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The ¹⁷O nmr chemical shifts of 20 acetyl and formylthiophenes, furans, and pyrroles are reported. The chemical shifts qualitatively correlate with the electronic character of the heterocyclic rings. The effect of steric factors are noted for the ¹⁷O chemical shifts of alkyl substituted acetylthiophenes and for *N*-methylpyrroles.

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The reactivity and physical properties of the five membered ring 6- π -heterocyclic systems thiophene, furan and pyrrole have intrigued chemists for decades [1]. In particular, the spectroscopy of the substituted heterocycles have received considerable attention [2]. Carbonyl containing derivatives of these ring systems have been examined with the goal of gaining insight into their electronic character, reactivity and conformational preferences [3]. An extensive and incisive review of the factors influencing the conformations of acyl groups in heterocyclic systems has recently appeared [4]. Oxygen-17 nuclear magnetic resonance is rapidly emerging as a powerful probe by which such questions can be explored [5]. Recent work has demonstrated the value of ¹⁷O nmr studies for assessing substituent electronic effects [6]. Even more recently ¹⁷O nmr methodology has been used to answer important conformational analysis questions [7]. The ¹⁷O nmr studies in heterocyclic chemistry have been largely limited to random studies of assorted systems [5] and a few detailed studies including systems such as heteroaromatic *N*-oxides [8], thiohydantoins [9], coumarins [10] and cyclic aromatic ethers [11]. This communication reports a ¹⁷O nmr study of several isomeric acetyl and formylthiophenes, furans and pyrroles. The purpose of this study is to report the ¹⁷O chemical shift characteristics of these important heterocyclic carbonyl compounds, to relate the results to their benzene analogs and to provide a basis for a detailed ¹⁷O nmr spectroscopy study of the electronic and steric effects in these heterocyclic systems.

The ¹⁷O nmr data for the carbonyl substituted five ring heterocycles, determined from 0.5 *M* solutions at natural abundance in dry acetonitrile at 75° are listed in Table 1. The formyl substituted heterocyclics (without additional substitution) exhibit ¹⁷O chemical shifts in the range of 496 to 557 ppm, which should be compared to the ¹⁷O chemical shift of benzaldehyde at 564 ppm [12]. The ¹⁷O chemical shifts of the acetyl analogs range from 490 ppm to 546 ppm which should be compared to the ¹⁷O chemical shift value of 552 ppm for acetophenone [13].

The data for the 2-substituted compounds show a num-

ber of interesting trends. The order of the carbonyl chemical shifts is thiophenes \geq furans \gg pyrroles for both the formyl and acetyl compounds. The chemical shifts for thiophenes **1** and **3** are only 2-3 ppm greater than the corresponding furans **10** and **12**; however, both systems exhibit values 35-40 ppm greater than the analogous pyrroles **16** and **18**. The signal for the *N*-methylpyrrole **19** is deshielded by about 15 ppm compared to its parent molecule **18**. This result is consistent with torsion angle rotation expected as a result of the proximate *N*-methyl group [7]. The general trend of carbonyl chemical shifts for the 2-substituted systems, thiophene \geq furan \gg pyrrole, is not in the order of aromaticity of these ring systems; this is in contrast to many other physical properties which parallel the order of aromaticity [2a]. The considerable upfield shift of the signal for the pyrrole compounds suggests significant electron donation from the heterocyclic nitrogen compared with donation from sulfur or oxygen and/or significant hydrogen bonding. This large upfield shift is analogous to that noted for the ¹⁷O chemical shift of *p*-aminoacetophenone [6b,6c]. Considerable evidence has appeared that suggests that some intramolecular hydrogen bonding occurs for **16** and **18** which could also contribute to the upfield position of the signals in these compounds [14]. A contribution to the observed chemical shift for **16** and **18** from intermolecular hydrogen bonding would be expected at the concentration used to obtain the ¹⁷O nmr data. Nevertheless, the chemical shift for *N*-methyl-2-pyrrolecarboxaldehyde **17** differs only 6 ppm from **16**, suggesting hydrogen bonding effects are relatively small. Despite the limited number of additionally substituted compounds included here, it is clear that substituent electronic effects are important for the thiophene and furan systems; compare **2**, **5**, **6** and **10**, **11**. For example, the nitro induced deshielding shift for the thiophene system is 29 ppm and the analogous result for the furan system is 38 ppm; this compares to the 17 ppm found for the analogous benzene system [6c]. Steric effects are exhibited in the thiophene system; compare **3** and **4** and **8** and **9**. The 8 ppm downfield shift of **4** relative to **3** is consistent in direc-

Table 1

¹⁷O NMR Chemical Shift Data for Acetyl and Formylthiophenes, Furans and Pyrroles

Compound No.	X	R ₁	R ₂	R ₃	δ (C=O)	δ (-O-)	Compound No.	X	R ₁	R ₂	R ₃	δ (C=O)	δ (-O-)
1	S	H	H	H	538.1		7	S	H	H	H	552.8	
2 [a]	S	H	H	NO ₂	567.0		8	S	CH ₃	H	H	539.1	
3	S	CH ₃	H	H	528.1		9	S	CH ₃	CH ₃	CH ₃	546.1	
4	S	CH ₃	CH ₃	H	535.8								
5	S	CH ₃	H	CH ₃	523.3								
6	S	CH ₃	H	Cl	531.0								
10	O	H	H	H	536.4	238.1	14	O	H	H	H	557.3	246.1
11	O	H	H	NO ₂	574.0	225.1	15	O	CH ₃	H	H	545.0	244.0
12	O	CH ₃	H	H	525.6	241.6							
13	O	CH ₃	H	CH ₃	516.3	249.6							
16	NH	H	H	H	496.0								
17	NMe	H	H	H	501.8								
18	NH	CH ₃	H	H	490.8								
19	NMe	CH ₃	H	H	505.4		20	NMe	CH ₃	H	H	509.4	

[a] Previously reported in ref [15].

tion with the shift attributed to torsional rotation noted for *o*-methylacetophenone; however, the magnitude of the shift difference is only approximately one-third that noted in benzene systems [13]. This result suggests a smaller torsion angle rotation for the thiophene, a larger carbonyl-ringing bond angle, an attractive van der Waals interaction between the sulfur and carbonyl group or a combination of these effects and merits further investigation.

As is the case for the 2-substituted carbonyl compounds, the 3-substituted thiophenes and furans exhibit comparable chemical shifts and the chemical shift for the one 3-substituted pyrrole **20** studied is considerably upfield of its furan and thiophene counterparts **8** and **15**. These results suggest that the chemical shifts for the carbonyl groups in the 3-acyl compounds are influenced in a generally comparable way to their 2-acyl analogs. However, the chemical shift values for the 3-substituted thiophenes **7** and **8** and the 3-substituted furans **14** and **15** are consistently downfield from the values of their 2-substituted counterparts **1** and **3** by 10-20 ppm. These chemical shift differences are consistent with the well known differences

in electronic density between the 2 and 3 position of these 5 ring heterocyclic systems [2,4]. Slight differences in torsion angles between 2- and 3-substituted compounds may exist which conceivably could contribute a very small amount to the downfield values for the 3-substituted compounds. The chemical shift of *N*-methyl-3-acetylpyrrole **20** is downfield by 4 ppm of the value for *N*-methyl-2-acetylpyrrole **19**. This small difference, compared to the analogous furans and thiophenes, doubtlessly reflects torsion angle rotation [7] for the 2-isomer as a consequence of the *ortho*-like *N*-methyl group and should not be inferred to indicate greater electron density on the 3-carbon of pyrrole. The data for the 3-substituted compounds are limited; however, it seems clear from comparison of the shifts for **8** and **9** that steric factors will influence the shifts for the 3-acyl compounds in an analogous fashion to that noted for the 2-substituted series.

It is clear from this preliminary report that ¹⁷O nmr is a useful methodology to probe electronic, conformational, and steric effects for acyl heterocyclic systems. Studies on other heterocyclic systems are in progress.

EXPERIMENTAL

The ^{13}C spectra were recorded on a JEOL GX-270 or on a Varian VXR-400 spectrometer equipped with a 10 mm broad-band probe. All spectra were acquired at natural abundance at 75° in acetonitrile (Aldrich, anhydrous gold label under nitrogen) containing 1% of 2-butanone as an internal standard. The concentration of the carbonyl compounds employed in these experiments was 0.5 M. The signals were referenced to external deionized water at 75° . The 2-butanone resonance (558 ± 1 ppm) was used as an internal check on the chemical shift measurements for these compounds. The instrumental settings for the GX-270 at 36.5 MHz were spectral width 25 kHz, 2K data points, 90° pulse angle (28 μs pulse width), 250 is acquisition delay, 40 ms acquisition time and 40,000-100,000 scans. The instrumental settings for the VXR-400 at 54.22 MHz were spectral width 35 kHz, 2 K data points, 90° pulse angle (40 μs pulse width), 300 μs acquisition delay, 29 ms acquisition time and ca. 20,000 scans. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying at 25 Hz exponential broadening factor to the FID prior to Fourier transformation. The data point resolution was improved to ± 0.1 ppm on the VXR-400 and ± 0.2 ppm on the GX-270 by zero filling to 8 K data points. The reproducibility of the chemical shift data is estimated to be $\geq \pm 1.0$. All the compounds were obtained from Aldrich, except **5** and **6** which were from Fairfield, **20** and **21** which were from TCI, and **15** which was synthesized by the addition of methyl lithium to 3-furoic acid.

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