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^{13}C-NMR STUDIES OF MARINE NATURAL PRODUCTS II. TOTAL ASSIGNMENT OF THE ^{13}C-NMR SPECTRUM OF ASPERDIOL

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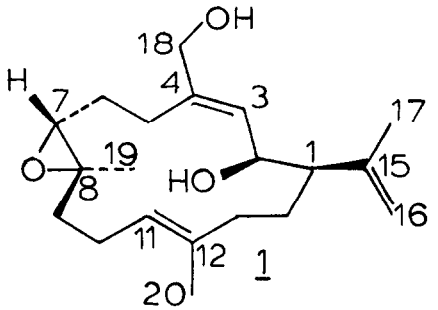
ABSTRACT

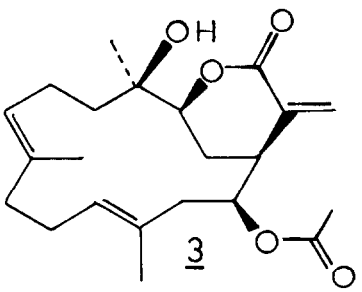
^{13}C-nmr spectral assignments for asperdiol are made with the aid of model compounds and T_1 relaxation behavior. Overall isotropic tumbling was inferred from the latter providing a supplemental means of multiplicity determination. Utilization of the T_1 relaxation times as an assignment criterion for select resonances in asperdiol is also described.

Cembranoid diterpenes are currently being isolated in burgeoning numbers from a variety of marine as well as terrestrial sources.[1] Although considerable ^{13}C-NMR spectral data has been reported for individual diterpenes,[2] only two papers have appeared that deal with the total spectral assignments for compounds of this class.[3,4] In a continuation of our ^{13}C-NMR studies of the marine cembranoids, we have now conducted a multi-faceted spectroscopic examination of asperdiol (1).[5] These studies have resulted in the total assignment of its ^{13}C spectrum, and have provided another example of the possibly general T_1 relaxation behavior observed for compounds in the cembrane series.

In conjunction with multiplicity information (vide infra), chemical shift assignments were made through detailed comparative studies with suitably constituted regions of model compounds. Limonene[6] served as a model for the isopropenyl side chain. Cecropia juvenile hormone[7] (2) served as a model for the C-1 to C-8 portion of the asperdiol ring, using appropriate chemical shift increments for the incorporation of the 2-hydroxyl[8] and geometry changes at the epoxide[9] and olefinic centers.[10] The balance of the ring resonances were related to crassin acetate (3), with modification for removal of the acetoxy residue.

T_1 inversion-recovery studies were performed to obtain a preliminary indication of signal multiplicities, and also for comparison with previously reported data on crassin acetate and its derivatives. Multiplicities inferred from the T_1 measurements were verified





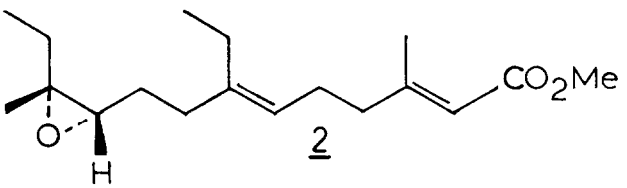


TABLE I

^{13}C-nmr Assignments and T_1 Values for Asperdiol at 25.2 MHz in Deuteriochloroform

Carbon	δ^{13}C(ppm)	Mult.	T_1(sec)[a]	Carbon	δ^{13}C(ppm)	Mult.	T_1(sec)[a]
1	50.40	d	0.56	11	128.54	d	0.51
2	68.26	d (b)	0.59	12	135.37	s	14.45
3	124.51	d	0.73	13	35.90	t	0.28
4	139.31	s	12.14	14	27.90	t	0.30
5	25.66	t	0.32	15	145.72	s	10.43
6	26.44	t	0.35	16	113.48	t	0.23
7	64.68	d (b)	0.60	17	22.18	q	7.01
8	60.21	s (b)	11.30	18	65.44	t (b)	0.45
9	37.32	t	0.28	19	15.66	q	10.45
10	23.87	t	0.29	20	16.46	q	4.74

(a) sample degassed

(b) multiplicity confirmed by SESFORD

using the SFORD technique, and where necessary due to overlap ambiguity, by acquisition of SESFORD spectra.[3] The results of these experiments, and the assignments of all resonances of the asperdiol molecule are summarized in Table I.

The values of the methine/methylene T_1 ratios observed previously for crassin, crassin acetate and crassin diacetate (Table II) indicated that these molecules were subject to overall isotropic motion in solution. The still higher ratio for asperdiol (side chain atoms excluded) reflects an even greater differentiation between its methine and methylene

resonances than those of the crassin group, and consequently more uniform isotropic tumbling.

Although it might be anticipated that the large size of the 14-membered carbocycle would permit independent regional (segmental) motion, it is evident that the ring is not sufficiently flexible for this to occur. Rather, all four of the cembranoid molecules appear to be sufficiently rigid to display isotropic behavior.

Because of its capability for free rotation about the C-4, C-18 single bond, the C-18 methylene resonance was excluded from consideration in determining the average T_1CH_2 relaxation time of the ring members. This additional motion imparts a shorter correlation time, and consequently a longer relaxation time, to this resonance relative to ring methylene resonances.[11,12] However, the rotational motion of the C-18 hydroxymethyl group in considerably slower than that of the freely rotating methyl groups, whose T_1 values are considerably longer. This relationship is not unexpected in view of the mass and bulk of the additional oxygen atom.

TABLE II

Comparative T_1 Relaxation Data

(for methine and methylene carbon resonances)

Compound	Avg. T_1CH_2 (sec)	Avg. T_1CH	T_1CH/T_1CH_2
Asperdiol	0.29[(a)]	0.60	2.04
Crassin Acetate	0.36	0.66	1.83
Crassin	0.27	0.51	1.85
Crassin Diacetate	0.39	0.71	1.81

(a) Excluding the C_{18} hydroxymethyl resonance and C_{16} methylene resonance of the isopropenyl group.

It is evident that careful consideration of T_1 relaxation data can provide useful structural information for compounds in the cembrane series, and presumbably also for other natural products which approximate to isotropic behavior. For such compounds, T_1 studies can assist spectral interpretation by providing an alternate approach to multiplicity determination which, like SFORD, is independent of a carbon atom's hybridization. As in the case of C-18 of asperdiol, disparate T_1 values pinpoint atoms external to a rigid nucleus, facilitating spectral assignment on the one hand, or conversely, assisting in structure elucidation.

We suspect that, as with the cembranes studied thus far, the characteristic requisites for isotropic behavior are probably more prevalent among many classes of natural products than is widely recognized. Relative rigidity of carbon skeleton is in fact commonplace in such compounds, but the absence of a preferred axis of tumbling in solution can be evaluated only by T_1 measurements. Although neither of these properties could safely have been predicted for the cembranes, their consequences provide a useful avenue of characterization,

which should also be applicable to other groups of natural products which display similar behavior. Further studies on additional members of the cembrane family as well as other marine natural products are presently underway in this laboratory.

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