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THE STEREOCHEMISTRY OF LYCORANE—II[1]

(−)β-LYCORANE

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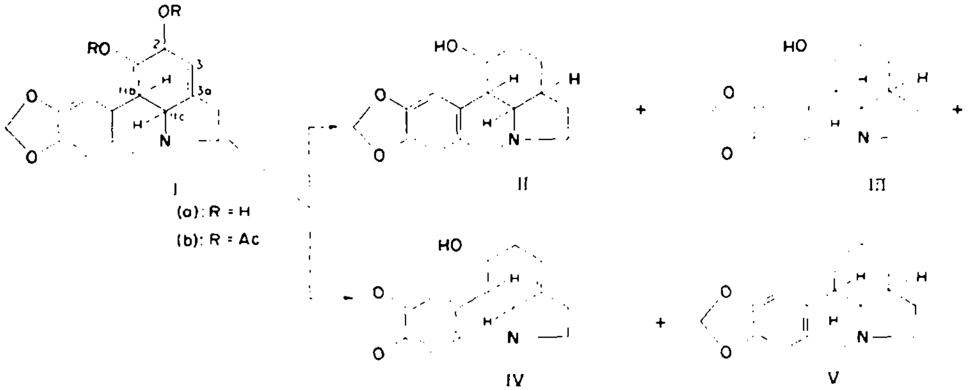
Abstract—Hydrogenation of diacetyllycorine (Ib) was found to be the most effective route for conversion of lycorine (Ia) into β-dihydrocaranine (II). The Hauptmann reduction of 1-deoxy-β-dihydrolycorin-2-one (XII) or the Clemmensen reduction of 1-O-acetyl-β-dihydrolycorinone (XI) followed by hydrogenation afforded (−)β-lycorane (X), which, in view of the sequence of reactions used in these transformations, is considered to have the same configurational structure as the skeleton of β-dihydrocaranine. This lycorane was also obtained by the Hauptmann reduction of β-dihydrocaranone (VIII). A procedure for preparing (−)α-lycorane (V) from 1-O-acetyllycorin-2-one (XIV) was also worked up.

In a preceding paper[1], we reported the preparation of (−)α-lycorane (V), which has the same configurational structure as the ring system of dihydrolycorine (VII) or α-dihydrocaranine (III).[2,3]



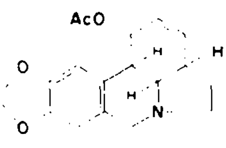
I
(a): R = H
(b): R = Ac

II

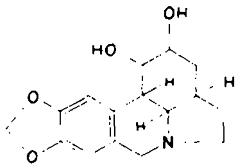
III

IV

V



VI



VII

The author next turned to the synthesis of the lycoranes having a β-configuration at C_{3a} hydrogen.

As the starting material for this purpose, β-dihydrocaranine (II), another hydrogenation product of caranine (IV), was first considered the most suitable.

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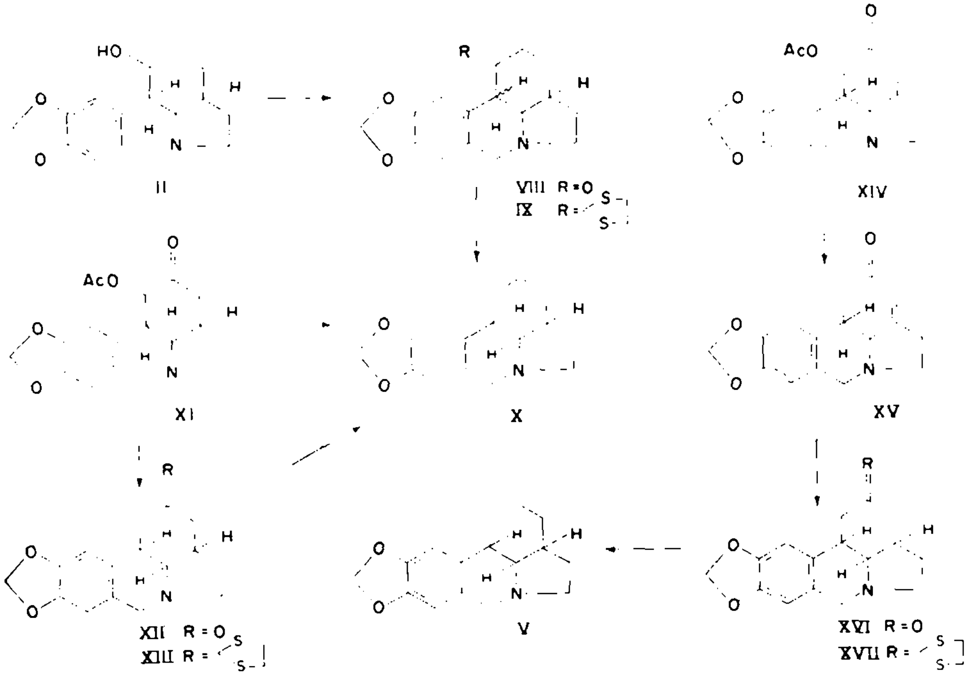
[1] Part I: K. Takeda, K. Kotera, S. Mizukami and M. Kobayashi, *Chem. Pharm. Bull.* **8**, 483 (1960).
[2] E. W. Warnhoff and W. C. Wildman, *J. Amer. Chem. Soc.* **79**, 2192 (1957); *Chem. & Ind.* 348 (1956).
[3] K. Takeda and K. Kotera, *Pharm. Bull.* **5**, 234 (1957); *Chem. & Ind.* 347 (1956).

Since, however, caranine has not yet been isolated from the bulbs of *Lycoris Radiata Herb.*, our sole natural source for obtaining the Amaryllidaceae alkaloids, it appeared at first very tedious to secure an amount of β-dihydrocaranine sufficient for the present work through the conversion of lycorine (Ia) into caranine and subsequent hydrogenation by the method reported earlier.[4] The author has, however, found a convenient procedure for the preparation of β-dihydrocaranine as follows. Hydrogenation of diacetyllycorine (Ib) with palladium–carbon in ethanol in the presence of a small amount of aqueous ammonia, followed by alkaline hydrolysis and chromatography, yielded β-dihydrocaranine in about 10 per cent yield along with small amounts of α-dihydrocaranine, caranine and (−)α-lycorane. Although the mechanism of this reduction may be complicated, it would be certain that caranine was a main intermediate formed by hydrogenolysis of the acetoxyl group allylic to the double bond in diacetyllycorine. Supporting this view, we have isolated, in a series of hydrogenation experiments carried out under a variety of conditions, caranine invariably as a by-product and in general its yields were inversely proportional to those of β-dihydrocaranine. Although convincing evidence for the formation of (−)α-lycorane as a by-product could not be obtained so far, it is possible to consider that some portion of diacetyllycorine used was converted by hydrogenolysis and simultaneous migration of the double bond[5] into acetyl isocaranine (VI) which immediately suffered further elimination of the second acetyl group attached to C_1 followed by saturation of the double bond to give (−)α-lycorane. It was shown previously that isocaranine gave on hydrogenation α-dihydrocaranine, indicating that the hydrogen atom attached to C_{3a} in isocaranine is α, like that in (−)α-lycorane.[4] It may be mentioned that in contrast to the result obtained above, catalytic reduction of



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[4] K. Takeda, K. Kotera and S. Mizukami, *J. Amer. Chem. Soc.* **80**, 2562 (1958).
[5] cf. W. G. Dauben and P. D. Hence, *J. Amer. Chem. Soc.* **77**, 2451 (1955).

diacetyllycorine with Adams catalyst in acetic acid followed by alkaline hydrolysis afforded predominantly dihydrolycorine (VII), though (—)α-lycorane and α-dihydrocaranine but no β-dihydrocaranine were obtained in an extremely low yield.

An approach to the lycorane derivative of the C_{3a} β-series from β-dihydrocaranine was considered to be the oxidation of the hydroxyl group to a ketone and subsequent reduction of the carbonyl to a methylene group. Modified Oppenauer oxidation of β-dihydrocaranine using potassium t-butoxide and benzophenone furnished β-dihydrocaranone (VIII).

Although this ketone had a sharp melting point at 159–161° and the crystals apparently were homogeneous, two spots were present in the paper chromatogram using butanol–acetic acid–water (10 : 1 : 5) as a solvent system. Furthermore, catalytic reduction of the ketone in acetic acid with Adams catalyst gave three isomeric products, compounds A, B, and C which had m.p. 164–165°, 225–228° (decomp) and 217–218° (decomp), respectively, analysed for $C_{16}H_{19}O_3N$ and characterized as the respective acetates, $C_{18}H_{21}O_4N$, m.p. 196–197°, 156–156·5° and 153–154°. In this case, the ratio of the amount of compounds A, B and C isolated was 1:1:3.

One or two of the above three products were also obtained by other methods. Treatment of the ketone with lithium aluminium hydride or catalytic reduction with Adams catalyst in dry ethanol in the presence of sodium ethoxide gave compounds A and B, the isolated amount being in the ratio of 1·4:1 in the former case and 13:1 in the later case. However, treatment with sodium and ethanol gave only compound B. Of the three products, compound A was identical with β-dihydrocaranine, while compounds B and C were neither identical with this nor with α-dihydrocaranine.

Although attempted replacement of the hydroxyl group in these two compounds with hydrogen by treatment with thionyl chloride followed by lithium aluminium hydride or catalytic hydrogenation according to the procedure employed by Uyeo *et al.*[6] was not successful, there is no doubt that compounds B and C are stereoisomeric to β-dihydrocaranine with respect to either C_1 or C_{11b}, or to both asymmetric centres. Since the author has isolated three compounds among the four theoretically possible isomers, at least either compound B or compound C must be epimeric to β-dihydrocaranine in respect to the asymmetric centre C_{11b}. Based on these discussions together with the chromatographic finding it is obvious that β-dihydrocaranone in solutions consisted of an equilibrium mixture of epimers, formed by keto-enol tautomerism.

Conversion of the ketone into the thioketal[7] (IX) and subsequent desulphurization gave in a 28 per cent over-all yield, a new lycorane, $C_{16}H_{19}O_2N$, m.p. 72–73°, $[\alpha]_D$ $-143·3°$ which was also characterized as its hydrochloride, m.p. 273–274° (decomp), $[\alpha]_D$ $-95·9°$. The base and its hydrochloride were in all respects distinctly different from (—)α-lycorane and its hydrochloride, respectively. As it is probable that this lycorane has the same configurations at all asymmetric centres as β-dihydrocaranine from the above mentioned experimental results, it was highly desirable to make clear the ambiguity as to its stereochemistry by making an approach to the same lycorane by another route which does not affect any symmetric centres in the molecule.

First, an attempt to replace the hydroxyl group in β-dihydrocaranine by a chlorine atom using thionyl chloride was not successful, since the only isolatable product was

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[6] S. Uyeo, W. C. Wildman, R. J. Highet and H. M. Fales, *J. Amer. Chem. Soc.* **80**, 2590 (1958).

[7] The paper chromatography of this thioketal in the same manner as that used in β-dihydrocaranone showed only one spot, differing from that of the parent ketone and indicated the thioketal probably to be homogeneous.

an oil which contained no chlorine atom and could not be induced to crystallize. The ultra-violet spectrum indicated that it contained β-anhydrodihydrocaranine.

In contrast, 1-0-acetyl-β-dihydrolycorinone (XI) which was obtained from diacetyllycorine in three steps and established to have the same configurations as β-dihydrocaranine at C_{11b}, C_{11c} and C_{3a} by Nakagawa and Uyeo[8], was found to be useful for the synthesis of β-lycorane, having the same configurations at C_{3a}, C_{11b} and C_{11c} as β-dihydrocaranine. Treatment of this with zinc dust in acetic anhydride according to the procedure used by Woodward[9] yielded 1-deoxy-β-dihydrolycorin-2-one (XII), m.p. 165–166°. This was first converted into its thioketal (XIII) by treatment with ethanedithiol and boron fluoride–etherate and then subjected to desulphurization by refluxing with Raney nickel in methanol. The product thus obtained, (—)β-lycorane, was in every respect identical with the above-mentioned lycorane.

With the preparation of (—)β-lycorane by a sequence of reactions in which there was less chance for involvement of asymmetric centres accomplished, it is now clear that (—)β-lycorane possesses the same configurations as β-dihydrocaranine so far as the ring system is concerned.

(—)β-Lycorane was also obtained by the Clemmensen reduction of 1-0-acetyl-β-dihydrolycorinone. Since, however, a small amount of an unsaturated compound seemed to be contaminated in the product, as in the case of 6-hydroxy-7-keto-1,12-p-phenylenedodecane,[10] the crude product was hydrogenated to give pure (—)β-lycorane.

It may be added here that when 1-0-acetyllycorin-2-one (XIV)[8] was reduced with zinc dust in acetic anhydride and *o*-xylene, 1-deoxylycorin-2-one (XV) was obtained as expected. Hydrogenation of this with palladium–carbon in ethanol gave 1-deoxy-α-dihydrolycorin-2-one (XVI) which was convertible into (—)α-lycorane by reduction of its thioketal (XVII) with Raney nickel.

EXPERIMENTAL[11]

Hydrogenation of diacetyllycorine (Ib)

(a) *With Adams catalyst in acetic acid.* Diacetyllycorine (1 g) in acetic acid (55 ml) was shaken in hydrogen with Adams catalyst (150 mg) for 4 hr (hydrogen uptake: 79 ml, calc. for 1 H_2: 66 ml). After removal of the catalyst, the mixture was evaporated to dryness *in vacuo* and the residue in ethanol (100 ml) and KOH (5 g) was refluxed for 2 hr. The reaction mixture was evaporated under reduced press, dissolved in dil HCl, filtered, basified with 10% Na_2CO_3 and extracted with benzene. The solid which remained undissolved in benzene gave dihydrolycorine (VII) (305 mg), needles (from methanol), m.p. and mixed m.p. 239–240°. The infra-red spectrum was also identical with that of an authentic specimen. The dried benzene solution was evaporated to dryness under reduced press, the residue (140 mg) dissolved in benzene and chromatographed over alumina (5 g). Elution with benzene furnished on recrystallization with pet ether (—)α-lycorane (V, 22 mg), m.p. and mixed m.p. 82–83°. The infra-red spectrum in carbon disulphide solution was identical with that of an authentic specimen. Elution with 10:1 benzene-methanol gave α-dihydrocaranine (III, 25 mg), prisms (from acetone), identical with an authentic specimen in m.p., mixed m.p. (168–169°) and infra-red spectrum.

(b) *With palladium–carbon in 95% ethanol and ammonia.* Diacetyllycorine (2 g) in 95% ethanol (200 ml) and 28% ammomia (1 ml) was shaken in hydrogen in the presence of 10% palladium–carbon

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[8] Y. Nakagawa and S. Uyeo, *J. Chem. Soc.* 3736 (1959).

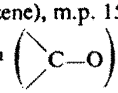
[9] R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. Maclamore, *J. Amer. Chem. Soc.* **74**, 4223 (1952).

[10] D. J. Cram, N. L. Allinger and H. Steinberg, *J. Amer. Chem. Soc.* **76**, 6132 (1954).

[11] All melting points are uncorrected. Unless otherwise stated, the ultra-violet spectra were taken in 95% ethanol using a Beckman Model DU spectrophotometer. Alumina used for chromatography in this experiment was Merck's Reagent Grade standardized according to the method of Brockmann. The infra-red spectra were determined with a Perkin-Elmer single-beam infra-red spectrophotometer, Model 12C, or a Koken infra-red spectrophotometer, Model, DS 301.

(3 g) for 4 hr. Hydrogen uptake was 288 ml (calc. for $2H_2$: 267 ml). After removal of the catalyst, water (30 ml) and KOH (3 g) were added and the mixture was refluxed on a water-bath for 1 hr, evaporated to dryness *in vacuo*, acidified with dil acetic acid, filtered, basified with Na_2CO_3 and extracted with benzene. The dried benzene layer was evaporated to dryness under reduced press and the residue (812 mg) in benzene-petroleum ether (1:1) was chromatographed over alumina (30 g). Elution with benzene-pet ether (1:1) and benzene gave (−)α-lycorane (V, 170 mg), prisms (from pet ether), identical with an authentic specimen in m.p., mixed m.p. and infra-red spectrum. The second benzene eluate gave β-dihydrocaranine (II, 190 mg), prisms (from ethyl acetate), identical in m.p., mixed m.p. (164–166°) and infra-red spectrum with an authentic specimen. Elution with benzene-ether (20:1, 10:1, 1:1) and ether afforded caranine (IV, 70 mg), prisms (from ethyl acetate), m.p. and mixed m.p. (177–178°). The infra-red spectrum was perfectly superimposable upon that of an authentic sample. A fraction eluted with benzene-methanol (20:1) gave on recrystallization from acetone α-dihydrocaranine (III, 25 mg) as prisms, m.p. 168–169°, identical in mixed m.p. and infra-red spectrum with an authentic specimen.

Modified Oppenauer oxidation of β-dihydrocaranine (II)

Potassium metal (100 mg) was dissolved under nitrogen in t-butanol (10 ml) which was freshly distilled over sodium metal. To the solution was added under stirring benzophenone (600 mg) and β-dihydrocaranine (200 mg), and the mixture was refluxed under nitrogen at 105–110° in an oil-bath for 2·5 hr. The excess of t-butanol was evaporated *in vacuo* over a period of 5–10 min, the residue was taken up in benzene (20 ml) and extracted repeatedly with dil HCl. The combined extracts were filtered, basified with 10% Na_2CO_3 and extracted with benzene (30 ml). The dried benzene was concentrated to 15 ml under reduced press and chromatographed over less active alumina (5 g).[12] Elution with benzene-ether (50:1) gave *β-dihydrocaranone* (VIII, 70 mg), prisms (from a small amount of benzene), m.p. 159–161°, $[\alpha]_D^{31^\circ}$ −268·9° (*c* 0·876, chloroform), λ_{max} 290 mμ, log ε 3·66; ν_{max}^{Nujol} 1712 cm⁻¹ . (Found: C, 71·08; H, 6·54; N, 5·16. $C_{16}H_{17}O_3N$ requires: C, 70·83; H, 6·32; N, 5·16%).

From fractions eluted with benzene-ether (10:1) the starting material (20 mg) was recovered unchanged. The paper chromatography of β-dihydrocaranone by an ascending method using butanol–acetic acid–water (10:1:5) gave two spots (R_f 0·55 and 0·66) by Dragendorff's reagent.

Reduction of β-dihydrocaranone (VIII)

(a) *With lithium aluminium hydride.* β-Dihydrocaranone (65 mg) in dry ether (20 ml) was added under stirring to a suspension of lithium aluminium hydride (40 mg) in dry ether (10 ml) and the whole refluxed for 3 hr. The excess of lithium aluminium hydride was destroyed by dropwise addition of water (10 ml), the ethereal layer separated, and the aqueous layer extracted with benzene (20 ml × 2).

The combined organic layers were dried over sodium sulphate and evaporated to dryness, and the residue (67 mg) was dissolved in benzene (6 ml) and passed through a column of alumina (2 g). Elution with benzene and benzene-ether (50:1, 30:1, 10:1, 5:1) gave crude compound A (35 mg) which was recrystallized from ethyl acetate to give pure β-dihydrocaranine (II, 20 mg), m.p. 162–164°, identical in mixed m.p. and infra-red spectrum with an authentic specimen. The eluate with benzene-ether (1:1) and ether gave crude *compound* B (30 mg) which was purified by recrystallization from acetone to give scales (14 mg), m.p. 225–227° (decomp), $[\alpha]_D^{26^\circ}$ −62·4° (*c* 0·596, ethanol), λ_{max} 237, 291 mμ, log ε 3·62, 3·68; ν_{max}^{Nujol} 3165 cm⁻¹, $\nu_{max}^{CHCl_3}$ 3600 cm⁻¹ (−OH). (Found: C, 70·37; H, 7·21; N, 5·27. $C_{16}H_{19}O_3N$ requires: C, 70·31; H, 7·01; N, 5·13%).

The acetate of compound B was prepared with acetic anhydride and pyridine, m.p. 156–156·5°, needles (from ethanol), $[\alpha]_D^{21^\circ}$ −55·8° (*c* 0·500, ethanol), λ_{max} 237, 292 mμ, log ε 3·59, 3·66; ν_{max}^{Nujol} 1731 cm⁻¹ (CH_3COO—). (Found: C, 68·31; H, 6·61; N, 4·34. $C_{18}H_{21}O_4N$ requires: C, 68·55; H, 6·71; N, 4·44%).

The acetate gave compound B on hydrolysis.

(b) *With sodium and ethanol.* To a solution of β-dihydrocaranone (70 mg) in dry ethanol (20 ml) was added in portions sodium metal (850 mg) in an atmosphere of nitrogen and the mixture was

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[12] Alumina used in this experiment was Merck's Reagent, the activity of which was reduced by addition of 6% water.

refluxed for 3 hr. The reaction mixture was evaporated to dryness under reduced press in nitrogen, and the residue was dissolved in water (10 ml) and extracted with benzene (45 ml). Evaporation of the dried extract gave an oil (48 mg) which was dissolved in benzene and chromatographed over alumina (5 g). Elution with benzene–ether (10:1, 5:1, 3:1) gave crude compound B (23 mg) which was recrystallized from acetone to give a pure sample (12 mg), m.p. and mixed m.p. (225–227° decomp).

(c) *With Adams catalyst in ethanol and sodium ethoxide.* β-Dihydrocaranone (50 mg) in dry ethanol (8 ml) containing sodium ethoxide (22 mg) was shaken in hydrogen with Adams catalyst (25 mg) for 3·5 hr. After removal of the catalyst the ethanol was evaporated to dryness. Water (10 ml) was added and the residue extracted with benzene. The dried benzene was evaporated, the residue dissolved in benzene and chromatographed over alumina (1·5 g). Elution with benzene–ether (50:1, 30:1, 20:1, 10:1) gave β-dihydrocaranine (II, 13 mg), m.p. and mixed m.p., 164–166°. Further elution with benzene–ether (5:1, 1:1) afforded compound B (1 mg), m.p. and mixed m.p., 225–227° (decomp).

(d) *With Adams catalyst in acetic acid.* A solution of β-dihydrocaranone (100 mg) in acetic acid (7 ml) was shaken in hydrogen with Adams catalyst (40 mg) for 4 hr. Hydrogen uptake was 9·7 ml (calcd. for 1 H_2: 8·77 ml). After removal of the catalyst, the acetic acid was evaporated to dryness and the residue was dissolved in water (5 ml), filtered, basified with Na_2CO_3 and extracted with benzene (40 ml). The dried extract was evaporated and the residue (69 mg) was chromatographed in benzene over alumina (2 g). Elution with benzene–ether (50:1, 30:1, 10:1) gave crude β-dihydrocaranine (II, 15 mg) which was recrystallized from ethyl acetate to give a pure sample (3 mg), m.p. and mixed m.p. 164–166°. The eluate with benzene–ether (5:1, 1:1) furnished crude compound B (8 mg) which on recrystallization from acetone gave a pure sample (4 mg), m.p. and mixed m.p. 225–226° (decomp). Elution with benzene–ethyl acetate (1:1) and ethyl acetate gave crude *compound* C (45 mg) which was recrystallized from ethyl acetate to give a pure sample (15 mg), m.p. 217–218°, $[\alpha]_D^{20^\circ}$ −22·0° (*c* 0·509 ethanol), λ_{max} 238, 291 mμ, log ε 3·58, 3·66; ν_{Max}^{Nujol} 3164, 3104 cm^{-1}, $\nu_{Max}^{CHCl_3}$ 3600 cm^{-1} (−OH) (Found: C, 70·40; H, 7·29; N, 5·47. $C_{16}H_{19}O_3N$ requires: C, 70·31; H, 7·01; N, 5·13%).

The acetate was prepared with acetic anhydride and pyridine, plumes (from acetone), m.p. 153–154°, $[\alpha]_D^{21^\circ}$ −103·7° (*c* 0·483, ethanol), λ_{max} 239, 292 mμ, log ε 3·59, 3·67; ν_{max}^{Nujol} 1741 cm^{-1} (CH_3-COO−). (Found: C, 68·54; H, 6·80; N, 4·05. $C_{18}H_{21}O_4N$ requires: C, 68·55; H, 6·71; N, 4·44%).

The acetate gave compound C on hydrolysis.

Thioketalization of β-dihydrocaranone (VIII)

Boron fluoride-etherate (0·3 ml) was added under cooling with ice to a mixture of β-dihydrocaranone (100 mg) in ethanedithiol (0·3 ml) and the mixture was allowed to stand at room temp for 20 hr. After addition of water (5 ml) and 10% NaOH (4 ml), the reaction mixture was extracted with a mixture of ether (50 ml) and benzene (10 ml), and the extract washed several times with 2% NaOH (12 ml) and then with water. The dried organic layer was evaporated to dryness under reduced press and the residue in benzene (20 ml) was chromatographed over alumina (10 g). Elution with benzene and benzene–ether (9:1) gave *thioketal* (IX, 70 mg), prisms (from ethanol), m.p. 144–145°, $[\alpha]_D^{21^\circ}$ −64·5° (*c* 0·51 chloroform), λ_{max} 291 mμ, log ε 3·64. (Found: C, 62·30; H, 6·02; N, 4·21; S, 18·39. $C_{18}H_{21}O_2NS_2$ requires: C, 62·21; H, 6·09; N, 4·03; S, 18·46%).

In contrast to the result obtained in the case of β-dihydrocaranone, the paper chromatography of this thioketal by an ascending method using butanol–acetic acid–water (10:1:5) as a solvent system showed one spot (R_f 0·74) by Dragendorff's reagent.

Desulphurization of thioketal (IX)

Thioketal (53·1 mg) in methanol (6 ml) was refluxed with freshly prepared Raney nickel (600 mg). After removal of the catalyst, the filtrate was evaporated under reduced press and the residue in pet ether (10 ml) was chromatographed over alumina (3 g). Elution with pet ether–benzene (5:1, 4:1, 2:1, 1:1) furnished (−)*β-lycorane* (X, 20 mg), plates (from pet ether), m.p. 72–73°, $[\alpha]_D^{20^\circ}$ −143·3° (*c* 1·04, ethanol), λ_{max} 291 mμ, log ε 3·67. (Found: C, 74·26; H, 7·53; N, 5·32. $C_{16}H_{19}O_2N$ requires: C, 74·68; H, 7·44; N, 5·44%).

Hydrochloride, needles from ethanol, m.p. 273–274° (decomp), $[\alpha]_D^{22^\circ}$ −95·9° (*c* 0·366, chloroform). (Found: C, 64·31; H, 6·90; N, 4·65; Cl, 12·35. $C_{16}H_{19}O_2N{\cdot}HCl{\cdot}1/4H_2O$ requires: C, 64·42; H, 6·93; N, 4·70; Cl, 11·89%).

Reaction of 1-O-*acetyl-β-dihydrolycorinone* (XI) *with zinc in* o-*xylene and acetic anhydride*

1-O-Acetyl-β-dihydrolycorinone (200 mg) and zinc dust (3 g) in acetic anhydride (3 ml) and dry *o*-xylene (5 ml) were refluxed under nitrogen for ½ hr. Zinc was removed and washed with benzene, the filtrate and washings were evaporated to dryness *in vacuo* and the residue was dissolved in dil HCl, filtered, basified with Na_2CO_3 and extracted with benzene. The dried benzene layer was evaporated under reduced press and the residue (124 mg) dissolved in benzene was chromatographed over alumina (4 g). Elution with benzene gave 1-*deoxy-β-dihydrolycorin-2-one* (XII, 55 mg), plates after repeated crystallizations from ethanol, m.p. 165–166°, $[\alpha]_D^{18°}$ −78·4° (*c* 0·589, ethanol), λ_{max} 291 mμ, log ε 3·68; ν_{Max}^{Nujol} 1711 cm^{-1} $\left(>C{=}O\right)$. (Found: C, 70·96; H, 6·44; N, 5·27. $C_{16}H_{17}O_3N$ requires: C, 70·83; H, 6·32; N, 5·16%).

Thioketalization of 1-*deoxy-β-dihydrolycorin-2-one* (XII)

To a mixture of 1-doxy-β-dihydrolycorin-2-one (50 mg) and ethanedithiol (0·2 ml) was added boron fluoride-etherate (0·2 ml) under cooling with ice. The mixture was kept at room temp for 16 hr. Water (5 ml) and 10% NaOH (4 ml) were added and the whole was extracted with a mixture of ether (40 ml) and benzene (10 ml). The extract was washed with 10% NaOH (2 ml) and water (10 ml), dried with anhyd sodium sulphate and evaporated to dryness under reduced press. The residue (50 mg) in pet ether–benzene (3:1) was chromatographed over alumina (1·5 g). Elution with pet ether–benzene (3:1, 2:1) gave *thioketal* (XIII, 34 mg), needles (from ether), m.p. 117–118°, $[\alpha]_D^{22°}$ −94·4° (*c* 0·566, ethanol), λ_{max} 291 mμ, log ε 3·76. (Found: C, 62·61; H, 6·12; N, 3·97; S, 18·49. $C_{18}H_{21}O_2NS_2$ requires: C, 62·21; H, 6·09; N, 4·03; S, 18·45%).

Desulphurization of thioketal (XIII)

Thioketal (57 mg) in methanol (4 ml) was refluxed with freshly prepared Raney nickel (500 mg) for 4 hr. After filtration of the catalyst and concentration of the filtrate, the residue (29 mg) in pet. ether–benzene (1:1) was chromatographed over alumina (1 g). Elution with pet ether–benzene (1:1) gave (−)β-lycorane (X, 17 mg), plates (from pet ether), m.p. 72–73°, $[\alpha]_D^{16°}$ −143·0° (*c* 0·57, ethanol), λ_{max} 291 mμ, log 3·67. A mixed m.p. of this with (−)α-lycorane (V) was depressed to 53–59° and the infra-red spectrum was not identical with that of V. (Found: C, 74·50; H, 7·52; N, 5·74. Calcd. for $C_{16}H_{19}O_2N$: C, 74·68; H, 7·44; N, 5·44%).

Clemmensen reduction of 1-O-*acetyl-β-dihydrolycorinone* (XI) *and hydrogenation of the product with Adams catalyst*

1-O-Acetyl-β-dihydrolycorinone (300 mg) in conc HCl (6 ml) was added dropwise to zinc-amalgam (1·5 g) which was prepared by amalgamating zinc (1·5 g) with mercuric chloride (276 mg) in water (4·8 ml) and conc HCl (1·8 ml). The mixture was stirred at 60–70° for 3 hr. After filtration, the filtrate was made alkaline with Na_2CO_3, extracted with a mixture of benzene–ether and the dried extract evaporated to dryness under reduced press. The residue (145 mg) in ethyl acetate (4 ml) was shaken in hydrogen with Adams catalyst (40 mg) for 2 hr. After filtration of the catalyst and evaporation of the filtrate, the residue was dissolved in dil HCl, filtered, basified with Na_2CO_3 and extracted with pet ether. The dried organic layer was evaporated and the residue (61 mg) in pet ether–benzene (2:1) passed through a column of alumina (3 g). A pet ether–benzene (2:1) eluate gave (−)β-lycorane (X, 25 mg), plates (from pet ether), m.p. 72–73°, identical in m.p., mixed m.p. and infra-red spectrum with the sample mentioned above.

Reaction of 1-O-*acetyl-lycorin-2-one* (XIV) *with zinc in* o-*xylene and acetic anhydride*

1-O-Acetyl-lycorin-2-one (200 mg) was dissolved in dry *o*-xylene (3 ml) and acetic anhydride (2 ml) under heating at 145–150° in an oil-bath, zinc dust (2 g) was added in one portion to the solution and the mixture was refluxed under nitrogen for 8 min. After removal of zinc the filtrate and washings were evaporated to dryness *in vacuo* and the residue was dissolved in dil acetic acid, filtered, basified with Na_2CO_3 and extracted with benzene–ether (1:1). The dried extract was evaporated under reduced press and the residue (130 mg) gave, on repeated crystallizations from acetone, 1-*deoxy-lycorin-2-one* (XV, 50 mg) as colourless needles, m.p. 157–158° (decomp), $[\alpha]_D^{24°}$ −169° (*c* 0·490, dioxane), λ_{max} 231, 290 mμ, log ε 4·20, 3·70: ν_{Max}^{Nujol} 1664 cm^{-1} (α,β-unsaturated ketone). (Found: C, 71·35; H, 5·65; N, 4·99. $C_{16}H_{15}O_3N$ requires: C, 71·36; H, 5·61; N, 5·20%).

Hydrogenation of 1*-deoxy-lycorin-*2*-one* (XV) *with palladium–carbon in ethanol and dioxane*

1-Deoxy-lycorin-2-one (92 mg) in ethanol (3 ml) and dioxane (4 ml) was shaken in hydrogen in the presence of 15% palladium-on-carbon (200 mg) for 5 hr (hydrogen uptake: 8·7 ml, calc. for 1 H_2: 7·6 ml). After removal of the catalyst, the filtrate was evaporated, the residue dissolved in dil HCl, filtered, made alkaline with Na_2CO_3 and extracted with benzene. The dried benzene was evaporated under reduced press and the residue (42 mg) in benzene–pet ether (1:1, 5 ml) chromatographed over alumina (2 g). Elution with benzene–pet ether (7:3) gave 1*-deoxy-α-dihydrolycorin-*2*-one* (XVI, 30 mg), plates (from acetone), m.p. 147–148°, $[\alpha]_D^{21°}$ −234·4° (*c* 0·748 ethanol), λ_{max} 292 mμ, log ε 3·67; ν_{max}^{Nujol} 1711 cm^{-1} (>C=O). (Found: C, 70·82; H, 6·39; N, 5·01. $C_{16}H_{17}O_3N$ requires: C, 70·83; H, 6·32; N, 5·16%).

Thioketalization of 1*-deoxy-α-dihydrolycorin-*2*-one* (XVI)

1-Deoxy-α-dihydrolycorin-2-one (103 mg) was treated in the usual manner with ethandithiol (0·3 ml) and boron fluoride-etherate (0·3 ml) to give the *thioketal* (XVII, 80 mg). It formed needles (from ether), m.p. 107–108°, $[\alpha]_D^{20°}$ −37·5° (*c* 0·787, ethanol), λ_{max} 292 mμ, log ε 3·69. (Found: C, 62·42; H, 6·13; N, 3·89; S, 18·18. $C_{18}H_{21}O_2NS_2$: C, 62·21; H, 6·09; N, 4·03; S, 18·46%).

Desulphurization of thioketal (XVII)

Thioketal (56 mg) in methanol (5 ml) was refluxed with Raney nickel (600 mg) for 5 hr. After working up in an usual manner, the product (13 mg) was chromatographed in benzene–pet ether (1:1, 4 ml) over alumina (1 g). Elution with benzene–pet ether (1:1) gave (−)α-lycorane (V, 8 mg), m.p. 82–83°, plates (from pet ether), identical in m.p., mixed m.p. and infra-red spectrum with an authentic specimen.

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