Tetrahedron. Vol. 24, pp. 1107 to 1111. Pergamon Press 1968. Printed in Great Britain

THE STRUCTURE AND STEREOCHEMISTRY OF SPERGULAGENIC ACID

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(*Received in the UK* 1 *May* 1967; *accepted for publication* 23 *June* 1967)

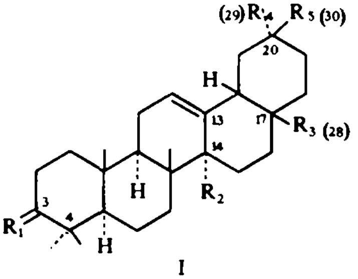
Abstract—The structure and stereochemistry of spergulagenic acid—a new triterpenoid sapogenin from *Mullugo spergula* has been established as 3β-hydroxy-olean-12-ene-28, 30-dioic acid.

SPERGULAGENIC acid, a new triterpene isolated from *Mollugo spergula*,[1] was earlier shown to be 3β-hydroxy-olean-12-ene-28, x-dioic acid by its conversion to oleanolic acid.[2] The second carboxyl group in spergulagenic acid was located either at C-4 or at C-20 on the basis of ease of saponification of the corresponding carbomethoxy group in dimethyl spergulagenate (Ib). The former position was ruled out because 3-keto dimethyl spergulagenate (Ie) does not undergo decarboxylation on saponification. The configuration of the C-20 carboxyl group in spergulagenic acid was considered to be α (equatorial, i.e. C-29) but further studies described in this paper show it to be β (axial, i.e. C-30) and accordingly the structure and stereochemistry of spergulagenic acid is represented as 3β-hydroxy-olean-12-ene-28, 30-dioic acid (Ia).

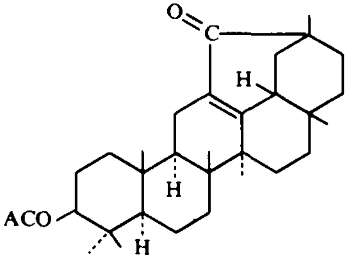
The mass spectrum (Fig. 1) of acetyl dimethyl spergulagenate (Ic, M = 556) is in complete agreement with the assigned structure and shows typical retro-Diels–Alder fragmentation pattern expected of olean-12-enes.[3] The principal ion fragments are summarized in scheme I. The mass spectrum (Fig. 2) of the triol (If, M = 458) obtained by LAH reduction of Ib provides further evidence for the proposed structure (*vide* scheme II).

The mass spectral analysis clearly shows that both the carboxyl groups in spergulagenic acid must be located in rings C, D and E. One of them has already been shown[2] to be at C-17. Mass spectral studies, however, cannot eliminate C-14 as another possible site for the second carboxyl group in addition to C-20. However, the non-identity of acetyl dimethyl spergulagenate (Ic) with acetyl dimethyl cincholate (Ig)[4] as shown by direct comparison of their mixed m.p., leaves hardly any doubt about the location of the second carboxyl group at C-20.

Earlier the second carboxyl group in spergulagenic acid was thought to be α (equatorial, i.e. C-29) firstly because the carbomethoxy group at C-20 in dimethyl spergulagenate could easily be saponified to yield the dicarboxylic acid monomethyl ester (Id), which was previously represented as Ih, and secondly because the optical rotations of 3-ketodimethyl spergulagenate, m.p. 204–206°, $[\alpha]_D^{33^\circ}$ +113° and the dicarboxylic acid monomethyl ester, m.p. 292–294°, $[\alpha]_D^{32^\circ}$ +97° (EtOH) prepared



I



II

a $R_1 = <^{H}_{OH}; R_2 = R_4 = CH_3; R_3 = R_5 = COOH$

b $R_1 = <^{H}_{OH}; R_2 = R_4 = CH_3; R_3 = R_5 = COOCH_3$

c $R_1 = <^{H}_{OAc}; R_2 = R_4 = CH_3; R_3 = R_5 = COOCH_3$

d $R_1 = <^{H}_{OH}; R_2 = R_4 = CH_3; R_3 = COOCH_3; R_5 = COOH$

e $R_1 = O; R_2 = R_4 = CH_3; R_3 = R_5 = COOCH_3$

f $R_1 = <^{H}_{OH}; R_2 = R_4 = CH_3; R_3 = R_5 = CH_2OH$

g $R_1 = <^{H}_{OAc}; R_2 = R_3 = COOCH_3; R_4 = R_5 = CH_3$

h $R_1 = <^{H}_{OH}; R_2 = R_5 = CH_3; R_3 = COOCH_3; R_4 = COOH$

i $R_1 = <^{H}_{OH}; R_2 = R_4 = CH_3; R_3 = COOH; R_5 = CH_2OH$

j $R_1 = <^{H}_{OH}; R_2 = R_5 = CH_3; R_3 = COOH; R_4 = CH_2OH$

k $R_1 = <^{H}_{OAc}; R_2 = R_5 = CH_3; R_3 = R_4 = COOCH_3$

l $R_1 = <^{H}_{OH}; R_2 = R_3 = R_5 = CH_3; R_4 = COOH$

m $R_1 = O; R_2 = R_5 = CH_3; R_3 = COOCH_3; R_4 = COOH$

n $R_1 = <^{H}_{OAc}; R_2 = R_4 = CH_3; R_3 = COOCH_3; R_5 = COOH$

o $R_1 = <^{H}_{OAc}; R_2 = R_4 = CH_3; R_3 = COOCH_3; R_5 = CO.O.COCH_3$

from dimethyl spergulagenate (Ib) were found to be quite different from those of the two degradation products (Ie), m.p. 199–201°, $[\alpha]_D$ +73° and (Id), m.p. 292–293°, $[\alpha]_D$ +59° (EtOH) prepared from queretaroic acid (Ii) by Djerassi *et al.*[5] Unfortunately, authentic samples of these two degradation products were not available for comparison purposes. Recently Tursch *et al.*[6] has fully elucidated the structure and stereochemistry of mesembryanthemoidigenic acid as (Ij) and they also showed its non-identity with queretaroic acid by direct comparison of their methyl esters. Acetyl dimethyl spergulagenate (Ic) has been found to be different from compound (Ik) prepared from mesembryanthemoidigenic acid (Ij) by direct comparison of mixed m.p. The configuration of the C-20 carboxyl group in spergulagenic acid cannot, therefore, be α (equatorial, i.e. C-29) as in that case acetyl dimethyl spergulagenate would have been identical with compound (Ik). Therefore the C-20 carboxyl group in spergulagenic acid appears to be β (axial, i.e. C-30).

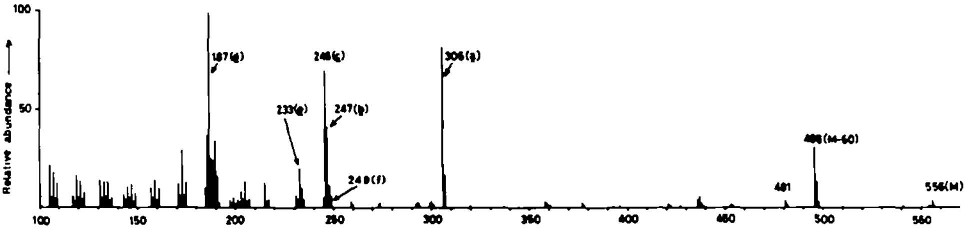
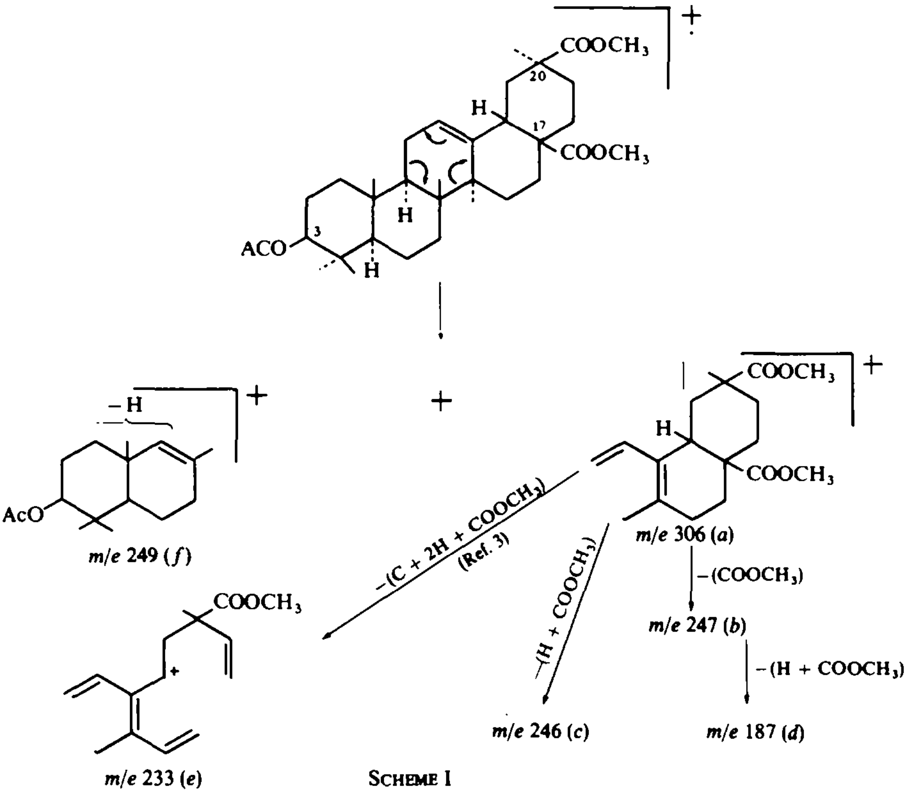


FIG. 1



SCHEME I

Katonic acid (II) which contains a C-20 α carboxyl group (i.e. C-29), when treated with acetic anhydride and perchloric acid furnished a product showing UV absorption max at 273 mμ (ε = 8900). King and Morgan[7] represented the product as II, the validity of which was, however, questioned by Tursch *et al.*[6] The compound Im, a degradation product of mesembryanthemoidigenic acid, also furnished under the same condition, a product showing UV-absorption maximum at 269 mμ (ε = 7500). The monoacetyl derivative* In of the dicarboxylic acid monomethyl ester (Id)

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* The monoacetyl derivative (In) of the dicarboxylic acid monomethyl ester (Id) described before[2] has now been found to be a mixture of the acetate (In) and the mixed anhydride (Io) (vide experimental).

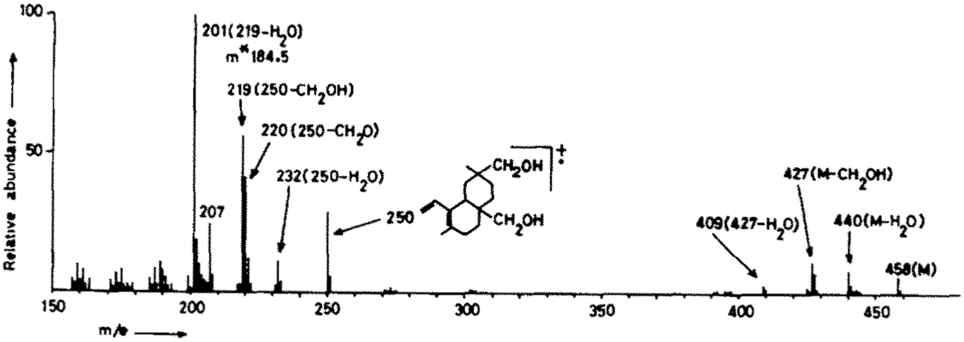
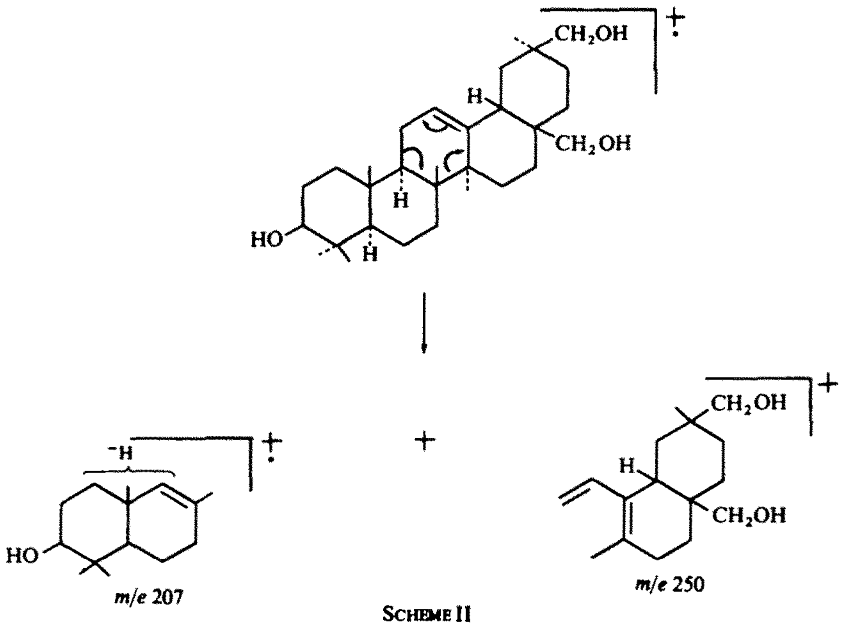


Fig. 2



Scheme II

prepared from dimethyl spergulagenate did not yield any product showing characteristic UV absorption max when treated with acetic anhydride in presence of perchloric acid and this evidence supports the β (axial, i.e. C-30) rather than α (equatorial, i.e. C-29) orientation of the C-20 carboxyl group in spergulagenic acid. Moreover, the molecular rotation change (+35·5°) on methylation of the dicarboxylic acid monomethyl ester (Id) yielding dimethyl spergulagenate (Ib) also suggests β-orientation (C-30) of the carboxyl group attached to C-20 in spergulagenic acid (*vide* Table 1). Thus spergulagenic acid is represented as 3β-hydroxyolean-12ene-28,30-dioic acid (Ia).

TABLE 1

Compound	$[M]_{(COOCH_3)}-[M]_{(COOH)}$
Deoxyglycyrrhetic acid acetate (3β-acetoxy-olean-12-en-30-oic-acid) Acetyl methyl deoxy glycyrrhetate	+55°[8]
3β-Acetoxy-16-oxo-13β,28-epoxyoleanan-30-oic acid Corresponding methyl ester	+43°[9]
Katonic acid (3α-hydroxy olean-12-en-29-oic-acid) Methyl katonate	+5·5°[7]
Dicarboxylic acid monomethyl ester (Id) Dimethyl spergulagenate (Ib)	+35·5°[2]

EXPERIMENTAL

M.ps are uncorrected and recorded in a bisulphate bath. Optical rotations are in $CHCl_3$ unless specified otherwise and UV absorption spectra in EtOH solution. IR spectra are determined as Nujol mulls. Mass spectra are recorded in an A.E.I. MS 9 mass spectrometer operating at 70 eV.

Preparation of the monoacetyl derivative (In) *of the dicarboxylic acid monomethyl ester* (Id). Compound Id (500 mg) was heated with Ac_2O (8 ml) and pyridine (5 ml) over steambath for 3 hr and then worked up in the usual way. The crude product showed two spots in TLC. It was crystallized from $CHCl_3$–MeOH, m.p. 260–263°, but TLC experiment still showed two spots. IR spectrum: ν_{max} 1800 (anhydride), 1735 and 1244 (OAc) and 1720 (COOMe and COOH) cm^{-1}. The above mixture (Io + In; 100 mg) was refluxed with EtOH (95%, 50 ml) for 8 hr. The product showed only one spot in TLC. On crystallization from $CHCl_3$–MeOH a product In, m.p. 198–204°, was obtained. Its IR spectrum showed bands at 1735 and 1242 (OAc) and 1715 (COOMe and COOH) cm^{-1}, but no band at 1800 cm^{-1} for anhydride, thus ensuring complete conversion of Io, a mixed anhydride of In and AcOH, to In. (Found: C, 73·35; H, 8·91; $C_{33}H_{50}O_6$ requires: C, 73·06; H, 9·23%.)

Treatment of In *with acetic anhydride and perchloric acid.* A soln of In (20 mg) in Ac_2O (10 ml) was kept with perchloric acid (0·5 ml) overnight at room temp. On working up in the usual way, a product was obtained which showed only a terminal absorption at 208 mμ for trisubstituted double in the UV spectrum. TLC experiment showed it to be the starting material.

Acknowledgement—The authors are indebted to Dr. D. M. Bose, Director and Dr. A. Sen, Head of the Department of Chemistry, Bose Institute, Calcutta and Prof. E. Lederer, Director, Institut de Chemie des Substances Naturelles, Gif-Sur-Yvette, Essonne, France, for their interest in the work. Thanks are due to Prof. R. Tschesche, Bonn University, W. Germany and Dr. B. Tursch, Free University of Bruxelles for generous gifts of authentic samples of acetyl dimethyl chincolate and the compound Ik, respectively. The authors are grateful to Dr. S. C. Pakrashi, Scientist, Indian Institute for Experimental Medicine, Calcutta, for the IR spectra.

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