BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 47(2), 509—510 (1974)

Hydroxyl Stretching Frequencies and Conformations of 4-Chromanol, 4-Thiochromanol, and 4-Thiochromanol 1,1-Dioxide

Kaoru HANAYA, Shinji ONODERA,* Sachio AWANO,** and Hideaki KUDO
Department of Chemistry, Faculty of Science, Yamagata University, Koshirakawa-cho, Yamagata 990
**Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Katahira-2-chome, Sendai 980*
***Department of Industrical Chemistry, Tsuruoka Technical College, 104 Inooka, Tsuruoka, Yamagata 997*

(Received September 3, 1973)

Synopsis. Conformations of ten epimeric alcohols have been examined by the measurements of the OH stretching absorptions. The preference of the OH quasi-axial conformations was shown.

Iwamura and Hanaya[1)] measured the O–H stretching absorption bands of epimeric 1-tetralols and 4-chromanols in carbon tetrachloride and pointed out that the epimer with the quasi-axial OH group shows a singlet absorption band and that with the quasi-equatorial OH group a doublet band. The doublet OH absorption of tetralol (**1**) was ascribed to the coexistence of the isomers with the quasi-axial and quasi-equational OH groups with the ratio 1 : 0.54.[2)] The apparent conformational energy ($-\Delta G_{25^\circ C}$) of the benzylic OH group was estimated to be 0.37 kcal/mol.

This paper reports on the measurements of the OH stretching absorptions and an estimation of the conformational energies for 4-chromanol (**2**), 4-thiochromanol (**3**), 4-thiochromanol 1,1-dioxide (**4**), and their derivatives which are considered to have a configuration similar to that of 1-tetralol. The OH absorption bands are analyzed in a similar way to that used for 1-tetralol.[1)] The NMR spectra of these compounds were also examined to confirm the conformations.

Results and Discussion

The OH stretching absorption maxima of 4-chromanol (**2**), 4-thiochromanol (**3**), 4-thiochromanol 1,1-dioxide (**5**), and their derivatives (**5a**∼**7b**) including 5,8-dimethyl-4-chromanol (**8**) are given in Table 1. The NMR measurements are summarized in Table 2 for the signals assigned to the protons at 4-positions of these compounds. Bolger and co-workers[3)] have determined the conformations of **5a** and **5b** by NMR study. The NMR spectra of **6a**, **6b**, **7a**, and **7b** are interpreted in a similar manner to those of **5a** and **5b**. A double doublet signal due to the proton at 4-position of **6a** indicates that the hydroxyl group of this compound has quasi-equatorial conformation as regards the heterocyclic ring. The same situation is also suggested for the conformation of **7a**. The triplet signals observed for the protons at the 4-positions of **6a** and **7b** indicate quasi-axial conformations.

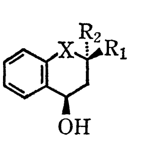
Epimers with a quasi-axial OH group each show a single absorption maximum, while those with the quasi-equatorial OH group have a doublet absorption band (Table 1). From the fact that the infrared spectra of these epimers are similar to those of 1-tetralols, it is assumed that these compounds have a similar conformation to that of 1-tetralol, in which the heterocyclic ring prefers a half-chair conformation.

The conformational free energies ($-\Delta G$) of the benzylic OH group for compounds **2**, **3**, and **4** were calculated by means of the graphical devision of the infrared OH absorptions in a similar manner to that for 1-tetralol[1)] (Table 3). These values lead to the conclusion that the quasi-axial OH conformation is predominant in compounds **2**, **3**, and **4** and component of the epimer with this conformation increases in the order **1**<**4**≈**3**<**2**. This is consistent with the results by Katekar and Moritz,[4)] who showed the preference of the quasi-axial OH conformation in **2** and **3** by examination of their infrared and NMR spectra.

From the half-chair conformations of the heterocyclic rings in **2**, **3**, and **4**, preference of the quasi-axial OH conformation should be attributed to the large steric repulsion between the equatorially oriented OH group and the aromatic hydrogen atom disposed parallel to the OH group, over the one 1,3-diaxial H···OH interaction in the heterocyclic ring.[5)] The assumption is consistent with the result for 5,8-dimethyl-4-thiochro-

TABLE 1. ν_{OH} ABSORPTION MAXIMA OF 4-CHROMANOL, 4-THIOCHROMANOL, 4-THIOCHROMANOL 1,1-DIOXIDE AND THEIR ALLIED COMPOUNDS

Compound	ν_{max} (cm^{-1})	$\Delta\nu^a{}_{1/2}$ (cm^{-1})	ε
2	3616	16	84
	3597	14	20
3	3614	15	66
	3595	14	14
4	3611	21	108
	3586	13	23
5a	3623	23	34
	3596	14	75
5b	3616	16	89
6a	3625	18	32
	3594	12	52
6b	3613	18	91
7a	3617	27	30
	3588	15	74
7b	3612	22	145
8	3616	16	91



2 : $X=O,\ R_1=R_2=H$
3 : $X=S,\ R_1=R_2=H$
4 : $X=SO_2,\ R_1=R_2=H$
5a : $X=O,\ R_1=Ph,\ R_2=H$
5b : $X=O,\ R_1=H,\ R_2=Ph$
6a : $X=S,\ R_1=CH_3,\ R_2=H$
6b : $X=S,\ R_1=H,\ R_2=CH_3$
7a : $X=SO_2,\ R_1=CH_3,\ R_2=H$
7b ; $X=SO_2,\ R_1=H,\ R_2=CH_3$

Table 2. NMR spectra of 4-chromanol, 4-thiochromanol and 4-thiochromanol 1,1-dioxide and their derivatives

Compound	Position of peaks in ppm	Assignment	Remarks (Hz)
5a[a]	6.55	4-H	Double doublet $J_{3a.4}+J_{3e.4}=16.2$
5b[a]	6.26	4-H	Triplet $J_{3a.4}+J_{3e.4}=6.0$
6a	4.65	4-H	Double doublet $J_{3a.4}+J_{3e.1}=15.3$
6b	4.47	4-H	Triplet $J_{3a.4}+J_{3e.4}=5.9$
7a	4.77	4-H	Double doublet $J_{3a.4}+J_{3e.4}=15.3$
7b	4.83	4-H	Triplet $J_{3a.4}+J_{3e.4}=6.8$

a) NMR spectrum of benzoyloxyflavan.

Table 3. Conformational free energies ($-\Delta G_{25°C}$) for the benzylic OH groups of **1**, **2**, **3**, and **4**

Compound	$-\Delta G_{25°C}$ (kcal/mol)[a]
1	0.37
2	0.65
3	0.56
4	0.51

a) With an error of about ±0.1 kal/mol.

manol (**8**). The infrared spectrum of **8** shows a singlet OH absorption maximum at 3616 cm^{-1} which can be assigned to the quasi-axial OH group. In this case, the steric repulsion between the equatorially oriented OH group and the bulky methyl group at 8-position would be more serious than that between the OH group and the hydrogen atom at 8-position, leading to an overwhelming selection of the quasi-axial conformation in **8**.

Experimental

Materials. *cis*-(**5a**) and *trans*-4-Flavanol (**5b**),[6] 4-chromanol (**2**),[7] 4-thiochromanol (**3**),[8] and 4-thiochromanol 1,1-dioxide (**4**)[9] were prepared by standard procedures. *cis*-(**6a**) and *trans*-2-Methyl-4-thiochromanol (**6b**), *cis*-(**7a**) and *trans*-2-methyl-4-thiochromanol 1,1-dioxide (**7b**) were prepared by the sodium borohydride reduction or the Merewein-Ponndorf reduction of 2-methyl-4-thiochromanone 1,1-dioxide, respectively. *cis*-2-Methyl-4-thiochromanol (**6a**): mp 74—75 °C (lit, 74—75.5 °C).[10] *trans*-2-Methyl-4-thiochromanol (**6b**): bp 116—118 °C/1 mmHg; the *p*-nitrobenzoate crystallized from ethyl acetate, mp 156—157 °C. Found: C, 61.75; H, 4.69; N, 4.25%. Calcd for $C_{17}H_{15}O_4NS$: C, 62.00; H, 4.25%. *cis*-2-Methyl-4-thiochromanol 1,1-dioxide (**7a**): mp 130—131.5 °C. Found: C, 56.70; H, 5.95%. Calcd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70%. *trans*-2-Methyl-4-thiochromanol 1,1-dioxide (**7b**): mp 105—106 °C. Found: C, 56.82; H, 5.74%. Calcd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70%. 5,8-Dimethyl-4-chromanol (**8**): Reduction of 5,8-Dimethyl-4-chromanone with sodium borohydride yielded 5,8-dimethyl-4-chromanol (**8**) as colorless needles from ligroin, mp 108—110 °C. Found: C, 73.75; H, 7.80 %. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%.

Measurements. The NMR spectra were measured in $CDCl_3$ using a Hitachi H-60 spectrometer with TMS as an internal standard. The infrared spectra were recorded with a Perkin-Elmer 125 or a JASCO DS-403G double beam grating spectrophotometer. A KCl cell of 30 mm in optical length was used. The concentration of the solution was *ca.* 0.005 mol/l in carbon tetrachloride purified by distillation over phosphorus pentoxide. The band due to intermolecular hydrogen bonding was not observed at this concentration.

The authors wish to express their gratitude to Associate Professor Hiizu Iwamura, the University of Tokyo, for his helpful discussions and suggestions during this work.

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