Colchicine and Related Compounds. Part XIV. Structure of β- and γ-Lumicolchicine.*

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The action of sunlight on dilute aqueous solutions of colchicine leads to the formation of α-, β-, and γ-lumicolchicine, each isomeric with colchicine (Grewe and Wulf, *Chem. Ber.*, 1951, **84**, 621). Degradative and spectroscopic evidence suggests that β- and γ-lumicolchicine are stereoisomers and indicates that they have tetracyclic structures which arise from a rearrangement of the bonds in the tropolone ring of colchicine.

It has been known for some time that colchicine (I) and its solutions undergo some change when exposed to sunlight (Hübler, *Arch. Pharm.*, 1865, **171**, 205; Struve, *Z. anal. Chem.*, 1873, **12**, 164). Jacobi (*Arch. exp. Path. Pharmak.*, 1890, **27**, 129) isolated an amorphous product, which, by reason of its analysis, he called oxydicolchicine. These experiments were probably concerned mainly with photo-oxidation, since air was invariably present. Later, it was shown (Macht, *Science*, 1927, **66**, 653) that only the short-wave portion of sunlight was capable of effecting any change. By irradiating solutions of colchicine in water with a powerful source of ultraviolet light, Grewe (*Naturwiss.*, 1946, **33**, 187) was able to effect a photo-isomerisation, which gave a small quantity of crystalline material. When very dilute solutions of pure colchicine were exposed to the available sunlight for 5—7 weeks, air being excluded from the system, there was obtained an almost theoretical yield of transformation product (Grewe and Wulf, *Chem. Ber.*, 1951, **84**, 621). This

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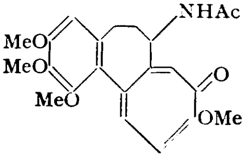
material was separated into three crystalline substances designated α-, β-, and γ-lumicolchicine, each isomeric with colchicine.

Concurrently, Šantavý (*Coll. Czech. Chem. Comm.*, 1951, **16**, 655), using less defined conditions, obtained " lumicolchicine " I by the action of sunlight on aqueous solutions of colchicine and " lumicolchicines " I and II by the action of ultraviolet radiations. In fact, lumicolchicines I and II are identical with the β- and the γ-isomer isolated by Grewe and Wulf (Šantavý, *loc. cit.*). It is of interest that these two compounds are identical with substances I and J, which are obtained, along with colchicine, from the meadow saffron, *Colchicum autumnale* (*idem, loc. cit.*), since it provides an example of a transformation which sunlight is capable of effecting in the plant, presumably without the connivance of enzymes.

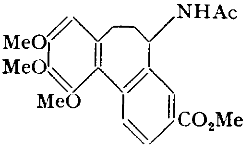
In the present work, dilute solutions of colchicine in water, under an atmosphere of nitrogen, were exposed to summer sunlight during 8—10 weeks. The transformation product was separated by fractional crystallisation from methanol into three isomeric compounds whose properties are in excellent agreement with those recorded for α-, β-, and γ-lumicolchicine by Grewe and Wulf (see Experimental section). They obtained the three isomers in roughly comparable amounts whereas here there was formed a preponderance of β-lumicolchicine, the other isomers being present in much smaller amounts. This discrepancy may well be due to a difference in the actinic value of the incident sunlight or to the different transparencies, toward ultraviolet light, of the glass of the containing vessels.

The near identity of the ultraviolet spectra (maxima at 225, 266, and 340 mμ) of β- and γ-lumicolchicine, together with the close resemblance of their infrared curves in the higher-frequency region, suggests a stereochemical rather than a structural relation between them, and this paper seeks to present a body of facts in favour of this assignment.

It was shown (Grewe and Wulf, *loc. cit.*) that on catalytic hydrogenation with Adams catalyst at atmospheric pressure, β- and γ-lumicolchicine absorbed only two mols. of hydrogen to give tetrahydro-compounds, in contrast to colchicine which forms a hexhydro-derivative (Bursian, *Ber.*, 1938, **71**, 245; Kemp and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 243). Further, it was shown (Grewe and Wulf, *loc. cit.*) that these tetrahydro-compounds absorbed rapidly only one atom of oxygen when titrated with perbenzoic acid, indicating the presence of one remaining aliphatic double bond, so that these compounds contain a fourth ring. Such a transformation (apart from any others which might have occurred) is most easily envisaged as a rearrangement of the bonds of the tropolone ring. On this basis, if stereochemical considerations are ignored, three structures (III—V) are possible. In each the extended conjugation of the colchicine molecule has been interrupted, requiring a shift of some of the light absorption maxima to shorter wavelengths. Indeed for β- and γ-lumicolchicine the intense maxima are located at 228 and 266 mμ (shoulder at 280 mμ) as against 247 and 350 mμ in colchicine. Moreover β- and γ-lumicolchicine show carbonyl activity as required by these tetracyclic structures. In addition to simple oximes and semicarbazones, they form osazones and dioximes (in pyridine), the latter by the loss of a methoxyl group. The dioximes react with nickel and copper salts to form brown and green complexes which are soluble in chloroform.



(I)



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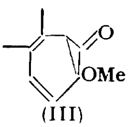

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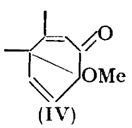

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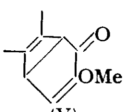


(V)

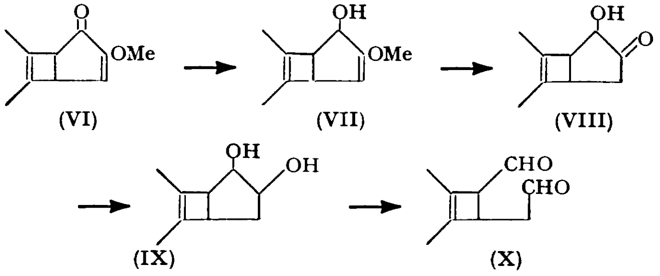
The usual methods of attack on the tropolone moiety of the colchicine molecule proved ineffectual when applied to β- and γ-lumicolchicine, *e.g.*, sodium methoxide in methanol [under more vigorous conditions than are required to rearrange colchicine to *allo*colchicine (II)], and very dilute acid at 100°. Stronger acid hydrolysed simultaneously the methoxyl and the amide group, and led to intractable products.

β-Lumicolchicine was smoothly reduced by sodium borohydride in methanol to a dihydro-compound, which contains four methoxyl groups and forms a monoacetate, but not an oxime. Its infrared spectrum shows no absorption in the carbonyl region other than that due to the amide group at 1642 $cm.^{-1}$.

At 100° N-hydrochloric acid hydrolysed dihydro-β-lumicolchicine almost instantaneously to demethyldihydro-β-lumicolchicine, $C_{21}H_{25}O_6N$, which contains only three methoxyl groups and forms a monoacetate and, moreover, an oxime. Its infrared absorption curve shows a peak at 1742 $cm.^{-1}$ (carbonyl stretching) in addition to that at 1654 $cm.^{-1}$ (amide CO). The ready hydrolysis of the methoxyl group indicates its presence as an enol ether. This points to formula (V) for β-lumicolchicine and precludes (III) and (IV) which are aliphatic ethers, as would be the dihydro-derivatives obtained by reduction of the keto-group. Structure (V) incorporates the monoenol ether of a 1 : 2-diketone and is consistent with the fact that the hydrolysis of β-lumicolchicine is less easy than that of dihydro-β-lumicolchicine, since the competition of the keto-group for the available hydrogen ions no longer pertains in the derived hydroxy-compound. These reactions may now be represented by partial formulæ (VI)—(VIII).

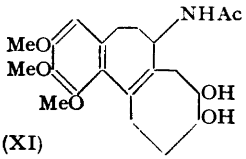
As required by structure (VIII), demethyldihydro-β-lumicolchicine has the properties of an acyloin. It reduced Fehling's solution and formed osazones with phenylhydrazine and its derivatives. In fact the 2 : 4-dinitrophenylosazone was identical with that obtained directly from β-lumicolchicine, by the loss of a methoxyl group, thus showing that the molecule had undergone no skeletal rearrangement during the previous stages. In addition demethyldihydro-β-lumicolchicine formed a dioxime, which differed from the two isomeric dioximes obtained from β-lumicolchicine (by the loss of a methoxyl group) and is presumably the third of the four possible isomers (see Experimental section).

Demethyldihydro-β-lumicolchicine was reduced in aqueous methanol by sodium borohydride to a 1 : 2-glycol (IX), which showed no carbonyl absorption in the infrared other than that of the amide group. This glycol was not separated into its stereoisomers but straightway oxidised with sodium metaperiodate in aqueous ethanol at pH 7—the use of periodic acid led to side reactions. The product, which gave a positive Angeli–Rimini reaction for an aldehyde, was isolated as its 2 : 4-dinitrophenylhydrazone, whose analysis corresponded to that of the bis-derivative of the dialdehyde (X). The bis-2 : 4-dinitrophenylhydrazone is light orange and shows a maximum in the ultraviolet spectrum at 353 mμ, both features characteristic of the derivative of a saturated carbonyl compound as required by (X). The formation of a dialdehyde, which does not undergo ring-closure under the acidic conditions of dinitrophenylhydrazone formation, is compatible with structure (X) and may be cited as evidence for the formation of a bridge across ring C of the colchicine molecule during its photoisomerisation. Had this not occurred the resultant 1 : 7-dialdehyde would almost certainly have suffered internal aldol condensation to give a monoaldehyde as occurs when hexahydrocolchicine (XI) is treated similarly (Arnstein, Tarbell, Scott, and Huang, *J. Amer. Chem. Soc.*, 1949, **71**, 2448).



(VI) (VII) (VIII) (IX) (X)

The possibility of a second double bond (not susceptible to hydrogenation at atmospheric pressure), instead of a fourth ring, in demethyldihydro-β-lumicolchicine (VIII) was precluded by the result of titrating its acetate with a molar excess of monoperphthalic acid in chloroform: only 1·15 atoms of oxygen (as determined by iodine–thiosulphate titration) were absorbed in 24 hr., indicating the presence of only one aliphatic double bond. The epoxide could not be obtained crystalline.



(XI)

Micro-hydrogenation of demethyldihydro-β-lumicolchicine and its acetate gave some support for their tetracyclic nature. With Adams catalyst in acetic acid, the acetate absorbed one mol. of hydrogen as required for the carbonyl group; but demethyldihydro-β-lumicolchicine surprisingly absorbed two mols. of hydrogen, a result which is not easy to explain: hydrogenolysis of the hydroxyl group and rupture of the *cyclo*butenering are possibilities. When palladium was substituted for Adams catalyst neither demethyldihydro-β-lumicolchicine nor its acetate absorbed hydrogen, compatibly with formula (VIII) for the acyloin.

γ-Lumicolchicine undergoes an analogous series of reactions which yield compounds whose chemical properties closely resemble those of the β-isomer. On reduction with sodium borohydride in aqueous methanol, γ-lumicolchicine yielded a dihydro-compound which contains four methoxyl groups and forms an acetate. Dihydro-γ-lumicolchicine was readily hydrolysed by dilute acid to demethyldihydro-γ-lumicolchicine, $C_{21}H_{25}O_6N$, which contains only three methoxyl groups and shows the properties of an acyloin. When treated with sodium borohydride demethyldihydro-γ-lumicolchicine was reduced to a glycol, which was then cleaved by sodium metaperiodate at pH 7. The resulting carbonyl compound was isolated as its 2:4-dinitrophenylhydrazone whose analysis showed the presence of two carbonyl groups. This derivative was orange and showed an ultraviolet maximum at 356 mμ, both characteristic of a saturated carbonyl compound. As expected, its ultraviolet spectrum closely resembles that of the corresponding β-derivative but their melting-point behaviour establishes their non-identity Further, when treated with an excess of monoperphthalic acid in chloroform, demethyldihydro-γ-lumicolchicine acetate took up only one atom of oxygen, corresponding to one double bond. These results indicate that γ-lumicolchicine is a tetracyclic compound and that, by the same arguments as those cited for the β-isomer, it may be represented by (V), but not (III) or (IV). The sequence of reactions may again be interpreted by partial formulæ (VI)—(X).

Thus, with the assumption that no photochemical change has occurred in colchicine other than the bridging of the tropolone ring, β- and γ-lumicolchicine may be assigned a stereochemical relation which involves the two forms of (V) which can be obtained by *cis*-fusion of the four- and five-membered rings (*trans*-fusion would result in excessive strain in the *cyclo*butene ring); so that if ring A, ring B, and the four-membered ring are considered as a planar system, from the point of view of stereoisomerism, the acetamido-group and the fused five-membered ring would be either *cis* or *trans* to one another. If, in addition, the optically active centre in colchicine has been involved in the transformation, then the enantiomorphic forms of the *cis*- and the *trans*-isomer already mentioned become possible structures; so that β- and γ-lumicolchicine may be either geometrical isomers or a pair of enantiomorphs.

For the rest of the molecule only certain features are clear. Ring A and its junction with ring C in the colchicine molecule have remained intact, as is shown by the isolation of 3:4:5-trimethoxyphthalic anhydride on permanganate oxidation of β-lumicolchicine. The acetamido-group as in colchicine is clearly indicated by the infrared spectrum of both β- and γ-lumicolchicine, and an almost quantitative *C*-methyl determination.

The size of ring B cannot be inferred from any of the above reactions, but the close similarity of the ultraviolet spectra of the dihydro-compounds, which concerns only ring A and the attendant conjugation in ring B—both show maxima at 230 and 280 mμ—suggests that it is the same in both isomers. Work is in progress to elucidate this point, to obtain direct evidence for the size of the other rings and to determine the configuration of the point of attachment of the acetamido-side-chain.

EXPERIMENTAL

Irradiation of Colchicine and Separation of the Products.—The irradiations were carried out according to the directions of Grewe and Wulf (*loc. cit.*) with some modifications: the separation of the products followed a different procedure.

Colchicine (5 g.) was dissolved in hot distilled water (2 l. at 80°) through which a stream of nitrogen was being passed. The solution was poured, whilst still hot, into cylindrical tubes (90 × 5 cm.) which were sealed immediately under nitrogen. After 10 days' exposure on the roof of the laboratory, the solution began to deposit crystals. These had a characteristic needle shape and grew steadily for about 3—4 weeks; then the edges began to lose their form. About this time the solution deposited a light amorphous precipitate which grew until it filled the whole of the liquid. After 8—10 weeks, depending upon the amount of sunshine, the tubes were opened and the contents worked up as follows.

The solutions were filtered (filtrate A), and the solid was washed with water and dried at room temperature. The dried material (14 g. from 20 g. of colchicine) was finely powdered and suspended in boiling methanol (150 c.c.) for 15 min.; the hot solution was filtered. After being washed with methanol, the residue (1·0 g.) consisted of almost pure α-lumicolchicine. A further crop (0·05 g.) was obtained from the mother-liquors on cooling. One recrystallisation from ethanol afforded colourless needles, m. p. 165°, $[\alpha]_D$ +80° (*c* 0·53 in $CHCl_3$) (Found: C, 63·2; H, 6·5; N, 3·5; OMe, 29·3. Calc. for $C_{22}H_{25}O_6N,H_2O$: C, 63·3; H, 6·5; N, 3·4; 4OMe, 29·7%). Grewe and Wulf (*loc. cit.*) give m. p. 165°, $[\alpha]_D$ +81°.

After removal of α-lumicolchicine, the solution was concentrated to 75 c.c. and left overnight. The wool-like precipitate which had formed was then filtered off and washed with ethanol. It consisted of long slender needles of pure γ-lumicolchicine (1·1 g.), m. p. 272° (decomp.), $[\alpha]_D$ −434° (*c* 0·66 in $CHCl_3$) [Found: C, 66·0; H, 6·2; N, 3·7; OMe, 31·1%; *M* (Rast, in camphorquinone), 416. Calc. for $C_{22}H_{25}O_6N$: C, 66·2; H, 6·3; N, 3·5; OMe, 31·1%; *M*, 399]. Grewe and Wulf (*loc. cit.*) give m. p. 268°, $[\alpha]_D$ −445°.

Further concentration of the mother-liquors yielded successive fractions of β-lumicolchicine of different m. p.s owing to a mixture of two crystalline forms. The first fractions consisted of the high-melting form, m. p. 204—205°; these were followed by intermediate fractions, m. p. 198—202°, which invariably softened at about 180°; finally there was a fraction of the lower-melting form, m. p. 179—180°. All fractions showed much the same optical rotation, indicating that they consisted of almost pure β-lumicolchicine. The combined yield was 10·7 g. Recrystallisation from aqueous ethanol afforded the higher-melting form in long needles, m. p. 206°: the lower-melting form was obtained from ethyl acetate–ethanol in rosettes of needles, m. p. 181°. Both gave $[\alpha]_D$ +308° (*c* 0·53 in $CHCl_3$) [Found: C, 66·1; H, 6·5; OMe, 31·1%; *M* (Rast), 410]. Grewe and Wulf (*loc. cit.*) give m. p. 183° and 207°, $[\alpha]_D$ +309°.

Extraction of filtrate A with ethyl acetate afforded a further quantity (4·0 g.) of β-lumicolchicine, m. p. 179—180°. A final extraction with chloroform yielded, first, γ-lumicolchicine (0·2 g.; m. p. 265—267°) followed by β-lumicolchicine (1·1 g.; m. p. 204—205°).

Total yields were: α-, 1·05 g., β-, 15·8 g., and γ-lumicolchicine, 1·3 g. Grewe and Wulf (*loc. cit.*) record yields in the ratios 4 : 3 : 2.

β-Lumicolchicine oxime was prepared in aqueous alcohol by hydroxylamine hydrochloride and sodium acetate. It crystallised from aqueous ethanol in fine matted needles, m. p. 263° (decomp.) (Found: C, 63·5; H, 6·3; N, 7·2. Calc. for $C_{22}H_{26}O_6N_2$: C, 63·7; H, 6·3; N, 6·8%). Šantavý (*loc. cit.*) records m. p. 274—276° (corr.).

The *dioxime* of demethyl-β-lumicolchicine was obtained when a solution of β-lumicolchicine (200 mg.) and hydroxylamine hydrochloride (100 mg.) in ethanol (1 c.c.) and pyridine (2 c.c.) was heated under reflux for 2 hr. After removal of solvents the residue was triturated with methanol, affording the solid *dioxime*, which crystallised from methanol in colourless plates, m. p. 184—186° (Found: C, 58·4; H, 6·4; N, 9·7. $C_{21}H_{25}O_6N_3,H_2O$ requires C, 58·2; H, 6·2; N, 9·7%). The mother-liquors afforded an *isomer* which crystallised from ethanol in small colourless needles, m. p. 233—234° (Found: C, 58·5; H 5·7%).

γ-Lumicolchicine oxime, prepared in aqueous ethanol, crystallised from aqueous ethanol in silky needles, m. p. 284—286° (decomp.) (Found: C, 63·8; H, 6·3; N, 6·9%). Šantavý (*loc. cit.*) records m. p. 309—311° (corr.).

2 : 4-*Dinitrophenylosazone of Demethyl*-β-*lumicolchicine*.—A warm solution of 2 : 4-dinitrophenylhydrazine (30 mg.) in methanol (3 c.c.) containing a drop of concentrated hydrochloric acid was added to a solution of β-lumicolchicine (30 mg.) in methanol (2 c.c.). After 15 min. the deep red crystalline precipitate was collected, washed with methanol, and recrystallised from nitromethane. The *osazone* was deposited overnight in deep-red feathery needles, m. p. 212° (Found: C, 52·8; H, 4·2; N, 16·8. $C_{33}H_{39}O_{12}N_9$ requires C, 53·2; H, 4·0; N, 17·0%). Light absorption: $\lambda_{max.}$ at 221, 270, 355, and 452 mμ.

Oxidation of β-*Lumicolchicine*.—A suspension of β-lumicolchicine (0·5 g.) in 5% aqueous potassium hydroxide (5 c.c.) and acetone (5 c.c.) was treated with a 4% solution of potassium permanganate (25 c.c.). When the colour had almost disappeared the mixture was heated on a steam-bath for 2 hr. During this time a concentrated solution of potassium permanganate (7 g.) in water (35 c.c.) was added gradually. The resulting solution, which was still pink, was acidified, whilst hot, with dilute sulphuric acid. When the effervescence had subsided, the mixture was rendered alkaline and filtered from manganese dioxide. The straw-coloured filtrate was acidified and extracted with ethyl acetate (3 × 25 c.c.). The combined extracts were dried, the solvent was removed, and the residue sublimed at 160°/0·2 mm., giving a pale yellow solid, which was taken up in ether and treated with charcoal. After removal of the ether, the residue was sublimed at 120°/0·2 mm., giving a colourless solid (50 mg.) which, on crystallisation from ether or carbon tetrachloride, afforded 3 : 4 : 5-trimethoxyphthalic anhydride as needles, m. p. and mixed m. p. 144° (Found: C, 55·8; H, 4·7. Calc. for $C_{11}H_{10}O_6$: C, 55·5; H, 4·2%).

Dihydro-β-*lumicolchicine* (VII).—A solution of β-lumicolchicine (500 mg.) and sodium borohydride (50 mg.) in methanol (15 c.c.) was set aside overnight. Dilute acid was then added until the solution was neutral to B.D.H. universal-indicator paper, and the bulk of the solvent was removed *in vacuo*. Addition of water to the residue produced a crystalline prepipitate of *dihydro*-β-*lumicolchicine* (460 mg.), which crystallised from aqueous ethanol in colourless prisms, m. p. 195° (Found: C, 65·6; H, 6·4; N, 3·7. $C_{22}H_{27}O_6N$ requires C, 65·8; H, 6·7; N, 3·5%).

The *acetate*, prepared in acetic anhydride and a large excess of pyridine, crystallised from aqueous ethanol in needles, m. p. 221° (Found: C, 64·7; H, 6·3; OMe, 27·8. $C_{24}H_{29}O_7N$ requires C, 65·0; H, 6·6; 4OMe, 28·0%).

Dihydro-γ-*lumicolchicine* (VII).—A solution of sodium borohydride (25 mg.) in water (1 c.c.) was added to a suspension of γ-lumicolchicine (100 mg.) in methanol (4 c.c.). After 1 hr. the solid had dissolved, and the solution was left overnight. After the solution had been brought to pH 7, the bulk of the solvent was removed *in vacuo*; a viscous oil separated. After addition of water, the aqueous layer was decanted, and the residual gum boiled with water. After a minute it had completely solidified and was removed (76 mg.). On crystallisation from aqueous ethanol it afforded *dihydro*-γ-*lumicolchicine* in rosettes of colourless needles, m. p. 204° (Found: C, 65·6; H, 6·8; N, 3·7%).

Demethyldihydro-β-*lumicolchicine* (VIII).—N-Hydrochloric acid (5 c.c.), previously heated to 100°, was added in one portion to a solution of dihydro-β-lumicolchicine (200 mg.) in hot ethanol (0·75 c.c.), giving a clear solution which began to deposit crystals after a few seconds. After 30 min. the crystals (177 mg.) were separated and crystallised from aqueous ethanol, whence *demethyldihydro*-β-*lumicolchicine* was obtained in colourless blades, m. p. 208° (Found: C, 65·2; H, 6·6; N, 3·7; OMe, 23·8. $C_{21}H_{25}O_6N$ requires C, 65·1; H, 6·5; N, 3·6; 3OMe, 24·0%).

The *acetate*, prepared in pyridine, crystallised from benzene–light petroleum in plates, m. p. 192° (Found: C, 64·4; H, 6·3. $C_{23}H_{27}O_7N$ requires C, 64·3; H, 6·3%). The *oxime*, prepared in aqueous alcohol, crystallised from the same solvent in short colourless needles, m. p. 238° (Found: C, 62·7; H, 6·4; N, 7·3. $C_{21}H_{26}O_6N_2$ requires C, 62·9; H, 6·5; N, 7·0%). The dinitrophenylosazone (prepared as for β-lumicolchicine) crystallised from nitromethane in deep-red feathery needles, m. p. 212° alone and when mixed with the osazone from β-lumicolchicine. Light absorption in EtOH: $\lambda_{max.}$ at 221, 270, 355, and 452 mμ. The *dioxime*, prepared in pyridine, was obtained from ethanol in colourless needles, m. p. 175—176° (Found: N, 9·6. $C_{21}H_{25}O_6N_3,H_2O$ requires N, 9·7%).

Demethyldihydro-γ-*lumicolchicine* (VIII).—Dihydro-γ-lumicolchicine (200 mg.) in ethanol (1 c.c.) was treated with N-hydrochloric acid (4 c.c.) previously heated to 100°. The clear solution so produced slowly deposited *demethyldihydro-γ-lumicolchicine* on cooling. It crystallised from aqueous ethanol in massive prisms, m. p. 238° (Found: C, 65·1; H, 6·4; OMe, 24·1%).

The *acetate*, prepared in acetic anhydride–pyridine, crystallised from ethyl acetate–light petroleum (b. p. 80—100°) in flat needles, m. p. 237° (Found: C, 64·3; H, 6·3%). The *oxime*, prepared in aqueous ethanol, crystallised from benzene–ethanol in small needles, m. p. 193° (Found: N, 6·8%).

Treatment of Demethyldihydro-β- and -γ-lumicolchicine Acetates with Monoperphthalic Acid.—Demethyldihydro-β-lumicolchicine acetate (157 mg.) in chloroform (10 c.c.) was treated with monoperphthalic acid in chloroform (4 c.c. containing 0·1364 g.). The volume was made up to 25 c.c., and the solution set aside at 0°. After 24 hr. the consumption of peracid, determined by iodine–thiosulphate titration, was 77 mg., corresponding to 1·15 mols. The chloroform solution afforded only a gum.

Similarly demethyldihydro-γ-lumicolchicine acetate (68 mg.) in chloroform (3 c.c.) was treated with monoperphthalic acid in chloroform (1·5 c.c. containing 51·1 mg.), the volume then being made up to 10 c.c. After 24 hr. the consumption of peracid was 32 mg. (1·1 mols.). Working up the solution did not give a crystalline epoxide.

Reduction of Demethyldihydro-β-lumicolchicine with Sodium Borohydride.—A solution of sodium borohydride (20 mg.) in water (1 c.c.) was added to a suspension of demethyldihydro-β-lumicolchicine (100 mg.) in methanol (2 c.c.). After 15 min. dissolution was complete, and the mixture was left overnight. After addition of acid to pH 7, the solution was evaporated under reduced pressure to a small bulk. Addition of a saturated solution of sodium sulphate in water (5 c.c.) then precipitated the glycol (IX) as a gum, which was extracted with chloroform (3 × 10 c.c.). The combined chloroform extracts were dried and evaporated, and the residual gum was taken up in benzene (5 c.c.). After removal of the benzene the glycol which remained as a colourless glass was not separated into its stereoisomers.

Periodate Oxidation of the Glycol from Demethyldihydro-β-lumicolchicine.—A solution of the glycol, prepared as above, in methanol (2 c.c.) was treated with one of sodium metaperiodate (55 mg., 1 mol.) in water (2 c.c.). After 48 hr., the solution was diluted with water (10 c.c.) and extracted with chloroform (3 × 10 c.c.). The combined chloroform extracts were dried and evaporated, and the residual gum was taken up in ethanol (1 c.c.)—this solution gave a positive Angeli–Rimini test for an aldehyde group. On addition of 2 : 4-dinitrophenylhydrazine (150 mg.) in methanol (5 c.c.) containing a drop of concentrated hydrochloric acid, a red crystalline precipitate was slowly formed. After 2 hr., the solid was collected, washed with methanol, and recrystallised from glacial acetic acid. The *bis-2 : 4-dinitrophenylhydrazone* of the dialdehyde (X) was thereby obtained in clusters of orange needles, m. p. 150° after drying for 4 hr. at 110°/1 mm. (Found: C, 52·9; H, 4·2; N, 16·7. $C_{33}H_{31}O_{12}N_9$ requires C, 53·1; H, 4·2; N, 16·8%). Light absorption in EtOH: $\lambda_{max.}$ 353 mμ.

Reduction of Demethyldihydro-γ-lumicolchicine with Sodium Borohydride.—A suspension of demethyldihydro-γ-lumicolchicine (100 mg.) in methanol (3 c.c.) was treated with a solution of sodium borohydride (30 mg.) in water (1 c.c.). After standing overnight, the resulting solution was worked up, as described above for the β-isomer, to give the glycol as a colourless glass.

Periodate Oxidation of the Glycol from Demethyldihydro-γ-lumicolchicine.—A solution of the glycol in methanol (1 c.c.) was treated with a solution of sodium metaperiodate (55 mg.) in water (2 c.c.). After 36 hr., the dialdehyde (X) was isolated as its *bis-2 : 4-dinitrophenylhydrazone*, m. p. 144° depressed on admixture with the analogous compound of the β-series (Found: C, 52·9; H, 4·3; N, 16·6%). Light absorption in EtOH: $\lambda_{max.}$ 356 mμ.

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