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CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTRA OF OPHIBOLINS

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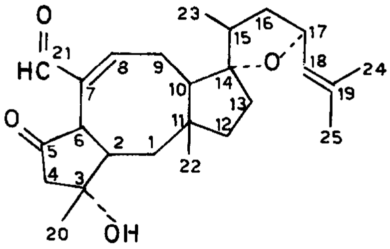
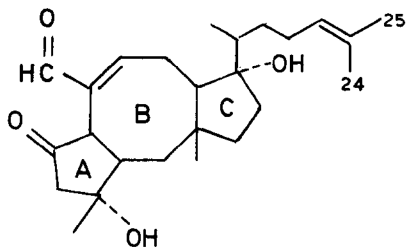
In continuation of our ^{13}C nmr study of terpenoic natural products with dicyclopenta (a, d) cyclooctene backbone (fusiccoccin and its cometabolites) (1) the natural abundance carbon-13 nmr spectra of the sesterterpenoic ophiobolin A(I), B(II), C(III), D(IV) (2) and their synthetic derivatives were recorded and analysed (3). We report here the assignment of the ^{13}C nmr spectra of the naturally occurring molecules I to IV (4). Apart from the presence of an additional isoprene unit in the side chain and the lack of the glucosidic moiety, the major differences in stereochemistry between I, II, III and fusicoccin consist of the appearance of new centres of asymmetry at C-2, C-10, C-14 and the loss of chirality at C-7, C-8 (displacement of double bond) and at C-9, C-12 (missing substituents) coupled with the simultaneous change of configuration at C-6. Structural differences between the molecules studied here are seen on the respective formulae.

Because of their similarity the spectra of I to III were interpreted first; spectral changes reflecting structural alterations in IV were treated separately. Inferences deduced from standard FT ^{13}C nmr procedures, experimental correlations with ^{1}H chemical shifts (3), evaluation of substituent effects, and considerations of known empirical rules (5) led to the assignments listed in the Table.

Comparison of the proton noise decoupled (PND) and single frequency off-centre decoupled (SFOCD) spectra immediately gave the assignments of the sp^2 carbons C-5, C-7, C-8, C-18 and C-19. Distinction between resonances due to C-19 and C-7 was facilitated by the large geminal ^{13}C-^{1}H coupling of the latter with the aldehydic proton giving rise to ^{13}C-^{1}H splitting under the conditions of SFOCD. Identification of the quaternary C-3 and C-11 resonances in the spectra of I, II and III was straightforward; the comparison of the spectra of I and II with



I



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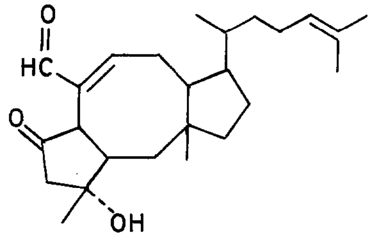
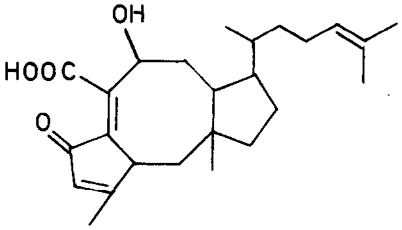


III



IV

that of III, on the other hand, provided designation of C-14 in the latter compound.

Of the methine carbon resonances in the spectra of I to III, those due to the angular C-2 and C-6 were expected to appear at nearly the same frequencies, while signals arising from C-10, C-15 and, in III, C-14 were evidently subject to substitution effects. Through the prior knowledge of the ^{1}H chemical shift of C-6H (3. 28 ppm), measurement of the residual splittings in the SFOCD spectra permitted the assignment of the resonance at approx 48. 7 ppm to C-6 and the other nonchanging methine signal at approx 50. 7 ppm to C-2 in I to III. Consideration of known substituent effects and published data on the isooctene side chain resonances in similar molecular environment (6) led to the assignments of C-10, C-15 in I to III, and C-14 in III.

The lowest field methylene resonance in the spectra of I to III exhibited only slight variations (from 54.6 to 54.8 ppm) and gave rise to a "sharp" triplet when using SFOCD. This finding suggested it was due to C-4, the only "isolated" methylene group in these molecules (7). On the basis published data for side chain methylene carbons (6), resonances at 37. 14 and 26. 05 ppm in the spectrum of III were respectively attributed to C-16 and C-17. Substitution shifts arising from the cyclic ether formation in I corroborated these assignments. The two methylene signals at 42. 80 and 23. 04 ppm in the spectrum of III gave rise to rather broadened off-resonance triplets (7) and thus were ascribed to the vicinally located C-12 and C-13, respectively. Supporting this conclusion were the good agreement of the above values with the chemical shifts

Table. Carbon-13 Chemical Shifts of Ophiobolins (a)

	I	II	III	IV
C- 1	35.31	37.35	36.10	48.74
C- 2	50.03	50.67	50.84	43.51
C- 3	76.54	76.65	76.72	178.12
C- 4	54.63	54.80	54.85	129.73
C- 5	217.08	217.29	217.35	195.75
C- 6	48.60	48.76	48.78	138.57
C- 7	141.96	141.35	141.81	137.27
C- 8	159.40	161.58	162.02	72.03
C- 9	23.12	23.98	24.67	31.50
C-10	60.92	66.50	53.66	47.02
C-11	42.69	44.82	44.01	43.72
C-12	41.09	40.37	42.80	43.41
C-13	30.15	31.98(b)	23.04	24.65
C-14	94.79	85.95	45.48	43.41
C-15	36.55	40.37	32.83	32.24
C-16	43.07	32.22(b)	37.14	37.66
C-17	70.89	26.53	26.05	26.07
C-18	126.79	125.54	124.99	124.76
C-19	134.51	130.56	131.12	130.71
C-20	25.81	25.86	25.80	17.24
C-21	194.50	195.00	195.47	172.00
C-22	17.65	18.56	18.91	21.36
C-23	17.93	16.38	16.62	16.96
C-24	18.10	17.64	17.61	17.54
C-25	25.65	25.70	25.73	25.64

(a) In parts per million relative to internal TMS; in the solvent mixture of $CDCl_3$-DMSO-d_6(2:1)
(b) Assignments may be reversed.

found for the same methylene carbons in related diterpenoids displaying identical structural environments (8), and shift variations attributable to the oxygen substitution at C-14 derived from the spectra of I and II. The remaining two methylene resonances at 24 and 36 ppm exhibiting only slight shift variations in the spectra of I to III were ascribed, respectively, to C-9 and C-1. Corroboration for this assignment was provided by measurements of the residual splittings in the SFOCD spectra correlating the higher field resonance with ^1H chemical shift of the allylic C-9 methylene group.

The five methyl carbon resonances of I to III appeared in two groups, with two methyl signals at approx.26 ppm and a further three in the range from 16 to 19 ppm. Distinction between the two lower field resonances, arising obviously from C-20 and C-25, was aided by measurements of the residual splittings and by single frequency selective ^1H decoupling (SFSD) experiments. Of the higher field methyl resonances the one due to C-24 was readily identified by its typically lower signal intensity connected with a relatively longer T_1 relaxation time, and also by the agreement of its shift value, 17.6 ppm, with published data (6). An unambigous assignment of the three high field methyl resonances was inferred from SFSD experiments based on the ^{1}H chemical shift differences of the respective methyl groups.

Structural differences occurring in IV leave ring C and isooctene side chain resonances practically unchanged. Therefore signals arising from carbons C-11 to C-19 and C-23 to C-25 appear in the spectrum of IV with only minor shift variations as compaired with their values in III. By similar reasoning as outlined above, designation of carbons C-4, C-5, C-8, C-10, C-20, C-21 and C-22 presented no difficulties. Identification of the allylic C-2 resonance was aided by establishing, via SFOCD, experimental correlation with its directly bonded C-2H pmr shift (4.03 ppm). SFSD measurements were performed to differentiate between resonances due to methylenic C-1 and C-9 and olefinic C-6 and C-7.

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