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# REACTION OF FURAN DERIVATIVES WITH AMMONIA

## VI. REACTION OF 2-FURYL-ARYLKETONES WITH AMMONIA\*

By

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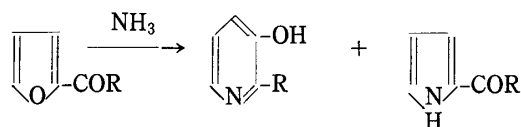
It was previously reported (1) that 2-alkyl-3-hydroxy-pyridines and 2-alkyl-pyrrylketones were formed from 2-furyl-alkylketones by reacting with ammonia.

The reaction of 2-furyl-arylketones with ammonia was reported by Dunlop (2), Gruber (3) and Leditischke (4), although their investigations in their procedure dealt almost exclusively with the formation of 2-aryl-3-hydroxy-pyridines, they did not mention the formation of 2-aryl-pyrrylketones.

In general, furan derivatives having a electron attractive group were cleaved at the furan nucleus by reacting them with ammonia, and obtained both 2-alkyl-3-hydroxy-pyridines and 2-alkyl-pyrrylketones by similar reaction, however, it was uncertain whether the reaction is ammonolytic cleavage (3, 4) or some other competitive reaction (2, 5).

This investigation was on a similar reaction in the hope that 2-aryl-3-hydroxy-pyridines and 2-aryl-pyrrylketones might be synthesized from 2-furyl-arylketones, and these were obtained by reacting 2-furyl-arylketones with ammonia under the same condition as mentioned previously.

Here we report on our findings of this investigation.



R : C<sub>6</sub>H<sub>5</sub> ( I ) ..... ( II ) ..... ( III )  
C<sub>6</sub>H<sub>4</sub>·CH<sub>3</sub> ( IV ) ..... ( V ) ..... ( VI )  
C<sub>6</sub>H<sub>3</sub> ( OCH<sub>3</sub> ) CH<sub>3</sub> ( VII ) ..... ( VIII ) ..... ( IX )  
C<sub>6</sub>H<sub>3</sub> ( OH ) CH<sub>3</sub> ( X )

\* The original report in Japanese of this work was contributed to Nippon Nogeikagaku Kaishi for publication (J. Agr. Chem. Soc. of Japan). (1960) 34, 411

## Experimental

### A) The syntheses of 2-furyl-arylketones.

#### 1) 2-Furyl-phenylketone (I), (6).

2-Furyl-phenylketone was prepared by Friedel-Crafts reaction using boron-trifluoride as a catalyst. Furan 50g, benzoic anhydride 100g were placed in a three-neckflask and stirred well under anhydrous condition for 30 min at 10°C. Addition of 1 ml of boron-trifluoride acetic acid solution caused a slight rise in temperature. The mixture was kept at 10–15°C for 1 hr with stirring, after stirring was continued at 35–40°C for 1.5 hr. The ketone was taken up with ether, washed with Na<sub>2</sub>CO<sub>3</sub> solution, and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, 47g of crude ketone was distilled under reduced pressure, b.p.<sub>10</sub> 170°C. After cooling, this substance formed a white crystalline, m.p. 43–44°C, and the yield was 69 per cent.

#### 2) 2-Furyl-*p*-tolylketone (2-[4-methyl-benzoyl]-furan) (IV), (7).

12 g of furoylchloride and toluene 30 g were heated in a reflux apparatus for 3 hr with the addition of anhydrous AlCl<sub>3</sub> 25 g several times. Reaction began at the first addition of AlCl<sub>3</sub> with copious evolution of HCl gas, and the temperature was regulated so as to keep the mixture in a state of gentle boiling. After heating for 3 hr, the resulting mixture was submitted to distillation under reduced pressure. The first portion of distillation contained a small amount of toluene, the ketone was distilled at 180–183°C/20 mm. and the yield was about 12 g (70 per cent), m.p. 41–42°C.

#### 3) 2-[3-Methyl-4-methoxy-benzoyl]-furan (VII), (8).

Tamura and Kuyama (8) prepared this compound from furoylchloride and *o*-cresyl-methylether (*o*-methoxytoluene) by Friedel-Crafts reaction using anhydrous AlCl<sub>3</sub> as a catalyst, VII was kindly supplied for this investigation by them.

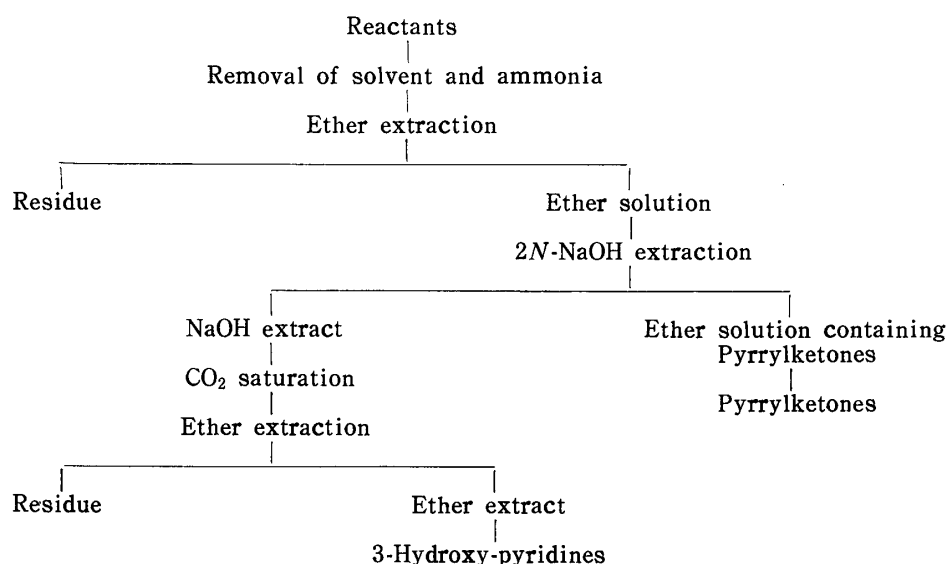
### B) The reaction of 2-furyl-arylketones with ammonia and the isolation of reaction products.

The reactants as shown in Table 1 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. After removal of the solvent and ammonia at reduced pressure, the residue was taken up with ether. Ether solution containing hydroxy-pyridines and pyrrolketones was extracted to isolate hydroxy-pyridines having a phenolic character with 2*N*-NaOH solution, pyrrolketones remained in the ether solution, and NaOH solution was saturated with CO<sub>2</sub> and then extracted again with ether for 48 hr. Hydroxy-pyridines were obtained from the ether extract.

The isolation method of hydroxy-pyridines and pyrrolketones is shown in the following.

**Table 1.** The yields of 2-aryl-3-hydroxy-pyridines and 2-aryl-pyrrylketones.

|   |                       |          |
|---|-----------------------|----------|
| (1) Reactants (180°C, 20 hr)  | Yield % (theoretical) |          |
| (I) 2g, Liq. NH <sub>3</sub> 10 ml, MeOH 10 ml                            | (II) 25               | (III) 15 |
| (I) 2g, Liq. NH <sub>3</sub> 10 ml, NH <sub>4</sub> Cl 0.5g               | 15                    | 10       |
| (I) 2g, 28% NH <sub>4</sub> OH 20 ml, MeOH 20 ml                          | 22                    | 10       |
| (2) Reactants (180°C, 20 hr)  | Yield % (theoretical) |          |
| (IV) 2g, Liq. NH <sub>3</sub> 10 ml, MeOH 10 ml                           | (V) 30                | (VI) 25  |
| (IV) 2g, Liq. NH <sub>3</sub> 10 ml, NH <sub>4</sub> Cl 0.5g              | 25                    | 20       |
| (IV) 2g, 28% NH <sub>4</sub> OH 20 ml, MeOH 20 ml                         | 40                    | 20       |
| (3) Reactants (180°C, 20 hr)  | Yield % (theoretical) |          |
| (VII) 2g, Liq. NH <sub>3</sub> 10 ml, MeOH 10 ml, NH <sub>4</sub> Cl 0.5g | (VIII) 40             | (IX) 5   |
| (VII) 2g, Liq. NH <sub>3</sub> 10 ml, NH <sub>4</sub> Cl 0.5g             | 35                    | 30       |
| (VII) 2g, 28% NH <sub>4</sub> OH 25 ml, MeOH 15 ml                        | 25                    | 10       |
| (VII) 2g, 10% Alcoholic ammonia 20 ml                                     | 20                    | 20       |

**2-Phenyl-3-hydroxy-pyridine (II), (2, 3, 4)**

II was purified by the method of sublimation under reduced pressure, and then recrystallized from methanol, colorless prism, m.p. 202°C. The yield of II is shown in Table 1. Anal. Found: C, 77.12; H, 5.32; N, 8.23 per cent. Calcd. for C<sub>11</sub>H<sub>9</sub>NO: C, 77.17; H, 5.30; N, 8.18 per cent. II indicated a deep red color with FeCl<sub>3</sub> solution, and a deep green color with Folin-Denis reagent. The ultra-violet spectrum of II is shown in Fig. 1,  $\lambda_{\max}$  300 m $\mu$ ,  $\lambda_{\min}$  260m $\mu$ . The infra-red spectrum of II had characteristic absorption bands as shown in Fig. 3, and also showed the hydroxyl group to be present in bonded form since it had two very broad bands centered at 2500 cm<sup>-1</sup> and 1800 cm<sup>-1</sup>. OH-N intermolecular hydrogen bond existed and this accounted for the wide spread for

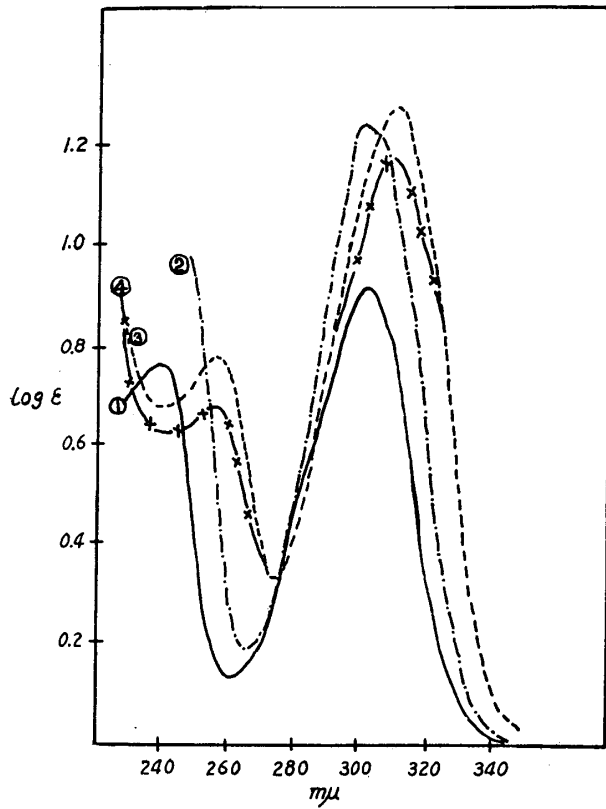


Fig. 1. The ultra-violet spectrum of 2-aryl-3-hydroxy-pyridines.

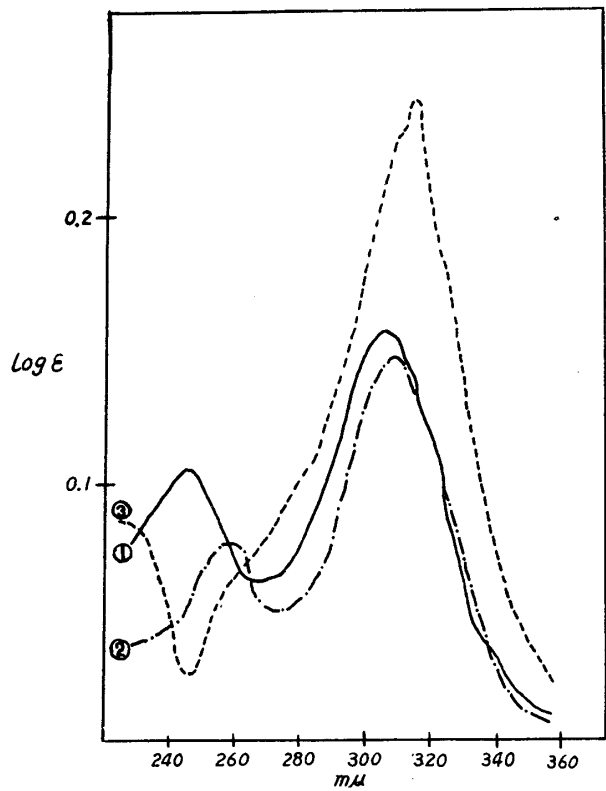
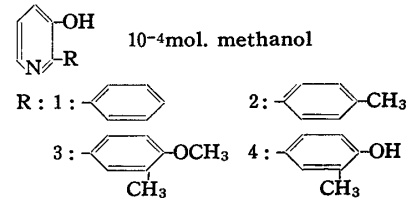
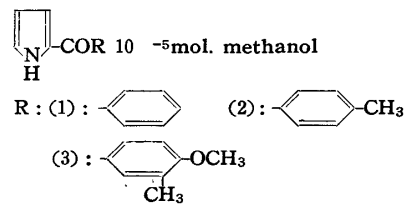


Fig. 2. The ultra-violet spectrum of 2-aryl-pyrrolylketones.



absorption.

*2-Phenyl-pyrrylketone* (III), (9).

III was recrystallized from hot-water, colorless needle, m.p. 78–79°C. Anal. Found: N, 8.32 per cent Calcd. for  $C_{11}H_9NO$ : N, 8.18 per cent. This melting point was identical with that of 2-phenyl-pyrrylketone described by Oddo (9). The ultra-violet spectrum of III is shown in Fig. 2,  $\lambda_{max}$  307m $\mu$ ,  $\lambda_{min}$  270m $\mu$ .

*2-Tolyl-3-hydroxy-pyridine* (V), (4).

V was recrystallized from methanol, colorless prism, m.p. 200°C. Anal. Found: C, 78.02; H, 5.94; N, 6.96 per cent Calcd. for  $C_{12}H_{11}NO$ : C, 77.81; H, 5.95; N, 7.56 per cent. V indicated a deep red color with  $FeCl_3$  solution, and a deep green color with Folin-Denis reagent. The ultra-violet spectrum of V is shown in Fig. 1,  $\lambda_{max}$  300m $\mu$ ,  $\lambda_{min}$  265m $\mu$ . The infrared spectrum of V is shown in Fig. 3.

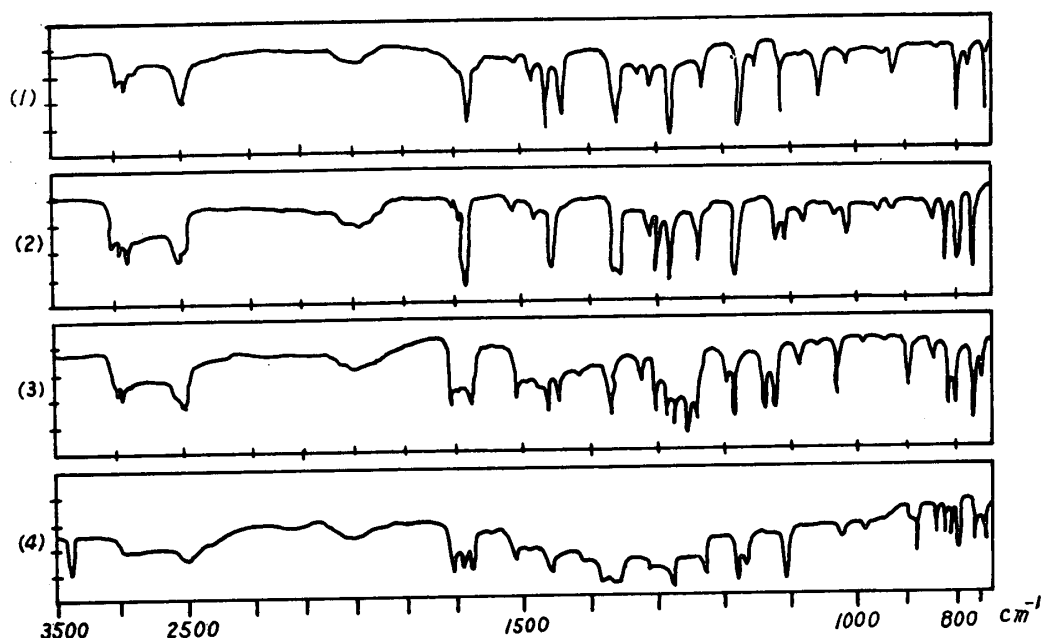
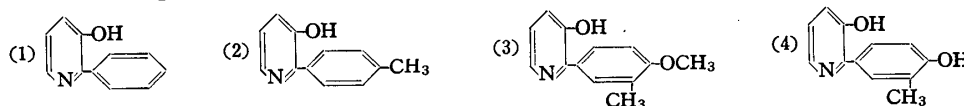


Fig. 3. The infra-red spectrum of 2-aryl-3-hydroxy-pyridines.



*2-Tolyl-pyrrylketone* (VI).

VI was recrystallized from hot-water, colorless needle, m.p. 119–120°C. Anal. Found: N, 7.62 per cent Calcd. for  $C_{12}H_{11}NO$ : N, 7.56 per cent. This substance showed no color reaction with Ehrlich reagent (dil. HCl solution of *p*-dimethylamino-benzaldehyde) in the cold, however, it showed a deep red color when heated, and showed a substitute group to be present in  $\alpha$ -position. The ultra-violet spectrum of VI is shown in Fig. 4,  $\lambda_{max}$  308m $\mu$ ,  $\lambda_{min}$  272m $\mu$ .

The infra-red spectrum of VI is shown in Fig. 4, and shows the characteristic absorption bands as following ( $\text{cm}^{-1}$ ), 3300, 1615, 1605, 1565, 1540, 1425, 1395, 830, 750.

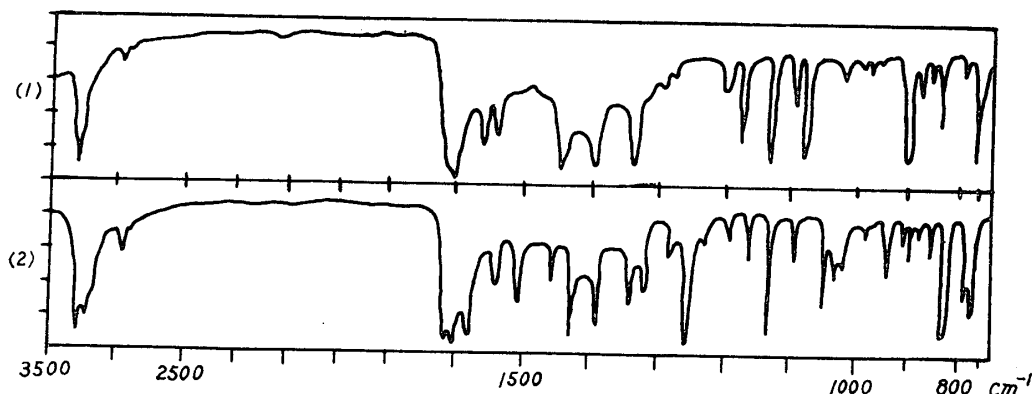
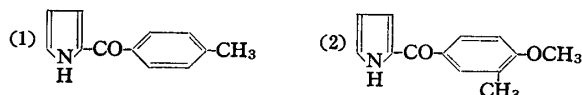


Fig. 4. The infra-red spectrum of 2-aryl-pyrrolketones.



*2-(3-Methyl-4-methoxy-phenyl)-3-hydroxy-pyridine (VIII).*

By reacting 2-furyl-arylketones having a hydroxyl group with ammonia, it was thought that both reaction products have phenolic character, and it is very difficult to isolate them from the reaction mixture, so in this work the same reaction as described above was carried out using methylated VII as the starting material.

VIII was recrystallized from ethanol, colorless prism, m.p. 181–182°C. Anal. Found: C, 72.57; H, 6.20; N, 6.10 per cent Calcd. for  $\text{C}_{13}\text{H}_{13}\text{NO}_2$ : C, 72.55; H, 6.04; N, 6.05 per cent. VIII indicated a deep red color with  $\text{FeCl}_3$  solution, and a deep green color with Folin-Denis reagent. Its picrate was prepared by the usual method, recrystallized from hot-water, yellowish needle, m.p. 205°C. Anal. Found: N, 12.85 per cent Calcd. for  $\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_9$ : N, 12.61 per cent. The ultra-violet spectrum of VIII is shown in Fig. 1,  $\lambda_{\text{max}}$  309 $\text{m}\mu$ ,  $\lambda_{\text{min}}$  272 $\text{m}\mu$ . The infra-red spectrum of VIII is shown in Fig. 3, and shows the characteristic absorption bands as follows ( $\text{cm}^{-1}$ ); phenyl radical at 3030, 2990, 1610, 1585, 1515; cyclic C=N 1575; methyl group 1465, 1370; methoxy group of benzene 1255;  $\alpha$ ,  $\beta$ -di-substituted pyridine 1185, 1055, 990; 1, 3, 4-tri-substituted benzene 895, 817;  $\beta$ -hydroxy-pyridine 800.

*2-(3-Methyl-4-methoxy-phenyl)-pyrrolketone (IX).*

IX was recrystallized from hot-water, colorless prism, m.p. 139°C. Anal. Found: C, 72.63; H, 6.15; N, 5.93 per cent Calcd. for  $\text{C}_{13}\text{H}_{13}\text{NO}_2$ : C, 72.55; H, 6.04; N, 6.05 per cent. This substance indicated a deep red color by heating with Ehrlich reagent as mentioned above. The ultra-violet spectrum of IX is shown

in Fig. 2,  $\lambda_{\max}$  317m $\mu$ ,  $\lambda_{\min}$  246m $\mu$ . The infrared spectrum of IX is shown in Fig. 4, and shows the characteristic absorption bands in the following ( $\text{cm}^{-1}$ ); NH absorption bands at 3298, 1548; phenyl radical 3020, 2990, 1577, 1508; the overlap of carbonyl group and phenyl radical 1615~1595; methyl group 1457, 1378; methoxy group of benzene 1255; 1, 3, 4-tri-substituted benzene 895, 814. 2-(*o*-Cresyl)-3-hydroxy-pyridine (X).

0.2g of VIII and 10 ml of 47 per cent HBr were heated in a reflux apparatus for 1.5 hr. After removal of HBr under reduced pressure, the residue was taken up with 2*N*-NaOH solution. NaOH solution was saturated with CO<sub>2</sub> and then extracted with ether for 48 hr. 0.15g of X was obtained from the ether extract. X was recrystallized from ethanol, colorless prism, m.p. 241—242°C. Anal. Found: C, 71.62; H, 5.61; N, 6.91 per cent. Calcd. for C<sub>12</sub>H<sub>11</sub>NO<sub>2</sub>: C, 71.64; H, 5.47; N, 6.96 per cent. X indicated a deep red color with FeCl<sub>3</sub> solution, and a deep green color with Folin-Denis reagent. The ultra-violet spectrum of X is shown in Fig. 1,  $\lambda_{\max}$  309m $\mu$ ,  $\lambda_{\min}$  273m $\mu$ . When the infra-red spectrum of X was compared with that of VIII, X has the characteristic absorption bands as shown in Fig. 3. Absorption band of hydroxyl group appeared at 3340  $\text{cm}^{-1}$ , but absorption band of methoxy group of benzene at 1255  $\text{cm}^{-1}$  displaced with that of hydroxy group.

VIII, IX and X described above are the hitherto unknown compounds, however, from the facts presented above, the authors believe these compounds to be VIII, IX and X respectively.

### Summary

2-Aryl-3-hydroxy-pyridines and 2-aryl-pyrrylketones were obtained by reacting 2-furyl-arylketones with ammonia under the same condition as mentioned previously, that is 2-phenyl-3-hydroxy-pyridine (II) and 2-phenyl-pyrrylketone (I) with ammonia; 2-tolyl-3-hydroxy-pyridine (V) and 2-tolyl-pyrrylketone (VI) from 2-furyl-*p*-tolylketone (IV); 2-(3-methyl-4-methoxy-phenyl)-3-hydroxy-pyridine (VIII) and 2-(3-methyl-4-methoxy-phenyl)-pyrrylketone (IX) from 2-(3-methyl-4-methoxy-benzoyl)-furan (VII); and also 2-(3-methyl-4-hydroxy-phenyl)-3-hydroxy-pyridine (X) by de-methylation of 2-(3-methyl-4-methoxy-phenyl)-3-hydroxy-pyridine (VIII).

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**References**

- 1) Sugisawa, H. and K. Aso (1959). *Nippon Nogei-kagaku Kaishi*, **33**, 259, 351, 353.
- 2) Dunlop, A. P. and S. Swadesh (1953). U. S. pat., 2,636,882.
- 3) Gruber, W. (1953). *Can. J. Chem.*, **31** 564.
- 4) Leditischke, H. (1952). *Ber.*, **85**, 202.
- 5) Aso, K. (1937). *Bull. of Inst. Phys. Chem. Res.*, **18** 171.
- 6) Hartough, H. D. (1950). U. S. pat., 2,515,123.
- 7) Borsche, W. and H. Leditischke (1937). *Ann.*, **529**, 108.
- 8) Tamura, T. and S. Kuyama, Unpublished.
- 9) Oddo, B. (1910). *Ber.*, **43**, 1012.