On the Nitration of 2-Pyrone

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A 1:1 adduct of 2-pyrone and nitronium fluoroborate has been detected by nmr and is a possible precursor of 5-nitro-2-pyrone, a subsequently formed product. From comparison of the nmr spectra of the 1:1 adduct and 2-methoxypyrylium fluoroborate, the adduct is believed to be the pyrylium fluoroborate derived from nitration of the carbonyl oxygen of 2-pyrone.

As part of a study of 2-pyrone chemistry, the feasibility of effecting electrophilic substitutions upon this ring system has been investigated. On the basis of its reactivity toward dienophiles and nucleophilic reagents, 2-pyrone has been considered a "non-aromatic" system (1), although some substituted 2-pyrones have been reported to undergo what appear to be electrophilic substitution reactions. However, efforts to effect nitration, sulfonation, chlorosulfonation or chloromethylation of 2-pyrone itself have been unsuccessful under conditions for which substituted 2-pyrones are reported to undergo such reactions (2-6). Moreover, halogenation of 2-pyrone has been found to proceed *via* addition-elimination sequences rather than by direct substitution (7).

Treatment of nitromethane solutions of 2-pyrone (I) with nitronium fluoroborate affords a substitution product, 5-nitro-2-pyrone (III) identified on the basis of its elemental composition and its spectral properties. The position of substitution is unambiguously assigned on the basis of the spin-spin coupling constants observed for the remaining three protons (8). Preferential substitution at the 5 rather than the 3- position is perhaps surprising in view of prior reports (2-6) of substitution reactions upon substituted 2-pyrones and in view of predictions based upon LCAO-MO calculations (9). However, precedent and calculations should not warrant much credence, since the nitropyrone may well come from some precursor other than 2-pyrone.

When the course of the nitration reaction is followed by nmr spectroscopy, a profound downfield shift of the two 2-pyrone complex multiplets (8) is initially observed, followed by the slow appearance of 5-nitro-2-pyrone resonances. Under the conditions of the nmr experiment, no other signals are detectable and the magnitudes of the initial downfield shifts are proportional to nitronium fluoroborate concentration until the nitronium fluoroborate concentration equals that of 2-pyrone. Beyond this value, there is little change in the chemical shifts of the ring protons (Figure 1). This observation clearly requires there to be a rapid reversible equilibrium between 2-pyrone,

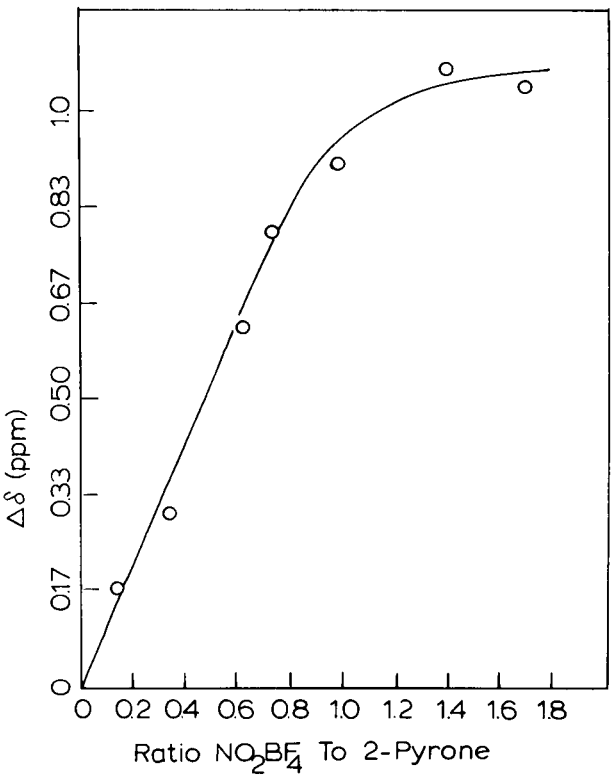
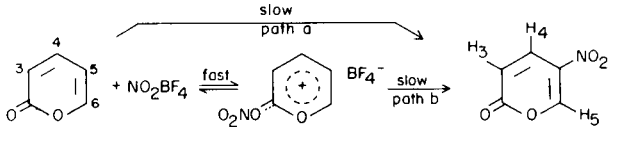


Figure 1. Influence of NO_2BF_4 concentration upon the apparent chemical shift of 2-pyrone. Plotted $\Delta\delta$ values represent the average of the shifts for both 2-pyrone multiplets. However, these shifts were essentially identical.

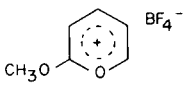
nitronium fluoroborate and some stable 1:1 adduct. This initial reaction is then followed by slower (*i.e.* $t_{1/2}$ *ca.* 5 hours at 25°) formation of 5-nitro-2-pyrone. *A priori*, the nature of the initial adduct is uncertain; it may be either an oxygen nitrated pyrylium salt (II), a π-donor acceptor complex, a ring-oxygen nitrated oxonium ion or a carbon σ-complex. Although the 1:1 adduct may be a direct precursor of the nitropyrone III (path b), this is not necessary, since free 2-pyrone (present in equilibrium with the adduct) might itself undergo electrophilic attack by nitronium ion to afford III (path a). There is presently no reason to prefer either path a or path b.



I II III

$J_{3,4}$ 10.5 Hz
$J_{5,6}$ 1.0 Hz
$J_{4,6}$ 3.0 Hz

Of the four possibilities considered for the structure of the 1:1 adduct, pyrylium ion II is deemed most likely in view of its nmr spectrum which is quite similar in appearance and chemical shift to that of the methoxypyrylium salt (IV). The spectral similarity suggests that charge densities about the ring carbons may be similar in both instances. For this reason, the 1:1 adduct is tentatively suggested to be pyrylium salt II. Attempts to examine the infrared spectrum of the adduct (which could not be isolated) led to no clear-cut result.



IV

The nmr spectrum of the ring protons of 2-methoxypyrylium fluoroborate (IV) afforded by the action of trimethyloxonium fluoroborate upon 2-pyrone, is very similar to that of 2-pyrone except for a downfield shift of 1.1 ppm which presumably arises from the delocalized positive charge. Apparently, the *relative* chemical shifts and spin-spin coupling constants of the ring protons of these two compounds are quite similar. The infrared spectrum of the pyrylium salt IV is free of carbonyl absorption, consistent with its proposed structure.

EXPERIMENTAL

NMR spectra were run on a Varian A-60-A spectrometer using *ca.* 15% solutions in deuteriochloroform containing 2% tetramethylsilane. Infrared spectra were run on a Perkin-Elmer 521 Spectrophotometer using 10% carbon tetrachloride solutions unless noted otherwise. Ultraviolet spectra were determined on a Perkin-Elmer 202 instrument. Melting points were taken on a Reichert block and are uncorrected. Analyses were conducted by Mr. J. Nemeth and his associates of these laboratories; mass spectra were obtained by Mr. J. Wrona using an Atlas CH-4 spectrometer.

5-Nitro-2-pyrone (III).

In a nitrogen filled dry bag, 1.327 g. of 2-pyrone in 10 ml. of nitromethane was added dropwise over a period of 5 minutes to a solution of 1.796 g. of nitronium fluoroborate (Ozark Mahoning Co.) in 50 ml. of dry nitromethane. After 1.25 hours of magnetic stirring, the homogeneous solution was concentrated to near dryness and the last traces of nitromethane were removed on a vacuum line. The reddish slushy residue (3.116 g.) was triturated with two 30 ml. portions of ether and the combined extracts were evaporated to *ca.* 6 ml. with a stream of dry nitrogen. The resultant crystals were collected, washed once with cold ether and vacuum dried to yield 0.466 g. of faintly yellow 5-nitro-2-pyrone (III), m.p. 108°. An additional 0.200 g. of this material was subsequently obtained from the mother liquors, bringing the overall yield to 35%. After one sublimation, the nitropyrone, m.p. 111-111.5°, has in chloroform, an infrared spectrum which shows a strong absorption at 1750-1770 cm^{-1}, sharp bands at 1645, 1565, 1515 and 1350 cm^{-1} and an ultraviolet spectrum having λ max (chloroform) 276 mμ (ϵ, 13,000).

Three equal area quartets are apparent in the nmr spectrum of the compound, centered at δ 6.45, 8.10 and 8.80 and coupling constants of 10.5, 1.0 and 3.0 Hz are observed (8). The product is exceedingly sensitive to nucleophiles, forming deep red to violet solutions with alcohols, water, amines or anions such as acetate and iodide.

Anal. Calcd. for $C_5H_3NO_4$: C, 42.55; H, 2.10; mol. wt., 141.09. Found: C, 42.79; H, 2.12; mol. wt., 141 (mass spectrometric).

NMR Detection of the 1:1 Adduct.

Portions (0.5 ml.) of a nitromethane solution 2.4 *M* in 2-pyrone were added to seven nmr tubes containing, respectively, 0.027, 0.060, 0.098, 0.116, 0.155, 0.217 and 0.270 g. of nitronium fluoroborate. The spectra of the solutions were measured (40°) as soon as possible after mixing. The results are summarized in Figure 1. Tube seven, after standing at 27° for one day, was shown by nmr to contain about equal amounts of 5-nitro-2-pyrone and the 1:1 adduct.

2-Methoxypyrylium Fluoroborate (IV).

In a dry nitrogen atmosphere, trimethyloxonium fluoroborate (0.04 mole) was placed in a 50 ml. centrifuge tube with 30 ml. of dry methylene chloride and the tube was stoppered with a serum cap and placed in an ice bath. With a syringe, 3.15 ml. of freshly distilled 2-pyrone (0.04 mole) was added dropwise to the nitrogen swept tube and the mixture was allowed to warm to room temperature. After two days at 27°, the supernatant methylene chloride was decanted from the crystalline mass which was then washed twice with 25 ml. portions of methylene chloride, once with dry ether, and finally dried under nitrogen. The infrared spectrum (Nujol) of the 2-methoxypyrylium fluoroborate thus obtained (4.208 g., 53.4%; m.p. 100-100.5° in a sealed tube)

shows two relatively broad but weak bands at 1645 and 1525 cm^{-1} as well as a very broad absorption at 1020-1170 cm^{-1} attributable to fluoroborate absorptions. The proton nmr spectrum (acetonitrile) shows two multiplets at *ca.* δ 7.50 and 8.56, and the methyl singlet at δ 4.46.

Heating the salt either in vacuum, in high boiling solvents, or in a sealed tube gave rise to no detectable organic products save 2-pyrone. Recovery of 1.797 g. of 2-pyrone was effected upon aqueous rinsing of the supernatant methylene chloride solution.

Anal. Calcd. for $C_6H_7O_2BF_4$: C, 36.38; H, 3.56. Found: C, 36.42; H, 3.61.

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