with 20 ml of chloroform–ethanol (20:0.5). The fractions were combined and evaporated. The residue was recrystallized from aqueous ethanol. This gave 0.16 g of the ketoepoxylactone (IV) with the composition $C_{15}H_{20}O_4$, mp 165-166°C (from aqueous ethanol).

Preparation of Tauremisin (V). The ketoepoxylactone (IV) (0.15 g) in 20 ml of methanol was boiled with 0.06 g of KOH in 2 ml of water. The reaction mixture was acidified with dilute HCl and was extracted with chloroform, and the extract was washed with water, dried, filtered, and evaporated. The residue was recrystallized from chloroform–hexane. This gave 0.07 g of acicular crystals with the composition $C_{15}H_{20}O_4$, mp 178-179°C (from aqueous ethanol).

LITERATURE CITED

1. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 75 (1978).
2. S. V. Serkerov, Khim. Prir. Soedin., 326, 488 (1979).
3. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 636 (1985).
4. A. Romo de Vivar and H. Jimenez, Tetrahedron, 21, 1741 (1965).
5. K. H. Lee and T. A. Geissman, Phytochem., 9, 403 (1970).
6. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 196 (1985).

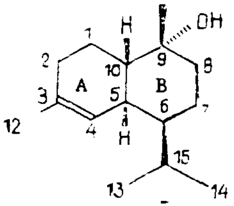
CONFORMATION OF δ-CADINOL IN SOLUTION

A. V. Tkachev and A. Yu. Denisov

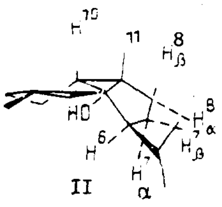
UDC 547.913.3:543.422.25

An assignment of the signals in the ^{13}C and ^{1}H NMR spectra of the natural sesquiterpene alcohol δ-cadinol has been made by the NMR method (INADEQUATE, 2D-INADEQUATE, two-dimensional C–H correlation on $^{1}J_{CH}$ constants, two-dimensional homonuclear J-spectroscopy) and the spin–spin coupling constants $^{1}J_{CC}$ and some J_{HH} constants have been determined. By comparing the experimental and calculated values of the spin–spin coupling constants J_{HH} it has been shown that the predominant conformation of the δ-cadinol molecule in solution is that in which ring A has the half-chair form and ring B the chair form with an equatorial arrangement of the hydroxy and isopropyl groups.

δ-Cadinol (I) is a sesquiterpenoid widely distributed in the vegetable kingdom, the structure and conformation of which have been the subject of prolonged discussion in the literature. In [1], on the basis of an analysis of the ^{13}C NMR spectra the δ-cadinol molecule (I) was assigned conformation (II), which, however, did not agree with the calculated figures obtained by the method of molecular mechanics [2]. In an analysis of the ^{13}C NMR spectrum of δ-cadinol (I) we found that an error had been admitted into [1] in the assignment of the signals of some of the carbon atoms, and since it was precisely the values of the chemical shifts that played a key role in the paper mentioned in determining the conformation of δ-cadinol (I) we undertook an additional investigation of this compound by the NMR method.



I



II

Analysis of the ^{13}C NMR spectra of δ-cadinol (I) recorded under the INADEQUATE and 2D-INADEQUATE regimes permitted an unambiguous assignment of the signals of the carbon atoms to be made (Table 1). A comparison of the assignment of the signals made in this way with

---

Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 635-638, September-October, 1990. Original article submitted January 3, 1990.

0009-3130/90/2605- 0539 $12.50

TABLE 1. Parameters of the ^{13}C NMR Spectrum of δ-Cadinol (I)

C^i	δC^i, ppm	$^1J_{(C^i-C^j)}$, Hz $(j)^a$
1	18,28	34,0(2), 34,1(10)
2	30,91	34,0(1), 39,4(3)
3	134,06	39,4(2), 43,3(12), 72,1(4)
4	124,38	72,1(3), 42,3(5)
5	36,52	42,3(4), 33,1(6), 32,1(10)
6	43,83	33,1(5), 33,1(7), 35,6(15)
7	21,25	33,1(6), 32,6(8)
8	34,96	32,6(7), 36,8(9)
9	72,25	36,8(8), 37,7(10), 39,8(11)
10	45,32	34,1(1), 32,1(5), 37,7(9)
11	27,71	39,8(9)
12	23,41	43,3(3)
13	21,45	35,4(15)
14	15,07	35,0(15)
15	26,16	35,6(6), 35,4(13), 35,0(14)

---

[a] ±0,1 Hz

TABLE 2. Parameters of the PMR Spectrum of δ-Cadinol (I)[a]

H^i	δH^i, ppm	$J_{H^i-H^j}$, Hz (±0,2 Hz)
H-1α	[1,82]*	13,5 (gem.)
H-1β	[1,45]*	13,5 (gem.)
2H-2	[1,89]	
H-4	5,43 dddq	5,6, 1,5, 1,5, 1,5
H-5	[1,92]	
H-6	[1,22] dddd	13,0, 11,0, 3,5, 3,5
H-7α	[1,40]	12,5 (gem.)
H-7β	1,01 dddd	13,0, 12,5(gem.), 12,0, 4,0
H-8α	[1,48]**	12,0 (gem.)
H-8β	[1,41]**	12,0 (gem.)
H-10	[1,59]	
3H-11	1,20 d	1,0
3H-12	1,57 dddd	1,5, 1,5, 0,5, 0,5
3H-13	0,80 d	7,0
3H-14	0,72 d	7,0
H-15	[1,88]dqq	3,5, 7,0, 7,0

---

[a] The chemical shifts given in square brackets and the values of the constants of geminal interaction (gem.) were obtained from a two-dimensional C–H correlation spectrum on the constants $^1J_{C-H}$; the values of the other constants were obtained from a two-dimensional J-resolved spectrum; the chemical shifts marked with asterisks should possibly be interchanged.

that given in [1] showed that in the paper mentioned the assignment of one pair of signals (the signals of the C-1 and C-8 atoms) had been interchanged.

Basing ourselves on the accurate assignment of the signals in the ^{13}C NMR spectrum and having recorded a two-dimensional C–H correlation spectrum on direct $^1J_{C-H}$ constants, we determined the chemical shifts in the PMR spectrum for all the hydrogen atoms of the δ-cadinol molecule, and from the results of the two-dimensional J-resolved proton spectrum and experiments on homonuclear double resonance we also determined the values of some spin-spin coupling constants J_{HH} (Table 2). We may note that the experimental parameters of the splitting of the signals in the PMR spectrum that were found do not agree with conformation (II). Thus, the methyl group geminal to the hydroxy group appeared in the PMR spectrum in the form of a doublet with the constant J_{HH} = 1 Hz, which is due to spin–spin coupling through four bonds with one of the H-8α,β or H-10 hydrogen atoms. However, this value of the constant can be observed only with the antiperiplanar arrangement of the carbon atom of the methyl group and the hydrogen atom vicinal to this carbon atom [3]. But in conformation (II) the carbon atom

TABLE 3. Values of the Spin–Spin Coupling Constants J_{HH} in the δ-Cadinol Molecule (I) and the Calculated Values of the Constants Characterizing Conformation (III)

H^i	H^j	$J_{H^i-H^j}$, Hz	
		experimental values[a,b]	calculation for conformation (III)[c]
H-4	H-5	5,6	5,2
	H-2α	1,5*	—2,3 (—1,4)
	H-2β	1,5*	—0,6 (—1,4)
	3H-12	1,5	
H-6	H-5	11,0	12,0
	H-7β	13,0	12,8
	H-7α	3,5*	3,7
	H-15	3,5*	3.9
H-7β	H-8α	12,0*	12,7
	H-8β	4,0*	4.4
3H-11	H-8α	1,0*	1,0
	H-8β	0.0	—0,2
	H-10	0,0	—0,2
3H-12	H-5	1.5	
	H-2α	0,5*	
	H-2β	0,5*	
3H-13	H-15	7,0	
3H-14	H-15	7,0	

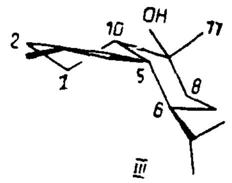
[a] Observed splitting, signs of the constants not determined.

[b] The values of the splittings marked by asterisks were determined from an analysis of the form of the H^i signal but the fact that it was just this splitting that belonged to the constant $J_{H^i-H^j}$ was not confirmed experimentally.

[c] The splitting in the spectrum calculated from the values of the spin–spin coupling constants and with allowance for the fact that the signals of the H-2α and H-2β atoms have the same chemical shift is given in parentheses.

of the C^{11} methyl group is located synclinally with respect to the H-8α,β and H-10 hydrogen atoms and in such a situation the constant $^4J_{HH}$ must be close to 0 Hz. Furthermore, the vicinal constant $^3J_{HH}$ between the H-6 atoms and one of the hydrogen atoms of the neighboring C^7H_2 methylene group amounts to 13.0 Hz, which is possible only with the 1,2-diaxial arrangement of the interacting atoms, but such a situation is excluded in the twist form of ring B, as in conformation (II).

Nevertheless, the experimental values of the spin-spin coupling constants are in harmony with conformation (III) in which ring A is present in the half-chair conformation and ring B in the chair conformation with equatorial hydroxy and isopropyl groups. Table 3 gives the calculated values of the spin–spin coupling constants J_{HH} for conformation (III). On the basis of the circumstance that the calculated and experimental splitting parameters agree well with one another, it may be concluded that the predominant conformation of the δ-cadinol molecule (I) in solution must be conformation (III). It must be mentioned that it is precisely this conformation of the δ-cadinol molecule that is the most stable according to calculations by the method of molecular mechanics [2].



III

EXPERIMENTAL

The spectra of δ-cadinol (I) isolated from the oleoresin of the Siberian stone pine Pinus sibirica were recorded on a Bruker AM 400 instrument (^{1}H – 400.13 MHz; ^{13}C NMR – 100.61 MHz) using the usual set of programs; the internal standard was the solvent (deuterochloroform), with δ_H 7.24 ppm and δ_C 76.90 ppm. The $^{13}C-\{^1H\}$ NMR spectrum, the two-dimensional $^{13}C-^{13}C$ two-quantum coherence correlation (2D-INADEQUATE) spectrum, the one-dimensional INADEQUATE spectrum, and the $^{13}C-^1H$ heteronuclear correlation two-dimensional spectrum on direct $^1J_{CH}$ constants were recorded for a 0.75 M solution in deuterochloroform. For the 2D spectra: a 2K × 2K matrix was obtained by the Fourier transformation (FT) of the matrix of free induction decays (FIDs) of 4K × 256 points with 32 accumulations for each decay in the case of 2D-INADEQUATE and 8 accumulations in the case of C–H correlation. The INADEQUATE spectra were optimized for J_{CC} = 40 Hz, and the C–H spectra for J_{CH} = 125 Hz. The PMR spectra and the two-dimensional homonuclear J-resolution spectrum were recorded for a 0.09 M solution in $CDCl_3$–CD_3OD (9:1). For the 2D spectrum: a matrix of 4K × 1K points was obtained after the FT of 4K × 256 FID points, with 16 accumulation for each FID.

The calculations by the method of molecular mechanics were carried out by the MM2 program [4]. The spin–spin coupling constants $^3J_{H-C(sp^3)-C(sp^3)-H}$ were calculated by point geometry as described in [5], and the constants of the other types were calculated in the same way using the following equations [3, 6]:

$$^3J_{H-C(sp^2)-C(sp^3)-H} = 6{,}6\cos^2\varphi + 2{,}6\sin^2\varphi\,(0^\circ \leqslant \varphi \leqslant 90^\circ) = 11{,}6\cos^2\varphi +$$
$$+\,2{,}6\sin^2\varphi\,(90^\circ \leqslant \varphi \leqslant 180^\circ),$$
$$^4J_{H-C=C-C(sp^3)-H} = 1{,}3\cos^2\varphi - 2{,}6\sin^2\varphi\,(0^\circ \leqslant \varphi \leqslant 90^\circ) =$$
$$= -2{,}6\sin^2\varphi\,(90^\circ \leqslant \varphi \leqslant 180^\circ),$$
$$^4J_{H-C(sp^3)-C(sp^3)-C(sp^3)-H} = A\cos^2\varphi_1\cos^2\varphi_2 - 0{,}35$$
$$A = 0{,}31 \text{ at } \varphi_1,\ \varphi_2 \leqslant 90^\circ,$$
$$A = 3{,}61 \text{ at } \varphi_1,\ \varphi_2 \geqslant 90^\circ,$$
$$A = 1{,}06 \text{ — for remaining cases.}$$

LITERATURE CITED

1. A. I. Rezvukhin, V. A. Khan, and Zh. V. Dubovenko, Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 1310 (1975).
2. Yu. V. Gatilov and Zh. V. Dubovenko, Khim. Prir. Soedin., No. 2, 234 (1979).
3. N. M. Sergeev, NMR Spectroscopy [in Russian], Izd-vo MGU, Moscow (1981), p. 88.
4. U. Burkert and N. L. Allinger, Molecular Mechanisms, ACS Monograph 177, American Chemical Society, Washington, DC (1982).
5. A. V. Tkachev, O. V. Toropov, G. E. Sal'nikov, Yu. V. Gatilov, and I. Yu. Bagryanskaya, Zh. Org. Khim., 25, 249 (1989).
6. E. W. Garbisch, J. Am. Chem. Soc., 86, No. 24, 5561 (1964).