151°. Recrystallization of A from ethanol raised the m.p. to 163–164°, and a third recrystallization failed to change the melting point. The crystallization filtrates were concentrated and chilled to yield 7 g. of yellow solid (B), m.p. 195–197°. Recrystallization of B raised the melting point to 198–200° (C). A sample of A, after storage for several years in a glass-stoppered bottle, was found to melt at 198–200°.

(A) *Anal.* Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.0; H, 4.4; N, 12.4. Found: C, 69.2; H, 4.6; N, 12.4. (B) *Anal.* Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.0; H, 4.4; N, 12.4. Found: C, 68.9; H, 4.6; N, 11.9.

The ultraviolet and solution spectra of samples A, B, and C were identical.

Method 3.—A mixture of the picoline (1.0 mole), the aldehyde (1.0 mole), and 2 g. of anhydrous zinc chloride was placed in an autoclave and heated at 200° for 16 hr. The product was isolated by distillation of the reaction mixture under reduced pressure. This method of isolation was used in all cases except those of the 4′-dimethylamino- and 4′-nitrostyrylpyridines. In preparing these, the crude reaction mixtures were dissolved in dilute hydrochloric acid, and the solution steam distilled to remove any unreacted aldehyde. The reaction product was then made basic again by the addition of solid sodium carbonate. The resulting solid was isolated by filtration, washed with water, and dried before being recrystallized from an appropriate solvent.

Method 4. a. 2-Styrylpyridine.—To a solution of sodium ethoxide prepared from 3.9 g. (0.17 mole) of sodium and 400 ml. of absolute ethanol was added, with vigorous stirring in a nitrogen atmosphere, 84.2 g. (0.194 mole) of benzyltriphenylphosphonium bromide, followed by 16.5 g. (0.154 mole) of 2-pyridinealdehyde. The resulting mixture was stirred 60 hr., poured into 2 l. of ice–water, and extracted with four 250-ml. portions of ether. After the combined ether extract was washed with 200 ml. of cold water, it was dried over anhydrous magnesium sulfate. The drying agent was filtered, and the ether distilled using a steam bath to give 61 g. of pale yellow residue, which was then slurried with 100 ml. of petroleum ether (b.p. 60–90°). The slurry was filtered and the filtrate concentrated on a steam bath at the water pump. After the residue, which weighed 18 g., was dissolved in 150 ml. of 2 *N* hydrochloric acid, it was extracted with two 50-ml. portions of benzene. The aqueous layer was separated and made alkaline with 2 *N* sodium hydroxide. The alkaline solution was extracted with three 50-ml. portions of benzene. The benzene extract was distilled, to give 14 g. of pale yellow liquid, b.p. 122–145° (1 mm.), $n^{25}D$ 1.6392. The solid which separated from the distillate was removed by filtration, and the remaining oil redistilled to give 7.0 g. (25%) of colorless *cis*-2-styrylpyridine, b.p. 93–96° (0.4–0.5 mm.), $n^{25}D$ 1.6267. Gas chromatography of the *cis*-2-styrylpyridine showed that it contained a maximum of 0.2% *trans*-2-styrylpyridine.

Anal. Calcd. for $C_{13}H_{11}N$: C, 86.2; H, 6.1; N, 7.7. Found: C, 86.5; H, 6.3; N, 7.9.

The residues which solidified upon cooling were combined from the distilling pot with the solid from the first distillation and recrystallized from 200 ml. of petroleum ether (b.p. 30–60°) to give 2.7 g. (9.9%) of *trans*-2-styrylpyridine, m.p. 92–93.5°.

b. 4-Styrylpyridine.—The procedure used was identical with that used for the preceding preparation (a) for *cis*-2-styrylpyridine, except that 18.0 g. (0.168 mole) of 4-pyridinealdehyde was used. The crude product obtained from concentration of the filtrate from the petroleum ether slurry was distilled directly to give 12.7 g. (42%) of colorless *cis*-4-styrylpyridine, b.p. 107–116° (0.4 mm.), $n^{25}D$ 1.6216.

Anal. Calcd. for $C_{13}H_{11}N$: C, 86.2; H, 6.1; N, 7.7. Found: C, 86.5; H, 6.1; N, 7.2.

The distillate was taken up in 150 ml. of 2 *N* hydrochloric acid and put through the rest of the purification procedure used for the *cis* 2-isomer. Distillation gave 5.8 g. of *cis*-4-styrylpyridine, b.p 105–106° (0.4 mm.), $n^{25}D$ 1.6215. Gas chromatography showed that the product was 100% pure *cis*-4-styrylpyridine.

4,5-Diphenyl-3-nitrofurfurylideneaniline from the Reaction of Sodium 2-Nitro-3-oxosuccinaldehydate with Aniline Hydrochloride and Benzaldehyde[1]

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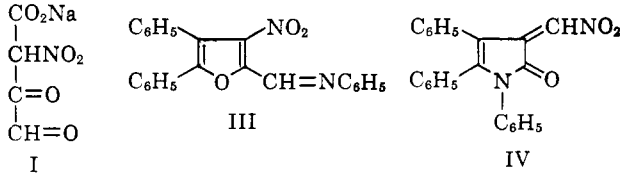
Treatment of sodium 2-nitro-3-oxosuccinaldehydate with aniline hydrochloride and benzaldehyde gave 4,5-diphenyl-3-nitrofurfurylideneaniline (III). The structure was assigned to III on the basis of spectral data and chemical reactions, and evidence for the mechanism of the reaction was obtained by isolation of several proposed intermediates.

When sodium 2-nitro-3-oxosuccinaldehydate (I)[4] was treated with aniline hydrochloride and benzaldehyde in aqueous ethanol with the expectation of obtaining an imidazole,[5] there was obtained instead a yellow, crystalline substance which was shown by elemental analysis and molecular weight determination to have a formula corresponding to the product (II) of equation 1. Analogous products were obtained by the reaction of compound I with anisaldehyde and aniline; *p*-chlorobenzaldehyde and aniline; or benzaldehyde and *p*-chloroaniline.

$$\underset{\text{I}}{C_4H_2NO_6Na} + C_6H_5NH_2\cdot HCl + 2C_6H_5CHO \longrightarrow \underset{\text{II}}{C_{23}H_{16}N_2O_3} + 3H_2O + CO_2 + NaCl \quad (1)$$

The high carbon to hydrogen ratio, as well as the infrared and ultraviolet absorption spectra suggested a cyclic and highly conjugated or aromatic structure for II. Two conceivable structures fitting these requirements are 4,5-diphenyl-3-nitrofurfurylideneaniline (III) and the unsaturated lactam IV. Degradative evidence and the isolation of reaction intermediates supported structure III and excluded the alternative formulation.



I III IV

Treatment of III with catalyst and hydrogen at low pressure resulted in the uptake of one mole of hydrogen and the formation of a secondary amine (Va). Although Va failed to react with nitrous acid to give the anticipated N-nitroso derivative, it readily formed the

(1) Supported in part by research grant no. CY-2240 of the National Institutes of Health, U. S. Public Health Service.

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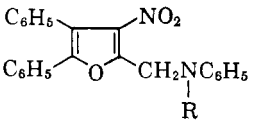
(4) Previously called sodium β-formyl-β-keto-α-nitropropionate; P. E. Fanta, R. A. Stein, and R. M. W. Rickett, *J. Am. Chem. Soc.*, **80**, 4577 (1958).

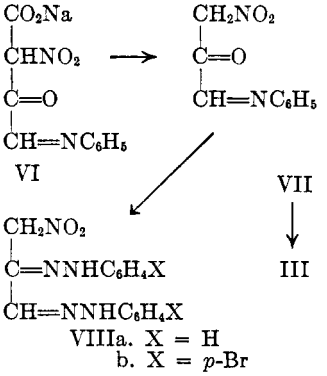
(5) An imidazole is the product of the well known Radziszewski reaction of a 1,2-dicarbonyl compound with an aldehyde and a primary amine; K. Hofmann, "Imidazole and Its Derivatives," Part I, Interscience Publishers, Inc., New York, N. Y., 1953.

benzoyl (Vb) and benzenesulfonyl (Vc) derivatives. Treatment of Va with diazomethane gave a tertiary amine (Vd), which gave Va on treatment with hot, concentrated hydriodic acid.[6] The structures assigned to these products were supported by the infrared absorption spectra.



Va. R = H
b. R = COC_6H
c. R = $SO_2C_6H_5$
d. R = CH_3

Evidence for a probable intermediate in the over-all reaction represented by equation 1 was obtained by the isolation of sodium 2-nitro-3-oxosuccinaldehydate monoanil (VI) from the reaction of compound I with aniline hydrochloride in the presence of sodium acetate. Compound VI was further characterized by the preparation of the S-benzylisothiouronium salt, and on acidification was converted by decarboxylation to the unstable nitropyruvaldehyde monoanil (VII), which could not be prepared in analytically pure form. On treatment with phenylhydrazine, VII gave nitropyruvaldehyde bisphenylhydrazone (VIIIa) and on treatment with benzaldehyde VII gave III. On the other hand, attempts to isolate a product from the reaction of compound I with benzaldehyde alone were unsuccessful.



VIIIa. X = H
b. X = *p*-Br

When the reaction mixture used for the preparation of III was made basic and then cooled to −15° after twenty-four hours, an unstable, yellow compound was obtained, which could not be fully purified. However, the analytical results, as well as the ultraviolet and infrared absorption spectra supported structure IX, a benzylidene derivative of the monoanil. Evidently, IX is the product of the aldol condensation of VII with benzaldehyde, followed by dehydration.

Evidence for the rather ready reversibility of this dehydration and aldol condensation was the observation that on treatment with *p*-bromophenylhydrazine, IX gave nitropyruvaldehyde bis-*p*-bromophenylhydrazone (VIIIb). Furthermore, on standing for a few hours with benzaldehyde in ethanol, IX gave the furan derivative III.

These observations may be rationalized by the reaction scheme summarized in Fig. 1, picturing the aldol

(6) References to the dealkylation of alkylanilines are given by W. J. Hickinbottom, "Reactions of Organic Compounds," 3rd ed., Longmans Green and Co., New York, N. Y., 1957, p. 416.

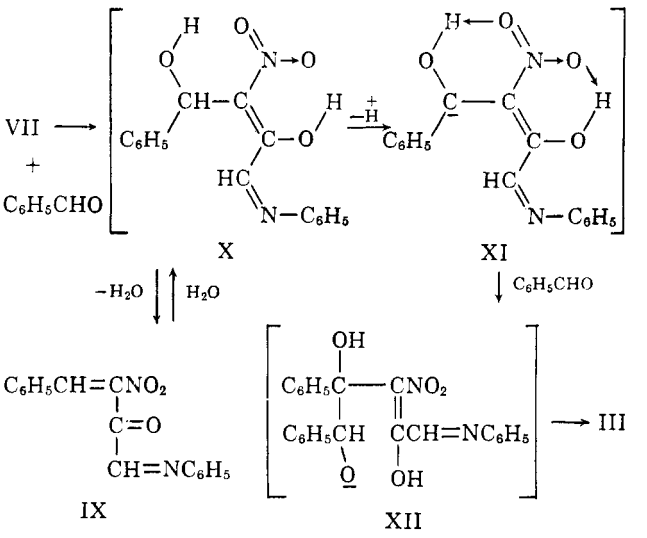
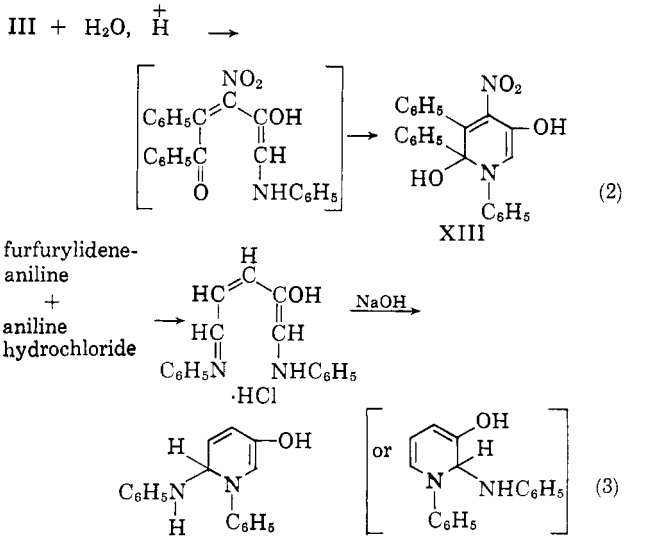


Fig. 1.—Reaction scheme for the formation of III. Hypothetical intermediates are in brackets.

condensation product X as a common intermediate in the formation of IX and III. The loss of a proton from X gives a resonance-stabilized carbanion XI, which reacts with the second molecule of benzaldehyde to give the intermediate XII. Cyclization of XII with the loss of hydroxide ion and a molecule of water to form III may readily be visualized. In this scheme, the hypothetical steps bear a formal similarity to the benzoin condensation, and the nitro group has the role of contributing to the stabilization of the carbanion XI by maintaining planarity through intramolecular hydrogen bonding.

Additional evidence for the structure of III was provided by treatment with hydrochloric or sulfuric acid to give a compound corresponding to the addition of a molecule of water, which is formulated as the dihydropyridine derivative, XIII. Further support for structure XIII was provided by the infrared absorption spectrum, and the observation that benzoylation resulted in the formation of a monobenzoyl derivative.



This sequence of reactions is analogous to the reaction of furfurylideneaniline with aniline hydrochloride to give an open-chain intermediate which is immediately cyclized to a dihydropyridine derivative on neutraliza-

tion with sodium hydroxide, as summarized in equation 3.[7] This dihydropyridine derivative also forms only a monoacetyl derivative.

A by-product of the reaction yielding XIII was benzaldehyde, which may be visualized as resulting from a reversal of the reactions leading to the formation of III.

It is noteworthy that the reaction summarized in Fig. 1 represents a novel synthesis of the furan ring.

Experimental

Sodium 2-nitro-3-oxosuccinaldehydate dihydrate (I) was prepared as previously described.[4] The crude salt contains sodium nitromalonaldehyde.

4,5-Diphenyl-3-nitrofurfurylideneaniline (III).—To a solution of 21.9 g. of crude compound I in 250 ml. of water was added a solution of 25.9 g. of aniline hydrochloride in 50 ml. of water. A yellow precipitate was immediately formed, and after 1 min. the reaction mixture was filtered to remove about 1.5 g. of crude nitromalonaldehyde monoanil. To the filtrate was added a solution of 20.2 ml. of benzaldehyde in 225 ml. of ethanol. The mixture was stirred at room temperature for 4 days, while the product was collected by filtration each day. The total yield of crude product was 16.9 g. (46%). Repeated recrystallization from ethanol–ethyl acetate gave yellow needles, m.p. 233–236° dec.; infrared absorption: ν_{max}^{KBr} 1685 (s) (C=N), 1530 (s) and 1347 (s) (C—NO_2); ultraviolet and visible absorption; λ_{max}^{EtOH} 244 mμ (log ε 4.2), 328 mμ (log ε 4.4), 418 mμ (log ε 4.1).

Anal. Calcd. for $C_{23}H_{16}N_2O_3$ (368): C, 74.98; H, 4.38; N, 7.61. Found: C, 74.75, 74.89; H, 4.50, 4.68; N, 7.87, 7.86; 375 (Rast).

The following analogous compounds were prepared in a similar way.

4,5-Dianisyl-3-nitrofurfurylideneaniline was obtained by using anisaldehyde in place of benzaldehyde. Recrystallization from ethanol–chloroform gave orange needles, m.p. 225–228°, from which water of crystallization was not removed by heating at 80° in a vacuum for several hours; infrared absorption: ν_{max}^{KBr} near 3500 (broad) (water OH), 1675 (s) (C=N), 1510 (s) and 1350 (m–s) (C—NO_2).

Anal. Calcd. for $C_{25}H_{20}N_2O_5 \cdot {}^1/_2H_2O$; C, 68.64; H, 4.84; N, 6.40. Found: C, 68.30; H, 4.64; N, 6.89.

4,5-Di(*p*-chlorophenyl)-3-nitrofurfurylideneaniline was prepared by treatment of nitropyruvaldehyde monoanil (VII) with *p*-chlorobenzaldehyde in ethanol. Warming and standing for a day gave a solid which was recrystallized from ethanol–chloroform, orange needles, m.p. 256.4–257.5° dec.; infrared absorption: ν_{max}^{KBr} 1680 (s) (C=N), 1530 (s) and 1350 (s) (C—NO_2).

Anal. Calcd. for $C_{23}H_{14}N_2O_3Cl_2$: C, 63.17; H, 3.23; N, 6.41; Cl, 16.21. Found: C, 62.90; H, 3.24; N, 6.65; Cl, 16.34.

4,5-Diphenyl-3-nitrofurfurylidene (*p*-**chloroaniline**) was obtained by using *p*-chloroaniline and an excess of concentrated hydrochloric acid in place of aniline hydrochloride. The crude product, obtained in 37% yield, m.p. 238–239°, was recrystallized repeatedly from ethanol–chloroform to obtain an analytical sample, orange crystals, m.p. 266–269° dec.; infrared absorption: ν_{max}^{KBr} 1680 (s) (C=N), 1535 (s) and 1355 (s) (C—NO_2).

Anal. Calcd. for $C_{23}H_{15}N_2O_3Cl$: C, 68.57; H, 3.75; N, 6.96; Cl, 8.80. Found: C, 68.38; H, 3.70; N, 7.05; Cl, 8.62.

N,4,5-Triphenyl-3-nitrofurfurylamine (**Va**).—A solution of 2.0 g. of III in 200 ml. of tetrahydrofuran containing 0.2 g. of 10% palladium-on-charcoal catalyst was stirred under a hydrogen pressure of 1 atm. Reaction ceased after 15 min., when one mole equivalent of hydrogen had been taken up. Filtration and evaporation of the solution gave a deep orange oil which crystallized on trituration with ethanol, giving an 81% yield of crude product. Recrystallization from ethanol gave orange plates, m.p. 137.5–138.4; infrared absorption: ν_{max}^{KBr} near 3400 (m) (NH), 1635 (s) (NH), 1530 (m) and 1360 (s) (C—NO_2); ultraviolet and visible absorption: λ_{max}^{EtOH} 255 mμ (log ε 4.1); 307 mμ (log ε 4.1); 375 mμ (shoulder) (log ε 3.2).

Anal. Calcd. for $C_{23}H_{18}N_2O_3$ (370): C, 74.59; H, 4.87; N, 7.56. Found: C, 74.39; H, 5.13; N, 7.95; 375 (ebullient in benzene).

The **benzoyl derivative** (**Vb**) was prepared by treatment of Va with benzoyl chloride in hot, 5% aqueous sodium hydroxide. Recrystallization from ethanol gave pale yellow needles, m.p. 158.0–158.6°.

Anal. Calcd. for $C_{30}H_{22}N_2O_4$: C, 75.93; H, 4.67; N, 5.91. Found: C, 76.01; H, 4.69; N, 6.08.

The **benzenesulfonyl derivative** (**Vc**) was prepared by treatment of Va with benzenesulfonyl chloride in hot, 10% aqueous sodium hydroxide. Repeated recrystallization from ethanol gave light yellow crystals, m.p. 138.0–139.0°.

Anal. Calcd. for $C_{29}H_{22}N_2O_5S$: C, 68.23; H, 4.34; N, 5.49. Found: C, 68.35; H, 4.39; N, 5.48.

Similarly, hydrogenation of 4,5-diphenyl-3-nitrofurfurylidene (*p*-chloroaniline) gave **N-*p*-chlorophenyl-4,5-diphenyl-3-nitrofurfurylamine**, orange plates from ethanol, 144.0–145.0°; infrared absorption: ν_{max}^{KBr} near 3450 (m) and 1630 (s) (NH), 1525 (m) and 1360 (s) (C—NO_2).

Anal. Calcd. for $C_{23}H_{17}N_2O_3Cl$: C, 68.23; H, 4.23; N, 6.92. Found: C, 68.23; H, 4.35; N, 6.94.

N-Methyl-N,4,5-triphenyl-3-nitrofurfurylamine (**Vd**).—Treatment of 11 mmoles of compound Va with a solution of 40 mmoles of diazomethane in 100 ml. of ether and 25 ml. of ethanol for 1 hr. followed by evaporation of the solvent under reduced pressure gave a yellow solid. Recrystallization from ethanol gave Vd, stubby, yellow needles, m.p. 119–120°; infrared absorption: $\nu_{max}^{CHCl_3}$ 1357 (s) and 1525 (m) (C—NO_2).

Anal. Calcd. for $C_{24}H_{20}N_2O_3$: C, 74.98; H, 5.24; N, 7.29. Found: C, 74.86; H, 5.47; N, 7.40.

Dealkylation of Vd.—A mixture of 0.1 g. of Vd and 1 ml. of 47% hydriodic acid was refluxed gently for 15 min. Cooling and filtration gave a solid which was washed with a little ethanol and recrystallized from ethanol to give orange crystals of Va, m.p. 135–138°, undepressed on admixture with an authentic sample of Va.

Sodium 2-Nitro-3-oxosuccinaldehydate Monoanil (**VI**).—A mixture of 14.2 g. of aniline hydrochloride and 23.1 g. of sodium acetate in 47 ml. of water was added to a solution of 12.3 g. of crude compound I in 123 ml. of water. After 1.5 hr. of stirring, the reaction mixture was filtered to remove 1.84 g. of nitromalonaldehyde dianil, m.p. 95°. Continued stirring of the filtrate for 24 hr. gave a precipitate of 7.5 g. of crude VI. Recrystallization from ethanol gave yellow plates which did not liquefy at all when the temperature of the melting point bath was raised slowly to 300°, but decomposed vigorously when placed suddenly in a melting point bath at 200°. The water of crystallization was not removed on heating in a vacuum at 80° for several hours. Infrared absorption: ν_{max}^{KBr} near 3500 (s) and 3400 (s) (water OH), 1740 (s) (keto C=O), 1661 (s) (broad) (water OH), 1529 (m—s) and 1345 (s) (C—NO_2), 1415 (s) (CO_2^-).

Anal. Calcd. for $C_{10}H_7N_2O_5Na \cdot {}^1/_2H_2O$: C, 44.95; H, 3.02; N, 10.49. Found: C, 45.20; H, 3.01; N, 11.07, 10.83.

The S-benzylisothiouronium salt of VI was prepared by adding an aqueous solution of S-benzylisothiouronium chloride to an aqueous alcoholic solution of VI. Recrystallization from ethanol gave yellow crystals, m.p. 144.5–146°.

Anal. Calcd. for $C_{10}H_8N_2O_5 \cdot C_7H_{10}N_2S \cdot H_2O$: C, 51.42; H, 4.79; N, 13.33. Found: C, 51.34; H, 4.78; N, 13.37.

Nitropyruvaldehyde Monoanil (**VII**).—Addition of 0.7 ml. of concentrated hydrochloric acid to a solution of 1.37 g. of VI in a mixture of 40 ml. of water and 20 ml. of ethanol, followed by cooling in an ice chest for 3 hr. gave 0.55 g. of pale yellow needles of VII. Attempted recrystallization resulted in decomposition. A sample dried over phosphorus pentoxide in a vacuum desiccator for 2 days at room temperature melted at 142° dec. Infrared absorption: ν_{max}^{KBr} near 3400 (m) (enol OH), 1729 (m–s) (keto C=O), 1680 (s) (C=N), 1568 (s) and 1340 (m) (C—NO_2).

Anal. Calcd. for $C_9H_8N_2O_3$: C, 56.25; H, 4.19; N, 14.58. Found: C, 58.19, 58.14; H, 4.89, 4.75; N, 12.90, 12.76.

On treatment with phenylhydrazine hydrochloride in aqueous ethanol, VII gave nitropyruvaldehyde bisphenylhydrazone (VIIIa), shown to be identical to the authentic material[4] by comparison of the infrared spectra. Furthermore, treatment of an alcoholic solution of VII with benzaldehyde at room temperature for several hours gave III.

N-(3-Nitro-2-oxo-4-phenyl-3-butenylidene)aniline (**IX**).—To a solution of 21.9 g. of compound I in 200 ml. of water was added a solution of 25.9 g. of aniline hydrochloride in 50 ml. of water. After 1 min., the solution was filtered to remove nitromalonaldehyde monoanil, and a solution of 10.1 ml. of benzaldehyde in 300 ml. of ethanol and 30.6 g. of 40% aqueous trimethylbenzylammonium hydroxide was added. After stirring

(7) J. C. McGowan, *J. Chem. Soc.*, 777 (1949).

for 24 hr. at room temperature the reaction mixture was cooled to −15° for 1 hr. Filtration gave 12.2 g. of yellow solid product. Attempted recrystallization from a variety of solvents always resulted in decomposition. An analytical sample was prepared by successive trituration and filtration first with cold 6 *M* acetic acid and then with two portions of ethanol, to give a yellow powder, m.p. 143–145°, infrared absorption: ν_{max}^{KBr} near 3550 (m) and 3400 (m) (water OH), 1730 (m–s) (keto C=O), 1658 (m–s) (water OH), 1529 (s) and 1340 (m–s) (C—NO_2); ultraviolet absorption: λ_{max}^{EtOH} 233 mμ, 314 mμ, 420 mμ.

Anal. Calcd. for $C_{16}H_{12}N_2O_3 \cdot {}^1/_2H_2O$: C, 66.43; H, 4.53; N, 9.68. Found: C, 66.80; H, 5.59; N, 10.43.

On standing for a few hours at room temperature, an alcoholic solution of IX and benzaldehyde gave III, identified by mixture melting point with an authentic sample.

Nitropyruvaldehyde Bis(*p*-bromophenyl)hydrazone (VIIIb).—A solution of 0.5 g. of IX, 0.6 g. of *p*-bromophenylhydrazine hydrochloride, and 4 drops of acetic acid in 30 ml. of ethanol was refluxed for 0.5 hr. Cooling and filtration gave a yellow solid which was recrystallized from ethanol, yellow crystals, m.p. 175.4–176.2°. This material was shown by comparison of melting point and infrared spectrum to be identical to authentic material prepared in a similar way from compound I, *p*-bromophenylhydrazine, and hydrochloric acid in ethanol.

Anal. Calcd. for $C_{15}H_{12}N_5O_2Br_2$: C, 39.58; H, 2.89; N, 15.39; Br, 35.11. Found: C, 39.81; H, 3.11; N, 15.03; Br, 34.87.

2,5-Dihydroxy-4-nitro-1,2,3-triphenyl-1,2-dihydropyridine (XIII).—A suspension of 2.0 g. of III in 200 ml. of ethanol containing 100 ml. of concentrated hydrochloric acid was heated to reflux. After 5 to 10 min. all of the material dissolved, and then almost immediately bright orange crystals precipitated from the mixture. After 1.5 hr. of refluxing, the mixture was cooled and filtered to give 1.46 g. of product. Successive recrystallization from ethanol–ethyl acetate gave orange crystals, m.p. 225–226° dec.; infrared absorption: $\nu_{max}^{CH_2Cl_2}$ near 3450 (m–s) (OH), 1640 (m–s) (C=C), 1500 (s) and 1360 (s) (C—NO_2).

Anal. Calcd. for $C_{29}H_{18}N_2O_4$: C, 71.49; H, 4.69; N, 7.25. Found: C, 71.70; H, 4.64; N, 8.25.

Treatment of the filtrate from the above reaction with 2,4-dinitrophenylhydrazine gave less than 0.1 g. of benzaldehyde 2,4-dinitrophenylhydrazone, identified by mixture melting point with an authentic specimen.

The **monobenzoyl derivative of XIII** was obtained by treating a chloroform solution of XIII with benzoyl chloride and 5% aqueous sodium hydroxide solution. After several hours of stirring at room temperature, the chloroform solution was separated, dried, and distilled, and the residue was recrystallized from ethanol–chloroform to give yellow crystals, m.p. 254–261° (uncor.), infrared absorption: $\nu_{max}^{CH_2Cl_2}$ near 3500 (m) (OH), near 1750 (s) (C=O).

Anal. Calcd. for $C_{30}H_{22}N_2O_4$: C, 73.46; H, 4.52. Found: C, 73.46; H, 4.43.

The Synthesis of Several 4,6-Dimethylquinolizinium Salts, Possible Precursors of Cycl[3.3.3]azine[1a]

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The preparation of 2,4,6-trimethyl- and 2-phenyl-4,6-dimethylquinolizinium salts has been accomplished by the reaction of 2,6-lutidyllithium with the appropriate protected β-diketone, followed by cyclodehydration of the intermediate pyridyl ketone with hydrobromic acid and acetic anhydride. Various functional derivatives of these and other quinolizinium salts have been obtained. The 4,6-dimethylquinolizinium salts were desired as intermediates in the synthesis of cycl[3.3.3]azine. Numerous reagents and conditions were employed in an attempt to bring the 4- or 6-methyl groups into reaction. These attempts were uniformally unsuccessful.

Preparation of Quinolizinium Salts.—While a number of quinolizinium salts are known, none of these contains methyl groups at the 4- and 6-positions, as may be considered desirable for ring closure to cycl[3.3.3]azine. Thus the object of the work reported here was to prepare quinolizinium salts such as (IX), and to explore the routes whereby these salts might be converted to cycl[3.3.3]azines.

Quinolizinium salts have been known to exist in certain complex alkaloids for some time. However, synthetic routes to relatively simple quinolizinium cations have been developed only recently. One of the most general of these approaches, discovered by Woodward and MacLamore[2] and further elaborated by Richards and Stevens,[3] consists of the reaction of picolyllithium (Ia) with the mono ketal or enol ether of a β-dicarbonyl compound (II), followed by cyclodehydration of the intermediate adduct (IIIb) to the corresponding quinolizinium compound (IX) with acid (sequence A).

Richards and Stevens[3] have used this method to advantage in the preparation, among others, of 2,4-dimethyl- and 2-phenyl-4-methyl-(IXb)quinolizinium picrates. These two compounds were of considerable interest to us, since the substitution of 2,6-lutidine for picoline in the initial step should provide quinolizinium salts with methyl groups in the 4- and 6- positions as required for the preparation of cycl[3.3.3]azines. In accord with their postulated mechanism, Richards and Stevens have isolated the picrate of the pyridyl ketone (IVb) analogous to IVa as an intermediate in the formation of 2-phenyl-4-methylquinolizinium picrate (IXb). In addition, we have isolated the hydrobromide of the unsaturated ketone (Vb) analogous to Va as an intermediate in the preparation of 4,6-dimethyl-2-phenylquinolizinium bromide (IXc), although Va, itself, could not be isolated in pure form. Further, we have obtained spectral evidence for the formation of (IVa) on mild acid treatment of the adduct (IIIa). Nesmeyanov[4] has reported the isolation of an intermediate, formulated as the hydroxydihydroquinolizinium salt (X), in the preparation of 2-methylquinolizinium bromide (IXd). Lacking further information, since this work is available to us only in abstract form, and in view of our experience with the ketone (Vb), it would seem that this could be formulated as the iso-

(1) (a) Taken from the Ph.D. dissertation of H. V. Hansen. Present address, Metcalf Laboratory of Chemistry, Brown University, Providence, R. I; (b) Lehigh Student Chemistry Foundation Fellow, 1959–1961.

(2) R. B. Woodward and W. M. MacLamore, *J. Am. Chem. Soc.*, **71**, 379 (1949).

(3) A. Richards and T. S. Stevens, *J. Chem. Soc.*, 3067 (1958).

(4) A. N. Nesmeyanov and M. I. Rybinskaya, *Dokl. Akad. Nauk SSSR*, **116**, 93 (1957).