(−)-Cotinine from Metabolic (+)-Hydroxycotinine.—A solution of 645 mg. of chlorocotinine (obtained from metabolic (+)-hydroxycotinine) in 75 ml. of ethanol was hydrogenated at atmospheric pressure and room temperature in the presence of 350 mg. of 5% palladium on charcoal until 1 equivalent of hydrogen had been consumed. After removal of the catalyst, the solution was evaporated to dryness. A solution of the residue in ammonia water was extracted with chloroform. The chloroform solution was dried over sodium sulfate and then placed upon a column of alumina. The column was eluted with methanol to obtain 420 mg. of (−)-cotinine. To this was added 1 equivalent of picric acid in methanol. The crystalline monopicrate melted at 105–106° after recrystallization from methanol. The picrate was decomposed in dilute hydrochloric acid. After extraction of picric acid with ethyl acetate, the aqueous solution was adjusted to pH 10 with ammonia water and extracted with chloroform. The cotinine base from evaporation of the chloroform was treated with one equivalent of hydrobromic acid to give (−)-cotinine hydrobromide. The analytical sample was recrystallized from isopropyl alcohol and dried at 25° and 1 mm., m.p. 187–188° dec. $[\alpha]^{30}_{6461}$ −32.6°, (*c*, 7.4 in methanol).

Anal. Calcd. for $C_{10}H_{13}N_2OBr$: C, 46.71; H, 5.09; N, 10.90. Found: C, 46.65; H, 4.96; N, 10.92.

The foregoing hydrobromide had a melting point and optical rotation in substantial agreement with the samples prepared[7] from metabolic and synthetic (−)-cotinine.

Isolation of Hydroxycotinine from Smokers' Urine.—Smoker's urine (60 l.) was obtained as voluntary daytime contributions from male laboratory workers, made alkaline, and then continuously extracted with chloroform as previously described.[7] The chloroform solution upon evaporation yielded a dark-brown oily residue (7.0 g.). The residue was treated with 40 ml. of boiling water, and the cooled mixture was filtered. The filtrate was adjusted to pH 2 with 5 *N* hydrochloric acid. The acidic solution was placed on a column of (4 × 30 cm.) of Dowex 50 (H^+). The column was washed thoroughly with water. Koenig positive material of R_f values 0.34, 0.61, 0.73, and 0.90 (base) was removed by exhaustive elution with 0.1 *N* ammonia water. The ammonical solution was placed upon a column (4 × 30 cm.) of Dowex 21K (OH^-). The ammoniacal effluent and exhaustive water wash were combined and concentrated to an oily residue (1.1 g.). The residue was dissolved in 20 ml. of chloroform and placed on a column of acid-washed alumina (30 g.). An elution with ether containing successively increasing amounts of methanol (0–100% by vol.) served to remove a fraction with Koenig positive material, R_f 0.75 (base), which was identified as cotinine. Subsequent fractions contained material with R_f 0.61 (base) and the final fractions contained material showing a single Koenig positive zone at R_f 0.84 (base), which was cochromatographed with nicotine but was not identified as such. The combined R_f 0.61 fractions yielded upon evaporation an oily residue (118 mg.). The residue was treated with 1 ml. of dry pyridine and 1 ml. of acetic anhydride. After standing overnight at room temperature, the mixture was concentrated under diminished pressure. The oily residue (143 mg.) was dissolved in 5 ml. of chloroform and then placed upon a column of acid-washed alumina (5 g.). Elution with ether containing increasing amounts of methanol (0–100%) gave fraction A, which showed a single Koenig positive spot upon paper chromatography (R_f 0.75, base), and fraction B (R_f 0.61, base). The oil (17 mg.) from fraction B cochromatographed on paper with authentic crystalline (−)-demethylcotinine[6] in both acid and base. It failed to crystallize and was not identified. Fraction A was obtained as an oil (30 mg.). A sample (15 mg.) in 0.5 ml. of ethanol was treated with one equivalent of picric acid (15% water) as a saturated solution in ethanol. The resultant crystalline acetoxycotinine picrate (75 mg.) was recrystallized from ethanol, m.p. 165°. The analytical sample corresponded in melting point[17] to acetoxycotinine picrate which was obtained from studies on the dog.[5] Admixture produced no depression of the melting point. The two samples cochromatographed, R_f 0.77 (acid) and R_f 0.74 (base). For analysis the compound from smokers' urine was dried at 60° and 1 mm. over potassium hydroxide.

Anal. Calcd. for $C_{18}H_{17}N_5O_{10}$: C, 46.67; H, 3.70; N, 15.12. Found: C, 46.62; H, 3.74; N, 15.19.

Acknowledgment.—The authors wish to thank Mr. James E. Mann for his invaluable assistance and Dr. John Chemerda of Merck and Co. for supplies of alumina. Microanalyses were made by Spang Microanalytical Laboratory.

(17) This corrected capillary melting point was obtained at a heating rate of 0.30° per min. At approximately 140° a change in crystalline form was observed. At higher rates of heating the melting point is somewhat elevated (ref. 5).

A Comparison of Methods for the Preparation of 2- and 4-Styrylpyridines[1]

J. L. R. WILLIAMS, R. E. ADEL, J. M. CARLSON, G. A. REYNOLDS, D. G. BORDEN, AND J. A. FORD, JR.

Kodak Research Laboratories, Eastman Kodak Company, Rochester, New York

Received August 27, 1962

Derivatives of 2-styrylpyridine, 5-ethyl-2-styrylpyridine, and 4-styrylpyridine bearing CH_3O, NO_2, CH_3, and $N(CH_3)_2$ in the 4′-position have been prepared by the following routes: (1) pyrolysis of the corresponding methiodides; (2) reaction of a benzaldehyde with a picoline in refluxing acetic anhydride; and (3) the zinc chloride condensation of a benzaldehyde and a picoline at 200°. A (2:5) mixture of *cis*- and *trans*-2-styrylpyridine was obtained from the reaction between a phosphorus ylid and 2-pyridylaldehyde. An analogous preparation gave *cis*-4-styrylpyridine from 4-pyridylaldehyde.

In preceding papers,[2] it was shown that the reaction of benzaldehyde with 2-picoline in refluxing acetic anhydride gave *trans*-2-styrylpyridine. Irradiation of *trans*-2-styrylpyridine, its hydrochloride or methiodide in solution with ultraviolet light gave the *cis* modification. In order to extend this study to include substituted and structurally isomeric styrylpyridines, it was necessary to examine various preparative methods for convenience, yields, and the isomer configurations obtained by these procedures.

Four methods were employed for the preparation of the styrylpyridines and are described in order as follows.

Method 1.—Phillips[3] prepared styrylpyridine methiodides by condensation of benzaldehydes with 2-picoline methiodide in methanol solution using piperidine as the catalyst. Horwitz[4] showed that the *trans* salts resulted when the same reaction was conducted using quinaldine methiodides in place of 2-picoline methiodide. On the basis of previous spectroscopic results from these laboratories,[2b] we have assigned the *trans* configuration to styrylpyridine methiodides prepared using piperidine as the catalyst. The physical properties of the styryl-

(1) Communication no. 2312 from the Kodak Research Laboratories, Eastman Kodak Co., Rochester, N. Y.

(2)(a) J. L. R. Williams, *J. Org. Chem.*, **25**, 1839 (1960); (b) J. L. R. Williams, S. K. Webster, and J. A. VanAllan, *ibid.*, **26**, 4893 (1961).

(3) A. P. Phillips, *ibid.*, **12**, 333 (1947).

(4) L. Horwitz, *J. Am. Chem. Soc.*, **77**, 1687 (1955).

TABLE I

PHYSICAL CONSTANTS OF STYRYLPYRIDINE METHIODIDES

Pyridine methiodide	4'-Substituent	Empirical formula	Found (Calcd.) C	H	N	I	M.p., °C.	λ_{max}, mμ	$\epsilon \times 10^{-3}$
2-Styryl	H	$C_{14}H_{14}NI$	51.6	4.5	4.4	39.4	229.5	333	27.5
			(52.0)	(4.4)	(4.3)	(39.3)			
	OCH_3	$C_{15}H_{16}NIO$	51.0	4.6	4.6	36.3	235	362	29.3
			(51.0)	(4.6)	(4.6)	(35.9)			
	NO_2	$C_{14}H_{13}N_2O_2I$	45.7	3.3	7.2	34.5	246–248	336	34.9
			(45.7)	(3.6)	(7.6)	(34.5)			
	CH_3	$C_{15}H_{16}NI$	53.4	4.8	4.1	37.6	263	344	28.9
			(53.5)	(4.8)	4.2	(37.6)			
	$N(CH_3)_2$	$C_{16}H_{19}N_2I$	52.8	5.4	7.7	34.5	248–250	474	44.2
			(52.8)	(5.2)	(7.7)	(34.7)			
5-Ethyl-2-styryl	H	$C_{16}H_{18}NI$	54.7	5.1	4.0	35.8	237	335	28.3
			(54.7)	(5.2)	(4.0)	(36.1)			
	OCH_3	$C_{17}H_{20}NIO$	53.3	5.3	3.3	32.9	217	360	31.0
			(53.5)	(5.3)	(3.7)	(33.3)			
	NO_2	$C_{16}H_{17}N_2O_2I$	48.4	4.3	6.8	32.0	209	340	29.6
			(48.5)	(4.3)	(7.1)	(32.0)			
	CH_3	$C_{17}H_{19}NI$	55.6	5.6	3.5	34.7	238	242	22.8
			(55.8)	(5.5)	(3.8)	(34.8)			
	$N(CH_3)_2$	$C_{18}H_{23}N_2I$	54.6	6.0	6.9	31.1	160	425	23.0
			(54.8)	(5.9)	(7.1)	(32.2)		356	21.6
4-Styryl	H	$C_{14}H_{14}NI$	51.7	4.4	4.4	39.3	218	345	33.0
			(52.0)	(4.4)	(4.3)	(39.3)			
	OCH_3	$C_{15}H_{16}NIO$	50.5	4.6	3.9	35.6	210	371	32.7
			(51.0)	(4.6)	(4.0)	(35.9)		251	20.3
	NO_2	$C_{14}H_{13}N_2O_2I$	45.9	3.6	4.0	37.6	222	343	36.9
			(45.7)	(3.6)	(4.2)	(37.6)		268	12.0
	CH_3	$C_{15}H_{16}NI$	53.2	4.8	4.0	37.2	237	352	24.7
			(53.5)	(4.8)	(4.2)	(37.6)			
	$N(CH_3)_2$	$C_{16}H_{19}N_2I$	52.6	5.3	7.7	34.6	254	448	27.5
			(52.8)	(5.2)	(7.7)	(34.7)		265	11.5

pyridine methiodides prepared using piperidine as the catalyst in this work are summarized in Table I. Pyrolysis of 2-styrylpyridine methiodide or its photodimer to the corresponding free bases was reported earlier.[2b] This reaction was extended to the other styrylpyridine methiodides listed in Table I, and the yields of the free bases are included in Table III.

Method 2.—Shaw and Wagstaff[5] prepared styrylpyridines by treating a picoline and a benzaldehyde in refluxing acetic anhydride. Horwitz[4] showed that the analogous reaction with quinaldines produced the *cis* isomers, and he suggested that a quasi-stable cyclic intermediate acetate underwent *cis* elimination. We have carefully examined the products resulting when 2-picoline reacted with benzaldehyde in refluxing acetic anhydride. No *cis*-2-styrylpyridine was found during any stages of the preparation. Under identical conditions, 4-picoline was converted to *trans*-4-styrylpyridine. The ultraviolet absorption spectra of the styrylpyridines listed in Table III prepared by method 2 indicated that only the *trans* forms were present. 4'-Nitro-4-styrylpyridine can, however, be isolated in either of three polymorphic forms, depending on the conditions of crystallization. These forms have identical ultraviolet and infrared spectra in solution. Many of the compounds prepared by Horwitz[4] in the quinaldine series carried substituents which would be expected to interfere sterically with isomerization of the *cis* to the *trans* forms. The styrylpyridines considered in the present work would be expected to be more labile. In order to check this, solutions of *cis*-2-styrylpyridine and *cis*-4-styrylpyridine were heated under reflux for one hour in 10% hydrochloric acid solution, glacial acetic acid, and acetic anhydride. The per cent isomerization of the *cis* to the *trans* forms was determined by gas chromatography of the isolated free bases and is shown in Table II.

TABLE II

PER CENT ISOMERIZATION OF *cis*-2-STYRYLPYRIDINE AND *cis*-4-STYRYLPYRIDINE DURING ONE-HOUR REFLUXING

	10% Hydrochloric acid, % *trans*	Acetic acid, % *trans*	Acetic anhydride, % *trans*
cis-2-Styrylpyridine	2	9.7	29
cis-4-Styrylpyridine	0.7	83	98

Both *cis* isomers are rapidly converted to the *trans* forms in refluxing acetic anhydride. The reflux times of up to eighteen hours employed during the preparations using acetic anhydride therefore caused complete isomerization of any *cis* isomers to the corresponding *trans* forms.

Method 3.—Preparation of styrylpyridine bases from benzaldehydes and picolines at 200° using zinc chloride as catalyst[6] provides a convenient synthesis. When applied to the series of compounds of interest to us, the yields were as shown in Table III. The method is particularly effective for 2-styrylpyridine (yield, 76%), which is obtained in low yield by the other procedures. In all cases, this method produced only the *trans* form.

(5) B. D. Shaw and E. A. Wagstaff, *J. Chem. Soc.*, 77 (1933).

(6) C. Langer, *Ber.*, **38**, 3704 (1905).

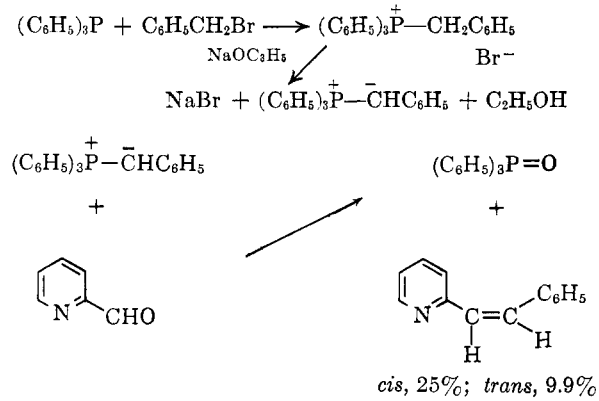
TABLE III

PHYSICAL CONSTANTS AND YIELDS OF STYRYLPYRIDINES

Pyridine	4′-Substituent	M.p., °C.[a] *trans* form	λ_{max}, mμ *trans* form	$\epsilon \times 10^{-3}$[g] *trans* form	% Yields[h] Method 1	Method 2	Method 3	Method 4
2-Styryl	H	93.5	309	25.1	72.5	20–30	76	25 *cis*, 9 *trans*
	OCH_3	69	325	36.9	44	0	35	
	NO_2	126	335	30.0	33	80	55	
	CH_3	88	314	33.9	35	10	45	
	$N(CH_3)_2$	139	365	29.2	58	0	46	
5-Ethyl-2-styryl	H	57	311	32.7	54	14	48	
	OCH_3[c]	57	325	29.4	33	0	30.4	
	NO_2	116	341	31.1	40	72	0	
	CH_3	89	316	33.0	54	17	32	
	$N(CH_3)_2$[d]	129	365	36.4	42	0	33	
4-Styryl	H	128	306	29.6	38	60	20	42 *cis*
	OCH_3	131	371	40.2	0	36	0	
	NO_2[b]	149–151	345	37.6	0	76	44	
	CH_3[f]	157	311	32.8	52	58	17	
	$N(CH_3)_2$[e]	241	375	32.5	0	0	25	

[a] Melting points agree with the literature except where noted. [b] As isolated, see Experimental. [c] O. Bialon, *Ber.*, **35**, 2789 (1902), no melting point. Present work. Calcd. for $C_{16}H_{17}NO$: C, 80.4; H, 7.2; N, 5.9. Found: C, 80.2; H, 7.5; N, 5.8. [d] New compound. Calcd. for $C_{17}H_{20}N_2$: C, 81.0; H, 8.0; N, 11.1. Found: C, 80.6; H, 8.1; N, 11.1. [e] *Anal.* Calcd. for $C_{15}H_{16}N_2 \cdot C_2H_5OH$: C, 76.6; H, 8.2; N, 10.4. Found: C, 76.3; H, 7.7; N, 11.4. [f] E. During, *Ber.*, **38**, 164 (1905), m.p. 101–102°, present work, m.p. 157°. Calcd. for $C_{14}H_{13}N$: C, 86.2; H, 6.7; N, 7.2. Found: C, 85.9; H, 6.8; N, 7.2. [g] Ultraviolet spectra determined in methanol, 2.5×10^{-5} molar. [h] Yields figures are for *trans* isomers except where noted otherwise.

Method 4.—A novel method for the preparation of a mixture of *cis*- and *trans*-stilbene employing an ylid intermediate was reported by Trippett[7] and has been applied by us to the synthesis of 2- and 4-styrylpyridines.



cis, 25%; *trans*, 9.9%

When the same ylid reacted with 4-pyridinealdehyde, a yield of 42% *cis* was realized. Seus and Wilson[8] found that diethyl benzylphosphonate, sodium methoxide, and 2-pyridylaldehyde in dimethylformamide gave only *trans*-2-styrylpyridine.

The physical constants for the styrylpyridines prepared in this work are summarized in Table III. The method most generally useful is condensation of the aldehyde and the picoline in the presence of zinc chloride. However, this must be carried out in an autoclave capable of containing the reactants at 200°. 4′-Methoxy-4-styrylpyridine and 5-ethyl-4′-nitro-2-styrylpyridine could not be prepared under these conditions, and only tarry residues resulted. The acetic anhydride method often led to unidentifiable tars, as shown in the cases where zero yields are listed in Table III. The synthesis using an ylid intermediate has not been extended to substituted styrylpyridines, because of the necessity of obtaining the necessary substituted benzyl chlorides. Depite the fact that the yields are somewhat low in a number of cases, the pyrolysis of the corresponding methiodides is a convenient and facile preparative method. It did, however, fail in the case of 4-substituted styrylpyridines.

(7) S. Trippett, "Advances in Organic Chemistry. Methods and Results," Vol. 1, R. A. Raphael, E. C. Taylor, and H. Wynberg, ed., Interscience Publishers, Inc., New York, N. Y., 1960, p. 83.

(8) E. J. Seus and C. V. Wilson, *J. Org. Chem.*, **26**, 5243 (1961

Experimental

Method 1.—The styrylpyridine methiodides were prepared according to the method described by Phillips.[3] It was very important that short reaction times be used to minimize side reactions. For our purposes a mixture of 0.1 mole of the picoline methiodide and 0.2 mole of the aldehyde was dissolved in a minimal quantity of refluxing methanol. After the addition of 5 ml. of piperidine to the solution, refluxing was continued for 1 hr. The styrylpyridine methiodides crystallized from the cooled reaction mixtures and were recrystallized from appropriate solvents.

The styrylpyridine methiodides were converted to the corresponding styrylpyridines by pyrolysis using a modification of the method described previously.[2] A typical run was as follows: In a 500-ml. distillation flask equipped with a side arm and a water-cooled receiver was placed 150 g. (0.45 mole) of 2-styrylpyridine methiodide. The receiver flask was then attached to a Dry Ice-cooled trap connected in series to a vacuum pump. The pressure was reduced to 0.1–0.5 mm., at which time the flask was heated gently over a direct flame. By carefully controlling the heat input to the flask, the quaternary salt was smoothly decomposed into methyl iodide and 2-styrylpyridine which collected in the receiver. After recrystallization of the crude distillate (78 g.) from 600 ml. of hexane, there was obtained 60 g. (72.5%) of *trans*-2-styrylpyridine, m.p. 91.5–93°.

Method 2.—A solution consisting of 0.3 mole of the picoline, the aldehyde (0.3 mole) and 50 ml. of acetic anhydride was heated under reflux for 16 hr. The cooled solution was poured onto ice, and the mixture then made alkaline with 40% aqueous sodium hydroxide. When the product was a solid, it was isolated by filtration and recrystallized from a suitable solvent. When the product was an oil, it was extracted from the water mixture with benzene. Distillation of the dried benzene extracts under reduced pressure yielded the desired styrylpyridine. The yields from both methods of isolation are shown in Table III.

4′-Nitro-4-stilbazole.—A mixture of 25 g. of *p*-nitrobenzaldehyde, 15 g. of 4-picoline, and 50 ml. of acetic anhydride was refluxed overnight, poured onto ice, and neutralized with 50% sodium hydroxide solution. The solid was collected and crystallized from ethanol to yield 18 g. of tan solid (A), melting at 149–

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]

DANIEL S. JAMES[2] AND PAUL E. FANTA[3]

Department of Chemistry, Illinois Institute of Technology, Chicago 16, Illinois

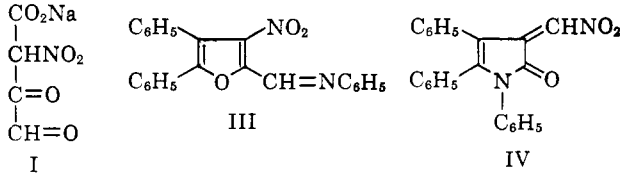
Received September 24, 1962

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.

(2) United States Steel Foundation Fellow, 1960–1962.

(3) To whom inquiries should be addressed.

(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.