CHEMISTRY LETTERS, pp. 1191-1194, 1977. Published by the Chemical Society of Japan

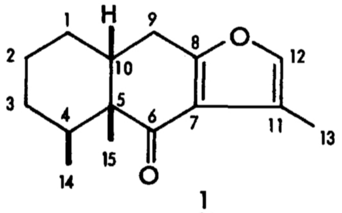
NMR AND CD SPECTRAL STUDIES OF CONFORMATIONAL ISOMERS OF ISOLIGULARONE AND FUKINONE, NATURALLY OCCURRING cis-DECALIN DERIVATIVES

Toshichika SATO,* Masahiro TADA,* Takeyoshi TAKAHASHI,* Isao HORIBE,** Hiroshi ISHII,**
Tatsuo IWATA,** Kaoru KURIYAMA,** Youko TAMURA,** and Kazuo TORI**

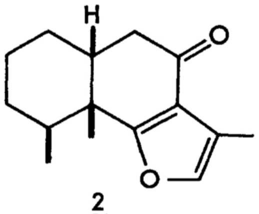
* Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo, 113 and ** Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553

NMR and CD spectroscopic evidence showed that cis-decalin types of sesquiterpenic ketones, isoligularone (2) and fukinone (3), predominantly adopt "steroid-like" conformations in solution in contrast with ligularone (1) which prefers the "non-steroid-like" one. ^{13}C NMR signal assignments and anomalies in the CD of the furanoketones are also reported.

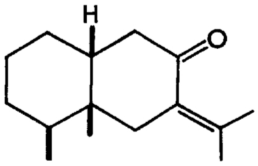
Generally, description of the conformations of naturally occurring cis-decalin derivatives is difficult because of the presence of a possible equilibrium between so-called "steroid-like" (A) and "non-steroid-like" (B) chair-chair conformational isomers. In a previous paper,1) we reported the first evidence for an equilibrium between the two conformers of cis-decalin type sesquiterpenes, ligularone (1) and ligularol acetate.2) As a further extension of this study, we examined variable-temperature ^{13}C and ^{1}H NMR, and CD spectra of isoligularone (2)3) and fukinone (3)4) as well as 1 to investigate factors controlling the equilibrium conditions between the two conformers. We report here evidence that they exist in solution in equilibrium between the two conformations, that 2 and 3 predominantly adopt conformation A in contrast to the case of 1 which was reported to have conformation B, mainly in a ratio of 4:1,1) and that Cotton effects of these furanoketones are reversed in sign predicted from "Snatzke's rule" for enones having regular half-chair forms in CD spectroscopy.5)



1



2



3

"Steroid-like" (A)

"Non-steroid-like" (B)

The ^{13}C NMR spectrum of **2** in $(CD_3)_2CO$-$CDCl_3$ (2:1) shows one set of relatively sharp signals (see Table 1). As the temperature was lowered, the signals broadened below -70°; at -130°, one set of sharp signals due to the predominant conformer was observed only because another set of signals corresponding to the minor conformer was too weak to be detected. Thus the population of the minor conformer at -130° should be less than 5%. The variable-temperature ^{1}H NMR spectra of **2** in CS_2-$CDCl_3$ (2:1) below -70° and in $(CD_3)_2CO$ below -65° also showed only the signals belonging to the major conformer. The dominant conformer of **2** was probably the "steroid-like" (A) one on the basis of $J_{9\alpha,10\beta}$ (ca. 15 Hz) and $J_{9\beta,10\beta}$ values (ca. 4 Hz) ($\delta_{H-9\alpha}$ 2.95; $\delta_{H-9\beta}$ 2.17); the J values at room temperature were ca. 13.5 and 4 Hz ($\delta_{H-9\alpha}$ 2.83; $\delta_{H-9\beta}$ 2.20).

The ^{13}C NMR spectrum of **3** in $(CD_3)_2CO$ at -130° showed two sets of signals in a ratio of about 10:1 (see Table 1). In the ^{1}H NMR spectra of **3** in CS_2 below -70°, only one set of signals due to the predominant conformer could be observed and assigned to those resulting also from "steroid-like" conformation (A) from the observed J values [($J_{9\alpha,10\beta}$ = 13.5 and $J_{9\beta,10\beta}$ = 4.5 Hz) ($\delta_{H-9\alpha}$ 2.78; $\delta_{H-9\beta}$ 2.18)]; the J values at room temperature were ca. 11 and 6 Hz ($\delta_{H-9\alpha}$ 2.54; $\delta_{H-9\beta}$ 2.23).

The variable-temperature ^{13}C NMR spectra of **1** were also examined in $(CD_3)_2CO$ and two sets of signals appeared below -65° in a ratio of 2.1:1 (see Table 1). The Gibbs' free energy difference, $\Delta G°$ at -65° was estimated to be 0.30 kcal/mole from the ^{13}C signal peak heights, agreeing well with the result from ^{1}H NMR spectroscopy.[1)]

The ^{13}C NMR signals were assigned in $CDCl_3$ using known chemical shift rules, several ^{1}H decoupling techniques,[6)] shift-reagent[$Yb(fod)_3$]-induced shifts (see Table 1) which were particularly useful for the purpose, and chemical-shift comparisons from compound to compound. The chemical shifts (Table 1) assessed for the conformers at low temperatures agree well with their stereochemical relationships.

The CD spectra of **3** in E.P.A. showed negative n-π* and positive π-π* Cotton effects as shown in Table 2. Application of the rules[5,7)] for the cisoid-enone indicates the predominance of the "steroid-like" conformation for **3**, too. The $\Delta G°$ value was calculated to be about 0.9 kcal/mole from the temperature variation in $[\theta]_{243}$, roughly agreeing with the NMR result.

On the other hand, the CD curves of **2** showed positive n-π* and negative π-π* Cotton effects whose signs were opposite to those expected from the Snatzke[5)] and Helicity[8)] rules for the preferred "steroid-like" conformation of **2** (see Table 2). This reversed sign seems to indicate that the furanoketone moiety of **2** with "steroid-like" conformation adopts a deformed sofa form than the regular half-chair one. This finding is similar to that observed for the aromatic ketones.[9)] This was similarly observed in the CD curve of **1** which mainly adopts the "non-steroid-like" (B) conformation as reported previously.[1,10)] Since the CD curve observed for **1** has an opposite sign to that predicted for conformation B as shown in Table 2, this fact can readily be explained by considering the deformed sofa conformation in contrast with the regular half-chair conformation of the furanoketone moiety.

Thus, the equilibria between the "steroid-like" and the "non-steroid-like" conformations in solution were confirmed for naturally occurring cis-decalin derivatives with an α,β-unsaturated ketone moiety (**2** and **3** as well as **1**), and the former two predominantly adopt the "steroid-like" conformation in contrast with **1**. It seems not immediately possible to explain the reversal of conformations between the former two and **1**. Simple conformational analyses attempted were not enough to explain the phenomena.

Table 1. Carbon-13 Chemical Shifts, δ_C, of Compounds Examined[a]

Carbon No.	Ligularone (**1**)			Isoligularone (**2**)			Fukinone (**3**)		
	$CDCl_3$	$(CD_3)_2CO$		$CDCl_3$	$CDCl_3$+$(CD_3)_2CO$(1:2)		$CDCl_3$	$(CD_3)_2CO$	
	30°[b]	45°	-65°[c]	30°[b]	38°	-130°[d]	30°[b]	30°	-130°[e]
1	28.6[f]	28.9[f]	h	20.4	20.7	20.5	21.6[f]	21.3	21.0
	[18]		(h)	[8]			[9]		(h)
2	20.2	20.7	23.4	30.0[f]	30.4[f]	30.0[f]	27.3	27.8	26.7
	[13]		(14.0)	[8]			[7]		(h)
3	29.9[f]	30.4[f]	h	26.1[f]	26.4[f]	25.6[f]	30.2	30.7	30.6
	[22]		(h)	[9]			[6]		(h)
4	31.1	31.7	31.4	34.8	35.2	34.6	32.5	32.8	30.8
	[42]		(h)	[11]			[11]		(h)
5	49.7	50.1	49.8	39.7	40.0	40.0	36.7	37.3	37.5
	[61]		(49.8)	[17]			[17]		(36.5)
6	199.8	198.7	199.4	174.4	174.8	174.5	40.7	41.0	41.6
	[130]		(199.4)	[30]			[29]		(38.4)
7	117.9	118.2	117.5	118.5	119.1	118.0	139.9	138.9	137.6
	[59]		(118.1)	[53]			[48]		(140.1)
8	164.2	164.6	164.6	195.7	194.9	195.7	205.4	204.0	205.3
	[33]		(165.6)	[127]			[126]		(h)
9	26.8	27.0	h	41.3	41.4	40.7	44.0	44.3	44.0
	[22]		(24.9)	[53]			[51]		(46.2)
10	39.0	39.7	37.7	42.1	42.4	42.4	41.4	42.0	43.1
	[28]		(41.0)	[22]			[20]		(49.0)
11	119.8	120.1	119.6	119.1	120.3	118.0	131.2	131.8	131.8
	[33]		(119.6)	[34]			[47]		(132.3)
12	139.2	140.1	140.5	139.1	140.0	139.7	22.6	22.3	22.5
	[17]		(140.5)	[18]			[36]		(h)
13	9.1	9.1	9.7	9.1	9.0	9.5	21.6[f]	21.7	21.0
	[18]		(9.7)	[24]			[17]		(25.1)
14	15.0	15.2	14.0	16.6[g]	16.8[g]	15.4[g]	16.0	16.3	16.8
	[20]		(17.3)	[10]			[8]		(15.3)
15	19.2	19.1	20.2	17.0[g]	17.0[g]	17.6[g]	20.5	20.9	20.7
	[39]		(20.8)	[9]			[5]		(h)

[a] ^{13}C NMR spectra were recorded on a Varian NV-14 FT NMR spectrometer at 15.087 MHz using TMS as an internal reference (δ_C 0) in 8-mm tubes. FT measurement conditions were: spectral width, 3923 Hz; pulse flipping angle, ca 16°; acquisition time, 0.6 sec; number of data points, 4820. [b] Values in square brackets are those for LIS (in ppm) obtained from the shift curves. [c] Values in parentheses are those for the minor conformer (A) (ratio, 2:1). [d] Exists as the major conformer A solely. [e] Values in parentheses are those for the minor conformer B (ratio, 10:1). [f,g] Assignments may be reversed. [h] Not assignable.

Table 2. Variable-temperature CD Spectral Data in E.P.A.

	1[1)]				**2**				**3**			
	$[\theta]_{max}$				$[\theta]_{max}$				$[\theta]_{max}$			
		+24.5°	-68°	-190°		+24°	-68°	-190°		+24°	-68°	-190°
n→π*	327 nm	+610	+1650	+2650	311 nm	+7810	+14200	+23600	325 nm	-1240	-1740	-1520
π→π*	287 nm	-630(dioxane)			267 nm	-2440	-3160	-5280	243 nm	+11300	+16900	+23800

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10) In the previous paper,1) 2-acetoxy-5β,[25R]-spirost-2-en-1-one was described to show Cotton effects similar to **1**; the A-ring of this compound has also a deformed sofa. However, 5β,[25R]-spirost-1-en-3-one was observed to have normal Cotton effects for a regular half-chair.

(Received August 16, 1977)