*Dihydropyridine Derivatives. I. The Reaction of 1,4-Diphenyl-3,5-diacetylpyridinium Salts with Inorganic Bases**

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During the structural studies of 1, 4-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (I), a chromium-containing compound was isolated by Inouye⁽¹⁾ from a reaction mixture of I with chromium trioxide in acetic acid, although its structure has not yet been determined. In the present investigation, this compound was found to be 1, 4-diphenyl-3, 5-diacetylpyridinium bichromate (II) on the basis of its analysis, its infrared spectrum and its reaction with inorganic bases. In addition, some new pyridinium salts have been prepared and their reactions with inorganic bases studied.

Mumm⁽²⁾ and Borsche⁽³⁾ reported that 1, 4-dihydropyridine derivatives were oxidized to pyridine derivatives with chromium trioxide. However, the isolation of bichromates of pyridine or its derivatives has not been reported. In the present investigation, I was oxidized to II with chromium trioxide in acetic acid. It was found that II is stable even when heated in water, but in organic solvents such as acetic acid, alcohols or acetone, it was decomposed by long heating. A characteristic blue fluorescence was observed with I, but not with II, either in the solid state or in solution. The infrared spectrum of I has an absorption band at 1645 cm^{-1} ($\nu_{C=O}$) which is attributed to a vinylogous amide gruop,⁽⁴⁾ while that of II has a band at 1700 cm^{-1} ($\nu_{C=O}$). These facts indicate that the dihydropyridine ring of I was oxidized to a pyridinium ring. The elementary analysis of II also supports the pyridinium salt structure.

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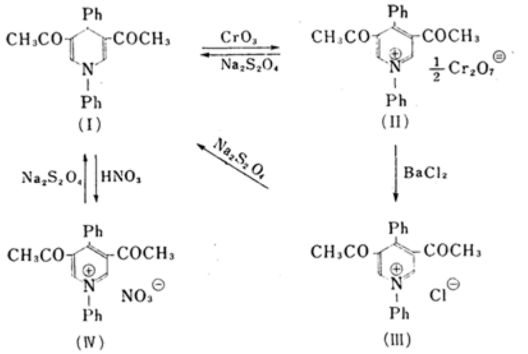
1) G. Inouye, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **79**, 1243 (1958).

2) O. Mumm and W. Beth, *Ber.*, **54**, 1591 (1921).

3) W. Borsche and H. Hahn, *Ann.*, **537**, 219 (1939).

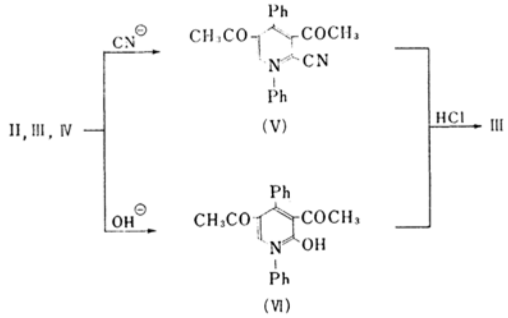
4) A. G. Anderson and G. Berkelhammer, *J. Am. Chem. Soc.*, **80**, 992 (1958).

By treatment with barium chloride, II was converted to 1, 4-diphenyl-3, 5-diacetylpyridinium chloride (III). By oxidation with nitric acid, I gave 1, 4-diphenyl-3, 5-diacetylpyridinium nitrate (IV). Infrared spectra of III and IV, like those of II, show their carbonyl band at 1700 cm^{-1}. Also, they did not show fluorescence, as was expected from the pyridinium structure.

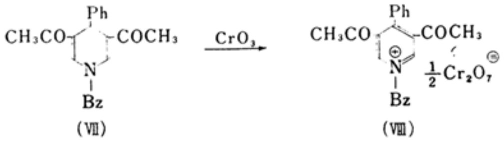


The reaction of II, III and IV with sodium dithionite gave a yellow crystalline compound (m. p. 181°C), which was identified with I by a study of their infrared spectra and by a mixed melting point determination. It has been known that the reduction of a pyridinium derivative with sodium dithionite affords a 1, 4-dihydropyridine derivative.[5]

Mumm[2] reported the formation of an addition compound of the cyano group by the treatment of pyridinium derivatives with potassium cyanide. II, III and IV were converted to 2-cyano-1, 2-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (V) by reaction with potassium cyanide. The infrared spectrum of V exhibits split carbonyl bands at 1672 cm^{-1} and 1646 cm^{-1} instead of a single band at 1645 cm^{-1} this can be attributed to two acetyl groups at the 3 and 5 positions. The shift to the higher frequency (1672 cm^{-1}) seems to be due to the decrease in the conjugation of the acetyl group with the dihydropyridine ring. It is reasonable that this decrease may be caused by the interaction of the bulky phenyl group and the cyano group.[6] The reaction of II, III and IV with such bases as sodium hydroxide, potassium carbonate or sodium acetate afforded 2-hydroxy-1, 2-dihydro-1, 4-diphenyl-3,5-diacetylpyridine (VI). No compound analogous to VI has yet been isolated by the reaction of pyridinium salt, similar to the cases of II, III or IV with hydroxide ions. VI is unstable and can be recrystallized only from ethylene dichloride. The infrared spectrum of VI shows bands at 1660 and 1608 cm^{-1} ($\nu_{C=O}$); the latter band is attributed to the 3-acetyl group hydrogen-bonded with the 2-hydroxy group. V and VI show a bluish-green fluorescence in the solid state as well as in solution. They were decomposed by being heated in organic solvents for a long time. After acidifying an ethanolic solution of V and VI with hydrochloric acid, the solvent was removed under reduced pressure to give colorless crystals. These were identified with III by mixed melting point determination and by a study of the infrared spectrum.



In the same way, 1-benzyl-4-phenyl-1, 4-dihydro-3, 5-diacetylpyridine (VII) was also oxidized to 1-benzyl-4-phenyl-3, 5-diacetylpyridinium bichromate with chromium trioxide.



Experimental

1, 4-Diphenyl-3, 5-diacetylpyridinium Bichromate (II).—A solution of 1 g. of chromium trioxide in 1 ml. of water and 2 ml. of acetic acid was added gradually to a solution of 0.5 g. of 1, 4-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (I) in 10 ml. of acetic acid. The resulting solution immediately became yellowish brown and cloudy, and then an oily product separated. The mixture was heated at 50°C for ten minutes, and 10 ml. of water was added. After standing at room temperature, 0.42 g. of orange crystals were obtained. Recrystallization from water gave 1, 4-diphenyl-3, 5-diacetylpyridinium bichromate (II) as orange-yellow plates; these did not show a definite decomposition point, but gradually turned black above 150°C.

Found: C, 59.44; H, 4.33; N, 3.27. Calcd. for $C_{21}H_{18}O_{21}N \cdot 1/2(Cr_2O_7)$: C, 59.43; H, 4.24; N, 3.30%.

1, 4-Diphenyl-3, 5-diacetylpyridinium Chloride (III).—To a solution of 0.5 g. of II in 100 ml. of hot water, 0.1 g. of barium chloride in 10 ml. of

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[5] D. Mauzerall and F. H. Westheimer, ibid., 77, 2261 (1958); R. F. Hutton and F. H. Westheimer, *Tetrahedron*, 3, 73 (1958).

[6] Curiously the infrared spectrum of V has not a band due to C≡N bond stretching. Reasonable explanation can not be given at present.

water was added in one portion. The solution immediately became yellowish and cloudy. The mixture was heated in a water bath for 1 hr. After the solution had cooled, the precipitate was filtered off and the filtrate was concentrated to dryness under reduced pressure. Ethanol (10 ml.) was added to the residue, the insoluble substance was filtered off, and the filtrate was concentrated to dryness under reduced pressure. The same procedures were repeated several times. The final residue was recrystallized from ethanol-ethyl acetate to give 1, 4-diphenyl-3, 5-diacetylpyridinium chloride (III) (0.35 g.) as colorless needles (m. p. 245～247°C (decomp.)).

Found: N, 3.99. Calcd. for $C_{21}H_{18}O_2NCl$: N, 3.96%.

1, 4-Diphenyl-3,5-diacetylpyridinium Nitrate (IV). I (0.5 g.) was dissolved in 30 ml. of methanol, and 0.5 ml. of concentrated nitric acid was added. The mixture was allowed to stand at room temperature overnight. The solvent was distilled off under reduced pressure, and the residue was recrystallized from ethanol-ethyl acetate. 1, 4-Diphenyl-3, 5-diacetylpyridinium nitrate (IV) (0.32 g.) was obtained as pale brownish needles (m. p. 177～178°C (decomp.)).

Found: N, 7.17. Calcd. for $C_{21}H_{18}O_5N_2$: N, 7.40%.

The Reduction of III with Sodium Dithionite.—To a solution of 0.1 g. of III in 10 ml. of water, 0.5 g. of sodium dithionite was added. The solution became yellowish and exhibited a blue fluorescence. After standing at room temperature for 3 hr., the separated precipitate was collected by filtration. Recrystallization from ethanol gave greenish yellow prisms (0.07 g., m. p. 181°C). No depression of melting point was observed on admixture with an authentic sample of I.

The Reduction of II and IV with Sodium Dithionite.—When the reduction of II and IV with sodium dithionite was carried out as described above for III, I was obtained in both cases.

2-Cyano-1, 2-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (V).—(i) To a solution of 0.4 g. of II in 100 ml. of water, 1.5 g. of potassium cyanide in 5 ml. of water was added. The solution became yellowish and cloudy. After the solution had stood overnight in an ice box, the yellowish crystals were collected by filtration. Recrystallization from ethanol-water gave 2-cyano-1, 2-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (V) (0.28 g.) as yellowish green needles (m. p. 154～155°C).

Found: C, 77.35; H, 5.10; N, 7.87. Calcd. for $C_{22}H_{18}O_2N_2$: C, 77.19; H, 5.26; N, 8.18%.

(ii) The similar reaction of III or IV with potassium cyanide afforded the same compound V.

The Reaction of V with Hydrochloric Acid.—To a solution of 0.2 g. of V in 5 ml. of ethanol, 0.1 ml. of concentrated hydrochloric acid was added. The solution turned from yellowish to colorless. After ten minutes, the solvent was distilled off under reduced pressure and the residue was recrystallized from ethanol-ethyl acetate to give colorless needles (0.12 g.) (m. p. 245～247°C). No depression of melting point was observed on admixture with an authentic sample of III.

2-Hydroxy-1, 2-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (VI).—To a solution of 0.3 g. of III in 5 ml. of water, 0.2 g. of potassium carbonate in 4 ml. of water was added. The solution immediately became yellowish and cloudy. After a few minutes, the yellow precipitates which had separated out were collected by filtration and the crude product was dissolved in ethylene dichloride at 20～30°C. The solution was cooled in an ice box, and 2-hydroxy-1, 2-dihydro-1, 4-diphenyl-3, 5-diacetylpyridine (VI) (0.2 g.) was obtained as yellowish prisms (m. p. 145～147°C (decomp.)).

Found: N, 4.14. Calcd. for $C_{21}H_{19}O_3N$: N, 4.20%.

II and IV also afforded VI by similar procedures. VI was also obtained by the treatment of II, III or IV with sodium hydroxide or sodium acetate instead of potassium carbonate.

1-Benzyl-4-phenyl-3, 5-diacetylpyridinium Bichromate (VIII).—A solution of 0.2 g. of chromium trioxide in 1 ml. of water and 3 ml. of acetic acid was added to a solution of 0.06 g. of 1, 4-dihydro-1-benzyl-4-phenyl-3, 5-diacetylpyridine (VII) in 3 ml. of acetic acid. The mixture was heated at 40°C for ten minutes, and 10 ml. of water was added. After cooling, 0.04 g. of orange crystals were obtained by filtration. Recrystallization from water gave orange yellow plates which decomposed at 350°C.

Found: C, 60.10; H, 4.57; N, 3.25. Calcd. for $C_{22}H_{20}O_2N \cdot 1/2Cr_2O_7$: C, 60.27; H, 4.60; N, 3.19%.

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