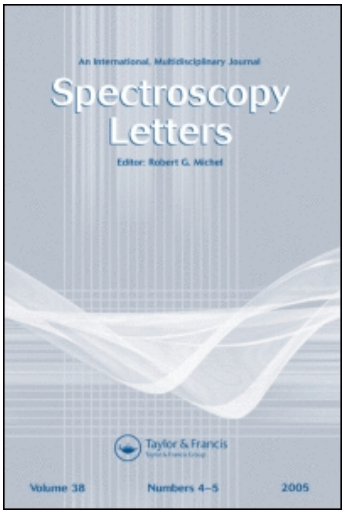

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Benzene Induced ^{1}H NMR Shifts of Chromeno-Compounds: An Aid to Differentiate Linear and Angular Chromenoflavones

A. Banerji[a]; D. L. Luthria[a]
[a] Chemical Ecology Section, Bio-Organic Division, Bhabha Atomic Research Centre, Bombay, India

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BENZENE INDUCED ^{1}H NMR SHIFTS OF CHROMENO-COMPOUNDS: AN AID TO DIFFERENTIATE LINEAR AND ANGULAR CHROMENOFLAVONES

Key Word : Benzene Induced Shifts, ^{1}H NMR, Chromeno-compounds, Differentiation of linear and angular chromenoflavones

A. Banerji and D. L. Luthria

Chemical Ecology Section, Bio-Organic Division,
Bhabha Atomic Research Centre, Trombay,
Bombay 400 085, India.

ABSTRACT: Benzene-induced shifts (BIS) in the ^{1}H NMR spectra of nine chromeno-compounds have been studied. It provides a simple non-destructive technique for distinguishing linear isomers of chromenoflavones from

their angular counterparts. BIS also assists in the assignment of chromene proton signals in chromeno-compounds.

INTRODUCTION

Solvent induced ^1H NMR shift is one of the simple and non-destructive spectroscopic techniques which has been utilized extensively in solving structural, stereochemical and conformational problems [1]. Use of this technique for the structural analysis of simple flavonoids has been reported previously [2]. We have studied benzene induced shifts (BIS) {$\Delta ppm = \delta(CDCl_3) - \delta(C_6D_6)$} to get an insight into the molecular architecture of structurally related chromenoflavones (1a-c, 2a-c). This technique not only provides a simple method for differentiation of angular and linear isomers, but is also useful in the assignment of signals due to chromene protons. The present paper reports the BIS studies of nine compounds containing chromene ring (FIG. 1).

RESULTS AND DISCUSSIONS

Recently, we have isolated two new chromenoflavones *viz.* atalantoflavone (2d) and racemoflavone (2e) from *Atalantia racemosa* [3]. Assignment of the position of chromene ring presents a major problem in the elucidation of structures of such compounds [4]. Color reactions such as Gibbs test have

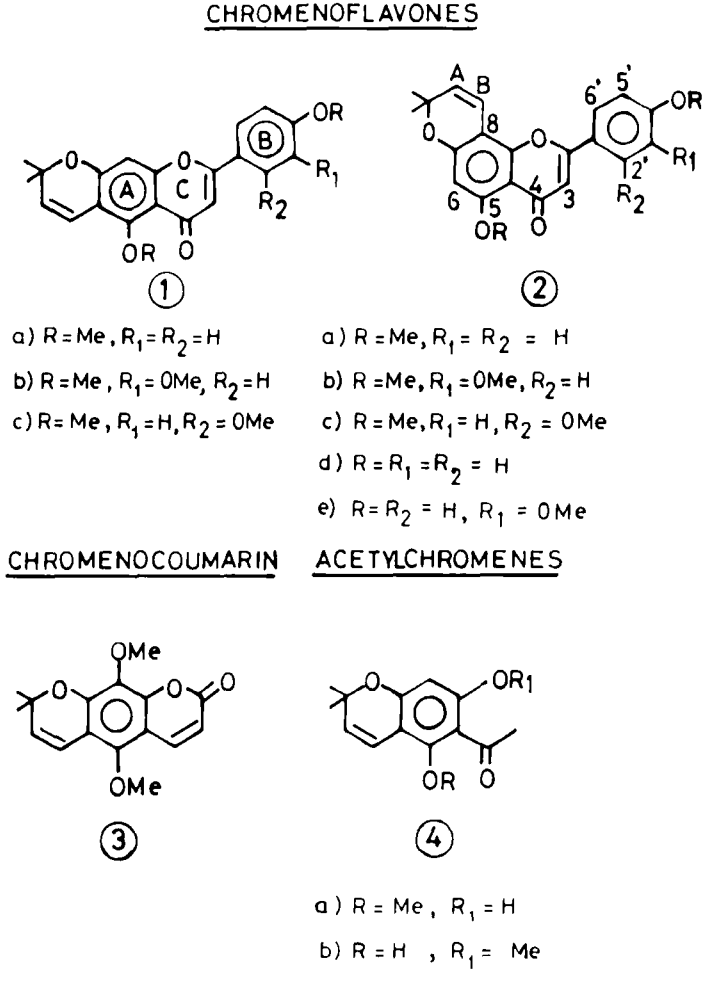

FIG. 1. Structure of Chromeno-compounds.

been used in determining the position of the fused chromene moiety [5,6], but this method has often proved to be inadequate in many instances [4,7,8], thereby resulting in the erroneous assignment of structures. Differences in the chemical shifts of unsubstituted A

ring proton (H-6 or H-8) can also be utilized for the differentiation of isomers. This too has limitation, due to occasional overlapping of signals of H-3, H-6 and H-8 protons [4]. This prompted us to explore the possibility of utilizing BIS for the characterization of chromenoflavones. Therefore, BIS of nine chromenocoumpounds of known structures were studied.

In the present study on chromenoflavones,the C-5 methoxyl protons of the linear isomers (1a-c) showed small downfield shifts ($\approx$ -0.06) due to their proximity to the negative end of the carbonyl dipole. However in contrast, the angular isomers (2a-c) exhibited marked upfield shifts ($\approx$ +0.51) because of the presence of free ortho protons (H-6). Thus, the shifts of C-5 methoxyl protons are of diagnostic value for the differentiation of angular and linear isomers. Methoxyl protons of the B ring having free ortho proton(s) also exhibited expected upfield shifts (FIG.2). These BIS for the methoxyl proton are in agreement with the observations made by Wilson *et al.*[9]

BIS studies of the chromene ring protons (gem dimethyl, A and B) of compounds (1a-c, 2a-c, 3 and 4a,b) revealed some interesting features. According to carbonyl plane rule[10] a downfield shift of chromene proton B and an upfield shift of chromene proton A are expected for linear isomers (1a-c), while in the case of angular isomers (2a-c) both the chromene protons (A

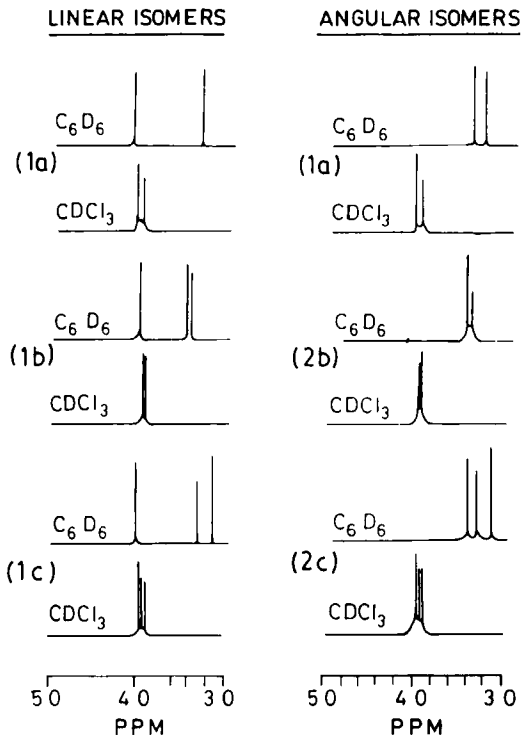

FIG. 2. Chemical Shifts of the Methoxyl Protons in $CDCl_3$ and C_6D_6 of Chromenoflavones.

and B) are expected to show an upfield shift. Suresh *et al.*[11] have reported similar effects in dihydropyranoisoflavones. However, in the present study it was observed that irrespective of the position of the chromene ring in chromenoflavones, B protons always showed downfield shifts of small magnitude (-0.02 to -0.08) while marked upfield shifts (+ 0.27 to +0.38) were observed for A protons.

Thus carbonyl functionality does not seem to influence shifts of chromene protons. Other compounds *viz.* racemosin (3), evodionol (4a) and isoevodionol (4b) having different disposition of carbonyl groups also showed marked upfield shifts in the range of +0.3 to +0.5 for A protons. However, shifts of smaller magnitude (-0.03 to +0.17) were observed for B protons. The marked downfield shift (-0.35) in case of compound 4b for B proton was due to the presence of free hydroxyl group at position 5. These differences in the shifts of A and B protons of the chromene ring may be due to the diffused solute solvent interaction arising from the steric effect of gem dimethyl groups. The gem dimethyl group of the linear isomers (1a-c, 3 and 4a) showed upfield shifts of higher magnitude (+0.20 to +0.40) as compared to the corresponding shifts ($\approx$+0.14) observed for the angular isomers (2a-c, 4b) (Table 1).

The H-3 proton of 4'-monomethoxylated B ring chromenoflavones (1a, 2a) exhibited insignificant downfield shift ($\approx$ -0.01), which increased marginally (-0.09) for 3',4' dimethoxylated compounds (1b, 2b) but significantly (-0.26) in case of 2', 4'dimethoxylated B ring chromenoflavones (1c, 2c). Thus the magnitude of the down shifts of the H-3 protons were found to be dependent on the proximty of the methoxyl group of the B ring of chromenoflavones. The A ring aromatic protons (H-6 or H-8) of chromenoflavones

TABLE 1
Chemical shifts of chromene ring protons (gem dimethyl, A and B) in $CDCl_3$ and C_6D_6.

COMPOUND	PROTONS		
	gem dimethyl	A	B
LINEAR ISOMERS			
1a	1.47,s 1.27,s (+0.20)	5.69,d,10 5.31,d,10 (0.38)	6.74,d,10 6.76,d,10 (-0.02)
1b	1.47,s 1.27,s (+0.20)	5.69,d,10 5.32,d,10 (+0.37)	6.74,d,10 6.77,d,10 (-0.03)
1c	1.46,s 1.26,s (+0.20)	5.67,d,10 5.31,d,10 (+0.36)	6.74,d,10 6.77,d,10 (-0.03)
3	1.52,s 1.22,s (+0.30)	5.74,d,10, 5.25,d,10 (+0.49)	6.58,d,10 6.41,d,10 (+0.17)
4a	1.44,s 1.20,s (+0.24)	5.60,d,10 5.20,d,10 (+0.40)	6.49,d,10 6.34,d,10 (+0.15)
ANGULAR ISOMERS			
2a	1.49,s 1.34,s (+0.15)	5.60,d,10 5.31,d,10 (+0.29)	6.83,d,10 6.82,d,10 (-0.01)
2b	1.50,s 1.34,s (+0.16)	5.60,d,10 5.30,d,10 (+0.30)	6.81,d,10 6.84,d,10 (-0.03)
2c	1.48,s 1.34,s (+0.14)	5.56,d,10 5.29,d,10 (+0.27)	6.79,d,10 6.87,d,10 (-0.08)
4b	1.44,s 1.31,s (+0.13)	5.45,d,10 5.12,d,10 (+0.33)	6.65,d,10 7.00,d,10 (-0.35)

1. δ Values in ppm relative to TMS, J values in Hz, s = singlet, d = doublet.
2. Normal values are obtained with $CDCl_3$ as solvent, while the underlined values are obtained with C_6D_6 as solvent.
3. Values in the parenthesis indicate Benzene Induced Shifts (BIS) [$\Delta = \delta CDCl_3 - \delta C_6D_6$].

showed small upfield shifts (+0.02 to +0.10) except in case of compound 4c where a slight downfield shift (-0.03) was observed. However, Vyas *et al.*[12], during their study on polymethoxylated flavones have differentiated H-3 protons (which showed small downfield shifts between -0.01 to -0.15) from aromatic protons (H-8) where marked upfield shifts (+0.30 to +0.50) were observed. Thus a clear distinction between H-3 and A ring aromatic protons as observed by Vyas *et al.*is not possible in the present study. The B ring aromatic protons showed upfield shifts of varying magnitudes which were not of much diagnostic value (Table 2).

Thus,it can be concluded that BIS study is a simple complementary technique which provides useful information for structural elucidation of chromenoflavones. This technique is particularly useful for natural products where characterization by chemical methods becomes difficult due to their limited availability.

EXPERIMENTAL

The physical and the spectral data of the compounds (1a,c; 2a,b; 3a,b; 4) were in perfect agreement with those reported in the literature [3,6,13,14]. Compounds (1b and 2c) were synthesized and their structures were established by physical and spectral analyses (mp, microanalysis, ^{1}H NMR, UV, IR, MS) [15].

Table 2
^{1}H NMR data of chromenoflavones (1a-c, 2a-c).

PROTONS	COMPOUNDS					
	1a	1b	1c	2a	2b	2c
H-3,s	6.52 6.54 (-0.02)	6.53 6.62 (-0.09)	6.85 7.11 (-0.26)	6.54 6.55 (-0.01)	6.55 6.63 (-0.08)	6.85 7.11 (-0.26)
H-6,s	-	-	-	6.31 6.21 (+0.10)	6.32 6.22 (+0.10)	6.29 6.21 (+0.08)
H-8,s	6.67 6.64 (+0.03)	6.69 6.67 (+0.02)	6.63 6.66 (-0.03)	-	-	-
2'	7.78,d,8 7.46,d,8 (+0.32)	7.33,d,2 7.11,d,2 (+0.22)	-	7.79,d,8 7.47,d,8 (+0.32)	7.32,d,2 7.11,d,2 (+0.21)	-
6'		7.46,dd,8,2 7.23,dd,8,2 (+0.23)	7.76,d,8 7.65,d,8 (+0.11)		7.47,dd,8,2 7.24,dd,8,2 (+0.23)	7.76,d,8 7.65,d,8 (+0.11)
3'	6.99,d,8 6.65,d,8 (+0.34)	-	6.54,d,2 6.26,d,2 (+0.28)	6.99,d,8 6.66,d,8 (+0.33)	-	6.55,d,2 6.28,d,2 (+0.27)
5'		6.96,d,8 6.51,d,8 (+0.45)	6.60,dd,8,2 6.34,dd,8,2 (+0.26)		6.97,d,8 6.52,d,8 (+0.45)	6.61,dd,8,2 6.34,dd,8,2 (+0.27)
C-5 methoxyl	3.92 3.98 (-0.06)	3.93 3.99 (-0.06)	3.93 3.98 (-0.05)	3.93 3.42 (+0.51)	3.94 3.39 (+0.55)	3.93 3.42 (+0.51)

1. δ Values in ppm relative to TMS, J values in Hz, s = singlet, d = doublet, dd =double doublet.
2. Normal values are obtained with $CDCl_3$ as solvent, while underlined values are obtained with C_6D_6 as solvent.
3. Values in the parenthesis indicate Benzene Induced Shifts (BIS) [$\Delta = \delta CDCl_3 - \delta C_6D_6$].

The ^1H NMR spectra were recorded on a Bruker AM-500 MHz FT-NMR spectrometer at 500.13 MHz under following conditions: mode FT; internal lock, from $CDCl_3$ or C_6D_6; the residual proton signal of $CDCl_3$ or C_6D_6 were used as secondary reference for chemical shift (7.24 or 7.16) from TMS respectively; spectra were recorded in a 5 mm o.d. tube; pulse width, 9.5 μs (flip angle 90°); aquistion time 0.8192 or 1.6384s; 8K or 16K data points were accumalated for a spectral width of 5000 Hz, corresponding to a digital resolution of 1.22 or 2.44 Hz per point.

The spectra of compounds (3, 4a and 4b) were recorded at ambient temperature. However, owing to the poor solubility of compounds (1a-c, 2a-c) in C_6D_6 their spectra were recorded at 65°C both in $CDCl_3$ and C_6D_6. The concentrations of the compounds (3, 4a and 4b) were 10mg/0.3ml, while for compounds (1a-c, 2a-c) were 2mg/0.3ml. Accuracies of chemical shifts are within ± 0.02 ppm.

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