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Reference Data

^{13}C NMR Study of Dihydropyrimidinedione and Dihydropyrimidine-2-thione Derivatives

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The ^{13}C NMR spectral data for 18 dihydropyrimidinediones and their 2-thio analogues are presented. The influence of substituents on the shielding of neighbouring atoms was analysed and the resonances were unambiguously assigned. ^{13}C NMR spectroscopy was shown to be useful for structural determination of dihydropyrimidinediones and thioanalogues and allowed the facile distinction of otherwise similar compounds from the two classes. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

N-Carbamoyl- and *N*-thiocarbamoyl-*N*-(3,4-substituted phenyl)-*β*-alanines have been obtained from the title compounds and show a growth-stimulating effect on wheat sprouts.[1] The present study, based on compounds **1**–**18** (Scheme 1), was undertaken in order to investigate the applicability of ^{13}C NMR spectroscopy for structural determination of dihydropyrimidinediones and their sulphur analogues. The effect of substituents on chemical shifts was also investigated.

EXPERIMENTAL

The ^{13}C NMR spectra were obtained at 75.43 MHz on a Varian XL-300 spectrometer operating in the Fourier transform mode. Spectra were recorded for solutions of 20 mg of each compound in 0.7 ml of DMSO-d_6, which was also used as internal standard. Chemical shifts are reported as δ (ppm) downfield from TMS. Samples were spun in 5 mm o.d. tubes at ambient temperature. The following conditions were used: spectral width, 16.5 kHz; acquisition time, 1 s; pulse width, 29°; number of transients, 9500; number of data points, 64K; and pulse repetition time, 1 s. Continuous decoupling conditions were low power 5 DB, Waltz-16 modulated.

The synthesis of compounds **1**–**18** has been described previously.[1]

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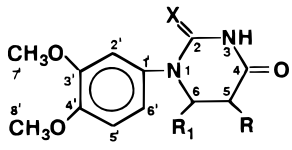
RESULTS AND DISCUSSION

The ^{13}C spectral data for compounds **1**–**18** are given in Tables 1–3.

Tentative assignment of ^{13}C resonances are based on the additivity effects induced by the substituents.[2] The final data were derived from the typical intensities of some signals and compared with suitable literature data.[2–9]

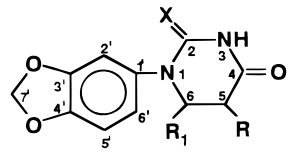
The identification of the carbon resonances of the benzene ring in **1**–**18** was complicated because of a considerable deviation from additivity caused by the *ortho* substitution[2,10] and an unknown shielding effect by the third substituent, the heterocyclic ring. Therefore, 1-phenyldihydro-4(1*H*,3*H*)pyrimidine-2-thione[11] was synthesized to determine the shielding influence of the heterocyclic ring on the aromatic carbons. Averaged chemical shift increments induced by the heterocyclic ring of both oxygen and sulphur analogues are given in Table 4. These data indicate that the aromatic carbons of dihydropyrimidinedione derivatives are more shielded than those of the sulphur analogues.

The chemical shifts of C-2 and C-4 of the heterocyclic ring are characteristic[2,10] due to their nature as carbonyl or thiocarbonyl carbons and the contributions of the adjacent atoms. The C-2 atoms in the dihydropyrimidinediones resonate at higher field than C-4, whereas in the sulphur analogues C-2 is more deshielded than C-4. The downfield shift of the C-6 resonances in the sulphur analogues indicated an enhanced *β*-deshielding effect of the thiocarbonyl group



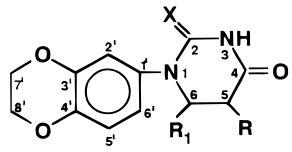
1-6

1 R = R_1 = H, X = O
2 R = CH_3, R_1 = H, X = O
3 R = H, R_1 = CH_3, X = O
4 R = R_1 = H, X = S
5 R = CH_3, R_1 = H, X=S
6 R = H, R_1 = CH_3, X = S



7-12

7 R = R_1 = H, X = O
8 R = CH_3, R_1 = H, X = O
9 R = H, R_1 = CH_3, X = O
10 R = R_1 = H, X = S
11 R = CH_3, R_1 = H, X=S
12 R = H, R_1 = CH_3, X = S



13-18

13 R = R_1 = H, X = O
14 R = CH_3, R_1 = H, X = O
15 R = H, R_1 = CH_3, X = O
16 R = R_1 = H, X = S
17 R = CH_3, R_1 = H, X=S
18 R = H, R_1 = CH_3, X = S

Scheme 1.

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Reference Data

Table 1. ^{13}C NMR chemical shifts (ppm) of compounds 1–6

Carbon	1	2	3	4	5	6
C-2	152.48	152.48	151.80	179.59	179.54	178.61
C-4	170.88	173.51	170.32	167.20	170.17	166.79
C-5	31.30	35.13	38.03	30.60	34.39	37.17
C-6	45.26	51.52	51.73	49.26	55.08	55.58
C-1′	135.33	135.26	133.68	138.28	138.19	136.80
C-2′	110.61	110.51	111.70	111.31	111.23	111.62
C-3′	148.74	148.75	148.91	148.95	148.37	149.03
C-4′	147.29	147.26	147.82	148.09	148.08	148.28
C-5′	111.72	111.74	112.20	111.73	111.75	112.21
C-6′	118.00	117.92	120.17	119.16	119.12	120.37
C-7′, C-8′	55.79	55.81	55.83	55.80	55.81	55.77
	55.88	55.89		55.85	55.85	55.90
Other						
(CH_3)		12.43	18.70		12.15	17.95

Table 2. ^{13}C NMR chemical shifts (ppm) of compounds 7–12

Carbon	7	8	9	10	11	12
C-2	152.51	152.15	151.86	179.78	179.41	178.84
C-4	170.84	173.14	170.27	167.19	169.79	166.78
C-5	31.26	34.89	38.03	30.55	34.23	37.16
C-6	45.29	51.32	51.78	49.20	54.88	55.54
C-1′	136.28	135.88	134.65	139.24	138.82	137.77
C-2′	107.75	107.35	108.13	108.36	108.04	108.31
C-3′	147.30	147.01	147.48	147.49	147.23	147.57
C-4′	145.54	145.22	146.65	146.49	146.13	146.69
C-5′	108.03	107.35	109.37	108.59	108.04	109.51
C-6′	119.15	118.73	121.37	120.52	120.15	121.67
C-7′	101.58	101.29	101.68	101.79	101.55	101.83
Other						
(CH_3)		12.24	18.68		12.03	17.96

Table 3. ^{13}C NMR chemical shifts (ppm) of compounds 13–18

Carbon	13	14	15	16	17	18
C-2	152.42	152.40	151.75	179.59	179.50	178.62
C-4	170.82	173.49	170.29	167.19	170.16	166.78
C-5	31.24	35.09	37.98	30.55	34.36	37.13
C-6	45.08	51.34	51.70	49.16	54.98	55.57
C-1′	135.51	135.44	133.96	138.51	138.42	137.10
C-2′	114.98	114.91	116.89	116.11	116.06	117.09
C-3′	143.13	143.13	143.28	143.38	143.39	143.45
C-4′	141.81	141.78	142.43	142.80	142.78	143.02
C-5′	116.91	116.91	117.08	117.30	117.31	117.29
C-6′	118.84	118.74	120.84	120.09	120.02	121.19
C-7′, C-8′	64.21	64.22	64.24	64.24	64.24	64.24
	64.28	64.28				
Other						
(CH_3)		12.46	18.69		12.18	17.92

Reference Data

Table 4. ^{13}C NMR chemical shift increments ($\Delta\ \delta$, ppm) induced by the heterocyclic ring on the aromatic carbons

Compound	C-*i*	C-*o*	C-*m*	C-*p*
1-Phenyldihydro-4(1*H*,3*H*)-pyrimidine-2-thione	16.59	−1.52	0.53	−1.09
Oxygen analogues of studied compounds (**1**–**3**, **7**–**9**, **13**–**15**)	14.44	−1.93	−0.47	−2.17
Sulphur analogues of studied compounds (**4**–**6**, **10**–**12**, **16**–**18**)	17.37	−0.94	−0.26	−1.30

compared with the carbonyl group while the C-4 resonances show opposite trends. The presence of a CH_3 group attached to C-5 induces a β-deshielding influence on C-4 of *ca.* 3 ppm for both types of compounds. The attachment of a CH_3 group to C-6 causes some changes of the shielding effects of the heterocyclic ring on the benzene carbons in the dihydropyrimidinediones and also in the sulphur analogues.

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