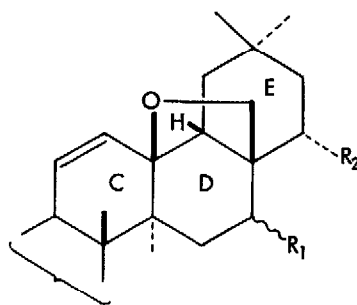
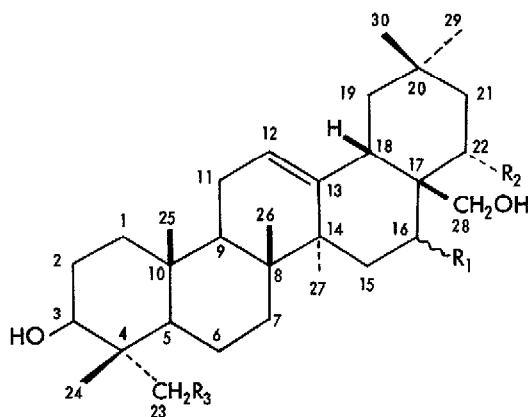


CARBON-13 NMR SPECTRA OF SAIKOGENINS.  
 STEREOCHEMICAL DEPENDENCE IN HYDROXYLATION EFFECTS UPON CARBON-13  
 CHEMICAL SHIFTS OF OLEANENE-TYPE TRITERPENOIDS

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(Received in Japan 11 September 1976; received in UK for publication 1 October 1976)

Knowledge of the chemistry of triterpenoid saponins, such as saikosaponins isolated from Bupleurum falcatum L.,<sup>1</sup> has become important with the discovery of their antiinflammatory<sup>2</sup> and antiviral<sup>3</sup> activities. Carbon-13 NMR spectroscopy has proved powerful for solving problems of structure elucidation and biosynthesis of triterpenoids.<sup>4-6</sup> In connection with studies of saikosaponin structures,<sup>1</sup> we have assigned <sup>13</sup>C FT NMR signals of saikogenins E (8), F (9) and G (7), their derivatives (6, 10),<sup>7</sup> and related olean-12-enes (2-5)<sup>7</sup> in CDCl<sub>3</sub>, and found that C-16 hydroxylation effects on <sup>13</sup>C chemical shifts δ<sub>C</sub> reflect the difference in D-ring conformations. These results will be useful in structural studies of not only saikosaponins<sup>8</sup> but also other triterpenoids and their saponins.



	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
23-HydroxyerythrodioI <sup>5a</sup> (1) :	H	H	H : 16-Dehydroxysaikogenin G (6)
23-Hydroxyprimulagenin A (2) :	α-OH	H	OH : Saikogenin G (7)
Longispinogenin (3) :	β-OH	H	H : Saikogenin E (8)
23-Hydroxylongispinogenin (4) :	β-OH	H	OH : Saikogenin F (9)
Camelliagenin C (5) :	α-OH	OH	OH : 22α-Hydroxysaikogenin G (10)

TABLE. Carbon-13 Chemical Shifts,  $\delta_C$ , of Olefin-12-enes (1-5), Saikogenin Derivatives (6-10) and Their Peracetates (in parentheses) in  $CDCl_3^a$ 

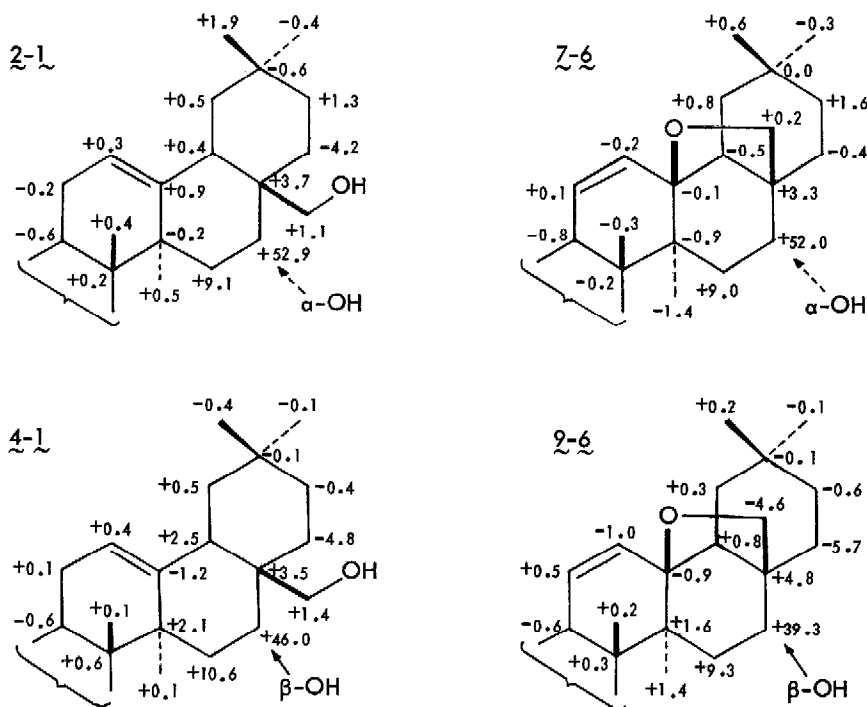
Carbon No.	1 <sup>b</sup>	2	3	4	5 <sup>c</sup>	6 <sup>c</sup>	7 <sup>c</sup>	8 <sup>c</sup>	9 <sup>c</sup>	10 <sup>c</sup>
1	38.3	38.4 (37.8)	38.8 (38.3)	38.5 (38.0)	38.5 (38.0)	38.0	38.0 (37.6)	38.4 (37.9)	38.2 (37.5)	38.2 (37.6)
2	26.0	26.4 (23.0)	26.9 (23.5)	26.7 (23.0)	26.3 (23.0)	26.2	26.1 (22.8)	26.9 (23.4)	26.1 (22.8)	26.2 (22.8)
3	76.7	76.7 (74.4)	78.9 (80.8)	76.5 (74.4)	76.0 (74.2)	75.9	75.6 (74.3)	78.7 (80.7)	75.4 (74.2)	75.2 (74.3)
4	41.8	41.9 (40.6) <sup>d</sup>	38.8 (37.7)	42.0 (40.6)	41.8 (40.6)	41.9	42.0 (40.6)	39.0 (37.9)	42.0 (40.6)	42.2 (40.6)
5	49.8	49.9 (48.0)	55.3 (55.2)	49.9 (47.9)	49.3 (47.9)	49.3	49.2 (47.7)	54.9 (54.9)	49.1 (47.6)	49.0 (48.0)
6	18.5	18.5 (17.9)	18.4 (18.1)	18.7 (17.9)	18.4 (17.8)	17.7	17.7 (17.2)	17.9 (17.5)	17.8 (17.2)	17.8 (17.2)
7	32.4	32.6 (32.5)	32.6 (32.6)	32.6 (32.3)	32.6 (32.4)	31.1	31.1 (31.0)	31.5 (31.4)	31.3 (31.1)	31.2 (31.0)
8	39.8	40.0 (39.8)	39.9 (39.7) <sup>d</sup>	40.0 (39.8) <sup>d</sup>	39.8 (39.8)	41.6	41.4 (41.4)	41.8 (41.8)	41.9 (41.7)	41.8 (41.6)
9	47.6	47.0 (46.9)	46.8 (46.7)	47.0 (46.9)	46.7 (46.7)	53.3	52.5 (52.5)	52.7 (52.4)	52.7 (52.4)	52.8 (52.6)
10	36.9	36.9 (36.7)	36.9 (36.8)	37.0 (36.6)	36.9 (36.6)	36.3	36.3 (36.1)	36.4 (36.3)	36.3 (36.1)	36.4 (36.1)
11	23.6	23.4 (23.5)	23.6 (23.5)	23.7 (23.6)	23.5 (23.6)	132.5	132.6(132.2)	132.9(132.6)	133.0(132.2)	133.2(132.7)
12	122.3	122.6(123.9)	122.6(123.6)	122.7(123.5)	122.9(124.9)	130.7	130.5(130.4)	129.7(129.7)	129.7(129.8)	130.3(129.9)
13	144.2	143.1(141.8)	142.8(141.8)	143.0(141.9)	142.7(140.4)	85.2	85.1 (84.3)	84.1 (83.8)	84.3 (83.6)	85.5 (83.8)
14	41.8	41.6 (41.1) <sup>d</sup>	43.7 (43.4)	43.9 (43.3)	41.8 (41.0)	43.9	43.0 (42.8)	45.4 (45.2)	45.5 (45.1)	43.8 (43.1)
15	25.6	34.7 (30.9)	35.8 (31.7)	36.2 (31.6)	33.4 (30.6)	25.7 <sup>d</sup>	34.7 (31.8)	35.1 (31.9)	35.0 (31.8)	34.3 (31.4)
16	22.0	74.9 (75.9)	67.7 (68.7)	68.0 (68.7)	67.9 (70.8)	25.3 <sup>d</sup>	77.3 (78.0)	64.7 (68.7)	64.6 (68.5)	70.5 <sup>d</sup> (72.2) <sup>d</sup>
17	36.9	40.6 (37.8)	40.0 <sup>d</sup> (40.0) <sup>d</sup>	40.4 <sup>d</sup> (40.0) <sup>d</sup>	43.9 (41.7)	41.6	44.9 (44.0)	46.3 (45.2)	46.4 (45.1)	47.5 (41.6)
18	42.4	42.8 (42.1)	44.7 (43.2)	44.9 (43.3)	42.4 (41.4)	51.1	50.6 (50.1)	51.7 (51.6)	51.9 (51.6)	50.4 (49.6)
19	46.5	47.0 (47.1)	46.7 (46.2)	47.0 (46.3)	47.2 (46.7)	37.2	38.0 (37.6)	37.5 (37.3)	37.5 (37.3)	37.4 (37.0)
20	31.0	30.4 (30.6)	30.8 (30.7)	30.9 (30.7)	31.4 (31.2)	31.7	31.7 (31.5)	31.5 (31.4)	31.6 (31.3)	33.2 (32.8)
21	34.1	35.4 (35.6)	33.6 (33.7)	33.7 (33.7)	44.8 (41.4)	34.9	36.5 (35.8)	34.3 <sup>d</sup> (34.2)	34.3 <sup>d</sup> (34.1)	45.7 (47.7)
22	31.0	26.8 (29.7)	26.2 (23.5)	26.2 (23.6)	75.5 (72.1)	30.9	30.5 (29.5)	25.1 (25.4)	25.2 (25.3)	74.3 <sup>d</sup> (74.5) <sup>d</sup>
23	72.0	71.9 (65.4)	28.1 (28.0)	71.7 (65.3)	70.8 (65.2)	70.7	70.3 (65.3)	27.8 (27.8)	70.0 (65.1)	69.6 (65.3)
24	11.4	11.5 (13.1)	15.6 (16.7) <sup>e</sup>	11.6 (13.1)	11.7 (13.1)	11.1	11.1 (12.5)	15.0 (16.1)	11.2 (12.5)	11.3 (12.5)
25	15.9	16.1 (16.1)	15.6 (15.6)	16.0 (16.0)	16.0 (16.0)	18.2	18.3 (18.3)	17.9 (17.9)	18.3 (18.2)	18.4 (18.3)
26	16.8	17.2 (16.8)	16.7 (16.8) <sup>e</sup>	16.9 (16.9)	16.8 (16.7)	19.3	19.0 (18.9)	19.5 (19.5)	19.5 (19.4)	19.1 (18.9)
27	26.8	27.3 (26.5)	26.9 (26.9)	26.9 (26.9)	27.0 (26.5)	19.3	17.9 (17.9)	20.7 (20.5)	20.7 (20.5)	18.1 (18.1)
28	69.7	70.8 (71.4)	70.9 (66.4)	71.1 (66.4)	71.1 (67.5)	77.1	77.3 (77.1)	72.4 (73.2)	72.5 (73.1)	76.9 (76.1)
29	33.2	32.8 (33.1)	33.2 (32.9)	33.1 (32.9)	33.2 (33.1)	33.7	33.4 (33.7)	33.6 (33.4)	33.6 (33.3)	33.2 (33.4)
30	23.6	25.5 (24.2)	23.9 (23.5)	24.0 (23.6)	24.9 (24.5)	23.6	24.2 (24.2)	23.7 (23.7)	23.8 (23.6)	25.2 (25.0)

<sup>a</sup>  $^{13}C$  NMR spectra were recorded on a Varian NV-14 FT NMR spectrometer at 15.087 MHz in  $CDCl_3$  with TMS as an internal reference ( $\delta_C 0$ ) in 8-mm spinning tubes at 30°; concentrations were about 0.1-0.5 mmole/cm<sup>3</sup>. FT measurement conditions were as follows: spectral width, 3923 Hz; pulse flipping angle, ca. 16°; acquisition time, 0.6 sec; number of data points, 4820. Data on OAc signals,  $\delta_C$  20.5-21.9 and 169.0-171.1, are not described. <sup>b</sup> Cf. ref 5a for the data in  $CDCl_3$ - $CD_3OD$ . <sup>c</sup> A small amount of  $CD_3OD$  was added to  $CDCl_3$  solutions to dissolve the sample. <sup>d/e</sup> Assignments may be reversed in each vertical column.

The  $^{13}\text{C}$  signals of oleanene-type triterpenes 2-5 were assigned using known chemical shift rules<sup>9</sup> such as OH substituent shifts,<sup>10</sup> acetylation shifts,<sup>11</sup> and steric  $\gamma$ ,<sup>11</sup> and  $\delta$ <sup>11,12</sup> effects, and by chemical-shift comparisons with previously reported data<sup>4-6</sup> as well as those on 1<sup>5a</sup> (see the TABLE). Based on our results obtained here and the usual procedures,<sup>9-12</sup> we assigned signals of saikogenins and derivatives 6-10 (see the TABLE). However, Me signals were difficult to assign completely; thus, some unequivocal assignments were further confirmed by selective  $^1\text{H}$  decoupling of the Me protons<sup>13,14</sup> in 7, 9, and their acetates.

The almost ordinary chair conformation of ring D of both  $16\alpha$ - and  $16\beta$ -hydroxyolean-12-enes was confirmed by X-ray crystallographic analyses<sup>4a,15</sup> as well as  $^1\text{H}$  NMR spectroscopy in solution,<sup>14a</sup> while the slight deformation of the chair D-ring of saikogenins was pointed out by  $^1\text{H}$  NMR.<sup>14</sup> The latter fact was further confirmed by detailed spin-decoupling and INDOR experiments of 100-MHz  $^1\text{H}$  NMR spectra of the peracetates of 2, 4, 7, and 9 in  $\text{CDCl}_3$  and  $\text{C}_6\text{D}_6$ : the  $J_{15\alpha,16}$  and  $J_{15\beta,16}$  values obtained ( $\pm 0.1$  Hz) were 3.2 and 3.2; 5.4 and 11.9;  $\sim 0.5$  and 4.9; and 6.8 and 9.6 Hz; respectively.

Thus, the  $16\alpha$ - and  $16\beta$ -OH substitution effects on  $\delta_{\text{C}}$  of neighboring carbons can be expected to differ from each other, depending on the D-ring conformation. As shown in the SCHEME, the OH effects ( $\Delta\delta_{\text{C}}$  in ppm) in the 28-hydroxyoleanene system can reasonably be explained by  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -shifts as suggested previously;<sup>4a,5a,10</sup> a considerable amount of an upfield shift of the C-22 signal should be noted. In the case of the bridged  $13\beta,28$ -epoxyoleanene (saikogenin) system, the substituted  $16\alpha$ -OH is deformed out of the D-ring, and accordingly its syn-diaxial interaction ( $\delta$ -effect) with 27-Me are



SCHEME. 16-Hydroxylation effects,  $\Delta\delta_{\text{C}}$  in ppm.

reduced; in fact, the C-27 signal is shifted upfield considerably. An increase in steric  $\gamma$ -interactions of the 16 $\beta$ -OH in **2** with 22-CH and 28-CH due to the bridge formation cause changes in magnitudes of the  $\alpha$ - and  $\beta$ -effects,<sup>10</sup> and the C-22 and C-28 signals are shifted upfield by -5.7 and -4.6 ppm, respectively. Thus, caution should be exercised in assigning <sup>13</sup>C signals by use of steric interaction because a minor change in the stereochemistry can sometimes cause considerable changes in  $\Delta\delta_C$  values expected from the general rules.

Some applications of the present results are reported in the following paper.<sup>8</sup>

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