Natural Abundance ^{17}O NMR Spectroscopy of Heteroaromatic Nitro Compounds

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The ^{17}O chemical shift data, at natural abundance, for selected nitroquinolines, nitroindoles, nitroindazoles and nitrothiophenes are reported. In the absence of a *peri* or a lone-pair repulsion effect, the nitroquinolines' chemical shifts differ little from those of their carbocyclic analogs. However, the signal for 5-nitroquinoline, **2**, is deshielded by 25 ppm compared to 6-nitroquinoline, **1**, and the ^{17}O nucleus in 8-nitroquinoline, **3**, is deshielded by 49 ppm compared to that in **1**. Both these shifts are attributed to rotation of the nitro group from the plane of the heteroaromatic ring arising from *peri* hydrogen interaction and lone pair repulsion, respectively. The signals for nitro groups on electron excessive ring systems (*e.g.*, indoles and thiophenes) are shielded relative to corresponding ones in electron deficient heterocyclic ring system analogs. The chemical shifts for the π-excessive systems are interpreted in terms of electronic effects.

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The influence of structure on the ^{17}O chemical shift of the aromatic nitro group has been examined in several systems in recent years. Christ and Diehl, in pioneering work, examined several substituted nitrobenzenes and qualitatively noted the influence of steric effects on their ^{17}O chemical shift [1]. More recently, we have noted a quantitative relationship between the ^{17}O chemical shift of aromatic nitro compounds and the torsion angle, obtained from x-ray diffraction data, between the nitro group and the aromatic ring [2]. The influence of electronic factors on the ^{17}O chemical shift of aromatic nitro compounds [3-5] including nitrostyrenes [6] has been studied in detail. The previously described ^{17}O nmr results have primarily focused on carbocyclic systems. This report describes the ^{17}O chemical shift of selected heteroaromatic nitro compounds, including π-deficient and π-excessive heterocyclic systems.

Nitroquinolines.

The ^{17}O nmr data for the four nitroquinolines, **1-4**, and one nitroisoquinoline, **5**, is listed in Table 1 along with data for nitroaromatic reference compounds [2]. The ^{17}O chemical shift value, 577 ppm, for 6-nitroquinoline, **1** is essentially the same as that of nitrobenzene (575 ppm) [2]. This indicates that the fusion of the π-deficient heteroaromatic ring has little influence on the nitro resonance in this case. The chemical shifts of 5-nitroquinoline, **2** (602 ppm), and 5-nitroisoquinoline, **5** (600 ppm), differ little from the value for 1-nitronaphthalene (605 ppm), again indicating only a small influence attributable to the fusion of the π-deficient heteroaromatic ring. Interestingly, the chemical shift of **2** is deshielded by 25 ppm compared to its 6 isomer **1**; a similar difference was noted for the shifts o f

1- and 2-nitronaphthalenes [2]. The results suggest a similar torsional angle between the nitro group and the ring for both the heterocycles and carbocycles.

Since the results for **1** and **2** indicate only small influences arising from π-deficient heteroaromatic ring fusion, 8-nitroquinoline, **3**, is an interesting molecule which can be used to study the lone pair-nitro group interaction. The ^{17}O chemical shift for 8-nitroquinoline, **3**, is 626 ppm, 24 ppm downfield from that of **2** and 51 ppm downfield from the value for nitrobenzene. This result indicates that the ring nitrogen lone pair-nitro group interaction is substantially greater than a nitro group-*peri* hydrogen interaction. If it is assumed that the relationship developed for carbocyclic nitro compounds [2] is applicable to 8-nitroquinoline, the torsional angle under discussion for **3** is predicted to be approximately 69 degrees. 7-Methyl-8-nitroquinoline, **4**, represents a case in which additional steric effects could influence the chemical shift of the nitro group. The ^{17}O chemical shift value for **4** is 633 ppm, downfield from that of **3** by 7 ppm. This suggests that the contribution of the methyl group in **4** to rotation of the nitro group from the plane is small. In view of the magnitude of the shift attributed to the interaction of the ring-nitrogen non-bonding electron pair, presumably reflecting a large torsional angle, further rotation of the nitro group caused by steric interaction of the methyl group appears to be small. Resolution of this question must await determination of the nitro group-ring torsion angle for **3** and **4** by an independent method.

Nitroindoles, Nitroindolines, Nitroindazoles and Nitrothiophenes.

In general nitro groups in π-excessive heterocycles are expected to have more single bond character for the nitrogen-oxygen bond, so their ^{17}O chemical shift should be upfield, compared to values for π-deficient systems [3]. The ^{17}O chemical shift of 5-nitroindole, **6**, is 562 ppm. This cor-

responds to approximately a 15 ppm upfield shift compared to both nitrobenzene and the heterocycle **1**, confirming expectations. The ^{17}O chemical shift for 7-nitroindole, **7**, which should be electronically equivalent to its isomer **6**, is slightly downfield from **6** at 568 ppm. This small downfield shift is in the correct direction for a *peri*-type compressional effect; however, hydrogen-bonding would be expected to cause shielding. A significant contribution from the latter effect seems unlikely since it is known that nitro groups form weak hydrogen bonds [7]. The two nitroindoles **8** and **9** represent electronically equivalent systems and, consequently, their differing ^{17}O chemical shift of 566 and 578 ppm, respectively, indicate that *peri* type interactions, although small compared to quinolines, are also operative for the indoles.

Table 1

^{17}O Chemical Shifts (PPM) for Heteroaromatic Nitro Compounds

Number	Name	Chemical Shift (PPM) [a]
1	6-nitroquinoline	577
2	5-nitroquinoline	602
3	8-nitroquinoline	626
4	7-methyl-8-nitroquinoline	633
5	5-nitroisoquinoline	600
6	5-nitroindole	562
7	7-nitroindole	568
8	6-nitroindole	566
9	4-nitroindole	578
10	5-nitroindoline	546
11	6-nitroindoline	572
12	5-nitroindazole	571
13	6-nitroindazole	575
14	2-nitrothiophene	569
15	5-nitrothiophene-2-carboxaldehyde	578 (567) [b]
16	nitrobenzene	575 [c]
17	*o*-nitrotoluene	602 [c]
18	*p*-nitrotoluene	572 [c]
19	1-nitronaphthalene	605 [c]
20	2-nitronaphthalene	575 [c]

[a] Taken in dried acetonitrile as 0.5 *M* solution at 75° [1.0% 2-butanone $\delta = 558 \pm 1$ ppm as internal check]. [b] The resonance for the aldehyde group. [c] Taken from ref [2].

The two indolines, 5-nitroindoline, **10**, and 6-nitroindoline, **11**, contain saturated heterocyclic ring systems and are expected to give ^{17}O nmr results similar to those reported for nitroanilines [3]. The chemical shift of 546 ppm for **10** is substantially upfield to that of **6** as expected from electron donation by a *para* amino function and the shift of 572 ppm for **11** reflects the smaller shift expected from a *meta* amino substituent [3].

The indazole ring represents a system which is more electron rich than quinoline and more electron deficient than the indoles. The ^{17}O chemical shift for 5-nitroindazole, **12** (571 ppm), falls between that of the quinoline **1** (577 ppm) and the indole **6** (562 ppm). Similarly, the chemical shift of 6-nitroindazole, **13** (575 ppm) is slightly downfield with respect to that of **8**.

The ^{17}O nmr signal for 2-nitrothiophene **14** occurs at 569 ppm, which is somewhat upfield of that of nitrobenzene (575 ppm). The ^{17}O chemical shift for the nitro group of 5-nitrothiophene-2-carboxaldehyde **15** occurs at 578 ppm. Compound **15** shows two signals at 578 and 567 ppm. The assignment given above was confirmed by enriching the aldehyde functional group, using ^{17}O enriched water by employing conditions similar to those previously reported [8]. The nitro group of **15** is deshielded by 9 ppm compared to **14** just as the nitro group of *p*-nitrobenzaldehyde is deshielded by 8 ppm compared to nitrobenzene [3].

EXPERIMENTAL

The nitro compounds studied were commercially available (Aldrich and Lancaster Synthesis). The ^{17}O spectra, natural abundance, was taken on a JEOL GX-270 Spectrometer equipped with a 10 mm broad band probe operated at 36.5 MHz. The nmr spectra were acquired at natural abundance on 0.5 *M* solutions in dried acetonitrile (molecular sieves) at 75°. The chemical shift data were referenced to external water (1.0% 2-butanone was added as an internal check, 558 ± 1 ppm). The instrument settings were: 25 KHz spectral width, 2 K data points, 90° pulse angle (28 μs pulse width), 0.3 ms acquisition delay, and 41 ms acquisition time or 30.12 KHz spectral width, 0.25 ms acquisition delay and 34 ms acquisition time. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying a 25-50 Hz exponential broadening factor to the FID prior to Fourier transformation. The data point resolution was improved to ±0.2 ppm by zero filling to 8 K data points. Generally, spectra with S/N of about 10/1 were obtained after ~ 10^5 scans. Under these conditions, the half height band widths were 230 ± 30 Hz. The reproducibility of the chemical shifts is estimated to be ±2 ppm.

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