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POLYENE CYCLIZATION : CYCLIZATION STUDIES ON AN ACYCLIC FURANODITERPENE AND ITS EPOXIDE

U. C. PANDEY, P. SARMAH and R. P. SHARMA*

Natural Products Chemistry Division

Regional Research Laboratory, Jorhat-6, Assam, India

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Abstract : Reaction of an acyclic diterpene alcohol 1c with chlorotrimethylsilane and sodium iodide or $SnCl_4$ furnishes compounds 7 and 8. This cyclization is reminiscent of the biosynthesis of pallescensins E-G - an analogous compounds in sesquiterpenoids. Reaction of the epoxide 2 with $SnCl_4$ furnishes only the acyclic compounds 12, 13, 14a, 14c and 15a. Photolysis of 2 results in the formation of ($\pi^4+\pi^2$) photocycloaduct 21.

A furanoditerpene acid 1a was first isolated by Bohlman et al from Centipeda orbicularis[1] whose constituents were later investigated by us[2,3]. Since pallescensins E-G isolated from the marine sponge Disidea pallescens and possessing the basic skeleton 23 are apparently biosynthesized from an analogous sesquiterpene alcohol 24 (or its biological equivalent), compound 1a attracted our attention for carrying out cyclization studies on it[4]. Structure of the acid 1a was based purely on spectroscopic data, it was therefore decided to confirm this structure, especially the geometry of the double bonds by chemical degradation and correlation studies which are described in sequel.

The methyl ester 1b obtained by methylation of 1a with excess diazomethane was reduced with $LAH/AlCl_3$ in dry ether to furnish the alcohol 1c in 80% yield. MnO_2 oxidation of 1c provided the aldehyde 1e in whose nmr spectrum the chemical shift of the aldehyde proton at 10.0 ppm conclusively established the geometry of the double bond, which originally carried the acid group, as trans.

It was decided to convert the alcohol 1c into its mesylate whose LAH or $NaBH_4$ reduction was expected to provide ambliofuran 1g[5]. However, reaction of the alcohol 1c with mesyl chloride in pyridine invariably furnished the pyridinium compound 1h. Change in base or the acid chloride furnished the analogous salts as shown in Scheme 1[6]. Reduction of the pyridinium salt 1h with $NaBH_4$ and nickle boride furnished the tetrahydro and the hexahydro compounds 1l & 1m respectively. When this route failed to give any mesylate or tosylate, the alcohol 1c was converted to its chloride 1f with triphenyl phosphine in refluxing carbon tetrachloride[7] which on reduction with $NaBH_4$ in DMSO[8] furnished a product whose direct comparison with ambliofuran (Kindly provided by Prof D J Faulkner) confirmed its identity as 1g.

The position of the acid group at C-6 in 1a was confirmed as follows : The acetate 1d obtained by acetylation of 1c, was treated with perbenzoic acid to furnish a mixture of two monoepoxides 2 and 3 and a diepoxide 4. Reaction of the epoxide 3 with acidic $NaIO_4$ furnished the ketone 5 thus proving the location of

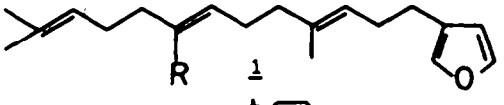
the acetoxy group in 3 at C-6 and theredore the acid group in 1a must be at C-6. A small amount of the product 6 was also isolated in the above reaction.

Having assureu of the location of acid group in 1a as well as the geometry of the double bonds, we proceeded to study its cyclization. Reaction of the alcohol 1c with chlorotrimethylsilane (CTMS) and sodium iodide[9] in acetonitrile furnished a mixture of two products which were separated by preparative TLC and were identified as 7 (minor) and 8 (major) on the basis of spectroscopic data (experimental), mechanistic considerations and analogies in polyene cyclization[10]. Significant peaks in the mass spectrum of 7 and 8 at m/z 161 and 147 respectively, which appeared to have arisen through cleavage as shown with the wavy lines fully support the above formulation. Isomerization of 7 to 8 was effected with TsOH in refluxing benzene. Hydrogenation of 7 and 8 over 10% Pd-C furnished compounds 9 and 10 respectively. Reaction of the alcohol 1c or the acetate 1d or the chloride 1f with $SnCl_4$ in refluxing benzene furnished 7 and 8 as the minor and the major products respectively. Cyclization of ambliofuran 1g with $SnCl_4$ in refluxing benzene furnished compound 11.

Reaction of the monoepoxide 2 with $SnCl_4$ in benzene at r.t. gave a mixture of three major and two minor products which were separated by preparative TLC and identified as 12, 13, 14a, 14c and 15a on the basis of IR, NMR and Mass spectral data and some chemical transformations as shown in Scheme 2. Reaction of the monoepoxide 2 with BF_3 etherate furnished essentially a single product 12 whereas with BF_3-Ac_2O the sole product fluorohydrin acetate 14b was obtained.

Comparison of the results obtained through cyclization studies on the alcohol 1c and the epoxide 2 clearly suggest that these two compounds possess absolutely different conformations in solution.

Since halo compounds have been photolyzed to obtain cyclized products[11], we decided to study the photolysis of the chlorohydrin 14a. Irradiation of 0.1% benzene solution of 14a in a pyrex flask resulted in the formation of a complex mixture. However, photolysis of 0.1% benzene solution of 1d furnished essentially a single product which was found to be unstable and slowly converting to a more polar product (TLC). NMR of the crude product was devoid of any signals due to protons on the furan ring, other signals were at 4.20-5.50 ppm (overlapping signals integrating to seven protons), 2.00 ppm (acetate) and 1.55 ppm (9H for three methyls). On the basis of above data structure 21 was assigned to this product. During purification on silica gel TLC compound 21 was completely transformed into a more polar product whose spectral characteristics (experimental) were fully consistent with the structure 22.



a R = CO_2H
b R = CO_2Me
c R = CH_2OH
d R = CH_2OAc
e R = CHO
f R = CH_2Cl
g R = CH_3

h R = CH_2–N$^+$ Cl^-

i R = CH_2–N$^+$ O_3S^-–CH_3

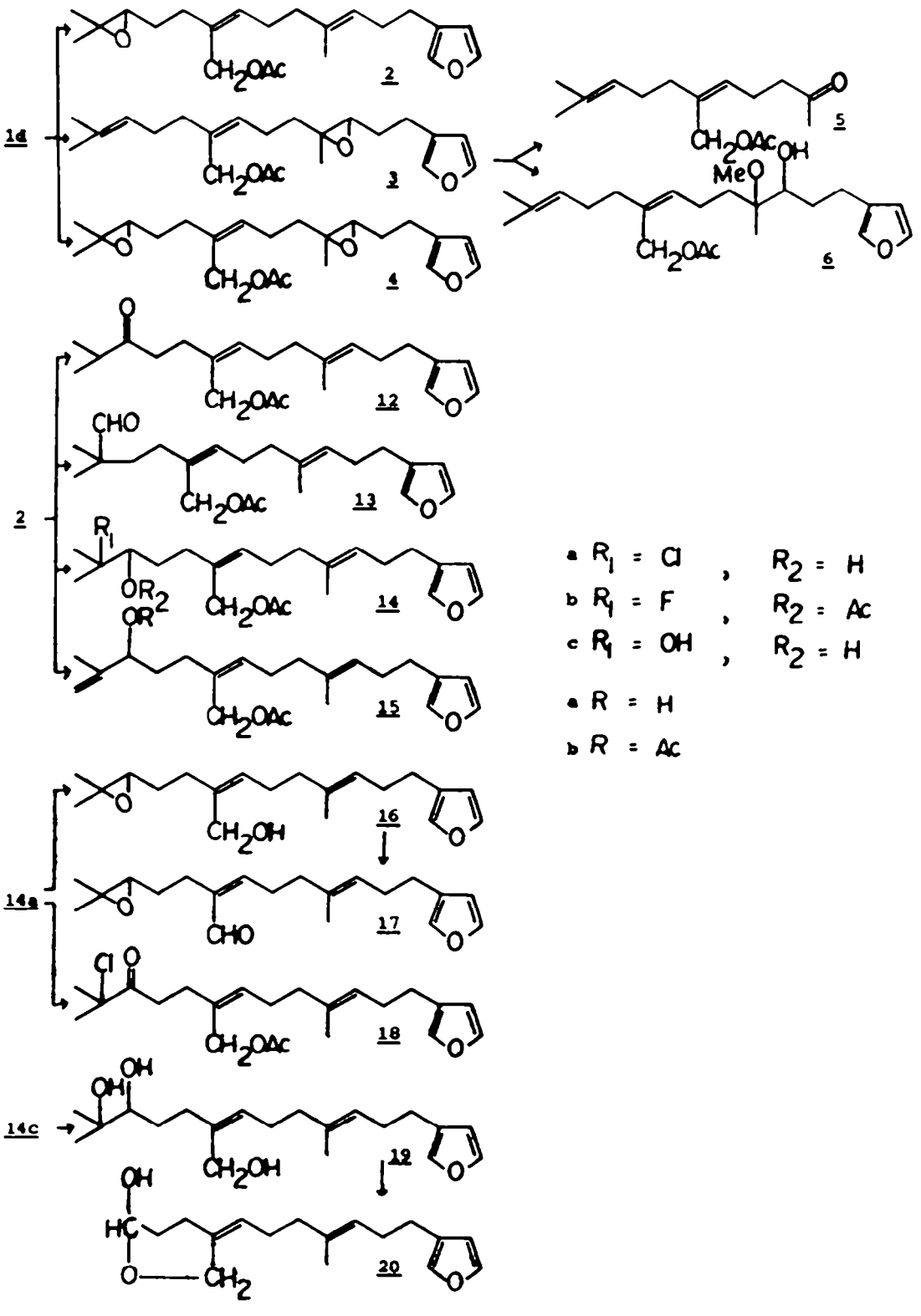
j R = CH_2–N$^+$ Cl^-–CH_3

k R = CH_2–N

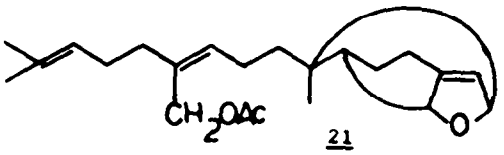
l R = CH_2–N

m R = CH_2–N

Scheme 1


1d
2
3
4
5
6
2
12
13
14
15
a R1 = Cl , R2 = H
b R1 = F , R2 = Ac
c R1 = OH , R2 = H
a R = H
b R = Ac
14a
16
17
18
14c
19
20

Scheme 2



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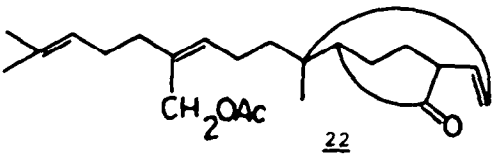

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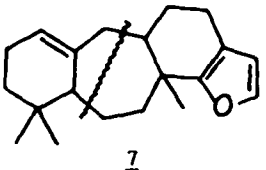

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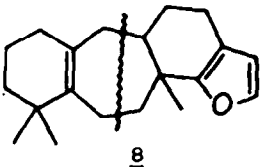

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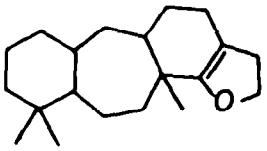

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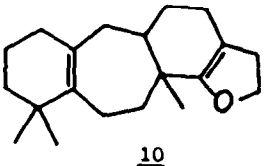

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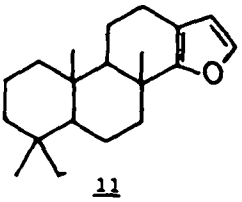

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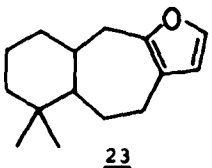

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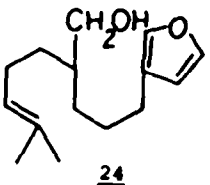

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EXPERIMENTAL

The NMR spectra were recorded at 60 MHz (T-60) in $CDCl_3$ with TMS as internal standard. Chemical shifts are expressed as δ in ppm. IR spectra were determined in $CHCl_3$ unless otherwise stated on Perkin Elmer 237B spectrophotometer. Mass spectra were recorded under electron impact at 70eV on MS-30 spectometer. For preparative TLC silica gel-G (BDH, India) was used. Petroleum ether refers to the fraction b.p. 60-80°. Work up reaction mixtures were dried over anhydrous Na_2SO_4.

Methyl ester 1b

A solution of 100 mg of the acid 1a in dry ether was treated with excess diazomethane solution in ether for half an hour at r.t. Excess of diazomethane was destroyed by adding a few drops of acetic acid and evaporation of the solvent furnished the methyl ether 1b as a gum in quantitative yield. IR: 1700, 1430, 1360, 1015 & 875cm^{-1}; NMR: 7.25 s br (H-16), 7.10 s br (H-17), 6.15 s br (H-15), 5.75 t (J=7.00 Hz, H-7), 5.00 (Overlapping signals of H-3 & H-11), 3.65 (OMe), 1.60 s (H-18) & 1.55 s (H-19, H-20); MS:m/z at 330, 271, 95 and 81.

LAH reduction of 1b

A solution of 100 mg of 1b in 15 ml dry ether was cooled at 0°C, 100 mg of LAH and 100 mg of $AlCl_3$ were added to it and the reaction mixture stirred at 0°C for one hour. The reaction was quenched with a saturated solution of ammonium chloride and extracted with ethyl acetate (5x100 ml). Evaporation of the washed and dried extract furnished a residue which was purified by preparative TLC (EtOAc:Bz, 1:50) to yield 1c as an oil (72 mg). IR: 3600-3700 (br), 1565, 1490, 1430, 1355, 1060, 1010 & 870cm^{-1}; NMR: 7.20 s br (H-16), 7.10 s br (H-17), 6.12 s br (H-15), 5.05 m (3H), 3.98 s br (H-19), 1.60 s (3-H), 1.55 s (6H). MS:m/z at 302, 286, 269, 252, 241, 231, 189, 95 & 81.

Acetylation of 1c with acetic anhydride and pyridine furnished the acetate 1d as a gum in quantitative yield. IR: 1730, 1430, 1370, 1210, 1055, 1020, 870cm^{-1}; NMR: 7.20 s br (H-16), 7.05 s br (H-17), 6.10 s br (H-15), 5.00 (overlapping signals of the H-3 & H-11), 4.47 s br (H-18), 1.95 (acetate), 1.55 (H-1, H-18 & H-20). MS:m/z at 344, 284, 95 & 81.

MnO_2 oxidation of 1c

60 mg of compound 1c was oxidised with MnO_2 as described earlier to yield 35 mg of the aldehyde 1e as an oil. IR: 1680, 1505, 1450, 1380, 1220, 1165, 1065, 1075 & 875cm^{-1}; NMR: 10.00 s br (H-19), 7.23 s br (H-16), 7.08 s br (H-17), 6.30 s br (H-7), 6.13 s br (H-15), 5.05 (overlapping signals of H-3 and H-11), 1.60 s br (H-1, H-18, & H-20). MS:m/z at 300, 285, 271, 95 & 81.

Preparation of the chloride 1f

A solution of 50 mg of 1c in 4 ml CCl_4 was treated with 400 mg triphenylphosphine and refluxed for 3 hr on a water bath. The reaction mixture was directly purified by PLC (Pet-ether) to obtain the chloride 1f (40 mg) as a gum. IR: 1430, 1240, 1160, 1110, 1025, 995, 875; NMR: 7.20 s br (H-16), 7.10 s br (H-17), 6.12 s br (H-15), 5.05 m (3H), 4.00 s (H-19), 1.60 s (3H) and 1.55 s (6H). MS:m/z at 320, 201, 199 & 131.

Reduction of 1f with $NaBH_4$

A solution of 30 mg of the chloride 1f in 2 ml DMSO was treated with 75 mg of $NaBH_4$. The reaction mixture was stirred at r.t. for one hr and worked up by adding water followed by extraction with CH_2Cl_2. The washed and dried extract was evaporated and purification of the crude product by preparative PLC (Pet-ether) furnished 16 mg of ambliofuran 1g as a gum. IR: 1450, 1375, 1025, 875cm^{-1}; NMR: 7.25 s br (H-16), 7.15 s br (H-17), 6.18 s br (H-15), 5.12 t (J=7 Hz), 5.05 m (2H), 1.65 s (3H) and 1.60 s (9H). MS:m/z at 286, 284, 269, 241, 215 & 187.

Reaction of 1c with mesyl chloride in pyridine

A solution of 75 mg of 1c in 2 ml dry pyridine was cooled to 0°C and treated with 0.75 ml of methanesulfonyl chloride. The reaction mixture was left overnight at r.t. and worked up by diluting with water followed by extraction with chloroform (4x100). The washed and dried extract was evaporated and the

residue purified by preparative TLC (MeOH:$CHCl_3$, 1:8). Compound 1h (70 mg) was obtained as a gum. IR: 1635, 1575, 1435, 1375, 1150, 1060, 1020 and 870cm^{-1}; UV λ_{max}^{EtOH} 259 nm (ϵ 5783); NMR: 8.66 d br (J=6.5 Hz, H-2' & H-6'); 8.35 m (H-4'), 8.15 m (H-3' & H-5'), 7.25 s br (H-16), 7.15 s br (H-17), 6.15 s br (H-15), 5.35 s br (H-19), 5.00 m (H-3, H-7 & H-11), 1.60 s br (H-1 & H-20), 1.55 s br (H-18). MS:m/z at 284 ($M^+-C_5H_6NCl$).

Reaction of 1c with tosyl chloride in pyridine

To a solution of 10 mg of 1c in 2 ml dry pyridine was added 50 mg of tosyl chloride and the reaction mixture left overnight at 5°C. Usual work up procedure followed by preparative TLC (1:9, MeOH:$CHCl_3$), furnished 8 mg of 1i as a gum. IR: 1640, 1515, 1465, 1440, 1375, 1210, 1035, 1020, 920 and 870cm^{-1}; NMR: 7.20 s br (H-16), 7.10 s br (H-17), 6.10 s br (H-15), 5.20 s br (H-19), 4.8-5.0 (overlapping signals of H-3, H-7 and H-11), 1.55 s br (H-1, H-18 and H-20); (Signals for the tosyl group appeared at 2.20 s br (3H), 7.60 d (J=7 Hz) and 7.00 d (J=7 Hz). MS:m/z at 284 ($M^+-C_{12}H_{13}SNO_3$).

Reaction of 1c with mesyl chloride in γ-picoline

A solution of 30 mg of 1c in 2 ml of γ-picoline was treated with methanesulphonyl chloride as described above. Preparative TLC (MeOH:$CHCl_3$, 1:9) furnished 20 mg of 1j as a gum. IR: 1650, 1580, 1525, 1475, 1455, 1380, 1225, 1050, 1030 & 880cm^{-1}; NMR: 8.60 d br (J=6.5 Hz, H-2' & H-6'), 8.0 d (J=6.5 Hz, H-3' & H-5'), 7.24 s br (H-16), 7.13 s br (H-17), 6.20 s br (H-16), 5.40 s br (H-19), 5.00 m (H-3, H-7 & H-11), 2.60 s (3 protons), 1.60 s br (H-1 & H-20), 1.55 s br (H-18). MS:m/z at 284($M^+-C_6H_8NCl$).

Reaction of 1c with mesyl chloride in quinoline

A solution of 30 mg of 1c in 2 ml dry quinoline was treated with methanesulphonyl chloride as described above. After usual work up compound 1k (30 mg) was obtained as a gum. IR: 1640, 1625, 1600, 1530, 1500, 1450, 1380, 1210, 1160, 1060, 1040, 1020 & 870cm^{-1}; NMR: 7.60-8.50 (aromatic proton), 7.27 s br (H-16), 7.17 s br (H-17), 6.20 s br (H-15), 4.80-5.80 (overlapping signals of H-3, H-7, H-11 & H-19), 1.67, 1.53 and 1.50 s br (H-1, H-18 and H-20). MS:m/z at 284 ($M^+-C_9H_8NCl$)

Reaction of 1h with $NaBH_4$

A solution of 50 mg of 1h in 4 ml MeOH was cooled to 0°C and treated with 25 mg $NaBH_4$. The reaction mixture was stirred at 0°C for 15 mints. and then diluted with water followed by extraction with dichloromethane (4x100 ml). The washed and dried extract was evaporated to furnish 1l (38 mg) as an oil. IR: 1630, 1510, 1490, 1470, 1390, 1360, 1300, 1175, 1100, 1075, 1030, 950 & 875cm^{-1}; NMR: 7.22 s br (H-16), 7.12 s br (H-17), 6.15 s br (H-15), 5.60 s br (H-3' & H-4'), 5.10 m (H-3, H-7 & H-11), 3.00 s (H-19), 2.95 m (H-2'), 1.65 s br (H-18), 1.60 s br (H-1 & H-20). MS:m/z at 367, 297, 285, 269, 241, 215, 95 & 81.

Reaction of 1h with NiB_2

To 100 mg of $NiCl_2$ in 5 ml ethanol was added a solution of 600 mg of $NaBH_4$ in 2 ml water with stirring at r.t. A black ppt. was formed immediately. 50 mg of the pyridinium salt 1h was added to this NiB_2 ppt. and the reaction mixture stirred for 5 hr at r.t. It was worked up by diluting with water followed by extraction with $CHCl_3$. The product was purified on preparative TLC (1:9, MeOH:$CHCl_3$) to furnish compound 1m (60 mg) as a gum. IR: 1505, 1450, 1380, 1215, 1160, 1110, 1065, 1025 & 875cm^{-1}; NMR: 7.24 s br (H-16), 7.13 s br (H-1), 6.20 s br (H-15), 5.10 (overlapping signals of H-3, H-17 & H-11), 3.15 s br (H-19), 1.60-1.70 (H-1, H-18 & H-20). MS:m/z at 369, 300, 288, 241, 234, 270, 206, 149, 95 & 81.

Epoxidation of 1d

A solution of 100 mg of 1d in 4 ml chloroform was cooled to -5°C and treated with 1 ml perbenzoic acid solution (8%) in chloroform. The reaction was followed on TLC and when 80% of the starting material had reacted, the reaction mixture was diluted to 100 ml of chloroform and successively washed with dilute KI solution, sodium thiosulphate solution and water. Evaporation of the dried extract gave an oily residue which was purified by preparative TLC (EtOAc:Bz, 1:50) to furnish 3 as the least polar product (10 mg) as a gum. IR: 1740, 1510, 1450, 1390, 1230, 1160, 1065, 1025 & 875cm^{-1}; NMR: 7.25 s br (H-17), 7.10 s

br (H-16), 6.20 s br (H-15), 5.0-5.40 (overlapping signals of H-3 & H-7), 4.55 (H-19), 2.00 (acetate), 1.70 and 1.60 s br (H-1 and H-20), 1.20 s (H-18). MS:m/z at 360, 300, 288, 95 & 81.

The next in polarity was the monoepoxide 4 (50 mg) obtained as a gum. IR: 1730, 1450, 1375, 1240, 1175, 1110, 1060, 1015, 955 & 870cm^{-1}; NMR: 7.25 s br (H-16), 7.15 s br (H-17), 6.20 s br (H-15), 5.25 m (overlapping signals of H-7 and H-11), 4.55 s (H-19), 2.00 (acetate), 1.55 (H-18) & 1.20 (H-1 & H-20). MS:m/z at 360, 300, 290, 288, 285, 254, 201, 95 & 81.

The most polar compound was the diepoxide 5 (10 mg) obtained as an oil. IR: 1730, 1500, 1445, 1370, 1225, 1150, 1105; NMR: 7.25 s br (H-16), 7.15 s br (H-17), 6.15 s br (H-15), 5.27 t (J=7 Hz, H-7), 4.45 s (H-19), 1.95 (acetate), 1.0-1.20 (H-1, H-18 & H-20). MS:m/z at 376, 317, 301, 95 & 81.

The unreacted starting compound 1d (20 mg) was also recovered.

Reaction of the epoxide 3 with sod. metaperiodate

A solution of 50 mg of the epoxide 3 in 4 ml methanol was treated with 0.5 ml of sodium metaperiodate solution (100 mg dissolved in 1 ml water) and two drops of 6N H_2SO_4. The reaction mixture was stirred for 4 hr at r.t. when TLC indicated complete disappearance of the starting material. The reaction mixture was diluted with water and extracted with $CHCl_3$ (4x100 ml). The washed and dried extract was evaporated and the residue purified by preparative TLC (Bz:EtOAc: 50:1). The less polar product was identified as 5 (18 mg) obtained as a gum. IR: 1730, 1710, 1375, 1200, 1025cm^{-1}; NMR: 5.0-5.40 (overlapping signals of H-3 & H-7), 4.65 s br (H-12), 2.10 & 2.05 s (H-11 & acetate), 1.70 & 1.65 s (H-1 & H-13). MS:m/z 251, 209, 191, 177, 159, 149, 134 & 119. The more polar compound 6 (10 mg) was also obtained as a gum. IR: 3600-3200 (br), 1735, 1520, 1440, 1375, 1220, 1090, 1020 & 870cm^{-1}; NMR: 7.25 s br (H-16), 7.10 s br (H-17), 6.70 s br (H-15), 5.0-5.40 (overlapping signals of H-3 & H-7), 4.55 s br (H-19), 3.15 s (OCH_3), 2.00 (acetate), 1.63 & 1.57 s (H-1 & H-20), 1.07 s (H-18). MS:m/z at 392, 374, 360, 332, 95 & 81.

Reaction of 1c with CTMS/NaI

To a solution of 40 mg of the alcohol 1c in 4 ml dry acetonitrile was added 400 mg NaI followed by 10 drops of chlorotrimethylsilane and the reaction mixture stirred at r.t. for 45 mints., when TLC indicated disappearance of the starting material. The reaction was quenched by addition of water and extracted with dichloromethane. The washed and dried extract was evaporated to furnish the crude which was purified by PLC (Pet-ether) to yield the more polar compound 7 (5 mg) as an oil. IR: 1450, 1210,& 875cm^{-1}; NMR: 7.10 s br (1H), 6.05 s br (1H), 0.95 s (6H),& 0.90 s (3H). MS:m/z at 284, 269 & 239, 161, 94 and 81. High resolution MS: MW 284, 2124 ($C_{20}H_{28}O$ requires 2.84.2140). The less polar compound 8 (20 mg) was also obtained as an oil. IR: 1460, 1205,& 875cm^{-1}; NMR: 7.12 s br (1H), 6.10 s (1H), 5.05 t (J=6 Hz, 1H), 0.98 s (6H) & 0.92 s (3H). MS:m/z at 284, 269, 239, 147, 94 & 81.

Reaction of 1c with $SnCl_4$

To a solution of 40 mg of 1c in benzene was added 400 mg of $SnCl_4$ and refluxed on a water bath for 20 mints. The reaction mixture was diluted with CH_2Cl_2, washed several times with water and dried. Evaporation of the solvent followed by purification on preparative TLC (Pet-ether) furnished 7 (40 mg) and 8 (10 mg).

Similarly, reaction of the chloride 1f or the acetate 1d with $SnCl_4$ in refluxing benzene furnished 7 as the major and 8 as the minor products.

Hydrogenation of 7

A solution of 20 mg of 7 in 25 ml ethyl acetate was hydrogenated in the presence of 20 mg of 10% Pd-C catalyst for 2 hr. Catalyst was filtered, and the product purified by PLC (Pet-ether) to yield 9 (16 mg) as a gum. NMR: 3.5 m (2H), 1.00-1.20 (overlapping signals for three methyl groups). MS:m/z at 288, (M^+), 273, 258, 243, 96 & 83.

Similarly, hydrogenation of 8 furnished 10 as a gum. NMR: 3.50 (2H), 1.00-1.20 (Signals for three methyl groups). MS:m/z at 286 (M^+), 271, 256, 241, 149, 96 & 83.

Isomerization of 7 to 8

A solution of 10 mg of 7 in 2 ml benzene was treated with 10 mg TsOH and refluxed on water bath for 10 mints. The reaction mixture was diluted with

CH_2Cl_2 and washed several times with water. Evaporation of the dried extract furnished a crude product which was purified by PLC (Pet-ether) to obtain 8 as a gum (8 mg).

Cyclization of ambliofuran 1g

A solution of 20 mg of 1g in 4 ml benzene was treated with 200 mg $SnCl_4$ and refluxed for 20 mints. on a water bath. The reaction mixture was diluted with CH_2Cl_2 and washed several times with water. The dried extract on evaporation followed by purification on PLC (Pet-ether) furnished 11 (18 mg) as a gum. IR: 1225 & 890cm^{-1}; NMR: 7.10 s br (1H), 6.05 s br (1H) and 0.90-1.00 (12H). MS:m/z at 286 & 271.

Reaction of the epoxide 2 with $SnCl_4$

A solution of 66 mg of the epoxide 2 in 3 ml dry benzene was treated with 150 mg of $SnCl_4$ with stirring at r.t. After 40 mints when no more of the starting material was present (TLC), the reaction mixture was diluted with 100 ml $CHCl_3$ and washed with water. Evaporation of the solvent furnished a residue which showed five spots on TLC (referred to as bands A-E in the order of polarity). These were separated by preparative TLC (EtOAc:Bz, 1:50).

The least polar band 'A' was identified as 13 (10 mg) obtained as a gum. IR: 2850, 1735, 1710, 1390, 1025, 875cm^{-1}; NMR: 9.44 s (aldehyde), 7.32 s br (H-16), 7.22 s br (H-17), 6.27 s br (H-15), 5.0-5.4 (overlapping signals of H-7 & H-11), 4.60 s (H-19), 2.05 s (acetate), 1.65 s br (H-18), 1.18 s (H-1 & H-20). MS:m/z at 360, 300, 290, 288, 95 & 81.

The next in polarity was band 'B' which identified as 12 (30 mg) obtained as a gum. IR: 1735, 1710, 1530, 1500, 1475, 1400, 1265, 1025 & 875cm^{-1}; NMR: 7.30 s br (H-16), 7.20 s br (H-17), 6.25 s br (H-15), 5.0-5.4 (overlapping signals of H-7 and H-11), 4.60 (H-17), 2.02 (acetate), 1.65 (H-18), and 1.20 (H-1 & H-20). MS:m/z at 360, 300, 290, 288, 95 & 81.

The next polar band 'C' was identified as 14a (10 mg) obtained as a gum. IR: 3200-3600 br, 1735, 1575, 1375, 1025 and 875cm^{-1}; NMR: 7.27 s br (H-16), 7.12 s br (H-17), 6.70 s br (H-15), 5.0-5.40 (overlapping signals of H-7 & H-11), 4.58 s (H-19), 3.45 dd (J=17 and 3 Hz, H-3), 2.00 (acetate), 1.60 s (H-1, H-18 and H-20). MS:m/z 398, 396 (3:1), 360, 338, 336, 300, 201, 95 & 81.

The next polar band 'D' was identified as 15a (2 mg) obtained as a gum. IR: 3200-3600 br, 1735, 1570, 1020 and 870cm^{-1}; NMR: 7.20 s br (H-16 & H-17) (intensity of two protons), 6.10 s br (H-15), 5.5-4.20 m (overlapping signals of H-7, H-11 and H-20), 4.50 s br (H-19), 3.1 br (OH), 2.00 (acetate), 1.65 and 1.55 s br (H-1 and H-18). MS:m/z at 360, 300, 299, 282, 193, 95 & 81.

Acetylation of compound 15a with acetic anhydride and pyridine after usual work up furnished the acetate 15b in quantitative yield as a gum. NMR: 7.20 s br (H-16), 7.10 s br (H-17), 6.10 d (J=2 Hz, H-15), 5.5-4.7 (overlapping protons of H-7, H-11 & H-20), 4.5 s br (H-19), 2.00 (two acetate), 1.65 s br & 1.55 s br (H-1 & H-18). MS:m/z at 402, 342, 300, 299, 282, 213, 193, 95 and 81.

The most polar band 'E' was identified as 14c (3 mg) obtained as a gum. IR: 3600-3200 br, 1725, 1225, 1075 and 875cm^{-1}; NMR: 7.25 s br (H-16), 7.10 s br (H-17), 6.20 s br (H-15), 5.0-5.4 (overlapping signals of H-7 & H-11), 4.55 s (H-19), 3.30 dd (J=7, 3 Hz, H-3), 2.05 (acetate), 1.60 s br (H-18), 1.20 and 1.18 (H-1 & H-20). MS:m/z at 378, 360, 318, 300, 201, 95 and 81.

Alkaline hydrolysis of 14a

A solution of 40 mg of the chlorohydrin 14a in 4 ml methanol was treated with two drops of 5% aqueous KOH at r.t. and the reaction mixture stirred under nitrogen for half an hour. It was then neutralized with dilute acetic acid and extracted with $CHCl_3$ (4x100 ml). The washed and dried extract was evaporated and the residue purified by preparative TLC (EtOAc:Bz, 1:50) to furnish 16 as an oil (19 mg). IR: 3600-3200 br, 1420, 1405, 1370, 1240, 1170, 1110, 1060, 1075 & 875cm^{-1}; NMR: 7.27 s br (H-16), 7.10 s br (H-17), 6.15 s br (H-15), 5.0-5.40 (overlapping signals of H-7 and H-11), 4.00 s br (H-19), 1.55 s br (H-18), 1.25 s br (H-1 & H-20). MS:m/z at 318, 300, 259, 201, 168, 95 & 81.

MnO_2 oxidation of 16

A solution of 33 mg of compound 16 in 4 ml dry chloroform was treated with 300 mg of active MnO_2 and the reaction mixture stirred at r.t. for one and a half hour. It was filtered and MnO_2 washed with chloroform (40 ml). The filtrate and washings were evaporated under reduced pressure to furnish the aldehyde 17 as an oil (25 mg). IR: 1675, 1650, 1510, 1455, 1390, 1225, 1170, 1075, 1030 & 880cm^{-1}; NMR: 10.00 s br (H-19), 7.25 s br (H-16), 7.10 s br (H-17),

6.30 t (J=7 Hz, H-7), 6.15 s br (H-15), 5.10 d (J=7 Hz, H-11), 1.55 s br (H-18), 1.20 s br (H-1 & H-20). MS:m/z at 316, 298, 257, 95 & 81.

CrO_3-pyridine oxidation of 14a

A solution of 70 mg of 14a in 2 ml dry pyridine was treated with 100 mg anhydrous CrO_3 and the resultant mixture left at r.t. for 30 hr. The excess CrO_3 was destroyed by adding ethyl alcohol and the reaction mixture was diluted with water followed by extraction with chloroform (4x100 ml). The washed and dried extract was evaporated and the residue purified by preparative TLC (Bz:EtoAc, 1:50) to furnish 18 as an oil (10 mg). IR: 1740, 1725, 1450, 1380, 1370, 1250, 1155, 1115, 1060, 1070, 955 & 875cm^{-1}; NMR: 7.26 s br (H-16), 7.10 s br (H-17), 6.20 s br (H-16), 5.0-5.40 (overlapping signals of H-7 & H-11), 4.60 s (H-19), 2.05 (acetate), 1.65 s br (H-1 and H-20), 1.60 s br (H-18). MS:m/z 394, 358, 298, 260, 253, 185, 167, 95 & 81.

Alkaline hydrolysis of 14c

A solution of 22 mg of the diol 14c in 2 ml methanol was treated with four drops of 5% aqueous KOH and the reaction mixture was stirred at r.t. under nitrogen atmosphere for 20 mints. The reaction mixture was worked up as described earlier to furnish 19 as a gum (15 mg). IR: 3600-3200 br, 1170, 1025 & 875cm^{-1}; NMR: 7.27 s br (H-16), 7.15 s br (H-17), 6.20 s br (H-15), 5.70 (overlapping signals of H-7 & H-11), 4.05 s br (H-19), 3.30 m (H-3), 1.60 s br (H-18), 1.20 s br (H-1 & H-20). MS:m/z 336, 318, 300, 262, 201, 175, 95 & 81.

Reaction of 19 with sod. metaperiodate

A solution of 30 mg of 19 in 1 ml MeOH was treated with four drops of sod. metaperiodate solution (100 mg dissolved in 1 ml of water) and the reaction mixture was left at r.t. for 1 hr. It was then diluted with water and extracted with chloroform. The washed and dried extract was evaporated to furnish 20 (15 mg) as an oil. IR: 3600-3200 br, 1590, 1400, 1070, 1055, 950, 925 & 870cm^{-1}; NMR: 7.27 s br (H-16), 7.16 s br (H-17), 6.10 s br (H-15), 5.10 (H-3, H-7 & H-11), 4.20 s (H-19, centre of the AB system), 1.60 s br (H-18). MS:m/z 276, 260, 243, 233, 214, 201, 95 & 81.

Reaction of 2 with BF_3 etherate

A solution of 30 mg of 2 in 2 ml dry benzene was cooled to 0°C and treated with two drops of BF_3 etherate. The reaction mixture was worked up after 15 mints. by diluting with water, neutralizing with dilute sodium bicarbonate solution followed by extraction with $CHCl_3$ (4x100 ml). Evaporation of the solvent provided a oily residue which was purified by preparative TLC (Bz:EtOAc, 4:1) to furnish 20 mg of an oil, identical in IR, NMR, Mass and TLC with 12.

Reaction of 2 with BF_3-Ac_2O

A solution of 30 mg of compound 2 in 5 ml dry ether and 1 ml acetic anhydride was cooled to 0°C and treated with four drops of freshly distilled BF_3-etherate. The reaction mixture was left at r.t. for 1 hr and worked up by diluting with water followed by extraction with $CHCl_3$ (4x100 ml). The chloroform extract was washed with dilute solution of sodium bicarbonate, water and dried. Evaporation of the solvent furnished 16b (20 mg) as an oil. IR: 1740, 1725, 1525, 1510, 1475, 1450, 1380, 1240, 1025 & 875cm^{-1}; NMR: 7.25 s br (H-16), 7.10 s br (H-17), 6.20 s br (H-15), 5.0-5.40 (H-3, H-7 & H-11), 4.55 (H-19), 2.00 s br (acetate), 1.60 s br (H-18), 1.30 d (J=22 Hz, H-1 & H-20). MS:m/z 422, 402, 362, 341, 300, 285, 282, 261, 95 & 81.

Photolysis of 1d

A solution of 50 mg of 1d in dry benzene was photolysed in a pyrex flask using a 125 W bare arc mercury lamp for 5 hr. Evaporation of the solvent furnished one major compound (TLC) (20 mg) as a gum identified as 21 on the basis of following data. IR: 1735, 1200, 1025 and 925cm^{-1}; NMR: 4.20-5.50 (7H), 2.00 (acetate) 1.55 (9H for three methyls). MS:m/z at 344 (M^+), 284, 254, 213, 159. Purification of 20 mg of compound 21 on preparative TLC (EtOAc:Pet-ether, 1:9) furnished exclusively 22 (18 mg) as a gum. IR: 1755, 1735, 1450, 1380, 1200, 1025 and 925cm^{-1}; NMR: 5.80 m (1H), 5.40 m (1H), 5.00 m (2H), 4.50 s br (H-19), 2.00 (acetate), 1.60 (9H for three methyls). MS:m/z at 344, 284 & 254. High resolution MS MW 344.2368 ($C_{20}H_{32}O_3$ requires 344.2352).

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