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^{17}O NMR SPECTROSCOPY OF LACTONES

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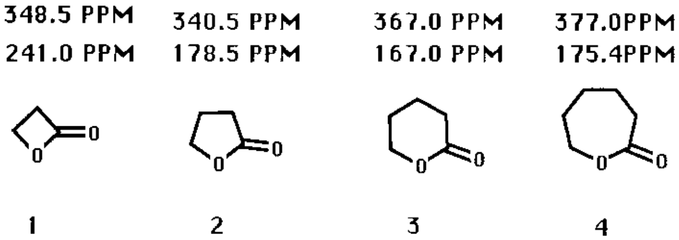
Abstract - Natural abundance ^{17}O nmr spectroscopic data for 30 lactones acquired in acetonitrile at 75°C are reported: relationships between ^{17}O chemical shift and structure are discussed.

The ^{17}O nmr chemical shifts for both types of ester oxygens have been shown to be influenced by substituents attached either to the carbonyl group or to the single bonded oxygen. Both ^{17}O nmr signals of aromatic esters have been shown to be sensitive to electronic effects of substituents.[1-3] Variation of the structure of the group attached to the single bonded oxygen significantly influences the signal for the single bonded oxygen and to a lesser extent that of the carbonyl oxygen.[3-6] Quantitative relationships have been found between ^{17}O nmr chemical shifts and torsion angles for aryl esters.[7] The ^{17}O nmr chemical shifts of a limited number of lactones have been reported in connection with other studies.[8-11] In sterically hindered rigid-planar lactones, ^{17}O chemical shifts were shown to be related to repulsive van der Waals interactions.[11] Recently, we reported the results of an ^{17}O nmr study of a significant number of lactams which provided insights into the influence of structure on the ^{17}O chemical shift of the lactam carbonyl group.[12] This paper reports the ^{17}O chemical shifts of 30 related lactones ranging in size from 4- to 7-membered rings. In this study the influence of structure on the ^{17}O chemical shift of both the carbonyl oxygen and the single bonded oxygen will be assessed.

The ^{17}O nmr data for the lactones determined, at natural abundance, from 0.5 M solutions in dry acetonitrile at 75°C are listed below. The ^{17}O nmr chemical shifts of the carbonyl group range from approximately 325 ppm, for lactones in which the carbonyl group is delocalized by conjugation, to approximately 375 ppm for lactones in which the carbonyl group is somewhat electronically isolated from the single bonded oxygen. In the case of thiolactones the carbonyl oxygen resonance is substantially deshielded compared to oxygen analogs, appearing as far downfield as 494 ppm.

The carbonyl ^{17}O chemical shift values for the unsubstituted lactones **1-4**, presented in Scheme 1, show no general trend with increasing ring size. Similar results are noted for the single bonded oxygens in this series. Comparable results were noted for the same ring size lactams;[12] however, the lactam carbonyl resonances were displaced approximately 40 ppm upfield compared to those of the lactones.

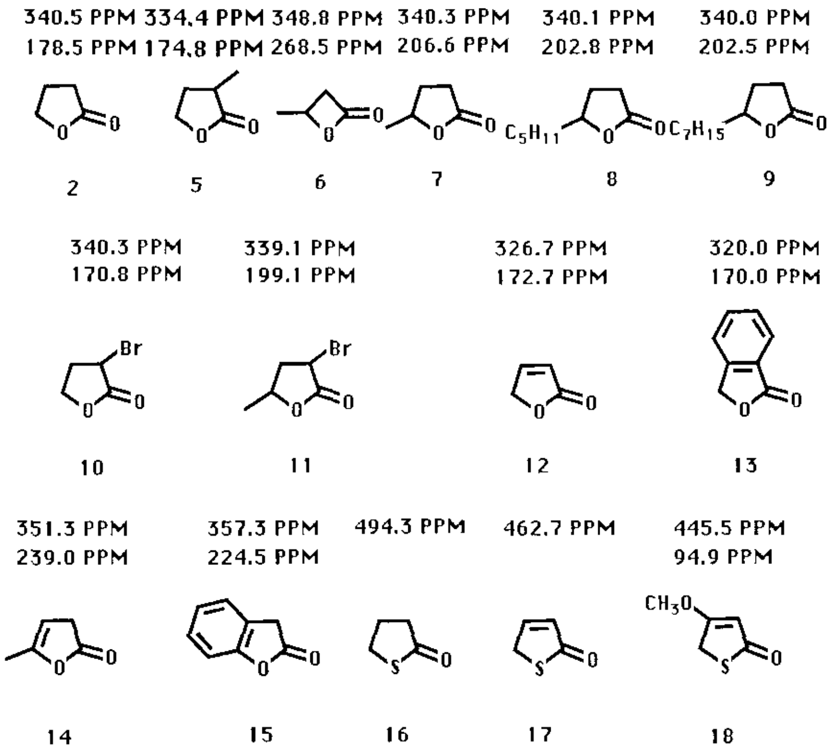
SCHEME 1



The influence of structural variation on the ^{17}O nmr chemical shift of one example of a 4-membered ring lactone and several examples of 5-membered ring lactones can be explored by examination of the results depicted in Scheme 2. Alkyl group substitution at the α-position (**5**) results in a 6 ppm shielding shift consistent with the γ-effect noted for acyclic esters[6] and cyclic ketones;[13] a concomitant upfield shift, but of somewhat smaller magnitude, was noted for the single bonded oxygen signal. Substitution of an alkyl group at the 4-position of the propiolactone ring **6** or at the 5-position of the butyrolactone ring (**7-9**) has no effect on the carbonyl resonance but significantly deshields the single bonded oxygen signal. Similar results have been noted for acyclic esters.[6] The introduction of an α-bromo group (**10** and **11**) has only a slight effect on both the carbonyl and the single bonded oxygen signal.

Introduction of double bonds in conjugation with either the carbonyl group or the single bonded oxygen produced the expected shifts. In the cases in which the carbonyl group is in conjugation with a double bond (**12** and **13**) the carbonyl ^{17}O nmr chemical shift is shielded 15-20 ppm compared with the signal of **2**. The upfield shift is consistent with the increased single bond character of the carbonyl group as a consequence of delocalization. A smaller shielding shift is also seen for the single bonded oxygen resonance. In systems **14** and **15** the introduced double bond is conjugated with the single bonded oxygen but not the carbonyl group. In these systems downfield shifts of 10-15 ppm for the carbonyl chemical shift values occur. This is as expected in view of the competition between the carbon-carbon double bond and the carbon-oxygen double bond for overlap of the single bond oxygen lone-pairs. Consequently, the carbonyl group is, in part, deconjugated from the single bond oxygen in **14** and **15** when compared to the carbonyl group of **2**.

SCHEME 2

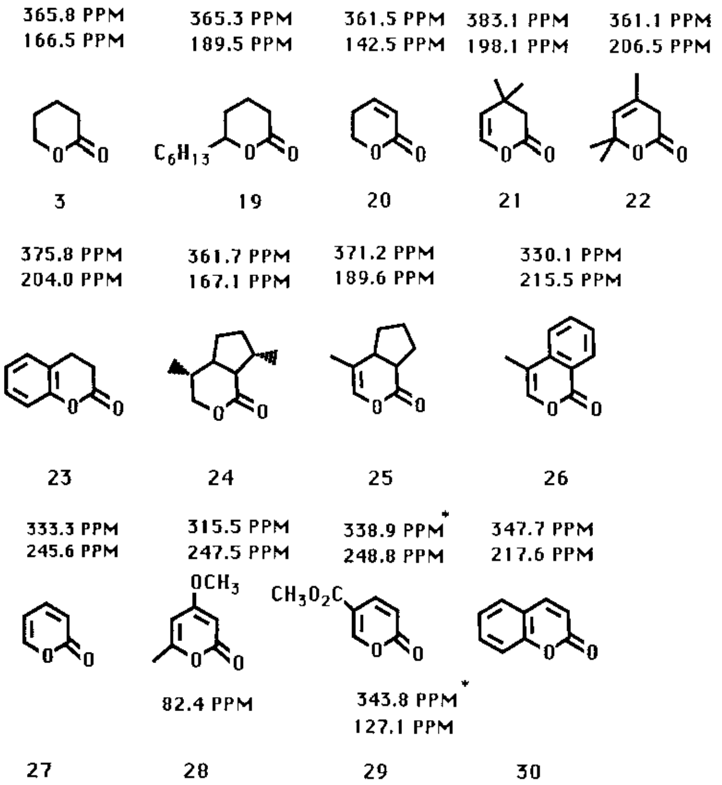


The thiobutyrolactone series **16-18** reveals interesting trends in the ^{17}O chemical shifts for this type of carbonyl group. The most striking feature is that the carbonyl group chemical shift of **16** is 154 ppm downfield of its parent system **2**. This result suggests that the electron density of the carbonyl oxygen of **16** is greatly reduced from that of **2**. Such a result is consistent with the atomic dimensions of sulfur and its reduced orbital overlap with the adjacent carbonyl group. Introduction of a double bond into conjugation with the carbonyl group of the thiolactone **17** has the expected shielding effect; the magnitude of the upfield shift for the thiolactone (compare **16** and **17**) is approximately twice as large as noted for the corresponding lactones (**2** and **12**). The introduction of a β-methoxy group into the enethiolactone system (**18**) causes shielding (17 ppm) consistent with methoxy lone-pair participation in the α,β-unsaturated carbonyl system.

The ^{17}O chemical shift values for a number of 6-membered ring lactones are depicted in Scheme 3. A comparable influence on ^{17}O chemical shifts upon double bond introduction is noted for both the 5-membered ring and 6-membered ring lactones. Location of a double bond in conjugation with the carbonyl group, compare **3** and **20**, results in a modest upfield shift of the carbonyl signal; the effect was not as great in the 6-membered ring case as was noted for the 5-membered ring one. The presence of a double bond directly bound to the single bonded oxygen, just as was the case for the 5-membered ring system, results in a downfield shift of both the lactone ^{17}O nmr signals; compare the chemical shifts of **3** with **21, 23** and **25.** The 6-membered ring lactones provide the opportunity for a more extended conjugated system; in fact, one in which one of the single bonded oxygen lone-pairs can be localized throughout the ring and ultimately on the carbonyl oxygen. Such participation should result in the ring oxygen assuming considerable double bond character. The ^{17}O nmr results from **26-30** suggest that such delocalization is important since the single bonded oxygen signal appears considerably downfield from the single bonded oxygen resonance of **3**. Accordingly, the carbonyl signals in these systems are upfield of the analogous signals for **3** and **20**. The three 6-membered ring lactones **27-29** provide the opportunity for a limited examination of the effect on chemical shifts of substituents with different electronic characteristics. As expected, the electron donating group in **28** causes shielding of the carbonyl signal, whereas the electron attracting group of **29** causes modest deshielding of the carbonyl resonance. Small effects are noted on the chemical shift of the ring oxygen chemical shift for both cases.

The above data show that the ^{17}O nmr chemical shifts of both oxygens of lactones are sensitive to a variety of structural changes. Consequently, ^{17}O nmr spectroscopy provides a method to analyze lactone structure and is one which allows direct detection of the influence of structural variation on the properties of the oxygen atoms.

SCHEME 3



EXPERIMENTAL

Lactones **22-24** are described in the Ph.D. dissertation of D.W.S. at O.S.U.; the remaining lactones were commercially available from Aldrich. The ^{17}O nmr 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°C in acetonitrile (Aldrich, anhydrous gold label under nitrogen) containing 1% of 2-butanone as an internal standard. The concentration of the lactones employed in these experiments was 0.5 M. The signals were referenced to external deionized water at 75°C. 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), 200-μs acquisition delay, 40-ms acquisition time, and 40,000-100,000 scans were required. The instrumental settings for the VXR-400 at 54.22 MHz were: spectral width 35 kHz, 2K data points, 90° pulse angle (40-μs pulse width), 200-μs acquisition delay, 29-ms acquisition time, and 20,000-40,000 scans. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying a 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 8K data points. The reproducibility of the chemical shift data is estimated to be ≤±1.0 ppm.

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