Phytochemistry, 1971, Vol 10, pp. 1367 to 1372 Pergamon Press. Printed in England

CYCLOMAHOGENOL, A NEW TETRACYCLIC TRITERPENE FROM *SWIETENIA MAHAGONI**

D. P. CHAKRABORTY and S. P. BASAK
Dept of Chemistry, Bose Institute, Calcutta 9, India

and

B. C. DAS and R. BEUGELMANS
Institute de chimie des substances Naturelles, C N R S , Gif-Sur-Yvette (Essone), France

(*Received* 12 *June* 1970, *in revised form* 22 *September* 1970)

Abstract—Cyclomahogenol, a new tetracyclic triterpene in the leaves of *Swietenia mahagoni* (Meliaceae) is shown to have structure (I)

INTRODUCTION

THE TETRANORTRITERPENOIDS of the Meliaceae have been considered to reflect its taxonomic closeness to the Rutaceae and Simaroubaceae.[1-3] The bicyclononanolides of the swietenine group[4-6] are added novelty to these group of compounds. The ring B cleaved nor-triterpenoids has been assumed to be the progenator of these bicyclononanolide system. On biogenetic and taxonomic considerations we were interested to examine the seeds of *Swietenia mahagoni* Jacq. from which two ring B cleaved tetranortriterpenoids, mahoganin[7] and 6-hydroxy methyl angolensate[8] as well as their biogenetic precursor 7-deacetyl-7-oxogedunin[9] have been reported. The occurrence of 7-deacetyl-7-oxogedunin in the seeds and cycloeucalenol[10] in the hard wood of the plant prompted us to look for triterpenes biogenetically related to the hypothetical precursor[11] of the furanolactones of the genus *Swietenia*

* Part XXIV in the series 'Chemical Taxonomy', Partly presented at the 5th Indian Chemical Society Convention at Roorkee, India 1967 and at the Indian Science Congress Session at Bombay, 1969 Partly from the D Phil thesis of S. P. Basak, Calcutta University (1968).
Part XXIII· D P CHAKRABORTY, K C DAS, A ISLAM, *J Ind. Chem. Soc* in press

[1] D P CHAKRABORTY, *Bull Bot. Soc Bengal* **18**, 103 (1964)
[2] D. L DREYER, *Experientia* **20**, 297 (1964)
[3] J B-SON BREDENBERG, *Chem & Ind* 73 (1964)
[4] J D CONNOLLY, R HENDERSON, R MCCRINDLE, K. H OVERTON and N S BHACCA, *J. Chem Soc* 6935 (1965)
[5] J D. CONNOLLY, R MCCRINDLE, K H OVERTON and W D C WARNOCK, *Tetrahedron Letters* 2937 (1965)
[6] J D CONNOLLY, R MCCRINDLE and K. H OVERTON, *Chem Commun* **8**, 162 (1965)
[7] D P CHAKRABORTY, K C DAS and C F HAMMER, *Tetrahedron Letters* 5015 (1968) D A. H. TAYLOR has claimed mahoganin to be a mixture of 6-hydroxymethylangolensate and methylangolensate *Chem. Commun* 58 (1969)
[8] K. C DAS, S P BASAK and D P CHAKRABORTY, *J Ind Chem Soc* **46**, 273 (1969)
[9] B K. CHOWDHURY and D P CHAKRABORTY, *J Ind Chem Soc.* **46**, 273 (1969)
[10] L AMOROS-MARIN, W I. TORRES and C F. ASEUJO, *J Org Chem.* **24**, 411 (1959)
[11] D ARIGONI, D H R BARTON, E J COREY, O JEGER, L CAGLIOTI, S. DEV, P G FERINI, E R GLAZIER, A MELERA, S K PRADHAN, K SCHAFFNER, S STERNHELL, J. F. TEMPLETON and S. TOBINAGA, *Experientia* **16**, 41 (1960)

in the leaves of the plant. The present communication relates to the structure of a new tetracyclic triterpene named cyclomahogenol (I) isolated from the leaves of the plant.

RESULTS

The neutral fraction of the petroleum extract of the mature leaves of *Swietenia mahagoni* collected from West Bengal* on chromatography over alumina furnished a colourless homogeneous compound which on crystallization from mixture of petroleum–benzene furnished cyclomahogenol, $C_{31}H_{52}O_2$, $(\alpha)_D$ + 42° (M^+ 456). The compound is soluble in benzene, chloroform, ethyl acetate and methanol but almost insoluble in petroleum.

The i.r. spectrum of the compound showed bands at 3600 (hydroxyl) 3100 (methylene group of a cyclopropane bridge) and 880 cm^{-1} (terminal methylene group). Its NMR spectrum (60 mc in $CDCl_3$) showed the presence of a terminal methylene group (δ 4·75, a broad singlet for 2H); two hydroxyl groups (δ 1·37, 2H singlet disappears on deuteration); multiplets for hydrogen adjacent to hydroxyl groups (δ 3·28, $J = 7$ c/s and δ 4·4, $J = 7$ c/s); the characteristic doublets for cyclopropane group at (δ 0·60 and 0·32 c/s); singlets for 4 C-methyl groups (δ 1·1, 1·15, 0·88, 0·80, 3H singlet each), the singlet for 2 C-methyl groups (δ 1·1, 6H singlet) and doublet for one secondary C-methyl group (δ 0·99, $J = 5$ c/s; 3H). The C_{31} molecular formula, the nature of the methyl groups, and the physical data showed that cyclomahogenol is a tetracyclic triterpene with a terminal methylene group, and a cyclopropane bridge. The multiplets at δ 3·28 could be assigned to the α-hydrogen of the 3β-hydroxyl group.[12]

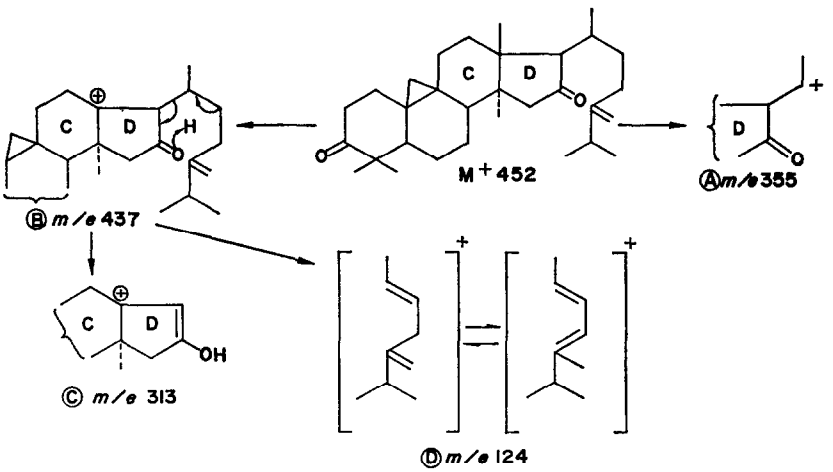
Cyclomahogenol yielded a diacetate (II), $C_{35}H_{56}O_4$, m.p. 125–127°, $(\alpha)_D$ + 102°, (M^+ 540), the i.r. spectrum of which has a strong peak at 1710 cm^{-1} for acetoxy group and the absence of hydroxyl group. In the NMR spectrum of (II), the six proton singlet (δ 2·02) for acetoxy groups replaces the hydroxyl signals in cyclomahogenol. The hydrogen adjacent to the hydroxyls in (I) at δ 3·28 and 4·4 moved to δ 4·45 and 5·53 in the diacetate. Cyclomahogenol diacetate on hydrogenation in acetic acid in presence of PtO_2 furnished a homogeneous dihydroderivative (III), $C_{35}H_{58}O_4$, m.p. 122–126°, $(\alpha)_D$ + 80·5°, M^+ 542. Deacetylation of dihydrocyclomahogenol diacetate furnished dihydrocyclomahogenol (IV), $C_{31}H_{54}O_2$, m.p. 172–173°, $(\alpha)_D$ + 23° (i.r. ν_{max} 3240, 2855, 1394 cm^{-1}).

The secondary nature of the hydroxyl groups of cyclomahogenol has been proved by its behaviour on Jones or Sarret oxidation when a diketo derivative (V), $C_{31}H_{48}O_2$, m.p. 133–134°, $(\alpha)_D$ − 114°, (M^+ 452) was obtained. The i.r. spectrum showed the presence of two ketonic groups one belonging to the five membered ring (1725 cm^{-1}) and other to the cyclohexanone system (1700 cm^{-1}). It turns out, therefore, that one of the hydroxyl groups in cyclomahogenol belongs to ring D while the other at 3 position (*vide infra*). Deuteration of the diketo derivative in alkali (deuteromethanol in sodium and drop of D_2O) produced a mass increase of 5. This proves the position of the five membered ring ketone at 16 instead at 15, since the location at 15 position would require a mass increase of 4. The position of the hydroxyl at 16 is also consistent with the mass spectral fragmentation of the diketo compound, as shown below. Diketocyclomahogenol on hydrogenation furnished the corresponding dihydroderivative (VI), $C_{31}H_{50}O_2$, m.p. 164–165°, M^+ 454, u.v. $\lambda_{max}^{ethanol}$ 278 nm (log ϵ 1·73).

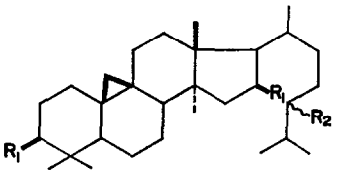
On ozonolysis diketocyclomahogenol furnished formaldehyde, identified as its 2 4-

* We thank Dr S. K. Mukherjee, Herbarium Curator, Indian Botanic Garden, Shibpur, Howrah, for kindly identifying the leaf specimen.

[12] D. SHIENGHONG, A. VARASARN, P. NANONGGAI-SUWANRATH and E. W. WARNHOFF, *Tetrahedron* **21**, 917 (1965).



DNPH derivative and a crystalline colourless product (VII), $C_{30}H_{46}O_4$, m.p. 147–148° (M^+ 470). The mass spectral data showed that, instead of being the expected triketone, this compound had an additional hydroxyl group. The structure of (VII) is being examined in light of the recent findings that ozonization of 24-methylenecycloartenol causes hydroxylation at the 7-position.[13]



	R_1	R_2
(I)	OH	$=CH_2$
(II)	OAc	$=CH_2$
(III)	OAc	$-CH_3$
(IV)	OH	$-CH_3$
(V)	$=O$	$=CH_2$
(VI)	$=O$	$-CH_3$
(VIII)	H	$=CH_2$
(X)	H	$-CH_3$

It follows, therefore, that cyclomahogenol is 24-methylenecycloartanol with an additional hydroxyl group at 16-position. To prove this, diketocyclomahogenol was converted to the known members of the cycloartenol series. Thus cyclomahogenone (V) on Wolff–Kishner reduction provided 24-methylenecycloartane (VIII) and 24-methylcycloartane* (IX). 24-methylcycloartane (IX) was also obtained by Wolff–Kishner reduction of dihydrodiketocyclomahogenol. This was identical to the hydrocarbon (X) obtained by Wolff–Kishner reduction of cyclolaudanone.† These results satisfy the 24-methylene-16-hydroxy cycloartanol formulation of cyclomahogenol. The assignment of the stereochemistry of the hydroxyl groups will lead to a complete structure of cyclomahogenol.

* A specimen of 24-methylenecycloartenol was supplied (to B.C.D) by Dr. Ponsimet Strasborough to whom our thanks are due.

† A specimen of cyclolaudanol was supplied by Prof. G. Berti, University De Pisa, Italy, to whom our thanks are due. Results consistent with lit, FURST *et al*, *Chem. Rev.* 51 (1965).

[13] W. LAWRIE, J. MCLEAN and O. O. OLUBAJO, *Tetrahedron Letters* 4143 (1969).

The C_3-hydroxyl group has been assumed to have a β-configuration on the basis of the NMR data. In consideration of the molecular rotation difference[14] of cyclomahogenol, dihydrocyclomahogenol and their corresponding diacetates, $(M)_D^+$ 359·28° and +330·97° respectively, both the hydroxyl groups have been considered to have β-configuration.[15] The reduction of cyclomahogenone (V) to cyclomahogenol (major product) with KBH_4 also supports this conclusion. The band width[16] of 3-H of cyclomahogenol diacetate (15 c/s/sec) is in agreement with the proposed stereochemical assignments.

In view of the occurrence of furanolactones in the genus *Swietenia*, cyclomahogenol is of some biogenetic interest. The ring 16-ketone of a tetracyclic triterpene of the apoeuphol or apotirucallol group has been considered to be a precursor of the ring D-lactone of the furanolactones. Gandifolione[17] may be cited as an intermediate in the biosynthetic sequence of the conversion of ring D to ring D-lactone. In plants elaborating furanolactones, tetracyclic triterpenes with 16-hydroxyl groups were unknown previous to our work.*,[18] The oxygenation at 16 position may be expression of an intermediate in an alternative biosynthetic pathway. With the recent demonstration of the conversion oxidosqualene to cycloartenol in cell free bean leaves,[19] biogenesis of cyclomahogenol could be readily rationalized as it may arise by C-methylation and hydroxylation cycloartenol at 24 and 16 position respectively. The results of ozonization of 24-methylenecycloartanol and cyclomahogenol may throw some light on the stepwise oxidation of a tetracyclic triterpene of apoeuphol type to ring B cleaved triterpenes.

EXPERIMENTAL

All m ps are uncorrected Petrol. refers to light petroleum b p 60–80°. All solvent extracts were dried over Na_2SO_4 Optical rotations were measured in $CHCl_3$ Samples were analysed after drying in vacuum at 80° over P_2O_5 for 24 hr The u v spectra were taken in 98% EtOH; i r spectra were recorded in KBr; NMR spectra were taken in CDl_3 with TMS as the internal indicator. Brockmann's alumina was used as the adsorbent for the column chromatography

Isolation of Cyclomahogenol (I)

Air dried finely powdered mature leaf of *Swietenia mahagoni* Jacq (1 kg) was extracted in a soxhlet (48 hr) with petrol The extract was freed from the solvent The residue was taken up in ether. The ethereal layer was fractionated in (i) basic (ii) acidic or phenolic and (iii) neutral fractions The neutral ethereal layer was dried and the solvent distilled off The residue was taken up in C_6H_6 and chromatographed over alumina (450 g; 35 × 5 6 cm) Elution were carried out successively with different solvent systems

Fraction 1 Petrol	4 × 300 ml	Oily mass
Fraction 2 Petrol –ether (1 1)	3 × 300 ml	Oily mass
Fraction 3 Petrol –ether (1 1)	3 × 300 ml	An amorphous compound m p 72–85°
Fraction 4 Petrol –C_6H_6 (1 1)	5 × 300 ml	Solid m p 137–138° identified as β-sitosterol
Fraction 5 Petrol –C_6H_6 (1 2)	6 × 300 ml	White residue m p 138–145°.

Residue m p 138–145° from fraction 5 on repeated crystallisation from C_6H_6 furnishes colourless crystals m p 151–152° (100 mg) TLC (silica gel G, solvent C_6H_6–$CHCl_3$, 3 1, R_f 0 357); $(\alpha)_D$ + 42° I r. bands

* When our work was complete, the structure of kulinone was published which has also a 16-β-hydroxyl group and thus similar biogenetic significance

[14] W KLYNE and W M STOKES, *J Chem Soc* 1979 (1954)
[15] A. BOWERS, T G HALSALL and G C SAYER, *J Chem Soc* 596 (1955).
[16] C W L BEVAN, D E U EKONG, T G HALSALL and P TOFT, *J Chem Soc* (C) 821 (1967)
[17] J D CONNOLLY, K L HANDA, R MCCRINDLE and K H OVERTON, *J Chem. Soc.* (C), 2227 (1968)
[18] C CHANG FREDERIC and CHIANG CHAO-KUO, *Chem Commun* 1156 (1968)
[19] H H REES, L J GOAD and T W GOODWIN, *Tetrahedron Letters* 723 (1968)

at 3600 (—OH group), 3100 (methylene group of a cyclopropane bridge) and 880 cm^{-1} (terminal methylene). (Found: C, 81·95; H, 11 41; $C_{31}H_{52}O_2$ requires: C, 81 52; H, 11·48%.)

Cyclomahogenol Diacetate (II)

To a solution of cyclomahogenol (100 mg) in pyridine (3 ml), AC_2O (3 ml) was added and the mixture was warmed at 100° for 4 hr. The solution cooled and poured into crushed ice (15 g) Solid obtained was filtered, dried and then chromatographed over alumina (5 g; 15 × 1 6 cm) Petrol eluent furnished a solid residue which was crystallized from MeOH in needles m p. 125–127° (72 mg). TLC (silica gel G, solvent: petrol –C_6H_6–$CHCl_3$, 10:30:1, R_f 0 5); $(\alpha)_D$ + 102° I r bands at 2890 (methylene group of the cyclopropane bridge), 1710 (acetoxy) and 892 cm^{-1} (terminal methylene). (Found· 3, 77·66; H, 10 72; $C_{35}H_{56}O_4$ requires· C, 77·73; H, 10 44%)

Dihydro Cyclomahogenol Diacetate (III)

Cyclomahogenol diacetate (40 mg) was hydrogenated in AcOH (2 5 ml) in presence of PtO_2 (30 mg) The crystalline (MeOH) dihydrodiacetate melted at 124–126° (32 mg) TLC (silica gel G, solvent· petrol.–C_6H_6–$CHCl_3$, 10 30 1, R_f 0 58), $(\alpha)_D$ + 80 5°.

Dihydrocyclomahogenol (Cyclomahoganol) (IV)

Dihydrocyclomahogenol diacetate (40 mg) was refluxed with 3% alcoholic KOH for 3 hr. The solution cooled, poured into crushed ice (10 g) and extracted with ether. The ether solution was washed, dried and the solvent distilled off. The residue was crystallized (petrol), m.p 172–175° (30 mg) TLC (silica gel G, solvent: petrol –C_6H_6, 3 1, R_f 0 73); $(\alpha)_D$ + 23°. I r. bands at 3240 (OH group) and 2855 cm^{-1} (methylene group of the cyclopropane bridge) (Found· C, 81 32; H, 11·40; $C_{31}H_{54}O_2$ requires C, 81·16; H, 11 86%.)

Diketocyclomahogenol (Cyclomahogenone) (V)

A solution of chromic acid (48 mg) in AcOH (10 ml) was added dropwise to the solution of cyclomahogenol (100 mg) in AcOH (20 ml) with constant stirring within 0 5 hr. It was then kept for 24 hr at room temp After discharging excess chromic acid by the addition of MeOH (0 2 ml), the solution was poured into crushed ice (20 g). A precipitate obtained was extracted with ether The ether solution was made acid free, washed, dried and the solvent distilled The solid residue was chromatographed over alumina (5 g; 10 × 1 4 cm), petrol –C_6H_6, 1 1, eluent furnished a solid which was crystallized from MeOH m p 133–134° (72 mg) TLC (silica gel 6, solvent, C_6H_6–$CHCl_3$, 3 1, R_f 0 58), $(\alpha)_D$ − 114° λ_{max} 280 nm (log ϵ 1 85), i r. bands at 2920 (methylene group of the cyclopropane bridge), 1725 (five membered ring ketone), 1700 (six membered ring ketone) and 888 cm^{-1} (terminal methylene) (Found C, 82 58; H, 10 31, $C_{31}H_{48}O_2$ requires C, 82 25; H, 10 69%)

Hydrogenation of Diketocyclomahogenol (Cyclomahoganone) (VI)

Diketocyclomahogenol (60 mg) was hydrogenated in AcOH (15 ml) in presence of PtO_2 catalyst (20 mg). The crystalline (MeOH) dihydrodiketo derivative melted at 164–165° (50 mg) TLC (silica gel G, solvent: petrol –C_6H_6, 1·2, R_f 0 52) λ_{max} 278 nm (log ϵ 1 73) (Found· C, 80 92, H, 11 23; $C_{31}H_{50}O_2$ requires C, 81 88; H, 11 08%)

Ozonolysis of Cyclomahoganone

Diketocyclomahogenol (50 mg) in dry $CHCl_3$ (5 ml) was treated at 0° with ozonized oxygen for 0 5 hr The solution was treated with AcOH (0 5 ml) and Zn dust (100 mg) during 0 5 hr at room temp. After 1 hr stirring the solution was washed with water. The combined aqueous washings were added to a freshly prepared DNPH solution (10 ml) and kept overnight.

Treatment with the DNPH Derivative

The DNPH derivative separated was extracted with CCl_4, washed, dried and chromatographed over alumina (2 g, 8 × 1 3 cm) Petrol –C_6H_6, 1:1, eluent on evaporation and crystallization (petrol) furnished needles m p 165–166° identical with DNPH of formaldehyde (mixed m p 164–165°), TLC (silica gel G, solvent petrol –C_6H_6, 1 2, R_f 0 28)

Treatment of the Nonvolatile Ketone (VII)

The $CHCl_3$ layer was washed, dried and the solvent distilled off The solid residue was then chromatographed over alumina (2 5 g; 8 × 1 3 cm) Petrol –C_6H_6, (1 3) eluents on evaporation gave a residue crystallized in needles (MeOH) m p 147–148° (10 mg) TLC (silica gel G, solvent·C_6H_6–$CHCl_3$, (3·1) R_f 0 79)

24-Methyl Cycloartane (IX)

A mixture of dihydrodiketocyclomahogenol (12 mg), hydrazine hydrate (100%, 0·4 ml) and NaOEt (from 30 mg Na) in EtOH (1 ml) was kept at 200° for 14 hr. The solution was cooled and poured into crushed ice (5 g) and extracted with ether The ether solution was washed, dried and evaporated. An oil mass obtained

was then chromatographed over alumina (2 g; 8 × 1 3 cm.) Petrol. eluent on evaporation furnished an oily mass which on crystallisation (MeOH) furnished a semisolid mass. The mass spectral and TLC behaviour was similar to that of 24-methylcycloartane obtained from cyclolaudanone.

Wolff–Kishner Reduction of Cyclolaudanone (X)

A mixture of cyclolaudanone (obtained by Jones oxidation of cyclolaudanol, 50 mg), hydrazine hydrate (100%, 0·5 ml) and NaOEt (from 70 mg Na) in EtOH (4 ml) was reduced by above method. The solid obtained was chromatographed over alumina (3 g; 10 × 1·4 cm) Petrol. eluent furnished a solid crystallized from MeOH m.p. 81°.

24-Methylcycloartane as obtained from both the compounds (IX) and (X) were found identical in the TLC (silica gel G; solvent MeOH–C_6H_6–AcOH, 88.2:0·5, R_f of hydrocarbon obtained from diketocyclomahogenol 0 32).

Borohydride Reduction of Diketocyclomahogenol

Diketocyclomahogenol (25 mg) in MeOH (2 ml) was heated under reflux for 3 hr with KBH_4 (50 mg). The reaction product was chromatographed (3 g 8 × 1 3 cm). The major product obtained from petrol.–C_6C_6, 1:1, eluent on recrystallization from C_6H_6 furnished colourless crystals m.p 151–152°; m.m p. with cyclomahogenol 151–152°; TLC (silica gel G; solvent·C_6H_6–$CHCl_3$, 3·1; R_f of the borohydride reduction product 0 36, R_f of cyclomahogenol 0 36).

Acknowledgements—The authors thank Prof. S. M. Sircar, Director, Dr. D. M. Bose, Dr A. Sen, Head of the Department of Chemistry, Bose Institute and Prof. E. Lederer, Director, Institut de Chimie Des Substances Gif Sur Yvette, for their interest in the work. The authors' thanks are also due to Dr. C. P. Dutta, University of Connecticut, Storrs, U S A for running some i r spectra. The financial support by C.S I.R., India is gratefully acknowledged