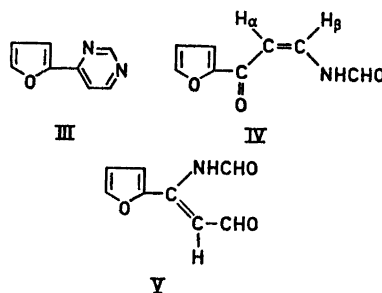


On the Reaction of
4-(2'-Furyl)pyrimidine with Nitric
Acid in Acetic Anhydride-Acetic
Acid

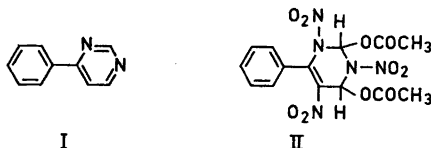
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A recent publication by Lynch and Poon¹ on the reaction of 4-phenylpyrimidine (I) with acetyl nitrate has prompted us to report our somewhat different results in the reaction of 4-(2'-furyl)pyrimidine with nitric acid in acetic anhydride-acetic acid mixture.

Lynch and Poon¹ found that acetyl nitrate in acetic anhydride, generated from fuming nitric acid and acetic anhydride at 15–20°C attacked the pyrimidine nucleus



of I, yielding a compound analyzing for $C_{14}H_{13}N_5O_{10}$. Based on its NMR-spectrum and IR-spectrum the structure 2,4-acetoxy-6-phenyl-1,3,5-trinitro-1,2,3,4-tetrahydropyrimidine (II) was assigned to this product.

They found, however, that nitration of I with fuming nitric acid (d 1.50) in conc. sulphuric acid or trifluoroacetic anhydride led to nitration in the phenyl ring.

In connection with our work on the directing effect of heterocyclic aromatic rings on electrophilic substitution,² we have started an investigation of the electrophilic substitution of 4-(2'-furyl)pyrimidine (III). We observed to our astonishment that the reagent nitric acid in acetic acid-acetic anhydride mixture so often used in the nitration of furans and thiophenes^{3,4} preferred to attack the highly π -deficient pyrimidine ring, instead of the π -excessive furan nucleus. The primarily formed product was rather unstable and was trans-

formed, when chromatographed on silica, or on standing (giving off acidic fumes) to a compound (A), m.p. 112–113.5°C, which analyzed correctly for $C_8H_7NO_3$.

As the mass spectrum of this compound confirmed the molecular weight of 165, and the NMR-spectrum clearly demonstrated the presence of three furanic hydrogens, reasonable structure alternatives are limited to IV and V, both of which can formally have been formed by hydrolytic ring-opening of the pyrimidine ring, with the elimination of ammonia from the 3- and 1-position, respectively.

Reaction of the crude product with hydrochloric acid followed by reaction with hydrazine yielded 2-(2'-furyl)pyrazole, which has been recently synthesized from the hydroxymethylene derivative of 2-acetylfuran and hydrazine.⁵ This provides additional evidence that the structure of A is IV or V.

Due to the poor solubility of A in most solvents, it was difficult to obtain a good NMR-spectrum. In acetone solution the three furan hydrogen resonances were observed at 2.12 τ (hydrogen 5), 2.78 τ (hydrogen 3) and 3.26 τ (hydrogen 4). The assignments are based on the characteristic coupling constants of furans.⁶ These shifts are quite similar to that of a -I-M-substituted furan like 2-acetylfuran, having τ_5 at 2.35 ppm, τ_3 at 2.68 ppm, and τ_4 at 3.35 ppm in acetone solution. In addition two doublets with splittings of 8.0 c/s and 4.9 c/s were observed at 0.05 τ and 0.28 τ . These two bands had a relative intensity of about 1:2, but a total intensity equal to one of the furan hydrogen resonances. Two broadened doublets with a total intensity corresponding to one furan hydrogen are also observed at 1.19 τ and 1.37 τ . These doublets have splittings of 7.5 c/s and 4.7 c/s, respectively. In the

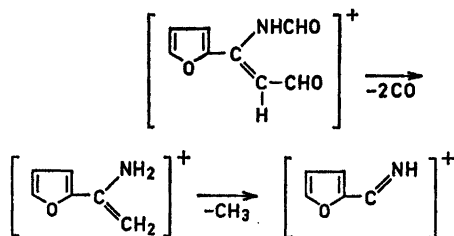
NMR-spectrum of A in trifluoroacetic acid solution, this band gives only rise to one peak at 1.25 τ . A doublet with a splitting of 5.0 c/s and with the same intensity as the doublet centered at 0.28 τ is observed at 3.91 τ . Finally a doublet partly overlapping the furan resonance at 2.78 τ is also observed.

Structure IV is the formamide of an enamine ketone. The NMR-spectra of enamine ketones have recently been studied by Dudek and Volpp⁷ and by Dabrowski.⁸ They have found that in solution rapid equilibration to a mixture of the chelated *cis* isomer and the *trans* isomer occurred. They found that α -hydrogen resonances occurred at about 4.6–5.0 τ and those for β -hydrogens between 2.35 and 3.35 τ , depending on the configuration at the double bond. Coupling constants of the order of 13 c/s were observed for the *trans* isomers and of 7–8 c/s for the *cis* isomers.

It is rather improbable that the presence of the formyl group in A would shift the β -hydrogen down to 1.2 τ , and furthermore the band at 3.91 τ in A is too low to be assigned to the α -hydrogen. Also the observed coupling constants are not compatible with IV. However, the NMR-spectrum can be interpreted as that of a mixture of the *cis* and *trans* isomers of V, as it is quite reasonable to assume that this enamine aldehyde will also easily equilibrate in solution. The two doublets at 0.05 τ and 0.28 τ are assigned to the aldehydic resonances of the *cis* and *trans* forms, while the two broad doublets at 1.19 τ and 1.37 τ are assigned to the amide CHO in the *cis* and *trans* forms. The coupling is to the NH, which is observed as a broad band below 0 τ . These couplings disappear in trifluoroacetic acid. The bands at 3.91 τ and 2.75 τ are those of the ethylenic hydrogens in the two forms.

The mass spectrum of A also confirms the structure V. The molecular ion loses consecutively two fragments of mass 28, giving strong peaks at $m/e = 137$ (90%) and $m/e = 109$ (100%) confirmed by metastable peaks at 114.1 and 86.9. This is interpreted as the loss of carbon monoxide.* A further loss of methyl leads to $m/e = 94$ (47%). For a structure such as IV a strong peak from the furoyl cation at $m/e = 95$ would certainly be expected. The strong

* Unfortunately no high-resolution mass spectrometer was available to check this interpretation.



peak at $m/e = 146$ (50%) could be due to the loss of the formyl group from the aldehyde function. The mass spectrum of A also shows peaks at m/e 29 (25%) and m/e 39 (53%) observed in furan derivatives.⁹⁻¹¹

At present it is difficult to rationalize the formation of V from an intermediate analogous to II. We are continuing our investigation on this new reaction of pyrimidine derivatives.

Experimental. A nitrating mixture was prepared by mixing 31.6 ml of conc. nitric acid (d 1.40) and 0.5 g of urea and diluting to 50 ml with glacial acetic acid. 2.25 ml of this solution was added at room temperature to a solution of 3.0 g of 4-(2'-furyl)pyrimidine¹² in 75 ml of acetic anhydride and the mixture stirred for 3 h. The mixture was poured onto ice, neutralized with bicarbonate and the yellow crystals filtered off, washed with water and dried, yielding 2.48 g of a product, m.p. 97–102°C, which was rather unstable. When 250 mg of this product was chromatographed on silica gel (100–200 mesh) with chloroform as an eluent, 200 mg of 3-formamido-3-(2'-furyl)acrolein, m.p. 112–113.5°C, was obtained after recrystallization from acetone. It was also obtained when the crude product was allowed to stand.

Mass spectrum: (m/e , %) 26, 8.2; 27, 25.5; 28, 54.1; 29, 36.8; 36, 6.1; 37, 9.2; 38, 22.4; 39, 71.4; 40, 18.4; 41, 28.6; 42, 18.4; 43, 15.3; 44, 12.3; 50, 9.2; 51, 18.4; 52, 22.4; 53, 42.8; 54, 15.3; 55, 11.2; 62, 5.1; 63, 16.3; 64, 14.3; 65, 22.4; 66, 9.2; 68, 32.6; 69, 9.2; 70, 5.1; 78, 5.1; 79, 5.1; 80, 56.2; 81, 28.6; 82, 7.1; 83, 12.2; 91, 5.1; 92, 30.6; 93, 25.5; 94, 49.0; 95, 9.2; 108, 16.3; 109, 100; 110, 9.2; 136, 48.0; 137, 85.7; 138, 7.1; 149, 7.1; 165, 21.4. (Found: C 58.87, H 4.3; N 8.53. Calc. for $C_8H_7NO_3$ (165.1), C 58.18; H 4.27; N 8.48).

3-(2'-Furyl)pyrazole. 230 mg of the crude product described above was dissolved in 10 ml 2.5 N hydrochloric acid at 30°C. When the

solution became dark-red, 0.35 ml of hydrazine hydrate was added with cooling. After 5 min the solution was neutralized with sodium bicarbonate solution and extracted with ether. Evaporation of the dried ether solution yielded 95 mg of crude 3-(2'-furyl)pyrazole, having the same IR-spectrum as an authentic sample.⁵ NMR-spectra were obtained with a Varian A-60 high resolution spectrometer and the mass spectra with an LKB 9000 mass spectrometer.

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The Probe Method for Measurement of Equilibrium Vapour Pressures

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An elegant way for determination of relative vapour pressures is the "dew-point" method applied among others by Hargreaves¹ to copper-zinc alloys and by Birchenall and Cheng² to silver-cadmium alloys. In this method a furnace with two independently heated zones is employed. The alloy sample to be investigated is placed in one end of an evacuated silica tube. This tube is placed in the furnace in such a way that the sample is kept at a constant temperature, while the temperature of the other end of the tube is lowered until pure droplets of the volatile component just start to condense. This temperature, the "dew-point", is accurately determined by repeated heating and cooling of this coolest zone of the furnace. The vapour pressure of the pure volatile component has of course to be known as a function of temperature. The crucial point of the method is the accurate determination of the dew-point which often is difficult and besides imposes the restriction that the sample container has to be made of a transparent material to permit ocular observation. This note describes a similar method in which these drawbacks are avoided as the vapour to be determined need not reach the dew-point, but is instead allowed to come to equilibrium with a probe in the form of a small piece of metal foil with which it forms an alloy.

Consider the sample tube arrangement in Fig. 1. The system consists in this case of an evacuated and closed tube containing the sample in the bottom part and the probe fixed on a hook in the top. The tube is placed in a vertical or nearly vertical position in a furnace to allow the sample to be a melt if necessary. The furnace has two well defined and controlled temperature zones covering the top and the bottom parts of the sample tube. Radiation shields of thin molybdenum metal arranged to avoid radiation from the hotter top to the cooler bottom zone but allowing the vapour to pass freely are placed between the probe and the sample. Indentations in