Carbon-13 Magnetic Resonance Spectra. Synthetic Presqualene Esters, Related Cyclopropanes, and Isoprenoids

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^{13}C N.m.r. spectra of isoprenoids, both acyclic and containing a cyclopropane ring, have been measured. These include *cis*- and *trans*-chrysanthemic acid and its relatives, presqualene esters, and compounds containing part-structures of the latter. The data are employed to derive stereochemical assignments in the presqualene series.

In the preceding paper [1] we have described syntheses of (±)-presqualene alcohol, prephytoene alcohol, and a number of closely related cyclopropanes. As well as products with the natural configuration, stereoisomers were produced and isolated. It was of utmost importance to decide the geometry of acyclic precursors containing trisubstituted double bonds, and to ascertain the configuration of products with respect to the cyclopropane ring and to side-chain double bonds. Early information on these features relied heavily on evidence from ^1H n.m.r. spectra.[2] Further valuable information emerged from ^{13}C n.m.r. when suitable instrumentation became available. We now report analysis and assignment of spectra for presqualene esters [(18) and (19)], some related cyclopropanes (7)—(17), and acyclic synthetic forerunners. These data are of potential value in studies of the biosynthesis of squalene (and other triterpenoids) and phytoene (and other carotenoids), since excellent incorporations of presqualene pyrophosphate into squalene have been reported, in various biological systems. Both noise-decoupled and off-resonance spectra were obtained.

Table 1 lists the ^{13}C assignments (δ in p.p.m. from internal standard Me_4Si) for a series of C_5, C_{10}, and C_{15} acyclic isoprenoid compounds. These are 3-methylbut-2-en-1-ol (1a), 3-methylbut-2-enyl phenyl sulphone (1b), ethyl senecioate (1c), geraniol (2a), nerol (3a), geranyl and neryl phenyl sulphones [(2b) and (3b)], methyl geranoate (2d), methyl neroate (3d), (2*E*,6*E*)-farnesol (4a), (2*E*,6*E*)- and (2*Z*,6*E*)-farnesyl phenyl sulphones [(4b) and (5b)], methyl (2*E*,6*E*)-farnesoate (4d), and (2*Z*,6*Z*)-farnesal (6e).

TABLE 1

^{13}C N.m.r. data for acyclic terpenoids (δ in p.p.m. from Me_4Si)

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	3-Me	7-Me	11-Me	Others
(1a)	58·8	124·2	134·9	25·7									17·7			
(1b)	56·1	110·4 [a]	138·6	25·7									17·6			Ph: 145, 126, 133
(1c)	166·6	116·2	156·1	27·3									20·1			OEt: 59·3, 14·3
(2a)	58·6	125·3	136·9	39·8	26·8	124·4	131·1	25·6					16·1	17·6		
(2b)	55·8	110·7	138·9	39·5	26·1	123·6	131·4	25·6					15·9	17·6		Ph: 145, 128, 133
(2d)	167·0	115·4	159·7	41·0	26·2	123·2	132·3	25·6					18·7	17·6		OMe: 50·5
(3a)	58·7	124·7	139·1	32·1	26·6	123·9	132·1	25·6					23·4	17·6		
(3b)	55·8	110·9	138·8	31·7	26·0	123·4	131·9	25·6					23·4	17·6		Ph: 145, 128, 133
(3d)	166·5	115·9	160·3	33·5	26·9	123·8	132·0	25·6					25·3	17·6		OMe: 50·6
(4a)	59·3	123·8	139·5	39·7	26·4	123·5	135·3	39·6	26·8	124·4	131·2	25·6	15·9	16·2	17·6	
(4b)	55·1	110·5	138·9	39·1	26·2	123·2	135·4	39·7	26·7	124·2	131·1	25·6	15·9	16·2	17·6	Ph: 146, 128, 133
(4c)	166·6	115·8	159·4	41·0	26·1	123·0	136·0	39·7	26·8	124·3	131·1	25·7	18·7	16·0	17·6	OEt: 59·3, 14·4
(5b)	55·9	110·8	138·8	31·8	25·9	123·1	135·8	39·6	26·6	124·1	131·1	25·6	23·5	16·0	17·6	Ph: 146, 128, 133
(6e)	190·5	128·6	163·6	32·9	26·8 [b]	123·1	137·1	31·9	26·4 [b]	124·0	131·5	25·6	25·7	23·3	17·6	

[a] Assignment checked by decoupling with the ^1H signal at δ 5·17. [b] These assignments may be interchanged.

Every carbon signal is resolved in the spectra of the C_{15} compounds and the assignments can be made with reasonable certainty by comparison within the group.[3,4]

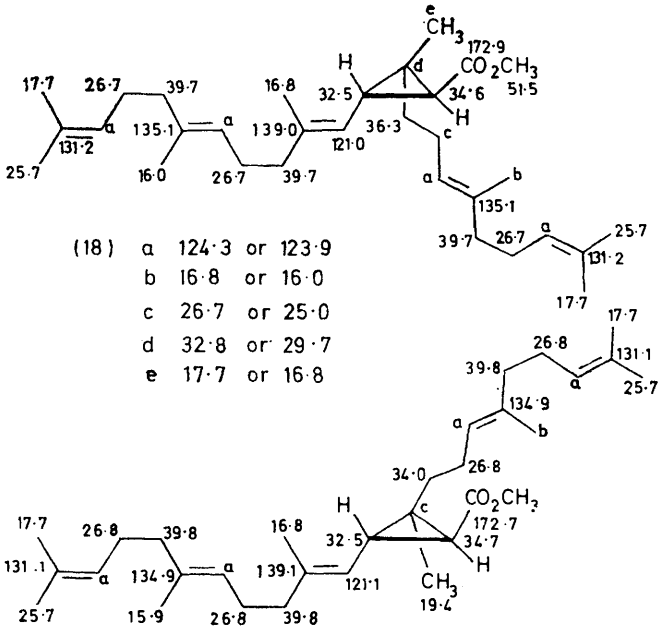
[1] R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden, and D. A. Whiting, preceding paper.

[2] A. F. Bramwell, L. Crombie, P. Hemesley, G. Pattenden, M. Elliott, and N. F. Janes, *Tetrahedron*, 1969, **25**, 1727.

[3] M. Jautelat, J. B. Grutzner, and J. D. Roberts, *Proc. Nat. Acad. Sci. (U.S.A.)*, 1970, **65**, 288.

[4] M. W. Duch and D. M. Grant, *Macromolecules*, 1970, **3**, 165.

The terminal methyls resonate at almost the same values (*Z* 17·6, *E* 25·6) in all the cases except (1c) where electron



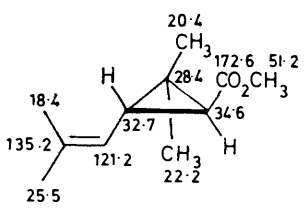
(18) a 124·3 or 123·9
b 16·8 or 16·0
c 26·7 or 25·0
d 32·8 or 29·7
e 17·7 or 16·8

(19) a 124·5 or 124·1
b 15·9 or 16·8
c 32·8 or 29·8

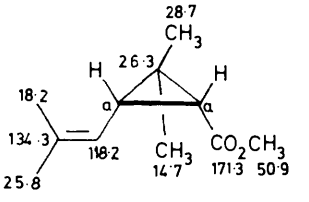
withdrawal by the ester function operates [shown by the +21·2 p.p.m. shift at C-3, from (1a) to (1c)]. The sp^2 carbons C-3, C-7, and C-11 in the farnesyl molecules show an interesting progression in shift along the chain [assignments based on (*a*) near-constant values at the 'head' of the terpenoid chains, and (*b*) variations caused by substituent R at the 'tail' of the chain; similar considerations permit allocation of the monoalkylated sp^2 carbons C-2, C-6, and C-10]. The C-2 geometry in the C_{10} and C_{15} series is clearly diagnosed by the ^{13}C resonances. Thus in the (2*E*)-compounds, C(3)–Me and C(3)–CH_2 absorb near δ 17 and 40, respectively, whereas the (2*Z*)-terpenoids show the corresponding signals around δ 24 and 32. On the other hand C-1 (CO_2R, CH_2OH, or $CH_2{\cdot}SO_2Ph$) is not sensitive to the geometry of the 2,3-double bond. Figures in Table 1 for the resonance positions of the 3- and 7-methyl carbons and the 4- and 8-methylene carbons of (2*Z*,6*Z*)-farnesal (6e) demonstrate clearly the *cis,cis*-geometry of the main chain in this example.

The aromatic carbons in the phenyl sulphones generally give rise to three signals, near δ 133, 128, and 145. The last value is appropriate for carbon attached to sulphur; signal heights indicate that the *ortho*- and *meta*-carbon signals may be at δ 128 with those of the *para*-carbons at 133 (—*M* effect of $-SO_2-$).

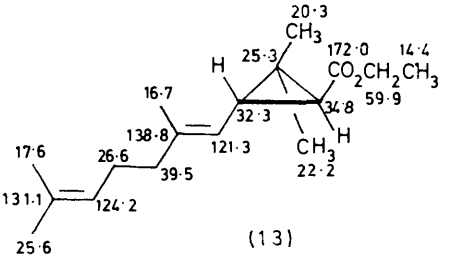
Data for various cyclopropane systems are shown in Table 2 and formulae (11)—(19). For *trans*- and *cis*-chrysanthemic acids, (7) and (8), and the corresponding esters [(11) and (12)] and alcohols [(9) and (10)] certain signals can be attributed without difficulty. Allocation of the two close cyclopropane methyl absorptions in the *trans*-series was decided by specific ^1H–^{13}C decoupling



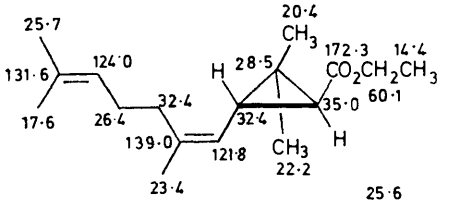
(11)



(12) a 32·2 or 30·9



(13)



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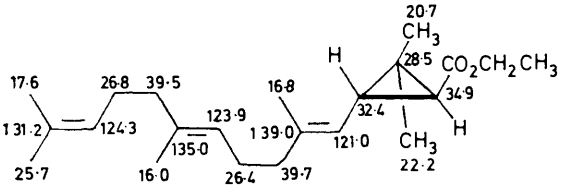

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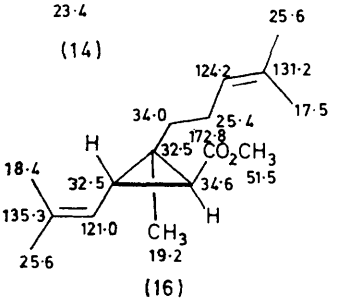

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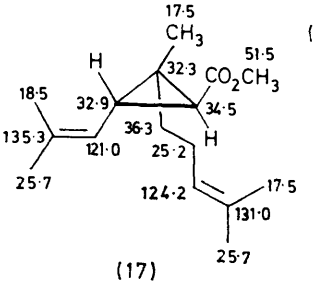


(17)

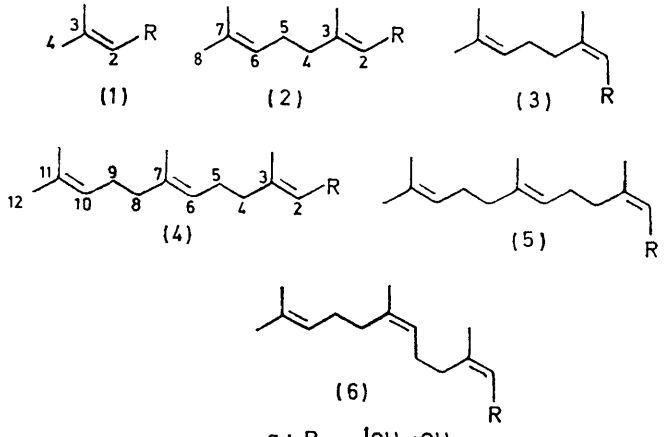
with the ^1H methyl resonance.[5] In the ester (11) and the acid (7) the cyclopropane methyl *cis* to the acid/ester function has the more shielded carbon (δ 20·4; *trans*-CH_3 δ 22·2) but the more deshielded protons (δ 1·25; *trans*-CH_3 δ 1·11). In the *cis*-series [(8), (10), and (12)] the cyclopropane methyl signals are well separated, the case of methyl *trans*-chrysanthemate (32·7 and 34·6), the assignments shown in (11) have been established by double irradiation, first at the C-1 proton frequency (δ 1·37) and then at that of the C-2 proton (δ 2·10).

TABLE 2

^{13} N.m.r. data for chrysanthemyl derivatives

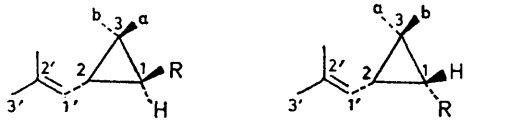
Cpd.	C-1	C-2	C-3	C-1′	C-2′	C-3′	3′-Me	3-Me [a]	3-Me [b]	Others
(7)	33·6/34·6 [c]		29·7	120·8	135·7	25·5	18·5	20·4	22·2	CO_2H: 179·3
(8)	31·1/33·2 [c]		27·4	117·8	134·8	25·8	18·3	14·7	28·8	CO_2H: 178·1
(9)	28·6	35·0	22·3	123·5	132·9	25·6	18·2	21·4	22·7	CH_2OH: 63·4
(10)	26·1	30·9	20·7	119·1	134·8	25·7	18·2	15·4	28·8	CH_2OH: 60·4

[a] *r* — 1, *cis*. [b] *r* — 1, *trans*. [c] Relative assignment uncertain.



(1) (2) (3) (4) (5) (6)

a; R = $^1CH_2{\cdot}OH$
b; R = $^1CH_2{\cdot}SO_2Ph$
c; R = $^1CO_2Et$
d; R = $^1CO_2Me$
e; R = ^1CHO



(7) R = CO_2H (8) R = CO_2H
(9) R = $CH_2{\cdot}OH$ (10) R = $CH_2{\cdot}OH$

more shielded being *cis*- to C-2 and C-3 substituents. C-1′ is also more shielded in the *cis*-series.

The cyclopropane ring carbons give rise in the off-resonance spectra to two doublets and one singlet. The last must be allotted to C-3 (quaternary); its shift varies with the nature of the C-1 substituent [δ 29·7 in (7), 22·3 in (9)]. The C-1 and C-2 lines are close. In the

[5] L. Crombie, G. Pattenden, and D. Simmonds, unpublished work.

On this basis, similar interpretations were made for the C_{15} and C_{20} prenylogues (13)—(15). Signals of all carbons in these three esters can be distinguished: the geometry about the ring is clearly shown to be *trans* by the cyclopropane Me and C-1′ shifts, and olefin geometry in the chain [(13) and (14)] is readily diagnosed by comparing C-2′ methyl and methylene resonances.

The cyclopropanes (16) and (17), closely resembling the presqualene esters (18) and (19), were examined, and spectral lines were assigned as shown. Little of compound (17) was available, and multiplicities were not in this case assigned with confidence. The spectra of (16) and (17) were very similar, the greatest differences being observed for bands at δ 19·2 (q) and 34·0 (t) in (16), moving to δ 17·5 (and coincident with a chain-terminal methyl signal) and 36·3 in (17). These signals evidently arise from the methyl and methylene at C-3; the more shielded of the pair of methyls/methylenes is *cis* to the C-1 ethoxycarbonyl group, in accord with the assignments above. The C-1′ signal is in the position expected for a C-1/C-2 *trans*-stereochemistry.

Finally the presqualene esters (18) and (19) were examined. The stereochemistry attributed to the two isomers [1] is fully confirmed by ^{13}C n.m.r. Thus the C-1′ signal [δ 121·0 and 121·1 (d)] is in accord with the C-1/C-2 *trans*-relation, and the resonances of the methyl and methylene attached to C-3 diagnose the C-1/C-3 stereochemistry.

EXPERIMENTAL

^{13}C N.m.r. spectra were obtained by using a JEOL JNM-PS-100 spectrometer at 25·15 MHz, interfaced with a Nicolet 1085 20 K computer. Deuterium lock was provided by the sample ($CDCl_3$). The pulse width was 3 μs (22° tip) and the F.I.D.s were compiled by using 8 K data points over a spectral width of 6000 Hz.

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