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A STUDY OF INTRAMOLECULAR NUCLEAR OVERHAUSER EFFECT AND CONFORMATION OF ISOLINDERALACTONE, A FURAN-SESQUITERPENE.

AN EXAMPLE OF LARGE NOE VALUES BETWEEN OLEFINIC GEMINAL PROTONS

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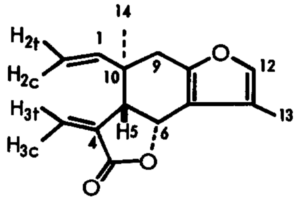
We report here the conformation of isolinderalactone (I), a furan-sesquiterpene isolated from Lindera strychinifolia Vill. (1), as determined by applications of the intramolecular nuclear Overhauser effect (NOE) (2) developed recently (3-6). In addition, we describe an example of large NOE values between olefinic geminal protons, believing that it is worthwhile to present our observations here, although two previous papers (4, 5) reported some examples. The results are briefly discussed.

Examination of molecular models shows that the six-membered ring of I can adopt four conformations; two of them have both the 10-Me and 9β-H axially-oriented, and the other two have both the 10-vinyl and 9α-H axially-oriented.



(I)

The 100-MHz PMDR and PMTR spectra of I have been examined in $CDCl_3$ and C_6D_6 to reveal the following facts: (a) the broader half (τ 7.32) of an AB-type quartet (J = (-)16.2 Hz) arising from one of the 9-H's is split by long-range spin-couplings (7) with 6β-H, 12-H, and 14-H ($|J|$ = 1.3, 0.7, and 0.5 Hz, respectively), whereas its sharper half (τ 7.44) is split by them with J's of less than 0.2 Hz, (b) the $J_{5β,14}$ value is clearly determined to be 0.3 Hz, and (c) no NOE's were observed for 9-H's, 5-H, and 3t-H on saturation of the 10-Me signal, or vice versa.

These facts demonstrate that the six-membered ring of I adopts the half-chair conformation with axially-oriented 10-Me, 9β-H, and 5-H (see the Figure).

The results of NOE experiments, shown in the Table, provide information about the conformation of the equatorial 10-vinyl group. The NOE's, $[H_5] \longrightarrow H_1$, $[H_{9α}] \longrightarrow H_1$, $[H_{9β}] \longrightarrow H_1$, and

[H_{14}] → H_{2c},[*1] imply that the vinyl group <u>mainly</u> adopts the conformation in which 2c-H is situated near the 10-Me, and 1-H is between 5-H and 9-H's (see the Figure). The fact that the long-range spin-coupling between 10-Me and 1-H was observed is compatible with this conformation.

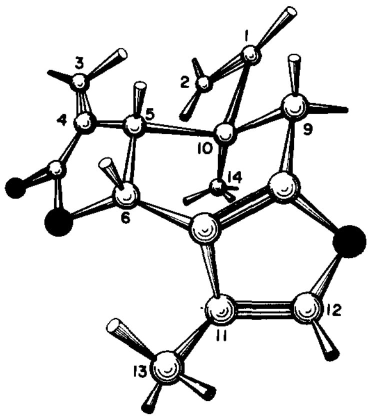
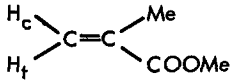
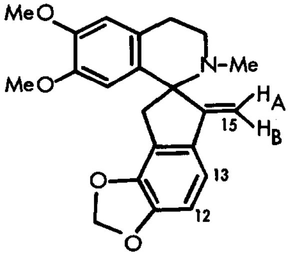


Figure. The conformation of isolinderalactone (I).

Fukumi, Arata, and Fujiwara (4) reported an NOE study of methyl metacrylate (II) by the use of the adiabatic rapid passage method (8),[*2] describing the large NOE values between olifinic geminal protons, [H_c] → H_t (48%) and [H_t] → H_c (42%). In an NOE study of ochotensimine (III), Bell and Saunders (5) also found large NOE values between similar protons, [H_{15A}] ↔ [H_{15B}] (40%), by employing the integration method.



(II)



(III)

As listed in the Table, the NOE's in the present molecule (I), [H_{3t}] → H_{3c} and [H_{3c}] → H_{3t}, were determined to be 46 and 37%, respectively, by the integration method.[*2] The latter smaller value obviously results from the fact that 3t-H is further relaxed by 5-H and 2c-H (the latter process could not at present be confirmed), whereas 3c-H can intramolecularly be relaxed by no other protons than 3t-H (2). Similar

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[*1] [H_i] → H_j denotes the NOE observation of the H_j signal on saturation of the H_i signal.

[*2] The adiabatic rapid passage method possesses the distinct advantages of the accurate determination of NOE values (5, 7) and of the measurements of spin-lattice relaxation times of the relevant protons at the same time (5). The integration method is, however, thought to be more convenient to organic chemists, particularly when examining complicated molecules, if much caution can be exercised.

TABLE

The Nuclear Overhauser Effects (increases in integrated signal intensities, %) and Chemical Shifts (τ) for Isolinderalactone in $CDCl_3$ and C_6D_6 (in parentheses)[a]

Observed signal	Irradiated signal											
	H_1 τ 4.16 (4.64)	H_{2t} 4.79 (5.13)	H_{2c} 4.94 (5.31)	H_{3t} 4.36 (4.84)	H_{3c} 3.70 (3.82)	H_5 6.99 (7.69)	H_6 4.74 (5.31)	$H_{9\alpha}$ 7.44 (7.76)	$H_{9\beta}$ 7.32	H_{12} 2.88 (3.13)	H_{13} 7.92 (8.07)	H_{14} 9.02 (9.25)
H_1	—	c (c)	c (c)	c (c)	0 (0)	6 (d)	c (c)	12 (d)	12	b (b)	b (b)	2 (0)
H_{2t}	c (c)	—	c (c)	c (c)	0 (0)	0 (0)	c (c)	0 (0)	0	b (b)	b (0)	-4 (-4)
H_{2c}	c (c)	c (c)	—	c (c)	0 (0)	0 (1)	c (c)	0 (1)	0	b (0)	b (0)	20 (18)
H_{3t}	c (c)	c (c)	0 (b)	—	37 (36)	0 (0)	c (c)	b (0)	b	b (b)	0 (b)	0 (0)
H_{3c}	c (c)	c (c)	0 (0)	46 (45)	—	0 (0)	0 (0)	b (0)	b	b (b)	0 (b)	0 (0)
H_5	c (c)	c (c)	c (c)	8 (c)	-5 (c)	—	12 (c)	c (c)	c	b (c)	-5 (c)	0 (c)
H_6	b (c)	c (c)	c (c)	c (c)	0 (0)	9 (c)	—	c (c)	c	0 (-1)	7 (7)	0 (0)
$H_{9\alpha}$	c (c)	c (c)	b (c)	b (c)	b (c)	c (c)	b (c)	—	c	b (c)	c (c)	2 (c)
$H_{9\beta}$	c	c	b	b	b	c	b	c	—	b	c	0
H_{12}	c (c)	c (c)	b (b)	0 (0)	0 (0)	0 (0)	-5 (-4)	b (b)	b	—	23 (26)	0 (0)

[a] The experimental procedures are similar to those previously described (6). Accuracies are about ± τ 0.01 for chemical shifts and about ±2% for NOE's.

[b] Not measured.

[c] Undeterminable.

[d] $[H_5, H_{9\alpha}, H_{9\beta}] \rightarrow H_1 = 30\%$ in double resonance. Other values in triple resonance are $[H_{3t}, H_6] \rightarrow H_5 = 21\%$ and $[H_5, H_{13}] \rightarrow H_6 = 16\%$.

relationship is seen between $[H_{3t}] \rightarrow H_5$ (8%) and $[H_5] \rightarrow H_{3t}$ (0%); 3t-H is strongly relaxed by 3c-H.

Much caution should, therefore, be exercised when discussing the relationship between the NOE value and the interatomic distance, and also, when showing a pair of protons to be distant from each other on the basis of no NOE between them.

As can be seen in the Table, negative NOE values were obtained between protons A and C when both protons have the relaxation paths to proton B, as previously reported (5, 9).

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