Reaction of Styrylpyridine Methiodides with Aniline

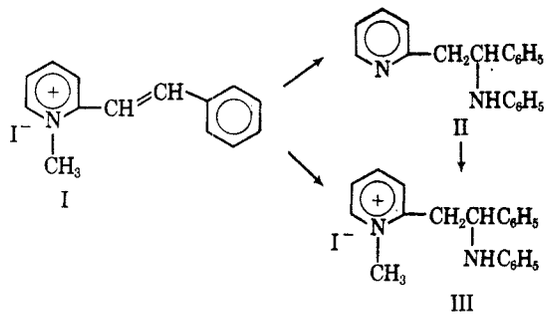
P. J. GRISDALE, J. C. DOTY, T. H. REGAN, AND J. L. R. WILLIAMS

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received December 16, 1966

The reaction between aniline and *trans*-2-styrylpyridine methiodide has been studied in detail and found to yield a mixture of diaminotriphenylmethanes, 2-picoline, N-methylaniline, and N,N-dimethylaniline. A mechanism for this reaction has been proposed which makes it possible to predict certain intermediates which have also been isolated. The reaction has been applied to other styryl derivatives of the methiodides of pyridine and quinoline.

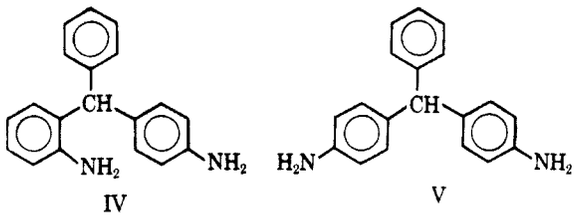
While studying the demethylation of *trans*-2-styrylpyridine methiodide (I) with various aromatic amines including aniline, we considered the possibility that addition of aniline to the double bond could take place.



The addition of various nucleophiles to similar systems has been reported. The reaction between 2-styrylquinoline (free base) and phenylmagnesium bromide furnished 2-(β,β-diphenyl)ethylquinoline,[1] although no reaction was reported between 2-styrylquinoline and sodiomalonic ester.[2] Doering and Weil have reported the addition of a variety of nucleophiles to the 2- and 4-vinylpyridines.[3] Included in their study was the unexpectedly rapid addition of the bisulfite ion, which was thought to be due to the enhanced activation of the double bond by protonation of the pyridine nucleus. In the case of styrylpyridine methiodide, similar activation of the double bond exists because of the charged pyridinium nucleus. In the case of aniline, one would anticipate either II or III as possible reaction products. Compound II would be formed if the addition were more rapid than the demethylation, probably *via* III. If the demethylation were more rapid than the addition, one would expect to obtain 2-styrylpyridine which would not be sufficiently reactive to yield II.

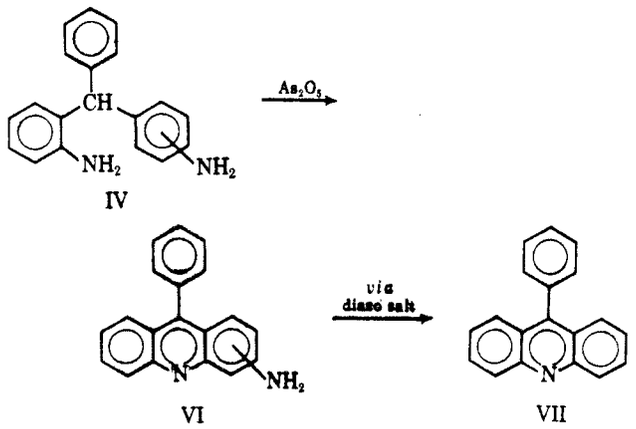
Results and Discussion

When 2-styrylpyridine methiodide was heated under reflux with aniline, we obtained a material which crystallized from benzene as a solvate and had the molecular formula $C_{19}H_{18}N_2C_6H_6$, the composition expected for the benzene-solvated, demethylated adduct, II. Thin layer chromatography revealed that this was a mixture from which two major components were separated by chromatography on silicic acid. Neither component, however, had an nmr spectrum in accord with the expected structures. Particularly evident was the absence of absorption characteristic of the proton α to nitrogen on pyridine (δ 8.3–9.2 ppm). Rather surprisingly, the methiodides of 4-styrylpyridine and 2-styrylquinoline furnished this same solvated mixture under the same conditions, whereas 3-styrylpyridine methiodide was demethylated and the free base, 2-styrylpyridine, failed to react. These two unknown products can also be separated *via* their diacetyl derivatives and have been identified as the 2,4′- and 4,4′-diaminotriphenylmethanes (IV and V).



The slower moving isomer (on thin layer chromatography) was assigned the structure V on the basis of analytical data and infrared, nmr, and mass spectra and by a comparison of the free base and its N,N′-diacetyl derivative with authentic samples.[4]

Throughout this project we were troubled by solvation of the various products. Many solvates of 4,4′-diaminotriphenylmethane are reported.[4] Despite the fact that no other diaminotriphenylmethanes are reported in the literature, the elemental analysis and spectral data (infrared, ultraviolet, nmr, and mass) indicated that the faster moving component was indeed isomeric with V. The increased complexity of the aromatic nmr absorption implied a less symmetrical substitution pattern. The fact that IV did contain an *o*-amino group was established by this degradation.



2,4′,4″-Triaminotriphenylmethane is known to undergo oxidative cyclization to a diaminoacridine when fused

(1) A. Hoffmann, R. T. Farlow, and R. C. Fuson, *J. Am. Chem. Soc.*, **55**, 2000 (1933).

(2) D. Vorlander, *Ann. Chem.*, **320**, 66 (1902).

(3) W. E. Doering and R. A. N. Weil, *J. Am. Chem. Soc.*, **69**, 2461 (1947).

(4) H. Weil, E. Sapper, E. Kramer, K. Kloter, and H. Selberg, *Ber.*, **61**, 1294 (1928).

with arsenic acid. The yield was not reported.[5] Compound IV was successfully converted to an aminophenylacridine (VI), though in poor yield. Compound VI was deaminated *via* the diazonium salt to give 9-phenylacridine identical in every respect with an authentic sample.[6]

The position of the second amino group was established by examination of a purified sample of VI, whose analytical data, infrared, ultraviolet, and mass spectra fully supported the assignment as an amino-9-phenylacridine. We had anticipated that cyclization would take place into the ring containing the second amino group, giving a 1-, 2-, 3-, or 4-amino-9-phenylacridine. Because the introduction of a 9-phenyl group into acridines has little effect on their ultraviolet spectra[7] and because we observed a close correspondence between the spectrum of VI and the spectra of 2- and 3-aminoacridine, we were able to assign VI as the 2- or 3-amino derivative. The 2-amino compound has been reported,[8] but its physical constants do not agree with those for isomer VI which has therefore been assigned as the 3-amino derivative and IV as 2,4′-diaminotriphenylmethane.

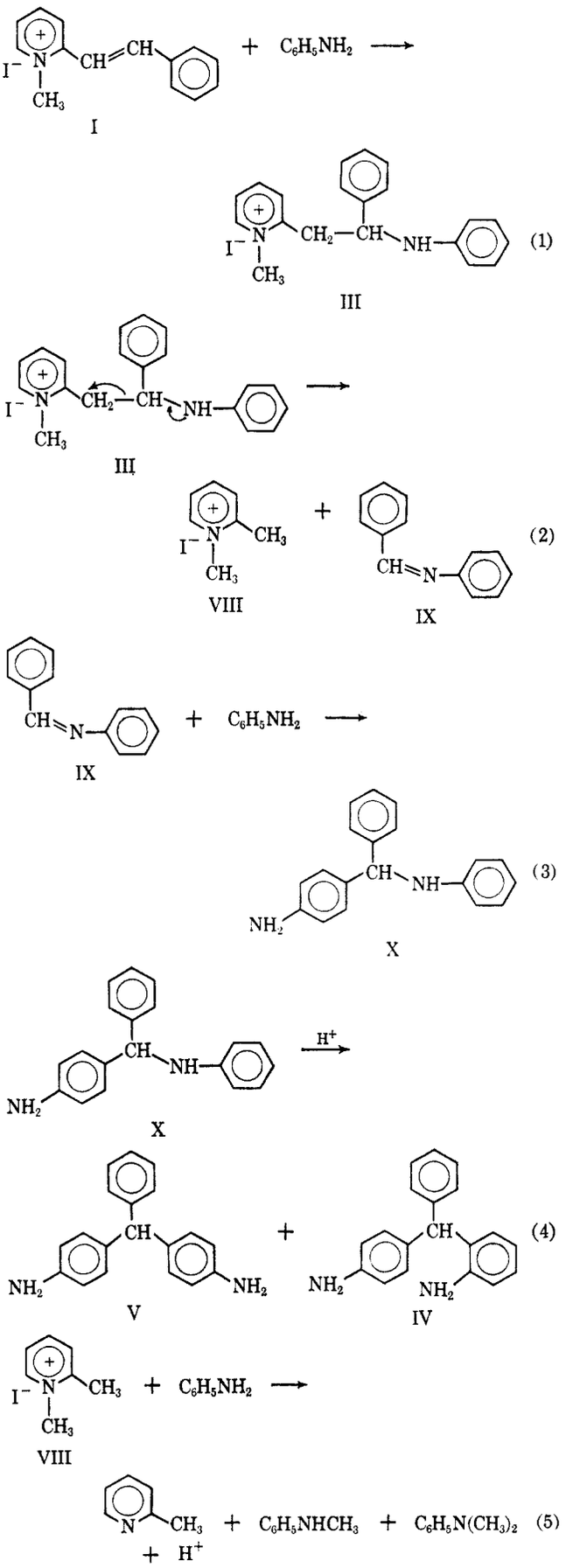
An interesting side light developed during the examination of IV and V. Initial attempts to determine their nmr spectra were carried out in acetone-d_6 solution. The tertiary proton appeared as a double or triple peak (unequal intensities) for both isomers. The solutions were allowed to stand overnight and the intensity of the acetone-d_5 multiplet increased severalfold. This was interpreted as being due to a rapidly established equilibrium between the diaminotriphenylmethanes and their corresponding acetone anils during the course of which the NH protons were

$$ArNH_2 + CH_3COCH_3 \rightleftharpoons ArN{=}C(CH_3)_2 + H_2O$$

eventually exchanged for D of the acetone-d_6, presumably through the intermediacy of the acetone enol. We were able to confirm this by a combination of gas chromatographic and mass spectrometric techniques. Acetone solutions of the diaminotriphenylmethanes were allowed to stand overnight, then injected onto a $^1/_8$-in.-diameter, 4-ft-long, vapor phase chromatography column, packed with 20% DC 200 on Anakrom ABS. The column was maintained at 250°. Compound IV gave one additional peak; V gave two peaks in addition to the diamine. The new peak from IV was collected from the effluent of the glpc column and examined by means of mass spectrometry. The fraction showed a major peak at *m/e* 274 corresponding to $Ar(NH_2)_2$, with smaller amounts of *m/e* 314 and 354 corresponding to $Ar(NH_2)(N{=}CMe_2)$ and $Ar(N{=}CMe_2)_2$, respectively. We tentatively conclude that this glpc peak is the diacetone anil and the parent diamine and monoanil arose from partial hydrolysis before the sample was introduced into the ionization chamber of the mass spectrometer.

The mechanism shown (eq 1–5) for the reaction between aniline and styrylpyridine methiodide is consistent with the above findings.

Aniline and both *cis*- and *trans*-2-styrylpyridine methiodides, when allowed to stand together at room

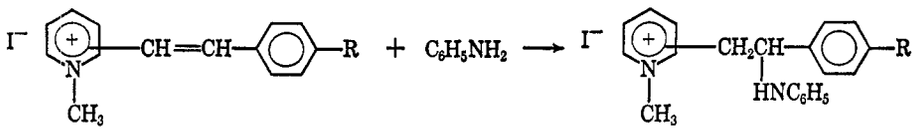


temperature, have yielded the adduct III, which has been characterized by elemental analysis and spectral data. The effect of the introduction of substituents into the phenyl ring of the styrylpyridine molecule has

(5) O. Fischer and G. Körner, *Ann. Chem.*, **226**, 189 (1884).
(6) A. Bernthsen, *ibid.*, **224**, 1 (1884).
(7) V. Zanker and G. Schiefele, *Z. Elektrochem.*, **62**, 86 (1958).
(8) F. Ullmann and H. W. Ernst, *Ber.*, **39**, 298 (1906).

TABLE I

PHYSICAL DATA FOR THE ADDUCTS FROM THE REACTION



Pyridine methiodide starting material	Yield of adduct, %	Reaction time, days	Mp, °C	Formula	Registry No.	Calcd, % C	H	I	N	Found, % C	H	I	N
trans-2-Styryl	66	13	173	$C_{22}H_{21}IN_2$		57.7	5.1	30.5	6.7	57.6	4.8	30.5	6.7
cis-2-Styryl	84	8	173	...		...	...	...	...	...	...	...	...
trans-4-Styryl	20	35	176–178	$C_{20}H_{21}IN_2$	13145-03-4	57.7	5.1	30.5	6.7	57.3	5.0	30.8	6.6
trans-2-Styryl-4′-chloro	72	6	166	$C_{20}H_{20}ClIN_2$	13145-04-5	53.3	4.4	28.2	6.2	52.9	4.3	28.5	5.9
trans-4-Styryl-4′-chloro	20	35	151	$C_{20}H_{20}ClIN_2$	13145-05-6	53.3	4.4	28.2	6.2	53.5	4.6	28.9	5.6
trans-2-Styryl-4′-nitro	55	3	195	$C_{20}H_{20}IN_3O_2$	13145-06-7	52.1	4.3	27.6	9.1	51.8	4.3	27.8	8.9
trans-4-Styryl-4′-nitro	10	35	149	$C_{20}H_{20}IN_3O_2$	13145-07-8	52.1	4.3	27.6	9.1	52.5	4.3	27.9	8.9

been studied. The yields and physical data for the adducts are shown in Table I. Some 4-styrylpyridine methiodides are included. In the presence of electron-donating groups, 4′-CH_3, 4′-OCH_3, and 4′-$N(CH_3)_2$, we were unable to isolate any adducts and no decrease in the extinction of the long-wavelength band in the ultraviolet spectrum owing to the loss of the conjugated >C=C< was observed. When attempts were made to determine the mass spectrum of III, it decomposed in the heated vaporization inlet of the instrument[9] to 2-picoline, methyl iodide, aniline, and N-benzylideneaniline. Similarly, attempts to sublime III yielded N-benzylideneaniline (IX), and the adducts from XII and XIV (Table I) gave 4-chloro- and 4-nitrobenzylideneaniline, respectively. The addition of aniline to N-benzylideneaniline to give X and its rearrangement to V is reported,[10] but no isomer formation was mentioned. Catalytic amounts of acid were used.

The final step is a simple transmethylation. We have examined all the products from the reaction between *trans*-2-styrlpyridine methiodide and hot aniline by glpc analysis. The results of duplicate runs are shown in Table II. The presence of dimethylaniline, methylaniline, and 2-picoline was confirmed by thin layer chromatography and by comparison with authentic samples; 2-picoline was also isolated as its picrate.

Step 4 is a Hofmann–Martius rearrangement, but the high *ortho–para* ratio (see Table II) was unprecedented for two reasons. First, very few *ortho* rearranged products are usually observed for such rearrangements[11] and, second, no isomeric products were reported by the early workers who used catalytic amounts of acid.[10] We are at present investigating this interesting rearrangement. It should be pointed out that this high *ortho–para* ratio is in agreement with the results of the Japanese workers,[12] who observed a rearrangement during an attempted synthesis of N-phenylbenzhydrylamine, which produced a high percentage of *o*-aminotriphenylmethane, together with the *para* isomer.

(9) The system is described by V. J. Caldecourt, *Anal. Chem.*, **27**, 1670 (1955), but modified by using all-glass construction.

(10) German Patent 111,041 (1898); *Chem. Zentr.*, II, 548 (1900).

(11) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 615–618.

(12) Z. Horii, T. Sakai, and Y. Tamura, *Pharm. Bull.* (Tokyo), **5**, 132 (1957); *Chem. Abstr.*, **51**, 16364*g* (1957).

TABLE II

PER CENT COMPOSITION OF THE PRODUCTS FROM THE REACTION OF 2-STYRYLPYRIDINE METHIODIDE (1.25 g) WITH ANILINE (2.5 ml) UNDER REFLUX

	Volatiles[a]	
Experiment no.	1	2
Aniline	83.0	83.6
N-Methylaniline	10.7	10.9
N,N-Dimethylaniline	Trace	Trace
2-Picoline	6.2	5.3
	Nonvolatiles[b]	
Experiment no.	1	2
2,4′-Diaminotriphenylmethane	39.8	37.8
4,4′-Diaminotriphenylmethane	52.0	54.5
Unknown[c]	8.2	7.7

[a] Volatiles determined by glpc analysis by using an 8-ft, 1/8-in. column packed with 20% DC 200 fluid on Anakrom ABS at 139°. [b] Nonvolatiles separated on a similar 4-ft column at 250°. [c] Available evidence indicates this unknown may be an N-methyl derivative of diaminotriphenylmethane, mass spectrum parent ion *m/e* 288, with three exchangeable protons.

Experimental Section

All melting points are corrected. Thin layer chromatography was performed on Eastman Chromogram Type K301R and developed by using ethyl acetate–hexane, 30:70 by volume, unless otherwise stated. Spectra were determined by means of a Cary Model 15 ultraviolet spectrometer, a Varian Model A-60, Baird Atomic NKI (infrared), and 60° sector-type mass spectrometer equipped with an all-glass inlet system heated to 235°.

Preparation and Chromatographic Separation of 2,4′-Diaminotriphenylmethane (IV) and 4,4′-Diaminotriphenylmethane (V).—A mixture of *trans*-2-styrylpyridine methiodide (25.0 g) and aniline (50.0 g) was heated under reflux for 1 hr. The cooled reaction mixture was washed with dilute ammonium hydroxide solution and organic material was extracted with ether. The ether extract was washed with water and dried over anhydrous magnesium sulfate. The excess aniline and ether were removed under reduced pressure to give a brown oil which crystallized from benzene to yield colorless prisms (15.0 g). A portion of this material (4.25 g) was chromatographed on silicic acid with an increasing percentage of ethyl acetate in benzene as eluent. The eluent was monitored by thin layer chromatography. The desired portions were evaporated to yield 2,4′-diaminotriphenylmethane (IV, 0.6 g) and 4,4′-diaminotriphenylmethane (V, 1.95 g). An intermediate cut yielded a mixture of IV and V (1.15 g). The

4,4′ isomer (V) crystallized from benzene as colorless prisms, 1.2 g, mp 137–138° (lit.[4] mp 106°, fast; approximately 130°, slow, for V with 1 mole of benzene). A sublimed sample had mp 142–144° (lit.[4] 139°) and mmp (with an authentic sample) 142–144°. Both the isolated and the authentic samples had identical mass spectra, mol wt 274, with four exchangeable protons. The nmr spectrum of the benzene-solvated compound showed absorption bands at δ^{CDCl_3} 7.30 (singlet, 6.8 H); 7.14 (singlet, 4.0 H); 6.93, 6.80, 6.52, 6.38 (characteristic AA′BB′ pattern of a *para*-disubstituted benzene, 8.0 H); 5.28 (singlet, 1.0 H); and 3.35 (singlet, 4.0 H). The latter peak was exchanged on shaking the solution with D_2O. This spectrum could be accommodated by 4,4′-diaminotriphenylmethane containing slightly more than 1 mole of benzene of solvation. A sublimed sample had the following analysis.

Anal. Calcd for $C_{19}H_{18}N_2$: C, 83.2; H, 6.6; N, 10.2. Found: C, 83.2; H, 6.8; N, 10.0.

The 2,4′ isomer (IV) crystallized from benzene as colorless prisms, 0.4 g, mp 99–104°, containing benzene of crystallization as judged by spectral data. A sample when sublimed at 120° (0.1 mm) had mp 131–132°, mol wt (mass spectrum) 274, and four exchangeable protons. The infrared spectrum established the presence of a primary amino group. The nmr spectrum showed absorption bands at δ^{CDCl_3} 6.6–7.3 (complex, 18.0 H); 5.82 (singlet, 1.0 H); 4.75 (broadened singlet, exchanged with D_2O, 3.4 H). The sublimed sample had the following analysis.

Anal. Calcd for $C_{19}H_{18}N_2$: C, 83.2; H, 6.6; N, 10.2. Found: C, 82.9; H, 6.2; N, 10.2.

Separation of the Isomeric Diaminotriphenylmethanes (IV + V) *via* Their Diacetyl Derivatives.—The crude mixture of diaminotriphenylmethanes (100 g, once recrystallized from benzene) was dissolved in benzene (900 ml) and treated with acetic anhydride (100 g). The mixture was allowed to stand for 2 days; the precipitated 4,4′-diacetylaminotriphenylmethane was removed by filtration. The crude product was crystallized from chloroform–petroleum ether (bp 65–75°) to yield 42 g of crystals, mp 230–234°. A sample recrystallized from dilute acetic acid had mp 244–246°, authentic sample mp 243–246°,[4] and mmp 242–246°. A sample dried at 100° analyzed as the hemihydrate.

Anal. Calcd for $C_{23}H_{22}N_2O_2 \cdot {}^1/_2H_2O$: C, 75.2; H, 6.1; N, 7.6. Found: C, 75.6; H, 6.1; N, 7.5.

A sample dried at 200° (0.1 mm) for 6 hr analyzed as the free diacetyl derivative.

Anal. Calcd for $C_{23}H_{22}N_2O_2$: C, 77.0; H, 6.0; N, 7.8. Found: C, 77.0; H, 6.0; N, 7.8.

The mother liquors from the precipitation of the crude 4,4′ isomers were evaporated and the residue was crystallized from chloroform–petroleum ether (bp 65–75°) to yield 19.0 g of crude product, mp 181–191°. A sample recrystallized from dilute acetic acid had mp 212–214° and, after drying at 100°, analyzed as a hemihydrate.

Anal. Calcd for $C_{23}H_{22}N_2O_2 \cdot {}^1/_2H_2O$: C, 75.2; H, 6.1; N, 7.6. Found: C, 75.5; H, 6.3; N, 7.6.

After drying at 180° (0.1 mm) for 6 hr, the free diacetyl derivative was obtained.

Anal. Calcd for $C_{23}H_{22}N_2O_2$: C, 77.1; H, 6.1; N, 7.8. Found: C, 76.5; H, 5.9; N, 7.6.

Both these diacetyl derivatives were hydrolyzed in dilute ethanolic hydrochloric acid to yield the free bases which were identical in every way with the samples separated by chromatography.

Reactions of Some Substituted Styrylpyridine Methiodides with Aniline.—Under the conditions outlined in the previous sections, the following observations were made. *trans*-4-Styrylpyridine and *trans*-2-styrylquinoline methiodides with aniline under reflux yielded the mixture of isomeric diaminotriphenylmethanes. *trans*-3-Styrylpyridine methiodide yielded aniline-solvated 3-styrylpyridine which crystallized from cyclohexane as white needles, mp 71–73°. Authentic *trans*-3-styrylpyridine had mp 80–81° (lit.[13] 77–79°), but crystallized from cyclohexane containing traces of aniline as an aniline-solvated species, mp 72–74°. The appearance of additional peaks in the infrared spectrum of *trans*-3-styrylpyridine due to aniline confirmed that the compound melting at 71–73° was a solvate and not an adduct. *trans*-4′-Chloro-2-styrylpyridine methiodide yielded a product assigned as a mixture of 2,4′- and 4,4′-diamino-4″-chlorotriphenylmethane by analogy.

(13) F. H. Clarke, G. A. Felock, G. B. Silverman, and C. M. Watrick, *J. Org. Chem.*, **27**, 533 (1962).

Anal. Calcd for $C_{19}H_{17}ClN_2$: C, 73.9; H, 5.5; N, 9.1. Found: C, 73.7; H, 5.3; N, 8.9.

Conversion of 2,4′-Diaminotriphenylmethane (IV) to 9-Phenylacridine (VII) *via* 3-Amino-9-phenylacridine (VI).—2,4′-Diaminotriphenylmethane (3.5 g) and syrupy arsenic acid (12 g) were heated to 160° in an oil bath for 30 min. The brown liquid was cooled, extracted with hot water, and filtered, and the filtrate made basic with sodium hydroxide solution. The brown precipitate (2.0 g) was collected, washed with cold water, and dried. Extraction of the material with ether in a Soxhlet extractor yielded a brown-yellow gum which gave a yellow solid on crystallization from ligroin (bp 65–45°). Thin layer chromatography (25% ethyl acetate in hexane) showed only one major component which exhibited bright fluorescence under ultraviolet light. The solid turned to a glass at 80° and became a liquid at 161–166°. Chromatography of the solid on Florosil with benzene and an increasing percentage of ethyl acetate yielded similar material (0.3 g) homogeneous on thin layer chromatography; it became a glass at 80° and a liquid at 171–175°. This substance had mol wt (mass spectrum) 270 and a peak at *m/e* 242 (M − CNH_2). The fragmentation pattern was similar to that of 3-aminoacridine. The infrared spectrum showed a primary amino group; the position and nature of the bands were very similar to those of 3-aminoacridine. The ultraviolet spectrum showed bands [λ_{max} mμ (ϵ)] at 435 (4900), 356 (6200), 339 (3600). 3-Aminoacridine had [λ_{max} mμ (ϵ)] 430 (6500), 352 (6600), 335 (3550).

Anal. Calcd for $C_{19}H_{14}N_2 \cdot {}^1/_2H_2O$: C, 81.7; H, 5.4; N, 10.0. Found: C, 81.2; H, 4.8; N, 10.0.

The mother liquors and residues from the isolation of the sample of 3-amino-9-phenylacridine were evaporated to dryness and the crude residue (0.75 g) was dissolved in dilute hydrochloric acid (30 ml) and treated with sodium nitrite (0.5 g) at 0°. The resulting suspension was filtered and the filtrate treated with ice-cold hypophosphorous acid (30 ml) and kept at 0° for 2 days. The suspension was filtered and the filtrate made basic with dilute sodium hydroxide solution and extracted with two 30-ml portions of ether. The ether layer was dried and evaporated to yield the crude 9-phenylacridine, 0.02 g, mp 170–176°. It was sublimed at 150° (0.05 mm) to give a pure sample identical in every respect with an authentic[6] sample: mp 179–182°, authentic sample mp 184–186°, mmp 179–182°. The ultraviolet spectra and thin layer chromatograms of the two samples were identical.

2-(β-Anilino-β-phenyl)ethylpyridine Methiodide (III) (Adduct of Aniline and I).—A mixture of *trans*-2-styrylpyridine methiodide (20 g, 0.1 mole) and aniline (35.4 g, 0.36 mole) was stirred in a stoppered flask at room temperature. After 1 week a portion of the suspension was withdrawn and diluted with methanol to give an approximately 5×10^{-4} *M* solution (based on starting material). The reduction of the 340-mμ band in the ultraviolet spectrum showed that little starting material remained. Acetonitrile (50 ml) was added and the suspension cooled; the solid was collected by filtration. The solid (A) which had mp 141–146° weighed 23.0 g. The filtrate was diluted with petroleum ether (50 ml, bp 35–60°) and, on cooling, deposited starting material, 3.0 g, mp 218–225°. On further cooling, the filtrate deposited solid B, 1.0 g, mp 174°, which proved to be the desired adduct (analyses in Table I). The nmr spectrum of B showed absorption at δ^{DMSO-d_6} 9.09 (doublet of multiplets 1.0 H characteristic of H α to N^+ on a pyridinium ring); complex absorption at 8.8–6.5 (14.0 H); a multiplet centered at 5.21 (four broad peaks approximately equal intensity (1.0 H); 4.40 (broad singlet, 3H, CH_3N^+); 3.62 (very broad single peak, 2.0 H). Both the nmr and infrared spectra of A showed additional absorptions due to aniline when compared with those of B. A sample of solid A was submitted for analysis.

Anal. Calcd for $C_{20}H_{19}IN_2 \cdot C_6H_5NH_2$: C, 61.4; H, 5.5; I, 24.9; N, 8.3. Found: C, 61.0; H, 5.8; I, 25.1; N, 8.3.

The solvated species (A, 3.0 g) in benzene (20 ml) was heated under reflux for 1 hr. On cooling, the unsolvated adduct (B) was deposited and was collected by filtration, 2.2 g, mp 172–174°. The filtrate was freed from benzene and the oily residue was identified as aniline by conversion to acetanilide: mp 120°, authentic sample mp 118–120°, mmp 118–120°.

Preparation of Adduct of Aniline and XII–XVI (Table I).—A mixture of the substituted styrylpyridine methiodide (XII–XVI, 5.0 g) and aniline (20 g) was stirred in a stoppered flask. Portions were withdrawn at weekly intervals and examined for the disappearance of the long-wavelength band in the ultraviolet spectra due to the conjugated *trans* >C=C< group. When the reaction was deemed complete, the mixtures were treated with

benzene (400 ml) and the crude products collected by filtration. These products were crystallized from acetonitrile–ethanol. The unreacted starting materials precipitated first and the desired adducts were recovered from the mother liquors by crystallization. The yields, reaction times, and analyses are listed in Table I.

Decomposition of III to N-Benzylideneaniline (IX).—The adduct III (2.0 g) was sublimed at 190° (0.1 mm). The sublimate was crystallized from hexane to yield N-benzylideneaniline, mp 43–44°, identical in every way with an authentic sample.

Anal. Calcd for $C_{13}H_{11}N$: C, 86.2; H, 6.1; N, 7.7. Found: C, 85.5; H, 6.4; N, 7.4.

Registry No.—III, 13144-99-5; IV, 13168-31-5; IV diacetyl derivative, 13145-00-1; V, 603-40-7; V diacetyl derivative, 13145-01-2; VI, 13145-02-3; VII, 602-56-2; IX, 538-51-2; 2,4′-diamino-4″-chlorotriphenylmethane, 13145-08-9; 4,4′-diamino-4″-chlorotriphenylmethane, 13145-09-0.

Catalytic Effects of Substituted Pyridines and Quinolines on the Reaction of Phenyl Glycidyl Ether and Benzoic Acid

YOSHIO TANAKA

Institute of Material Science and Engineering, Faculty of Engineering, Yokohama National University, Yokohama, Japan

Received December 21, 1966

The catalytic effect of methyl-substituted pyridines and quinolines on the reaction between phenyl glycidyl ether and benzoic acid in xylene was studied at various temperatures and comparative catalytic coefficients were evaluated for these catalysts. The reaction rates decrease from pyridine to 2-picoline, from 2-picoline to 2,6-lutidine, and from quinoline to 2-methylquinoline. Introduction of a methyl group into the 3 or 4 position of pyridine increases the rate, while substitution in the 2 position decreases the rate. This should be due to a steric hindrance, which does not seem to be additive, of larger size than in the reaction of methyl iodide with 2-alkylpyridines and of smaller size than in the reaction of boron trifluoride with these bases. A deviation from a linearity between the rates and the pK_a values can be interpreted neither by a nucleophilicity of the pyridines, by an electrophilicity of their conjugated acids, nor by a linear combination of these two factors. This hindrance might be related to steric strains primarily in the activated complex and secondly in molecular addition compounds in the reaction process.

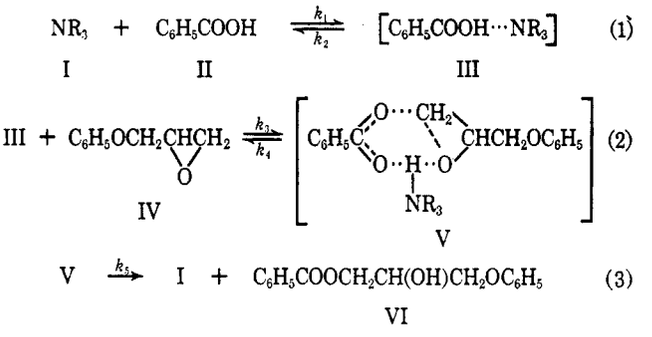
Pyridine catalyzes the solvolyses of acetic anhydride[1-3] and tetramethylphosphorodiamidic chloride,[4] whereas 2-picoline and 2,4- and 2,6-lutidines, which are stronger bases, have no effect on those reactions. This phenomenon has been ascribed to steric requirement of nucleophilic attack by the bases on the electrophiles. Subjection to steric hindrance is one of the criteria which might be considered to characterize nucleophilic as opposed to general base catalysis.

Recently, however, some reactions which are considered to proceed by general base or acid catalysis are found to be subjected to steric hindrance. Gutsche and his co-workers[5] have found that the aldol condensation is promoted by pyridine but hardly by 2,6-lutidine. Covitz and Westheimer[4] have shown that the hydrolysis of methyl ethylene phosphate, mutarotation of glucose, and inversion of menthone are dependent on steric requirement by substituted pyridines used as catalyst.

Pritchard and Long[6] examined the nucleophilic activity of various hindered amines toward propylene oxide in buffered aqueous solutions, while Swain[7] showed that "specific oxonium ion catalysis" for ethylene oxide reactions is observed only at so low buffer concentrations that neither the undissociated buffer acid nor the buffer base participates detectably.

In a previous paper,[8] we suggested and discussed that a hydrogen-bonded complex (III) of a tertiary amine (I) and benzoic acid (II) would play an important role for the tertiary amine catalyzed reaction of phenyl glycidyl ether (IV) and benzoic acid (see Scheme I). If an activated complex or a transition species is of the type V in Scheme I, its stability may be affected by steric requirement.

SCHEME I



Because an appropriate choice of substituents and their position permits one to vary, simultaneously or independently, both the donor tendency of the N-ring atom and the steric requirements of the molecule, substituted pyridines appear to be especially suited to the investigation of the factors which influence the stereochemistry of the transition-state species or the activated complex. This paper reports a catalytic effect of the pyridines on the reaction of phenyl glycidyl ether (PGE) and benzoic acid (BA) in xylene.

Experimental Section

Materials.—Reagent grade PGE was dried over calcium hydride for several days and distilled at reduced pressure. The fraction boiling at 103° (6 mm) was collected for use. Reagent grade benzoic acid was recrystallized from its aqueous

(1) (a) S. L. Bafna and V. Gold, *J. Chem. Soc.*, 1406 (1953); (b) V. Gold and E. G. Jefferson, *ibid.*, 1409 (1953); (c) V. Gold and E. G. Jefferson, *ibid.*, 1416 (1953).
(2) A. R. Butler and V. Gold, *ibid.*, 4362 (1961).
(3) S. L. Johnson, *J. Phys. Chem.*, **67**, 495 (1963).
(4) F. Covitz and F. H. Westheimer, *J. Am. Chem. Soc.*, **85**, 1773 (1963).
(5) C. D Gutsche and R. S. Buriks, *ibid.*, **84**, 3775 (1962).
(6) J. G. Pritchard and F. A. Long, *ibid.*, **79**, 2365 (1957).
(7) C. G. Swain, *ibid.*, **74**, 4108 (1952).
(8) H. Kakiuchi and Y. Tanaka, *J. Org. Chem.*, **31**, 1559 (1966).