then distilled. A quantitative yield, 1.3 g., of solid ketone (+)-VII was obtained, m.p. 55–55.5°, [α] 141° (*c* 1, ethanol). The melting point and specific rotation were the same after two crystallizations from hexane. The n.m.r. spectrum was identical with that of the racemic sample.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 82.7[17]; H, 7.41.[17]

In one model experiment a batch of racemic ketone VII, prepared by our method, crystallized after being stored in the refrigerator. Subsequently all samples of the ketone crystallized if they did not contain detectable amounts of the *exo*-phenyl epimer. The ketone has previously been reported[2] as a liquid. It was crystallized from ice-cold hexane; m.p. 33–35°.

(+)-3-*endo*-Phenyl-2-*exo*-norbornanol ((+)-X).—Partially resolved (−)-3-*exo*-phenyl-2-*endo*-norbornylamine ((−)-VIII) was recovered from the mother liquors after resolution of (+)-VIII. It was converted to the (+)-2-phenylnorbornylene-2, [α] 103.7° (57.5% optically pure). This olefinic material, 5.9 g., was dissolved in 43 ml. of diglyme, and 1.1 g. of sodium borohydride was added. To the mixture was then slowly added 4.5 g. of boron trifluoride dietherate in 10 ml. of diglyme. The mixture was stirred for 3.5 hr. after which 7.5 ml. of 3 *N* sodium hydroxide was added, followed by 7.5 ml. of 30% hydrogen peroxide. Stirring was continued for 0.5 hr. and the contents of the flask were washed with ether and water into a separatory funnel. The water layer was removed and the ether layer was washed three times with water. The ether was evaporated and the residue was distilled. Most of the material, 4 g., was collected at 125–126° at 0.15 mm. It partially crystallized; [α] 52.8° (*c* 1, ethanol).

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.06; H, 8.37.

Oxidation of (+)-X to (+)-VII.—To 17 ml. of pyridine cooled in an ice bath was carefully added 2 g. of chromium trioxide. After the yellow complex had been formed, there was added 2 g. of carbinol (+)-X dissolved in 5 ml. of pyridine. The mixture was stirred at room temperature for 2 hr., after which time it was mixed with 200 ml. of water. The aqueous solution was extracted with three portions of ether, and the ether extracts were washed with water and dilute hydrochloric acid. After evaporation of the ether, the product was distilled to give 1 g. of ketone (+)-VII; b.p. 103–106° at 0.1 mm., [α] 74.8° (*c* 1, ethanol, 53% optical purity). The infrared spectrum indicated the presence of a small amount of unreacted carbinol.

Summary of Evidence for Assignment of *endo*-Phenyl Configuration in Ketone VII.—At the suggestion of a referee we summarize our evidence which establishes the *endo* configuration of the phenyl group in ketone VII: (1) Borohydration of olefin IV gave 3-*endo*-phenyl-2-*exo*-norborneol (X) whose configuration is assumed from the established[18] stereochemical course for borohydration of norbornene, α-pinene, camphene, and other similar bicyclic olefins. Oxidation of X with chromium trioxide in pyridine afforded a ketone (VII) whose n.m.r. spectrum was identical with that of the ketone VII obtained upon rearrangement of VI in sulfuric acid.

Further evidence for the correctness of the assigned *endo*-phenyl configuration of VII can be obtained by comparing its n.m.r. spectrum with that of 3-*exo*-phenylnorbornanone-2 obtained by the Nef reaction[2] or by isomerization of VII in alkaline solution. The signal for the tertiary proton at C-3 of ketone VII appears as a doublet, J = 4.5 c.p.s. at 3.27 p.p.m. downfield from the signal for tetramethylsilane. The signal for the same proton of the "Nef" ketone appears as a doublet, J = 3.1 c.p.s. at 2.93 p.p.m. It has been shown[19] that the *exo* protons in bicycloheptyl compounds are less shielded than *endo* protons and appear at lower fields. This then establishes VII as having a 3-*exo* proton. The doublet separation of 3.1 c.p.s. for the "Nef" ketone probably arises from coupling of the 3-*endo* proton with the 7-*anti* proton[20] rather than with the 4-bridgehead proton (which should be nearly zero).[21] Details of the n.m.r. spectra of several phenyl-substituted norbornane compounds will be the subject of a later paper.

(17) Carbon and hydrogen analyses were performed by Huffman Microanalytical Laboratories, Wheatridge, Colo. The analysis of the ketone is somewhat low, about 1%, because this compound reacts with oxygen from the air and is converted to a mixture of *cis*-3-benzoylcyclopentanecarboxylic acid and other oxygen-containing compounds.

(18) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, pp. 126–131.

(19) J. I. Musher, *Mol. Phys.*, **6**, 93 (1963).

(20) J. Meinwald and Y. C. Meinwald, *J. Am. Chem. Soc.*, **85**, 2514 (1963).

(21) P. Laszlo and P. von R. Schleyer, *ibid.*, **86**, 1171 (1964).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME, NOTRE DAME, INDIANA]

Aromatic N-Oxides. IV. The Mechanism of the Reaction of 2-Alkylpyridine N-Oxides with Acetic Anhydride[1,2]

BY VINCENT J. TRAYNELIS AND PIER L. PACINI

RECEIVED JULY 23, 1964

The reaction of 1-acetoxy-2-methylpyridinium perchlorate and the corresponding 2-benzyl and 2-*p*-nitrobenzyl compounds with base to produce the corresponding 2-pyridylmethyl acetates is reported. Attempts to detect the intermediacy of the anhydro base IV in the above reactions spectrally were all negative. These results along with the absence of deuterium exchange are interpreted mechanistically.

Since the reaction of 2-alkylpyridine N-oxides with acid anhydrides to produce 2-(α-acetoxyalkyl)pyridines was reported about 10 years ago,[3,4] considerable attention has been directed toward the mechanism of this reaction. In a recent report, Oae[5] reviewed the contributions of various workers toward elucidating the mechanism of this reaction and provided important evidence about the nature of the bond-breaking process leading to the rearranged product. The present paper offers a discussion about the anhydro base intermediate and the rate-controlling step of this reaction.

The generally accepted mechanism as diagrammed below requires a nucleophilic attack by the N-oxide (I) oxygen on acetic anhydride (II) with the generation of the 1-acetoxy-2-alkylpyridinium ion (III) and an acetate anion. Abstraction of a proton from III by the acetate anion produces acetic acid and the anhydro-base IV which undergoes an intramolecular rearrangement to V. Direct evidence for the nature of step 1 is not available; however, studies in the 2-methylquinoline N-oxide system[6,7] provided spectral evidence that 2-methylquinoline N-oxide in acetic anhydride was

(1) Grateful acknowledgment is made to the National Science Foundation for a research grant (NSF-G13154) in support of this work.

(2) For paper III in this series see V. J. Traynelis, Sr., A. I. Gallagher, and R. F. Martello, *J. Org. Chem.*, **26**, 4365 (1961).

(3) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954); G. Kobayashi and S. Furukawa, *Pharm. Bull. Japan*, **1**, 347 (1953); *Chem. Abstr.*, **49**, 10948*e* (1955).

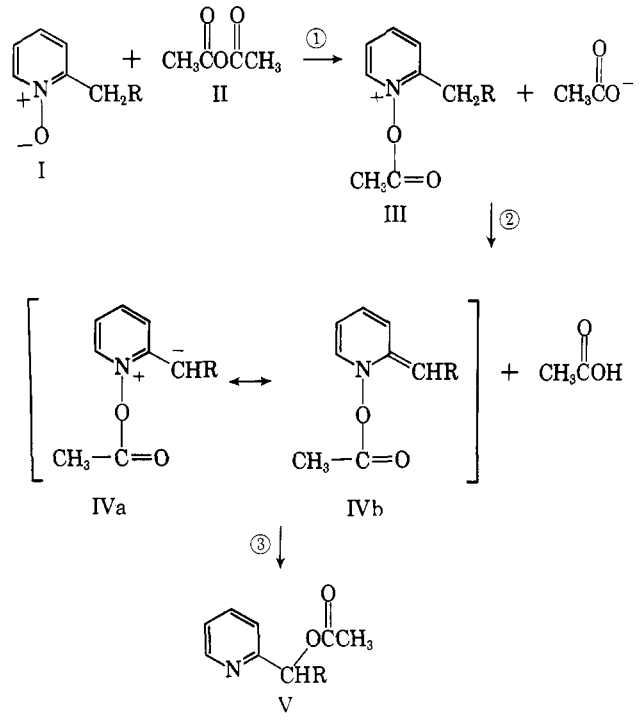
(4) For leading references see V. J. Traynelis and R. F. Martello, *J. Am. Chem. Soc.*, **80**, 6590 (1958).

(5) S. Oae, T. Kitao, and Y. Kitaoka, *ibid.*, **84**, 3359 (1962).

(6) S. Furukawa, *J. Pharm. Soc. Japan*, **79**, 492 (1959); *Chem. Abstr.* **53**, 18029*b* (1959).

(7) C. W. Muth and R. S. Darlak, private communication.

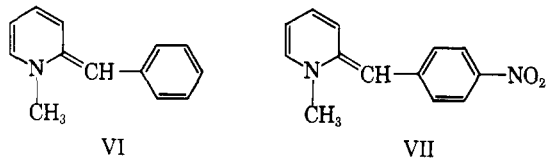
converted completely to the 1-acetoxyquinolinium cation similar to III. By analogy, one may expect a good conversion of I to III after mixing the reactants.



The isolation of cation III was accomplished as the perchlorate salt[7] from the reaction of I and II in the presence of perchloric acid and the picrate salt[2] from the reaction of 2-picoline N-oxide with picryl acetate. When the latter salt was treated with triethylamine, equal amounts of 2-pyridylmethyl acetate and triethylammonium picrate resulted, which supports the suggestion of III as an acceptable intermediate in this reaction.[2] In addition, the need for base to convert III to V requires a proton abstraction in step 2. The intramolecular nature of the rearrangement, step 3, was supported by experiments in the presence of foreign anions (chloride,[4] other acid anions;[4] and aryl oxide ions[2]) which were *not* incorporated in the products. Oae[5] strengthened this position by showing, through labeling experiments, that the N-oxide oxygen was retained in the ester product. Further, Oae demonstrated that the nitrogen–oxygen bond of IV must be broken before the carbon–oxygen bond of ester V was formed.

A free-radical chain mechanism has been excluded[4,5] for this reaction, but free radicals appeared to be present in the reaction medium.[4] An attractive explanation consistent with the above discussion involves a homolytic rupture of the nitrogen–oxygen bond in IV with the generation of a radical pair in a cage. Thus recombination of these species leads to ester products, or, alternatively, separation of the radicals followed by reactions characteristic of the species generated (acetoxy radicals and 2-picolyl radicals) leads to the by-products of the reaction.

Our current efforts have been directed toward gathering evidence for the anhydro base IV and the rate-limiting step of the over-all reaction. An attractive approach to detect the presence of the anhydro base IV in the reaction medium appeared to be by spectral measurements. Two model anhydro bases, 1-methyl-2-benzal-1,2-dihydropyridine (VI) and 1-methyl-2-*p*-nitrobenzal-1,2-dihydropyridine (VII), were prepared as described in the literature and their ultra-



violet and visible spectra recorded (see Experimental section). Both compounds showed strong absorption maxima in the ultraviolet and visible regions. The most promising study for spectral detection of the N-acetoxy anhydro bases analogous to VI and VII appeared to be the reaction of 1-acetoxy-2-benzyl(or-2-*p*-nitrobenzyl)pyridinium perchlorate and triethylamine.

Preliminary to this study, the reactions of 2-benzylpyridine N-oxide (I, R = C_6H_5) and 2-*p*-nitrobenzylpyridine N-oxide (I, R = *p*-$NO_2C_6H_4$) with acetic anhydride were investigated and produced phenyl-2-pyridylmethyl acetate (V, R = C_6H_5) (80%) and *p*-nitrophenyl-2-pyridylmethyl acetate (V, R = *p*-NO_2-C_6H_4) (48%), respectively. The former ester was identified by physical constants and preparation of its picrate, while the later ester had the correct analysis, an appropriate infrared spectrum, and was saponified to the corresponding *p*-nitrophenyl-2-pyridylmethanol. When equimolar amounts of 2-benzylpyridine N-oxide and acetic anhydride were refluxed in acetonitrile for 2 hr., only a 60% yield of ester resulted.

1-Acetoxy-2-alkylpyridinium (III) perchlorates were prepared by the procedure of Muth[8] and are listed in Table I. Structural assignments were based on analysis and the characteristic carbonyl absorption at 5.42–5.45 μ.[2] A study of the reaction of 1-acetoxy-2-benzylpyridinium perchlorate (III, R = C_6H_5) and triethylamine in anhydrous acetonitrile did not reveal the presence of any anhydro base, but reaction proceeded and gave phenyl-2-pyridylmethyl acetate (V, R = C_6H_5) in 56–60% yield (note the reaction of 2-benzylpyridine N-oxide and acetic anhydride in acetonitrile produced ester in 60% yield). Similarly, the reaction of 1-acetoxy-2-*p*-nitrobenzylpyridinium perchlorate (III, R = *p*-$NO_2C_6H_4$) and triethylamine failed to provide spectral evidence for the anhydro base but produced ester in 51–56% yield. When the reaction of III (R = C_6H_5 or R = *p*-$NO_2C_6H_4$) and triethylamine was followed by the disappearance of the characteristic 5.4 μ carbonyl absorption of III, the results indicated a rapid conversion of III to V. The reaction of III with triethylamine in anhydrous acetonitrile at 0° was complete before a sample of the reaction mixture could be removed and its infrared spectrum determined. This surprising observation led to a study of the reaction of III (R = C_6H_5) with several bases under various conditions. These results are recorded in Table II and suggest that the conversion of III to V is dependent on base strength.

Reasonable mechanistic pathways for the reaction of 1-acetoxy-2-alkylpyridinium ions (III) and base to produce the ester V include a direct conversion of III

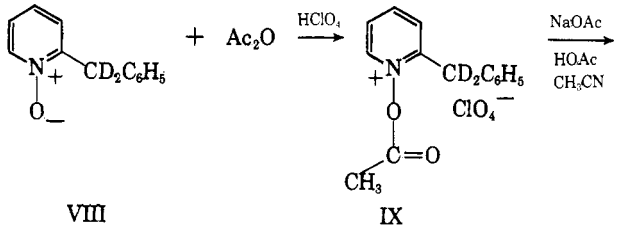
(8) C. W. Muth, R. S. Darlak, W. H. English, and A. T. Hamner, *Anal. Chem.*, **34**, 1163 (1962).

to V or the intervention of an intermediate anhydro base IV. The direct route to ester V requires a transition state in which a proton abstraction from the α-side chain carbon must be accompanied by rupture of the nitrogen–oxygen bond with recombination of fragments producing the ester alkyl–oxygen bond. This mechanism does not appear attractive in view of the extensive bond-breaking and bond-making acts required. Oae[5] has shown *via* oxygen-18 studies that the two oxygens in the acetoxy moiety in III become equilibrated during rearrangement to V. These observations are not compatible with the above mechanism of a simultaneous proton abstraction and acetoxy migration in III. The alternative path involving the anhydro base IV may proceed by a reversible or irreversible conversion of III to IV followed by an intramolecular rearrangement of IV to V.

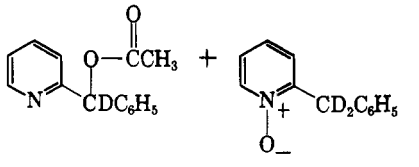
$$\text{III} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \text{IV} \xrightarrow{k_4} \text{V}$$

The absence of absorption maxima of the reaction medium in the ultraviolet and visible spectrum corresponding to the spectrum of the similar, stable, classical anhydro bases VI and VII requires, at best, a very low concentration of anhydro base. This lack of accumulation of anhydro base immediately excludes the possibility that $k_3 > k_{-3}$ or k_4. This leaves as alternatives $k_{-3} >> k_4$ in which case step IV to V is rate determining, or $k_4 >> k_{-3}$ in which case step III to IV is rate determining. A study with deuterium-labeled compounds was undertaken to settle this point.

2-(α,α-Dideuteriobenzyl)pyridine N-oxide (VIII) was prepared by an exchange reaction of 2-benzylpyridine N-oxide in deuterium oxide promoted by triethylamine. The replacement of the two α,α-benzyl hydrogens by deuterium was nearly complete (calcd.: 18.18 atom % excess deuterium; found: 17.55%) and the n.m.r. spectrum showed the absence of proton resonance in the region of the benzyl hydrogens. The N-oxide VIII was converted to 1-acetoxy-2-(α,α-dideuteriobenzyl)pyridinium perchlorate (IX) which was hygroscopic and regenerated the starting N-oxide VIII upon treatment with water. When IX was treated with sodium acetate in the presence of acetic acid and



VIII IX



X

acetonitrile under conditions which led to 50% reaction (see Table II for conditions and results with undeuterated compounds), no deuterium loss was observed in the rearranged ester IX (calcd.: 7.69 atom % excess deuterium; found: 7.34%) and the N-oxide VIII (found: 17.65 atom % excess deuterium), formed from IX by hydrolysis. These results require the conclusion that the rate of conversion of IV to V is much faster than the reverse reaction of IV returning to III; *i.e.* $k_4 >> k_{-3}$. Therefore the mechanism of this reaction requires a slow rate-controlling conversion of III to IV with a rapid rearrangement of IV to V. This conclusion is consistent with the absence of accumulated anhydro base IV, the absence of deuterium exchange during reaction, and the effect of base strength on the reaction. These suggestions require further testing *via* a kinetic study. One interesting consequence of this mechanism is the rapid rearrangement of anhydro base IV.

In previous work[2] the reaction of 1-acetoxy-2-methylpyridinium picrate with triethylamine produced 2-pyridylmethyl acetate in 20% yield. A similar result was observed with 1-acetoxy-2-methylpyridinium perchlorate and triethylamine with the added observation that the reaction was very rapid. When the two reactants were mixed under conditions of high dilution, the yield of 2-pyridylmethyl acetate increased threefold (see Table IV). These results suggest the formation of the intermediate anhydro base which rearranges to ester in competition with a second reaction which apparently is at least bimolecular. The nature of the products from the second reaction is unknown.

One practical application which arises from this work is a more rapid method for converting certain 2-alkylpyridine N-oxides (I) to the corresponding esters V. The generation of the 1-acetoxypyridinium perchlorates III is rapid and in high yield and these salts are converted instantly to the corresponding ester V by reaction with triethylamine. This procedure is faster than the standard method of direct reaction of the N-oxide I with acetic anhydride and leads to a cleaner product. One disadvantage of the two-step method is the limitation to the size of reaction in view of the use of perchlorate salts.

Experimental[9]

2-Benzylpyridine N-oxide, m.p. 98–100° (lit.[10] m.p. 100.5°), was prepared by oxidation of 2-benzylpyridine[11] by the procedure of Hands and Katritzky.[10] The n.m.r. spectrum[12] had the following peaks: triplet, center at 1.8 τ, (α-proton in pyridine); multiplet, 2.6–3.2 τ with a sharp peak at 2.7 τ (phenyl and β,γ-pyridine protons); and singlet, 5.8 τ (benzylic protons).

2-*p*-Nitrobenzylpyridine N-oxide, m.p. 163–165° (lit.[10] m.p. 166.5–167°), resulted from the nitration of 2-benzylpyridine N-oxide using the method of Hands and Katritzky.[10]

1-Methyl-2-benzylpyridinium Methosulfate.—A solution of dimethyl sulfate (3.7 g., 0.029 mole) in anhydrous benzene (10 ml.) was added with vigorous stirring to 2-benzylpyridine[11] (5.0 g., 0.029 mole) dissolved in anhydrous benzene (10 ml.). After stirring at room temperature for 2 hr. the precipitate was filtered, washed with anhydrous ether, and dried. The yield of 1-methyl-2-benzylpyridinium methosulfate, m.p. 60–65°, was 8.1 g. (93%). This compound was very hygroscopic. An analytical sample, m.p. 72–74° (sealed tube), was prepared by repeated crystalliza-

(9) All melting points and boiling points are uncorrected. The microanalyses were carried out by Midwest Microlab, Inc., Indianapolis, Ind., while deuterium analysis were performed by J. Nemeth, Urbana, Ill. Infrared spectra were determined on a Perkin–Elmer Infracord spectrophotometer; the ultraviolet and visible spectra were recorded on a Perkin–Elmer Spectracord; and the n.m.r. spectra were determined by Mr. W. E. Hunter with a Varian Associates 60 Mc. high-resolution n.m.r. spectrometer, Model V-4300B.

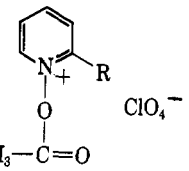
(10) A. R. Hands and A. R. Katritzky, *J. Chem. Soc.*, 1754 (1958).

(11) The authors wish to thank Dr. F. E. Cislak, Reilly Tar and Chemical Co., Indianapolis, Ind., for a generous gift of 2-benzylpyridine.

(12) Determined in deuteriochloroform solution with tetramethylsilane as an internal standard.

TABLE I

1-ACETOXY-2-ALKYLPYRIDINIUM PERCHLORATES[a]



R	Normality $HClO_4$ soln.	M.p.,[a] °C.	Yield,[b] %	Ultraviolet spectrum, mμ	Analyses, % Calcd.	Found
CH_3	0.5	148–150[c]	83		C 38.18	38.40
					H 4.00	4.11
$C_6H_5CH_2$	0.5	132–135	94	$\lambda_{max}^{CH_3CN}$ 264.5	C 51.31	51.40
				ϵ_{max} 7840	H 4.30	4.47
p-$NO_2C_6H_4CH_2$	0.1	161–164	80	$\lambda_{max}^{CH_3CN}$ 269	C 45.11	45.49
				ϵ_{max} 17,800	H 3.51	3.79

[a] Sealed tube; the compounds melted with decomposition. [b] The yields reported represent material precipitated during reaction. If the reaction mixture was evaporated to dryness, the perchlorate salts were isolated quantitatively. [c] C. W. Muth and R. Darlak, private communication; m.p. 153–154.5°.

tion from anhydrous acetone–ether mixture. The ultraviolet spectrum was determined in acetonitrile and showed λ_{max} 267 mμ, ϵ_{max} 8510.

Anal. Calcd. for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80. Found: C, 56.46; H, 5.93.

1-Methyl-2-*p*-nitrobenzylpyridinium Methosulfate.—After dimethyl sulfate (4.8 g., 0.038 mole) in anhydrous benzene (20 ml.) was added slowly to a stirred solution of 2-*p*-nitrobenzylpyridine[13] (6.0 g., 0.028 mole) in anhydrous benzene (20 ml.), the resulting mixture was refluxed 3.5 hr. and the crystalline precipitate was filtered, washed with anhydrous ether, and dried. The yield of 1-methyl-2-*p*-nitrobenzylpyridinium methosulfate, m.p. 153–156°, was 9.3 g. (98%). Repeated crystallization from ethanol provided an analytical sample, m.p. 157.5–159°; $\lambda_{max}^{CH_3CN}$ 268 mμ, ϵ_{max} 17,500.

Anal. Calcd. for $C_{14}H_{16}N_2O_6S$: C, 49.40; H, 4.73. Found: C, 49.60, 49.58; H, 4.71, 4.64.

1-Methyl-2-benzal-1,2-dihydropyridine.—The action of 15 ml. of 10% sodium hydroxide soution on 1-methyl-2-benzylpyridinium methosulfate (206.7 mg., 0.70 mmole) produced 1-methyl-2-benzal-1,2-dihydropyridine, a red-colored oil.[14a] This oil was extracted into cyclohexane and the ultraviolet and visible spectra recorded in that solvent: λ_{max} 336 mμ, ϵ_{max} 15,700; λ_{max} 422–423 mμ, ϵ_{max} 2740.[15] The extinction coefficients should be considered as minimum values since the compound appeared to decompose on standing.

1-Methyl-2-*p*-nitrobenzal-1,2-dihydropyridine.—When 1-methyl-2-*p*-nitrobenzylpyridinium methosulfate (9.3 g., 0.027 mole) in water (150 ml.) was treated with 50 ml. of 10% sodium hydroxide solution, an intense blue solid precipitated immediately.[14b] Crystallization of this solid from ethyl acetate gave 5.3 g. (85%) of 1-methyl-2-*p*-nitrobenzal-1,2-dihydropyridine, m.p. 149°[16] (lit.[14b] m.p. 160°); $\lambda_{max}^{C_2H_5OH(95\%)}$ 267 mμ, ϵ_{max} 15,500; $\lambda_{max}^{CH_3CN}$ 547 mμ, ϵ_{nax} 10,600. The extinction coefficients should be considered as minimum values since the compound in solution appeared to be light sensitive.

1-Acetoxy-2-alkylpyridinium Perchlorate.[8] General Procedure.—A solution of the appropriate N-oxide (5–10 g.) in acetic anhydride (5–10 ml.) and acetic acid (5–10 ml.) was mixed with the stoichiometric amount of 0.1–0.5 *N* perchloric acid in acetic acid.[17] After standing for 30–60 min., the crystalline precipitate which formed was filtered and washed with anhydrous ether. The infrared spectra of the various compounds in acetonitrile showed a characteristic carbonyl absorption at 5.42–5.45 μ.[2] Table I contains the pertinent experimental data for the compounds studied.

Reaction of 2-Benzylpyridine N-Oxide and Acetic Anhydride.[18] Acetic Anhydride Solvent.—2-Benzylpyridine N-oxide (10 g., 0.054 mole) was added in small portions and with stirring to refluxing acetic anhydride (22 g., 0.215 mole). After the mixture was refluxed 2 hr., the excess acetic anhydride was removed, and distillation of the residue gave 9.8 g. (80%) of phenyl-2-pyridylmethyl acetate, b.p. 139–140° (1.6 mm.), $n^{20}D$ 1.5602; $\lambda_{max}^{C_6H_{12}}$ 257 mμ, ϵ_{max} 3340 [lit.[19] b.p. 101–104° (0.04 mm.)]

The picrate was prepared in the usual manner, and after recrystallization from ethanol melted at 150.5–152° (lit.[19] m.p. 154–155°).

The liquid ester after standing for 2 months crystallized. An analytical sample, m.p. 46.5–47°, was prepared by crystallization from petroleum ether (b.p. 60–70°). The n.m.r. spectrum[12] had the peaks at: doublet, center at 1.5 τ (α-proton in pyridine); multiplet, center at 2.7 τ (phenyl and β,γ-pyridine protons); singlet, 3.2 τ (benzylic proton); and singlet, 7.5 τ (methyl protons).

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.98; H, 5.76. Found: C, 74.24, 74.09; H, 5.89, 5.99.

Acetonitrile Solvent.—A solution of equimolar amounts of 2-benzylpyridine N-oxide and acetic anhydride in acetonitrile was heated at reflux for the prescribed time, the solvent removed, and the residue dissolved in ether. After the ether solution was washed with 10% sodium carbonate, dried over potassium carbonate, and the ether removed, the residue was crystallized from petroleum ether (b.p. 60–70°) and gave phenyl-2-pyridylmethyl acetate. These results are summarized in Table III.

An alternative isolation procedure involved removal of the solvent from the reaction mixture and chromatography of the residue on Fluorosil with benzene–ether as eluents.

Reaction of 1-Acetoxy-2-benzylpyridinium Perchlorate with Base.—A solution of the perchlorate salt in dry acetonitrile and the base in dry acetonitrile were mixed and subjected to the conditions described in Table II. The reaction was processed by one of the following procedures.[20] (A) After the volatile liquid was removed, the residue was extracted with cyclohexane, the cyclohexane removed, and the ester crystallized from petroleum ether (b.p. 60–70°). (B) The reaction mixture was poured into water, made strongly alkaline, and extracted with chloroform. After the extract was dried over potassium carbonate, the chloroform was removed, and the residue crystallized from an appropriate solvent. (C) Method B was followed and, after the chloroform was removed, the residue was chromatographed on Fluorosil using anhydrous benzene–chloroform as eluents. (D) The reaction mixture was concentrated and processed according to method B. The residue from the chloroform extract gave 2-benzylpyridine N-oxide and phenyl-2-pyridylmethyl acetate by fractional crystallization from petroleum ether (b.p. 60–70°). (E) The reaction mixture was poured into water and extracted with ether. After the ether extract was washed with sodium carbonate solution, the ether was removed and the resulting ester crystallized from petroleum ether (b.p. 60–70°). The

(13) 2-*p*-Nitrobenzylpyridine was prepared by the procedure of K. Schofield, *J. Chem. Soc.*, 2408 (1949).

(14) (a) H. Decker, *Ber.*, **38**, 2493 (1905); (b) E. Koenings, D. Köhler, and K. Blindow, *ibid.*, **58**, 933 (1925). These workers observed the same result from the action of base on 1-methyl-2-benzylpyridinium iodide.

(15) L. C. Anderson and N. V. Seeger, *J. Am. Chem. Soc.*, **71**, 343 (1949), reported the ultraviolet and visible spectra of this compound in ether; λ_{max} 357 mμ, ϵ_{max} 12,000; λ_{max} 431 mμ ϵ_{max} 2200. These data were calculated from the spectral curve reported in this publication.

(16) The end of the melting point was difficult to ascertain because of the very dark color of the compound and melt.

(17) J. S. Fritz, "Acid–Base Titrations in Nonaqueous Solvents," G. Frederick Smith Chemical Co., Columbus, Ohio, 1952, p. 13.

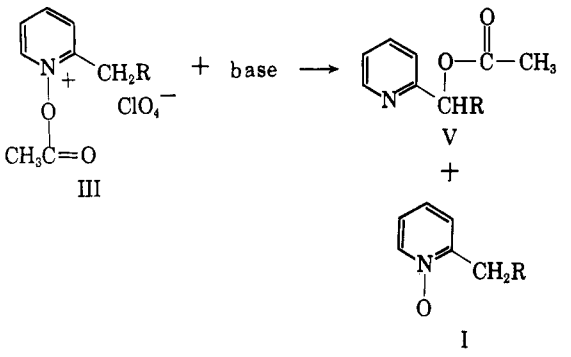
(18) F. E. Cislak, U. S. Patent 2,748,141, May 29, 1956; *Chem. Abstr.*, **51**, 2878*c* (1957).

(19) J. H. Boyer and L. T. Wolford, *J. Am. Chem. Soc.*, **80**, 2741 (1958).

(20) During the work-up procedure the product composition was followed by infrared, and led to the various modifications reported.

TABLE II

THE REACTION OF 1-ACETOXY-2-BENZYLPYRIDINE PERCHLORATES WITH BASE

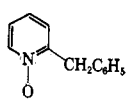


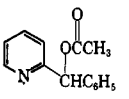
	III, mole	Base	Mole	Time	Temp., °C.	Method	Yield,[a] % V	Yield,[a] % I
				R = C_6H_5				
(1)	0.0114	$(C_2H_5)_3N$	0.114	12 hr.	Reflux	A	60	..
(2)	.0245	$(C_2H_5)_3N$	0.0245	1 hr.[c]	0[b]	A	57	..
(3)	.0245	$(C_2H_5)_3N$	0.0245	<5 min.[d]	0[b]	C	56	..
(4)	.046		0.046	2.5 hr.[f]	R.t.[e]	B	57	..
				15 min.[f]	R.t.[e]	B	46	..
(5)	.024		0.024	<5 min.	0[b]	C	6	82
(6)	.0305	CH_3CO_2Na[g]	0.0305	2 hr.	Reflux	D	49	23
(7)	.043	CH_3CO_2Na[g]	0.043	0.5 hr.[h]	Reflux	E	32	43
				5 min.[h]	R.t.[e]	B	0	93
				R = p-$NO_2C_6H_4$–				
(8)	.0188	$(C_2H_5)_3N$	0.0188	16 hr.	Reflux		56[i]	
(9)	.0188	$(C_2H_5)_3N$	0.0188	<5 min.[d]	0[b]		51[i]	

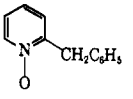
[a] The yields represent isolated and purified products. [b] The two solutions were precooled to 0° before mixing. [c] The course of the reaction was followed by observing the carbonyl region in the infrared. Reaction was complete when the first spectrum was taken after 5 min. [d] After the reactants were mixed, an infrared spectrum was recorded and showed the complete disappearance of the 5.45-μ carbonyl band of the salt and the presence of the 5.75-μ band of the ester. The reaction was immediately processed. [e] Room temperature. [f] The data for experiments 4 and 5 came from one reaction which was followed by observing the carbonyl region of the infrared. Half of the reaction was processed in 15 min. and the other half in 2.5 hr., after which time the infrared indicated no further change in the carbonyl region. The 5.45-μ band was absent. [g] Sodium acetate was dissolved in 36% acetic acid–64% acetonitrile (volume %). [h] These data were obtained from the same experiment where half the reaction was processed in 5 min. and the remainder after 30 min. [i] After the ester was eluted from the Fluorosil column with ether, continued washing with ether slowly removed a red band. Assuming this material was isomeric with the ester, the yield of the red compound was about 4%.

TABLE III

THE REACTION OF 2-BENZYLPYRIDINE N-OXIDE AND ACETIC ANHYDRIDE IN ACETONITRILE







	Mole	Ac_2O, mole	$(C_2H_5)_3N$, mole	Time, hr.	Yield, %	Yield, %
(1)	0.054	0.054	...	2	60	..
(2)	.026	.026	...	0.25	14[a]	18[a,b]
(3)	.054	.054	0.054	2	53	..
(4)	.026	.026	0.026	0.25	26[a]	6[a,b]

[a] These products were isolated by chromatography. [b] Much of the N-oxide was removed during the washing procedure and was not isolated.

sodium carbonate washings were mixed with the initial reaction mixture, made strongly alkaline, and extracted with chloroform. 2-Benzylpyridine N-oxide was recovered from the extract according to method B.

Reaction of 2-p-Nitrobenzylpyridine N-Oxide and Acetic Anhydride.—2-p-Nitrobenzylpyridine N-oxide (4.0 g., 0.017 mole) was added in small amounts over a period of 30 min. to refluxing acetic anhydride (7.1 g. 0.069 mole) under nitrogen. After the reaction mixture was refluxed for 2 hr., the solvent was distilled and the residue chromatographed on 100 g. of Fluorosil using anhydrous ether as eluent. The yield of p-nitrophenyl-2-pyridylmethyl acetate, m.p. 64–69° (from ethyl acetate–hexane; $\lambda_{max}^{CH_3CN}$ 266 mμ, ϵ_{max} 13,500), was 2.3 g. (48%). An analytical sample melted at 72–73°.

Anal. Calcd. for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44. Found: C, 61.74, 61.85; H, 4.78, 4.76.

p-Nitrophenyl-2-pyridylmethanol.—The above reaction was repeated using the same equivalents of reactants, and instead of chromatography the residue was treated with ether, the ether extract washed with 10% hydrochloric acid, and the acid layer made alkaline with 10% sodium hydroxide soution. From this solution phenyl-2-pyridylmethanol, m.p. 108–111°, was isolated in 46% yield by extraction with ether and crystallization from ethyl acetate–hexane. An analytical sample melted 111.5–112.5°.

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 62.60; H, 4.37. Found: C, 62.54; H, 4.64.

Reaction of 1-Acetoxy-2-p-nitrobenzylpyridinium Perchlorate and Base.—A solution of the perchlorate salt in dry acetonitrile and triethylamine in dry acetonitrile was mixed and subjected to the conditions described in Table II. The solvents were removed, the residue chromatographed on Fluorosil using anhydrous ether as the eluent, and the product was recrystallized from ethyl acetate–hexane.

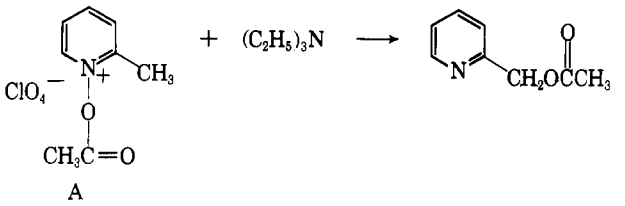
Reaction of 1-Acetoxy-2-Methylpyridinium Perchlorate with Triethylamine. Method A.—A solution of the perchlorate salt in dry acetonitrile and triethylamine in dry acetonitrile were mixed rapidly and subjected to the conditions described in Table IV. After the reaction mixture was poured into 10% sodium bicarbonate solution, the mixture was extracted with chloroform, and the extract dried and distilled using a Claisen head.

Method B.—This procedure followed method A with one modification: the triethylamine solution was added slowly and with stirring over the period of time listed in Table IV.

Deuterium Label Experiments. 2-(α,α-Dideuteriobenzyl)-pyridine N-Oxide.—A mixture of 2-benzylpyridine N-oxide (5.00 g., 0.027 mole), triethylamine (7.22 g., 0.072 mole), and deuterium oxide (15 ml.) was refluxed 20 hr., cooled, and extracted with chloroform. After the extract was dried and the chloroform removed, 4.7 g. (94%) of 2-(α,α-dideuteriobenzyl)pyridine N-

TABLE IV

THE REACTION OF 1-ACETOXY-2-METHYLPYRIDINIUM PERCHLORATE WITH TRIETHYLAMINE



A

	A, mole	CH_3CN, ml.	$(C_2H_5)_3N$, mole	CH_3CN, ml.	Method	Time, hr.	Temp., °C.	Yield,[a] %
(1)	0.018	40	0.018	10	A	1	0[c]	23
(2)	.0357	80	.0357	10	A	<5 min.	0[c]	22
(3)	.038	70	.038	20	B	1[b]	0	38
(4)	.040	200	.040	100	B	2[b]	Reflux	60
(5)	.040	200	.040	100	B	2[b]	R.t.[d]	57–62
(6)	.040	2850	.040	150	B	2[b]	R.t.[d]	64

[a] Based on distilled material. [b] This represents the time of addition of base. [c] Both solutions were precooled before mixing. [d] Room temperature.

oxide, m.p. 96–98°, was isolated. An analytical sample, m.p. 98.5–100°, was prepared by recrystallization from benzene.

Anal. Calcd. for $C_{12}H_9D_2NO$[21]: C, 76.97; H, 5.92; D, 18.18 atom % excess. Found: C, 76.75; H, 5.99; D, 17.55 atom % excess.

The n.m.r. spectrum[12] had peaks at: triplet, 1.8 τ (α-proton in pyridine) and multiplet, 2.6–3.2 τ with a sharp peak at 2.7 τ (phenyl and β,γ-pyridine protons). The 5–6 τ region (benzylic protons) showed no absorption.

Reaction of 1-Acetoxy-2-(α,α-Dideuteriobenzyl)pyridinium Perchlorate with Sodium Acetate in the Presence of Acetic Acid.—A solution of 1-acetoxy-2-(α,α-dideuteriobenzyl)pyridinium perchlorate[22] (5.9 g., 0.018 mole), sodium acetate (1.47 g., 0.018 mole) in acetonitrile (48 ml.), and acetic acid (27 ml.) was refluxed 30 min., diluted with water, and extracted with chloroform. After the extract was dried over anhydrous sodium sulfate and the chloroform, acetonitrile, and acetic acid removed under vacuum, the residue was chromatographed on 35 g. of Fluorosil using benzene and chloroform as eluents. The first compound eluted was phenyl(2-pyridyl)-1-deuteriomethyl acetate and weighed 0.85 g. (21%). The n.m.r. spectrum[12] had peaks at: doublet, center at 1.5 τ (α proton in pyridine); multiplet, center at 2.7 τ (phenyl and β,γ-pyridine protons); singlet, 7.8 τ (methyl protons). The 3.2 τ region (benzylic proton) showed no absorption. An analytical sample, m.p. 46°, was prepared by recrystallization from petroleum ether (b.p. 60–70°).

Anal. Calcd. for $C_{14}H_{12}DNO_2$[21]: C, 73.67; H, 5.74; D, 7.69 atom % excess. Found: C, 73.57; H, 5.77; D, 7.34 atom % excess.

A second compound eluted with chloroform was 2-(α,α-dideuteriobenzyl)pyridine N-oxide and weighed 1.2 g. (36%). The n.m.r. spectrum[12] was identical with that of an authentic sample and showed no absorption in the 5.8 τ region (benzyl hydrogens; see n.m.r. of 2-benzylpyridine N-oxide). An analytical sample, m.p. 101–102°, was prepared by recrystallization from anhydrous ether.

Anal. Calcd. for $C_{12}H_9D_2NO$[21]: C, 76.97; H, 5.92; D, 18.18 atom % excess. Found: C, 76.88; H, 6.12; D, 17.65 atom % excess.

(21) The % H was calculated by using the formula weight of the deuterated molecule and the number of hydrogen atoms × 1.008 of the undeuterated molecule. The conversion factor for regular water was used for the combustion water collected in the absorption tube.

(22) 1-Acetoxy-2-(α,α-dideuteriobenzyl)pyridinium perchlorate, m.p. 129–132°, was prepared in 98% yield by the procedure described above for the nondeuterated 1-acetoxypyridinium salts.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYMER RESEARCH INSTITUTE, POLYTECHNIC INSTITUTE OF BROOKLYN, BROOKLYN, N. Y.]

Stereochemistry of Poly-α-methylvinyl Methyl Ether

BY MURRAY GOODMAN AND YOU-LING FAN[1]

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We synthesized stereoregular poly-α-methylvinyl methyl ether (PMVME) employing various cationic catalysts at low temperature. In contrast to the stereochemical configurations of polyvinyl methyl ether (PVME), these polymers were found to be primarily syndiotactic in nature by high-resolution nuclear magnetic resonance and infrared spectroscopy. We interpreted these results in terms of the greater stability of the six-membered oxonium ring formed at the growing chain end which governs the stereochemical configurations of the main chain during the course of propagation. Examination by X-ray diffraction analysis indicates the identity period along the chain axis is 16.4 Å., which requires the main chain to be spiraled in the crystalline state presumably in an eightfold helix with three turns.

Introduction

α-Methylvinyl alkyl ethers were polymerized by Shostakovskii and co-workers.[2-4] In their work, the polymers varied from viscous liquids to transparent solids and were synthesized using a ferric chloride–dioxane catalyst at fairly low temperature. A cationic polymerization mechanism was described by these authors.

Although the chain configurations and crystalline structures of polyvinyl alkyl ethers have been investigated extensively,[5-9] no elucidation of the stereochemis-

(1) Submitted by Y. L. Fan in partial fulfillment of the requirements for the degree of Doctor of Philosophy to the Faculty of the Polytechnic Institute of Brooklyn.

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(3) M. F. Shostakovskii and E. P. Gracheva, *ibid.*, **27**, 355 (1957).

(4) M. F. Shostakovskii, E. P. Gracheva, and N. K. Kul'bovskaya, *ibid.*, **28**, 2344 (1958).

(5) S. Okamura, T. Kodama, and T. Higashimura, *Makromol. Chem.*, **53**, 180 (1962).