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TRANSANNULAR CYCLIZATIONS OF ZERUMBONE EPOXIDE

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Abstract—Formic acid catalyzed rearrangement of zerumbone epoxide **3** gives three major bicyclic products, **4–6**. The most important rearrangement is a conrotatory electrocyclic Nazarow reaction. The structures were deduced from spectral and chemical evidence. ^{13}C NMR data are presented. An X-ray study has independently confirmed the proposed structures.

The three mono-epoxides of humulene **1** occur in Nature and have been proposed to be *in vivo* precursors of several bi- and tricyclic sesquiterpenoids.[1] *In vitro* acid-catalyzed cyclizations of humulene and of its three mono-epoxides have been intensively studied.[2–4] We have investigated acid treatment of the epoxide **3** of the related ketone, zerumbone **2**, a constituent of *Zingiber zerumbet*. We were prompted to undertake this study by the interesting results obtained in the study of the action of formic acid on another medium-ring epoxy-enone, epoxylathyrol.[5] By the action of formic acid on zerumbone epoxide, we obtained two products, **4** and **5**, with the rare bicyclo[6.3.0]undecane skeleton, and one (**6**) with the bicyclo[5.3.0]decane (hydroazulene) skeleton. Sesquiterpenoids with the bicyclo[6.3.0]undecane skeleton have recently been isolated from a sea hare, *Aplysia dactylomela*,[6] and a soft coral, *Capnella imbricata*.[7] Furthermore, bicyclo[6.3.0]undecane sesquiterpenoids have been shown to be intermediates in *in vitro* biomimetic rearrangements of humulene to tricyclic sesquiterpene skeletons, such as the illudoid skeleton,[3] and to be possible biosynthetic precursors of the tricyclic capnellane skeleton.[7] Another compound with the bicyclo[6.3.0]undecane skeleton has been used as a key intermediate in the chemical synthesis of the tricyclic sesquiterpene isocomene.[8]

RESULTS AND DISCUSSION

Three major products, **4–6** (see Scheme 1), all more polar than the starting material, were formed on treatment of zerumbone epoxide **3** with formic acid at room temperature.

The mass spectrum of substance **6** shows a molecular ion with *m/e* 234 (isomeric with the starting material), while **4** and **5** both have molecular ions with *m/e* 280, corresponding to the addition of formic acid. The UV absorption maximum of **6** at 240 nm indicates that the compound still contains an α,β-unsaturated ketone grouping. The IR bands at 1703 and 1636 cm^{-1} indicate the presence of a 2-cyclopentenone system, and the bands at 2705 and 1730 cm^{-1} suggest the presence of an aldehyde group.

Substance **5**, according to UV and IR data, contains the same cyclopentenone system and a formate group.

In the case of substance **4**, the UV absorption at 235 nm and IR bands at 1727 and 1635 cm^{-1} indicate it to contain a 2-methylenecyclopentanone system.

After catalytic hydrogenation of **4** followed by hydrolysis (forming products **4e** and **4f**) the IR spectrum showed a carbonyl absorption at 1740 cm^{-1}, typical of cyclopentanones.

The ^1H and ^{13}C NMR data of **4–6** confirmed the IR and UV results, and the relative configurations can be explained as shown in Scheme 1.

The first step is proposed to be the opening of the epoxide to give a less strained intermediate for the cyclization to follow, which is a conrotatory electrocyclic reaction within a pentadienyl cation,[9,10] i.e. the well-known Nazarov reaction. This process leads to **5** and **4**, which according to the Woodward–Hoffmann rules both have a *trans* ring junction. The aldehyde **6** is formed from **5** by a pinacol rearrangement.

The ^1H NMR assignments were supported by spin-decoupling experiments. However, a complete, detailed interpretation, even at 250 MHz, was not possible due to the complexity of the spin systems, expecially in the case of **4**. Compound **4** shows two doublets, at δ 5.32 and δ 6.04, typical of an exocyclic methylene group adjacent to a carbonyl in a five membered ring.[11] The coupling of 2.5 Hz was due to allylic coupling with the proton at C-f, while the coupling between the geminal protons was not observable.

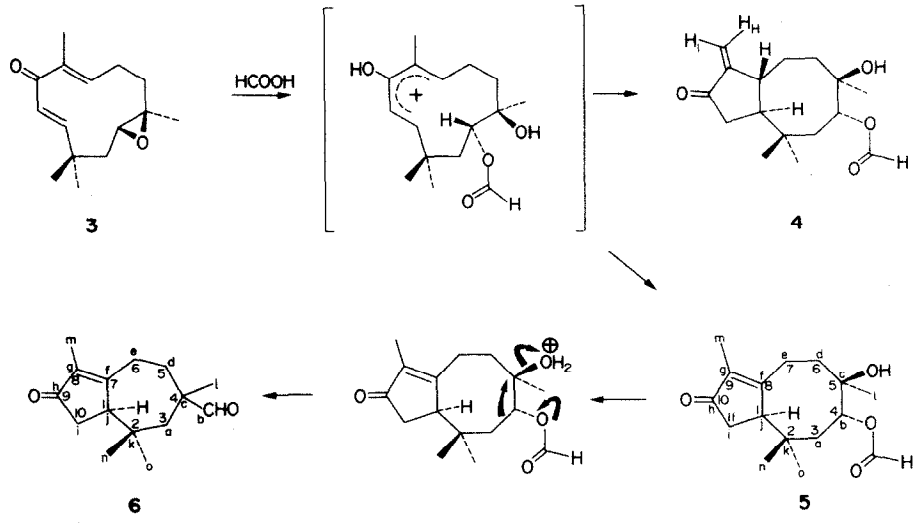
The methyl group at C-c shows up as a singlet at δ_H 1.25, while the geminal methyls appear at δ_H 0.96 and δ_H 1.00. The formate proton appears as a singlet at δ 8.16.

In the case of **5**, the geminal methyl signals are attributed to singlets at δ 0.73 and 1.08. The high field signal is assigned to C-n, since this methyl according to Dreiding models (and as confirmed by the X-ray analysis, see Fig. 1) is situated in the shielding region of the conjugated π-bond of the 5-membered ring.[11] the C-l methyl is seen as a singlet at δ_H 1.29 and the C-m methyl as a slightly split doublet.

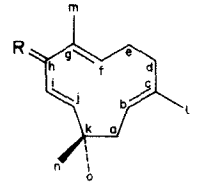
Compound **6** shows the C-n methyl at δ 0.58. The more strained bicyclo[5.3.0]decane system apparently tends to increase the shielding effect already observed in the case of **5**. The singlets at 1.03 and 1.07 are attributed to C-l and C-o methyls. The C-m methyl protons appear as a doublet (J = 1 Hz) at δ_H 1.66 and the aldehyde proton as a singlet at δ 9.54.

^{13}C NMR assignments were verified by gated decoupled spectra and for proton-bearing carbons by single resonance selective decoupling experiments, when the chemical shift of the proton was well defined. The ^{13}C NMR data are summarized in Table 1. The high field carbon signal at $\delta_C \sim 8$ in substances **5** and **6** is typical of

a methyl adjacent to the carbonyl function in a cyclopentenone ring.[12,13] The proximity of the two methyl signals in the ^{1}H NMR spectrum of **6** (δ 1.03 and 1.07) made their assignment difficult. Selective proton decoupling in ^{13}C NMR spectra showed that the methyl at δ_H 1.03 corresponds to the carbon at δ_C 32.3 and the methyl at δ_H 1.07 to δ_C 27.0. The absolute assignment was uncertain from these results. The position of the aldehyde near the methyl at C-c made it possible to consider long-range coupling for assignment of the methyls in the following way: when the single frequency heteronuclear decoupler was set to about $\delta_H = 2$ in the region of the methylene signals long-range coupling with the methyls was suppressed in the ^{13}C NMR spectrum. The carbon at δ_C 27.0 appeared as a "clean" quartet whereas the quartet at δ_C 32.3 was split by three-bond ($^3J_{CH}$) long-range coupling to the aldehyde proton (δ_H = 9.16, well outside the decoupling region). The peaks at δ_C 32.3 and δ_H 1.03 could thus be attributed to the methyl at C-c.



Scheme 1.



1 R=H_2
2 R=O

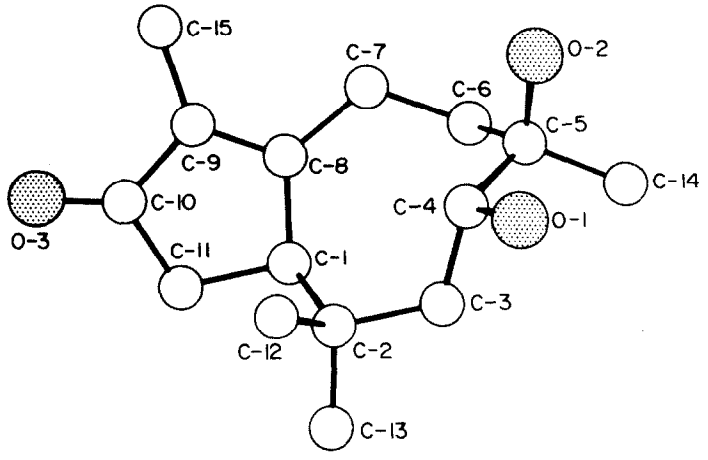


Fig. 1.

Table 1. ^{13}C NMR data (62.8 MHz, $CDCl_3$ ppm from TMS as internal standard, J (Hz) in parenthesis)

Carbon	4	4a	4b	4c	4d	5	5a	6
a†	47.4 t(126)	49.0 t(126)	49.0 t(126)	49.6 t(125)	51.2 t(125)	46.5 t(128)	47.5 t(124)	52.4 t(126)
b	76.0 d(146)	72.8 d(142)	216.0 s	72.8 d(150)	75.2 d(150)	75.0 d(148)	71.5 d(139)	205.2 d(170)
c	75.1 s	76.2 s	77.9 s	208.9 s	208.5 s	74.0 s	74.2 s	49.3 sd# (25)
d	35.3 t(130)	35.6 t(130)	32.9 t(130)*	40.5 t(125)	40.8 t(125)	33.9 t(127)	33.4 t(125)	30.7 t(125)
e	29.6 t(126)	29.7 t(126)	31.6 t(126)*	30.2 t(125)	31.0 t(125)	24.6 t(126)	25.0 t(126)	26.1 t(125)
f	38.5 d(130)	39.1 d(130)	38.5 d(125)	40.1 d(125)	39.1 d(125)	173.2 s	175.2 s	174.7 s
g	151.8 s	152.7 s	149.9 s	150.2 s	149.4 s	139.3 s	137.9 s	136.8 s
h	206.0 s	206.4 s	206.4 s	207.9 s	208.0 s	207.8 s	208.2 s	207.4 s
i	40.8 t(126)	40.9 t(126)	39.8 t(130)	56.1 d(125)	61.4 d(125)	41.3 t(129)	41.1 t(126)	38.0 t(125)
j	44.2 d(126)	44.8 d(122)	45.0 d(125)	54.2 d(125)	51.2 d(125)	50.0 d(131)	50.2 d(126)	51.9 d(125)
k	35.0 s	34.6 s	40.4 s	40.8 s	41.5 s	37.6 s	37.3 s	36.7 s
l	23.6 q(125)	22.3 q(125)	28.3 q(130)	30.1 q(125)	30.1 q	22.2 q(126)	20.9 q(126)	32.3 q(126)
m	118.5 t(161)	118.1 t(159)	119.0 t(160)	119.0 td# (160,4)	119.7 td# (160,4)	8.3 q(128)	7.9 q(125)	7.8 q(126)
n	18.9 q(124)	18.8 q(122)	18.3 q(125)	24.2 q(125)	23.2 q(125)	18.5 q(125)	17.6 q(126)	20.2 q(125)
o	31.6 q(125)	31.9 q(124)	31.3 q(125)	30.2 q	28.5 q(125)	32.5 q(120)	32.2 q(125)	27.0 q(125)
HCOO-	161.0 dd# (226,4)					161.0 dd# (225,4)		

† Numeration, see Scheme 1 and 2

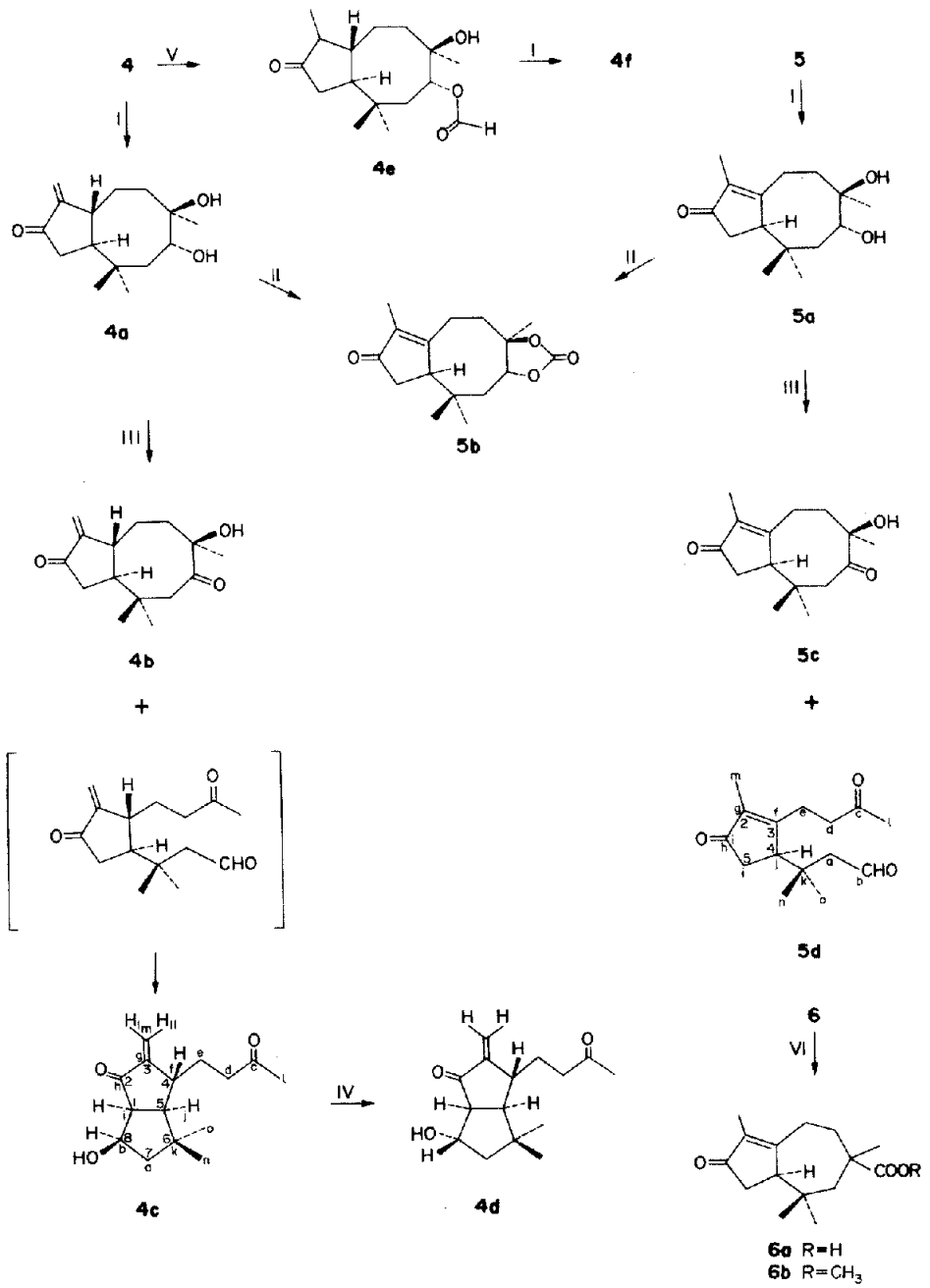
* Could be reversed

$^3J_{CH}$

The relative configurations were further confirmed by some chemical reactions as shown in Scheme 2.

Compound **5**, on hydrolysis, provided the diol **5a**, which on treatment with phosgene yielded **5b**. The carbonate group was shown to be in a five-membered ring by its IR absorption at 1816 cm^{-1} in CCl_4.[14] Compound **5a** was thus a vicinal diol and provided two further products on oxidation with pyridinium dichromate.[15] Of these, **5c** was the expected oxidation product. It had an additional carbonyl absorption at 1705 cm^{-1} in $CHCl_3$, typical of cycloöctanones. The other, **5d**, corresponds to a glycol cleavage product, thus showing that pyridinium dichromate can cleave α-diols, in the same way as periodic acid or chromic acid. **5d** obviously had the cyclopentenone ring intact, according to the IR absorption at 1695 and 1635 cm^{-1}.

Compound **4** yielded **4a** on basic hydrolysis. Even under very mild conditions, it was not possible to avoid partial dimerisation of **4a**. On treatment with phosgene and catalytic amounts of pyridine, **4a** provided the carbonate **5b**. The isomerisation, caused by the HCl formed, proved the close structural relationship between **4** and **5**.



(I) K_2CO_3/MeOH; (II) $COCl_2$/pyridine; (III) $(pyH)_2Cr_2O_7$; (IV) TFA/$CHCl_3$; (V) H_2/Pd/C; (VI) 6a Air oxidation of 6; 6b CH_2N_2 treatment of 6a.

Scheme 2.

Oxidation of **4a** with pyridinium dichromate gave two products, **4b** and **4c**. One, **4b**, was the expected hydroxy ketone. The other, **4c**, was a bicyclo[3.3.0]octane derivative. The formation of this product could be explained by a prior cleavage analogous to that observed for **5a**, the cleavage product then being cyclised by an intramolecular aldol condensation. Treatment of **4c** with trifluoroacetic acid resulted in isomerization at C-b to give **4d**. The structural isomers **4c** and **4d** are both supposed to have the *cis*-configuration at the ring junction, since *trans*-fused bicyclo[3.3.0]octanes are highly strained.[16]

The coupling constant ^3J H-i, H-j = 9.5 Hz fits with the theoretical value (Karplus)[11] for a bond angle of 0° and this confirms the *cis*-configuration.

The original five-membered ring was still intact as shown by IR and NMR spectra. The doublets at δ_H 5.34 and 6.08 have chemical shifts typical for the protons of an exocyclic methylene adjacent to the carbonyl in a cyclopentanone ring.[11] These values are almost identical in the series **4d**. The singlet at $\delta_C \sim 150$ and the triplet at $\delta_C \sim 118$ in the ^{13}C NMR spectra are also typical. Compound **4c** was also obtained by treatment of **4a** with periodic acid, while the simple cleavage product (a keto aldehyde) could not be detected.

6 was easily air-oxidized on standing to the acid **6a**, which on treatment with diazomethane provided **6b**.

The stereochemistry of **5a** was finally determined by X-ray analysis (see Fig. 1, which shows the structure of one enantiomer; all the substances described here are racemic). The proposed structure was thus shown to be correct. The 1,2-diol was *trans* as expected to result from the opening of an epoxide. Assuming the reaction to follow the Woodward-Hoffmann rules, the stereochemistry is determined as shown in Scheme 2.

EXPERIMENTAL

M.ps were recorded on a Reichert hot stage microscope and are corrected. NMR spectra were run at 250 MHz (^1H) and 62.8 MHz (^{13}C) in $CDCl_3$ with TMS as internal standard. In some cases, when it seemed reasonable, the NMR patterns were treated as first order, even if the requirement $(\Delta\nu/J) > 10$ was not fulfilled. Gated decoupled spectra were run with a pulsing time of 5–10 μsec and a recovery time of 1 sec; MS: Electron impact and chemical ionization mass spectra were recorded at high and low resolution using a Thomson THN 208 instrument, 70 eV, direct inlet; tlc was performed on Merck silica gel 60 F_{254} plates (0.25 mm); Flash column chromatography[17] (f.c.c.) was carried out with silica gel (Merck No. 9385 (40–63 μm). The X-ray measurements were recorded on a Philips PW 1100 automatic refractometer. All data concerning this X-ray study can be obtained on request.†

Zerumbone **2**, was isolated from *Zingiber zerumbet* as earlier described.[18]

Zerumbone epoxide **3**. Zerumbone (5 g) was dissolved in CH_2Cl_2 (20 ml) and treated at room temp. in small portions with a soln of m-chloroperbenzoic acid in CH_2Cl_2. The reaction was rapid and was followed by tlc (AcOEt–hexane, 1:1) to completion. Most of the m-chlorobenzoic acid formed could be precipitated on addition of hexane. The remainder in the filtrate could be removed most easily on a basic silica gel column.[19] The solution was evaporated to give crystals (5.2 g) of racemic zerumbone epoxide. A sample was recrystallized from n-heptane. M.p. 96°, analytical and spectral data were identical with those of the natural product.[18,20]

†This information is available on request from the Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 IEW.

Acid catalysed rearrangement of zerumbone epoxide. **3** (4 g) was dissolved in HCOOH–CH_2Cl_2 (8:2; 20 ml) and left at room temp. for 10 h. The reaction mixture was evaporated twice with 20 ml portions of toluene and the residue chromatographed by f.c.c. with AcOEt–hexane (1:1) as eluant. The separation was finished in about 15 min. The first fractions contained a mixture (1 g) of minor less-polar products which were not investigated further. The next fractions contained unreacted **3** (0.5 g) (R_f 0.6). Then followed three major products, **6** (0.4 g, R_f 0.45), **4** (1.5 g, R_f 0.3) and **5** (0.8 g, R_f 0.15).

4 - *Formyloxy* - 5 - *hydroxy* - 2,2,5 - *trimethyl* - 9 - *methylene* - trans - *bicyclo*[6.3.0]*undecan* - 10 - *one*, **4**, m.p. 124–126° (Et_2O, CH_2Cl_2), IR (CCl_4): 3540, 1727 and 1635 (2-methylene cyclopentanone and HCOO–), 1180 (HCOO–), 940 (C=CH_2) cm^{-1}. MS: *m/e* (rel. int.): 280.167 (M^+, $C_{16}H_{24}O_4$, 3), 265 (M^+-Me, 1), 262 (M^+-H_2O, 3) 234 (M^+-HCOOH, 4), 216 (23), 165 (62), 107 (100), 69 (38), 43 (68). UV (EtOH): λ_{max} 235 nm (log ϵ 3.55). ^1H NMR: δ 0.96 (3H, *s*, H-n), 1.00 (3H, *s*, H-o), 1.25 (3H, *s*, H-l), 1.46 (1H, *d*, *J* 16 Hz, H-a), 1.66 (1H, *dt*, *J* 16, 4 Hz, H-d), 1.87 (1H, *dd*, *J* 7.5, 16 Hz, H-a), 1.8–2.6 (6H, *m*, H-d, 2×H-e, 2×H-i, H-j), 3.05 (1H, br. *s*, H-f), 5.32 (1H, *d*, *J* 2.5 Hz, H_{II} on C-m, 5.49 (1H, br. *d*, *J* 6.8 Hz, H-b), 6.04 (1H, *d*, *J* 2.5 Hz, H_I on C-m), 8.16 (1H, *s*, OCOH). (^{13}C NMR, see Table 1.)

4,5 - *Dihydroxy* - 2,2,5 - *trimethyl* - 9 - *methylene* - trans - *bicyclo*[6.3.0]*undecan* - 10 - *one* **4a**, was obtained in 60% yield by hydrolysis of **4** (1 g) with K_2CO_3 in MeOH for 20 sec. A dimer of **4a** was the major byproduct, but was not further investigated. The mixture was purified by f.c.c., eluant AcOEt–hexane (5:1), to give **4a** as a colourless oil. MS (chemical ionisation, using isobutane as reacting gas): *m/e* 253.180 ($M^+ + 1$, $C_{15}H_{23}O_3$). Peak matching was carried out using zerumbone epoxide, $M^+ + 1$ = *m/e* 235.176 as reference. IR ($CHCl_3$): 3580 br. and 3440 br. (OH), 1716 and 1635 (2-methylene cyclopentanone), 940 (C=CH_2) cm^{-1}. ^1H NMR: δ 0.96 (3H, *s*, H-n), 1.01 (3H, *s*, H-o), 1.21 (3H, *s*, H-l), 1.21 (1H, *d*, *J* 13 Hz, H-e), 1.41 (1H, *d*, *J* 16 Hz, H-a), 1.41 (1H, *dm*, *J* 16 Hz, H-d), 1.75 (1H, *dd*, *J* 16, 7 Hz, H-a), 1.88 (2H, br. *s*, 2×OH), 1.94–2.08 (1H, *m*, H-j), 2.20–2.32 (1H, *m*, H-i), 2.40–2.54 (3H, *m*, H-i, H-e, H-d), 2.93 (1H, br. *m*, H-f), 4.06 (1H, br. *d*, *J* 7 Hz, H-b), 5.26 (1H, *d*, *J* 2.3 Hz, H_{II} on C-m), 6.02 (1H, *d*, *J* 3 Hz, H_I on C-m). (^{13}C NMR, see Table 1.)

On treatment of **4a** in CH_2Cl_2 with $COCl_2$ and catalytic amounts of pyridine the product isolated was **5b** (see later).

Oxidation of **4a** (10 mg) with pyridinium dichromate in CH_2Cl_2 provided two products, **4b** and **4c**, which were separated by tlc (AcOEt–hexane, 1:1), R_f 0.45 and 0.3.

4 - *Oxo* - 5 - *hydroxy* - 2,2,5 - *trimethyl* - 9 - *methylene* - trans - *bicyclo*[6.3.0]*undecan* - 10 - *one* **4b**, m.p. 97–98° (toluene) MS: *m/e* (rel. int.): 250.157 (M^+, $C_{15}H_{22}O_3$, 21), 232 (M^+-H_2O, 12), 206 (53), 165 (96), 136 (67), 107 (100), 95 (90), 71 (63), 43 (69). IR ($CHCl_3$): 3480 br. (OH), 1715 and 1635 (2-methylene cyclopentanone), 1695 (carbonyl in cyclooctanone), 940 (C=CH_2) cm^{-1}. ^1H NMR: δ 0.96 (3H, *s*, H-n), 1.06 (3H, *s*, H-o), 1.29 (3H, *s*, H-l), 1.9–2.6 (8H, *m*, 2×H-d; 2×H-e, 2×H-i, H-f, H-j), 2.10 (1H, *d*, *J* 11.5 Hz, H-a), 2.88 (1H, *d*, *J* 11.5 Hz, H-a), 3.94 (1H, br. *s*, OH) 5.27 (1H, *d*, *J* 1.5 Hz, H_{II} of C-m), 6.00 (1H, *d*, *J* 1.5 Hz, H_I of C-m).

4α - (3' - *Oxo* - *butyl*) - 8β - *hydroxy* - 6,6 - *dimethyl* - 3 - *methylene* cis - *bicyclo*[3.3.0]*octan* - 2 - *one*, **4c**. Colourless oil. MS: *m/e* (rel. int.): 250.157 (M^+, $C_{15}H_{22}O_3$, 9) 232 (M^+-H_2O, 29) 217 (23), 189 (34), 113 (27), 107 (100), 95 (30), 43 (77). IR ($CHCl_3$): 3500 br. (OH), 1715 and 1635 (2-methylenecyclopentanone), 1175 (CH_3CO–), 940 (C=CH_2) cm^{-1}. ^1H NMR: δ 0.93 (3H, *s*, H-n), 1.04 (3H, *s*, H-o), 1.60 (1H, *dd*, *J* 13, 4.5 Hz, β-H-a), 1.65–1.90 (2H, *m*, 2×H-e), 1.77 (1H, *dd*, *J* 13, 6.5 Hz, α-H-a), 2.02 (1H, *dd*, *J* 9.5, 2.5 Hz, H-j), 2.17 (3H, *s*, H-l), 2.50 2H, *t*, *J* 7 Hz, 2×Hd), 2.74 (1H, v.br. *t*, *J* 9 Hz, H-f) 2.92 (1H, br. *d*, *J* 2.5 Hz, OH) 3.08 (1H, *t*, *J* 9.3 Hz, H-i) 4.61 (1H, br. *ddd* *J* 9, 6.5, 4.5 Hz, H-b), 5.34 (1H, *d*, *J* 1 Hz, H_{II} at C-m) 6.08 (1H, *d*, 1.7 Hz, H_I at C-m). (^{13}C NMR, see Table 1.) **4c** was equally obtained on treatment of **4a** with periodic acid in etheral soln.

4α - (3' - *Oxo* - *butyl*) - 8α - *hydroxy* - 6,6 - *dimethyl* - 3 - *methylene* -cis - *bicyclo*[3.3.0]*octan* - 2 - *one*, **4d**, was obtained from **4c** (1.5 mg) in 0.5 ml $CDCl_3$ on addition of one drop of TFA.

The reaction was over in 4 h (followed by NMR). The solution was co-evaporated with toluene and the residue purified by tlc to give **4d** (0.9 mg), R_f (AcOEt–hexane, 1:1) 0.2, as a colourless oil. MS: *m/e* (rel. int.): 250.157 (M^+, $C_{15}H_{22}O_3$, 30), 232 (M^+-H_2O, 51), 217 (49), 189 (37), 174 (63), 159 (46), 131 (42), 105 (27), 91 (41), 57 (54), 44 (100), 43 (97). ^{1}H NMR: δ 0.59 (3H, *s*, H-n), 1.09 (3H, *s*, H-o), 1.59 (1H, *dd*, *J* 12.5, 8 Hz, β-H-a) 1.74 (2H, sl. br. *septet*, $J \approx 7$ Hz, 2 × H-e), 1.94 (1H, *dd*, *J* 12.5, 6.5 Hz, α-H-a), 2.17 (3H. *s*, H-1), 2.25 (1H, *d*, *J* 11 Hz, H-j), 2.51 (2H, *t*, *J* 7.5 Hz, 2 × H-d), 2.58 (1H, br. *t*, *J* 7 Hz H-f), 2.84 (1H, *dd*, *J*, 11, 3 Hz, H-i), 4.44 (1H, *ddd*, *J* 8, 6.5, 3 Hz, H-b), 5.36 (1H, *dd*, J_{gem} 0.8 Hz, $J_{allylic}$ 1.6 Hz, H_{II} at C-m), 6.07 (1H, *dd*, *J* 0.8, 1.6 Hz, H_I at C-m). (^{13}C NMR, see Table 1.)

4 - *Formyloxy* - 5 - *hydroxy* - 2,2,5,9 - *tetramethyl* - trans - *bicyclo*[6.3.0]*undecan* - 10 - *one*, **4e**, was obtained by hydrogenation of **4** with 10% Pd/C in AcOEt. Colourless oil. MS: *m/e* (rel. int.): 282.183 (M^+, $C_{16}H_{26}O_4$ 1.7), 267 (M^+-CH_3, 4), 236 (M^+-HCOOH, 5.5), 211 (42), 167 (40), 149 (100), 109 (40) 69 (34), 43 (38). IR ($CHCl_3$): 3460 br. (OH), 1740 (cyclopentanone), 1720 (HCOO–), 1180 (HCOO–) cm^{-1}. ^{1}H NMR: δ 0.94 (3H, *s*, H-n or H-o), 0.95 (3H, *s*, H-o or H-n), 1.10 (3H, *d*, *J* 6 Hz, H-m), 1.25 (3H, *s*, H-1), 1.6–2.5 (11H, *m*, 2 × H-a, 2 × H-d, 2 × H-e, H-f, H-g, 2 × H-i, H-j), 5.35 (1H, *d*, *J* 7 Hz, H-b), 8.14 (1H, *s*, OCOH).

4,5 - *Dihydroxy* - 2,2,5,9 - *tetramethyl* - trans - *bicyclo*[6.3.0]*undecan* - 10 - *one*, **4f** was obtained by hydrolysis of **4e** with K_2CO_3 in MeOH. Colourless oil. MS: *m/e* (rel. int.): 254.188 (M^+, $C_{15}H_{26}O_3$, 1.2) 239 (M^+-Me, 1.4), 236 (M^+-H_2O, 1.5), 205 (46). 183 (89), 149 (100), 109 (41), 84 (67), 69 (53), 56 (72), 41 (51). ^{1}H NMR: δ 0.95 (3H, *s*, H-n or H-o), 0.96 (3H, *s*, H-o or H-n), 1.07 (3H, *d*, *J* 7 Hz, H-m), 1.22 (3H, *s*, H-1), 1.6–2.2 (8H, *m*, H-a, 2 × H-d, H-e, H-f, 2 × H-i, H-j), 1.80 (1H, *dd*, *J* 16, 7 Hz, H-a), 1.84 (1H, *dd*, *J* 7, 11 Hz, H-g), 2.47 (1H, *ddd J* 18, 9, 1.5 Hz, H-e) 3.92 (1H, *d*, *J* 7 Hz, H-b).

4 - *Formyloxy* - 5 - *hydroxy* - 2,2,5,9 - *tetramethylbicyclo*[6.3.0]*undeca* - 8 - *en* - 10 - *one*, **5**, m.p. 157–158° (CH_2Cl_2). MS: *m/e* (rel. int.): 280.167 (M^+, $C_{16}H_{24}O_4$, 12) 265 (M^+-Me, 1), 262 (M^+-H_2O, 1), 234 (M^+-HCOOH, 10), 216 (19), 201 (17), 166 (43), 123 (63), 107 (54), 79 (40), 69 (73), 43 (100), 41 (54). IR ($CHCl_3$): 3580 br. (OH), 1720 (HCOO–), 1690 and 1620 (2-cyclopentenone), 1180 (HCOO–) cm^{-1}. UV (EtOH): λ_{max} 243 nm (log ϵ 4.03). ^{1}H NMR: δ 0.73 (3H, *s*, H-n), 1.08 (3H, *s*, H-o), 1.29 (3H, *s*, H-1), 1.49 (1H, *d*, *J* 16 Hz B of ABX, H-a), 1.75 (3H, *d*, *J* 1 Hz, H-m), 1.82 (1H, *dd*, *J* 15, 7 Hz, H-d), 1.88 (1H, *dd*, *J* 16, 7 Hz, A of ABX, H-a), 2.10 (1H, *dd*, *J* 12, 15 Hz, H-d), 2.37 (2H, br. *d*, $\Delta\nu$ = 3.5 Hz, AB of ABX, 2 × H-i), 2.48 (1H, br. *dd*, *J* 20, 7 Hz, H-e), 2.78 (1H, br. *s*, X of ABX, H-j), 3.06 (1H, br. *dd*, *J* 13, 20 Hz, H-e), 4.92 (1H, br. *d*, *J* 7 Hz, X of ABX, H-b) 8.11 (1H, *s*, OCOH). (^{13}C NMR, see Table 1.)

4,5 - *Dihydroxy* - 2,2,5,9 - *tetramethylbicyclo*[6.3.0]*undeca* - 8 - *en* - 10 - *one* **5a** was obtained by hydrolysis of **5** (100 mg) with K_2CO_3 in MeOH for 1 min and purified by f.c.c. to give crystals (80 mg) which were recrystallised from toluene to give colourless prisms, m.p. 165–166° MS: *m/e* (rel. int.): 252.172 (M^+, $C_{15}H_{24}O_3$, 27), 237 (M^+-Me, 4), 234 (M^+-H_2O, 7), 181 (36) 167 (53), 150 (42), 123 (78), 110 (100), 69 (52), 43 (84). IR ($CHCl_3$): 3560 and 3440 (OH), 1695 and 1625 (2-cyclopentenone) cm^{-1}. ^{1}H NMR: δ 0.73 (3H, *s* H-n), 1.08 (3H, *s*, H-o), 1.25 (3H, *s*, H-1), 1.41 (1H, *d*, *J* 16 Hz, H-a), 1.72 (3H, *d*, *J* 1.5 Hz, H-m), 1.76 (1H, *dd*, *J* 14, 6 Hz, H-d), 1.82 (1H, *dd*, *J* 15, 5.5 Hz, H-a), 1.89 (1H, br. *s*, OH), 1.93 (1H, br. *s*, OH), 2.07 (1H, *dd*, *J* 12, 14 Hz, H-d), 2.35 (2H, br. *d*, $\Delta\nu$ 3.5 Hz, H-i), 2.35 (1H, *dd*, *J* 6, 19 Hz, H-e) 2.72 (1H, br. *s*, H-j), 3.05 (1H, *dd*, *J* 12, 19 Hz, H-e), 3.43 (1H, br. *d*, *J* 5 Hz, H-b) (^{13}C NMR, see Table 1.) A quadrilateral bipyramidal crystal with the dimensions: 0.4 × 0.4 × 0.4 mm was used for X-ray analysis.

Carbonate of **5a**, **5b** was obtained by treatment overnight at room temp. of **5a** (10 mg) in CH_2Cl_2 (2 ml) with one drop of pyridine and a few drops of $COCl_2$ (20% in toluene). After purification by tlc, the yield was 5 mg of **5b**, which was recrystallised from CCl_4 to give colourless prisms m.p. 202–203°. MS: *m/e* (rel. int.): 278.152 (M^+, $C_{16}H_{22}O_4$, 13), 234 (M^+-CO_2, 11), 178 (35), 150 (19), 123 (79), 110 (49), 108 (100), 69 (78). IR (CCl_4): 1816 (carbonate in five-membered ring)), 1710 and 1635 (2-cyclopentenone). ^{1}H NMR: δ 0.79 (3H, *s*, H-n), 1.13 (3H, *s*, H-o), 1.51 (3H, *s*, H-1) 1.79 (3H, br. *s*, H-m), 1.79 (1H, *dd*, *J* 16, 1.5 Hz, A of ABX system H-a) 2.07 (1H, *d*, *J* 12.5 Hz, H-e), 2.09 (1H, *dd*, *J* 16, 6 Hz, B of ABX, H-a), 2.18 (1H, *d*, *J* 12.5 Hz, H-d), 2.29 (1H, *dd*, *J* 12.7 Hz, H-d), 2.35 (2H, br. *d*, $\Delta\nu$ 3.5 Hz, AB of ABX system, H-i), 2.47–2.53 (1H, non diss. *m*, X of ABX, H-j), 2.92 (1H, *dd*, *J* 13.7 Hz, H-e), 4.92 (1H, *dd*, *J* 6.5, 1.5 Hz, X of ABX, H-b).

Oxidation of **5a** (7 mg) with pyridinium dichromate[13] in CH_2Cl_2 provided two products, which were separated by tlc (AcOEt), **5c** (3 mg, R_f 0.6) and **5d** (1.5 mg, R_f 0.5).

5 - *Hydroxy* - 2,2,5,9 - *tetramethyl* - 4 - *oxo* - *bicyclo*[6.3.0]*undeca* - 8 - *en* - 10 - *one*, **5c**, m.p. 150–152°, MS: *m/e* (rel. int.): 251 (M^+ + 1, 51), 250.157 (M^+, $C_{15}H_{22}O_3$, 26), 232 (M^+-H_2O, 14), 166 (42), 123 (100), 108 (47), 43 (63). IR ($CHCl_3$): 3460 br. (OH), 1705 sh (cyclooctanone), 1695 and 1625 (2-cyclopentenone) cm^{-1}. ^{1}H NMR: δ 0.75 (3H, *s*, H-n), 1.18 (3H, *s*, H-o), 1.42 (3H, *s*, H-1), 1.65 (3H, sl. br. *s*, H-m), 1.90 (1H, *dd*, *J* 14, 8 Hz, H-d), 2.27–2.50 (5H, *m*, 2 × H-a, H-d, H-e, H-i), 2.67 (1H, *dd*, *J* 18.8 Hz, H-e), 2.87–2.97 (2H, br. *m*, H-i, H-j), 3.93 (1H, br. *s*, OH).

3 - (3′ - *Oxo* - *butyl*) - 2 - *methyl* - 4 - (1″,1″ - *dimethyl* - *propanal*) - 2 - *pentenone*, **5d**. Colourless oil. MS: *m/e* (rel. intl): 251 (M^+ + 1, 3), 250.157 (M^+, $C_{15}H_{22}O_3$, 2), 232 (M^+-H_2O, 4), 206 (85), 188 (38), 166 (27), 123 (77), 108 (100), 43 (58). IR ($CHCl_3$): 2740 (–CHO), 1720 (–CHO and –$COCH_3$), 1695 and 1635 (2-cyclopentenone) cm^{-1}. ^{1}H NMR: δ 1.07 (3H, *s*, H-n) 1.16 (3H, *s*, H-o), 1.73 (3H, sl. br. *s*, H-m), 2.19 (3H, *s*, H-l), 2.27 (1H, *dd*, *J* 18, 2 Hz, H-i), 2.35 (2H, *d*, *J* 2.5 Hz, 2 × H-a), 2.43 (1H, *dd*, *J* 18, 6 Hz, H-i), 2.5–2.9 (4H, *m*, 2 × H-d, 2 × H-e), 2.99 (1H, br. *d*, *J* 6 Hz, H-j), 9.84 (1H, *t*, *J* 2.5 Hz, H-b).

4 - *Formyl* - 2,2,4,8 - *tetramethylbicyclo*[5.3.0]*deca* - 7 - *en* - 9 - *one*, **6**, was isolated as colourless crystals, m.p. 99°, MS: *m/e* (rel. int.) 234.162 (M^+, $C_{15}H_{22}O_2$ 82), 219 (M^+-Me, 21), 216 (M^+-H_2O, 12), 206 (59), 191 (65), 161 (100), 125 (88), 122 (82), 110 (79), 83 (65), 55 (60), 41 (64). IR (CCl_4): 2705 (–CHO), 1730 (–CHO), 1703 and 1635 (2-cylopentenone). UV (EtOH): λ_{max} 240 nm (log ϵ 4.0). ^{1}H NMR: δ 0.58 (3H, *s*, H-n), 1.03 (3H, *s*, H-1), 1.07 (3H, *s*, H-o), 1.63 (1H, *d*, *J* 16 Hz, H-a), 1.66 (3H, *d*, *J* 1 Hz, H-m), 1.72 (1H, *t*, *J* 13 Hz, H-d), 2.06–2.20 (2H, *m*, H-d and H-i), 2.16 (1H, *d*, *J* 16 Hz, H-a), 2.50 (1H, *dd*, *J* 18, 6 Hz, H-i), 2.62 (1H, *dd*, *J* 19, 7 Hz, H-e), 2.76–2.92 (2H, *m*, H-e and H-j), 9.54 (1H, *s*, H-b). (^{13}C NMR, see Table 1.)

4 - *Carboxy* - 2,2,4,8 - *tetramethylbicyclo*[5.3.0]*deca* - 7 - *en* - 9 - *one*, **6a** was obtained from **6** by air-oxidation on standing m.p. 170–172° (toluene). MS: *m/e* (rel. int.) 250.157 (M^+, $C_{15}H_{22}O_3$, 20), 205 (47), 128 (100), 123 (92). IR ($CHCl_3$): 3200–2600 (–COOH), 1690 br. (2-cyclopentenone and –COOH), 1628 (C=C) cm^{-1}. ^{1}H NMR: δ 0.66 (3H, *s*, H-n), 1.00 (3H, *s*, H-o), 1.32 (3H, *s*, H-1), 1.51 (1H, *d*, *J* 14.5 Hz, H-a), 1.66 (3H, sl. br. *s*, H-m), 1.70 (1H, *ddd*, *J* 14, 12, 2 Hz, H-d), 2.17 (1H, *dd*, *J* 18, 2 Hz, H-i), 2.17 (1H, br. *dd*, *J* 14, 7 Hz, H-d), 2.41 (1H, *d*, *J* 14.5 Hz, H-a), 2.41 (1H, *dd*, *J* 18, 5 Hz, H-i), 2.64 (1H, *dd*, *J* 18, 7 Hz, H-e), 2.79 (1H, sl. br. *s*, H-j), 2.94 (1H, *dd*, *J* 18, 12 Hz, H-e).

4 - *Carboxymethyl* - 2,2,4,8 - *tetramethylbicyclo*[5.3.0]*deca* - 7 - *en* - 9 - *one*, **6b** was formed by CH_2N_2 treatment of **6a**, m.p. 105–106°, MS: *m/e* (rel. int.): 264.173 (M^+, $C_{16}H_{24}O_3$, 48), 249 (M^+-Me, 12), 205 (25), 142 (100), 123 (42). IR ($CHCl_3$): 1725 (ester), 1685 and 1630 (2-cyclopentenone). ^{1}H NMR: δ 0.56 (3H, *s*, H-n), 0.99 (3H, *s*, H-o), 1.24 (3H, *s*, H-1), 1.48 (1H, *d*, *J* 14.5 Hz, H-a), 1.66 (3H, sl. br. *s*, H-m), 1.67 (1H, *ddd*, *J* 14, 12, 2 Hz, H-d), 2.17 (1H, br. *dd*, *J* 14, 7 Hz, H-d), 2.17 (1H, *dd*, *J* 19, 2 Hz, H-i), 2.40 (1H, br. *dd*, *J* 19, 6 Hz, H-i), 2.41 (1H, *d*, *J* 14.5 Hz, H-a), 2.65 (1H, br. *dd*, *J* 19, 7 Hz, H-e), 2.80 (1H, br. *s*, H-j), 2.95 (1H, br. *dd*, *J* 19, 12 Hz, H-e), 3.68 (3H, *s*, OCH_3).

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