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The ^{13}C chemical shifts of 2-aryl and 3-arylbenzofurans are discussed. Pairs of isomers can be differentiated based on the chemical shifts of C-2 in 3-arylbenzofurans and C-3 in 2-arylbenzofurans. A signal near 100 ppm (101 ± 1.7) indicates a 2-arylbenzofuran and a signal near (141 ± 1.3) indicates a 3-arylbenzofuran.

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Introduction.

Benzofurans, particularly aryl-substituted benzofurans, have recently found widespread utility as medicinal agents. The antianginal/antiarrhythmic agent cordarone bears this heterocyclic nucleus and benzofurans are also described as antihypertensive, antiinflammatory and antihyperlipidemia agents (1-6).

In some of our benzofuran synthetic work we frequently dealt with 2- and 3-arylbenzofurans. In addition to being intermediates to 2-acyl-3-arylbenzofurans, 3-arylbenzofurans rearrange under thermal and acid catalysis with varying ease to the 2-aryl isomers (7,8,9). For example, a principle synthetic route to 2-(and 3)-arylbenzofurans utilizes ω-phenoxy acetophenone **3** as starting material (8); polyphosphoric acid at 80° causes a cyclodehydration reaction to give only 3-phenylbenzofuran **1**. Raising the cyclodehydration reaction temperature to 132° gives only 2-phenyl benzofuran **2**; intermediate temperatures give mixtures of the two isomers. Thus, it is of critical importance to differentiate between the two isomers. Physical properties have been used to characterize and separate pairs of isomers (10) but the correlation is tenuous. ^{1}H nmr is of some use in making structural assignments (chemical shift of 3-proton in 2-arylbenzofurans) but often assignment is left in doubt due to overlapping chemical shifts of the 2- and 3-protons with the other aromatic protons. Thus ^{1}H nmr cannot be relied upon for making a differentiation. We have found however, that such differentiation can be made quickly and unequivocally by use of ^{13}C nmr.

Results and Discussion.

Proton off-resonance decoupling experiments were used to determine degree of substitution of carbon atoms and thus were of critical importance in making peak assignments. Chemical shifts of the carbon atoms of the benzofuran nucleus were also consistent with chemical shifts of 2- and 3-methyl benzofurans reported by Platzer and coworkers (11) (see Table). Peak intensities were observed to vary directly to the number of directly-bonded hydrogen atoms, a relationship which frequently but not invariably holds (12,13). Assignments, however, were made independent of peak intensities. The methoxy and methyl resonances were assigned by their characteristic chemical shifts in comparison with literature values (14). Substituent chemical shift additivity principles (15,16) for chloro, methoxy, and methyl substituents on a benzene ring were used to assist in assignments. From the chemical shift table, one notices that the chemical shift of C-3 in 2-arylbenzofurans always appears around 100 ppm (101 ± 1.7) and that of C-2 in 3-arylbenzofurans around 140 ppm (141 ± 1.3). These peaks are thus diagnostic of the two types of substitution; a signal near 100 ppm indicates a 2-arylbenzofuran, a signal near 140 ppm indicates a 3-arylbenzofuran. In the case of a mixture of the two, such as might arise from an incomplete rearrangement reaction, both signals will appear and give an approximate percentage of the mixture. Both signals are very easy to identify since their chemical shifts are away from the aromatic region (120-130 ppm). The chemical shifts of these peaks appear, from this study, to be very insensitive to the effects of substitution on either of the aryl moieties of 2- and 3-arylbenzofurans.

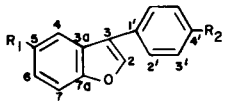
On the basis of some preliminary work we expect this correlation to be generally applicable to pairs of 2- and 3-arylbenzothiophenes and indoles.

EXPERIMENTAL

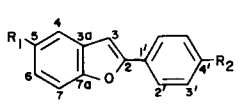
^{13}C nmr spectra were recorded at 20 MHz using a Varian CFT-20 Fourier-Transform Spectrometer. All spectra were run in deuteriochloroform solution with the exception of compound **2d** which was run in DMSO-d_6 solution. Saturated solutions were used with tetramethyl silane internal standard. Solvent effects were negligible. A good signal to noise ratio was obtained with scans ranging from 2,600 to 72,000 depending on the concen-

Table

^{13}C Chemical Shifts of 2- and 3-Arylbenzofurans (c)



1a, $R_1 = R_2 = H$
1b, $R_1 = H$, $R_2 = OCH_3$
1c, $R_1 = Cl$, $R_2 = H$



2a, $R_1 = R_2 = H$
2b, $R_1 = H$, $R_2 = OCH_3$
2c, $R_1 = Cl$, $R_2 = H$
2d, $R_1 = H$, $R_2 = Cl$
2e, $R_1 = H$, $R_2 = CH_3$

Carbon	1a	2a	1b	2b	1c	2c	2d	2e
C-2	140.18 (m)	155.99 (w) (a)	140.68 (m)	156.14 (w) (a)	142.44 (m)	157.47 (w)	154.34 (w) (a)	156.26 (w) (a)
C-3	121.33 (w)	101.31 (m)	122.02 (w)	99.71 (m)	121.98 (w)	100.79 (m)	102.67 (m)	100.59 (m)
C-4	119.34 (m)	120.90 (m)	120.41 (m)	120.61 (m)	120.03 (m)	120.43 (m)	121.24 (m)	120.74 (m)
C-5	121.91 (m)	122.94 (m)	122.90 (m)	122.86 (m)	128.71 (w)	128.56 (w)	123.28 (m)	122.84 (m)
C-6	123.47 (m)	124.26 (m)	124.46 (m)	123.78 (m)	124.71 (m)	124.41 (m)	124.80 (m)	123.98 (m)
C-7	110.69 (m)	111.17 (m)	111.76 (m)	111.00 (m)	112.60 (m)	112.10 (m)	111.09 (m)	111.08 (m)
C-3a	125.54 (w)	129.29 (w) (b)	126.89 (w)	129.58 (w)	127.78 (w)	130.62 (w) (a)	128.72 (w) (b)	129.68 (w)
C-7a	154.91 (w)	154.98 (w) (a)	155.94 (w)	154.79 (w) (a)	154.10 (w)	153.31 (w)	154.05 (w) (a)	154.88 (w) (a)
C-1′	131.14 (w)	130.56 (w) (b)	124.61 (w)	123.42 (w)	131.25 (w)	130.03 (w) (a)	128.91 (w) (b)	127.85 (w)
C-2′	126.50 (s)	124.97 (s)	128.75 (s)	126.46 (s)	127.34 (s)	125.09 (s)	126.32 (s)	124.93 (s)
C-3′	127.87 (s)	128.75 (s)	114.54 (s)	114.32 (s)	128.96 (s)	128.86 (s)	129.04 (s)	129.44 (s)
C-4′	126.36 (m)	128.50 (m)	159.31 (w)	160.11 (w)	127.64 (m)	128.98 (m)	133.32 (w)	138.47 (w)
$-OCH_3$	---	---	55.22 (m)	55.32 (m)	---	---	---	---
$-CH_3$	---	---	---	---	---	---	---	21.26 (m)

(a) Assignments may be reversed. (b) Assignments may be reversed. (c) Abbreviations (peak heights): s = strong; m = medium; w = weak.

tration of the solution. A flip angle of 32° or less was applied. The precision is 0.05 ppm (resolution 0.4 Hz). Decoupler frequency off-set was 10 ppm upfield from the center of ^{1}H nmr spectrum.

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