Tetrahedron Vol. 41, No. 12, pp. 2513 to 2516, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00
Pergamon Press Ltd.

APPENDIX - 1

REDUCTION OF KETONES TO EPIMERIC ALCOHOLS WITH POTASSIUM HYDROXIDE-DIETHYLENE GLYCOL

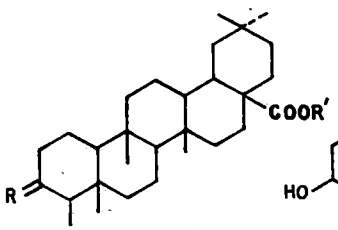
B. P. PRADHAN*, A. HASSAN and (Miss) T. RAY

Department of Chemistry, University of North Bengal,
P.O. North Bengal University, Darjeeling 734 430, India.

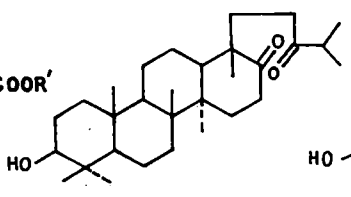
(*Received in UK* 4 *March* 1985)

Abstract - Triterpenoid ketones have been reduced to epimeric alcohols on boiling with potassium hydroxide in diethylene glycol. α,β-unsaturated ketone furnished saturated epimeric alcohols.

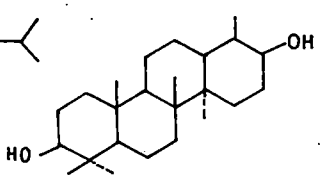
During the hydrolysis of 3-keto-methyl trichadenate[1] 1 with potassium hydroxide in diethylene glycol we observed that the 3-keto functional group of the triterpenoid being converted to epimeric alcohols (viz. trichadenic acid A and B[1]) 1a and 1b . A survey of the literature showed that during the degradation of hydroxydiketone 2 with potassium hydroxide in diethylene glycol, Barton et al[2] obtained the dihydroxy compound 3 . Similar observation was made by Halsall et al[3] (4 ⟶ 5). Doering et al[4,5] have reported the equillibration of ketones and alcohols in presence of their respective alkoxides under high pressure and temperature.



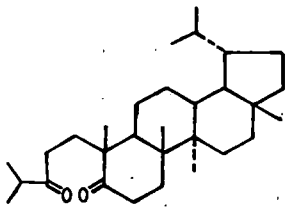
1, R=O, R'=CH_3
1a, R=, R'=H
1b, R=, R'=H



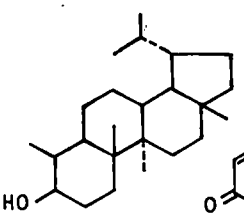
2



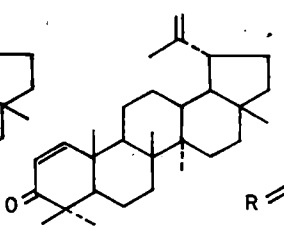
3



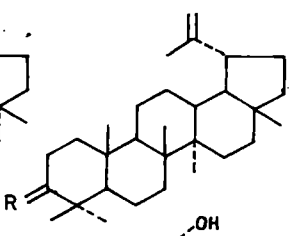
4



5



6



7, R=O 7a, R= 
7b, R= 

In order to examine the validity of the reaction on other keto compounds we carried out the reaction on a series of triterpenoid ketones (Entries 1 - 7) and one non-terpenoid ketone (Entry 8) as shown in Table I.

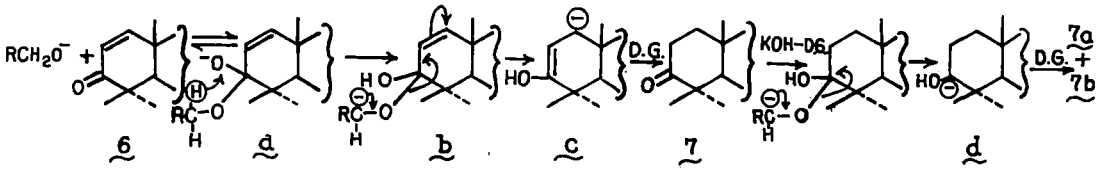
Table I

Entry No.	Ketones	Products (Yield in %)
1	Methyl trichadonate[1] 1	Trichadenic acid A[1] 1a (50) and Trichadenic acid B[1] 1b (15)
2	Friedelin[6]	Friedelanol[6] (45) and epi-friedelanol[6] (20)
3	Moretenone[7]	Moretenol[7] (50) and epi-moretenol[7] (15)
4	Taraxerone[6]	Taraxerol[6] (50) and epi-taraxerol[6] (15)
5	β-amyrone[6]	β-amyrin[6] (50) and epi-β-amyrin[6] (15)
6	Lupenone[6] 7	Lupeol[6] (50) and epi-lupeol[6] (15)
7	Glochidone[8]	Lupeol[6] (40), epi-lupeol[6] (15) and lupenone[6] (8)
8	Benzophenone	Benzhydrol (90)

Thus from the above observation we find that the ketones are reduced to the epimeric alcohols and the formation of the equatorial isomers predominate the less thermodynamically stable axial isomers.

Mechanism:- At the high temperature of the reaction mixture, potassium hydroxide probably forms potassium-glycoxide with diethylene glycol. The glycoxide so formed may reduce the ketone in a cyclic mechanism that may be considered parallel to the action of aluminium-alcoxides in the case of Meerwein-Ponndorf -Verley reduction[9]; but in the latter case the reduction of α,β-unsaturated ketones furnish only the allylic alcohols[10] whereas in the present case the entry 7 shows that along with the keto group, the α,β-unsaturation is also reduced which cannot be explained by the cyclic mechanism. A most probable mechanism for this reduction may follow the route as depicted in the Scheme I :

Scheme I



Under the high thermal condition, the ketone undergoes nucleophilic attack by the anionic glycoxide to form the intermediate anion a that undergoes hydride ion shift forming the carbanion intermediate b ; elimination of glycolaldehyde from b furnishes the tautomeric carbanion c which subsequently acquires a proton from the solvent, the glycol to form the saturated ketone. The isolation of a small amount of the ketone, lupenone 7 from the reaction mixture as shown in entry 7 of Table I confirms the proposed mechanism. Further nucleophilic attack by the glycoxide anion on the saturated ketone in a similar path furnishes the intermediate anion d which ultimately affords the epimeric alcohols.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were run in KBr disc in Beckman-20 and UV spectra were recorded in ethanol in Beckman DU-2 Spectrophotometers. Mass spectra were run in JMS-300 instrument. All the rotations were determined in $CHCl_3$ soln. Column chromatography were performed in silica gel (BDH 60-120 mesh) and TLC were run on plates coated with silica gel G and were developed in iodine chamber. All the analytical samples were routinely dried for 36 h in vacuo. Petrol used had the b. p. 60-80° and the ether extracts were dried over anhydrous Na_2SO_4.

Treatment of methyl trichadonate 1 with KOH-diethylene glycol: Preparation of trichadenic acid A 1a and trichadenic acid B 1b : A mixture of methyl trichadonate (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was heated in a r.b. flask (100ml) in a heating mantel initially without condenser till all the moisture escaped from the mixture. When the temperature rose above 160° in the vapour phase, the condenser was fitted in the r.b. flask and the mixture was refluxed for 2h. The mixture was then cooled, acidified with dil HCl and extracted with ether. The ether extract was washed with water, dried and the solvent was removed by distillation. The residue (0.45 g) was chromatographed over silica gel column (15 g). The column on elution with benzene:ether (4:1) furnished a solid (0.085 g) which was crystallised from $CHCl_3$-MeOH to afford a solid of m.p. 334-35°, $[\alpha]_D$ +41°, IR: 3425, 1690; M^+ 458. The acetate derivative prepared by Ac_2O-Py method had the m.p. 270-71 $[\alpha]_D$ +50°, M^+ 500; IR: 1725, 1690, 1240 cm^{-1}. The acetate was identified as O-acetyl trichadenic acid B by m.m.p., co-IR and co-TLC with an authentic sample. On further elution of the column with benzene:ether (7:3) a second solid was eluted which after crystallisation from $CHCl_3$-MeOH had m.p. 289-90°, $[\alpha]_D$ + 23°; M^+ 458; IR: 3410, 1688 cm^{-1}. Acetylation of the solid with Ac_2O-Py method and workup in the usual manner furnished an acetate m.p. 251-52°, $[\alpha]_D$ + 27°, M^+ 500; IR: 1740, 1688, 1240 cm^{-1}. The acetate was identified as O-acetyl trichadenic acid A by m.m. p., co-IR and co-TLC with an authentic sample.

Conversion of friedelin to epi-friedelanol and friedelanol: A mixture of friedelin (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was boiled in a r.b. flask (100 ml) in a heating mantel without condenser till the temperature of the escaping vapour started registering temperature above 160° when the condenser was fitted in. The mixture was allowed to reflux for 2 h and then cooled. The mixture was then acidified with dil HCl, extracted with ether, washed the ether extract with water and dried (Na_2SO_4). The solvent was removed and the residue (0.45 g) was chromatographed over silica gel (15 g). Elution of the chromatogram with benzene:Petrol (1:4) afforded a solid that was crystallised from $CHCl_3$-MeOH to furnish crystals m.p. 278-80°, $[\alpha]_D$ + 20°, IR: 3610 cm^{-1}. The acetate prepared by Ac_2O-Py method had m.p. 291-92°, $[\alpha]_D$ + 38°, IR: 1730, 1240 cm^{-1}; M^+ 470 was found identical (m.m. p., co-IR and co-TLC) with an authentic sample of epi-friedelanol acetate. Further elution of the column with benzene:petrol (3:2) furnished another solid that was crystallised from $CHCl_3$-MeOH had m.p. 300-302°, $[\alpha]_D$ + 18°; IR: 3620 cm^{-1}; its acetate prepared by Ac_2O-Py method had the m.p. 315-16°, $[\alpha]_D$ - 10°; IR: 1730, 1240 cm^{-1} was found identical with an authentic sample of friedelanol acetate by comparison of their m.p., TLC and IR spectra.

Reduction of moretenone to epi-moretenol and moretenol: Moretenone (0.5 g) and KOH (2 g) was mixed with diethylene glycol (50 ml) taken in a r.b. flask(100 ml) and heated as described before. The solid (0.45 g) obtained after usual workup was chromatographed. Elution of the chromatogram with benzene:petrol (1:4) yielded a solid (0.08 g) that was crystallised from MeOH ; the crystals had m.p. 223-24°, $[\alpha]_D$ - 2°, IR: 3460, 3080, 1640,890 cm^{-1}; M^+ 426; its acetate prepared by Ac_2O-Py method had m.p. 231-32°, $[\alpha]_D$- 18°; IR: 3070, 1725, 1640, 890 cm^{-1}; M^+ 468. The acetate was identical (m.m.p., co-IR and co-TLC) with an authentic sample of epi-moretenyl acetate. Further elution of the column with benzene:petrol (2:3) gave a solid (0.25 g) which on crystallisation from $CHCl_3$-MeOH furnished crystals of m.p. 228-30°, $[\alpha]_D$ + 27°; IR: 3480, 3070,1640,890 cm^{-1}; M^+ 426; the acetate prepared by Ac_2O-Py method had m.p. 276-78°, $[\alpha]_D$ + 20°; IR: 3070, 1725, 1640, 1250, 885 cm^{-1}; M^+ 468 was identified as moretenyl acetate by comparison of m.p., IR and TLC with an authentic sample.

Reduction of taraxerone to epi-taraxerol and taraxerol: A mixture of taraxerone (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was refluxed for 2 h as described above. The solid (0.45 g) obtained after usual workup was absorbed in a chromatogram (15 g) and the column on elution with benzene:petrol (1:4) yielded a solid (0.08 g). The solid on crystallisation from $CHCl_3$-MeOH furnished crystals m.p. 262-64°, $[\alpha]_D$ - 18°, IR: 3470, 810 cm^{-1}; M^+ 426; its acetate prepared by Ac_2O-Py method had m.p. 202-203°, $[\alpha]_D$ - 25°; IR: 1730, 1240, 820 cm^{-1}; M^+ 468 was identical in its m.p., TLC and IR with an authentic sample of epi-taraxeryl acetate. The chromatogram on further elution with benzene:petrol (3:2) yielded a solid (0.25 g) which on crystallisation from $CHCl_3$-MeOH furnished crystals of m.p. 278-79°, $[\alpha]_D$ + 3°, IR: 3460, 815 cm^{-1}. The solid on acetylation with Ac_2O -Py method formed acetate of m.p.297-99°, $[\alpha]_D$ + 8°; IR: 1730, 1240, 820 cm^{-1}; M^+ 468 which was identical (m.m.p., co-IR and co-TLC) with an authentic specimen of taraxeryl acetate.

Conversion of β-amyrone to epi-β-amyrin and β-amyrin: A mixture of β-amyrone (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was refluxed as described above. The solid (0.45 g) obtained after usual work-up was chromatographed over silica gel (15 g). Elution of the column with benzene:petrol (1:4) gave a solid that was crystallised from MeOH. The crystals had m.p. 220-22°, $[\alpha]_D$ + 70°; IR: 3540, 820 cm^{-1}; M^+ 426; its acetate (Ac_2O-Py) had m.p. 125-26°, $[\alpha]_D$ + 55°; IR: 1730, 1240, 810 cm^{-1}; M^+ 468 was identified (m.m.p., co-IR, and co-TLC) with an authentic sample of epi-β-amyrin acetate). Further elution of the column with benzene:Petrol (2:3) furnished a solid (0.25 g) which was crystallised from $CHCl_3$-MeOH. The crystals had m.p. 197-98°, $[\alpha]_D$ + 80°; IR: 3500, 810 cm^{-1}; Ac_2O-Py

method of acetylation formed an acetate m.p. 237-38°, $[\alpha]_D$+ 79°; IR: 1730, 1240, 820 cm^{-1}; M^+ 468 which was identical (m.m.p., co-IR and co-TLC) with an authentic sample of β-amyrin acetate.

Reduction of lupenone to epi-lupeol and lupeol: A mixture of lupenone (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was refluxed for 2 h as described above. The product (0.45 g) obtained after usual manner was chromatographed over silica gel (15 g). Elution of the chromatogram with petrol furnished a solid (0.08 g) that was crystallised from MeOH to afford crystals m.p. 200-201°, $[\alpha]_D$ + 17°; IR: 3320, 3060, 1640, 880 cm^{-1}; the acetate prepared with Ac_2O-Py had m.p. 159-60°; $[\alpha]_D$ - 5°; IR: 3060, 1730, 1640, 1250, 880 cm^{-1} was identical (m.m.p., co-IR and co-TLC) with an authentic sample of epi-lupenyl acetate. Further elution with benzene:petrol (2:3) and crystallisation of the solid with $CHCl_3$-MeOH furnished a solid of m.p. 214-16°, $[\alpha]_D$ + 26°; IR: 3340, 1640, 890 cm^{-1} which on acetylation with Ac_2O-Py formed an acetate m.p. 215-17°; IR: 1730, 1640, 1240, 880 cm^{-1} that was identical (m.m.p., co-IR and co-TLC) with lupenyl acetate.

Reduction of glochidone to lupenone, epi-lupeol and lupeol: A mixture of glochidone (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was refluxed for 2 h as in the previous cases. The product(0.45 g) obtained after usual workup was absorbed in a column of silica gel (15 g). Elution of the chromatogram with petrol furnished a solid (0.04 g) that was crystallised from $CHCl_3$-MeOH to afford fine crystals of m.p. 168-69°; IR: 1700, 1640,880 cm^{-1}; UV: no absorption between 220 - 270 nm; M^+ 424 was identified as lupenone by comparison of m.p., IR and TLC with an authentic specimen. Further elution with petrol furnished solid (0.08 g) that was crystallised from MeOH to give crystals m.p. 199-200°; $[\alpha]_D$ + 18°; IR: 3320, 3060, 1640, 880 cm^{-1}; M^+ 426 was directly compared with an authentic sample of epi-lupeol and was found identical. Elution of the column with benzene:petrol (2:3) yielded a solid (0.20 g)that crystallised from $CHCl_3$-MeOH to afford crystals of m.p. 215-16°, $[\alpha]_D$ + 24°, IR: 3340, 1640, 890 cm^{-1}; the acetate prepared with Ac_2O -Py had m.p. 214-15°:IR 1730, 1640, 1240, 880 cm^{-1} was found identical (m.m.p., co-IR and co-TLC) with an authentic specimen of lupenyl acetate.

Reduction of benzophenone to benzhydrol: A mixture of benzophenone (0.5 g) and KOH (2 g) in diethylene glycol (50 ml) was refluxed for 2 h as in the previous cases. After usual workup the solid (0.45 g) was chromatographed over silica gel (15 g) and elution of the column with benzene:petrol (3:2) furnished solid that was crystallised from $CHCl_3$-MeOH to afford crystals of m.p. 67-68°, IR: 3350, 1605, 1280, 1050,1030, 940, 920, 860, 765, 750, 700 cm^{-1}; M^+ 168. It was found identical (m.m.p., co-IR and co-TLC) with an authentic sample of benzhydrol.

Acknowledgements:- We thank Dr. A. Duffield, Biomedical Mass Spectrometry Unit, The University of New South Wales, Australia for the mass spectra; the Director, CDRI Lucknow for the mass spectra and optical rotations; Dr. S. K. Sengupta, EIPW Calcutta also for the optical rotations, and the CSIR (New Delhi) and the University of North Bengal for financial support.

REFERENCES

1. S. P. Gunasekera and M. U. S. Sultanbawa, J. C. S. Perkin I, 483, 1977.
2. D. H. R. Barton, P. De Mayo and J. C. Orr, J.Chem.Soc., 2239,1958.
3. G. V. Baddeley, T. G. Halsall and E. R. H. Jones, J.Chem.Soc., 1173, 1964.
4. W. von E. Doering, G. Cortis and L. H. Knox, J.Am.Chem.Soc., 1700, 1947.
5. W. von E. Doering and T. C. Aschner, J.Am.Chem.Soc., 838, 1949.
6. J. Simonsen and W. C. J. Ross, "The Terpenes", Cambridge University Press, Vol. IV, 1957.
7. H. N. Khastgir, B. P. Pradhan, A. M. Duffield and L. J. Durham, Chem.Commun. 1217, 1967.
8. A. K. Ganguly, T. R. Govindachari, P. A. Mohamed, A. D. Rahimtulla and N. Viswanathan, Tetrahedron, 1513, 1966.
9. R. B. Woodward, N. L. Wendler and F. J. Brutschy, J.Am.Chem.Soc., 1425,1945.
10. O. Wintersteiner and W. L. Ruigh, J.Am.Chem.Soc., 1177, 1942.

Indian Journal of Chemistry
Vol. 26B, May 1987, pp. 462-464

APPENDIX - 2

Reaction of Cholesterol with Benzophenone in Presence of Potassium Hydroxide in Dimethyl Sulfoxide

BHIM PRASAD PRADHAN* & (Miss) TANDRA RAY
Department of Chemistry, University of North Bengal
P.O. North Bengal University, Dist. Darjeeling 734430
and
PETER WEYERSTAHL
Institut für Organiche Chemie, Technische Universitat, Berlin
D-1000 Berlin 12, West Germany

Indian Journal of Chemistry
Vol. 26B, May 1987, pp. 462-464

Reaction of Cholesterol with Benzophenone in Presence of Potassium Hydroxide in Dimethyl Sulfoxide

BHIM PRASAD PRADHAN* & (Miss) TANDRA RAY
Department of Chemistry, University of North Bengal
P.O. North Bengal University, Dist. Darjeeling 734430
and
PETER WEYERSTAHL
Institut für Organiche Chemie, Technische Universitat, Berlin
D-1000 Berlin 12, West Germany

Received 18 *July* 1986; *accepted* 24 *September* 1986

Reaction of cholesterol and benzophenone in the presence of Potassium hydroxide in anhydrous dimethyl sulfoxide (DMSO) results in the formation of cholesta-3, 5-diene (**1**) and cholesta-5, 7-dien-3, 6-diol benzophenide (**2**).

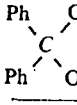
In a previous communication from our laboratory, Pradhan *et al.*[1] reported the reduction of triterpenoid ketones to isomeric alcohols and benzophenone to benzhydrol on treatment with KOH in diethyleneglycol. As the reaction involved a ketone and an alcohol we ventured to treat a mixture of cholesterol, an alcohol and benzophenone, a ketone, with KOH as the main initiator of the reaction in dimethyl sulfoxide (DMSO) as the aprotic solvent. The products obtained in this reaction have been fully characterised by spectral data.

Thus a mixture containing cholesterol (0.5 g), benzophenone (0.5 g) and KOH (3g) in DMSO (50 ml) was refluxed for 7 hr, cooled, poured into water and extracted with ether. The ether extract was washed with water, dried (Na_2SO_4) and concentrated to afford a residue (0.3 g) which was chromatographed over silica gel (15 g). Elution with petrol furnished compound **A** in the first four fractions (15 ml each). The column was further eluted with the same solvent and after rejecting two fractions (15 ml each), the next eight fractions (15 ml each) afforded compound **B**.

Compound (**A**) analysed for $C_{27}H_4$ (Found: C, 87.6; H, 12.0. $C_{27}H_{44}$ requires C, 88.0; H, 12.0%), m.p. 79-80°, $[\alpha]_D - 105°$. In its mass spectrun compound A exhibited peaks at *m/z* 358(M^+), 352, 260, 254, 247, 213, 111, 57 (base peak). Its IR spectrum was flat in the OH region while the olefinic double bonds appeared at 1655, 890, 850, 810, 740, 730, 625 cm^{-1}. Its UV spectrum displayed absorption at 234 nm (ε, 20,000), suggesting the presence of a heteroannular diene system in compound **A**. The compound **A** was finally identified as cholesta-3, 5-diene (**1**) by direct comparison (m.m.p, IR, PMR, mass) with an authentic sample prepared by Wolff-Kishner reduction of cholesta-3, 5-dien-7-one[2].

The compound (**B**) analysed for $C_{40}H_{52}O_2$ (Found: C, 85.2; H, 9.3. $C_{40}H_{52}O_2$ requires C, 85.1, H, 9.3%), m.p. 106-7° (from pet ether-acetone). Its mass spectrum showed the molecular ion peak at *m/z* 564(M^+) and other peaks at *m/z* 410, 395, 386, 372, 371, 370 (100%), 215 and 196. The appearance of λ_{max} at 268 nm (ε, 9000) in its UV spectrum was suggestive of the presence of a homoannular diene system. Its IR spectrum was flat in the OH and carbonyl regions but the peaks at 1640 (s) and 1220 (s) cm^{-1} were indicative

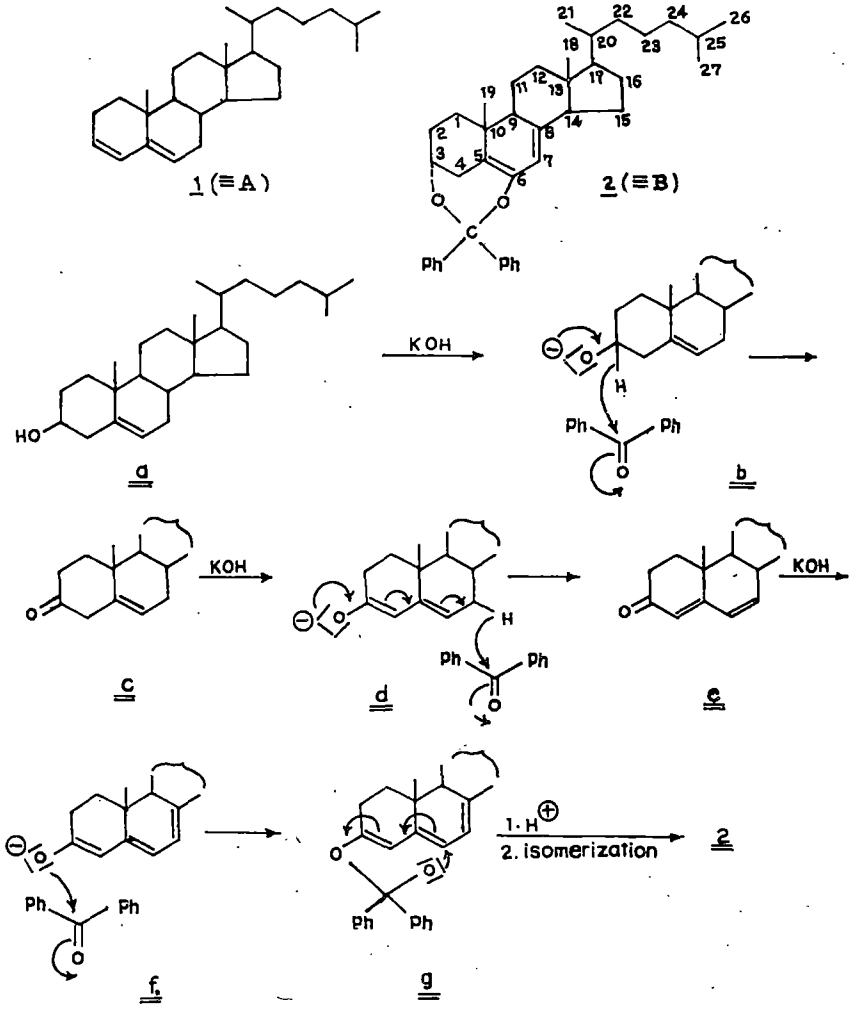
Table 1—Carbon-13 NMR Data of Compound **B**, Cholesta-5, 7-diene-3β-yl Acetate and Ergosteryl Acetate

Carbon No.	2	Cholesta-5,7-diene-3β-yl acetate[4]	Ergosteryl acetate[5]
1	37.1 *t*	38.4	37.9
2	28.8 *t*	28.5	26.1
3	82.6 *d*	72.9	72.7
4	37.1 *t*	37.1	36.6
5	137.9 *s*	138.8	138.3
6	126.3 *s*	120.7	120.0
7	144.1 *d*	117.0	116.2
8	141.1 *s*	141.3	141.2
9	50.1 *d*	46.5	46.0
10	36.7 *s*	37.5	37.1
11	21.0 *t*	21.4	25.1
12	39.4 *t*	39.7	39.0
13	42.3 *s*	43.3	42.8
14	56.2 *d*	54.8	54.5
15	24.3 *t*	23.3	23.0
16	28.2 *t*	28.5	28.1
17	56.8 *d*	56.5	55.7
18	11.9 *g*	12.1	12.1
19	18.7 *g*	16.3	16.1
20	35.8 *g*	36.6	40.4
21	19.4 *g*	19.2	19.7
22	36.2 *t*	36.6	135.4
23	23.8 *t*	24.3	131.8
24	39.8 *t*	39.9	42.8
25	28.0 *d*	28.3	33.0
26	22.6 *g*	22.8	20.0
27	22.8 *g*	23.0	21.1
28	—	—	17.7
Aromatic carbons (two Ph groups)	140.2(2*s*) 122.3 (1*d*) 126.2 (1*d*) 127.8 (*d*), 128.2(*d*) 128.5(*d*), 129.9(*d*)		
	120.0*s*		

of a vinyl ether linkage[3]; other peaks at 1140, 785, 780, 770, 715 and 710 (all sharp) cm^{-1} were indicative of the presence of benzene nucleus in (**B**).

PMR spectrum of **B** exhibited two singlets of three protons each at δ0.69 and 1.02; three doublets of three protons each at 0.86, 0.87 and 0.97 (J=7 Hz each) assignable to three secondary methyls; a one-proton quintet at 3.69 due to a proton geminal to ether linkage; a one-proton singlet at 6.50 due to an olefinic proton and a cluster of peaks between 7.2 and 7.45 integrating for ten protons due to two phenyl groups.

The ^{13}C NMR of **B** accounted for all the 40 carbons in its molecular framework. The attach proton test (APT) experiment indicated the existence of 5 quartets, 10 triplets, 17 doublets and 8 singlets (Table 1). The presence of only one signal (at 82.6 ppm) in the region 110 to 60 ppm showed that only one oxygen is attached to a sp^3-carbon having a geminal proton. The absence of a peak due to a carbonyl carbon indicated that the second oxygen is also in the form of an ether linkage which is probably attached to a sp^2-carbon. The carbonyl carbon of benzophenone appeared at 120.0 ppm as a singlet, with two oxygen atoms linked to it causing a downfield shift. The doublets at 127.8, 128.2, 128.5 and 129.9 ppm had heights double of those of other doublets at 122.4 and 126.2 ppm showing the presence of two phenyl groups with four pairs of protonated carbons in identical ironments, the last two being the *para*-carbons of the two phenyl rings. A comparison of the ^{13}C NMR signals of **B** with that of cholesta-5, 7-dien-3β-yl acetate[4] and ergesteryl acetate[5] (Table 1) indicated very close similarity, excepting the chemical shifts of carbons at C-6 and C-7. This observation confirmed the existence of a homoannular diene system in ring-B with an ether oxygen attached to the C-6 olefinic carbon in



Scheme 1

compound **B**. All the above facts lead us to assign structure (**2**) to compound (**B**) Dreiding model of **B** showed that a stable molecule is possible with ring-A in the twisted chain conformation with the ether oxygen α-orientated. The newly formed seven-membered ring is in the boat form.

The formation of **2** can be rationalised as follows (see Scheme 1). As suggested in the previous communication[1], potassium hydroxide forms an alkoxide with cholesterol which undergoes Oppenauer oxidation with benzophenone to give **C**. Repetition of the above process twice ultimately furnishes anion (**f**) which probably finds it easier to undergo nucleophilic addition to benzophenone (→**g**) followed by cyclization. Protonation and isomerization finally leads to **2**.

One of the authors (TR) is grateful to the University of North Bengal for financial assistance.

References

1 Pradhan B P, Hassan A & Ray T, *Tetrahedron*, **41** (1985) 2513.
2 Stavely H E & Bergmann W, *J Org Chem*, **1** (1937) 567, 575.
3 Silverstein R M, Bassler G C & Mortill T C, *Spectrometric identification of organic compound* (John Wiley, New York) 1981, 116.
4 Stothers J B & Blunt J W, *Org Magn Reson*, **9** (1977) 450.
5 Cushley R J & Filipenke J D, *Org Magn Reson*, **8** (1976) 30B.

Indian Journal of Chemistry
Vol. 27B, June 1988, pp. 592-593

APPENDIX - 3

Reaction of Acetophenone with Potassium Hydroxide in Diethylene Glycol

BHIM PRASAD PRADHAN* & (Miss) TANDRA RAY
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734 430

Received 6 *October*, 1986; *revised and accepted* 9 *November* 1987

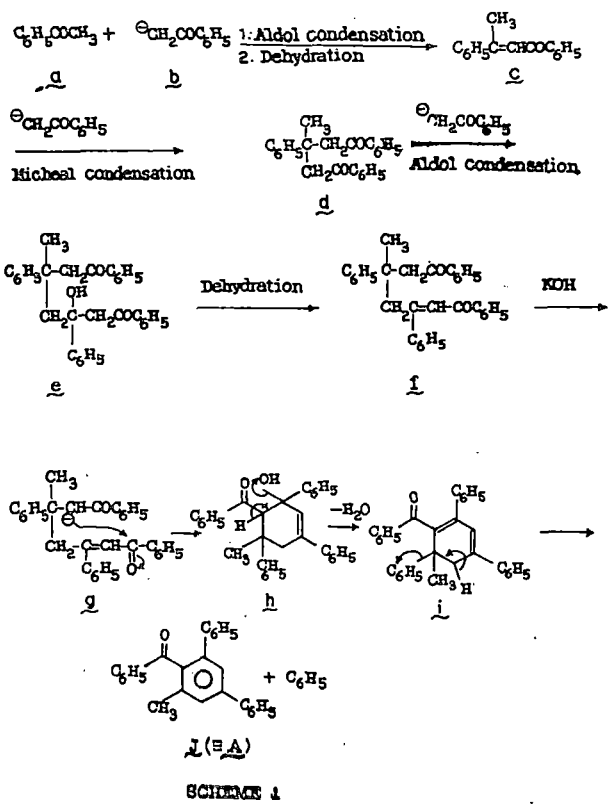
The reaction of acetophenone with potassium hydroxide in diethylene glycol under reflux furnishes 2-methyl-4, 6-diphenylbenzophenone (A).

In a previous communication[1] from this laboratory ketones with or without α,β-unsaturation were shown to furnish the saturated epimeric alcohols on reaction with potassium hydroxide in diethylene glycol. A reverse process of the reaction has also been reported[2] where cholesterol is oxidised to cholesta-3, 5-diene and cholesta-5, 7 -dinene-3, 6-diol-benzophenide on refluxing with potassium hydroxide in an aprotic solvent like dimethyl sulphoxide. In continuation of our study on the reductive effect of potassium hydroxide we ventured our attempt on an α,β-unsaturated ketone which is in conjugation with an aromatic ring. In order to prepare such a compound we took up acetophenone as an ideal starting material which is reported[3,4] to give 1, 3-diphenyl-2-buten-1-one under basic condition. The C-C double bond formed by Aldol condensation of acetophenone and subsequent dehydration is expected to be particularly stable as it is in conjugation with the aromatic ring. We report in this note the isolation of a product formed by condensation of acetophenone alone or with 1, 3-diphenyl-2-buten-1-one (c) on refluxing with potassium hydroxide in diethylene glycol.

The compound A obtained by refluxing a mixture of acetophenone and KOH in diethylene glycol (*vide infra*) was analysed for $C_{26}H_{20}O$. Its IR spectrum showed an absorption band at 1660 indicative of an α,β-unsaturated carbonyl group and the sharp peaks at 1280, 1270, 940, 880, 775, 760, 750, 720, 700 cm^{-1} due to aromatic nucleus. Its UV absorption at 245 nm with a high absorption coefficient (ϵ, 30,000) was typical of biphenyls[5]. Its mass spectrum exhibited the molecular ion peak at m/z 348 (M^+) with other peaks at m/z 271 ($M-C_6H_5$)$^+$, 242 ($M-C_6H_5CO$)$^+$, 228, 165 (171—C_6H_5)$^+$, 105 (C_6H_5CO)$^+$, and 77 (C_6H_5)$^+$.

The PMR spectrum of A showed a three proton singlet at δ 2.22 assignable to an aromatic methyl group and a cluster of peaks at 7.0-7.7 due to 17 aromatic protons. A combination of SFORD and B-B decoupled experiments of ^{13}C NMR showed the presence of a quarter centered at δ 19.7 due to the methyl carbon in an aromatic ring and doublets centered at 126.1, 127.1, 127.2, 127.6, 127.9, 127.95, (2C), 128.2 (2C,) 128.2 (2C), 129.1 (2C), 129.2 (2C), and 132.9 (2C) due to 17 protonated aromatic carbons. These data are in agreement with those of the PMR spectrum. The singlets at δ 135.7, 137.7, 137.75, 140.3 (2C), 140.6 and 141.8 indicated the presence of non-protonated aromatic carbons. Thus the total of 7 singlets and 17 doublets account for the presence of four benzene nuclei in A. The singlet at δ 199.5 was assignable to the carbonyl carbon. The m/z 105 peak in the mass spectrum indicated the carbonyl group to be attached to a phenyl group. The structure of A was finally arrived at by the mechanistic path-way as proposed in Scheme 1.

That the conversion of a and A proceeds via the formation of c and a when the reaction product did not contain c even in traces. The final product A is formed by elimination of benzene molecule from the intermediate i as indicated in Scheme 1. This was confirmed by collecting the distillate from the reaction mixture whose UV spectrum showed absorptions at 245, 149, 155 and 261 nm.



Preparation of 2-methyl-4, 6-diphenylbenzophenone (A)

(a) A mixture of acetophenone (1 ml) and KOH (3 g) in diethylene glycol (50 ml) was refluxed in a round bottomed flask initially without condenser. When the reaction temperature rose above 160° the condenser was fitted and the mixture refluxed for 2 hr. It was cooled, diluted with water and extracted with ether. The ether layer was washed with water, dil. HCl and finally with water till neutral, dried (Na_2SO_4) and the solvent removed. The residue (0.5 g) was chromatographed over silica gel (25 g) column. Elution with petrol afforded A as a solid (0.2 g) which was crystallised from $CHCl_3$-MeOH, m.p. 185-86° (Found: C, 89.7; H, 5.7. $C_{26}H_{20}O$ requires C, 89.6; H, 5.8%).

(b) A mixture of 1, 3-diphenyl-2-buten-1-one (c, 1 ml), acetophenone (a, 1 g) and KOH (3 g) in diethylene glycol (50 ml) was refluxed for 2 hr and worked-up as described above. The residue (0.9 g) was adsorbed over silica gel (50 g) column and eluted with petrol to furnish A, m.p. 185-86° ($CHCl_3$-MeOH). It was identical (m.m.p. and co-IR) with A prepared from acetophenone only as mentioned above.

The authors are thankful to the Director, CDRI, Lucknow for elemental analysis and spectral data. One of them (T R) is grateful to the University of North Bengal for the award of a senior research fellowship.

References

1 Pradhan B P, Hassan A & Ray T, *Tetrahedron*, **41** (1985), 2513.
2 Pradhan B P, Ray T & Weyerstahl P, *Indian J Chem*, **26B** (1987), 462.
3 Fieser L F & Fieser M, *Advanced organic chemistry*, (Asia Publishing House, New Delhi) 1961, 835.
4 Morrison R T & Boyd R N, *Organic chemistry*, 4th edition (Allyn & Bacon Inc, Boston) 1983, 870.
5 Silverstein R M, Bassler G C & Morrill T C, *Spectrometric identification of organic compounds*, 4th edition (John Wiley & Sons, New York) 1981, 322.

Indian Journal of Chemistry
Vol. 27B, September 1988, pp. 846-848

APPENDIX - 4

Action of N-Bromosuccinimide on Cholesteryl Acetate in Dimethyl Sulfoxide

BHIM PRASAD PRADHAN* & (Miss) TANDRA RAY
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734430
and
BIMAL PRASAD SHARMA†
The University of New South Wales, P.O. Box 1, Kensington NSW 2033, Australia

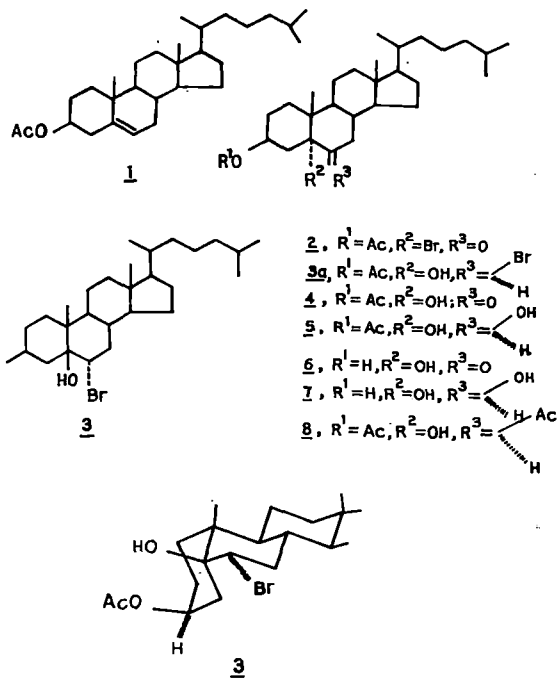
Received 6 July, revised and accepted 22 December 1987

Cholesteryl acetate (**1**) on oxidation with NBS in DMSO furnishes six different compounds which have been identified as 5α-bromo-6-keto-cholestan-3β-yl acetate (**2**), 6α-bromo-5β-hydroxycoprostan-3β-yl acetate (**3**), 5α-hydroxy-6-keto-cholestan-3β-yl acetate (**4**), 5α,6β-dihydroxycholestan-3β-yl acetate (**5**), 3β,5α-dihydroxycholestan-6-one (**6**) and cholestane-3β,5α,6β-triol (**7**) by chemical studies and spectral (IR, mass, PMR and ^{13}CNMR) data. Compound **3** is perhaps reported for the first time.

The action of NBS on cholesteryl acetate (**1**) or benzoate has been studied well in various solvents. Recently, in the reaction of NBS with methyl acetylbetulenate using DMSO as solvent it has been shown that allylic bromination of the isopropyl group takes place by bromonium ion attack to afford a dibromo compound[1]. We became interested to examine the nature of the products of **1** where the double bond could easily be attacked by a bromonium ion. The isolation and characterization of the various products formed in the reaction of **1** with NBS in DMSO are described in this note. The products which were separated by chromatography and purified by crystallisation were designated as **A, B, C, D, E** and **F**.

Compound **A** which analysed for $C_{29}H_{47}O_3Br$, m.p. 164°, $[\alpha]_D$ −130° was identified as 5α-bromo-6-ketocholestan-3β-yl acetate (**2**) on the basis of spectral data (IR, PMR, ^{13}CNMR and mass). Its CMR data were identical with those reported in literature[2].

Compound **B** (major product) analysed for $C_{29}H_{49}O_3Br$, m.p. 125°, $[\alpha]_D$ +12.4°; showed the mass fragments at *m/z* 509, 507 $(MH-H_2O)^+$, 465, 449 $(509-AcOH)^+$, 447 $(507-AcOH)^+$, 429 $(509-HBr)^+$, 427 $(507-HBr)^+$, 407, 385, 367, 285, 257, 229, 201 and 149 (base); responded to Beilstein test for halogen. Its IR spectrum showed the presence of a hydroxyl group as indicated by a sharp peak at 3410 cm^{-1} and an acetyl group)1710 and 1265 cm^{-1}). Absence of an olefinic double bond was indicated by negative TNM test. Resistance to oxidation with CrO_3-Py complex suggested the hydroxyl group to be at tertiary position (C-5). Attempts to acetylate **B** with Ac_2O-Py regenerated **1** in 100% yield suggesting that the two leaving groups (OH and Br) were in *trans*-disposition. The structure of **B** was derived from a close study of its PMR spectrum which exhibited three doublets centered at δ 0.85, 0.86 and 0.88 each integrating for three protons with the same coupling constant (J = 6.5 Hz) for the three secondary methyls, two singlets at 0.64 and 0.99 for two tertiary methyls and a singlet at 2.09 for the acetoxy methyl at C-3. However, the heptet due to the methine proton at C-3 in **1** vanished in the spectrum of **B** and instead a singlet like one-proton peak with a $W_{\frac{1}{2}}$ of 5 Hz appeared at δ 5.3. There appeared two additional peaks: one sharp singlet for a single proton that shifted its position from δ 3.02 to 4.81 on D_2O exchange was due to the hydroxyl proton and a double doublet centered at 4.53 with coupling constant of 14 and 5 Hz was assignable to an axially oriented proton having one axial and one equatorial neighbouring protons. Considering this proton



†Present address: M.M.A. Campus, Biratnagar, Nepal.

to be located at C-6, the bromine atom that may cause sufficient downfield shift should be equatorially oriented, but the stereochemistry of the hydroxyl group at C-5 could be either above or below the plane. The singlet like peak at δ 5.3 if considered to be due to C-3 methine proton suggests the acetoxy group to be axially oriented[3] in **B**. Such a change in stereochemistry at C-3 could be possible only if A/B ring junction is *cis*-fused (a coprostan derivative). This was found to be true from the mechanistic point of view (*vide infra*). The ^{13}CNMR spectrum of **B** exhibited 29 peaks and the APT experiment[4] showed the presence of six methyl carbons, including the acetoxy methyl, ten methylene carbons, eight methine carbons and four quarternary carbons (as quartets, triplets, doublets and singlets respectively). A comparison of the ^{13}CNMR data of with those of the previously known compound, 6β-bromo-5α-hydroxycholestan-3β-yl acetate[2] (**3a**), showed sharp differences for the carbons C-5 and C-6 (δ 75.1 and 62.4 in **B** and 76.1 and 56.4 in **3a** for C-5 and C-6 respectively) (Table 1), indicating different environments of the two carbons in **B** and **3a**. Thus compound **B** was assigned the structure **3** as 6α-bromo-5β-hydroxy-coprostan-3β-yl acetate. This is perhaps the first report on the formation of **3**.

Compound **C** analysed for $C_{29}H_{48}O_4$, m.p. 232-33°; $[\alpha]_D$ −56°; CD, −315 nm. Its IR spectrum showed the presence of a hydroxyl group (3380 cm^{-1}), an acetoxyl group (1735, 1280-1240 cm^{-1}), and a six-membered ring ketone (1707 cm^{-1}); MS: *m/z* 460 (M^+). PMR spectral analysis showed it to be 5α-hydroxy-6-keto-cholest-3β-yl acetate (**4**) which was further confirmed by its ^{13}CNMR spectra data (Table 1).

Compound **D** analysed for $C_{29}H_5O_4$, m.p. 205-6°, $[\alpha]_D$ −16°; TNM test showed the absence of olefinic double bond; IR spectrum displayed two hydroxyl peaks (3440 and 3390 cm^{-1}) and an acetoxyl peaks (1730-1710 br and 1290-1250 cm^{-1});MS: *m/z* 462 (M^+), 443, 385 (base) PMR spectral data led to the structure of **D** as 5α,6β-dihydroxycholestan-3β-yl acetate (**5**), the ^{13}CNMR spectrum of which was in consonance with that reported[2] for **5**. It was further confirmed by the conversion of **D** into 5α-hydroxycholestan-3β,6β-diyl acetate[5] (**8**) by treatment with Ac_2O-Py.

Compound **E**, $C_{27}H_{46}O_3$, m.p. 228-29°, $[\alpha]_D$ +28°; IR: 3500-3260 (br, OH), 1710 cm^{-1} (C=O); MS: *m/z* 398 $(M-H_2O)^+$, 380, 317; was identified as 6-keto-cholestane-3β,5α-diol[5] (**6**) by spectral data (PMR and ^{13}CNMR) and the preparation of its acetate (Ac_2O-Py) identical with **C**.

Table 1 – ^{13}CNMR Spectral Data (δ, ppm) of Compounds **B**, **C**, **E**, and **F** and Comparison of the Data of **B** (**3**) with those of Isomeric **3a**.

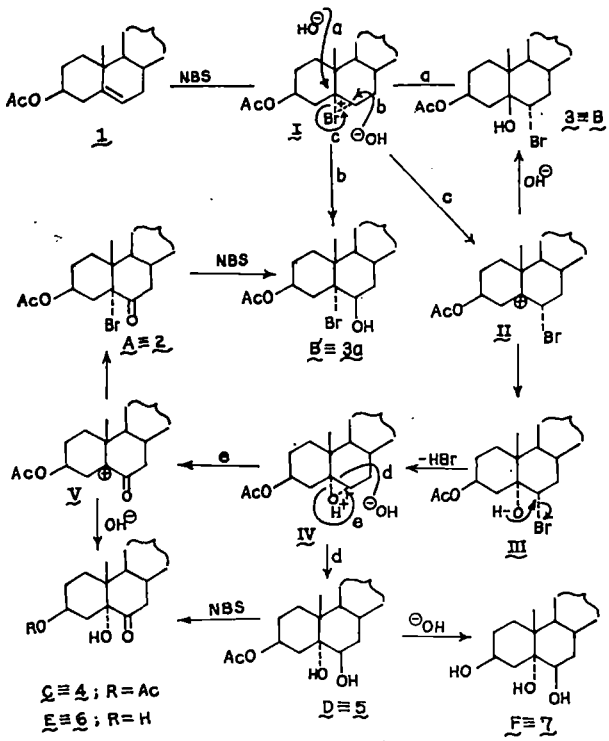
Carbon	B (3)	3a[2]	C (4)	E (6)	F (7)*
1	31.8	32.9	29.5	36.4	30.3(32.5)
2	26.6	26.6	26.3	29.9	31.0(33.4)
3	70.5	71.5	70.7	67.3	67.7(67.6)
4	39.5	30.1	37.3	37.4	40.9(42.1)
5	75.1	76.1	80.3	80.8	75.8(76.0)
6	62.4	56.4	212.3	212.4	76.2(76.3)
7	39.5	36.4	41.8	41.8	34.7(35.8)
8	36.8	30.6	32.5	30.5	32.5(31.3)
9	42.9	45.1	44.3	44.6	46.0(46.0)
10	43.2	39.4	42.5	42.5	38.4(39.2)
11	21.6	21.2	21.4	21.5	21.3(22.0)
12	40.4	40.0	39.5	39.7	40.1(40.8)
13	42.7	42.8	43.1	43.2	42.9(43.2)
14	56.1	55.3	56.3	56.5	56.0(56.8)
15	24.0	24.1	23.9	23.9	24.2(24.7)
16	28.1	28.3	28.0	28.1	28.3(28.7)
17	56.1	56.5	56.2	56.3	56.4(56.8)
18	12.0	12.2	12.1	12.1	12.2(12.6)
19	16.7	19.0	13.9	14.2	16.9(17.3)
20	35.7	35.9	35.7	35.8	35.9(36.3)
21	18.6	18.7	18.7	18.7	18.7(19.2)
22	36.1	36.3	36.1	36.2	36.3(36.6)
23	23.8	24.1	23.9	23.9	23.9(24.4)
24	39.7	39.5	39.5	39.5	39.6(39.9)
25	28.0	28.0	28.0	28.1	28.0(28.4)
26	22.6	22.6	22.6	22.6	22.6(22.9)
27	22.8	22.8	22.8	22.8	22.8(22.9)
$-OCOCH_3$	21.4	21.4	21.4		
$-OCOCH_3$	171.0		171.0		

*Literature[2] values are given in parentheses.

Compound **F** analysed for $C_{27}H_{48}O_3$, m.p. 238°, $[\alpha]_D$ +4.6°; gave TNM test for an olefinic double bond; IR: 3422-3340 cm^{-1} (OH); MS: (CI/CH_4): *m/z* 419 $(MH)^+$, 403, 401, 385, 367. PMR spectral analysis showed it to be cholestane-3β,5α,6β-triol (**7**) and its ^{13}CNMR data were very close to those of reported[2] for **7**.

Mechanism

It is very interesting to observe that there are only two products (**A** and **B**) that contain one bromine atom each below the plane (alpha). This suggests that the bromonium ion (Br^+) initially attacks the double bond from the less hindered α-side to form an intermediate three-membered ring cation (I) which can be attacked by HO^- ion either at C-5 or C-6 from above the plane to yield either **B** or the isomeric **B'**. The latter (**B'**) is perhaps susceptible to NBS oxidation to form **A**. The cation I can also open-up to generate carbonium



Scheme 1

ion at C-5 (II) that combines with HO^- ion from the rare position to form a *cis*-bromo-hydroxy derivative(III). The hydroxyl group in III is well poised for $S_{N}2$ neighbouring group participation to afford the epoxide intermediate IV which under the reaction condition opens-up in two ways to furnish either the *trans*diol **D** or the oxo-carbonium ion V to be attacked either by bromide ion to form **A** or by the hydroxide ion to form **C**. Oxidation of **D** by NBS yields **C**, and hydrolysis of **C** and **D** under the reaction condition furnishes **E** and **F** respectively (Scheme 1).

It is noteworthy to mention here that no allylic bromination takes place in this oxidation.

Melting points reported are uncorrected. Petrol used had b.p. 60-80°. PMR spectra were recorded in $CDCl_3$ on a Bruker WH-400 instrument and ^{13}CNMR spectra (off resonance, DEPT programme) in $CDCl_3$ on a Bruker WH-270 or a Varian CFT-20 spectrophotometer using TMS as internal standard (chemical shifts in δ, ppm), IR spectra in nujol on a Beckman IR-20 instrument and mass spectra on a Varian-Mat-711 or a JMS 300-D instrument at 70eV. Silica gel (BDH 60-120 mesh) was used for column chromatography.

Treatment of cholesteryl acetate (**1**) *with NBS in DMSO*

A solution of **1** (3 g) in $CHCl_3$ (150 ml) was mixed with DMSO (75 ml) and the solution cooled to 20°, NBS (3.5 g) added to it in small lots in order to keep the temperature below 25° and the mixture kept in the dark dor 13 days. It was extracted with $CHCl_3$ and the extract washed several times with water, dried (Na_2SO_4) and solvent removed under reduced pressure. The residue (3 g) was chromatographed over silica gel (75 g). Elution with solvents of increasing polarity furnished **A** [0.2 g, petrol-benzene (3:2)], **B** [0.7 g, petrol-benzene (2:3)], **C** [0.3 g, petrol-benzene (1:4)], **D** [0.3 g, petrol-benzene (1:4)], **D** (0.2 g, benzene), **E** [0.35 g, benzene-ethyl acetate (2:3)] and **F** (0.25 g, ethyl acetate).

Compound **B**: *6α-bromo-5β-hydroxy-cholestan-3β-yl acetate* (**3**)

IR: 3410 (OH), 1710, 1265 ($-OCOCH_3$), 1180, 1110, 1050, 1010, 840, 800, 730 cm^{-1}; MS: *m/z* 509 ($M_1H^+ - H_2O$)*, 507 ($M_2H^+ - H_2O$)*, 406(0.2), 445 (5), 429 (0.5), 407 (0.4), 385 (7), 367 (4.6), 285 (15), 257 (95), 229 (20), 201 (18) and 149 (100) (Found: C, 58.8; H, 8.6. $C_{29}H_{49}O_3Br$ requires: C, 58.8; H, 8.9%).

The authors are thankful to Prof. D St C Black, University of New South Wales, Australia, Prof. T A Hase, University of Helsinki, Finland and Prof. P Weyerstahl, Institut für Organische Chemie, Technische Universität, Berlin, West Germany for spectral data. One of them (T R) is grateful to the University of North Bengal for the award of a senior research fellowship.

References

1 Pradhan B P, Mukherjee M M, Chakraborti D K & Shoolery J N, *Indian J Chem*, **22B** (1983) 12.

2 Stothers J B & Blunt J W, *Org Magn Reson*, **42** (1977) 450.

3 Bhacca N S & Williams D H, *Application of NMR spectroscopy in organic chemistry* (Holden-Day Inc, Sanfrancisco) 1964.

4 (a) Cocq L & Lallemend J-Y, *Chem Commun*, (1981) 150.
(b) Shoolery J N & Patt S, *J Magn Reson*, (1982) 535.

5 Fieser L F & Fieser M, *Steroids*, (Asian Publishing House, Bombay) 1962.

*M_1H^+ and M_2H^+ refer to the protonated molecular ions with bromine atoms of atomic masses 81 and 79 respectively.

Indian Journal of Chemistry
Vol. 27B, February 1988, pp. 105-108

APPENDIX - 5

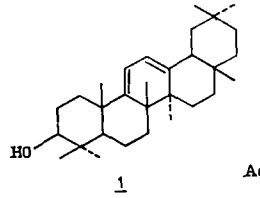
Action of Lithium/Ethylenediamine Reagent on Triterpenoid Conjugated Dienes

BHIM PRASAD PRADHAN*, SATYAJIT CHAKRABORTY & (Miss) TANDRA RAY
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734 430
and
PETER WEYERSTAHL
Institut fur Organische Chemie, Technische Universitat Berlin, D-1000 Berlin 12, West Germany

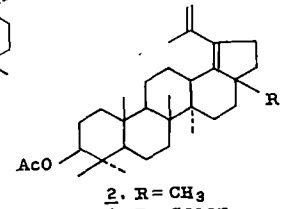
Received 25 *May* 1987; *accepted* 7 *September* 1987

The reaction of lithium in ethylenediamine (EDA) with olean-9(11), 12(13)-dien-3β-ol (**1**) results in the recovery of starting **1** while similar reaction on lup-18(19), 20(29)-dien-3β-yl acetate (**2**) furnishes lup-18(19)-en-3β-ol (**4**). Lithium in EDA reacts with methyl lup-18(19), 20(29)-dien-28-oate-3β-yl acetate (**3**) to afford 28-nor-lup-17(18)-en-3β-ol (**5a**), lup-18(19)-en-3β, 28-diol (**4a**), lupan-28-oic acid (**6**) and lup-18(19)-en-3β-ol-28-oic acid (**4c**). **4** on isomerization with HCl-AcOH furnishes lup-13(18)-en-3β-yl acetate (**7**) whereas **4c** furnishes lup-28 → 19β-olide-3β-yl acetate (**9**) and the acetate derivative (**4g**) of the unisomerized **4c**.

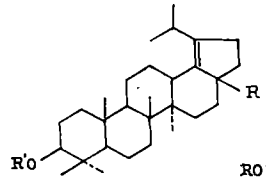
In our studies[1,2] on the action of lithium in ethylenediamine (EDA) on triterpenoids, it was observed[2] that the reduction of double bond in conjugated keto –ene system is dependent on the sterical environment. In order to see if conjugated diene systems would also respond differently to the reagent, we have presently studied the reaction of this reagent on conjugated dienes where one of the double bonds is tetrasubstituted and the other exocyclic, viz. lup-18(19), 20(29)-dien-3β-yl acetate (**2**) and lup-18(19), 20(29)-dien-28-carbomethoxy-3β-yl acetate (**3**). The reaction of this reagent on olean-9(11),12(13)-dien-3β-ol(**1**), resulted in the recovery of the starting **1**. This showed that when double bonds are tetrasubstituted at 1,4-position of a homoannular diene then no reduction of double bond occurs, probably due to steric factors.

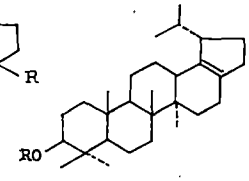


1



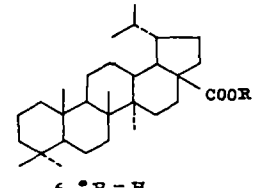
2, R = CH_3
3, R = $COOCH_3$





5a, R = H
5b, R = Ac

4, R = CH_3, R' = H
4a, R = CH_2OH, R' = H
4b, R = CH_2OAc, R = Ac
4c, R = COOH, R' = H
4d, R = CH_3, R' = Ac
4e, R = $COOCH_3$, R' = Ac
4f, R = $COOCH_3$, R' = H
4g, R = COOH, R' = Ac



6, R = H
6a, R = CH_3

It has been reported[3] that the heteroannular dienes where both the double bonds are trisubstituted readily produce tetrasubstituted mono-ene derivatives on reduction with Li-EDA.

Compound **2**[4-6] on reduction with Li-EDA furnished a solid after usual work-up and chromatography. It analysed for $C_{30}H_{50}O$ and on acetylation (Ac_2O/Py) furnished an acetate, $C_{32}H_{52}O_2$. The PMR spectrum of the acetate was indicative of the presence of six tertiary methyls, two secondary methyls, one acetoxymethyl and a C-3 methine proton geminal to acetoxy methyl. The presence of two secondary methyls indicated that the isopropenyl group in **2** has undergone reduction. Carbon-13 NMR of the acetate displayed two singlets downfield at δ 138.68 and 139.39 suggesting that the tetrasubstituted double bond has remained intact during the reduction. Thus the compound has been identified as lup-18(19)-en-3β-yl acetate (**4d**) and hence the corresponding alcohol as lup-18(19)-en-3β-ol (**4**).

Compound **3**[6,7] on similar treatment furnished after work-up and chromatography a compound in petrol-benzene (4:1) eluate which has been characterised as **5a** based on elemental analyses and spectral data. The appearance of two singlets at δ132.52 and

138.68 in ^{13}C NMR suggested that the double bond in **3** was no longer C-18(19) position. Acetylation of **5a** furnished an acetate, which was identical with 28-nor-lup-17(18)-en-3β-yl acetate[8] (**5b**).

The second compound that appeared in petrol-benzene (1:4) eluate could be likewise characterised as **6**. It afforded an ester on treatment with ethereal diazomethane, identical with methyl dihydrobetulanate[9] (**6a**). Thus the parent acid is lupan-28-oic acid (**6**).

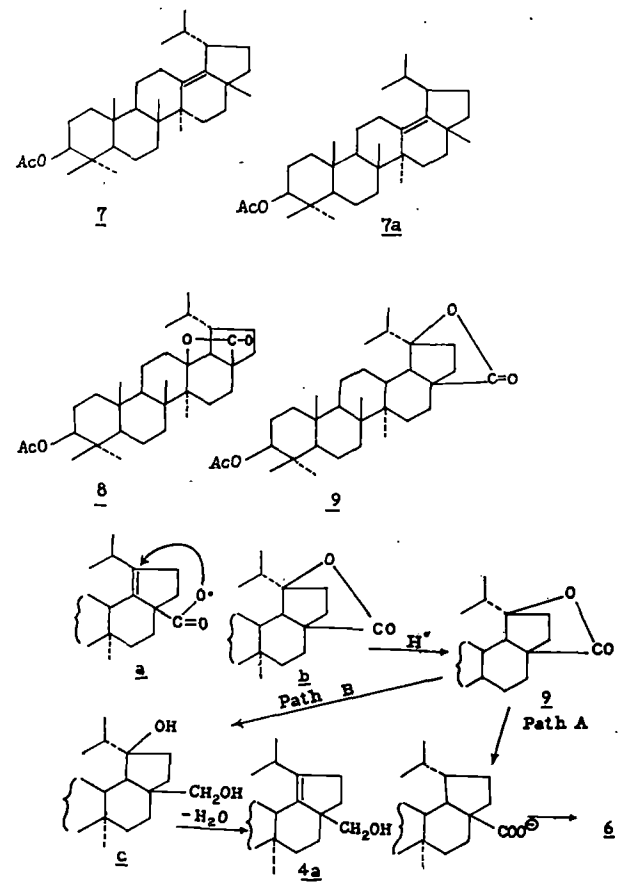
The third compound that was eluted by benzene-ethyl acetate (9:1) was characterised (IR, mass, PMR) as lup-18(19)-en-3β, 28-diol (**4a**). Further confirmation of the structure was provided by forming an acetate, which was identical with authentic lup-18(19)-en-3β, 28-diol (**4a**). Further confirmation of the structure was provided by forming an acetate, which was identical with authentic lup-18(19)-en-3β, 28-diol (**4b**).

The fourth compound that was eluted by benzene-ethyl acetate (4:1) was established as lup-18(19)-en-3β-ol-28-oic acid (**4c**) by its spectral data and by preparation of its acetate derivative which was found identical with methyl 3β-acetoxy lup-18(19)-en-28-oate (**4e**).

Thus from the above observations it is quite evident that only the isopropenyl group is easily reduced by Li-EDA as reported earlier[1]. But the formation of **6** and **4a**, though in small amounts, may be explained by assuming that the carboxylate radical (*a*) formed during reduction was converted into lactone (*b*) which then underwent cleavage by two different paths (A)[10] and (B)[11] giving the saturated carboxylic acid (**6**) and the triol (*c*). The OH group in (*c*) at C-19 underwent dehydration to furnish the diol (**4a**) (Scheme 1).

As there is no report of the isomerization of 18-19 double bond to 13-18 position, we attempted the isomerization of **4** and **4c** with conc. HCl and glacial acetic acid under refluxing condition. The reaction mixture from **4** after purification and crystallisation furnished a crystalline solid which was found to be an acetate (IR) different from **4d**. A detailed analysis of its PMR spectrum and its melting point showed that it was not the neolup-13(18)-en-3β-yl acetate (**7a**) prepared from lupenyl acetate[12]. This compound was designated as lup-13(18)-en-3β-yl acetate (**7**) where the stereochemistry of isopropyl group is alpha.

Similar isomerization of **4c**, which was envisaged to end up in the formation of 13-28 lactone derivative, led to a lactone identical with lup-28 → 19β-olide-3β-yl acetate (**9**) and an acid which gave an ester (diazomethane) identical with methyl 3β-acetyl lup-18(19)-en-28-oate (**4e**).



Scheme 1

Experimental Procedure

Melting points reported are uncorrected. Petrol used had b.p. 60-80°. PMR spectra were recorded in $CDCl_3$ on Bruker WH-400 instrument (Chemical shifts downfield from TMS internal reference), IR spectra in nujol on a Beckman IR-20 instrument and mass spectra on Varian mat 711 and JMS 300-D instrument at 70 eV. Silica gel was used for column chromatography.

Reduction of lup-18(19), 20(29)-*dien*-3β-yl acetate (**2**)

To a solution of **2** (0.4 g) in ethylenediamine (100 ml), Li metal (0.4g) was added in small pieces at intervals and the mixture was refluxed for 2 hr under N_2 blanket. After usual work-up, the residue (0.35g) was chromatographed over silica gel (10g). Elution with petrol-benzene (3:2) afforded a solid which crystallised from $CHCl_3$ – MeOH to furnish needle shaped crystals of **4**, m.p. 220-22°; IR: 3400-3450 cm^{-1}; yellow colour with TNM (Found: C, 87.7; H, 12.1. $C_{30}H_{50}O$ requires C, 87.7; H, 12.3%). It afforded acetate (**4d**) with Ac_2O-Py, m.p. 236-38°; IR: 1740, 1250 cm^{-1}; MS: *m/z* 468 (M^+). **4d** was found to be

identical with the product obtained by hydrogenation of **2** over Adams catalyst[5,6].

Reduction of methyl 3β-*acetoxy lup*-18(19), 20(29)-*en*-28-*oate* (**3**)

A solution of **3** (1g) dissolved in ethylenediamine (200 ml) was treated with Li metal (1g) in small pieces at intervals and the mixture refluxed for 2 hr under N_2 atmosphere. The residue (1g) obtained after usual work-up was chromatographed over silica gel (25g). Petrol-benzene (4:1) eluted **5a** (0.1g), m.p. 186-87°; IR 3400 cm^{-1}; yellow colour with TNM,; MS: *m/z* 412 (M^+); PMR ($CDCl_3$): δ0.6545 and 0.8851 (2*d*, 6H, 2× sec. CH_3, *J*=7 Hz), 0.7770, 0.8654, 0.8675, 0.9768 (4*s*, 5Xt—CH_3, 15H); 3.210 (*dd*, 1H, *H*—C—3—OH, *J*= 5, 11 Hz); ^{13}C NMR ($CDCl_3$):138.68 (*s*), 132.52 (*s*), 79.00 (*d*) and 24 other peaks in the region 56-13 ppm (Found: C, 84.3; H, 11.6. $C_{29}H_{48}O$ requires C, 84.4; H, 11.7%). **5a** (0.03g) with Ac_2O (1 ml) and pyridine (1 ml) furnished **5b**, m.p. 210-11°, identical with an authentic sample[8] (m.m.p). Elution of the column with petrol-benzene (1:4) afforded **6** (0.1 g) which crystallised from $CHCl_3$—MeOH, m.p. 290-92°; IR: 3300-2900, 1690 (−COOH) cm^{-1}; MS (CI-isobutane): *m/z* 442 (M^+), 395, 338, 279, 249, 205, 191, 117, 75; no colour with TNM. **6** in ether on treatment with CH_2N_2 formed the methyl ester (**6a**), m.p. 165-66°, identical (m.m.p) with methyl dihydrobetulanate (**6a**)[9].

Further elution of the column with benzeneethylacetate (9:1) yielded **4a** (0.1g), m.p. 28-09°; IR: 3320-3200 cm^{-1}; with TNM it developed yellow colouration; MS (CI): *m/z* 443 (M^+ + H), 425, 233, 197, 191, 177; MS (EI), *m/z* 411 (M^+—CH_2OH), 203, 189, 135, 95, 81, 69, 55 (base) (Found: C, 81.1; H, 11.2. $C_{30}H_{50}O_2$ requires C, 81.3; 11.4%). It formed the diacetate (**4b**), m.p. 205-07°; $[\alpha]_D$-13°; IR: 1735-1725, 1250, 1240 cm^{-1}.

Further elution of the column with benzene-ethyl acetate (4:1) furnished the acid (**4c**) with crystallised from $CHCl_3$—MeOH, m.p. 275-77°; IR: 3500-3400, 1710 cm^{-1} (Found: C, 78.8; H, 10.5. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%). **4c** on treatment with CH_2N_2 gave the ester (**4f**), m.p. 198-200°; IR: 3450, 1730 cm^{-1}; MS: *m/z* 470 (M^+); ^{13}C NMR ($CDCl_3$): 178.33 (*s*, COOMe), 144.33 (*s*, C−18), 134.28 (*s*, C-19), 79.00 (*d*, *C*−3−OH) and 27 other peaks between 61 and 14 ppm. Ac_2O—Py treatment of **4f** after usual work-up furnished ester acetate (**4e**), m.p. 214-15°; IR: 1740, 1730, 1250 cm^{-1}, identical (m.m.p. and co-IR) with the product obtained by hydrogenation of **3** Over Adams Catalyst[6,7].

Acid isomerization of lup-18(19-*en*-3β-ol (**4**): *Formation of lup*-13(18)-*en*-3β-*yl acetate* (**7**)

A solution of **4** (250 mg) in AcOH (200 ml) was refluxed with conc. HCl (5 ml) for 3 hr. The mixture was cooled, diluted with ice cold water and filtered. The residue was thoroughly washed with water and chromatographed over silica gel (10g). Petrol-benzene (4:1) eluted **7** (2.2g) which crystallised from $CHCl_3$—MeOH, m.p. 214-15°; IR: 1740, 1250 cm^{-1}; yellow colour with TNM; MS: *m/z* 468 (M^+); 453, 426, 408, 393, 249, 218, 205, 204, 203, 189; PMR ($CDCl_3$): 0.86 (6H, *d*, *J*=7 Hz, 2× s—CH_3), 0.853, 0.8675, 0.875, 0.91, 0.9675, 1.0825 (5*s*, 15H, 5×*t*—CH_3), 2.0425 (*s*, 3H, COCCH_3), 2.376 (*dd*, 10, 2 Hz, 1H, C-12-H), 2.4725 (*ABq*, *J*= 8 Hz, 1H, C—19—H), 4.5 (*m*, 1H, *H*—C—O—$COCH_3$); ^{13}C NMR: δ170.97 (*s*, —O*C*OCH_3), 141.12 (*s*, *C*-13), 133.37 (*s*, *C*-18), 80.95 (*d*, *C*—C—OCO) and 26 other peaks between 56 and 16 ppm.

HCL-AcOH treatment of lup-18(19)-*en*-3β-*ol*-28-*oic acid* (**4c**): *Formation of lactone* (**9**)

A solution of **4c** (0.5 g) in AcOH (200 ml) was refluxed with conc. HCl (6 ml) for 4 hr. The mixture was cooled, diluted with ice cold water and filtered. The residue was washed with water, dried (0.5g) and chromatographed over silica gel (15 g). Petrol-benzene (2:3) eluted **9** (0.4g), m.p. 299-300°; IR: 1770, 1725, 1245 cm^{-1}; with TNM it did not develop colouration; MS: *m/z* 498 (M^+, 2), 470 (M^+—CO, 38), 438(90), 411, 395, 351, 327, 261, 206, 205, 202 (78), 189 (base), 135; PMR ($CDCl_3$): δ0.825, 0.8375, 0.85, 0.87, 0.94 (5*s*, 15H, 5×*t*—CH_3), 0.934, 1.063 (2*d*, 6H, *J*=7 Hz each, 2× S−CH_3), 2.037 (*s*, 3H, O—$COCH_3$), 2.2875 (*heptet*, 1H, C—20—H), 4.455 (*m*, 1H, H—C—3—OCO—); ^{13}C NMR: δ179.71 (*s*, γ-lactone *C*-20), 170.94 (*s*, —O*C*OCH_3), 95.84 (*s*, O—C—19), 80.77 (d, H—*C*—3—O) and 28 other peaks in the region 56 to 13 ppm. It was found identical (m.m.p., co-IR) with authentic sample of **9** prepared by hydrogenation of 3β-acetyl lup-20(29)-en-28→19β olide[6] Over Adam's Catalyst. Further elution of the column with petrol-benzene (1:4) furnished **4g** (0.05g), m.p. 293-94°; IR: 3250-2900, 1735, 1690, 1245 cm^{-1}; MS: *m/z* 498 (M^+, 68), 452, 438, 392(66), 351(54), 234, 190(84), 189 (base); PMR ($CDCl_3$): δ0.8325, 0.845, 0.8879, 0.9125, 1.0 (5*s*, 15H, 5×*t*—CH_3), 0.9775, 1.025 (2*d*, *J*=7 Hz each, 6H, 2×*s*—CH_3), 2.05 (*s*, 3H, $OCOCH_3$), 3.1758 (*heptet*, 1H, C-20-H), 4.48 (*m*, 1H, H—C—3—O); ^{13}C NMR ($CDCl_3$): δ181.25 (*s*, *C*-28-OOH), 145.17 (*s*, C-18), 133.61 (*s*, —C—19); 80.91 (*d*, C—3—O), 171.04 (*s*, $OCOCH_3$) and 28 other peaks between 61 and 15 ppm.

9 on esterification with CH_2N_2 formed the ester acetate (**4e**), m.p. 213-14°; IR: 1740, 1730, 1250 cm^{-1}, identical with an authentic sample of **4e** obtained by hydrogenation of **3**.

Acknowledgement

One of us (SC) is grateful to the CSIR, New Delhi for the award of a senior research fellowship.

References

1 Pradhan B P, Chakrabarti D K & Chakraborty S, *Indian J Chem*, **23B** (1984) 1115.
2 Pradhan B P & Chakraborty S, *Indian J Chem*, **26B** (1987) 263.
3 Sengupta P, Sen M & Rao S N, *Indian J Chem*, **16B** (1978) 738.
4 Biedebach F, *Arch Pharm*, **281** (1943) 49.
5 Baddeley G V, Simes J J H & Watson T G, *Tetrahedron*, **26** (1970) 3795.
6 Adhikary S P, Lawrie W & McLean J, *J chem Soc (C)*, (1970) 1030.
7 Allison J M, Lowrie W, McLean J & Taylor G R, *J chem Soc*, (1961) 3353.
9 Simonsen J & Ross W C J, *The terpenes*, Vol 4 (The Cambridge Univesity Press, London), 1957.
8 Bose S N & Khastgir H N, *J Indian chem Soc*, **46** (1969) 860.
10 Pradhan B P, Hassan A & Shoolery J N, *Tetrahedron Lett*, **25** (1984) 865.
11 Pradhan B P & Chakraborty S, Unpublished work.
12 Ageta H, Shiojima K, Masuda K & Lin T, *Tetrahedron Lett*, **24** (1981) 2289.