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^{13}C NMR SPECTROSCOPY OF TETRACARBOCYCLIC DITERPENES AND RELATED SUBSTANCES[1]

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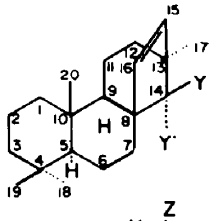
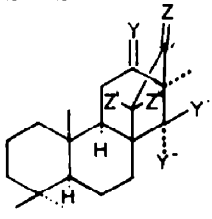
Abstract—A carbon shift analysis of hibaene, phyllocladene, isophyllocladene, cafestol, cafamarine, mascaroside and hibane-like substances is presented.

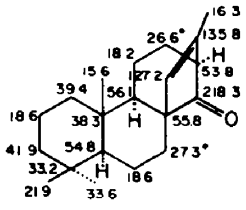
Structure analyses[2,3] and partial syntheses[4,5] of tetracarbocyclic diterpenes of the hibaene,[6] phyllocladene and kaurene[7] types have led to the accumulation of a number of structurally similar substances, whose close relationship made them good substrates for ^{13}C NMR analysis and hence for the acquisition of physical data of importance for future research in diterpene chemistry. Compounds **1–5** represent materials of mainly hibaene and some phyllocladene types, whose carbon shifts are listed in Table 1. The designation of the majority of the δ values derived from proton-decoupled as well as single-frequency off-resonance decoupled (SFORD) spectra was based on the analogy with especially ring A and some ring B carbon shifts for tricarbocyclic diterpenes,[8,9] on the δ values for model bicyclo[3.2.1]octanes[10,11] and on known substituent effects.[12]



1a: Y + Y′ = 0
b: 13-demethyl, Y + Y′ = 0
c: Y = Y′ = H
d: Y = H, Y′ = OH



2a: Y = Z = H_2, Y′ = Y″ = Z′ = Z″ = H
b: Y = Z = H_2, Y′ = Z′ = Z″ = H, Y″ = OH
c: Y = Z = H_2, Y′ = Z′ = H, Y″ = Z″ = OH
d: Y = Z = H_2, Y′ = Z″ = H, Y″ = Z′ = OH
e: Y = Z = H_2, Y′ = Z′ = H, Y″ = Z″ = OCHO
f: Y = Z = H_2, Y′ = Z′ = H, Y″ = OH, Z″ = $OSOC_6H_4Me(p)$
g: Y = Z = H_2, Y′ = Z″ = H, Y″ = OH, Z′ = $OSOC_6H_4Me(p)$
h: Y = Z = H_2, Y′ + Y″ = O, Z′ = Z″ = H
i: Y = 0, Z = H_2, Y′ = Y″ = Z′ = Z″ = H
j: Y = H_2, Z = O, Y′ = Y″ = Z′ = Z″ = H



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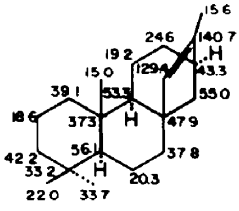

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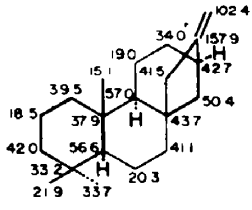

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Table 1. Carbon shifts of substances 1 and 2[a]

	1a	1b	1c	1d	2a[b]	2b[c]	2c[c]	2d[c]	2e	2f	2g	2h	2i	2j[d]
C(1)	39.3	39.3	39.1	39.3	39.7	39.7	40.8	41.9	39.5	39.6	40.1	40.0	39.7	39.6
C(2)	18.5	18.7	18.6	18.7	18.5	18.5	19.5[e]	20.3[e]	18.6[e]	18.6[e]	19.2[e]	18.3[e]	18.2	18.5
C(3)	41.9	41.9	42.0	42.2	42.0	42.0	43.1	43.3	41.8	42.0	42.0	41.8[f]	41.9	42.1
C(4)	33.1	33.2	33.1	33.3	33.1	33.2	24.0	34.2	33.1	33.2	33.3	33.1	33.1	33.4
C(5)	54.7	54.9	55.9	55.5	56.5	56.0	57.3	58.1	56.1	56.3	56.7	55.1	56.1	56.5
C(6)	18.5	18.7	20.0[e]	18.7	20.4[e]	19.2	20.5[e]	20.5[e]	18.4[e]	18.6[e]	19.2[e]	18.6[e]	19.5	20.1
C(7)	27.3	26.9[e]	37.2	33.6	41.2[f]	38.5	30.4[f]	39.4	29.8[f]	30.4[f]	37.8	32.2	39.2	39.6
C(8)	55.8	54.9	48.9	49.7	44.9	45.3	50.1	50.6	48.4	49.0	49.7	51.2	45.2	48.9
C(9)	56.0	56.6	52.7	44.7	56.9	46.8	47.0	49.2	47.1	55.9	47.9	60.2	57.8	55.6
C(10)	38.3	38.5	37.2	37.0	37.6	37.3	38.5	37.6	37.5	37.5	36.8	38.9	38.1	37.8
C(11)	19.1	18.1	20.1[e]	19.8	20.2[e]	19.9	19.6[e]	21.1[e]	19.2[e]	19.7[e]	20.0[e]	19.1	36.4	20.1
C(12)	35.4	27.8[e]	33.1	26.0	40.0[f]	32.4	31.7[f]	34.2	31.5[f]	30.2[f]	32.6	42.2[f]	215.4	37.8
C(13)	51.0	49.6	43.5	44.7	39.2	40.1	41.0	40.7	40.0	40.3	40.1	46.8	52.1	54.8
C(14)	219.6	218.0	61.1	85.3	57.7	83.8	81.3	81.2	80.8	81.0	80.8	222.7	56.1	54.8
C(15)	132.4[e]	126.8	135.1[f]	134.5[e]	37.6	31.9	46.4	44.4	42.8	42.7	40.7	30.3	37.2	211.8
C(16)	133.7[e]	134.7	136.0[f]	134.8[e]	33.6	29.6	69.9	81.6	71.4	83.4	90.3	27.8	32.6	48.9
C(17)	16.5	——	24.9	22.1	27.1	25.1	25.4	25.6	24.2	24.6	24.5	19.6	19.5	20.1
C(18)	33.6	33.6	33.6	33.6	23.7	33.6	34.2	34.2	33.6	33.6	33.6	33.6	33.6	33.9
C(19)	21.9	21.9	21.9	22.0	21.9	22.0	22.4	22.4	21.9	21.9	21.9	21.3	21.8	22.1
C(20)	15.6	15.6	15.0	15.8	15.1	15.5	15.8	16.8	15.1	15.5	19.1	15.4	14.8	15.2

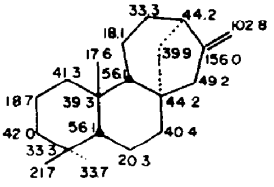
[a] In ppm downfield from TMS; $CDCl_3$ solutions containing TMS as standard. [b] Data from ref. 6a. [c] d_6-Acetone solution containing TMS. [d] $CDCl_3$ solution without TMS; $\delta(TMS) = \delta(CDCl_3) + 76.9$ ppm. [e,f] Signals in any vertical column may be interchanged.

Even though three methylenes, C(2), C(6) and C(11), in the olefins **1**,[13] **3** and **4** reveal similar chemical shifts, the δ value of C(11) can be differentiated from that of the other carbons by its *ca.* 1 ppm increase in the 13-methylated cases, in accord with previous observations among model bicyclo[3.2.1]octanes.[10] The saturated methines C(5) and C(9) have similar resonances, but can be distinguished by the latter being shielded in the 14α-hydroxy compounds, e.g. *cf.* **1d** and **2b** vs **1c** and **2a**,[14] respectively. Furthermore, the two methines exhibit strikingly different multiplicities in the sford spectra of compounds **1–5**, the C(5) signal appearing expectedly as a doublet but C(9) as a triplet. The olefinic methines of **1a**, **c** and **d** cannot be differentiated with the data at hand. Comparison of the C(7) and C(12) shifts among compounds **2i**, **2j**, and **5** permits the differentiation of the two carbons in phyllocladene (**5**).

Introduction of a 14-keto group into the hibaene skeleton leads to strong shielding of the *peri* carbon, C(7), reminiscent of the like phenomenon among tricarbocyclic diterpenic systems,[9] as well as long-range effects of more than 1 ppm at carbons 5, 6, 10 and 11. The 14α-hydroxy group shields predictably C(7) and exerts long-range effects on C(5) and C(6). Its shielding of the two-carbon bridge spanning C(8) and C(13) must be the consequence of their antiperiplanar relationship,[15] observable also in bicyclo[3.2.1]octan-8-ol of like stereochemistry[11] and affecting C(15) and C(16) of the hibaene-like structures unsymmetrically. The shielding effect in the bicyclooctanol is more powerful than the γ effect exerted by the 8-hydroxy group on the same carbon pair in the epimeric alcohol.[11] As the C(14) shift variation in the **2b–c** and **2b–d** pairs of substances indicates, the γ and antiperiplanar effects are nearly the same in the hibols. The γ effect is stronger than the antiperiplanar shifts in the bicyclo[3.2.1]octan-6-ol epimers.[11] The introduction of the two-carbon bridge, i.e. C(15) and C(16) of the hibanes, into ring C of the tricarbocyclic diterpene system[8,9] deshields the angular methyl group by *ca.* 1 ppm. These steric and accompanying NMR effects are enhanced dramatically by a 16-oxy substituent oriented toward the angular methyl group, as best illustrated by the C(20) shift perturbation of 3.6 ppm in hydroxyester **2g**. The strong buttressing is reflected even by 0.7 ppm deshielding of C(2).

A comparison of the carbon resonances of phyllocladene (**5**) with those published for kaurene (**6**)[7b] shows various shift changes, only three of which are of serious diagnostic value for structure analysis. The angular methyl group of kaurene (**6**) is more deshielded

than that of phyllocladene (**5**) by the extra δ effect from C(12) and C(14) and C(16) are affected differently in the two hydrocarbons.



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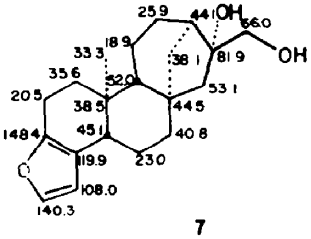

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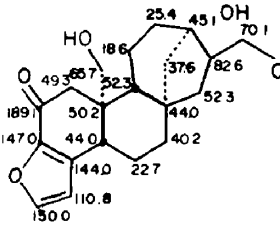
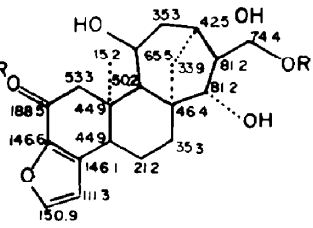


8(R = β-glucopyranosyl)



9(R = β-glucopyranoxyl)

The ^{13}C NMR analysis of the coffee constituents[2] cafestol (**7**), cafamarine (**8**) and mascaroside (**9**) can be carried out on the basis of *a priori* principles. The stereochemistry of the vicinal glycol moiety common to the three kaurene-like diterpenes is reflected by characteristic chemical shifts of ring D analogous to those in steviol.[7c] The ^{13}C NMR analysis of cafamarine constitutes the determination of the relative configuration of this diterpene glucoside.

The carbon shift designation of the oxahibanes (**10–14**) is illustrated on the formulas of these manool degradation products.[5] The C(8) epimers **10** and **13** show the same shift relationship as phyllocladene (**5**) and kaurene (**6**) (*vide supra*), the angular methyl group of **13** being more deshielded than that of **10** and the oxymethylene of the two substances showing the same variation. The stereochemistry on the oxa bridges of the ozonide **14** was unknown. As the angular methyl shift indicates, the compound's configuration is as depicted on the formula.

EXPERIMENTAL

The spectra were recorded on Varian CFT-20 and XL-100-15 NMR spectrometers, the latter operating at 25.2 MHz in the Fourier transform mode. The δ values on formulas **3–14** are derived from $CDCl_3$ solutions; $\delta(TMS) = \delta(CDCl_3) + 76.9$ ppm. The starred numbers indicate possible signal reversal.

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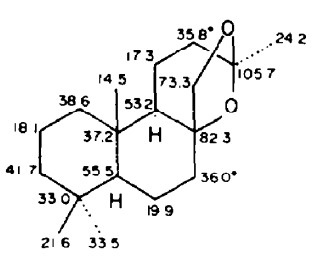

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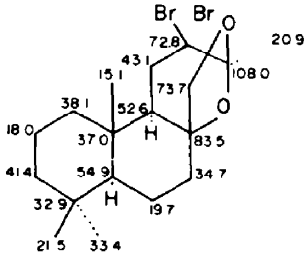

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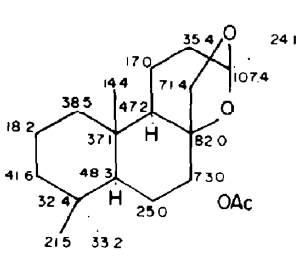

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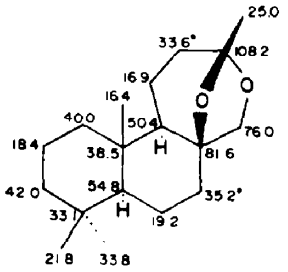

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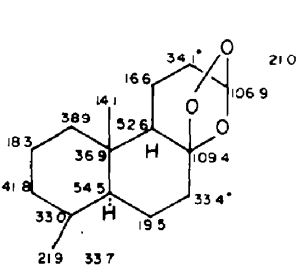

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