CHAPTER—IV

E X P E R I M E N T A L

Extraction:

Dried and powdered root of Leucas Aspera (5 kgs) was extracted directly with ethyl alcohol in a Soxhelt apparatus for twenty four hours. The solvent of the alcohol extract was concentrated to about 500 cc.

Hydrolysis of ethyl alcohol extract:

The ethyl alcohol extract was treated with 7% H_2SO_4 (20 cc) and the mixture was refluxed for 10 hours. Then it was cooled and extracted with ether. The ether layer was treated with 10% sodium hydroxide solution (3 x 100 ml) and the organic layer was washed with water to make it neutral and then dried over anhydrous sodium sulphate. The solvent was distilled off, which gave a gummy residue (5 gms).

Chromatography of the above gummy material:

The above gummy material (5 g) was dissolved in benzene (15 ml) and was placed on a column of alumina (400 g) deactivated with 16 ml of 10% aqueous acetic acid. The chromatogram was developed with petroleum ether and was eluted with the following solvents (Table—2):

Table—2

Chromatography of the above gummy material

Eluent	Fraction 50 ml each	Residue on evaporation
Petroleum (200 ml)	1—4	Nil
Petroleum ether:benzene (4:1) (200 ml)	5—8	Nil
Petroleum ether:benzene (3:2) (200 ml)	9—12	Nil
Petroleum ether:benzene (2:3) (300 ml)	13—18	White solid (300 mg) m.p.140—50°
Petroleum ether:benzene (1:4) (200 ml)	19—22	Nil
Benzene (200 ml)	23—26	Nil
Benzene:ether (4:1) (300 ml)	27—32	White solid (600 mg) m.p.270—90°

Further elution with more polar solvents did not afford any solid material

Isolation of stigmasterol:

Fraction 13—18 (table—2) were combined (300 mg) and was crystallised from a mixture of chloroform-methanol to afford crystals of $C_{29}H_{48}O$, m.p. 154—56°, $[\alpha]_D$ -50°. Its melting point was not depressed when mixed with an authentic sample of stigmasterol. IR spectra of the two were also superimposible.

Analysis report:

Found, C, 84.34% ; H, 11.71%

Required for $C_{29}H_{48}O$, C, 84.4% ; H, 11.72%

IR(nujol): ν_{max} at 3430 cm^{-1} (hydroxyl group)

Acetylation of stigmasterol : Preparation of stigmasteryl acetate:

Stigmasterol (0.1 g) was dissolved in 2 ml pyridine and acetic anhydride (2 ml) was added to the mixture and kept on water bath for 4 hours. It was cooled and poured into ice cold water. The white solid (0.09 g) separated out was filtered and washed with water. It was then crystallised from chloroform-methanol mixture which afforded crystals of $C_{31}H_{50}O_2$, m.p. 137--8°, $[\alpha]_D$ -34°. It showed no depression in m.p. when mixed with an authentic sample of stigmasteryl acetate. IR spectra of the two compounds were also superimposible.

Analysis report:

Found, C, 81.85% ; H, 11.07%

Calculated for $C_{31}H_{50}O_2$, C, 81.88% ; H, 11.08%

IR(nujol): ν_{max} at 1720 and 1240 cm^{-1} (acetate)

Mass : m/e at 454 (M^+), 453, 441, 439, 423, 395, 383, 255, 139 (base). Fig.1

Isolation of new triterpene dihydroxy lactone—leucolactone 1:

Fractions 27—32 (table—2) were combined (600 mg) and was crystallised from chloroform-methanol mixture to afford crystals of 1, m.p. 310° (500 mg).

Analysis report:

Found, C, 76.23% ; H, 9.58%

Required for $C_{30}H_{48}O_4$, C, 76.23% ; H, 10.23%

UV : No UV absorption between 200—350 nm.

IR(KBr): ν_{max} at 3607 and 3540 (two hydroxyl groups), 1750 (γ-lactone), 1380 and 1365 cm^{-1} (gem dimethyl group). Fig.2

PMR : 0.9, 0.98, 1.00, 1.21, 1.28 ppm (methyl groups), 2.6(1H, m), 3.18 (1H, $W_{\frac{1}{2}}$ = 8Hz), 3.85 (1H, $W_{\frac{1}{2}}$ = 18Hz) ppm.

Mass : m/e at 472 (M^+), 454, 439, 421, 411, 384, 251, 234, 253, 221, 220 (base), 203, 202, 207, 189, 187. Fig.13

Liebermann - Burtchard test positive, TNM test negative.

Acetylation of compound 1 ; Preparation of leucolactone diacetate 2 :

200 mg of the hydroxy lactone 1 was dissolved in 5 cc of pyridine and 5 cc of acetic anhydride was added.

The mixture was kept on water bath for 4 hours. Then it was cooled and poured into ice cold water when white solid separated out which was filtered. The residue (0.2 g) was dissolved in minimum amount of benzene and placed on a column of deactivated alumina (50 g). The chromatogram was developed with petroleum ether. The following solvents were used for chromatography (Table—3):

Table—3

Eluent	Fraction 50 ml each	Residue on evaporation
Petroleum ether	1—4	Nil
Petroleum ether:benzene (4:1)	5—8	Nil
Petroleum ether:benzene (3:2)	9—12	Nil
Petroleum ether:benzene (2:3)	13—20	White solid m.p. 270—80°

Further elution with more polar solvents did not afford any solid material

Fractions 13—20 (table—3) were combined and crystallised from a mixture of chloroform and methanol which afforded crystals of 2, m.p. 284—85° .

Analysis report:

Found, C, 73.35% ; H, 9.48%

Required for $C_{34}H_{52}O_6$, C, 73.35% ; H, 9.41%

IR(KBr): ν_{max} at 1728 and 1740, 1216 and 1235 cm^{-1} (two acetate), 1768 (lactone carbonyl), 1359 and 1379 cm^{-1} (gem dimethyl group) Fig.3

PMR : 0.85—1.28 (methyl groups), 2.05 (s) and 2.12 (s) (protons of acetomethoxy groups), 2.8 (d,d), 4.45(t), 4.9 (d) ppm Fig.5

^{13}C NMR: 176.09, 170.85, 169.79, 90.2, 80.53 and 71.64 ppm Fig.6

Mass : m/e at 556 (M^+), 496, 481, 453, 436, 421, 414, 393, 327, 301, 263, 262, 249, 233, 216, 212, 203, 189 (base), 187. Fig.14

Chromium trioxide - pyridine oxidation of the dihydroxy lactone 1 : Preparation of the diketoleucolactone 3 :

100 mg of the dihydroxy lactone, 1 dissolved in pyridine (2 ml), was added to CrO_3-Py complex prepared from pyridine (6 ml) and CrO_3 (0.6 g) at 10°C and the mixture was stirred for 12 hrs. Excess of CrO_3 was destroyed by adding methanol (4 ml), diluted with ethyl acetate and filtered. Ethyl acetate was removed and the concentrate was taken up in ether. The organic layer was washed with hydrochloric acid (5%), then with water till neutral and dried

over anhydrous sodium sulphate. Removal of solvent gave a gummy residue (0.9 g). The above residue was chromatographed over a column of deactivated alumina (30 g). The chromatogram was developed with petroleum ether and the product dissolved in benzene (5 ml) was poured on the column and eluted with the following solvents:

Table—4

Eluent	Fraction 50 ml each	Residue on evaporation
Petroleum ether	1—4	Nil
Petroleum ether:benzene (4:1)	5—8	Nil
Petroleum ether:benzene (3:2)	9—12	Nil
Petroleum ether:benzene (2:3)	13—20	White solid m.p. 310—20°

Further elution with more polar solvents did not afford any solid material

Fractions 13—20 (table—4) were combined and crystallized from chloroform-methanol mixture to give the crystals of 3, m.p. 323—4°.

Analysis report:

Found, C, 76.86% ; H, 9.45%

Required for $C_{30}H_{44}O_4$, C, 76.88% ; H, 9.46%

IR(nujol): ν_{max} at 1705—10 (broad peak), 1760 cm^{-1}

Fig.4

PMR : 0.82, 0.93, 1.02, 1.10, 1.18 and 1.30 ppm (tert-CH_3), 2.18 (d), 2.78 (d) ppm

Fig.9

Mass : m/e at 468 (M^+), 453, 425, 280, 250, 240, 219, 210, 205, 193, 189, 182 etc.

REFERENCES

1. The Welth of India, Raw materials, Vol.VI, New Delhi.

2. A.M.J. Shirazi, Ind.J.Pharm., 9, 116 (1947).

3. N.Adityachowdhury and (Miss) Dipali Ghosh, J.Ind.Chem. Soc., 46, 95 (1969).

4. J.D.Hooker, "Flora of British India", CSIR., New Delhi, Vol.IV, p.680, 690 and 604 (Reprinted on 1978).

5. M.Crowford, S.W.Hauson and M.E.S.Koker, Tet.Let., 3099 (1975).

6. A.S.R. Anjaneyulu and M.N.Rao, Phytochem., 19, 1163 (1980).

7. H.Budzikiewicz, J.M.Wilson and Carl. Djerassi, J.A.C.S., 85, 3688 (1963).

————————x:o):O:(o:x————————

R E P R I N T S

Reprint no - 1.

Tetrahedron Vol. 39, No. 17, pp. 2819 to 2824, 1983
Printed in Great Britain.

0040-4020/83 $3.00+.00

ACTION OF HYDROGEN PEROXIDE ON OLEAN-12,15-DIEN-3,11-DIOL: PREPARATION OF C-NOR-TRITERPENE LACTONES

B. P. PRADHAN,* M. M. MUKHERJEE and D. K. CHAKRABERTI
Department of Chemistry, University of North Bengal, Dist. Darjeeling—734 430, India

and

J. N. SHOOLERY
Varian Associates, Palo Alto, California, U.S.A.

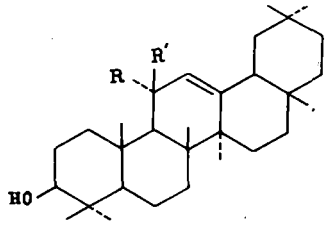
(*Received in UK 19 April 1982*)

Abstract—Treatment of olean-12,15-dien-3,11-diol with hydrogen peroxide containing p-toluenesulphonic acid furnished two isomeric γ-lactones identified as 3β-acetates of C-12-nor-olean-15-en-13α-carb→19α-olide and C-12-nor-olean-18(19)-en-13β-carb→15β-olide.

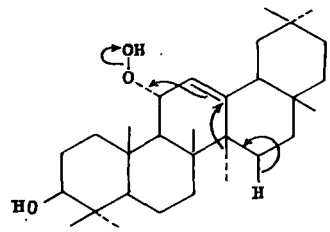
E. J. Corey *et al.*[1] synthesised epoxytaraxerol **2** from both the olean - 12 - en - 3β,11β - diol **1a** and olean - 12 - en - 3β,11α - diol **1b** and suggested that the formation of the same epoxide **2** from the isomeric (C-11) diols must proceed by C-11–O bond cleavage with the formation of the same C-11,12,13 allylic cation which then forms the hydroperoxide **3**. This **3** in turn undergoes O–O fission and carbon rearrangement to afford **2**.

that would undergo nucleophilic attack by OH^- ion producing a 16-hydroxytaraxerol derivative or to produce a cation at C-8 by migration of C-8–Me to C-14 position which was expected to eliminate a C-7 proton to give multiflorenol derivative **7**; but in actual practice, the findings were widely different from those expected and are discussed below:

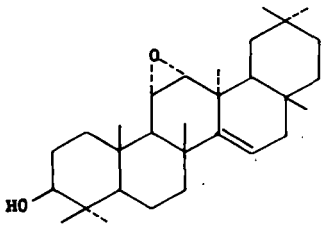
Treatment of taraxeryl acetate **8** with NBS afforded **9**,



1a, R=H, R'=OH
1b, R=OH, R'=H



3

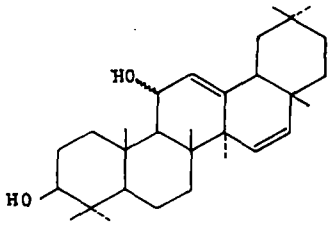


2

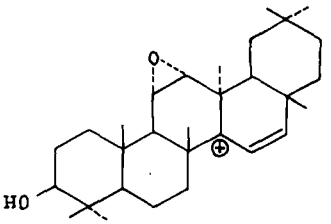
Chart I

This type of reaction under identical conditions was carried out on the diol **4** synthesised from taraxeryl acetate with a view to producing the allylic cation **5**. The intermediate **5** would further isomerize either to produce the allylic cation **6** by migration of C-15–16 double bond

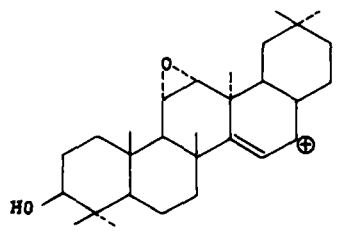
$C_{32}H_{51}O_2Br$ (M^+ 548, Br 81) m.p. 180–82°, $[\alpha]_D+47.4°$, ν_{max} 1720, 1250 (-$OCOCH_3$); ^1H NMR: δ 5.3 (m, 1H, $\diagdown C{=}C \diagup$ H), 4.53 (m, 1H, H–C–O–$COCH_3$), 4.3 (m, 1H, H–C–Br), 2.09 (s, 3H, –O–$COCH_3$) ppm. Treatment of **9**



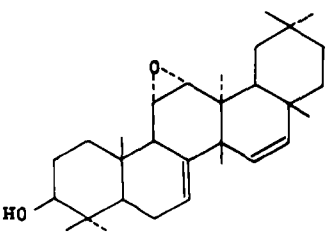
4



5

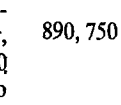


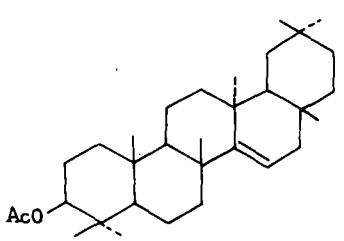
6



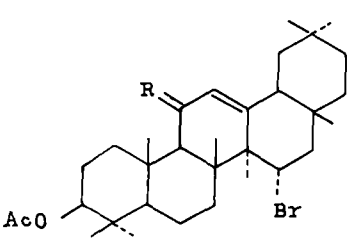
7

Chart II

with sodium dichromate and acetic acid furnished 11 - oxo - 15 - bromo - β - amyrenyl acetate[2] **10** $C_{32}H_{49}O_3Br$, m.p. 240–41°, $[\alpha]_D + 88°$, λ_{max} 249 nm; ν_{max} 1725, 1250 ($-OCOCH_3$), 1680 ($-C{=}C-C{=}O$) cm^{-1}. Attempts to dehydrobrominate **10** with dimethyl aniline/collidine gave the starting compound **10**. A reverse route was followed to prepare the 11 - oxo - 12,15 - diene by dehydrobrominating **9** which furnished compound **11**, $C_{32}H_{50}O_2$, m.p. 199–200°, $[\alpha]_D + 42°$; no UV absorption between 220–300 nm; ν_{max} 1730, 1240 ($-OCOCH_3$), 1650, 890, 750 () cm^{-1}; NMR: 5.2–5.6 (*m*, 3H, vinyl protons), 4.5 (*m*, 1H, H–C–$OCOCH_3$), 2.08 (*s*, 3H, $-O-COCH_3$), 0.8–1.2 (8-t-CH_3) ppm. The diene **11** was oxidised to give the desired 11-oxo-12,15-diene **12**, $C_{32}H_{48}O_3$, m.p. 243–45°, $[\alpha]_D + 28.6°$, λ_{max} 244 nm; ν_{max} 1730, 1240 ($-O-COCH_3$), 1660 ($C{=}C-C{=}O$), 1650, 890, 750

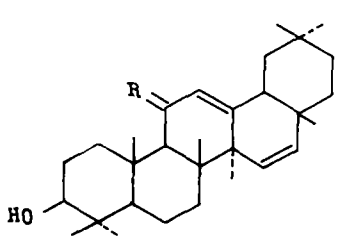


8



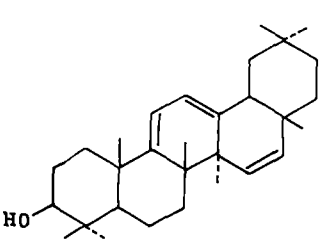
9 R = 

10 R = O



11 , R = 

12 , R = O



13

Chart III

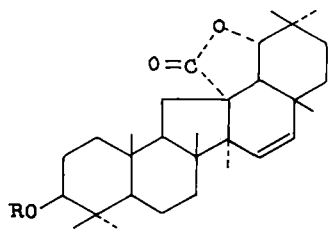
(), 820 () cm^{-1}. LAH reduction of the 11-oxo-diene **12** furnished a diene-diol **4**, $C_{30}H_{48}O_2$, m.p. 198–200°, ν_{max} 3460 (-OH), 820 () cm^{-1}; purification of the diol by chromatography yielded a homoannular diene **13**, $C_{30}H_{46}O$, m.p. 189–90°, λ_{max} 276 nm.

The diol **4** was directly treated with hydrogen peroxide containing p-toluenesulphonic acid following the procedure adopted by Corey *et al.*[1] The product furnished two compounds (**14** and **16**) of the same molecular formula $C_{30}H_{46}O_3$. The compound **14**, m.p. 240–41° showed IR bands at 3520 (-OH), 1775 (γ-lactone), 1650, 890, 870, 750 () cm^{-1}. Acetylation of **14** furnished the acetate **15** $C_{32}H_{48}O_4$, m.p. 215–16°; ν_{max} 1780 (γ-lactone), 1720, 1250 (-$OCOCH_3$), 1650, 890, 870, 750 () cm^{-1}. The formation of the lactone has thus been proved by the IR spectrum of the alcohol **14** and its acetate **15**. The structure **14** has been conclusively established from mass, ^1H and ^{13}C NMR spectra of the compound **15**.

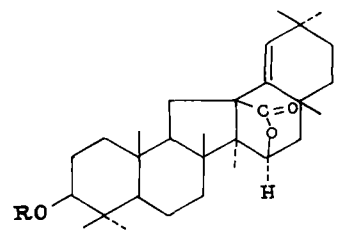
^1H NMR of **15** showed the presence of eight tertiary Me- groups between 0.5 and 1.5 ppm, the acetoxy Me-group at 2.05 ppm, the proton geminal to the lactonic O at 4.72 ppm as a doublet (J = 7.3 Hz), and the *cis*-disubstituted olefinic protons appeared at 5.27 ppm as an AB quartet (J = 10 Hz). Irradiation at 4.72 ppm gave a singlet at 1.7 ppm showing the proton at 1.73 ppm to be coupled to the one at 4.72 ppm with J = 7.5 Hz and weakly to other protons. Again irradiation at 1.73 ppm at a fairly low level gave a sharp line at 4.72 ppm which was a doublet otherwise. Hence the doublet at 4.72 ppm arises due to a single proton adjacent to the lactonic O that couples with the proton at 1.73 ppm. The multiplet at 4.5 ppm collapses to a broad singlet suggesting the presence of a proton at C-3 coupled with protons at C-2. The absence of any peaks between 2.2 and 3.5 ppm shows that the C-α to the lactonic -CO- possesses no proton. The above observations could be explained if the lactone -CO- group is attached to the C-13 position and the γ-lactone ring is formed with the C-19 carbon with a geminal β-H that has a single neighbouring β-axial proton at C-18 position, thus establishing the structure of **14**. This structure is corroborated by the ^{13}C NMR and mass (Experimental) spectra.

The compound **16** had m.p. 256–57° and showed IR absorptions at 3525 (OH), 1780 (γ-lactone), 820 () cm^{-1}. ^1H NMR showed a singlet at 5.3 ppm for the vinyl proton, a multiplet at 4.8 ($W_{1/2}$ = 20 Hz) ppm for the proton geminal to the lactonic oxygen which may have two neighbouring protons, a triplet at 3.23 ppm ($W_{1/2}$ = 20 Hz) for the proton geminal to the OH at C-3 present as an axial proton.[3] Acetylation of **16** gave the acetate **17**, $C_{32}H_{48}O_4$ m.p. 228–29°; ν_{max} 1780 (γ-lactone), 1715, 1250 (acetate), 820 (trisubstituted double bond) cm^{-1}. The mass spectrum of **17** was essentially identical with those of **15**.

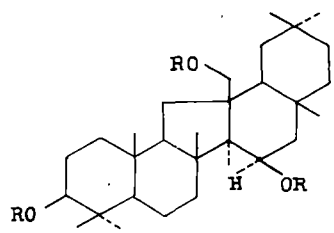
The ^1H NMR of **17** showed a multiplet at 4.8 ($W_{1/2}$ = 7 Hz) ppm (integrated for one proton) showing that the proton geminal to the lactonic O is equatorial which couples with axial and equatorial protons; the multiplet at 4.5 ppm was due to C-3 proton, the singlet at 5.3 ppm was due to C-19 olefinic proton. The absence of any peaks in the region 2.2–3.5 ppm showed that the lactone -CO- has no α-H as in **15**, and hence should be attached to the same carbon (C-13). The absence of AB quartet for the *cis* C-15–16 olefinic protons present in **4** indicated



14, R = H
15, R = CH_3CO



16, R = H
17, R = CH_3CO



18, R = H
19, R = CH_3CO

Chart IV

that this double bond must be involved in the formation of lactone **16** and the lactonic O should be attached to C-15 with an α-equatorial geminal proton that couples with C-16 protons. The structure **16** thus assigned to the lactone explains all the IR and NMR peaks.

LAH reduction of the lactone **16** afforded a triol **18** $C_{30}H_{50}O_3$ m.p. 280–82°, acetylation of which gave a triacetate **19**, $C_{36}H_{56}O_6$, m.p. 190–93°, ν_{max} 1735–40, 1250–40 (acetate groups), 820 cm^{-1}. ^1H NMR of the triacetate **19** showed peaks at 0.85–1.2 (eight t-Me groups), 2.05 (two acetoxyl Me- groups), 2.1 (one acetoxyl Me-), 3.65 (J = 11 Hz, AB-quartet for two methylene protons geminal to the acetate group), 4.45 (a multiplet for the proton at C-3 geminal to the acetate), 5.2 (J = 8 Hz, a doublet split into a multiplet for C-15-proton geminal to the acetate) and at 5.3 (a singlet for the C-19 vinyl proton which has no neighbouring proton) ppm.

Mechanism. Contrary to the formation of the proposed intermediates **5** or **6** the double bond at C-12–13 is pushed, during the formation of the epoxide **I-2**, from the hydroperoxide **I-1** towards ring E (to form a germanicol derivative) rather than to ring B or D due to the presence of double bond at C-15–16 position. Under the reaction condition the epoxide **I-2** is unstable due to the conformational strain caused by the double bonds at C-15–16 and C-18–19 positions and hence undergoes epoxide ring opening in presence of acid forming carbonium ion **I-4** probably by 1,3-hydride shift from C-13 to C-11 as shown in **I-3**. The intermediate carbonium ion **I-4** undergoes ring contraction producing the isomeric cations **I-5** and **I-5'** which in turn lose a proton to form isomeric aldehydes **I-6** and **I-6'** respectively. These aldehydes get oxidised in presence of hydrogen peroxide to the corresponding α and β carboxylic acids at C-13 positions.

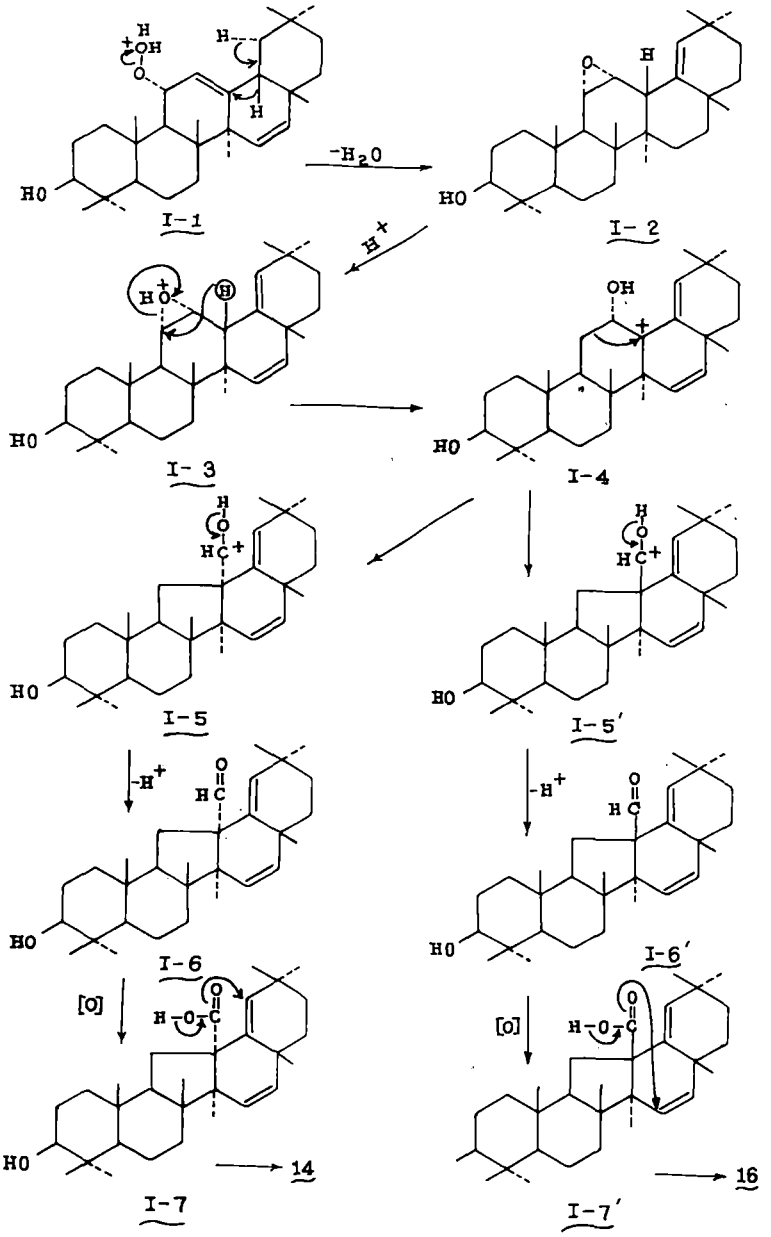


Chart V

The α-carboxyl group in **I-7** being at proximity to the double bond at C-18–19, undergoes lactonization furnishing the γ-lactone **14**, whereas the inetermediate **I-7'** having its carboxyl group in the β-position is at proximity to the C-15–16 double bond, lactonizes forming **16**. The Dreiding model of the lactones **14** and **16** showed that the lactones are strain free, thus stabilising the molecules. This is perhaps the first report on the formation of a lactone with the carbon skeleton rearrangement in ring C of a triterpenoid with hydrogen peroxide in presence of p-toluenesulphonic acid.

EXPERIMENTAL

M.ps are uncorrected. Petroleum used had b.p. 60–80°. All the rotations were determined in $CHCl_3$ at 1–2% solns. The ^1H NMR spectra were recorded with Varian A-60, T-60, FT-80A and XL-100 NMR spectrometers using $CDCl_3$ containing TMS as internal reference. All the UV spectra were determined in 95% ethanol and IR in nujol. Column chromatography were done on neutral alumina deactivated with 10% aqueous acetic acid (4 ml/100 g of alumina).

Oxidation of taraxeryl acetate **8** *with NBS in DMSO*

Preparation of 15-*bromo*-β-*amyrin acetate* **9**. To a soln of **8** (1 g) in $CHCl_3$ (50 ml) and DMSO (25 ml), was added NBS (1 g) in portions and kept in dark for 14 hr. The mixture was filtered and the filtrate extracted with $CHCl_3$, washed with water and dried ($NaSO_4$). Removal of the solvent and chromatography of the residue furnished **9** (0.9 g), m.p. 180–82°, $[\alpha]_D + 47.4°$. (Found: C, 70; H, 9.1. $C_{32}H_{51}O_2Br$ requires: C, 70.23; H, 9.3%.) Beilstein test for halogen—positive.

Oxidation of 15-*bromo*-β-*amyrin acetate* **9**

Preparation of 11-*oxo*-15-*bromo*-β-*amyrin acetate* **10**. To a refluxing soln of **9** (1 g) in benzene (40 ml) was added slowly a soln of $Na_2Cr_2O_7$ (1 g) in glacial AcOH (30 ml) with stirring while maintaining the temp at 70°. After the addition was complete the stirring was continued for 24 hr, maintaining the temp at 80–85°. At the end it was cooled and rectified spirit (5 ml) was added. The soln was concentrated to 1/3rd volume and poured into ice cold water. The ppt was filtered off, washed and crystallization from $CHCl_3$–MeOH gave **10** (0.75 g) m.p. 240–41°, $[\alpha]_D + 89°$. (Found: C, 68.2; H, 8.6. $C_{32}H_{49}O_3Br$ requires: C, 68.4; H, 8.7%.) Beilstein test—positive.

Attempted dehydrobromination of 11-*oxo*-15-*bromo*-β-*amyrin acetate* **10**

(a) *With dimethyl aniline.* Compound **10** (0.5 g) was refluxed with dimethylaniline (75 ml) for 6 hr. The mixture was cooled, acidified with HCl (6 N) and then extracted with ether. Removal of the solvent and chromatography of the residue furnished an eluate (with petroleum at eluent) which on crystallization with $CHCl_3$–MeOH afforded the starting **10**, m.p. (m.m.p.) 240–41°, Beilstein test—positive.

(b) *With s-collidine.* Compound **10** (0.2 g) was refluxed with s-collidine (15 ml) for 18 hr at 180° in an oil bath. Working up the mixture in the usual method gave back **10**, m.p. (m.m.p.) 240°, Beilstein test—positive.

Dehydrobromination of 15-*bromo*-β-*amyrin acetate* **9**

Preparation of olean - 12,15 - dien - 3 - β - yl acetate **11**. Acetate **9** (0.2 g) was refluxed with distilled dimethylaniline (30 ml) for 6 hr. The mixture was diluted with water, acidified with aq HCl and extracted with ether. The ether was distilled off and the residue chromatographed. Petroleum eluted a solid which on crystallization ($CHCl_3$–MeOH) gave **11**, m.p. 199–200°, $[\alpha]_D +$ 42°. (Found: C, 81.9; H, 10.8. $C_{32}H_{50}O_2$ requires: C, 82.35; H, 10.8%.) UV—no absorption in the region 220–300 nm. Beilstein test—negative.

Oxidation of olean-12,15-*dien*-3-β-*yl acetate* **11**

Preparation of 11 - *oxo* - *olean* - 12,15 - *dien* - 3 - β - *yl acetate* **12**. A soln of $Na_2Cr_2O_7$ (4 g) in glacial AcOH (100 ml) was added slowly during a period of 1 hr to a vigorously stirred soln of olean - 12,15 - dien - 3 - β - yl acetate (4 g) in refluxing benzene (50 ml). The mixture was refluxed for 24 hr and then cooled. Excess of dichromate was decomposed with EtOH (50 ml). The soln was concentrated to 1/3rd volume and the contents poured into ice cold water, extracted with ether, washed with water and dried (Na_2SO_4). Removal of the solvent and chromatography of the residue furnished a solid on elution with petroleum: ϕH (3:2). The solid on crystallization ($CHCl_3$–MeOH) gave 12, m.p. 243–45°, $[\alpha]_D + 28.8°$, λ_{max} 244 (ε, 11,376) nm, ^1H NMR: δ 0.82–1.04 (8 t-Me protons), 2.03 (s, 3H, $-OCOCH_3$), 2.23 (dd, 1H, C-1β-H), 2.42 (s, 1H, C-9α-H), 2.82 (t of d, 1H, C-1β-H),[4] 4.5 (t, 1H, H–C–3–O–CO–), 5.38 (s, 2H, 2 vinyl H), and 5.64 (s, 1H, 1 vinyl H) ppm. (Found: C, 79.86; H, 9.95. $C_{32}H_{48}O_3$ requires: C, 79.95; H, 10.06%.)

LAH reduction of 11 - *oxo* - *olean* - 12,15 - *dien* - 3 - β - *yl acetate* **12**

Preparation of olean - 12,15 - dien - 3,11 - diol **4**. A soln of **12** (2.5 g) in dry benzene (30 ml) and dry ether (70 ml) was refluxed with LAH (5 g) for 6 hr followed by stirring at room temp for another 12 hr. Excess LAH was destroyed by adding water dropwise at r.t. The etherial layer was separated and the aqueous layer was extracted with ether and the two ether soln were mixed, washed with water and dried (Na_2SO_4). The ether was removed and the residue yielded **4** (4.5 g), m.p. 198–200°, ν_{max} 3460, 1650, 890, 860, 820, 750 cm^{-1} (TLC single spot).

Compound **4** (0.2 g) was absorbed in a column of deactivated alumina (10 g) and elution with petroleum: ϕH (3:2) furnished **13** m.p. 189–90°, λ_{max} 276 nm, m/e 422 (M^+). (Found: C, 84.8; H, 11.30. $C_{30}H_{46}O$ requires: C, 85.25; H, 10.97% (TLC homogenous).)

Treatment of olean - 12,15 - dien - 3,11 - diol **4** *with* H_2O_2-*p*TsOH

Isolation of **14** *and* **16**. To a soln of **4** (1.9 g) in CH_2Cl_2 (100 ml) was added a soln (80 ml) prepared by mixing p-TsOH (3 g) and 30% H_2O_2 (5 ml) in t-BuOH (80 ml). The mixture was stirred slowly for 24 hr and then poured into water. It was then extracted with CH_2Cl_2, washed with water, dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue (1.5 g) was absorbed in an alumina column. Elution with benzene yielded a mixture of **14** and **16**, (Rf **14** = 49; **16** = 46 in EtOAc). The mixture was repeatedly crystallized from $CHCl_3$–MeOH when **14** (0.3 g) separated as the less soluble part. Further purification by crystallization from $CHCl_3$–MeOH afforded pure **14**, m.p. 240–41°, no UV absorption in the region 220–300 nm. (Found: C, 78.94; H, 9.89. $C_{30}H_{46}O_3$ requires: C, 79.25; H, 10.20%.)

Acetylation of lactone **14**. **14** (0.1 g) was heated with a mixture of Py (2 ml) and Ac_2O (2 ml) for 4 hr. The mixture was then poured into ice cold water and then filtered. The residue was washed with water and dried under suction. Crystallization of the solid furnished **15**, m.p. 215–16°; *m/e* 496 (M^+). 468 (M^+–CO), 452 (M^+–CO_2), 436 (M^+–AcOH), 421, 408, 392, 372, 313, 300, 269, 257, 244, 231, 217, 218, 206, 203, 191, 189, 187, 175, 171, 161, 147, 135; ^{13}C NMR (multiplicity): 175.5(*s*), 170.5(*s*), 132.75(*d*), 132.5(*d*), 82.0(*d*), 80.0(*d*), 75.8(*s*), 67.5(*d*), 55.75(*d*), 51.75(*d*), 45.25(*s*), 42.0(*s*), 38(3*t*, 1*s*), 36.8(*s*), 35.75(*t*), 34.8(*t*), 34.2(*s*), 32.8(*q*), 30.25(*s*), 29.0(*q*), 28.0(*q*), 25.0(*q*), 23.75(*q*), 23.5(*t*), 22.75(*q*), 21.25(*q*), 19.75(*t*), 18.6(*q*), 16.25(*q*) ppm. (Found: C, 77.25; H, 9.85. $C_{32}H_{48}O_4$ requires: C, 77.36; H, 9.74%.)

Isolation of lactone **16**. The more soluble fraction was crystallized twice and the purer product was isolated from the filtrate. Concentration of the filtrate gave **16** (0.2 g), m.p. 256–57°; *m/e* 454 (M^+), 436 (M^+–H_2O), 426 (M^+–CO), 410 (M^+–CO_2), 408, 392, 313, 269, 231, 205, 189, 187, 171. (Found: C, 79.45; H, 9.76. $C_{30}H_{46}O_3$ requires: C, 79.25; H, 10.20%.)

Acetylation of lactone **16**. **16** (0.01 g) was heated with Py (1 ml) and Ac_2O (1 ml) for 4 hr. The mixture on usual work up and crystallization from $CHCl_3$–MeOH gave the acetate **17**, m.p. 228–29°, *m/e* 496 (M^+), 468 (M^+–CO), 452 (M^+–CO_2), 436 (M^+–AcOH), 408, 392, 372, 313, 269, 257, 256, 217, 206, 203, 191, 189, 187, 171, 161, 147, 135. (Found: C, 77.38; H, 9.94. $C_{32}H_{48}O_4$ requires: C, 77.30; H, 9.74.)

LAH reduction of lactone **16**. A soln of 16 (0.2 g) dissolved in dry ether (50 ml) was refluxed with LAH 90.4 g) for 4 hr. Excess of LAH was decomposed with a saturated soln of Na_2SO_4 and the product extracted with ether (200 ml), washed with water and dried (Na_2SO_4). The solvent was distilled off and the residue when recrystallized from acetone furnished the triol **18** (0.15 g), m.p. 280–82° (TLC single spot). (Found: C, 78.42; H, 10.84. $C_{30}H_{50}O_3$ requires: C, 78.55; H, 10.99%.)

Acetylation of triol **18**—*preparation of triacetate* **19**. A mixture of 18 (0.12 g) in dry Py (2.0 ml) and Ac_2O (2.0 ml) was kept over a water bath for 12 hr. The mixture was poured into cold water when a solid which separated out was washed with water and dried under suction. It was then crystallized from $CHCl_3$–MeOH to afford the triacetate **19** (0.1 g), m.p. 190–93° (TLC-single spot); m/e 584 (M^+), 524 (M^+–AcOH), 432, 464 (M^+–2AcOH), 459, 389, 358, 343, 340, 269, 249, 215, 204, 189, 187; ^{13}C NMR (multiplicity): 170.5(*s*), 170.2(*s*), 170(*s*), 155.5(*s*), 122(*d*), 80.5(*d*), 78.5(*d*), 76.0(*t*), 55.5(*d*), 50.0(*d*), 46.8(*s*), 41.5(*s*), 39.5(*t*), 38.2(*s*), 38.0(*t*), 37.8(*s*), 37.5(*s*), 34.0(*t*), 33.9(*t*), 33.5(*t*), 32.0(*s*), 31.5(*t*), 31.0(*q*), 29.5(*q*), 28.0(*q*), 25.5(*q*), 23.8(*t*), 23.5(*q*), 22.5(*q*), 21.5(3*q*), 18.5(*t*), 16.0(*q*), 15.5(*q*) ppm. (Found: C, 73.50; H, 9.85. $C_{36}H_{56}O_6$ requires: C, 73.93; H, 9.65%.)

Acknowledgement—The authors' thanks are due to Dr. A. Duffield, University of New South Wales for the mass spectra; to Dr. S. K. Sengupta, East India Pharmaceutical Works Ltd. Calcutta for the optical rotations. Two of us (M. M. Mukherjee and D. K. Chakrabarti) are grateful to U.G.C. for the financial assistance.

REFERENCES

[1]I. Ageta, E. J. Corey, A. G. Hortmann, J. Klien, S. Proskow and J. J. Ursprung, *J. Org. Chem.* **30**, 1698 (1965).

[2]K. Chattopadhyay, D. R. Misra and H. N. Khastgir, *Indian J. Chem.* **14B**, 403 (1976).

[3]L. M. Jackman and S. Sternhell, *Application of Nuclear Magnetic Spectroscopy in Organic Chemistry*, 2nd Edn. Pergamon Press, Oxford (1969).

[4]H. S. Bhacca and D. H. Williams, *Application of NMR Spectroscopy in Organic Chemistry*. Holden-Day, New York (1964).

Reprint No. 2.

Indian Journal of Chemistry
Vol. 22B, January 1983, pp. 12-16

Action of N-Bromosuccinimide on Triterpene Acids & Esters in Dimethyl Sulphoxide

B P PRADHAN*, M M MUKHERJEE & D K CHAKRABARTI
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734430
and
J N SHOOLERY
Varian Associates, Palo Alto, California

Indian Journal of Chemistry
Vol. 22B, January 1983, pp. 12-16

Action of N-Bromosuccinimide on Triterpene Acids & Esters in Dimethyl Sulphoxide

B P PRADHAN*, M M MUKHERJEE & D K CHAKRABARTI
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734 430
and
J N SHOOLERY
Varian Associates, Palo Alto, California

Received 15 *April* 1982; *accepted* 11 *May* 1982

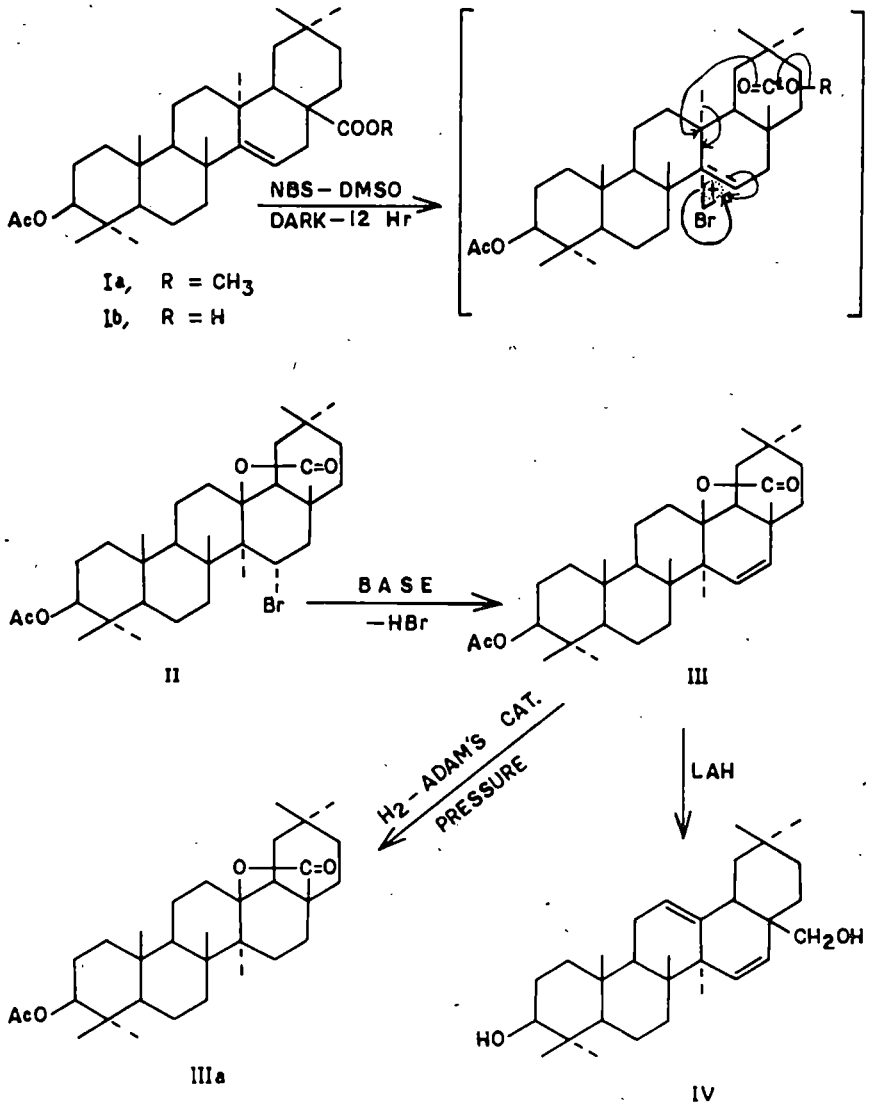
Action of N-bromosuccinimide on acetyloleanolic acid/methyl ester, acetylaleuritolic acid/methyl ester and acetylbetulenic acid/methyl ester in dimethyl sulphoxide has been studied and in each case a bromo γ-lactone is formed, and in the latter two compounds lactonization occurs with rearrangements. The compounds so formed have been identified as 3β-acetyl-12α-bromooleanan-28→13-olide (V), 3β-acetyl-15α-bromooleanan-28→13-olide (II) and 3β-acetyl-29,30-dibromo-18α-oleanan-28→19β-olide (IX) respectively.

Khastgir and coworkers[1] reported that taraxeryl acetate on treatment with N-bromosuccinimide (NBS) furnished 15-bromo-β-amyrin acetate. In order to examine the applicability of the reaction on other compounds of taraxerane skeleton, we have presently carried out the reaction on methyl acetylaleuritolate[2] (Ia), $C_{33}H_{52}O_4$, by treating it with NBS in dimethyl sulphoxide (DMSO) in dark for 12 hr. Usual work-up followed by chromatography and crystallization furnished a crystalline solid which analysed for $C_{32}H_{49}O_4Br$, m.p. 280-82°, $[\alpha]_D$ +19.51°. That it had γ-lactone moiety was supported by its IR spectrum in nujol, exhibiting bands at 1780, 1710, 1240 cm^{-1}. Its PMR spectrum indicated the absence of a vinyl proton and methoxycarbonyl protons originally present in the starting material, showing that the bromination was accompanied by the formation of a γ-lactone involving the double bond and the loss of a methyl group from the carbomethoxyl group. Repetition of the reaction on acetyl aleuritolic acid[2] (Ib), $C_{32}H_{50}O_4$, furnished the same bromolactone. The structure of the bromolactone has been established as II on the fact that the compound on dehydrobromination with dimethylaniline afforded 15,16-dehydro-lactone (III), $C_{32}H_{48}O_4$, m.p. 308-10°, $[\alpha]_D$ −8.42°; IR (nujol): 1770 (γ-lactone), 1730, 1250 (acetate), 900 cm^{-1} (*cis*-disubstituted olefin). III on LAH reduction furnished aegiceradiol[3] (IV), $C_{30}H_{48}O_2$, m.p. 235-36° identical (m.m.p., co-IR) with an authentic sample. III on catalytic hydrogenation over Adam's catalyst in acetic acid under pressure afforded 3β-acetyloleanan-28→13-olide[4] (IIIa), $C_{32}H_{50}O_4$, m.p. 293-94° (identical with the lactone prepared from 3β-acetyl oleanolic acid[4]). The formation of aegiceradiol (IV) showed that the double bond must be formed at 15-16 position on dehydrobromination of the bromine present at 15-position.

A study of the Dreiding model of the lactone (II) showed that the bromine at C-15 should be α-equatorial. This was confirmed by appearance of a proton centered at δ 4.3 (*d*, *d*) with coupling constants of 14 Hz (*J* a, a) and 3 Hz (*J* a, e) due to the axial proton geminal to the bromine having axial and equatorial protons on the vicinal carbon. The mechanism of formation of II probably involves the attack of the bromonium ion from NBS in DMSO at the double bond. Bromine being a bulky atom ultimately assumes the equatorial position so as to have the minimum strain and steric interaction. The next step involves concerted migration of the C-13 methyl to the C-14 position and elimination of the methoxyl methyl to form the 28→13-olide (II).

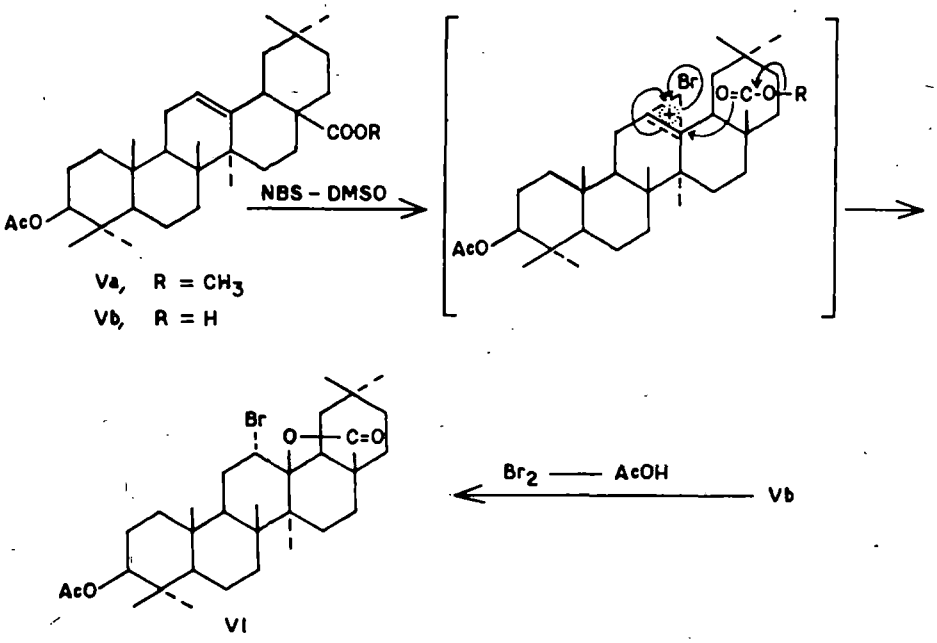
As no systematic work on the action of NBS in DMSO on a triterpene acid/ester has been reported, the formation of the lactone (II) prompted us to explore if the reaction could be applied to other triterpene acids and esters as well. Methyl acetyloleanolate (Va) was taken as another model compound for this reaction when we isolated the product (VI), $C_{32}H_{49}O_4Br$, m.p. 215-16°, IR (nujol): 1770 (γ-lactone), 1725, 1240 cm^{-1} (acetyl), which was found to be identical with 3β-acetyl-12α-bromo-oleanan-28→13-olide[5] (VI) prepared by treatment of 3β-acetyloleanolic acid with bromine in acetic acid. The same bromolactone (VI) was formed when 3β-acetyloleanolic acid (Vb) was treated with N-bromosuccinimide in dimethyl sulphoxide.

Methyl 3β-acetylbetulenate[6] (VIIa) on similar reaction with NBS in DMSO afforded two different bromo compounds, separated by chromatography.



The less polar one, $C_{33}H_{51}O_4Br$, m.p. 235-36°, $[\alpha]_D$ +42.55° was identified as methyl 30-bromo-3β-acetylbetulenate (VIII); IR (nujol): 1735 ($-COOCH_3$), 1725, 1240 ($-OCOCH_3$), 1260 ($-CH_2Br$), 1660, 876 cm^{-1} ($=CH_2$); PMR: δ 0.87-1.02 (15H, 5 tert. CH_3), 2.03 (*s*, 3H, $-OCOCH_3$), 4.1 (*m*, 2H, $-CH_2Br$), 3.75 (*s*, 3H, $-COOCH_3$), 4.9 (*m*, 2H, $=CH_2$), 4.5 (*m*, 1H, $CH-O-COCH_3$); VIII on treatment with zinc and acetic acid gave methyl 3β-acetylbetulenate (VIIa).

The more polar fraction (10%) was a dibromo lactone (IX), $C_{32}H_{48}O_4Br_2$, m.p. 303-4°, $[\alpha]_D$ +47; CD (*n*-hexane): 218 nm ($\varepsilon = -0.99$); IR (nujol): 1780 (γ-lactone), 1720, 1240 ($-OCOCH_3$), 1260 cm^{-1} ($-CH_2Br$); PMR: δ 0.87-0.92 (15H, 5 tert. CH_3), 2.03 (*s*, 3H, $-OCOCH_3$), 3.44 (*m*), 3.55 (*m*); 3.73 (*d*) and 3.78 (*d*) (4H, C-29-H_2Br and C-30-H_2Br, J_{AB} = 11 Hz), 4.34 (*s*, 1H, $HC-OCO$) and 4.5 (*m*, 1H, $HCOCOCH_3$). The methylene protons present at C-29 and C-30 as CH_2Br are non-equivalent and their position is fixed due to hindered rotation of these groups containing the bulky and highly electronegative bromine atoms which are at the farthest positions. The appearance of the C-19 proton adjacent to the lactonic oxygen as a singlet in the PMR spectrum of IX suggests that this proton has either no neighbouring proton or the conformation is such as to have no coupling with it. A Dreiding model of IX showed that the dihedral angle between the C-18 and C-19 protons is almost 90° if the C-18 proton is α-oriented. The appearance of a peak in the ^{13}C NMR of IX at 178.48 ppm revealed the presence of a lactonic carbonyl group in a five-membered ring whereas the one at 171 ppm indicated the presence of an acetoxyl carbonyl group. The doublets at 80.77 and 80.95 ppm due to *C*-H groups bonded to acetoxy and lactone oxygen atoms. The dibromolactone (IX) could not be dehydrobrominated with dimethylaniline but on debromination with Raney nickel-hydrogen gave X,



$C_{32}H_{50}O_4$, m.p. > 360°, $[\alpha]_D$ + 59°, identical with 3β-acetyloleanan-28→19β-olide prepared from 3β-acetylbetulenic acid. From these observations the dibromolactone (IX) has been assigned the structure of 3β-acetyl-29, 30-dibromo-18α-oleanan-28→19β-olide (IX).

3β-Acetylbetulenic acid (VIIb) also furnished the dibromolactone (IX) on treatment with NBS in DMSO and 3β-acetyl-30-bromobetulenic acid which was converted with the methyl ester (VIII) on esterification with diazomethane.

Methyl 3β-acetyl-30-bromobetulenate (VIII) is formed by allylic bromination of the methyl ester (VIIa) which on further attack by the bromonium ion on the double bond causes ring expansion and lactonization as in other acid isomerization[7] of the double bond to furnish the lactone (IX).

Methyl 3β-acetyldihydrobetulenate on similar treatment with NBS in DMSO gave back the starting material in 100% yield, suggesting that the attack by the bromonium ion on the double bond initiates the lactonization and no free radical is involved in this reaction.

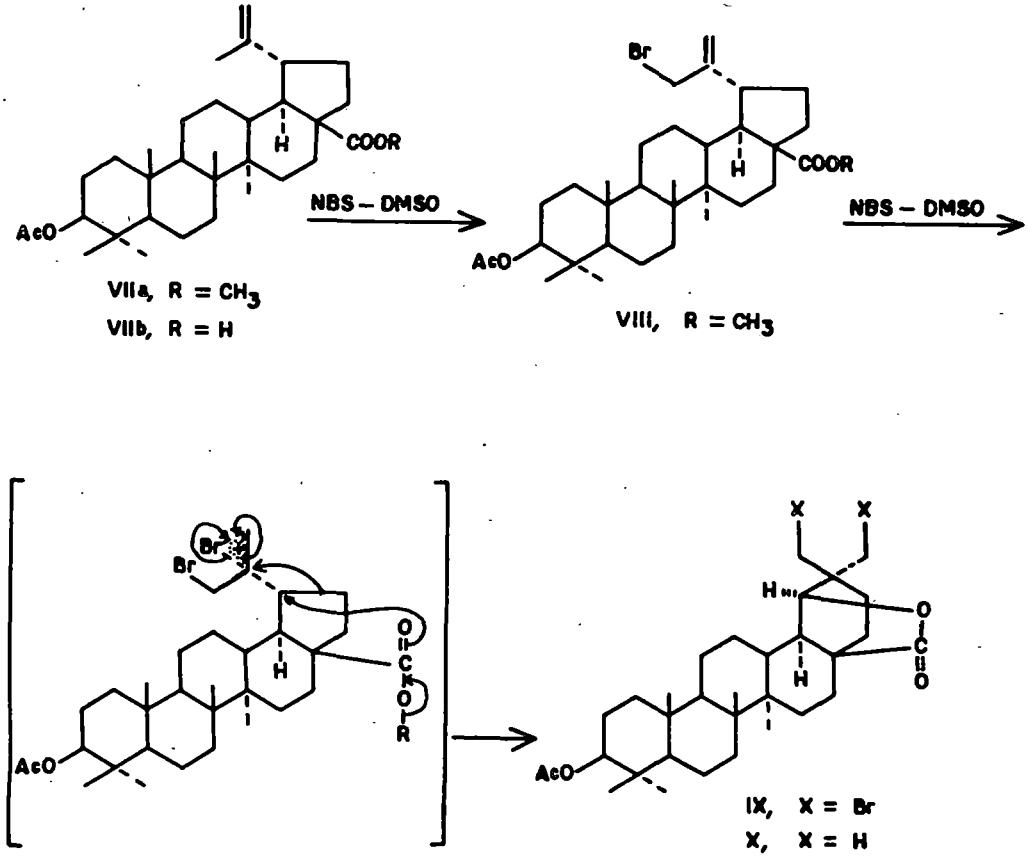
Experimental Procedure

Melting points are uncorrected. The petroleum used throughout had the b.p. 60-80°. Brockmann alumina (S. Merck) deactivated with 5% of 10% AcOH was used for column chromatography. TLC plates were coated with silica gel G (acc. to Stahl) having the thickness of about 0.2 mm and the spots located by exposing to iodine vapour. All the optical rotations were determined in chloroform solution. IR spectra were recorded as nujol mulls on a Beckman IR-20 spectrophotometer and the UV spectra in MeOH on a Beckman DU-2 spectrophotometer. NMR spectra were recorded on Varian A-60 or T-60 or EM-360 and FT-80A (^1H and ^{13}C) NMR instruments using $CDCl_3$ as solvent containing TMS as internal standard. Mass spectra were recorded by solid probe CI/CH_4 method.

Treatment of methyl 3β-acetylaleuritolate (Ia) with NBS: Formation of 3β-acetyloleanan-15α-bromo-28→13β-olide (II)—Ia (200 mg) dissolved in $CHCl_3$ (12 ml) was mixed with freshly distilled DMSO (6 ml). After cooling the reaction mixture, NBS (200 mg) was added, kept in dark for 12 hr, filtered, the filtrate extracted with $CHCl_3$, the organic layer washed with water and dried (Na_2SO_4). Chloroform was distilled off and the residue chromatographed over deactivated alumina. Elution with petroleum-benzene (3:2) furnished a solid which crystallized from $CHCl_3$ – MeOH to give II; PMR: δ 0.8 to 1.4 (7 tert. CH_3), 2.04 (*s*, 3H, O–$COCH_3$), 4.3 (*dd*, 1H, CHBr, J_{aa} = 14 Hz and J_{ae} = 3 Hz), 4.5 (*m*, 1H, H–C–O–$COCH_3$) (Found: C, 67.8; H, 8.8. $C_{32}H_{49}O_4Br$ requires C, 67.1; H, 8.6%).

Treatment of 3β-acetylaleuritolic acid (Ib) with NBS—Ib (150 mg) dissolved in $CHCl_3$ (10 ml) was mixed with DMSO (5 ml) and NBS (150 mg) and kept in dark for 24 hr. After usual work-up and chromatography, a solid was eluted by petroleum-benzene (3:2) which crystallized from $CHCl_3$ – MeOH to give II, identical (m.m.p., co-IR) with II obtained in the above experiment.

3β-Acetylolean-15,16-en-28→13β-olide (III)—II (150 mg) was refluxed for 4 hr with freshly distilled dimethylaniline (30 ml). The mixture was poured into water, acidified with 6*N* HCl and extracted with ether.



The ether layer was washed with water till neutral and dried (Na_2SO_4). The solvent was removed and the residue (130 mg) chromatographed. Elution with petroleum-benzene (3:2) furnished a solid which crystallised from $CHCl_3$–MeOH to furnish III; PMR: δ 0.8-1.3 (7 tert. CH_3), 2.04 (*s*, 3H, $-OCOCH_3$), 4.5 (*m*, 1H, $HC-OCOCH_3$), 5.5 (*AB* quartet $-\overset{|}{C}-CH=CH-\overset{|}{C}-$, J_{AB}=10 Hz) (Found: C, 77.1; H, 9.7. $C_{32}H_{48}O_4$ requires C, 77.4; H, 9.7%); Beilstein test-negative.

Hydrogenation of lactone (III): Formation of 3β-acetyloleanan-28→13β-olide (IIIa)—A mixture of III (200 mg) dissolved in ethyl acetate (50 ml), AcOH (50 ml) and Adam's catalyst (25 mg) was stirred under hydrogen atmosphere in a Pars hydrogenation apparatus (40 p.s.i). The solvent was removed under reduced pressure and the residue dissolved in benzene was passed through a column of alumina. The eluate on crystallization from $CHCl_3$–MeOH afforded IIIa, m.p. 293-94° (m.m.p. and co-IR identical with an authentic sample of 3β-acetyloleanan-28→13-olide[4]); IR: 1780 (γ-lactone), 1720, 1240 cm^{-1} (acetate) (Found: C, 77.0; H, 10.1. $C_{32}H_{50}O_4$ requires C, 77.1; H, 10.1%).

LAH reduction of III: Formation of aegiceradiol (IV)—III (50 mg) taken in dry ether (100 ml) was refluxed with LAH (100 mg) for 4 hr. The mixture was cooled, LAH decomposed with a saturated soln. of Na_2SO_4, extracted with ether, the ether extract washed with water, dried (Na_2SO_4) and the solvent removed. The residue (m.p. 225-28°) was chromatographed over alumina. Elution with benzene-ether (3:2) afforded a solid which crystallised from $CHCl_3$–MeOH to furnish aegiceradiol, m.p. 235-36° (m.m.p. and co-IR with authentic sample) (Found: C, 81.7; H, 10.9. Calc. for $C_{30}H_{48}O_2$: C, 81.6; H, 11.0%).

Treatment of methyl 3β-acetyloleanolate (Va) with NBS in DMSO: Formation of 3β-acetyloleanan-12α-bromo-28→13β-olide (VI)—Va (0.2 g) dissolved in $CHCl_3$ (10 ml) and DMSO (5 ml) was treated with NBS (0.2 g). The mixture was kept in the dark for 24 hr, washed with water, dried (Na_2SO_4) and the solvent removed. The oily residue (0.18 g) was chromatographed when a solid was eluted by petroleum-benzene (3:2). This on crystallization from $CHCl_3$–MeOH furnished VI (0.15 g), m.p. 215-16°; IR: 1770, 1180, 1160 (γ-lactone), 1725, 1240 cm^{-1} (acetate), identical (m.m.p., co-IR) with an authentic sample of 12α-bromo-3β-acetyloleanan-28→13-olide[5] (Found: C, 67.2; H, 8.6. Calc. for $C_{32}H_{49}O_4Br$: C, 67.1; H, 8.6%); Beilstein test-positive.

Treatment of 3β-acetyloleanolic acid (Vb) with NBS: Formation of bromo lactone (VI)—To a solution of Vb (0.2 g) in $CHCl_3$ (10 ml) containing DMSO (5 ml), NBS

(0.2 g) was added in one lot and the mixture kept in the dark for 24 hr. The mixture was diluted with water, extracted with $CHCl_3$, and the organic layer dried (Na_2SO_4). The solvent was distilled off and the residue again extracted with ether, stirred with aq. NaOH (5%) and separated into alkaline and neutral extracts. The alkali extract on acidification and extraction with ether did not furnish any solid residue indicating the absence of an acidic component in the reaction mixture. The neutral ethereal portion was concentrated to give a residue (0.15 g) which was homogeneous in TLC (single spot). It was crystallized from $CHCl_3$ – MeOH, m.p. 215-17° and found identical with VI obtained above.

Treatment of methyl 3β-acetylbetulenate (VIIa) with NBS: Formation of methyl 3β-acetyl-30-bromobetulenate (VIII) and 3β-acetyl-29,30-dibromooleanan-18α,28→19β-olide (IX)—To a solution of VIIa (0.4 g) in $CHCl_3$ (20 ml) and DMSO (10 ml), crystals of NBS (0.8 g) were added in lot of 100 mg each and the soln kept in dark for 24 hr. The mixture was diluted with water, washed the chloroform layer, dried and concentrated to give a residue (0.35 g) which was chromatographed. Elution with petroleum – benzene (4:1) furnished a solid which crystallized from $CHCl_3$ – MeOH to give VIII, m.p. 235-36°, $[\alpha]_D$ +42.55° (Found: C, 65.2; H, 8.6; Br, 13.5. $C_{33}H_{51}O_4Br$ requires C, 65.3; H, 8.6; Br, 13.5%). Beilstein test-positive.

Further elution of the column with petroleum-benzene (2:3) furnished a solid which crystallized from $CHCl_3$ – MeOH to give the dibromo lactone (IX), m.p. 303-4°, $[\alpha]_D$ +47.22°; CD: 218 nm, ε = 0.99; CMR: δ 178.48 (*s*, lactone $-O-C=O$), 171 (*s*, $-O-CO-CH_3$), 80.77 (*d*, $HC-O-C=O$), 80.95 (*d*, $HC-O-C=O$) and 28 other peaks between 55.60 to 13.67 ppm; MS†: 659 (M_1^+H, 10%), 657 (M_2^+H, 19%), 655 (M_3^+H, 10%), 599 ($M_1^+H-CH_3COOH$), 597 ($M_2^+H-CH_3COOH$), 595 ($M_3^+H-CH_3COOH$), 503 (599-CH_3Br† and 597-CH_3Br‡, 5%), 501 (597-CH_3Br† and 595-CH_3Br‡, 5%), 407 (503-CH_3Br† or 501-CH_3Br‡, 31%), 517 (599-HBr† and 597-HBr‡), 515 (597-HBr† and 595-HBr‡), 489 (517-CO), 487 (515-CO), 437 ($MH-Br_2$), 435 (517 – HBr† and 515 – HBr‡), 407 (503-CH_3Br† and 501-CH_3Br‡ or 487-HBr‡ and 489 – HBr†), 249, 191 (base), 189 (Found: C, 58.5; H, 7.3. $C_{32}H_{48}O_4Br$ requires C, 58.6; H, 7.4%).

Debromination of lactone (IX): Formation of 3β-acetyloleanan-18α,28→19β-olide (X)—X (0.2 g) dissolved in EtOH (50 ml) was refluxed with freshly prepared Raney Nickel (5 g) for 6 hr. The mixture was filtered and the filtrate on concentration furnished X (0.14 g), m.p. > 360°, $[\alpha]_D$ +59° identical (m.m.p. and co-IR) with an authentic sample of 3β-acetyloleanan-28 →19β-olide.

†M_1^+H refers to the protonated molecular mass with the two bromine atoms of isotopic mass 81; M_2^+H to mass with isotopic masses 79 and 81; and M_3^+H to mass with isotopic mass 79. Br† and Br‡ refer to bromine atoms of isotopic masses 81 and 79 respectively.

Acknowledgement

The authors thank Dr A Duffield, University of New South Wales, for mass spectra; Dr P M Scopes, Department of Chemistry, Westfield College, London for the CD and Dr S K Sengupta, East India Pharmaceutical Works Ltd, Calcutta for optical rotations. Two of the authors (MMM and DC) are grateful to the UGC, New Delhi for financial assistance.

References

1 Chattopadhyay K, Misra D R & Khastgir H N, *Indian J Chem*, **14B** (1976) 403.
2 Misra D R & Khastgir H N, *Tetrahedron*, (1970) 3017.
3 Rao K V & Bose P K, *Tetrahedron*, (1962) 461.
4 Barton D H R & Holeness N J, *J chem Soc*, (1952) 78.
5 (a) Dowle M D & Davies D I, *Chem Soc Rev*, (1979) 171; (b) Winterstein & Stein, *Z Physiol Chem*, **211** (1932) 5.
6 Simonsen J & Ross W C J, *The terpenes*, Vol. 5 (The Cambridge University Press, London) 1957, 317.
7 Davy G S, Halsall T G, Jones E R H & Meakins G D, *J chem Soc*, (1951) 2702.
8 Roy T K, Misra D R & Khastgir H N, *Phytochemistry*, (1975) 1876.