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LONG RANGE COUPLINGS IN BENZOFURANS

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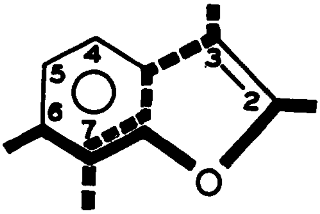
The proton nmr spectra of several benzofurans have been examined. Interring 2,6- and 2,4-couplings were found in addition to the previously reported 3,7- couplings (1-9). Evidence was also found for an interaction between H_3 and H_4 (9). The 2,6-couplings, analogous to those found in indole (10) and benzothiophenes (10-16), follow a straight zig-zag path (10), as do the 3,7-couplings (2). The 2,4-couplings, which do not conform to such a pattern, are much smaller. Notably, no evidence was found for any interaction between H_2 and H_5, which also conforms to a straight zig-zag pattern.



The interactions of H_2 with both H_4 and H_6 are illustrated clearly in the spectrum of 5,7-dichlorobenzofuran, where H_2 is coupled with all three protons in this molecule. This requires both interring 2,4- and 2,6-couplings in addition to the 2,3-coupling. In still another illustration, the H_4 and H_6 resonances in the 5-bromobenzofuran spectrum distinctly show the 2,4- and 2,6-couplings, respectively. These splittings are clearly absent in the spectrum of methyl 5-bromo-2-benzofurancarboxylate, where C_2 bears a substituent. No 2,5 or 2,7 interactions could be observed. Since the resonance shapes of H_2 in the spectra of 5-chloro-, 7-chloro-, and 5,7-dichlorobenzofurans are the same, then H_5 and H_7 must not interact with H_2. An analogous identity of H_2 line shapes are also observed in the spectra of 5- and 7-methoxybenzofurans. Deuterium labeling in 5-chlorobenzofuran-2-D further supports the absence of 2,7-couplings. The line shapes of the H_7 resonance in both the labeled and unlabeled spectra are essentially identical.

The 3,4-coupling was not seen directly, but its effect could be seen in the spectrum of 5,7-dichlorobenzofuran. Frequency sweep decoupling of H_3 sharpened the two broad lines of the H_4 resonance into two distinct doublets, which demonstrates the 2,4-coupling. A plotted spectrum, using the iterated values with $J_{3,4}$ set at -0.12 Hz, the value reported earlier (9), was identical with the observed single resonance spectrum. Using the iterated values for 7-methoxybenzofuran and setting $J_{3,4} = -0.12$ Hz caused no observable change in the line shapes of the plotted spectrum. In all other computations $J_{3,4}$ was set at zero.

In all of these benzofurans H_3 couples with H_2 and H_7 where possible. Any other interactions of H_3 except the 3,4-coupling were too small to be seen. The identical H_3 doublets in 7-chloro- and 5,7-dichlorobenzofurans rule out any coupling between H_3 and H_5.

These interring couplings are uniform for all of the benzofurans we have examined. Additional illustrations are shown in which these principles apply; *vis.*, 5-nitrobenzofuran and 5- and 6-fluorobenzofuran.

In the spectrum of 7-methoxybenzofuran a coupling was observed between the methoxyl protons and H_6 ($J_{CH_3O,6}$ 0.25 Hz). The 5-methoxybenzofuran spectrum showed no such coupling. Apparently the steric restrictions of an adjacent group is required, as illustrated by similar couplings in the spectra of 3- and 6-methoxysalicylaldehydes and 3- and 6-methoxy-2-hydroxyacetophenones, where the *ortho* $J_{CH_3O,H}$ = 0.25 Hz (17). Where the adjacent positions are not occupied, these couplings are absent, as in the spectra of 4- and 5-methoxysalicyaldehydes and 4- and 5-methoxy-2-hydroxyacetophenones (17).

The preparation and characterization of the compounds reported here are discussed elsewhere (18,19).

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Chemical Shifts (ppm) and Coupling Constants (Hz)[a]

Benzofuran	Solvent[b]	δ_2	δ_3	δ_4	δ_5	δ_6	δ_7	$J_{2,3}$	$J_{2,4}$	$J_{2,6}$	$J_{3,7}$	$J_{4,5}$	$J_{4,6}$	$J_{4,7}$	$J_{5,6}$	$J_{5,7}$	$J_{6,7}$
5-bromo	C_6D_6	7.10	6.18	7.42	--	7.13	7.00	2.19	0.28	0.42	0.94	--	2.08	0.57	--	--	8.8
5-bromo-2-carbomethoxy	C_6D_6	c	6.98	7.31	--	7.11	6.88	--	--	--	0.88	--	2.05	0.60	--	--	8.8
5-chloro	$CDCl_3$	7.53	6.60	7.48	--	7.18	7.33	2.30	0.08	0.38	0.97	--	2.22	0.58	--	--	8.8
5-chloro-2-D[d]	$CDCl_3$	--	6.18	7.26	--	7.00	7.06	--	--	--	0.6[e]	--	2.11	0.61	--	--	8.7
7-chloro	$CDCl_3/C_6D_6$	7.50	6.63	7.36	7.04	7.21	--	2.19	0.19	0.44	--	7.87	1.07	--	7.82	--	--
5,7-dichloro	$CDCl_3$	7.56	6.60	7.31	--	7.18	--	2.20	0.26	0.51	--	--	1.94	--	--	--	--
5-methoxy	$CDCl_3$	7.53	6.63	7.01	--	6.87	7.36	2.18	0.17	0.48	0.96	--	2.63	0.54	--	--	9.0
7-methoxy[f]	C_6D_6	7.36	6.50	7.10	7.04	6.57	--	2.17	0.16	0.37	--	7.85	0.65	--	8.33	--	--
5-nitro	$CDCl_3$	7.76	6.90	8.49	--	8.19	7.54	2.36	0.35	0.38	0.98	--	2.39	0.55	--	--	9.0
5-fluoro[g]	CD_3COCD_3	7.86	6.87	7.36	--	7.08	7.51	2.24	0.31	0.62	0.99	8.89	2.71	0.51	9.47	4.15	8.9
6-fluoro[g]	$CDCl_3$	7.52	6.64	7.42	6.96	--	7.19	2.25	0.23	0.27	0.95	8.60	5.44	0.40	9.50	2.30	9.0

(a) Varian A60 and HA 60 IL nmr spectrometers were used. Experimental line positions were obtained by interpolation with a precision of ± 0.05 Hz. These data are the result of iterative computations done with a modified version of LACOON II (Ref. 20), which takes into account magnetic equivalence factoring for groups of nuclei with spins $I \geq 1/2$. In all of these solutions $J_{3,4}$ was set at zero. Computed spectra plotted from the above data using Lorenz line shape gave the best fit to the experimental spectra. RMS errors were < 0.1 in all cases. Typical maximum errors in any line fit was 0.15 Hz.

(b) Different solvents were tried until sufficient clarity for complete assignment of the spectra was obtained. No effort was made to find a uniform solvent system. Concentrations varied. An internal reference of tetramethylsilane was used.

(c) $\delta_{CH_3} = 3.49$ ppm.

(d) Double resonance spectrum where H_3 was irradiated. The deuterium quadrupole relaxation broadened H_3.

(e) Measured directly from the spectrum.

(f) Double resonance spectrum where CH_3O ($\delta_{CH_3O} = 3.62$ ppm) was irradiated. Using these iterated values with $J_{CH_3O,6} = 0.25$ Hz gave a computed spectrum which was identical with the observed single resonance spectrum. Setting $J_{3,4} = -0.12$ Hz did not change the line shapes.

(g) $J_{H,F}$ values are included here.