Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally-occurring Substances
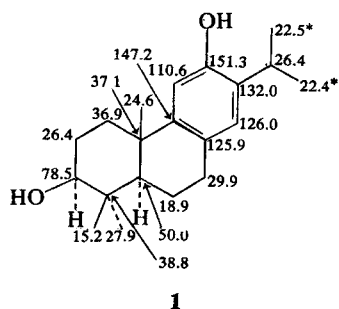
LVII.[†] Triterpenes Related to Lupane and Hopane

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The ^{13}C NMR spectra of lupeol and related triterpenes were recorded and all carbon shifts assigned. Their analysis aided in the shift assignment of the structurally related hopane-like triterpenes.

After early work on some tetracarbocyclic triterpenes[2,3] there appeared ^{13}C NMR analyses of α- and β-amyrinic pentacarbocyclic substances.[3,4] However, except for a report on two hopanes from an oil shale deposit[5] and the use of a limited number of friedelin shifts for the interpretation of β-effects in *trans*-decalin systems[6] little is known about the ^{13}C NMR spectroscopy of non-amyrin types of pentacarbocyclic triterpenes. The present communication concerns a ^{13}C NMR study of a large number of lupeol-derived substances and some hopane derivatives. Their shift assignments utilized off-resonance decoupling techniques for the determination of the substitution profile of carbon centers, functionality manipulation causing predictable shift variations, shift assessment utilizing ^{13}C NMR data for carbocyclic systems of known stereochemistry and conformation, especially those of decalins,[7,8] perhydrophenanthrenes,[9] diterpenes [e.g. $\mathbf{1}^{10-13}$ (the shift assignment of hinokiol (1) is based on that of ferruginol[10] and of ring A of lanosterol)[2]] and steroids [14] and lanthanide-induced shift measurements.

and melaleucic acid (**3f**). The shifts of carbons 1, 2, 3, 4, 5, 10, 23 and 24 were assigned by analogy with diterpene resonances (cf **1**).[10,11,13] The δ values of the remaining quaternary carbons, i.e. C-8, C-14 and C-17, could be recognized from the invariability of the C-8 shift on modification of the substituents in rings A and D, from the γ-*anti*-periplanar heteroatom effect of *c.* 1.3 ppm on C-14 by the introduction of 16β-oxy substituents[15] and from the predicted β-effects of 3–6 ppm by the 16- and 28-substituents on

2a: Y = OH, Y' = Y" = H
2b: Y = Y' = OH, Y" = H
2c: Y = OAc, Y' = Y" = H
2d: Y = Y' = OAc, Y" = H
2e: Y = Y = Y" = OAc
2f: Y = Y' = Y" = H
2g: Y = Y' = H, Y" = OH
2h: Y = Y' = H, Y" = OAc
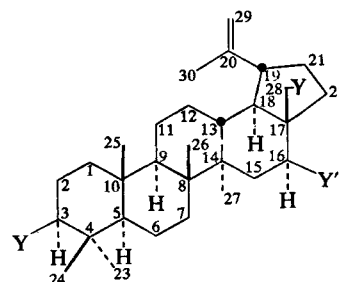2i: Y = Y' = Y" = OH

1

The lupane series

Much of the initial analysis of this family of compounds was based on derivatives of the natural products lupeol (**2a**), lup-20(29)-ene-3β,16β-diol (**2b**), lup-20(29)-ene-3β, 16β, 28-triol (**2i**), betulic acid (**3e**)

3a: R = R' = Me, Y + Y' = O
3b: R = Me, R' = CO$_2$Me, Y = Y' = H
3c: R = Me, R' = CO$_2$Me, Y = OH, Y' = H
3d: R = R' = CO$_2$Me, Y = OH, Y' = H
3e: R = Me, R' = CO$_2$H, Y = OH, Y' = H
3f: R = R' = CO$_2$H, Y = OH, Y' = H

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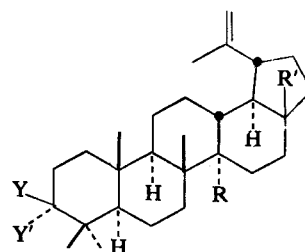† For part LVI see Ref. 1.
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C-17.[16] Whereas the C-14 and C-17 shifts are otherwise very similar, they were differentiated on the basis of a lanthanide shift study of lupeol (*vide infra*).

The remaining methine resonances, i.e. for C-9, C-13, C-18 and C-19, were distinguished by C-19 showing the largest residual coupling in off-resonance decoupling experiments,[10] C-18 experiencing the γ-*anti*-periplanar heteroatom effect on introduction of oxy-substituents at C-16,[15,17,†] C-9 being most deshielded because of many β-effects[16] and the C-13 signal being farthest upfield in view of two γ-effects by neighboring methyl groups.[16] (By analogy with the *change* of magnitude of the γ-effect of the 4β-methyl group on C-2 and C-6 among diterpenes on its conversion into a 4β-oxymethyl function[10] the introduction of an oxy substituent at C-28 shields C-13 by *c.* 0.6 ppm. The lower axiality of H-19β and H-21β minimizes this effect at C-19 and C-21.) By analogy with observations in the steroid[14] and decalin[8,13] series the entry of a keto group at C-3 and a 16β-alcohol unit into the lupane skeleton leads to shielding of C-9 and C-13, respectively.

The as yet undesignated methyl groups, C-25, C-26, C-27, C-28 and C-30 were assigned δ values on the basis of C-30 revealing the largest residual coupling and distinct long-range coupling with H-29 (such long-range coupling was also observed among other terpenes containing isopropenyl units, e.g. the monoterpene limonene),[18] C-28 being shielded by 16β-substitution and its signal disappearance upon its own functionalization, C-27 being most shielded in view of γ-effects by five axial hydrogens acting on it and C-25 and C-26 being distinguished albeit only in lupeol (2a) by the lanthanide shift study (*vide infra*).

The following arguments were advanced for the differentiation of the remaining methylenes, i.e. carbons 6, 7, 11, 12, 15, 16, 21 and 22. Functionalization of C-16 affects the lowest field (i.e. neopentyl) carbons, C-7, C-16 and C-22, discriminatingly,—C-7 remaining unchanged, the C-16 signal disappearing and C-22 being shielded by the 16β-oxy substituent. The C-16 functionalization also differentiates the medium-field methylenes, carbons 12, 15 and 21,—C-15 being deshielded and C-12 and C-21 remaining nearly unaffected. The latter two carbons are distinguished from each other by the lanthanide-induced shift modifications in lupeol (2a) (*vide infra*). Among the two high-field methylenes C-6 experiences more γ-effects than C-11 and hence more shielding on introduction of a 3β-oxy substituent into the lupane system.[8,13] (By analogy with the steroid series a 3-keto group deshields C-11.[14] However, in contrast to the steroid experience such functionalization of C-3 leads to *c.* 1 ppm deshielding of C-6. The latter phenomenon may reflect a conformational alteration of a 3-keto ring A by the C-4 geminal methyl groups.)

The replacement of an angular methyl group by a carbomethoxy function expectedly modifies the shifts of the quaternary site, the neopentyl neighbors and

the carbons attached thereto. Thus the difference of methyl betulate (3c) from lupeol (2a) amounts to 13.5 ppm deshielding of the α-carbon, 3–3.5 ppm shielding of C-16 and C-22 in view of the γ-effect from the oxygens and low deshielding of C-15 and C-21 due to a decreased γ-effect of C-28. The placement of an additional carbomethoxy group on to a bridgehead, i.e. at C-14 in dimethyl melaleucate (3d), causes a similar, but enhanced response by the neighboring carbons.

In order to confirm the carbon shift assignment of lupeol (2a), a lanthanide shift study with the use of the Yb(DPM)₃ agent was undertaken. A molar ratio of up to 0.4 reagent to substrate was utilized, leading expectedly to shift perturbation throughout the lupeol framework. The gradients $\Delta\delta$/Yb(DPM)₃ molar ratio, normalized to unit molar ratio of shift agent and obtained by the least-square fitting method, are shown on formula 4. The symmetrical shift perturbation in ring A and the similar gradients for the two 4-methyl groups show the ytterbium to assume a time-averaged position on the 3-hydroxy group of the complex, colinear with the carbon–oxygen axis and thus undistorted by the C-4 substituents.

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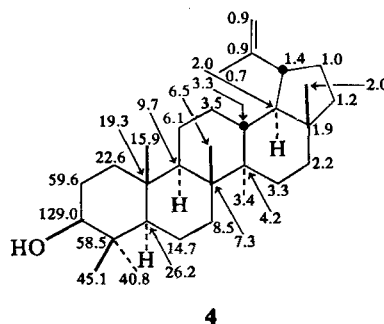
With the carbon shift data on the α-lupene derivatives in hand (Table 1) it was of interest to analyze ceanothic acid by the ^{13}C NMR method. For this reason the spectra of four ring A nor-α-lupene compounds, 5a–5d, and dimethyl ceanothate (5e), a soluble form of the acid, were compared with each other and with the shift data for α-lupene (2f) and methyl 3-deoxybetulate (3b), respectively. A line of demarcation through the C-6—C-7, C-8—C-9 and C-11—C-12 bonds separates those carbons whose shifts are affected by the shrinkage of ring A from those unperturbed. In the nor-α-lupene derivatives 5a–5d the quaternary center C-4 can be distinguished from C-10 by the stronger shift modification imposed on C-4 by the introduction of a 3-keto function. A similar argument based on the effect of the C-3 functionality permits the distinction of the methines C-5 and C-9. The proper methine shift choice is aided by the only minimal C-9 shift differences between the nor-α-lupenes and like 3-substituted α-lupenes and the major shift changes for C-5, a bridgehead center of the perhydroindane system of 5a–5d and of the decalin unit of 2. The shift invariance of C-11 among the nor-α-lupenes (5a–5d) differentiates this methylene from C-6 and the appearance of the C-11 signal *c.* 3 ppm downfield from its position in the spectra of the

† By analogy with the C-5 shift perturbation among diterpenes upon introduction of an oxy substituent on the 4β-methyl group, (Ref. 10) C-18 is inexplicably deshielded by 0.5 ppm on similar substitution of C-28.

Table 1. Carbon shifts of α-lupene derivatives[a]

	2a	2b	2c[b]	2d[b]	2e[b]	2f	2g	2h[b]	3a	3b[c]	3c[c]	3d[c,d]
C-1	38.7	38.9	38.3	38.3	38.1	40.3	40.2	40.3	39.5	40.2	38.7	39.5
C-2	27.4	27.4	23.6	23.6	23.4	18.7	18.6	18.6	34.0	18.6	27.3	27.3[e]
C-3	78.8	78.8	80.7	80.6	80.3	42.1	42.1	42.1	217.9	42.0	78.6	77.9
C-4	38.8	38.9	37.7	37.6	37.4	33.2	33.2	33.2	47.2	33.2	38.7	38.4
C-5	55.2	55.4	55.3	55.2	55.0	56.3	56.3	56.3	54.8	56.3	55.2	55.2
C-6	18.3	18.3	18.2	18.0	17.8	18.7	18.6	18.6	19.6	18.6	18.2	17.9
C-7	34.2	34.3	34.1	34.1	33.8[e]	34.3	34.2[e]	34.2[e]	33.5	34.2	34.2	33.9
C-8	40.8	41.0	40.7	40.9	40.7	41.0	41.1	41.1	40.7	40.8	40.5	40.3
C-9	50.4	50.0	50.2	49.7	49.4	50.5	50.4	50.4	49.7	50.6	50.4	51.0
C-10	37.1	37.1	37.0	36.9	36.7	37.5	37.4	37.4	36.8	37.4	37.0	37.1
C-11	20.9	20.9	20.9	20.7	20.4	20.8	20.7	20.7	21.4	20.7	20.8	20.3
C-12	25.1	24.9	25.0	24.5	24.5	25.2	25.3	25.3	25.1	25.5	25.4	27.0[e]
C-13	38.0	37.3	37.9	37.2	36.5	38.0	37.2	37.5	38.1	38.2	38.1	38.4
C-14	42.8	44.1	42.7	44.0	43.9	42.8	42.7	42.7	42.8	42.3	42.2	59.5
C-15	27.4	36.9[e]	27.4	33.4	33.6[e]	27.4	27.0	27.0	27.4	29.6	29.6	25.8
C-16	35.5	76.9	35.5	78.8	77.9	35.6	29.2[f]	29.6[f]	35.4	32.1	32.0	37.5[f]
C-17	42.9	48.6	42.9	47.2	50.1	43.0	47.7	46.3	42.9	56.5	56.4	55.8
C-18	48.2	47.7	48.2	47.6	48.1	48.3	48.7	48.8	48.2	49.4	49.3	51.7
C-19	47.9	47.6	47.9	47.4	47.1	47.9	47.7	47.6	47.8	46.9	46.8	46.5
C-20	150.6	149.8	150.5	149.4	148.6	150.6	150.2	149.8	150.5	150.3	150.1	149.3
C-21	29.8	30.0	29.8	29.6	29.8	29.9	29.8[f]	29.8[f]	29.8	30.6	30.5	30.0
C-22	39.9	37.8[e]	39.9	37.5	32.7	40.0	33.9[e]	34.5[e]	39.9	36.9	36.8	36.5[f]
C-23	28.0	28.0	27.9	27.8	27.6	33.4	33.3	33.3	26.6	33.3	27.9	27.7
C-24	15.4	15.4	16.5	16.4	16.2	21.6	21.5	21.5	21.0	21.5	15.3	15.3
C-25	16.1	16.1	16.1	16.1	15.9	16.1	16.0	16.1	15.8[e]	16.0	16.0[e]	16.4[g]
C-26	15.9	16.1	15.9	15.9[e]	15.9	16.1	16.0	16.1	15.9[e]	16.0	15.9[e]	16.8[g]
C-27	14.5	16.1	14.4	15.8[e]	15.5	14.6	14.8	14.8	14.4	14.7	14.6	175.3
C-28	18.0	11.8	18.0	12.7	61.1	18.0	60.4	62.7	18.0	176.3	176.2	176.1
C-29	109.2	109.6	109.2	109.8	110.0	109.2	109.4	109.6	109.2	109.4	109.3	109.5
C-30	19.3	19.4	19.2	19.1	19.0	19.3	19.1	19.1	19.3	19.3	19.3	18.6

[a] The δ values are in ppm downfield from TMS: $\delta(TMS) = \delta(CDCl_3) + 76.9$ ppm.
[b] The acetyl $\delta(Me) = 21.0 \pm 0.2$ ppm and $\delta(CO) = 170.4 \pm 0.7$ ppm.
[c] $\delta(OMe) = 51.1$ ppm.
[d] $\delta(OMe)$ of 14-ester is 50.1 ppm.
[e,f,g] Values bearing the same superscript may be interchanged.

α-lupenes (2) reflects the appreciable lowering of the γ-effect from C-1 in compounds of small ring A size. The shift perturbation induced by the 3-hydroxy group of the alcohols 5c and 5d on the C-4 gem-dimethyl group allows the differentiation of C-25 from C-23 and C-24 in the nor-α-lupenes and the last two sites from each other in all compounds except 5d. The total shift assignment for compounds 5a–5d, listed in Table 2, led to a ready analysis of dimethyl ceanothate (5e) which confirmed the 2α-carbomethoxy-3β-hydroxy configuration of the diester of the natural acid.[19] Thus the C-23 and C-24 shifts are characteristic of a 3β-hydroxy compound, whereas the invariance of the C-11 shift and the γ-effects of more than 5 ppm on C-5 and C-9 are compatible only with a 2α-ester configuration.

In order to assess the subtleties of side chain conformations, the ^{13}C NMR spectra of C-20-modified lupanes, 6a–6i, were examined. The shift assignment depends on the choice of proper models. Thus 30-norlupan-20-one (6a) shows major shift changes from α-lupene (2f) only in the immediate vicinity of the carbonyl group. Similarly, saturation of the double bond of α-lupene (2f) or lupeol (2a) modifies the C-19 shift. It was distinguished in 6b and 6c from the C-18 shift by the strong γ-effect exerted on C-18, as on C-22, by the axial 16α-hydroxy group of lupane-

3β,16α-diol (6d). Reduction of ketone 6a introduces shift changes in the vicinity of the 20-hydroxy group dependent on its stereochemistry. The shift assignment for the alcohols 6e and 6f as well as their acetates, 6g and 6h respectively, is buttressed nicely by a Yb(DPM)₃ shift study of the 20S-alcohol (6f). The lanthanide shift gradients are depicted on formula 7. When C-20 becomes fully substituted, as in lupan-20-ol (6i), there appear many shift alterations which may be associated with distortion of molecular geometry due to steric crowding. When compared with lupane (6b), not only are the C-12 and C-21 centers of 6i
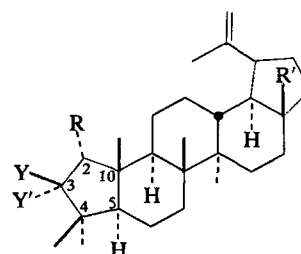
5a: R = Y = Y' = H, R' = Me
5b: R = H, R' = Me, Y + Y' = O
5c: R = Y' = H, R' = Me, Y = OH
5d: R = Y = H, R' = Me, Y' = OH
5e: R = R' = CO₂Me, Y = OH, Y' = H

Table 2. Carbon shifts of nor-α-lupene derivatives[a]

	5a	5b	5c	5d	5e[b]
C-2	40.7[c]	55.4	51.5	51.3	65.3
C-3	38.9[c]	224.5	82.3	81.2	84.6
C-4	37.8	45.7	44.4	41.9	43.2
C-5	61.6	59.2	61.8	61.1	56.4
C-6	18.8	18.1	18.6	19.0	19.4
C-7	34.7	33.8	34.4	34.4	33.9
C-8	41.4	41.2[c]	41.4	41.4	41.6
C-9	50.0	48.7	49.9	49.7	44.5
C-10	45.6	41.6[c]	43.4	40.9	49.3
C-11	23.6	23.7	23.6	23.6	23.5
C-12	25.1	24.8	24.9	24.9	25.4
C-13	38.3	38.1	38.2	38.2	38.5
C-14	43.0	42.9	42.9	42.9	42.8
C-15	27.8	27.5	27.6	27.6	29.8
C-16	35.7	35.5	35.6	35.6	32.1
C-17	42.9	42.9	42.8	42.8	56.5
C-18	48.4	48.2	48.3	48.3	49.3
C-19	48.0	47.9	47.9	47.9	46.8
C-20	150.7	150.4	150.5	150.5	150.1
C-21	29.9	29.8	29.8	29.8	30.6
C-22	40.1	39.9	40.0	40.0	36.8
C-23	32.7	27.7	31.8	25.4[c]	30.7
C-24	26.2	21.0	19.0	25.2[c]	18.4
C-25	16.1[d]	17.5	17.2	17.4	18.4
C-26	16.3[d]	16.2	16.1	16.2	16.5
C-27	14.7	14.6	14.6	14.6	14.7
C-28	18.0	18.0	18.0	18.0	176.4
C-29	109.2	109.3	109.2	109.2	109.4
C-30	19.4	19.3	19.3	19.3	19.1

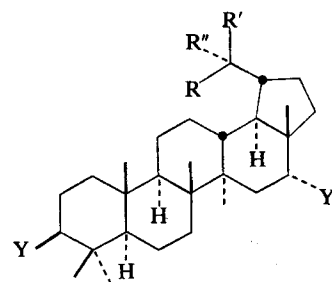[a] The δ values are in ppm downfield from TMS; $\delta(TMS) = \delta(CDCl_3) + 76.9$ ppm.
[b] $\delta(C=O) = 175.0$ ppm and $\delta(OMe) = 51.2$ ppm.
[c,d] Values bearing the same superscript may be interchanged.

6a: R + R′ = O, R″ = Me, Y = Y′ = H
6b: R = Y = Y′ = H, R′ = R″ = Me
6c: R = Y′ = H, R′ = R″ = Me, Y = OH
6d: R = H, R′ = R″ = Me, Y = Y′ = OH
6e: R = Y = Y′ = H, R′ = Me, R″ = OH
6f: R = Y = Y′ = H, R′ = OH, R″ = Me
6g: R = Y = Y′ = H, R′ = Me, R″ = OAc
6h: R = Y = Y′ = H, R′ = OAc, R″ = Me
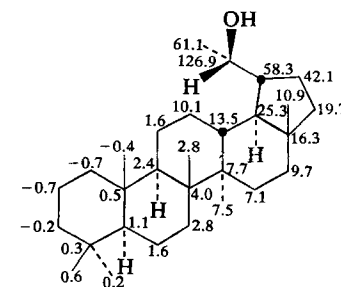**6i:** R = OH, R′ = R″ = Me, Y = Y′ = H

7

deshielded appreciably, but also ring D and E carbon sites quite distant from C-20 are affected by up to 1.5 ppm. All shifts of lupanes **6a–6i** are portrayed in Table 3.

The favored orientation of the isopropenyl sidechain of the α-lupenes (**2** and **3**) is known from the X-ray analysis of dimethyl melaleucate 3β-iodoacetate to be as shown in **8**.[20] In view of the minimal C-18 and C-21 shift changes between the α-lupenes and the nor-ketone **6a** the acetyl sidechain of the latter possesses a conformational disposition toward ring E related to **8**. The C-18 and C-21 shifts are diagnostic of the sidechain conformation of most of the lupanes (**6**). Thus the intense shielding of C-21 in the lupanes **6b–6d**, i.e. more than one γ-effect, is compatible with conformation **9**. The similarity of the two shifts in alcohols **6e** and **6f** and their acetates (**6g** and **6h**, respectively) with those of **6b–6d** indicates that these 20-oxy compounds possess a similar conformation, **10** for **6e** and **6g** and **11** for **6f** and **6h**.

The three lup-18-enes **12a–12c** were the last lupenic substances to be analyzed. They were chosen to obtain ¹³C NMR data on triterpenes containing non-protonated nuclear double bonds, functional groups not easily recognized and/or localized by other physical methods of analysis. [The diacetate **12c** is obtained readily by acid-catalyzed isomerization of the diester **2** (Y = Y″ = OAc, Y′ = H).[21] Treatment of α-lupene (**2f**) under the identical conditions and ¹³C NMR analysis

of the product mixture revealed the absence of any lup-18-ene (**12b**).] The ring A, B and C shifts of the nuclear olefins, except for those of C-12 and C-13, are nearly the same as those of related α-lupenes. Carbon-13 being allylic permits its recognition by its large residual coupling, while C-12 in two cases is undifferentiated from C-15. The ring D and E methylenes are most difficult to distinguish, although the coupling behavior of the allylic C-21 facilitates its shift selection. It is noteworthy that C-21 gives the same difference of shift response toward the isopropenyl group of **12a** and isopropyl group of **12b** and **12c** as earlier to the same sidechains of **2f** and **6b–6d**, respectively. The removal of selective shielding by H-18α leads to similarity in the shifts of C-29 and C-30. These facts imply that conformations like those depicted in **8** and **9** are maintained for diene **12a** and for mono-olefins **12b** and **12c**, respectively. All shifts of the lup-18-enes are recorded in Table 3.

The next ¹³C NMR challenge was the hopane family of pentacyclic triterpenes, of which four representatives were investigated,—29-acetoxyhopan-22ξ-ol (**13a**), zeorin 6-acetate (**13b**), leucotylin 6,16-diacetate (**13c**) and methyl leucotylate (**13d**). Dissection of the first three esters through the ring C C-8—C-14 and C-11—C-12 bonds and application of the known equatorial acetoxy substituent parameter (*vide supra*)[8,15] permits the shift assignment of the ring A and B carbons and two of the ring C carbons of the three pentacycles. The removal of the three-carbon sidechain from the vicinity of C-12 and the transplantation of the ring E angular methyl group on to C-18

Table 3. Carbon shifts of lupane derivatives[a]

	6a	6b	6c	6d	6e	6f	6g[b]	6h[b]	6i	12a	12b	12c[c]
C-1	40.2[d]	40.5	38.7	38.7	40.2[d]	40.3	40.2	40.2	40.2	40.5	40.5	38.3
C-2	18.6	18.8	27.4	27.3	18.6	18.6	18.6	18.6	18.6	18.7	18.6[d]	23.4
C-3	42.0	42.3	78.8	78.7	42.0	42.0	42.1	42.1	42.0	42.1	42.1	80.4
C-4	33.2	33.3	38.8	38.8	33.2	33.2	33.2	33.2	33.2	33.3	33.3	37.5
C-5	56.2	56.5	55.2	55.2	56.2	56.2	56.2	56.2	56.1	56.6	56.5	55.2
C-6	18.6	18.8	18.3	18.2	18.6	18.6	18.6	18.6	18.6	18.7	18.7[d]	17.9
C-7	34.1	34.6	34.4	34.4[d]	34.3	34.2	34.3	34.3	34.5	34.8	35.0	34.4
C-8	40.9	41.3	40.8	41.0	41.0	41.0	41.0	41.0	41.5	40.9	41.0	40.5
C-9	50.2	50.4	50.1	49.1	50.0	50.0	49.9	50.1	50.2	51.3	51.2	50.7
C-10	37.4	37.6	37.1	37.1	37.4	37.4	37.4	37.4	37.4	37.5	37.5	36.8
C-11	20.7	21.0	20.9	21.0[e]	20.7	20.7	20.7	20.7	21.2	21.2	21.5	21.4
C-12	27.2[e]	27.1[d]	26.8[d]	26.6	27.2	27.3	26.7[d]	27.0	29.1[d]	28.2[d]	28.4[e]	28.0
C-13	36.9	38.1	37.8	38.1	37.5	37.3	37.2	37.1	37.4	39.5	40.3	40.6
C-14	43.0[f]	43.2	43.0	43.1	42.9	42.8	42.9	42.8	43.5	43.5	43.7	43.0
C-15	27.6[e]	27.5[d]	27.4[d]	34.2[d]	27.2	27.1	27.2[d]	27.0	27.5	27.0[d]	28.3[e]	28.0
C-16	34.9	35.8	35.5	74.2	35.2	35.3	35.3	35.4	35.5	39.7[e]	37.7[f]	32.2[d]
C-17	42.6[f]	43.2	43.1	47.4	43.2	43.3	42.9	43.2	44.6	48.3	48.4	51.9
C-18	49.6	47.8	47.5	40.4	46.0[e]	48.7	47.0	48.5	48.2	141.4	139.0[g]	133.6
C-19	52.5	44.9	44.6	43.8	46.9[e]	45.7	44.1	42.3	49.9	135.7	138.7[g]	143.1
C-20	212.7	29.5	29.3	29.6	68.6	69.4	72.3	73.0	73.3	145.3	26.4	26.3
C-21	27.2[e]	22.0	21.9	21.3[e]	21.3	21.8	22.8	22.6	28.7[d]	37.4[f]	28.7	29.1
C-22	39.8[d]	40.5	40.4	33.2	40.1[d]	40.3	40.2	40.2	40.2	36.8[e,f]	39.2[f]	34.7[d]
C-23	33.3	33.4	28.0	27.9	33.3	33.3	33.3	33.3	33.3	33.3	33.3	27.6
C-24	21.5	21.7	15.4	15.4	21.6	21.5	21.6	21.5	21.5	21.5	21.5	16.6
C-25	16.0	16.1[e]	16.0	16.0	16.0	16.0	16.0	16.0	16.1[e]	16.0	16.6[h]	16.3
C-26	16.0	16.2[e]	16.0	16.0	16.0	16.0	16.0	16.0	16.2[e]	16.3	16.7[h]	16.3
C-27	14.4	14.6	14.4	17.2	14.5	14.3	14.2	14.3	14.8	15.4	15.4	15.3
C-28	17.9	18.2	18.0	19.1	18.1	17.9	17.9	17.9	19.2	16.7	23.7	66.6
C-29	29.0	15.2	15.1	15.2	23.0	17.0	19.8	14.0	24.8	111.7	21.4[i]	21.4[i]
C-30		23.0	23.0	22.9					31.4	23.6	21.9[i]	21.9[i]

[a] The δ values are in ppm downfield from TMS; δ(TMS) = δ(CDCl₃) + 76.9 ppm.
[b] Acetyl δ(C=O) and δ(Me) values are 170.4 and 21.4 ppm, respectively.
[c] Acetyl δ(C=O) values are 170.2 and 170.6 ppm and δ(Me) values are 20.7 and 21.0 ppm.
[d-i] Values bearing the same superscript may be interchanged.

shields C-12 in the hopanes vs the lupanes and de-shields dramatically C-13 in the former. The ring D carbon shift designation is aided by the perturbations introduced by the 16-acetoxy group of 13c. In view of the similarity of the environment of C-13, C-14 and C-18 of 13a and 13b with that of C-9, C-8 and C-10 of A-nor-α-lupene (5a), respectively, the assignment of the signals of the three hopane carbons is based also on the shift designation for 5a. The differentiation of C-17 and C-21 is based on the C-21 shift alteration by sidechain changes. Carbon-27 is deshielded in the hopanes vs the lupanes due to the loss of the γ-effect from C-18 and the gain of a δ-effect from C-28. The neopentyl nature of C-19 and the γ-effects of the sidechain on C-20 allow these methylenes to be distinguished from each other. Neither these carbons nor the other ring E sites maintain shift constancy through the hopane series of compounds, an omen of ring E conformational change. This argument is in conformity with results from the X-ray analyses of 6-ketoleucotylin 16β-O-p-bromobenzoate[22] and 6-O-p-bromobenzoylzeorin[23] which indicate that 13a and 13b belong to a different ring E conformational series from 13c and 13d. A dramatic revelation of this fact is the absence of any C-21 response on introduction of the 16β-oxy group into the hopane skeleton. Finally, the analysis of methyl leucotylate (13d) rests on the lupane data and equatorial ester parameters from the

resin acid field[10] for rings A, B and C and on the ¹³C NMR data of 13c for the remaining rings. All shifts are listed in Table 4.

The accumulated ¹³C NMR data on the lupanes and hopanes permitted the re-evaluation of an earlier shift assignment on hopane (13e) itself.[5] As Table 4 indicates, several shifts require redesignation.
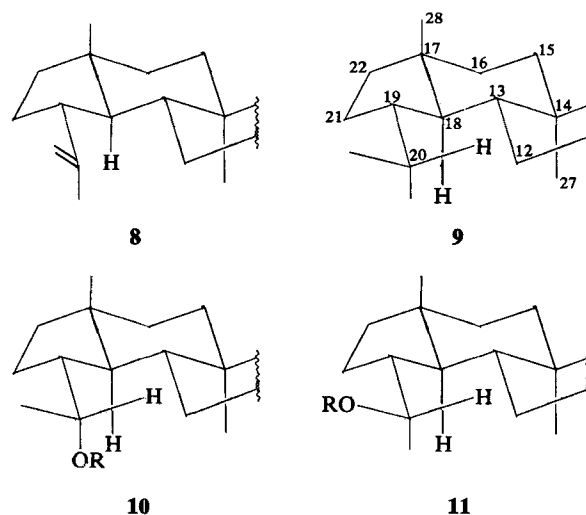

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Table 4. Carbon shifts of hopane derivatives[a]

	13a[b]	13b[c]	13c[c]	13d[d]	13e[e]	13e[f]
C-1	40.3	40.1	40.1	39.3	42.0	40.2
C-2	18.7	18.3	18.3	17.7	18.6	18.6
C-3	42.1	41.1[g]	40.9[g]	36.7	40.2	42.0
C-4	33.2	33.0	33.1	47.7	33.0	33.0
C-5	56.0	58.3	58.2	51.1[g]	56.0	56.0
C-6	18.7	71.7	71.6	21.6	18.6	18.6
C-7	33.4	40.8[g]	40.7[g]	32.8	20.8	32.9[g]
C-8	41.9	42.6	42.7	42.3	41.8	41.6[h]
C-9	50.3	49.2[h]	49.1[h]	50.5[g]	50.4	50.4
C-10	37.4	39.4	39.4	36.7	37.2	37.2
C-11	20.9	20.9	20.7	20.6	23.8	20.8
C-12	24.1	23.8	23.3	23.5	32.9	23.8
C-13	49.8, 49.8	49.7[h]	48.5[h]	49.0	49.2	49.2
C-14	41.8, 41.9	41.8	44.0	44.0	41.6	41.8[h]
C-15	34.3, 34.3	34.2	41.4[g]	41.5	33.5	33.5[g]
C-16	20.9	21.7	73.1	66.8	22.5	22.5
C-17	53.6, 53.7	53.8	56.8	60.6	54.5	54.5
C-18	44.0	43.8	46.5	45.8	44.2	44.2
C-19	41.2	43.4	43.3	43.7	41.5	41.5
C-20	25.4, 25.9	26.5	27.7	27.8	27.5	27.5
C-21	46.3, 47.1	50.9	51.6	49.8[g]	47.8	47.8
C-22	74.1, 74.5	73.5	72.9	74.1	31.9	31.9
C-23	33.2	36.2	36.2	179.3	33.2	33.2
C-24	21.6	22.0	22.0	16.6	21.4	21.4
C-25	15.8	17.0	16.9[i]	16.1[h]	16.4	15.6[i]
C-26	15.8	17.9	18.0	16.3[h]	16.5	16.4[i]
C-27	17.0	17.0	18.0	18.3	25.7	16.5[i]
C-28	16.0, 16.7	16.0	17.0[i]	17.1	15.6	22.7[j]
C-29	70.7, 71.3	28.7	27.4	26.6	22.7	23.7[j]
C-30	22.9, 24.8	30.8	30.3	30.8	23.7	25.7[j]

[a] The δ values are in ppm downfield from TMS; δ(TMS) = δ(CDCl₃) + 76.9 ppm.
[b] A mixture of 22-epimers; δ(C=O) = 170.9, 170.9 ppm and δ(Me) = 21.8, 22.1 ppm.
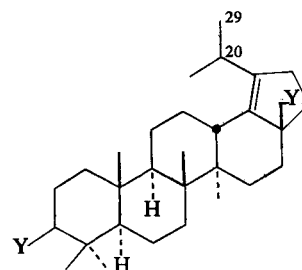[c] Acetyl δ(C=O) = 170.0 ppm, δ(Me) = 21.9 ppm.
[d] δ(OMe) = 51.7 ppm.
[e] From Ref. 5, translated into the TMS scale.
[f] Shifts from Ref. 5 reallocated.
[g-j] Values bearing the same superscript may be interchanged.

12a: Y = H, 20,29-dehydro
12b: Y = H
12c: Y = OAc
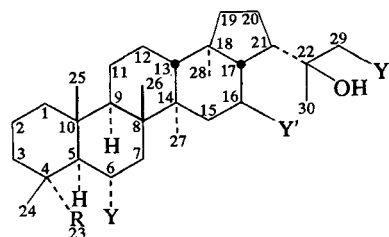
13a: R = Me, Y = Y' = H, Y" = OAc
13b: R = Me, Y = OAc, Y' = Y" = H
13c: R = Me, Y = Y' = OAc, Y" = H
13d: R = CO₂Me, Y = Y" = H, Y' = OH
13e: R = Me, Y = Y' = Y" = H, 22-deoxy

δ(CDCl₃) + 76.9 ppm. The starred values may be interchanged. All spectra were run under the following conditions: a digital resolution of ±0.6 Hz (spectral width of 5000 Hz with 8 K data points in the real spectrum), pulse flip angle of 55–65° and 1500–10 000 transients depending on the terpene concentration. The off-resonance decoupling experiments were carried out with the ¹H decoupler offset 0–1 ppm upfield from TMS and ¹H irradiating power adjusted to 118–119 dB.

EXPERIMENTAL

The ¹³C NMR spectra were recorded on a Varian XL-100-15 NMR spectrometer operating at 25.2.MHz in the Fourier transform mode. The shifts on formula 1 are in ppm downfield from TMS; δ(TMS) =

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3