaining reaction mixture yielded unchanged lactone (0·7 g.).

By omitting the treatment with methanolic sodium hydroxide, the *methyl* ester (VI; R = OMe) was obtained, by extracting with ether, washing the extract with dilute sodium hydroxide solution, drying ($K_2CO_3$), removing the ether, and distilling the residue, as a colourless mobile liquid, b. p. 108°/1 mm. (Found: C, 68·15; H, 7·35. $C_{11}H_{14}O_3$ requires C, 68·05; H, 7·2%).

o-*Methoxymethylphenylacetyl Chloride* (VI; R = Cl).—To a solution of the above acid (1·55 g.) in dry ether (5 c.c.), thionyl chloride (1·7 g.), followed by dry pyridine (1 drop), was added. After 14 hours at room temperature, the ether was removed (reduced pressure; room temperature) and the residue distilled rapidly, giving the *chloride* (1·52 g.) as a colourless liquid, b. p. 108°/1 mm. (Found: C, 60·1; H, 5·35. $C_{10}H_{11}O_2Cl$ requires C, 60·45; H, 5·55%). Slow distillation from a bath led to partial cyclisation to give the original lactone.

*Condensation of the Above Chloride with Tryptamine and Attempted Cyclisation of the Product.*—The chloride (0·4 g.) in benzene (5 c.c.) was added during 20 minutes to a vigorously stirred suspension of tryptamine (0·35 g.) in benzene (12 c.c.) and 0·5N-sodium hydroxide (4 c.c.). After being stirred for a further 20 minutes, the aqueous layer was made alkaline by the addition of a little more sodium hydroxide solution, the layers were separated, and the aqueous layer was extracted with ether. The combined ether–benzene extract was washed successively with dilute sodium hydroxide solution, dilute hydrochloric acid, and again dilute sodium hydroxide, and dried ($K_2CO_3$), and the solvents were removed. The resulting gum failed to crystallise. A benzene solution of it was poured through a column of alumina, and the latter washed through with much benzene, the filtrate being discarded. A mixture of benzene and alcohol (200 : 1) was then run through the column, the filtrate collected in 5 fractions, and each evaporated. Fractions (1) and (5) yielded only small residues and were discarded. Fractions (2), (3), and (4) yielded clear, pale yellow gums which failed to crystallise. These were combined (0·57 g.) and heated under reflux for 1 hour in an atmosphere of pure, dry nitrogen with phosphoryl chloride (8 c.c.). The chloride was removed by distillation from a water-bath, under reduced pressure, in a current of nitrogen. The residue was heated under reflux for 10 minutes in a current of nitrogen with concentrated hydrochloric acid (2 c.c.) and water (15 c.c.), the aqueous layer decanted, and the residue boiled with several portions of water. The combined acidic aqueous extract (total volume, 50 c.c.) was cooled rapidly, decanted from resinous material, and basified (30% NaOH). The resulting pale yellow precipitate was extracted with chloroform, the extract dried ($K_2CO_3$), and the chloroform removed, leaving a dark red gum. When this was stirred with a little cold chloroform, some solid separated; this was filtered off and washed with chloroform, giving a pink solid (50 mg. in one experiment; but generally much less), m. p. 200—210°. On recrystallisation twice from alcohol (charcoal), this afforded creamy-white needles, m. p. 214—215° (after drying at 80°/1 mm.) (Found: C, 78·65; H, 6·3. $C_{19}H_{18}ON_2$ requires, C, 78·6; H, 6·2. $C_{20}H_{20}ON_2$ requires C, 78·95; H, 6·6%). Light absorption in ethanol: $\lambda_{max.}$ 3230 A., log ε 4·11; $\lambda_{min.}$ 2730 A., log ε 3·42.

3 : 4-*Dihydro*-7 : 8-*benzindolo*(2′ : 3′-1 : 2)*pyridocoline* (I).—A solution of (II) (0·2 g.) in tetrahydrofuran (22 c.c.) was added to one of lithium aluminium hydride (0·13 g.) in ether (3·5 c.c.), and the mixture heated under reflux in an atmosphere of pure, dry nitrogen for 3 hours (water-bath). After being cooled, the reaction mixture was decomposed by the addition of water and acidified (HCl), and the tetrahydrofuran distilled off on a water-bath. On cooling, the clear solution deposited yellow needles, which were collected, washed with water, and recrystallised from boiling water, affording the *hydrochloride* (0·2 g.) as bright yellow needles. For analysis, this was dried for 3 hours at 100°/1 mm., whereafter it formed an orange-coloured powder, m. p. 298° (decomp.) (Found: C, 69·55; H, 5·5. $C_{19}H_{17}N_2Cl,H_2O$ requires C, 69·6; H, 5·8%). A solution of this in hot water was basified (NaOH), cooled, and the resulting solid (0·15 g.) filtered off, washed with water and recrystallised from aqueous alcohol (charcoal), affording the *base* as glittering, golden-yellow leaflets, m. p. 210—215° (decomp.), darkening at 190° (Found, after drying at 80°/1 mm.: C, 82·9; H, 5·8. $C_{19}H_{16}N_2$ requires C, 83·8; H, 5·9%). Light absorption in ethanol: (*a*) freshly prepared solution, $\lambda_{max.}$ 3520 A., log ε 4·46; 2430A., log ε 4·36; $\lambda_{min.}$ 2670 A., log ε 3·68 (this solution is almost colourless and stable in the dark, but when kept in daylight rapidly develops a yellow colour); (*b*) after 2 hours in daylight, $\lambda_{max.}$ 3510, 2520, and 2380 A., log ε 4·44, 4·48, and 4·48, respectively; $\lambda_{min.}$ 2720, and 2460 A., log ε 3·79, and 4·45, respectively; (*c*) after more prolonged action of light, $\lambda_{max.}$ 3510, 2800, 2520, and 2380 A., log ε 4·44, 395, 4·48, and 4·48, respectively; $\lambda_{min.}$ 3000, 2700, and 2460 A., log ε 3·72, 3·83, and 4·45, respectively. Light absorption in 0·01N-NaOH in ethanol: $\lambda_{max.}$ 3518 and 2300 A., log ε 4·45 and 4·46, respectively; $\lambda_{min.}$ 2780 A., log ε 3·67.

3 : 4 : 6 : 9-*Tetrahydro*-7 : 8-*benzindolo*(2′ : 3′-1 : 2)*pyridocoline* (III).—(*a*) The above crude base (0·2 g.) was hydrogenated with previously reduced Adams's catalyst (50 mg.) in glacial acetic acid (15 c.c.) at room temperature and pressure ($H_2$ absorption: 1 mole in 20 minutes). After filtration from the catalyst, the solvent was removed (water-bath; reduced pressure), the residue basified (dilute sodium hydroxide solution) and extracted with ether, the extract dried ($K_2CO_3$), the ether removed, and the residue recrystallised from benzene–light petroleum (charcoal), affording the base (0·17 g.) as colourless needles, m. p. 196—197°, not depressed by a specimen prepared by the method described in Part I

(Found : C, 82·6; H, 6·75. Calc. for $C_{19}H_{18}N_2$ : C, 83·2; H, 6·6%). (*b*) The same product was also obtained by reduction with hydriodic acid (*d* 1·7) and red phosphorus (heated under reflux for 4 hours), followed by basification.

*Action of Iodine on* 3 : 4 : 6 : 9-*Tetrahydro*-7 : 8-*benzindolo*-(2′ : 3′-1 : 2)-*pyridocoline.*—A warm solution of potassium acetate (0·7 g.) and iodine (0·35 g.) in absolute alcohol (10 c.c.) was added to one of the base (70 mg.) in alcohol (2 c.c.). The mixture was warmed on the water-bath for 5 minutes and then allowed to cool. The product was filtered off, washed with alcohol, suspended in hot water, treated with sulphur dioxide, filtered off, and washed with water and alcohol; it (0·1 g.) crystallised from alcohol as a felted mass of golden-yellow needles, m. p. 333° (decomp.) (Found : C, 57·1; H, 3·95. $C_{19}H_{15}N_2I$ requires C, 57·3; H, 3·8%). Light absorption in ethanol : $\lambda_{max.}$ 3520, 2810, 2520, and 2390 A., log ε 4·51, 3·97, 4·53, and 4·53, respectively; $\lambda_{min.}$ 2990, 2690, and 2470 A., log ε, 3·73, 3·84, and 4·48, respectively. This *iodide* (IX; X = I) (0·1 g.) was heated under reflux for 13 hours with excess of freshly prepared silver chloride in a mixture of alcohol (100 c.c.) and water (50 c.c.), the filtered liquid was evaporated to dryness (water-bath; reduced pressure), and the residue recrystallised from alcohol, affording the *chloride* (IX; X = Cl) as large orange-red needles (70 mg.), m. p. 330° (decomp.) (Found, after drying at 100°/1 mm. : C, 73·95; H, 5·25. $C_{19}H_{15}N_2Cl$ requires C, 74·4; H, 4·9%).

(*a*) Hydrogenation of the chloride (24·4 mg.) with Adams's catalyst (20 mg.) in glacial acetic acid (5 c.c.) ceased after the uptake of 2 moles of hydrogen in 70 minutes. The catalyst was filtered off after the solution had been heated to dissolve the partly precipitated hydrochloride. Isolation of the base yielded (from benzene–light petroleum) colourless needles, m. p. 197—198°, not depressed by admixture with 3 : 4 : 6 : 9-tetrahydro-7 : 8-benzindolo(2′ : 3′-1 : 2)pyridocoline.

(*b*) Hydrogenation of the chloride (21·1 mg.) with Adams's catalyst (20 mg.) in absolute alcohol (5 c.c.) containing AnalaR sodium hydroxide (4 mg.) ceased after the uptake of 1 mole of hydrogen in 10 minutes. Filtration, evaporation, and recrystallisation from aqueous alcohol yielded golden-yellow leaflets, m. p. 210—215° (decomp.) (darkening at 190°), not depressed by admixture with 3 : 4-dihydro-7 : 8-benzindolo(2′ : 3′-1 : 2)pyridocoline.

*Action of Iodine on* 3 : 4-*Dihydro*-7 : 8-*benzindolo*(2′ : 3′-1 : 2)*pyridocoline.*—A warm solution of the base (0·1 g.) in alcohol (10 c.c.) was treated with iodine (0·25 g.) and potassium acetate (0·5 g.) in alcohol (7·5 c.c.) as above. The product appeared to be identical with the above iodide (Found : C, 57·8; H, 4·1. Calc. for $C_{19}H_{15}N_2I$ : C, 57·3; H, 3·8%). Conversion into the chloride, and repetition of the above hydrogenations gave the same results as before.

*Action of Iodine on Sempervirine.*—Treatment of sempervirine (14 mg.) as described in the previous paragraph, and recrystallisation of the product from alcohol, afforded golden-yellow needles, m. p. 325—328°; mixed with sempervirine hydriodide, m. p. 325—327°. Boiling with dilute sodium hydroxide solution, extraction with chloroform, drying of the extract ($K_2CO_3$), evaporation, and recrystallisation of the residue from aqueous alcohol afforded brownish crystals, m. p. *ca.* 256°. A dilute solution of the base in alcoholic hydrochloric acid was very pale, with a blue-violet fluorescence; addition of dilute sodium hydroxide gave a deep yellow solution without fluorescence. The identity of the base with sempervirine was confirmed by measurement of the ultra-violet absorption spectrum in alcohol.

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