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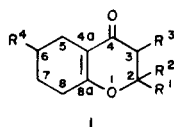
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The 25 MHz ^{13}C and 350 MHz ^1H -nmr spectra of the title compounds are reported. Conformational equilibria in variously substituted 5,6,7,8-tetrahydrochromanones are discussed. Compounds bearing a *t*-butyl group at the 6 position appear to be conformationally homogenous.

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Recently, we described the synthesis of 5,6,7,8-tetrahydrochromanone derivatives **1a-e,h**, as precursors of 1-oxa-4-decalones [1,2]. The lack of ^{13}C -nmr data of this class of compounds prompted us to determine the values of these data in order to investigate their conformational properties in combination with 350 MHz ^1H -nmr studies. Additional isomeric 6-*t*-butyl-2-methyl derivatives **1f,g** were prepared by acylation of 4-*t*-butyl-1-morpholino-1-cyclohexene with crotonoyl chloride.



	R ¹	R ²	R ³	R ⁴
a	H	H	H	H
b	Me	H	H	H
c	Me	Me	H	H
d trans	Me	H	Me	H
e cis	H	Me	Me	H
f cis	Me	H	H	<i>t</i> -Bu
g trans	Me	H	H	<i>t</i> -Bu
h	Me	Me	H	<i>t</i> -Bu

Table 2

Methyl substituent effects [a] at C-2, C-3 and C-4

Compound	Substituent	C-2	C-3	C-4
1b	2-methyl	7.2	6.8	0.7
1c	2,2-dimethyl	12	11.3	0.4
1d	<i>trans</i> -2,3-dimethyl	12.1	8.6	2.2
1e	<i>cis</i> -2,3-dimethyl	9.4	7.7	5.2
1f	<i>cis</i> -2-methyl	7.2	6.7	0.3
1g	<i>trans</i> -2-methyl	6.9	6.5	-0.1
1h	2,2-dimethyl	11.9	11.0	0.2

[a] In ppm; positive values indicate downfield shifts. All shifts are related to values in the parent compound **1a**.

The carbon shifts are listed in Table 1 and were assigned on the basis of ^{13}C -nmr off-resonance decoupled spectra, general chemical shift arguments and comparison of the ring carbon shifts with chromanones [3,4], 2-methyl-2,3-dihydropyran-4-one [5] and substituent effects in substituted 3,4-dihydro-2*H*-pyrans [6]. In the case of the 2,6-disubstituted derivatives, the formation of a mixture of *cis/trans* isomers is clearly revealed, since the ^{13}C -nmr spectrum of the crude material give rise to two resonances for all the carbon atoms in a 7:3 ratio. The problem re-

Table 1

 Carbon Chemical Shifts of Tetrahydrochromanones **1** (δ ppm, Deuteriochloroform)

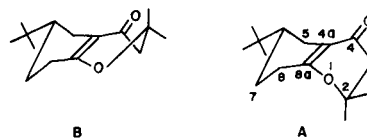
No. Compound	C-2	C-3	C-4	C-4a	C-8a	CH ₃	<i>t</i> -Bu	Other C [a]
1a	67.2	36.3	191.5	112.6	171.4			20.8, 22.0, 22.1, 28.6
1b	74.4	43.1	192.2	111.8	171.2	20.6		20.6, 21.9, 22.0, 28.6
1c	79.2	47.6	191.9	110.2	168.8	26.3		20.4, 22.1, 22.2, 29.1
1d trans	79.3	44.9	193.7	110.8	170.1	19.4 (C-2) 10.5 (C-3)		20.9, 21.9, 22.0, 28.6
1e cis [b]	76.6	44.0	196.7	110.0	170.3	16.2 (C-2) 9.5 (C-3)		20.8, 21.9, 22.1, 28.5
1f cis	74.4	43.0	191.8	111.5	170.9	20.7	32.1, 27.3	43.7 (C-6), 29.7, 23.2, 22.2
1g trans [c]	74.1	42.8	191.4	110.9	170.3	20.3	32.1, 27.3	43.9 (C-6), 29.7, 23.4, 21.7
1h	79.1	47.3	191.7	109.8	168.6	27.7 24.8	32.2, 27.3	43.9 (C-6), 30.2, 23.3, 21.8

[a] No attempt was made to assign C-5-C-8 resonances. [b] Recorded from a mixture of **1d** + **1e**. [c] Recorded from a mixture **1f** + **1g**.

mains of deciding which belong to *cis* and which to *trans* isomer. A choice cannot be made between them based upon ^{13}C shifts or 350 MHz ^1H -nmr. The major compound **1f** was obtained in a pure state by recrystallization. Therefore the crystal structure of **1f** was determined by an X-ray diffraction experiment. Unambiguous evidence to support the *cis* configuration was obtained [7]. In Table 2 are gathered data on the effects of methylation calculated from the chemical shifts in Table 1. A comparison of the heterocyclic ring carbons with chromanones [3,4] reveals that the C-2, C-3 and C-4 carbons were not significantly affected by the replacement of a phenyl by a cyclohexenyl moiety.

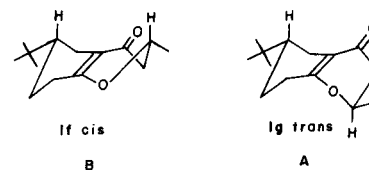
In order to obtain additional information about the conformation of compounds **1**, the coupling constant data were determined through 350 MHz ^1H -nmr analysis, by spin decoupling experiments (Table 3). It is reasonable to accept that the heterocyclic ring adopts a conformation with the ether-oxygen and four carbon atoms in one plane, only C-2 lying outside this plane, by analogy to chromanones and flavanones [8,9]. Moreover, it is well known that the half-chair conformation of the cyclohexene ring corresponds to an energy minimal [10]. The ^1H -nmr spectra of **1a** and **1c** showed magnetic equivalence of the H-3 and H-3' protons and of H-2 and H-2' (**1a**) or of the geminal 2-methyl groups (**1c**). These findings are consistent with the heterocyclic ring in rapid conformational equilibrium. By fixing the conformation of the cyclohexene ring by means of *t*-butyl group at the 6 position (**1h** compared to **1c**), the nonequivalence of the H-3 and H-3' protons and of the 2,2-methyl groups revealed a rigid conformation of the dihydropyran ring. Additional evidence comes from the ^{13}C -nmr spectrum of **1h** which displayed two different

methyl carbons. The remaining question, more difficult to answer, concerns the conformation of this molecule for which two possibilities exist: the C-2 and C-7 carbons could be either on the same side of the plane formed by C-4, C-5, C-8, C-4a and C-8a (**A**) or on the opposite side (**B**) (Scheme 1).



Scheme 1. Possible conformations of **1h**.

Interestingly, the 350 MHz ^1H nmr spectra of the isomeric 6-*t*-butyl-2-methyl derivatives **1f** and **1g** indicated that the 2-methyl groups are pseudoequatorially disposed in each isomer, since the 2-methine protons exhibited both axial-axial and axial-equatorial vicinal coupling constants (Table 3). Consequently, **1f** and **1g** exist in a fixed conformation **B** and **A** respectively (Scheme 2).



Scheme 2. *cis* and *trans* 6-*t*-Butyl-2-methyl-5,6,7,8-tetrahydro-4-chromanones.

It can be seen from the Table 1 that the ^{13}C chemical shifts of **1f** and **1g** are nearly identical, although all reson-

Table 3
Selected Chemical Shifts and ^1H Coupling Constants for Compounds **1**

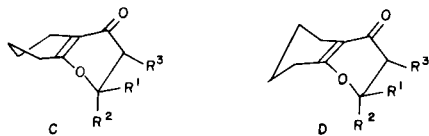
Compound	δ ppm, deuteriochloroform			CH ₃ (C-3)	JH-2-H-3	J (Hz)	J H-3-H-3'
	H-2	H-3	CH ₃ (C-2)				
1a	4.39	2.44			7		
1b	4.44	2.44	1.40		12.3		16.8
1c		2.37	1.37		4.5		
1d trans	4.01	nl	1.41	1.06	12.5		
1e cis [a]	4.45	nl	1.30	1.00	3.3		
1f cis	4.42	2.45	1.41		13.3		16.8
		2.34			3.8		
1g trans [b]	4.49	nl	1.40		11.9		
					4.5		
1h		2.56	1.41				16.5
		2.39	1.35				

nl = Not located unambiguously. [a] Recorded from a mixture **1d** + **1e**. [b] Recorded from a mixture **1f** + **1g**.

ances of the *trans* isomer are slightly upfield (0.2-0.6 ppm) as compared to those of the major *cis* isomer. The less favorable geometry of the *trans* isomer which differs from the *cis* by a greater interaction between the O-C₂ and C-7,C-8 bonds could explain these small differences. The conformational diagnosis of **1h**, by comparing its carbon chemical shifts with those of **1g** and **1f** is not conclusive; however, upon geometrical argument, conformation **B** would seem to be preferable [11].

For the compound **1b**, the vicinal coupling constants $J_{H-2,H-3}$ and $J_{H-2,H-3'}$ of 12.3 and 4.5 Hz suggest that the heterocyclic ring mostly exists in a conformation with the 2-methyl group in a pseudoequatorial disposition. In the case of the *trans* and *cis* 2,3-dimethyl derivatives **1d** and **1e** besides the establishment of the configuration from the H-2,H-3 coupling constants, the downfield position of H-2 (4.45 ppm) and the upfield shift of the 2-methyl carbon (16.2 ppm) of the *cis* isomer **1e**, as compared to the corresponding signals found for the *trans* isomer **1d** (4.01 and 19.4 ppm respectively), suggest that **1e** exists in a conformation with a pseudoaxial disposition of the 2-methyl group. However, the downfield shift of the carbonyl carbon in the *cis* isomer, probably due to the loss of conjugation with the double bond, suggests a slight distortion of the heterocyclic ring.

In contrast to **1f** or **1g** (6-*t*-butyl analogs), the compounds **1b,d,e** can adopt the conformation **C** or **D** by the half-chair inversion of the cyclohexenyl ring. For the geometrical reason discussed above, we favor the **C** conformation, however, our data do not allow to appreciate if a conformational equilibrium **C** \rightleftharpoons **D** occurred in solution.



Scheme 3. Possible conformations of compounds **1b,d,e**.

In summary, the dihydropyran ring prefers the conformation in which the 2-methyl group is pseudoequatorially disposed, with the exception of the *cis*-2,3-dimethyl derivative in which the 2-methyl group adopts a pseudoaxial position.

EXPERIMENTAL

Melting points were recorded on a Kofler hot plate. Boiling points

were uncorrected. Infrared and ultraviolet spectra were obtained with a Beckman Model Acculab 2 and DB spectrometers. The ¹H-nmr spectra were taken on a 350 MHz Cameca spectrometer. The following conditions were used: sweep width 2800 Hz, pulse angle 13°, repetition time 2.3 seconds, digitization and data processing 16K, temperature 20°C. The ¹³C-nmr spectra were performed on a Varian XL-100 12FT spectrometer operating at 25.2 MHz with ¹H noise decoupling at 100 MHz by FT technique using 45° pulse angle and a 1 second acquisition time, 5 kHz spectral width and 16 K FT. The samples were recorded in deuteriochloroform (5% W/v) used as lock signal in spinning 10 mm tubes at 22°C. All spectra are expressed per million from TMS. Elemental analyses were performed by Microanalytical Laboratory, Centre National de la Recherche Scientifique 69390 Vernaison, France. Compounds **1a-e** [1] and **1h** [2] have been previously described.

cis- and *trans* 6-*t*-Butyl-2-methyl-5,6,7,8-tetrahydro-4-chromanones **1f** and **1g**.

These compounds were obtained as described for **1a-e** [1] using 4-*t*-butyl-1-morpholino-1-cyclohexene and crotonoyl chloride. The material obtained after distillation bp 150-155° (4 mm Hg), yield 65% proved to be a mixture of *cis* and *trans* isomers **1f** and **1g** in a ratio of about 7:3 by 350 MHz ¹H-nmr; 350 MHz ¹H-nmr (deuteriochloroform): δ 0.92 (s, 9H), 1.40 and 1.41 (2d, 3H, J = 6.5 Hz, *trans* and *cis* respectively), 1.15-2.50 (m, 9H), 4.42 (m, 0.7 H, *cis*), 4.49 (m, 0.3 H, *trans*) ppm.

Anal. Calcd. for C₁₄H₂₂O₂: C, 75.63; H, 9.97. Found: C, 75.51; H, 10.08.

The *cis/trans* isomeric mixture crystallized on standing, recrystallization of the solid material from hexane afforded the pure *cis* isomer **1g**, yield 25%, mp 69°; ir (carbon tetrachloride): ν max 1680, 1630 cm⁻¹; uv (ethanol): 275 nm (ε 11800).

Attempts to isolate pure *trans* compound **1g** failed.

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