REACTION OF FURAN DERIVATIVES WITH AMMONIA VIII THE SEPARATION OF REACTION PRODUCTS OF 2-ACETYLFURAN WITH AMMONIA BY SUBLIMATOGRAPHY

REACTION OF FURAN DERIVATIVES WITH AMMONIA VIII*

THE SEPARATION OF REACTION PRODUCTS OF 2-ACETYLFURAN WITH AMMONIA BY SUBLIMATOGRAPHY**

By

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Sublimation has long been recognized as a valuable technique for the separation or purification of organic compounds. Recently, technique of fractional sublimation using oil bath, the temperature of which can be changed alternately, was reported by Kaufmann *et al.* (1), and another method giving the temperature gradient to sublimato-tube by wire-heater was reported by Melhnish (2), but the method of "Sublimatography" reported by Shibata *et al.* (3) was theoretical and highly instructive for our investigation. Shibata *et al.* recognized that each chemical compounds have a new characteristic temperature-scale property just as boiling point or melting point, and named it "vacuum condensing point" (v.c.p.). And then, they suggested the possibility of separating mixed substances by this method and named it "Sublimatography".

Now, I should like to report on the separation of 2-methyl-3-hydroxypyridine-NH_4Cl and 2-methyl-pyrrylketimine from the reaction products of 2-acetylfuran and ammonia by the application of the improved sublimatography.

Experimental

A) Sublimato-scope The apparatus was named sublimato-scope, and is shown in Fig. 1. In this sublimato-scope, thermo-gradient heater was the most important instrument containing squalan as the thermo-medium, and every part in this heater was regulated automatically to keep the temperature constant

* The original report of this work in Japanese will be published in the Nippon Nogeikagaku Kaishi (J. Agr. Chem. Soc. Japan).

** The outline of this work will be published in the Chemistry and Industry (1960).

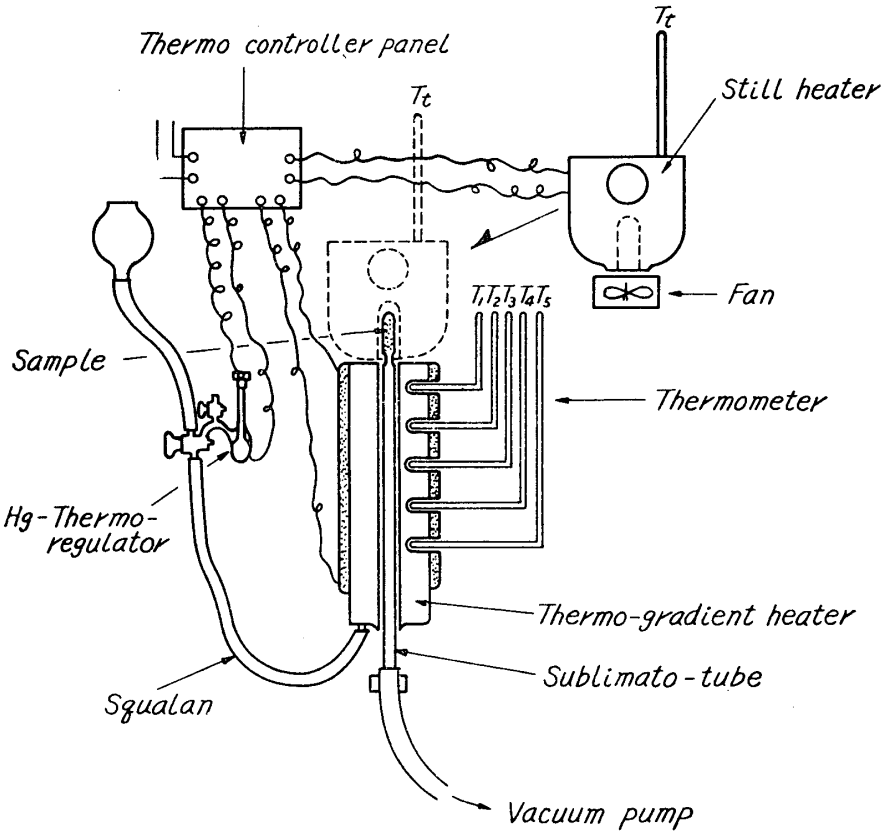

Fig. 1. The design of sublimato-scope.

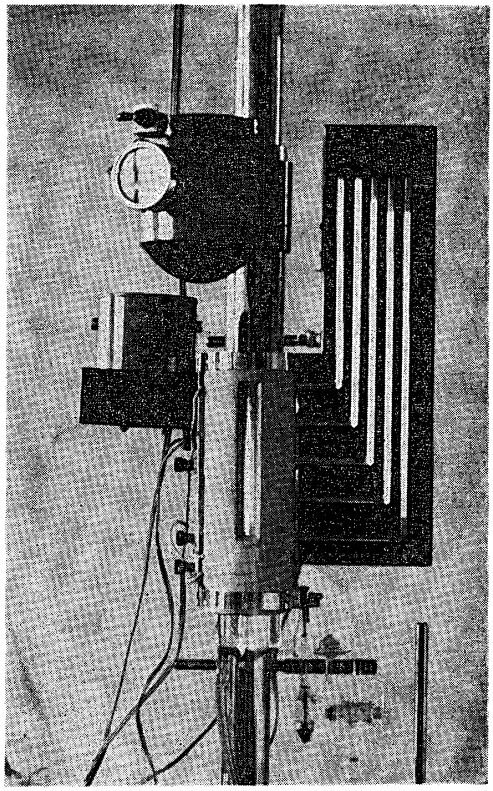

Photo. 1. Photography of the sublimato-scope.

by a thermo-regulator, moreover the temperature of each part was respectively different from each other, the temperature of the top-part was the highest in this heater, the lower the part of the heater went down, the lower the temperature of thermo-gradient heater became, that is a temperature gradient given thermometrically to the sublimato-tube, by this heater. The still heater in the top of this apparatus can heat until 300°C electrically, and the sample for sublimatography is heated in this still heater. The temperature of the still heater is explained by the term of T_t, the temperature of each part in thermo-gradient heater are shown by T_1, T_2, T_3, T_4 and T_5. Also the scale to measure the sublimed zone position is involved in the thermo-gradient heater.

B) Measuring of the vacuum condensing point.

The vacuum condensing point (v.c.p.) is calculated from the relationship between the zone position and the temperature of the thermo-gradient heater (T_1, T_2, T_3, T_4, T_5). The v.c.p. is a physical constant characteristic of every substance and is found to be independent of the temperature gradient and the diameter of the sublimato-tube used. The v.c.p. was calculated as shown in the following. In the figure, an axis of abscisses is the scale of the sublimed zone position, using cm as unit, and an axis of ordinates shows the temperatures of T_1, T_2, T_3, T_4 and T_5. Also the lines of T_1, T_2, T_3, T_4 and T_5 in the figure stand on the scale fit with a thermometer in the thermo-gradient heater. In the measuring of v.c.p., the temperatures of T_1, T_2, T_3, T_4 and T_5 are plotted on their lines, and the thermo-gradient curve is obtained by connecting every point as shown in Fig. 2. Next, the zone position is measured by the scale involved in the thermo-gradient heater, and its position is plotted on the thermo-gradient curve. The v.c.p. of substance can be calculated from the above curve.

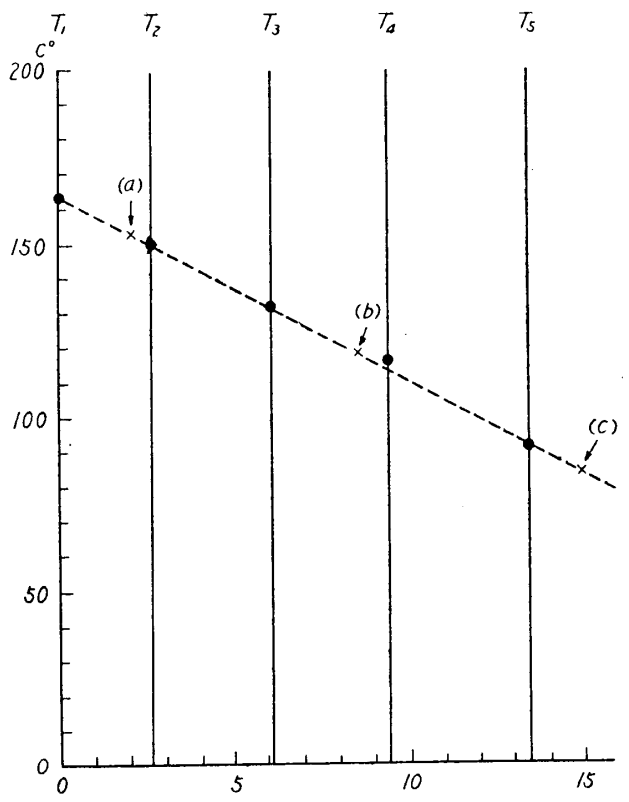

Fig. 2. The measuring of v.c.p.

C) The v.c.p. of β-hydroxy-pyridines

This work was carried out to consider the character of v.c.p., and v.c.p. of four kinds of β-hydroxy-pyridine which were measured as follows. From

the results, it was recognized that, v.c.p. was a physical constant characteristic of each substance, and was found to be independent of the temperature gradient and the diameter of the sublimato-tube used.

1) 2-Methyl-3-hydroxy-pyridine
   1st. T_t=178°C, T_1=137°C, T_2=121°C, T_3=105°C, T_4=84°C, T_5 =70°C
   zone position (cm)=3.5, reduced pressure=2 mmHg.
   v.c.p.=117°C/2 mm.
   2nd. T_t=180°C, T_1=152°C, T_2=140°C, T_3=122°C T_4=102°C, T_5=86°C
   zone position (cm)=6.5, reduced pressure =2 mmHg.
   v.c.p.=119°C/2 mm
2 2-Ethyl-3-hydroxy-pyridine
   1st. T_t=162°C, T_1=128°C, T_2=110°C, T_3=91°C T_4=72°C, T_5=60°C
   zone position (cm)=6.5, reduced pressure=2 mmHg.
   v.c.p.=90°C/2 mm
   2nd. T_t=186°C, T_1=150°C, T_2=140°C, T_3=123°C T_4=99°C, T_5=83°C
   zone position (cm)=11.0
   v.c.p.=92°C/2 mm
3) 2-Propyl-3-hydroxy-pyridine
   1st. T_t=163°C, T_1=121°C, T_2=109°C, T_3=93°C T_4=74°C, T_5=61.5°C
   zone position (cm)=5.5, reduced pressure=2 mmHg.
   v.c.p.=95°C/2 mm
   2nd. T_t=184°C, T_1=154°C, T_2=141°C, T_3=122°C T_4=98°C, T_5=82°C
   zone position (cm)=9.0, reduced pressure=2 mmHg.
   v.c.p.=96°C/2 mm
4) 2-[3-Methyl-4-methoxy-phenyl]-3-hydroxy-pyridine
   1st. T_t=226°C, T_1=177°C, T_2=160°C, T_3=139°C T_4=112°C, T_5=95°C
   zone position (cm)=1.5, reduced pressure=3 mmHg.
   v.c.p.=165°C/3 mm
   2nd. T_t=230°C, T_1=190°C, T_2=172°C, T_3=150°C T_4=128°C, T_5=105°C
   zone position (cm)=4.0, reduced pressure=3 mmHg.
   v.c.p.=163°C/3 mm

D) Separation of the reaction products by Sublimatography

2-Acetylfuran 3 g, liquid ammonia 10 *ml*, methanol 10 *ml* and NH_4Cl 0.5 g were heated in an autoclave at 180°C for 20 hr. The reaction mixture was diluted with 50 *ml* of methanol, and treated with active carbon. Drying after removal of the solvent and ammonia from the filtrate under reduced pressure, the dark brown syrup was obtained. Twenty mg of a sample was introduced in advance into one end of a glass tube (9 mm×40 cm), which is a sublimato-tube. The open end of the sublimato-tube was connected with the vacuum pump and the closed end containing the syrupy sample was closely inserted into the thermo-gradient heater having a thermo-regulator and temperature

gradient set up along the tube with the aid of squalan by heating it electrically. When the temperature of the sublimato-tube and thermo-gradient

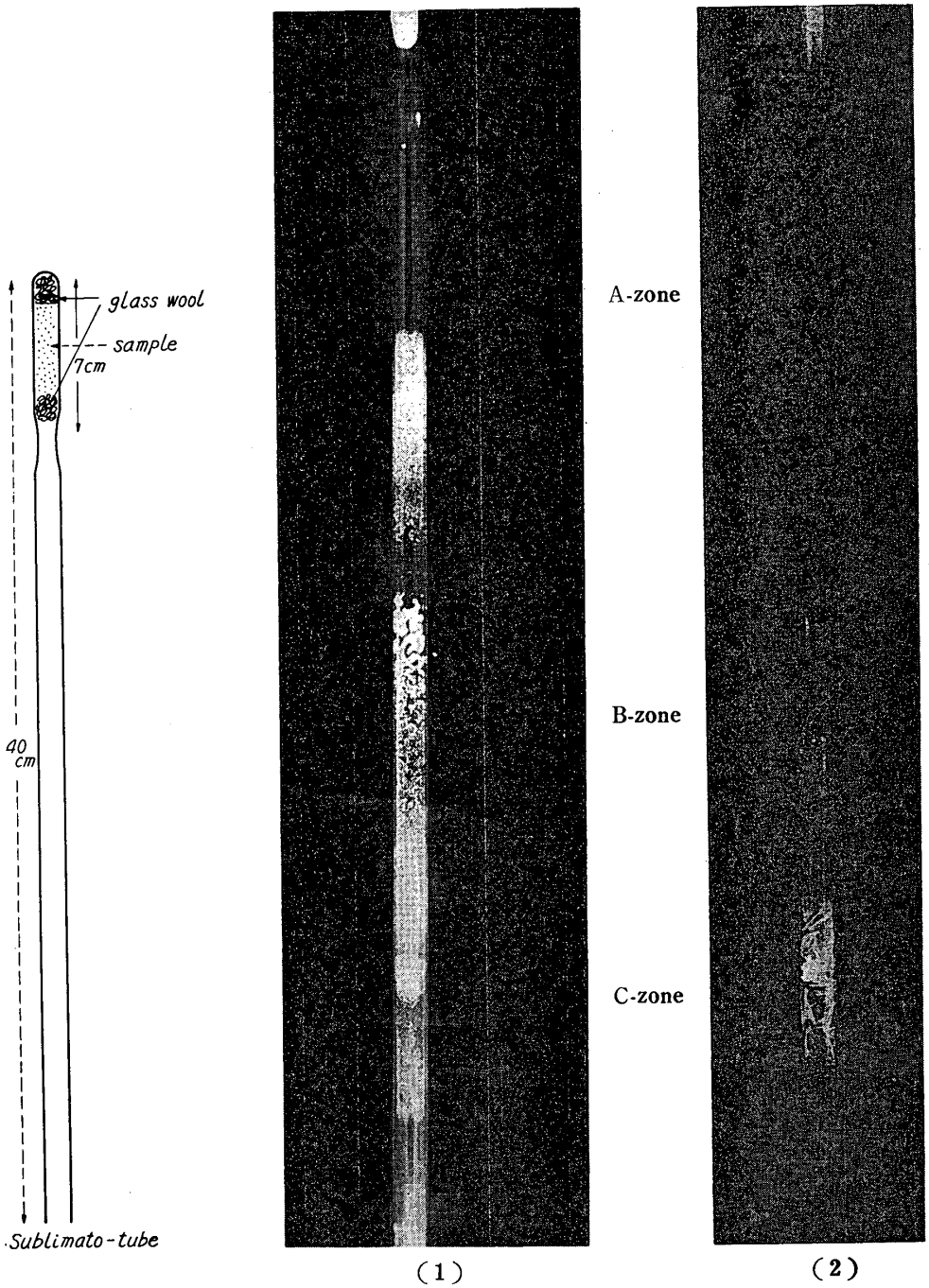

Photo. 2. Sublimatogram.
(1) A-zone, a mixture of white crystal and yellow oil
(2) A-zone, yellow oil

heater became equilibrium, 15~20 min. was required for the thermo-equilibrium, the closed end containing the sample was heated in a still heater under reduced pressure of 2 mmHg. The sample was fractionated into three zones, A,

B and C according to the difference of v.c.p. value of the components, and it took 10 min. to sublime. The v.c.p. was calculated from the relationship between the zone position and the temperature of thermo-gradient heater. The three zones could be separated by cutting the sublimato-tube carefully into three segments. The sublimatogram is shown in Photo. 2. A-zone: A-zone had the highest v.c.p. among the three zones, and was a mixture of colorless crystal and yellow oil. The v.c.p. of colorless crystal was 153°C/2 mm, the v.c.p. of yellow oil was 156°C/2 mm. The components of the A-zone is described in the following article. B-zone: The v.c.p. of B-zone was 119°C/2 mm, and B-zone was separated by cutting the sublimato-tube, m.p. 168~169°C, colorless prism, yield 7 mg. The melting point of this substance was not depressed on admixture with 2-methyl-3-hydroxy-pyridine. Also it was recognized to be identical with 2-methyl-3-hydroxy-pyridine by the application of the paper partition chromatographic method. C-zone: C-zone had the lowest v.c.p. among these products, and it was 83°C/2 mm, m.p. 91~92°C, a colorless needle, yield 3 mg. The melting point of this compound was not depressed on admixture with 2-acetylpyrrole, moreover it was recognized to be identical with 2-acetylpyrrole by the application of paper partition chromatography.

E) A mixture of A-zone

A-zone was a mixture of colorless crystal and yellow oil, and was dissolved into 5 *ml* of methanol. Methanol solution was spotted on filter paper, and was

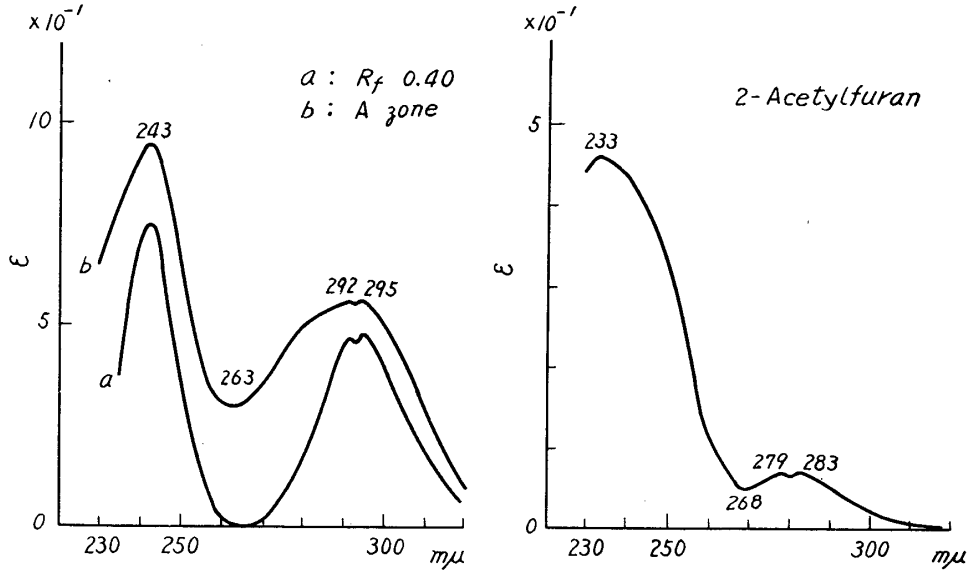

Fig. 3. The ultra-violet spectrums of A-zone, R_f 0.40-extract and 2-acetylfuran (MeOH).

submitted to paper partition chromatography as shown previously, two spots were detected in R_f 0.40 and R_f 0.55. The compound of R_f 0.40 agreed with the R_f value of presumed 2-methyl-pyrrylketimine, and then its spot was ex-

tracted with 5 *ml* of methanol, and the ultra-violet spectrum of methanol solution was compared with that of methanol solution described in Fig. 6 in the proceding report, it is shown in Fig. 3.

From the results, it was supposed that the compound of R_f 0.40, yellow oil might be identical with the compound mentioned in Part VII (I). R_f 0.55 was corresponding to that of 2-methyl-3-hydroxy-pyridine, but the melting point and v.c.p. values of this substance were different from that of 2-methyl-3-hydroxy-pyridine, m.p. of colorless crystal was 232°C, and this substance indicated a white color by $AgNO_3$ solution, a deep red color by $FeCl_3$ solution, a green color by Folin-Denis reagent. Its picrate was a yellow needle, m.p. 202~203°C, and was not depressed on admixture with the picrate of 2-methyl-3-hydroxy-pyridine. The infrared spectrum of this compound is shown in Fig. 4, and shows the absorption bands of NH^+ at 2870 and 2620 cm^{-1}, a cyclic C=N at 1570 cm^{-1}, CH_3 group at 1470 and 1380 cm^{-1}, β-hydroxy-pyridine at 800 cm^{-1}. From the above facts, it was supposed that this compound might be 2-methyl-3-hydroxy-pyridine-NH_4Cl.

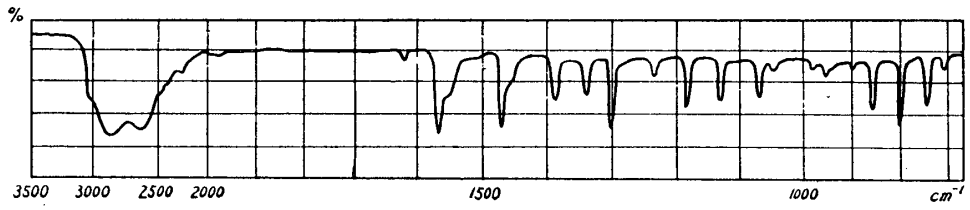

Fig. 4. The infrared spectrum of 2-methyl-3-hydroxy-pyridine-NH_4Cl.

F) 2-Methyl-3-hydroxy-pyridine-NH_4Cl.

2-Methyl-3-hydroxy-pyridine 70mg and 34 mg of NH_4Cl were dissolved into 10 *ml* of methanol, and this solution was allowed to stand over night. After removal of methanol under reduced pressure, the residue was dried over $CaCl_2$. The products were separated from the dried material by sublimatography, and two-zones were detected clearly in the zone positions of 1.5 cm and 6.0 cm. The former was v.c.p. 151°C/2 mm, and corresponding to that of 2-methyl-3-hydroxy-pyridine-NH_4Cl presumed above, a colorless prism, m.p. 230~232°C. The melting point of this 2-methyl-3-hydroxy-pyridine-NH_4Cl was not depressed on admixture with the compound mentioned in the above article. The compound of zone position 6.0 cm was v.c.p. 118°C/2 mm, 2-methyl-3-hydroxy-pyridine, colorless prism, m.p. 168~169°C.

G) 2-Methyl-pyrrylketimine (2-acetylpyrrole-imine).

When NH_4Cl was used as a catalyst, it was recognized that 2-methyl-3-hydroxy-pyridine-NH_4Cl was formed from 2-methyl-3-hydroxy-pyridine in the reaction product and NH_4Cl. Therefore, 2-acetylfuran 4 g, liquid ammonia 10 *ml* and 10 *ml* of methanol were heated in an autoclave at 180°C for 20 hr, and

the reaction mixture was diluted with 50 *ml* of methanol, and treated with active carbon. After removal of solvent under reduced pressure, 0.1 g of the residue for the sample of sublimatography was enveloped with thin tin-paper, and sublimatography was carried out to separate the reaction products. T_t= 214°C, T_1=160°C, T_2=148°C, T_3=130°C, T_4=104°C, T_5=87°C. Zone position (cm) 1.5, 8.0, 14.0, at reduced pressure 3 mmHg. The sample was fractionated into three zones, A, B and C-zone by the sublimatographic method. A-zone was yellow oil only, and did not contain 2-methyl-3-hydroxy-pyridine-NH_4Cl, v.c.p. 156°C/3mm. B-zone was 2-methyl-3-hydroxy-pyridine, v.c.p. 118°C/3 mm, m.p. 168~169°C, a colorless prism. C-zone was 2-acetylpyrrole, v.c.p. 84°C/3 mm, a colorless needle, m.p. 91°C. A-zone was cut carefully, this yellow oil was indicated a deep milky yellow color by the Mayer reagent, a deep red color by heating with the Ehrlich reagent. The yellow oil was dissolved into 5 *ml* of methanol, and methanol solution was submitted to paper partition chromatography, and one spot only was detected in the position of R_f 0.40. The ultra-violet spectrum of methanol solution is shown in Fig. 5, $\lambda_{max.}$ 243 mμ, 290 mμ, min. 260 mμ. From the above results, it was recognized that yellow oil separated by sublimatography might be 2-methyl-pyrrylketimine.

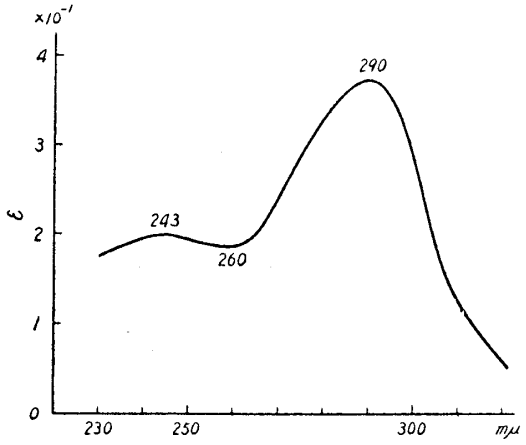

Fig. 5. The ultra-violet spectrum of 2-methyl-pyrrylketimine (MeOH).

i) $HgCl_2$ Salt: Yellow oil separated by sublimatography was dissolved in 5 *ml* of ethanol, and ethanol solution was poured into 10 *ml* of 10 per cent $HgCl_2$ solution, and it was allowed to stand overnight. The white yellow product was filtered, and dried over $CaCl_2$. The crude crystal was recrystallized from pyridine, and water successively. The $HgCl_2$ salt of 2-methyl-pyrrylketimine was obtained, a white yellow prism, m.p. 225°C. Anal. Found: N, 4.72 per cent, Calcd. for $C_6H_8N_2$. Hg. $HgCl_2$: N, 4.82 per cent.

ii) 2, 4-Dinitro-phenylhydrazone: Yellow oil was dissolved into 5 *ml* of

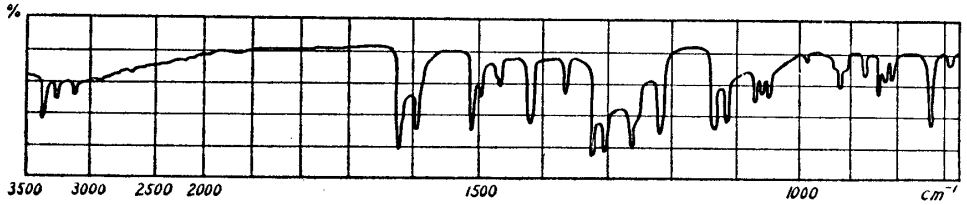

Fig. 6. The infrared spectrum of 2, 4-dinitro-phenylhydrazone of 2-methyl-pyrrylketimine.

methanol, 2, 4-dinitro-phenylhydrazone of 2-methyl-pyrrylketimine was prepared by the usual procedure, and recrystallized from methanol and ethylacetate, a red needle, m.p. 307°C. Anal. Found: C, 50.07; H, 3.91; N, 24.27 per cent. Calcd. for $C_{12}H_{11}N_5O_4$: C, 49.82; H, 3.81; N, 24.22 per cent. The infrared spectrum of this substance is shown in Fig. 6.

Summary

As a new technique of fractional sublimation, sublimatography was carried out to separate the reaction products of 2-acetylfuran with ammonia. 2-Methyl-3-hydroxy-pyridine, 2-acetylpyrrole, 2-methyl-3-hydroxy-pyridine-NH_4Cl and 2-methyl-pyrrylketimine were separated by the application of sublimatography.

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References

1) Kaufman, S., J. C. Medina and C. Zapata (1960). Anal. Chem., **32**, 192.
2) Melhnish, W. H. (1959). Nature, **184**, 1933.
3) Shibata, E. and S. Saito (1959). J. Chem. Soc. of Japan (ind. Chem Section.) **80**, 30.