

The Carbon-13 Nuclear Magnetic Resonance Spectra of Isoflavones

By **Andrew Pelter** and **Robert S. Ward,*** Department of Chemistry, University College of Swansea, Singleton Park, Swansea SA2 8PP
Robert J. Bass, Chemical Research Department, Pfizer Ltd., Sandwich, Kent CT13 9NJ

The ^{13}C n.m.r. spectra of a series of isoflavones and related compounds have been determined. Chemical shifts of the ring A carbon atoms are relatively insensitive to changes of substitution in the rest of the molecule but are markedly influenced by the presence of a double bond between C-2 and C-3.

As a continuation of our investigation of the ^{13}C n.m.r. spectra of flavonoids¹ we have studied the spectra of a series of isoflavones [(1)—(10) and (13)—(17)] and related compounds. The spectra were recorded for solutions in $(\text{CD}_3)_2\text{CO}$, CDCl_3 , or $\text{CDCl}_3-(\text{CD}_3)_2\text{SO}$ according to solubility. We have previously shown that only small solvent shifts are normally observed for these solvents.¹ The signals were assigned on the basis of their multiplicities in off-resonance decoupled spectra and by consideration of known substituent effects.^{2,3} In some cases the assignments were also confirmed by specific irradiation of ^1H signals, and by examination of the proton-coupled spectra before and after D_2O exchange.⁴

The signals of the benzopyrone nucleus are relatively insensitive to changes in the substitution of ring B. Thus in the series of isoflavones (1)—(10) which differ only in the substituent attached to ring B, the chemical

shifts of carbon atoms 2—8, 8a, and 4a are remarkably constant, the largest differences being seen at C-3 (directly attached to ring B), the chemical shift of which varies over a range of 3.5 p.p.m. (120.7—124.2 p.p.m.). Not surprisingly, introducing a pyridyl group (11), or a methoxy group (12) at C-3 has a more profound effect, but only on C-2, -3, and -4.

Thus it appears that ring A is effectively insulated from changes in the rest of the molecule. This conclusion is supported by comparing the spectra of the 7-hydroxyisoflavones (14) and (15) with that of the chromone (18). Furthermore, comparing the spectra of the isomeric isoflavones and flavones¹ shows that the ring A carbon atoms are not markedly affected by the position of attachment of ring B to the benzopyrone nucleus. However, comparing the isoflavone (15) with the dihydro-derivative (21) shows that the carbon atoms of ring A are

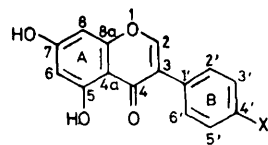
¹ A. Pelter, R. S. Ward, and T. I. Gray *J.C.S. Perkin I*, 1976, 2475.

² G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley-Interscience, New York, 1972.

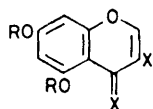
³ J. B. Stothers 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, New York, 1972.

⁴ F. W. Wehrli, *J.C.S. Chem. Comm.*, 1975, 663; see also H. Wagner, V. M. Chari, and J. Sonnerbichler, *Tetrahedron Letters*, 1976, 1799; K. R. Markham and B. Ternai, *Tetrahedron*, 1976, 2607.

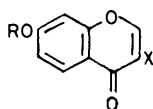
influenced by the presence or absence of a double bond between C-2 and C-3.



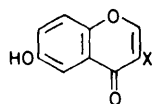
- (1) X = H (6) X = Cl
 (2) X = OH (7) X = Br
 (3) X = OMe (8) X = NO₂
 (4) X = Prⁱ (9) X = MeSO₂
 (5) X = F (10) X = Ph



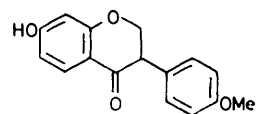
- (11) X = 4-pyridyl, R = H
 (12) X = OMe, R = H
 (13) X = *p*-MeO·C₆H₄, R = Me



- (14) X = *p*-HO·C₆H₄, R = H
 (15) X = *p*-MeO·C₆H₄, R = H
 (16) X = *p*-HO·C₆H₄, R = Me
 (17) X = *p*-MeO·C₆H₄, R = Me
 (18) X = cyclopentyl, R = H



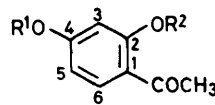
- (19) X = cyclohexyl
 (20) X = cyclopentyl



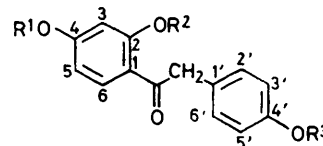
(21)

In order to assess the influence of the benzopyrone ring on the chemical shifts of the various carbon atoms the

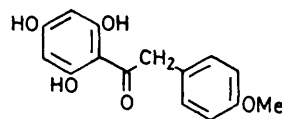
the presence of a free hydroxy group at C-2 in these compounds has a marked effect on the chemical shifts of the ring A carbon atoms, particularly C-1, and the carbonyl group [compare for example (23) and (24)].



- (22) R¹ = R² = H
 (23) R¹ = Me, R² = H
 (24) R¹ = R² = Me



- (25) R¹ = R² = R³ = H
 (26) R¹ = R² = H, R³ = Me
 (27) R¹ = R³ = Me, R² = H
 (28) R¹ = R² = R³ = Me



(29)

Secondly, by comparing the spectra of the isoflavones with those of the deoxybenzoin it can be deduced that the presence of a benzopyrone ring has very little effect on the carbon atoms of ring B, but does affect the chemical shifts of ring A carbon atoms [compare for example (14) and (25)]. It is particularly noteworthy that the spectrum of the deoxybenzoin (26) resembles that of the isoflavanone (21) more closely than that of the isoflavone (15). Thus the mean deviation of the chemical shifts of the ring A carbon atoms in (26) from those in (21) is *ca.* 1.9 p.p.m., while the mean deviation of the shifts of the same carbon atoms in (26) from those in (15) is *ca.* 4.7 p.p.m.

Finally, we note that the substituent effects of the

TABLE I

¹³C Chemical shifts of isoflavones and related compounds

| Compound | Solvent * | C-1' | C-2',-6' | C-3',-5' | C-4' | C-2 | C-3 | C-4 | C-5 | C-6 | C-7 | C-8 | C-8a | C-4a | OMe etc. |
|----------|-----------|--------|----------|----------|--------|----------|--------|--------|----------|----------|----------|---------|--------|--------|--------------------------------|
| (1) | a | 132.17 | 129.95 | 129.07 | 128.90 | 155.11 † | 124.17 | 181.34 | 163.97 † | 100.02 † | 165.10 † | 94.62 † | 159.06 | 106.23 | |
| (2) | a | 122.90 | 130.97 | 115.82 | 158.20 | 154.01 | 123.88 | 181.37 | 183.70 | 99.73 | 164.73 | 94.34 | 158.82 | 106.05 | |
| (3) | a | 123.84 | 131.09 | 114.54 | 160.70 | 164.46 | 124.20 | 181.57 | 183.94 | 99.91 | 165.01 | 94.54 | 159.05 | 106.21 | 55.60 |
| (4) | b | 127.60 | 128.80 | 126.59 | 149.17 | 153.13 | 123.76 | 180.70 | 182.06 | 99.61 | 162.72 | 94.18 | 157.79 | 105.66 | 33.86, 23.80 |
| (5) | a | 128.34 | 131.82 | 116.30 | 168.43 | 155.12 | 123.22 | 181.24 | 183.91 | 100.06 | 165.18 | 94.66 | 159.07 | 108.16 | |
| (6) | a | 130.95 | 131.50 | 129.13 | 134.39 | 155.28 | 122.95 | 181.01 | 183.89 | 100.10 | 165.20 | 94.67 | 158.99 | 106.10 | |
| (7) | a | 131.39 | 131.79 | 132.14 | 122.95 | 155.28 | 122.57 | 180.95 | 183.86 | 100.12 | 165.20 | 94.70 | 158.96 | 106.07 | |
| (8) | c | 138.08 | 129.75 | 123.13 | 147.07 | 155.49 | 120.73 | 179.23 | 182.29 | 99.65 | 164.89 | 94.10 | 157.82 | 104.60 | |
| (9) | a | 131.32 | 131.55 | 122.89 | 150.37 | 155.43 | 122.89 | 181.03 | 183.86 | 100.12 | 165.25 | 94.69 | 158.99 | 106.00 | 37.72 |
| (10) | a | 131.04 | 130.18 | 127.52 | 141.31 | 154.89 | 123.50 | 181.07 | 183.68 | 99.92 | 165.00 | 94.52 | 158.79 | 106.00 | 141.10, 129.57, 127.35, 128.16 |
| (11) | d | 144.65 | 144.95 | 124.57 | | 158.05 | 118.35 | 178.78 | 162.02 | 99.76 | 165.09 | 94.30 | 157.34 | 104.19 | |
| (12) | c | | | | | 140.54 | 142.79 | 176.52 | 162.06 | 98.83 | 164.56 | 93.80 | 157.61 | 104.83 | 57.26 |
| (13) | b | 124.31 | 130.20 | 113.60 | 159.31 | 149.80 | 125.86 | 175.34 | 161.37 | 96.09 | 163.71 | 92.51 | 159.74 | 109.69 | 55.23, 55.63, 56.27 |
| (14) | c | 122.67 | 129.97 | 115.06 | 157.25 | 152.15 | 123.89 | 175.03 | 127.16 | 115.06 | 162.54 | 102.16 | 157.59 | 116.83 | |
| (15) | c | 123.62 | 130.00 | 113.60 | 159.14 | 152.42 | 124.45 | 174.89 | 127.20 | 115.09 | 162.67 | 102.22 | 157.66 | 116.92 | 55.07 |
| (16) | c | 122.61 | 129.98 | 115.24 | 157.58 | 152.27 | 124.32 | 175.04 | 127.08 | 114.33 | 163.72 | 100.32 | 157.49 | 118.01 | 55.81 |
| (17) | b | 124.09 | 129.92 † | 113.79 | 159.36 | 151.82 † | 124.66 | 175.53 | 127.57 † | 114.33 | 163.72 | 99.96 | 157.71 | 118.27 | 55.22, 55.72 |
| (18) | c | | | | | 150.71 | 126.37 | 176.09 | 126.73 | 114.71 | 162.35 | 101.99 | 157.64 | 116.38 | 36.55, 31.03, 24.76 |
| (19) | c | | | | | 151.78 | 127.52 | 176.13 | 107.97 | 149.58 | 119.06 | 122.71 | 154.53 | 124.32 | 34.25, 31.74, 26.50, 25.89 |
| (20) | a | | | | | 152.28 | 127.10 | 177.39 | 109.04 | 151.17 | 120.23 | 123.41 | 155.38 | 125.64 | 38.03, 31.96, 25.77 |
| (21) | a | 129.10 | 130.55 | 114.78 | 159.96 | 72.57 | 51.74 | 190.98 | 130.17 | 111.39 | 165.13 | 103.44 | 164.43 | 115.34 | 55.48 |

* a, (CD₃)₂CO; b, CDCl₂; c, CDCl₃-(CD₃)₂SO(1:1); d, (CD₃)₂SO. † Assignment confirmed by specific irradiation of ¹H signals. ‡ Signals for C-5 and C-7 appear as a doublet and triplet, respectively, in the proton-coupled spectrum, after D₂O exchange.

spectra of a series of acetophenones and deoxybenzoin has also been examined (Table 2). We note first that

groups attached to ring B (Table 3) are in reasonably close accord with those previously reported.²

TABLE 2
¹³C Chemical shifts of acetophenones and deoxybenzoins

| Compd. | Solvent * | | CH ₃ | CO | C-6 | C-5 | C-4 | C-3 | C-2 | C-1 | OMe | | |
|--------|-----------|--------|-----------------|----------|--------|-----------------|--------|--------|--------|--------|--------|--------|--------|
| (22) | a | | 26.17 | 203.56 | 134.19 | 108.68 | 166.05 | 103.51 | 165.45 | 114.26 | | | |
| (23) | b | | 26.10 | 202.26 | 132.13 | 107.41 | 165.92 | 100.77 | 165.06 | 113.80 | 55.46 | | |
| (24) | b | | 31.79 | 197.22 | 132.52 | 105.37 | 164.68 | 98.19 | 161.20 | 121.02 | 55.41 | | |
| | | C-1' | C-2',-6' | C-3',-5' | C-4' | CH ₂ | CO | C-6 | C-5 | C-4 | C-3 | C-2 | C-1 |
| (25) | a | 126.70 | 131.19 | 116.20 | 157.11 | 44.27 | 203.71 | 134.18 | 108.84 | 166.69 | 103.65 | 165.63 | 113.41 |
| (26) | a | 127.83 | 131.20 | 114.70 | 159.52 | 44.17 | 203.48 | 134.12 | 108.81 | 166.67 | 103.68 | 165.52 | 113.45 |
| (27) | b | 126.40 | 130.38 | 114.16 | 158.68 | 43.82 | 202.33 | 132.05 | 107.65 | 166.14 | 101.05 | 165.83 | 113.13 |
| (28) | b | 127.80 | 130.57 | 113.74 | 158.26 | 49.03 | 198.01 | 132.95 | 105.35 | 164.49 | 98.26 | 160.62 | 120.85 |
| (29) | a | 128.78 | 131.52 | 114.30 | 159.25 | 49.16 | 203.97 | 165.40 | 95.86 | 195.50 | 95.86 | 165.40 | 104.98 |

* a, (CD₃)₂CO; b, CDCl₃; c, CDCl₃-(CD₃)₂SO (1 : 1).

TABLE 3

Effects (p.p.m.) of 4'-substituents in ring B of isoflavones

| X | C-4' | ortho | meta | para |
|-------------------|--------|--------|-------|-------|
| MeO | +31.80 | -14.53 | +1.14 | -8.33 |
| HO | +29.30 | -13.25 | +1.02 | -9.27 |
| Pr ⁱ | +20.27 | -2.48 | -1.15 | -4.57 |
| F | +39.53 | -12.77 | +1.87 | -3.83 |
| Cl | +5.49 | +0.06 | +1.52 | -1.22 |
| Br | -5.95 | +3.07 | +1.84 | -0.78 |
| NO ₂ | +18.17 | -5.94 | -0.20 | +5.91 |
| MeSO ₂ | +21.47 | -6.18 | +1.60 | -0.85 |
| Ph | +12.41 | -1.55 | +0.23 | -1.13 |

EXPERIMENTAL

The ¹³C spectra were determined using a Varian XL-100 instrument fitted with a 620L-100 computer. Chemical shifts are recorded as p.p.m. downfield from internal Me₄Si. The isoflavones were all prepared by the methods recently reported.^{5,6}

[7/1672 Received, 22nd September, 1977]

⁵ R. J. Bass, *J.C.S. Chem. Comm.*, 1976, 78.

⁶ A. Pelter and S. Foot, *Synthesis*, 1976, 326.