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Studies of Compounds Related to Azines. VII.[1] The Pyrorlysis of 2-Acetylthiophene- and 2-Acetylfuranketazine

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As part of a study attempting to elucidate the relation between the chemical structure of an azine and its pyrolysate, the pyrolyses of 2-acetylthiophene- (I) and 2-acetylfuranketazine (II) have been investigated. The pyrolysis of I at 270°C afforded principally nitrogen, ammonia, and 7-methyl-5-(2-thienyl)-thieno[2,3-*c*]pyridine (III), plus lesser quantities of thiophenecarbonitrile and 2-acetylthiophene. The reductive desulfurization of III, followed by oxidation, afforded pyridine 2,4,6-tricarboxylic acid *via* 5-*n*-butyl-7-methyl-thieno-[2,3-*c*]pyridine and 2-*n*-butyl-4-ethyl-6-methylpyridine. On the other hand, II was pyrolyzed to give nitrogen, ammonia, and tars as the major products, together with furan, furancarbonitrile, 2-acetylfuran, 5-(2-furyl)-7-methyl-furo[2,3-*c*]pyridine, and 2,4,6-tri(2-furyl)pyridine.

In order to elucidate the relation between the chemical structure of an azine and its pyrolysate, pyrolyses of various azines have been investigated,[2-6] and it has been found that aromatic ketazines are decomposed by a free-radical process, giving the corresponding Piloty-Robinson's reaction product as the main product in many cases.[3-5]

In this paper we wish to report the formation of novel products from the pyrolyses of 2-acetylthiophene-(I) and 2-acetylfuranketazine (II).

When I was pyrolyzed at 270°C for 1 hr, nitrogen, ammonia, and colorless crystalline compound III, mp 103—104°C, were obtained as major products, accompanied by lesser quantities of thiophenecarbonitrile and 2-acetylthiophene.

Although the compound III was in agreement with the expected molecular formula, $C_{12}H_9NS_2$, which corresponded to that of the Piloty-Robinson's reaction product, 2,5-dithienylpyrrole, its IR spectrum did not show any bands ascribed to the NH group, while it did show the C=N band at 1570 cm^{-1}. The NMR spectrum had signals at τ 7.48 (3H, CH_3, *s*) and 2.3—3.2 (6H, aromatic protons, *m*), while the mass spectrum exhibited the parent ion peak (M^+) at *m/e* 231, together with major peaks at *m/e* 216 (M^+–Me), 205 (M^+–C_2H_2), 186 (M^+–CHS), 148 (186$^+$—C_3H_2), and 133 (148$^+$–Me). On the basis of these spectral data and the following chemical transformations, it seems reasonable to assume that III is a methyl-thienyl-substituted thienopyridine.

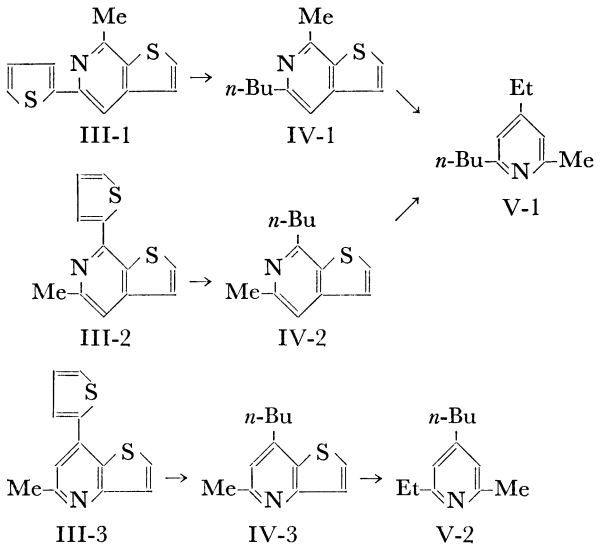
The relative desulfurization of III with Raney nickel catalyst was carried out. Treatment with Raney nickel catalyst (W-1 type) gave pale yellow oil IV and colorless oil V. On the further treatment of IV with Raney nickel catalyst (W-4 type), IV was transformed into V in a good yield.

The compound IV ($C_{12}H_{15}NS$) was assumed, by spectral studies as well as by elemental analysis, to be *n*-butyl-methyl-substituted thienopyridine, whose structure corresponded to that which will be derived from III under the reductive desulfurization of the thienyl group in III to the *n*-butyl group. The NMR spectrum exhibited signals at τ 9.1 (3H, $C\underline{H}_3$–$(CH_2)_3$–, *t*), 8.0—9.3 (4H, Me–$(C\underline{H}_2)_2$–CH_2–, *m*), 7.5 (3H, CH_3, *s*), 7.25 (2H, Me–$(CH_2)_2$–$C\underline{H}_2$–, *t*), 3.2 (1H, pyridine ring proton, *s*), 2.6 and 2.43 (each 1H, thieno ring proton, *dd*). In the mass spectrum, the parent ion peak (M^+) appeared at *m/e* 205, together with major peaks at *m/e* 190 (M^+–Me), 176 (M^+–Et), 163 (M^+–MeCH=CH_2), 148 (163$^+$–Me) and 122 (163$^+$–MeCN).

1) Part VI of this series: O. Tsuge, M. Tashiro, and K. Hokama, *Nippon Kagaku Zasshi*, **90**, 572 (1969).
2) O. Tsuge, M. Tashiro, and K. Hokana, *Kogyo Kagaku Zasshi*, **71**, 1293 (1968).
3) O. Tsuge, M. Tashiro, K. Hokama, and K. Yamada, *ibid.*, **71**, 1667 (1968).
4) O. Tsuge, K. Hokama, and H. Watanabe, *ibid.*, **72**, 1107 (1969).
5) O. Tsuge, K. Hokama, and H. Watanabe, *Yakugaku Zasshi*, **89**, 783 (1969).
6) O. Tsuge, K. Hokama, and M. Koga, *ibid.*, **89**, 789 (1969).

On the other hand, the compound V ($C_{12}H_{19}N$) was presumed, by spectral studies and chemical transformation, to be 2,4,6-trialkyl (*n*-butyl, ethyl, and methyl)pyridine. The IR and UV spectra of V were very similar to those of 2,4,6-collidine, while the NMR spectrum had signals at τ 9.1 (3H, $C\underline{H}_3$–$(CH_2)_3$–, *t*), 8.8 (3H, $C\underline{H}_3$–CH_2–, *t*), 8.0—9.3 (4H, Me–$(C\underline{H}_2)_2$–CH_2–, *m*), 7.8 (3H, CH_3, *s*), 7.1—7.6 (4H, Me–$(CH_2)_2$–$C\underline{H}_2$– and Me–$C\underline{H}_2$–, *m*) and 3.4 (2H, pyridine ring protons, *s*). The mass spectrum showed the parent ion peak (M^+) at *m/e* 177, together with major peaks at *m/e* 162 (M^+–Me), 148 (M^+–Et), 135 (M^+–MeCH=CH_2), 120 (135^+–Me), and 107 (135^+–C_2H_4).

Furthermore, V was oxidized with selenium dioxide in pyridine to give pyridine 2,4,6-tricarboxylic acid, which was identical with an authentic specimen prepared by the oxidation of 2,4,6-collidine.

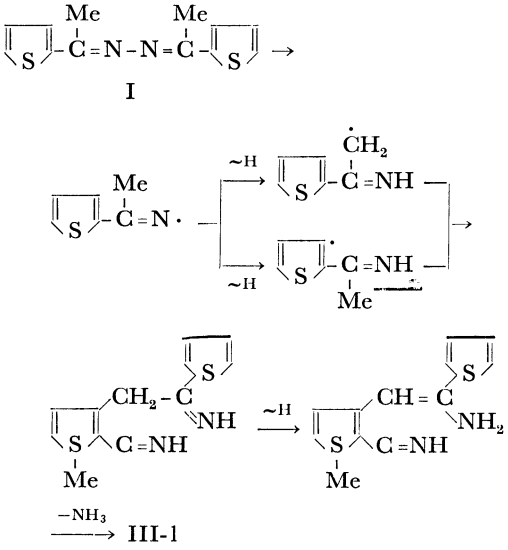


On the basis of the chemical shift of methyl protons in the respective NMR spectrum of III, IV, or V, it is evident that the methyl group is located at the α-position of the pyridine ring in the respective compound. Consequently, 2-*n*-butyl-4-ethyl-6-methyl- (V-1) and 4-*n*-butyl-2-ethyl-6-methylpyridine (V-2) are both possible structures for V.

It should be deduced that the compounds III and IV are 7-methyl-5-(2-thienyl)- (III-1) or 5-methyl-7-(2-thienyl)- (III-2) and 5-*n*-butyl-7-methyl- (IV-1) or 7-*n*-butyl-5-methylthieno[2,3-*c*]pyridine (IV-2) from the structure of V-1, and 5-methyl-7-(2-thienyl)- (III-3) and 7-*n*-butyl-5-methyl-thieno[2,3-*b*]pyridine (IV-3) from the structure of V-2. Unfortunately, it is very difficult to determine from spectral data which isomers would be more reasonable for III and IV.

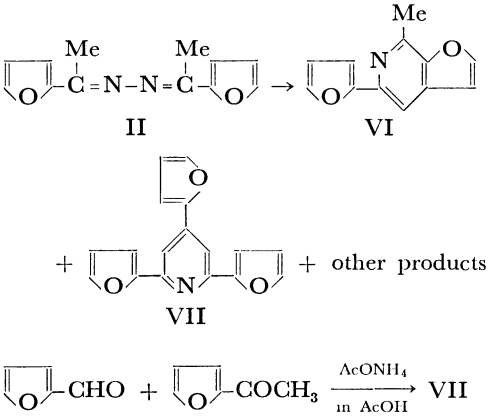
It has previously been found that the main pyrolytic pathway of aromatic ketazines is that through the homolysis of the N–N bond of ketazines.[3-5] For the formation of III-2 or III-3 from the ketazine I, anomalous homolyses of I and complicated reactions must take place.

In analogy with the pathway of the formation of 2,5-diphenylpyrrole from acetophenoneketazine,[4] however, the formation of III-1 from I can be illustrated by the homolytic dissociation of the N–N bond of I, followed by the rearrangement and recombination of the formed radicals and the subsequent elimination of ammonia.



On the basis of the spectral data and considerations of the pyrolytic pathway, it seems reasonable to conclude that III, IV, and V are 7-methyl-5-(2-thienyl)- (III-1), 5-*n*-butyl-7-methyl-thieno[2,3-*c*]pyridine (IV-1), and 2-*n*-butyl-4-ethyl-6-methylpyridine (V-1) respectively.

A similar pyrolysis of II gave 5-(2-furyl)-7-methylfuro[2,3-*c*]pyridine (VI) and 2,4,6-tri(2-furyl)pyridine (VII) in low yields, accompanied by other products and intractable tars. The structure of VI was assumed on the basis of spectral studies as well as the elemental analysis. The UV spectrum of VI was similar to that of III, while the parent ion peak (M^+) appeared at *m/e* 199, together with major peaks at *m/e* 184 (M^+–Me), 170 (M^+–CHO), 142 (184^+–CH_2C=O) and 132 (170^+–C_3H_2) in the mass spectrum. On the other hand, the compound VII was identified by



comparing its IR spectrum with that of an authentic sample prepared by the reaction of furfural with 2-acetylfuran in the presence of ammonium acetate according to the improved Chichibabin pyridine synthetic method.[7]

7) M. Weiss, *J. Amer. Chem. Soc.*, **74**, 200 (1952).

Experimental[8]

Materials. The 2-Acetylthiophene- (I) and 2-acetylfuranketazine (II) were prepared by the reaction of the corresponding 2-acetyl compound with hydrazine hydrate in acetic acid; each was then recrystallized from ethanol. The yield was quantitative.

I: mp 95—96°C (lit,[9] 93°C).

II: mp 102—103°C. Found: C, 66.62; H, 5.52; N, 13.07%. Calcd for $C_{12}H_{12}O_2N_2$: C, 66.65; H, 5.59; N, 12.96%.

Procedure. After the pyrolysis had been carried out in an apparatus similar to one described previously,[3] the products were analyzed by the following methods. The products were divided into three fractions: gaseous material (nitrogen, ammonia), a lower-boiling fraction, and a residual fraction.

The analyses of nitrogen and ammonia were carried out by the reported method.[3] The lower-boiling fraction was analyzed by gas chromatography. The conditions for the gas chromatography were as follows: column, 30% high-vacuum silicon grease (HVSG) (3 m) and 20% PEG - 0.5% adipic acid (0.75 m); temperature, 200°C; carrier gas, hydrogen 30 ml/min. From the areas of the individual peaks, mol% figures were calculated for each product after determining the relative response data by the internal standard method using *o*-chloronitrobenzene. Individual peaks were identified by means of the retention times of pure samples.

After the residual fraction had been extracted with benzene, the benzene extract was chromatographed on alumina, giving pure crystalline compounds. The quantitative estimation of the compounds was carried out by the gas-chromatographic internal standard method using 1-benzylnaphthalene. The conditions for the gas chromatography were as follows: column, 30% HVSG (0.75 m); temperature, 300°C; carrier gas, hydrogen 147 ml/min.

Pyrolysis of I. Five grams of I were pyrolyzed at 270°C for 1 hr. The respective yields (mol%) of products obtained from the average values of three runs under the same conditions were as follows: nitrogen, 12.3; ammonia, 96.7; thiophenecarbonitrile, 2.6; 2-acetylthiophene, 3.1; 7-methyl-5-(2-thienyl)-thieno[2,3-*c*]pyridine (III), 50.5 mol%.

III: mp 103—104°C, colorless prisms. UV λ_{max}^{EtOH} mμ (log ε): 276 (4.3), 304 (4.0), 324 (4.0). Found: C, 62.15; H, 4.02; N, 5.91%. Calcd for $C_{12}H_9NS_2$: C, 62.34; H, 3.92; N, 6.06%.

Reductive Desulfurization of III with Raney Nickel Catalyst (W-1). A solution of III (10.0 g) in ethanol (800 ml) was stirred with a freshly-activated W-1 Raney nickel catalyst (100 g) under reflux for 60 hr. After the reaction mixture had then been filtered, the filtrate was concentrated, leaving a brown oil. The oil was divided by distillation into the fraction F_1 (bp 60—70°C/5 mmHg, colorless oil, yield 0.9 g), F_2 (bp 140—144°C/5 mmHg, pale yellow oil, yield 3.0 g), and a residue (yield 2.1 g). The fractions F_1 and F_2 were then both submitted to gas chromatography: from each fraction 2-*n*-butyl-4-ethyl-6-methylpyridine (V) and 5-*n*-butyl-7-methylthieno[2,3-*c*]pyridine (IV) were obtained in the pure state.

IV: UV λ_{max}^{EtOH} mμ (log ε): 231 (3.4), 273 (2.9), 298 (2.8). Found: C, 70.26; H, 7.26; N, 6.78%. Calcd for $C_{12}H_{15}NS$: C, 70.22; H, 7.37; N, 6.82%.

V: UV λ_{max}^{EtOH} mμ (log ε): 265 (3.7), 272 (3.7). Found C, 81.19; H, 10.82; N, 7.61%. Calcd for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90%.

A benzene solution of the residue was chromatographed on alumina, giving 1.2 g of III.

Reductive Desulfurization of IV with Raney Nickel Catalyst (W-4). A solution of IV (0.6 g) in ethanol (150 ml) was stirred with a freshly-activated W-4 Raney nickel catalyst (10 g) under reflux for 11 hr. After the reaction mixture had then been treated in a manner similar to that described above, a pale yellow oil (0.45 g) which was found to be composed of 70.6% of V by the gas-chromatographic estimation was obtained.

Oxidation of V. A solution of V (1.0 g) in pyridine (20 ml) was stirred with selenium dioxide (15.2 g) under reflux for 15 hr. The reaction mixture was filtered, and the filtrate was subjected to steam distillation. After active charcoal and chips of filter paper had then been added to the residue, the mixture was refluxed and then filtered. The filtrate was concentrated to about 20 ml and then allowed to stand overnight, giving pyridine 2,4,6-tricaraoxylic acid, mp 227°C (decomp.) (lit,[10] 227°C (decomp.)), as colorless crystals. Yield, 0.6 g (50%). This compound was identical the authentic sample prepared by the oxidation of 2,4,6-collidine.

Pyrolysis of II. Five grams of II were pyrolyzed under several conditions; the results are shown in Table 1.

5-Furyl-7-methyl-furo[2,3-*c*]pyridine (VI); mp 68—69°C, colorless prisms. NMR: τ 7.4 (3H, CH_3, *s*), 3.5 (1H, *m*), 3.0 (2H, *m*), 2.5 (2H, *m*), 2.2 (1H, *d*). UV λ_{max}^{EtOH} mμ (log ε): 241 (4.2), 268 (4.0), 277 (3.9), 320 (4.1). Found:

Table 1. Pyrolysis of II[a]

Conditions		Products, mol%							
Temp. (°C)	Time (min)	N_2	NH_3	F[b]	N[b]	A[b]	VI	VII	II
240	75	48.2	57.8	1.0	1.0	6.2	0	3.3	22.4
250	50	no determined		1.5	0.8	8.7	1.2	4.6	3.3
275	20	37.0	68.0	3.0	3.0	9.8	1.5	5.2	0

a) Intractable tars were formed in a large amount.
b) F: furan, N: furancarbonitrile, A: 2-acetylfuran.

8) All the melting points are uncorrected. The IR spectra were recorded on a Nippon Bunko IR-S spectrophotometer, while the UV spectra were measured in ethanol with a Shimadzu SV-50A spectrophotometer. The NMR spectra were determined in a carbon tetrachloride solution at 60 MHz with a Hitachi R-20 NMR spectrometer, using TMS as the internal reference. The multiplicity of signals is indicated in abbreviated form; *s*: signlet, *d*: doublet, *dd*: double doublet, *t*: triplet, *m*: multiplet. The mass spectra were obtained on a Hitachi RMS-4 mass spectrometer using a direct inlet and an ionization energy of 70 eV.

9) H. H. Szmant and H. J. Planinrek, *J. Amer. Chem. Soc.*, **72**, 4981 (1950).

10) R. Craf and F. Zelle, *J. Prakt. Chem.*, [2], **1937**, 148.

C, 72.61; H, 4.42; N. 6.95%. Calcd for $C_{12}H_9O_2N$: C, 72.37; H, 4.55; N, 7.07%.

2,4,6-Tri(2-furyl)pyridine (VII). A mixture of 2-2-acetylfuran (3.3 g), furfural (1.5 g), and ammonium acetate (15 g) in acetic acid (38 m*l*) was refluxed for 1 hr. After the reaction mixture had been extracted with benzene (100 m*l*), the benzene-extract was washed with water, dried over sodium sulfate, and then concentrated. A benzene solution of the residue was chromatographed over alumina, giving VII, mp 128—129°C, as colorless needles. Yield, 0.6 g (14 %).

Found: C, 73.73; H, 3.94; N, 5.00%. Calcd for $C_{17}H_{11}O_3N$: C, 73.64; H, 4.00; N, 5.05%.

This compound was identified by comparing its IR spectrum with that of the product melting at 128—129°C obtained in the pyrolysis of II.