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CORYMBOL, A NEW DITERPENIC ALCOHOL*

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Abstract—The isolation of a new diterpenic alcohol is described and its structure and stereochemistry established as VII.

THE structure of turbincorytin, isolated as its glucoside from *Turbina corymbosa*, was recently established as a $C_{23}H_{40}O_6$ compound with a basic nucleus of an isoprenoid type.[1]

From the same plant a diterpenic alcohol has been isolated and named corymbol. This compound has a biogenetic interest as it may be the precursor of turbicorytin.

Corymbol (I), $C_{20}H_{34}O_3$, m.p. 282–283°, was obtained in low yield by fractional crystallization of the crude ethanolic extract of the seeds. The IR spectrum shows only hydroxyl functional groups and on acetylation it affords a di- and a tri-acetate. Corymbol gives a positive periodic acid test, indicating the presence of at least two vicinal hydroxyl groups in the molecule.

The two acetates were obtained on treatment of corymbol with acetic anhydride and pyridine and the mixture was separated by chromatography on alumina.

The diacetate (II), $C_{24}H_{38}O_5$, m.p. 141–142°, shows in the NMR spectrum two signals at 2·02 (3H) and 2·1 ppm (3H), characteristic of the acetoxy methyl groups; a multiplet centered at 5·1 ppm (1H), ascribed to the hydrogen at C-6, and a singlet at 4·23 ppm (2H) which corresponds to the hydrogens at C-20. The IR spectrum has a band at 3650 cm^{-1} corresponding to a tertiary alcohol, a carbonyl band at 1730 cm^{-1}, two bands at 1380 and 1368 cm^{-1} indicating a *gem*-dimethyl group and a band at 1240 cm^{-1} assigned to the C—O stretching frequency of the acetate function.

The triacetate (III), $C_{26}H_{40}O_6$, m.p. 180–182°, shows in the NMR spectrum the signals of the acetoxy methyl groups at 1·99 (3H), 2·02 (3H) and 2·07 ppm (3H), the same multiplet at 5·1 ppm (1H) as in the case of the diacetate, but instead of the singlet 4·23 ppm, there appeared two doublets (2H, AB system), centered at 4·95 and 4·40 ppm (J = 12·5 c/s). This splitting of the signal of the protons at C-20 may be due to the interaction between the acetate groups at C-16 and C-20 which hinders free rotation of the primary carbon atom, thus making the two hydrogens non-equivalent.† The IR spectrum shows a carbonyl band at 1720 cm^{-1} and an acetate band at 1240 cm^{-1}.

Corymbol, on treatment with periodic acid, used up one mole of the reagent, affording two degradation products, formaldehyde (one mole) and a hydroxyketone

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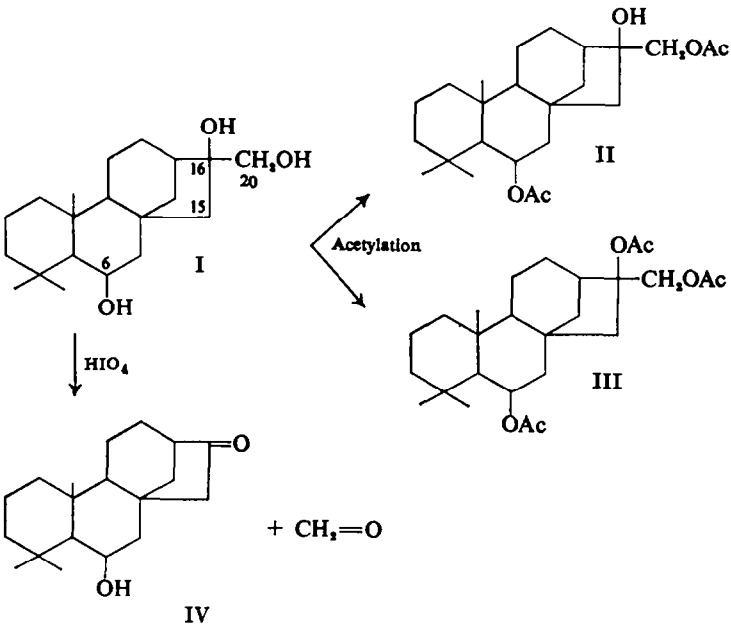
† This hindered rotation appeared to favor the preponderant formation of one conformer for the NMR spectra of acetate III, taken at different temp (60 to −30° with 10° interval), showed only minor differences in the chemical shift of protons A and B without any change of the coupling constant.

[1] M. C. Perezamador, F. García Jiménez, J. Herrán and S. E. Flores, *Tetrahedron* **20**, 2999 (1964).

(IV). Therefore, two of the hydroxyl groups must be vicinal, one being a tertiary and the other primary.

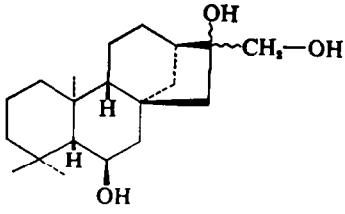
The hydroxyketone (IV) is identical in all respects with the one obtained in the turbicoryn series.[1] The oxime and the diketone derivatives of both compounds are also identical. This correlation enabled the complete structure of corymbol to be established.



SCHEME 1

The chemical evidence as well as the spectroscopic data are in accord with formulas I, II and III for corymbol and its di- and tri-acetate, respectively (scheme I).

Since the stereochemistry of the hydroxyketone (IV) in the turbicoryn series is known,[2] the partial stereochemistry for corymbol is as follows:



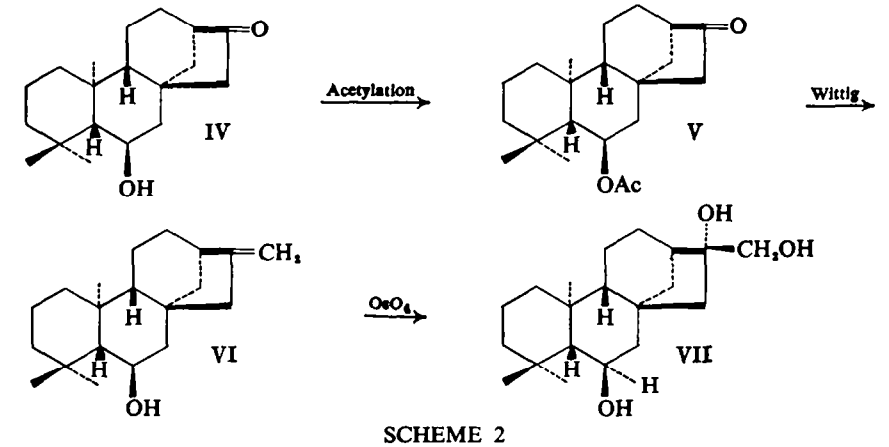
In order to determine the configuration at C-16, a stereospecific synthesis of corymbol was carried out (scheme 2), similar to that of the glycol side chain of cafestol.[3]

[1] F. García Jiménez, M. C. Perezamador, S. E. Flores and J. Herrán, *Tetrahedron Letters* No. 11, 621 (1965).

Due to an error in the typing of this communication, the signs of C. D. are changed and should be positive.

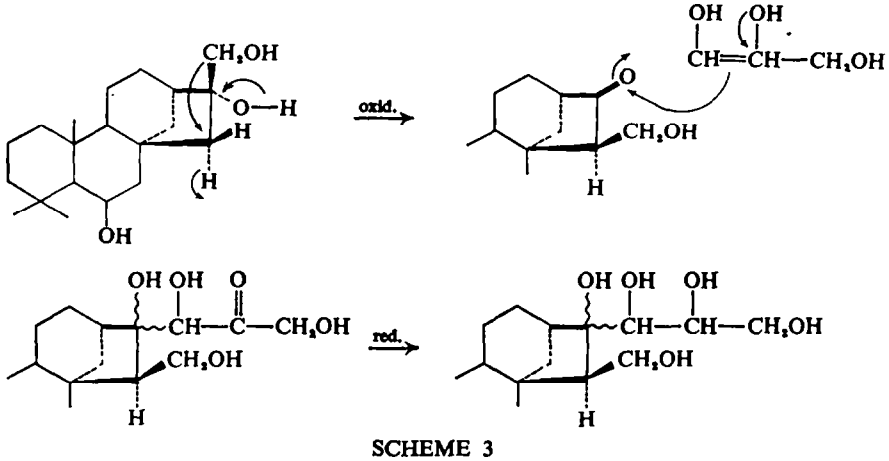
[2] R. A. Finnegan, *J. Org. Chem.* **26**, 3057 (1961).

On treatment with Wittig's reagent,[4] the acetate (V) was converted to the hydroxyolefin (VI), the structure of which is evident from its method of formation and its IR and NMR spectra. In the vinyl proton region, VI shows a doublet (2H), centered at 4·8 ppm (J = 1 c/s, typical of *gem*-vinyl protons), ascribed to the hydrogens at C-20. In the IR spectrum the bands at 1660 and 875 cm^{-1} infer the presence of the exocyclic methylene group.



SCHEME 2

When the hydroxyolefin (VI) was treated with OsO_4, only one of the two possible stereoisomeric glycols was obtained (VII), the relative configuration of which was established by the preferred steric course of the reaction. With a molecular model of VI it is possible to predict that OsO_4 will attack the exocyclic methylene from the back side of the molecule (α), since the β-face is sterically more hindered by the C-11 axial hydrogen.



SCHEME 3

The synthetic product was identical to corymbol in all respects and the acetates were also identical with the acetates from natural corymbol. Therefore, the absolute configuration of this compound is that shown in formula VII.

[4] G. Wittig and U. Schollkopf, *Chem. Ber.* **87**, 1318 (1954).

Taking into consideration the structure and stereochemistry of corymbol, it is possible that this product is the biogenetic precursor of turbicorytin. The transformation of corymbol to turbicorytin may be visualized as an oxidation-reduction process. The migration of the hydroxymethylene group from C-16 to C-15, on the β-side of the molecule, would give the corresponding C-15 substituent in turbicorytin with a β-configuration, in accord with its partial stereochemistry.[2] The next step would be attack by glyceraldehyde or an equivalent with a subsequent reduction of the keto group to form the C-16 side chain in turbicorytin (scheme 3).*

Hence, turbicorytin and corymbol belong to the kaurene series and their configurations are in accord with the biogenetic rule in its extension to the diterpenes.[5]

EXPERIMENTAL†

Isolation of corymbol (I)

The ethanolic extract (50 g) from the seeds of *Turbina corymbosa* in 100 ml MeOH was diluted with 500 ml water and concentrated to 100 ml. The solution was allowed to stand 72 hr at 0° and the precipitate formed filtered off and washed first with water and then with acetone. The acetone washings yielded on evaporation 1 g of a crystalline product which was a mixture (chromatoplate run with butanol–acetic acid–water 5:1:4) and purified by fractional crystallization from acetone–water, yielding 250 mg of corymbol, m.p. 282–283°, $[\alpha]_D^{20}$ −3·8° (c = 1·03; pyridine); ν_{max} 3550, 3470, 3410, 1063, 1034 and 1017 cm^{-1} (KBr pellet). (Found: C, 74·41; H, 10·26; O, 15·37. $C_{20}H_{34}O_3$ requires: C, 74·49; H, 10·63; O, 14·89%.)

Acetylation of corymbol

Corymbol (100 mg) was acetylated with Ac_2O (1 ml) and pyridine (1 ml) by heating the mixture for 10 hr on the steam bath. Working in the usual manner, 131 mg of a product were obtained, which gave two spots on a chromatoplate run with AcOEt–hexane (60:40). This mixture was separated by chromatography on 50 g neutral alumina I, eluted with AcOEt–hexane (1:1).

Corymbol triacetate (III)

From the first fractions, 87 mg of the triacetate (III), m.p. 180–182°, $[\alpha]_D^{20}$ −3·3° (c = 2·62; $CHCl_3$) were obtained; ν_{max} 1720 and 1240 cm^{-1}; NMR signals at 0·90, 0·93 and 1·12; 1·99, 2·02 and 2·06; 4·40 d (12·5); 4·95 d (12·5) and 5·1 ppm m. (Found: C, 69·65; H, 9·10; O, 21·52. $C_{26}H_{40}O_6$ requires: C, 69·61; H, 8·99; O, 21·40%.)

Corymbol diacetate (II)

From the last fractions, 30 mg of the diacetate (II), m.p. 141–142°, $[\alpha]_D^{20}$ −2·4° (c = 1·9; $CHCl_3$) were obtained; ν_{max} 3650, 1730, 1380, 1368 and 1240 cm^{-1}; NMR signals at 0·92, 0·93 and 1·12; 2·02 and 2·1; 4·23 and 5·1 ppm m. (Found: C, 70·65; H, 9·17; O, 19·94. $C_{24}H_{38}O_6$ requires: C, 70·90; H, 9·42; O, 19·68%.)

Periodic acid degradation of corymbol

(a) *Moles of periodic acid consumed.* To 100·9 mg corymbol in 30 ml MeOH, 50 ml of a H_5IO_6 solution (approximately 0·03 M; 6·8385 g in 1000 ml) were added and the mixture allowed to stand for 12 hr at room temp. Simultaneously, a blank was run under the same conditions. At the end of

* We wish to thank Dr. James D. White for the valuable advice regarding this mechanism.

† M.ps were determined on a Kofler block and are uncorrected. IR spectra were run on a Perkin–Elmer model 21 spectrophotometer in $CHCl_3$, unless otherwise specified. NMR spectra were determined by Mr. Eduardo Díaz on a Varian A-60 spectrometer in $CDCl_3$ containing TMS as internal standard. Mycroanalyses were determined by Dr. Franz Pascher, Bonn, Germany. Alumina Woelm was used for chromatography and Silica Gel G Merck for chromatoplates which were developed with ceric sulphate.

[5] A. I. Scott, F. MacCapra, F. Comer, S. A. Sutherland, D. W. Young, G. A. Sim and G. Ferguson, *Tetrahedron* **20**, 1339 (1964).

the reaction 5 g KI in 50 ml water and 10 ml H_2SO_4 (1:10) were added and the solutions titrated with 0·1N $Na_2S_2O_3$. In the titration 6·2 ml were required corresponding to 0·98 moles of periodic acid.

(b) *Moles of formaldehyde produced.* A solution of 100 mg corymbol in 30 ml MeOH was oxidized with 80 mg periodic acid in 15 ml water. The reaction was allowed to stand for 12 hr at room temp. Subsequent steam distillation removed the formaldehyde produced. To the distillate (250 ml), 50 ml of 1% dimedone ethanol–water (1:1) solution was added and it was allowed to stand 12 hr. On concentration, 72·7 mg of formaldimedone (corresponding to 0·80 moles formaldehyde). m.p. 189–190° were obtained. This compound did not give a depression in mixed m.p. with an authentic sample of formaldimedone.

Hydroxyketone (IV)

Corymbol (200 mg) was oxidized as above. The reaction mixture was neutralized with $NaHCO_3$ and extracted with AcOEt. On evaporation, 179 mg of the hydroxyketone (IV) were obtained. After sublimation at 155°/0·05 mm the product showed a m.p. of 165–166°. The IR and NMR spectra were identical with those of the hydroxyketone obtained in the turbicoryn series[1] and the m.p. of the mixture of both compounds showed no depression.

Oxime of the hydroxyketone

A solution of 90 mg of hydroxyketone (IV) in 10 ml EtOH with 90 mg hydroxylamine hydrochloride and 90 mg AcONa, was refluxed for 2 hr. The solvent was evaporated to dryness, water was added and the product filtered. After crystallization from MeOH, 86 mg of the oxime, m.p. 285–287° were obtained. This product gave no depression in m.p. with the oxime of the hydroxyketone in the turbicoryn series.[1]

Diketone

To a solution of 110 mg of IV in acetone were added dropwise and with stirring, 0·15 ml of Jones reagent[6] (250 g CrO_3 in 1000 ml). The mixture was neutralized with $NaHCO_3$, filtered and washed with acetone. On evaporation, 100 mg of the diketone were obtained. After sublimation at 150°/0·05 mm the product showed a m.p. of 139–140° and gave no depression in mixed m.p. with the corresponding diketone obtained in the turbicoryn series. The IR and NMR spectra of both compounds were identical in all respects.

Hydroxyketone IV *acetate* (V).

The hydroxyketone (IV; 2 g) was acetylated with Ac_2O (10 ml) and pyridine (10 ml) for 3 hr on the steam bath and allowed to stand for 21 hr at room temp. The reaction product was poured onto ice and the crystalline precipitate filtered and washed. After drying 2·162 g of the acetate (V) m.p. 119–120° were obtained.

Hydroxyolefin (VI)

The acetate (V; 500 mg) in anhydrous ether was added to Wittig's reagent[3,4] (0·01 mole triphenylmethylphosphonium iodide and 0·01 mole butyl-lithium in anhydrous ether and N_2 atmosphere) and the mixture stirred for 2 hr at room temp. The excess reagent was destroyed with 1 ml acetone and sufficient MeOH was added to dissolve the complex. The solution was diluted with water and extracted with AcOEt. The solvent was evaporated to dryness, the residue dissolved in benzene–hexane (1:10), filtered through celite to eliminate the triphenylphosphonium oxide and again evaporated. The crude product (1 g) was chromatographed on neutral alumina I (200 g), eluting with AcOEt–hexane (30:70). The first crystalline fraction (110 mg) corresponded to VI, m.p. 153–154°; ν_{max} 3640, 3502, 1717, 1660 and 875 cm^{-1}; NMR signals at 0·85, 0·91 and 1·05; 1·82, 2·07, 2·67 m, 3·95 m, and 4·80 d (1). The hydroxyketone (IV; 240 mg) was obtained from the last fractions of the chromatography.

Osmium tetroxide oxidation of hydroxyolefin VI (VII).

To VI (110 mg in 25 ml of anhydrous ether) were added 0·5 g OsO_4 in 10 ml anhydrous ether and 5 ml pyridine. The reaction was stirred for 5 hr and the excess OsO_4 destroyed with a solution of

[6] A. Bowers, T. G. Hasall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.* 2555 (1953).

2 g $NaHSO_3$ in 10 ml water and 15 ml pyridine. The product was poured into 200 g ice-water and the ether was allowed to evaporate at room temp. The crystalline precipitate was filtered, washed with water and dissolved in MeOH. Evaporation of the solvent afforded 105 mg of the product, m.p. 277–280°. Repeated recrystallizations from MeOH yielded 90 mg VII, m.p. 282–283°. No depression was observed in mixed m.p. with natural corymbol. Additional 10 mg of the product were obtained from the mother liquors.

Synthetic corymbol acetates

The synthetic corymbol (90 mg) was acetylated with Ac_2O (1 ml) and pyridine (5 ml) on the steam bath for 5 min and the reaction mixture allowed to stand overnight at room temp. The product was separated by the usual procedure, affording 105 mg acetates. The crude product was chromatographed on 75 g of neutral alumina I, eluting with AcOEt–hexane (1:1). From the first fractions, 9 mg of III, m.p. 180–182° were obtained, and from the last fractions, 90 mg of II, m.p. 140–141°, which showed no depression in mixed m.p. with the diacetate (II) from natural corymbol. The IR and NMR spectra of both diacetates were identical in all respects.