

Carbon-13 Nuclear Magnetic Resonance Spectroscopy of 1-Tetralols and Chroman-4-ols

By Yasuhisa Senda,* Jun-ichi Ishiyama, and Shin Imaizumi, Department of Applied Science, Tohoku University, Sendai, Japan
Kaoru Hanaya, Department of Chemistry, Yamagata University, Yamagata, Japan

¹³C N.m.r. spectra of 1-tetralol, chroman-4-ol, and their substituted homologues have been determined. The CH(OH) resonances of 1-tetralol and chroman-4-ol indicate that their hydroxy-groups prefer a pseudoaxial orientation, as a result of $A^{(1,2)}$ strain. ¹³C N.m.r. spectra of stereoisomeric flavanols support the configurational relationship reported by Clark-Lewis *et al.* and by others that the α -isomer corresponds to the *cis*- and the β -isomer to the *trans*-form.

SUFFICIENT evidence has been accumulated to establish that carbon shieldings depend, at least in part, on molecular geometry and conformation.¹⁻³ We have studied the ¹³C n.m.r. spectra of a range of 1-tetralols and chroman-4-ols, primarily to ascertain the influence of structure and stereochemistry on carbon chemical shifts.

RESULTS AND DISCUSSION

The natural-abundance 25.15 MHz ¹³C Fourier transform n.m.r. spectra were obtained by using the ¹H noise decoupling technique. ¹H Off-resonance decoupling was used to aid assignments of resonances to specific carbon atoms. The chemical shifts obtained are listed in Table 1. The assignments of CH(OH) signals of 1-tetralols are straightforward. The CH(OH) resonances of *cis*-3-methyl- (3) and *cis*-3-phenyl-1-tetralol (4) appear at lower field than those of their *trans*-counterparts. The CH(OH) chemical shifts of 2-methylcyclohex-2-enol (10), and *cis*- and *trans*-2-methyl-5-*t*-butylcyclohex-2-enols (11) are δ 68.87, 71.53, and 68.80, respectively.⁴ As in the case of the 2-methylcyclohex-2-enols the C-1 resonance of 1-tetralol (1) appears closer to those of *trans*- (3) and *trans*- (4) than to those of their *cis*-counterparts. It has been reported that the hydroxy-group of the cyclohexenol (10) prefers a pseudoaxial orientation as a result of strain between the hydroxy-group at the allylic position and the methyl group at the vicinal sp^2 hybridised carbon atom [$A^{(1,2)}$ strain⁵]. The magnitude of the interaction is estimated as *ca.* 1.95 kcal mol⁻¹.⁶ The equatorial methyl group of 4-methylcyclohexene hardly affects the chemical shift of C-6.⁷ An equatorial phenyl group at C-4 is also expected not to affect appreciably the chemical shift of C-6 in cyclohexene. The correlation of the chemical shift for C-1 of the tetralol (1) with that of the cyclohexenol (10) suggests that (1) exists in a conformation with the hydroxy-group in a preferred pseudoaxial

orientation, as also indicated by an i.r. study.⁸ Large $A^{(1,2)}$ strain may also exist between the hydroxy-group and the aromatic methine group at position 8. When *cis*- (3) is in a conformation with the hydroxy-group in a pseudoaxial orientation, there is a large 1,3-*syn*-axial-pseudoaxial interaction between the methyl and the hydroxy-group. The energy of this interaction is estimated as *ca.* 2.2–2.4 kcal mol⁻¹, the energy of the 1,3-*syn*-diaxial interaction on a cyclohexane ring,⁹ or less. By comparing the $A^{(1,2)}$ strain of the hydroxy-group and the 1,3-*syn*-axial-pseudoaxial interaction between a methyl and a hydroxy-group on a cyclohexene ring, *cis*- (3) is deduced to be stabilised in a conformation with the substituents in an equatorial and a pseudoequatorial orientation by 0.3–0.4 kcal mol⁻¹ or less. This indicates that, even when $A^{(1,2)}$ strain is large, the hydroxy-group of *cis*- (3) prefers a pseudoequatorial orientation. The C-3 resonances for the tetralols (3) and (4) are easily assigned by use of the off-resonance technique. If it is possible to apply the substituent parameters of a methyl group and a hydroxy-group on a cyclohexane ring to the saturated carbon atoms of a cyclohexene ring, other two resonances for the alicyclic carbon atoms can be assigned appropriately to C-2 and -4. The resonances for C-2, -3, and -4 of the *cis*-isomers appear at lower field than those of the *trans*-forms as in the case of C-1.

The C-2 resonances of chroman-4-ols are expected to appear close to the CH(OH) signals. The CH(OH) resonances of chroman-4-ol (5) and 4-methylchroman-4-ol (6) appear a few p.p.m. to higher field than those of the corresponding 1-tetralols because these carbon atoms are γ with respect to the ethereal oxygen.¹⁰ On the basis of the substituent effect of the ethereal oxygen, the resonances of the stereoisomeric 2-methylchroman-4-ols (8) and flavan-4-ols (9) which appear a few p.p.m. to higher field than those of the corresponding 1-tetralols, may correspond to C-4. In comparing the

¹ G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley-Interscience, New York, 1972.

² J. B. Stothers, 'Carbon-13 NMR Spectroscopy,' Academic Press, New York, 1972.

³ N. K. Wilson and J. B. Stothers, *Topics Stereochem.*, 1974, **8**, 1.

⁴ Y. Senda, S. Imaizumi, S. Ochiai, and K. Fujita, *Tetrahedron*, 1974, **30**, 539.

⁵ F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.*, 1965, **87**, 5492.

⁶ Y. Senda and S. Imaizumi, *Tetrahedron*, 1974, **30**, 3813.

⁷ T. Pehk, S. Rang, O. Eisen, and E. Lippmaa, *Eesti N.S.V. Tead. Akad. Toim. Keem. Geol.*, 1968, **17**, 296.

⁸ H. Iwamura and K. Hanaya, *Bull. Chem. Soc. Japan*, 1970, **43**, 3901.

⁹ E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 237.

¹⁰ E. L. Eiel, W. F. Bailey, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Scheli, and D. W. Cochran, *J. Amer. Chem. Soc.*, 1975, **97**, 322.

TABLE I

¹³C Chemical shifts (δ) of 1-tetralols and chroman-4-ols ^a

No.		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-8a	C-4a	C-1'	C-2',-6'	C-3',-5'	C-4'	CH ₃	
(1)		67.70	32.15	18.99	29.18	(128.68)	(125.89)	(127.16)	(128.68)	138.87	136.87						
(2)		70.43	39.61	20.44	29.91	(126.92)	(126.19)	(126.43)	(128.62)	143.00	136.08						30.76
<i>cis</i> - (3)		69.40	42.04	28.27	38.28	(126.86)	(125.95)	(126.86)	(128.25)	139.60	136.50						22.08
<i>trans</i> - (3)		67.95	39.92	23.66	38.10	(128.98)	(126.19)	(127.77)	(129.65)	137.78	137.17						21.84
<i>cis</i> - (4)		69.89	40.34	39.31	38.23	(126.37)	(126.85)	(127.20)	(128.44)	139.28	136.17	145.39	(126.71)	128.56	(126.37)		
<i>trans</i> - (4)		67.76	38.58	34.70	37.61	(126.72)	(127.94)	(128.95)	(129.79)	137.28	136.74	145.79	127.00	128.47	(126.37)		
(5)			61.88	30.82	62.91	129.77	120.43	129.47	116.91	154.46	124.31						
(6)			63.21	37.98	66.19	128.98	120.67	126.55	117.03	153.80	128.50						29.42
(7)			60.61	30.94	60.00	136.02	121.46	130.07	121.22	152.83	123.64						15.83 17.89
<i>cis</i> - (8)			71.22	39.55	65.28	128.86	120.49	127.04	116.36	154.52	125.77						21.41
<i>trans</i> - (8)			67.34	37.67	63.64	130.20	120.37	129.71	117.15	155.07	123.58						21.17
α - (9)			76.94	40.17	65.89	(128.70)	121.01	(128.25)	116.80	154.54	126.11	140.56	127.03	129.20	(125.80)		
β - (9)			73.04	38.22	63.76	(129.95)	120.79	(129.10)	117.45	154.83	125.77	140.93	126.19	128.56	(128.01)		
(10)		68.87	32.04	17.85	25.19												
<i>cis</i> - (11)		71.53	34.95	43.68	27.12												
<i>trans</i> - (11)		68.80	33.13	37.56	27.30												

Values in parentheses may be interchanged.

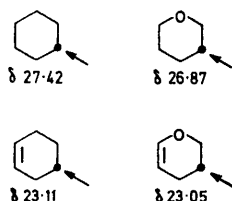
CH(OH) chemical shifts of the stereoisomeric alcohols (8) and (9) with those for (5), a similar correlation to that with the 1-tetralols is observed. This indicates that the hydroxy-groups of (5), *trans*-(8), and β -(9) also prefer the pseudoaxial orientation,¹¹ while those of *cis*-(8) and α -(9) prefer the pseudoequatorial position. The resonances for C-2, -3, and -4 of the *cis*-isomers appear at lower field than those of the *trans*-forms.

The stereochemistry of the flavanols (9) has been discussed extensively. Clark-Lewis *et al.*¹² and other authors¹³ have studied the ¹H n.m.r. spectra and deduced from coupling constants that α -(9) corresponds to the *cis*- and β -(9) to the *trans*-isomer. The ¹³C n.m.r. spectra of these compounds support this configurational relationship. The CH(OH) resonance of (7) appears at higher field than that of parent chromanol. This may be due to an increasing population of the conformer with the pseudoaxial hydroxy-group owing to the large hydroxy-methyl strain at the allylic and the *peri* positions and/or the steric compression shift caused by the methyl group at C-5.^{14,15}

The ¹³C n.m.r. spectra of the stereoisomeric 1-t-butyl-4-methylcyclohexanes show that the chemical shift of an axial methyl group in a cyclohexane ring is δ 17.53, and that of an equatorial methyl group is 22.53.¹⁶ If these values are applied to the methyl group at the homoallylic position on a cyclohexene ring, the observed carbon chemical shifts for the 3-methyl group of the stereoisomeric tetralols (3) indicate that these groups prefer an equatorial orientation. In comparing the carbon chemical shifts of cyclohexane and cyclohexene with those of tetrahydropyran and dihydropyran, respectively, no substituent effect on the β -carbon atom by replacement of a methylene with an oxygen atom was observed (Table 2). Therefore, the carbon chemical

TABLE 2

Comparison of ¹³C chemical shifts of six-membered ring compounds



shifts of the methyl groups in the stereoisomeric chromanols (8), which are β with respect to the ethereal oxygen atom, indicate that these groups are also in an equatorial conformation.

The resonances for substituted aromatic carbon atoms

* Positive values represent shifts to lower field.

¹¹ K. Hanaya, S. Onodera, S. Awano, and H. Kudo, *Bull. Chem. Soc. Japan*, 1974, **47**, 509.

¹² J. W. Clark-Lewis, T. M. Stopwood, and L. R. Williams, *Proc. Chem. Soc.*, 1963, 20; J. W. Clark-Lewis, T. M. Stopwood, and L. R. Williams, *Austral. J. Chem.*, 1963, **16**, 107.

of 1-tetralols and chroman-4-ols are easily assigned on the following basis. (i) For comparisons of the chemical shifts of the respective carbon atoms of allylic alcohols¹⁷ with those of the corresponding alkenes¹⁸ with the same number of carbons, the substituent parameters of the hydroxy-group on both β - and γ -carbon atoms are positive,* the former being larger than the latter. In 1-tetralols, the resonances for C-4a may appear at higher field than those for C-8a. (ii) The resonances for substituted carbon atoms of monoalkylbenzenes appear around δ 140–150.¹⁹ The resonances around δ 145 in (4) and those around δ 140 in (9) correspond to C-1'.

The chemical shifts for the aromatic carbon atoms in phenyl ethers such as anisole are usually in the order, substituted $>$ *meta*- $>$ *para*- $>$ *ortho*-positions, since the electronic effect of the oxygen atom produces an upfield shift of *ortho*- and *para*-carbon signals, the former appearing at higher field than the latter. The resonances around δ 116–117 in chroman-4-ols may correspond to C-8 and those around δ 120–121 to C-6. It has been reported that for toluene, the substituent of which is relatively small, the resonances of the *ortho*-carbon atoms appear at a field lower than those for the *meta*-carbon atoms, whereas an inverse tendency due to steric compression is found in monoalkylbenzenes which have a relatively large substituent such as a cyclohexyl or an isopropyl group.¹⁹ In the phenyl-substituted compounds such as (4) and (9), the resonances for C-2' and C-6' or C-3' and C-5' are expected to appear at the same position, those of the former two carbon atoms appearing at slightly higher field than those of the latter two. The signal intensity identifies these resonances. Other aromatic carbon signals are impossible to assign to the specific nuclei.

EXPERIMENTAL

N.m.r. Spectra.—¹³C Fourier transform n.m.r. spectra were obtained at 25.15 MHz with a JEOL JNM-MH-100 instrument equipped with a JNM-MFT-100 Fourier transform accessory; the instrument was controlled with a JEC-6 spectrum computer. Samples were dissolved into CDCl₃, the deuterium signal of which provided a field frequency lock; the concentrations were 20% (w/v). Measurement conditions were as follows; pulse width 27.5 μ s (ca. 45 °C); repetition time 4 s; spectral width 6.25 kHz; data points 8 192. Noise modulated proton decoupling was carried out at a nominal power of 20 W. All chemical shifts (δ) are expressed in p.p.m. downfield

¹³ C. P. Lillya, D. Kehoe, E. M. Philbin, M. A. Vickars, and T. S. Wheeler, *Chem. and Ind.*, 1963, 84; C. P. Lillya, S. E. Derwes, and D. G. Roux, *ibid.*, p. 783; H. G. Krishnamuity, T. R. Seshadri, and D. G. Roux, *Tetrahedron Letters*, 1965, 3689; B. G. Bolger, A. Hirwe, K. G. Marathe, E. M. Philbin, M. A. Vickars, and C. P. Lillya, *Tetrahedron*, 1966, **22**, 621.

¹⁴ Ref. 1, p. 84.

¹⁵ Ref. 2, p. 115.

¹⁶ Y. Senda and S. Imaizumi, *Tetrahedron*, 1975, **31**, 2905.

¹⁷ Ref. 2, p. 188.

¹⁸ R. A. Friedel and H. L. Retcofsky, *J. Amer. Chem. Soc.*, 1963, **85**, 1300.

¹⁹ Ref. 2, p. 97.

from internal Me_4Si . Each observed chemical shift is estimated to be accurate to within ± 0.06 p.p.m.

Materials.—All compounds employed in this work have

²⁰ F. Strauss and L. Lemmel, *Ber.*, 1921, **54**, 25.

²¹ T. Kusama and D. Koike, *Nippon Kagaku Zasshi*, 1951, **72**, 683.

²² K. Hanaya, *Nippon Kagaku Zasshi*, 1966, **87**, 995.

²³ G. D. Thakar, N. Janaki, and B. C. Subba Rao, *Indian J. Chem.*, 1965, **3**, 74.

been previously reported; (1),²⁰ (2),²¹ (3),²² (4),²² (5),²³ (6),²⁴ (7),¹¹ (8),²⁵ and (9).²⁶

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²⁴ F. Arndt and J. Pusch, *Ber.*, 1925, **58**, 1648.

²⁵ K. Hanaya and K. Furuse, *Nippon Kagaku Zasshi*, 1968, **89**, 1002.

²⁶ S. Mitsui and A. Kasahara, *Nippon Kagaku Zasshi*, 1958, **79**, 1382.
