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Note

Manganese dioxide oxidation of 18-acetoxy-12,19-dihydroxy geranyl nerol

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Oxidation of an 18-acetoxy-12,19-dihydroxy geranyl nerol **1**, a naturally occurring acyclic diterpene with ethereal solution of manganese dioxide affords a mixture of six products. Two of them have been characterised as monoformyl configurational isomers **2** and **3** and remaining identified as diformyl configurational isomers, **4** to **7**.

In pursuing our interest in diterpenoid constituents[1-3] we have reported the isolation of a new acyclic diterpene **1** alongwith heliangolides and guaianolides from aerial parts of *Blainvillea latifolia*[4]. The genus *Blainvillea* (Compositae, tribe Heliantheae) is placed in the subtribe Ecliptinae[5,6]. The structure of diterpene was deduced from highfield PMR and high resolution mass spectrometry. The PMR spectrum of **1** (see Table I) clearly showed that it may be a derivative of geranyl geraniol or geranyl nerol as signals for three olefinic methyls (δ 1.66, 1.75, 1.77) and four downfield triplets (δ 5.12, 5.33, 5.46, 5.74) were visible for olefinic protons. The protons of the oxygen bearing carbons led to a broad doublet at δ 4.07 (2H), a broad doublet at δ 4.09 (2H), a pair of doublet at δ 4.67 and 4.73 (2H) and a double doublet at δ 4.16 (1H) suggesting the presence of two hydroxymethylene, an acetoxymethylene and a hydroxy methine groups. Spin decoupling experiments have decisively established the relative position of the oxygen functions. Irradiation at the resonance frequency δ 5.12 (H-14) sharpened the broad singlets at δ 1.75 and 1.66 and hence these singlets were of H-16 and H-17 methyl protons. It also simplified the multiplet at δ 2.22 due to H-13. Irradiation at δ 5.33 (H-6) collapsed multiplet at δ 2.20 into a triplet for H-5 protons while decoupling of the triplet at δ 5.46 sharpened the broad doublet at δ 4.09 indicating this signal belonged to H-1 protons. Irradiation at δ 5.74 simplified the multiplet at δ 2.33 (H-9). The configuration of double bonds was determined by NOE difference spectroscopy. Clear effects were observed between H-17 and H-13 (5%), between H-16 and H-14 (10%), between H-20 and H-2 (10%), between H-18 and H-9, between H-19 and H-5 (3%) and also between H-12 and H-10 (10%). Thus the diterpene **1** was characterised as 18-acetoxy-12,19-dihydroxy geranyl nerol. Several geranyl nerol derivatives have earlier been isolated from *Aspilia*[7], *Balsamorhiza*[8], *Dimerostemma*[9,10], *Kingianthus*[11], *Zexmenia*[12] and *Zinnia*[13] all belong to subtribe Ecliptinae and tribe Heliantheae. In the present investigation the diterpene was subjected to manganese dioxide oxidation studies which led to the isolation of various oxidation products with simultaneous isomerisation of double bonds. The latter phenomenon is interesting in view of acyclic nature of diterpene. Oxidation with MnO_2 in ethereal solution of **1** gave a complex mixture of six products. The mixture was separated by preparative TLC (silica gel, PF_{254}, Et_2O-petrol, 3:1) giving rise two distinct bands. The highfield PMR spectrum of the product from band-I (R_f 0.15) revealed the presence of two compounds namely 18-acetoxy-12, 19-dihydroxy geranyl neral **2** and 18-acetoxy-12,19-dihydroxy geranyl geranal **3** in which primary alcoholic group at the end of the chain get oxidised. The product from band - II (R_f 0.20) showed the presence of four compounds viz. 18-acetoxy-12-hydroxy geranyl nera-1,19-dial **4**, 18-acetoxy-12-hydroxy geranyl gerana-1,19-dial **5**, 18-acetyoxy-12-hydroxy geranyl-6,7 E-nera-1,19-dial **6** and 18-acetoxy-12-hydroxy geranyl-6,7 E-gerana-1,19-dial **7**, in these isomers both-C-1 and C-19 primary alcoholic groups get oxidised with simultaneous isomerisation of C_6-C_7 double bonds in compounds **6** and **7**. Secondary alcoholic group at C-12 could not be oxidised under such mild conditions. The above bands could not be further separated into pure compounds, there is

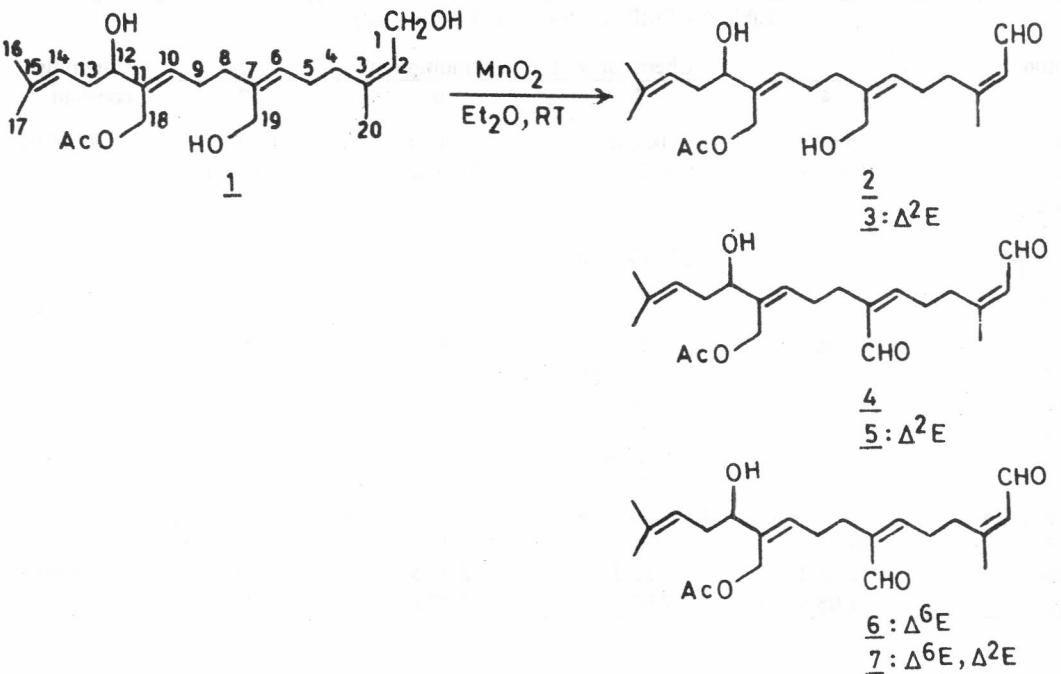

Table I—PMR spectral data of compounds **1,2** and **3**

Proton	Chemical shift (δ) and multiplicity			Coupling constant
	1	**2**	**3**	
H-1	4.09d br	9.90 d	9.99 d	J = 8 Hz
H-2	5.46 t	5.91d br	5.88d br	J = 8 Hz
H-4	2.18 m	2.20 m		
H-5	2.20 m	2.25 m		
H-6	5.33 t	5.30 t		J=7 Hz
H-8	2.30 m	2.30 m		
H-9	2.33m	2.33 m		
H-10	5.74 t	5.72 t	5.74 t	J = 7 Hz
H-12	4.16 dd	4.12t br		
H-13	2.22 m	2.30 m		
H-14	5.12 t	5.12 t		J = 7 Hz
H-16	1.75s br	1.73s br		
H-17	1.66s br	1.66s br		
H-18	4.73 d	4.72d		J = 12 Hz
H-18'	4.67 d	4.66 d		J = 12 Hz
H-19	4.07d br	4.15d br		
H-20	1.77 s	2.01 d	2.19d	J = 1 Hz
OAc	2.07 s	2.09 s		

precedent of non-separation of such configurational isomers of an acyclic diterpene[14].

Characterisation of compounds 2 and 3

The PMR spectral data of the product from band-I clearly indicated the presence of two isomers as the signals of protons H-1, H-2 and H-20 were doubled. Since these isomers were present in unequal amount in mixture hence the assignment of their signals has become easier. In case of major isomer **3**, C-20 methyl group appeared further downfield (δ 2.19) as doublet with coupling

Table II—PMR spectral data of compounds 4 to 7

Proton	Chemical shift (δ) and multiplicity				Coupling constant
	4	5	6	7	
H-1	9.90 d	10.0 d	9.93 d	10.01 d	J = 8 Hz
H-2	5.97d br	5.92dbr	5.90 dbr	5.90 dbr	
H-4, H-5, H-8, H-9, H-13		2.27 to 2.80 m			
H-6	6.40 t	6.42 t	6.46 t	6.48 t	
H-10		5.65 to 5.70 m			
H-12		4.10t br			
H-14		5.11t br			
H-16		1.74s br			
H-17		1.65s br			
H-18, H-18′		4.60 to 4.68 m			
H-19	10.09 s	10.10 s	9.39 s	10.10 s	
H-20	2.03 d	2.22 d	2.04 d	2.24 d	J = 1Hz
OAc	2.08 s	2.07 s	2.08 s	2.06 s	

constant 1 Hz due to the deshielding effect of an aldehydic group which is in its close proximity owing to the *E*-geometry of C_2-C_3 double bond. In addition to this it is β to the α,β-unsaturated carbonyl group. The signal of aldehydic proton also appeared downfield (δ 9.99) as doublet with coupling constant 8Hz being close in space to C-20 methyl group. Irradiation of the signal (H-2) at its resonance frequency δ 5.88 collapsed aldehydic doublet to a singlet and also sharpened broad singlet at δ 2.19. Accordingly the minor isomer **2** has *Z*-geometry at C_2-C_3 double bond. The chemical shifts of the remaining protons were closely related to those of diterpene **1** as depicted in Table I. The IR spectrum exhibited bands at 3510, 1730, 1690 cm^{-1} indicating the presence of hydroxyl, acetoxyl and conjugated carbonyl groups respectively in the product. The mass spectrum displayed molecular ion peak at *m/z* 378 corresponding to molecular formula $C_{22}H_{34}O_5$, some important fragments were at 360$[M-H_2O]^+$, 332$[360-CO]^+$, 318$[M-AcOH]^+$ and 43$[CH_3CO]^+$. From above spectral data compounds were characterised as 18-acetoxy-12,19-dihydroxy geranyl neral **2** and 18-acetoxy-12,19-dihydroxy geranyl geranal **3** respectively.

Characterisation of compounds 4 to 7

The PMR spectrum of the product from band-II clearly showed the presence of four diformyl isomers as evident by the appearance of four set of doublets centred at δ 9.90, 10.00, 9.93, 10.01 with coupling constant 8 Hz each and four set of singlets at δ 10.09, 10.10, 9.39 and 10.10 corresponding to C-1 and C-19 aldehydic protons of various isomers respectively. In case of isomers **5** and **7**, C-1 aldehydic proton and C-20 methyl protons being close in space due to the E geometry of C_2-C_3 double bond appeared comparatively more downfield. Similarly in isomers **6** and **7**, C-6 olefinic protons gave signals downfield (δ 6.46, 6.48) due to its proximity with C-19 aldehydic protons. Spin decoupling experiments helped in the identification of some of signals belong to different isomers. Irradiation of the broad doublet at δ 5.90 collapsed aldehydic doublets centred at δ 9.93 and 10.01 to singlets and sharpened the doublets at δ 2.04 and 2.24. Irradiation of the signal at δ 5.97 changed doublet at δ 9.90 to a singlet and sharpened the doublet at δ 2.03. Irradiation of the signals at resonance frequency δ 6.40 and 6.48 simplified the complex multiplet at δ 2.27 to 2.80. The chemical shifts of the remaining protons, which were not affected by oxidation studies, were almost similar in all isomers as shown in Table-II. The IR spectrum revealed the presence of hydroxy (3500 cm^{-1}), acetoxy (1730 cm^{-1}) and conjugated carbonyl functions (1690, 1685 cm^{-1}) and its mass spectrum showed molecular ion peak at *m/z* 376 corresponding to molecular composition $C_{22}H_{32}O_5$

alongwith prominent peaks at 348[M-CO]$^+$, 316[M-AcOH]$^+$ and 43[CH_3CO]$^+$. From spectral assignments above isomers were characterised as 18-acetoxy-12-hydroxy geranyl nera-1,19-dial **4**, 18-acetoxy-12-hydroxy geranyl gerana-1, 19-dial **5**, 18-acetoxy-12-hydroxy geranyl-6,7 E-nera-1,19-dial **6** and 18-acetoxy-12-hydroxy geranyl-6,7 *E*-gerana-1,19-dial **7.**

Experimental Section

IR spectra were recorded in CCl_4 on Beckmann IR 9 and Perkin Elmer 577 spectrometers, mass spectra on Varian MAT 711, 70 eV direct inlet, PMR spectra in $CDCl_3$ on a Bruker WM 400 MHz and JEOL FX 90 Q spectrometers, CC over silica gel (BDH, 60-120 mesh) and prep TLC over silica gel PF_{254}, $^{60}F_{254}$ E Merck plates. Melting points were recorded in soft glass capillaries in an electrothermal m.p. apparatus and are uncorrected. Chemicals shifts are reported in δ ppm.

Oxidation of 18-acetoxy-12,19-dihydroxy geranyl nerol 1. A mixture of 1 (0.079 m mole) and MnO_2 powdered (0.34 m mole) was stirred in ethereal solution at room temperature for 5 hr. The ether was removed *in vacuo* and the resulting mass was subjected to prep TLC, over silica gel, PF_{254}, Et_2O-petrol (3:1) displaying two bands on plate. Band-I (R_f 0.15) and band-II (R_f 0.20) after usual work-up gave colourless oil, 10 mg and 15 mg and their highfield PMR spectra revealed the presence of two and four compounds respectively. The above bands could not be further resolved into pure compounds by repeated prep. TLC in different solvent systems over silver nitrate impregnated silica gel plates and even by HPLC using analytical column.

18-Acetoxy-12,19-dihydroxy geranyl neral and geranyl geranal 2 and 3. Colourless oil, IR(CCl_4): 3510 (OH), 1730 (OAc), 1690 (C=C-CHO) and 1240 cm^{-1} ; MS: *m/z* 378 [M]$^+$ ($C_{22}H_{34}O_5$), 360[M-H_2O]$^+$, 332[360-CO]$^+$, 318[M-AcOH]$^+$, 43[CH_3CO]$^+$.

18-Acetoxy-12-hydroxy geranyl nera-1,19-dial and geranyl gerana-1,19-dial 4 and 5 and geranyl-6, 7 *E*-nera-1,19-dial and geranyl-6, 7 E-gerana-1,19-dial 6 and 7. Colourless oil, IR(CCl_4): 3500 (OH), 1730 (OAc), 1690, 1685 (C=C-CHO) and 1240 cm^{-1}; MS: *m/z* 376 [M]$^+$ ($C_{22}H_{32}O_5$), 348[M-CO]$^+$, 316[M-AcOH]$^+$, 43 [CH_3CO]$^+$.

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