was compared with those obtained in similar reactions performed at room temperature in the same solvent. In both room temperature runs, a solution of phenylacetic anhydride (50.8 g., 0.200 mole) and 4-picoline N-oxide (21.8 g., 0.200 mole) in 800 ml. of benzene was allowed to stand at room temperature for 12 days. In only one of the runs was nitrogen ebullition used (with consequent sweeping away of the evolved carbon dioxide). The results in Table III indicate that although the total yield of benzylpicolines does not vary appreciably as conditions are changed, the composition of the benzylpicoline fraction is greatly influenced by the reaction conditions. The reason for this behavior is not clear.
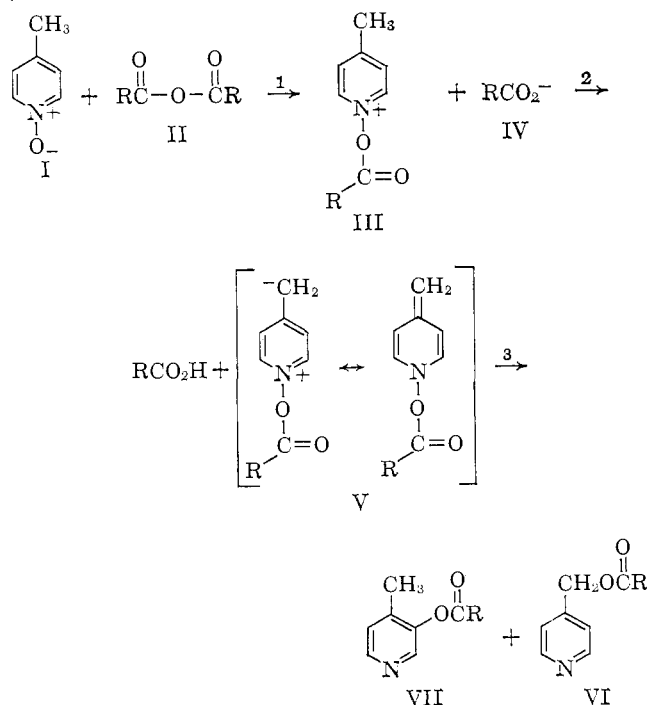
Aromatic N-Oxides. V. The Reaction of 4-Picoline N-Oxide with Various Anhydrides[1,2]

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A product study of the reactions of 4-picoline N-oxide with acetic, isobutyric, and pivalic anhydrides is reported. The product categories include carbon dioxide, esters (4-acyloxymethylpyridine and 3-acyloxy-4-methylpyridine), and alkylpyridines (4-alkylpyridines, 3,4-dialkylpyridines, and 2,4-dialkylpyridines). A rationalization of these results is made utilizing an intramolecular radical-pair mechanism via the intermediate anhydro base.

The various mechanisms which have been suggested to explain the formation of 4-pyridylmethyl acetate (VI, $R = CH_3$) and 3-acetoxy-4-methylpyridine (VII,

$R = CH_3$) from the reaction of 4-picoline N-oxide and acetic anhydride have been reviewed in a recent report by Oae.[4] In the generally accepted mechanistic scheme, as outlined above, both the initial step leading to the formation of 1-acyloxy-4-methylpyridinium ion (III) and its conversion, by proton abstraction with the acid anion IV, to the anhydro base V have been based on analogy with similar reactions, particularly the comparable reaction of 2-picoline N-oxide and acid anhydrides.[2] Recently, we have obtained evidence for III by isolation of this cation as its perchlorate and the conversion of III perchlorate by base to a mixture of esters VI and VII.[5] In addition, spectroscopic evidence is available for the anhydro base V and will be reported in the near future.[5]

A controversy still exists over step 3, the transformation of V to the ester mixture VI and VII. The intermolecular mechanism requires attack of the acid anion (IV) on the exocyclic methylene group of V with expulsion of the acid anion attached to nitrogen (path A) and the formation of ester VI. Ester VII would arise by attack of IV at the C-3 position of V and expulsion of the N acid anion (path B) followed by an allylic rearrangement of VIII to regenerate the pyridine ring. The alternate mechanism involves an intramolecular

rearrangement of V which may occur *via* a concerted, ion-pair or radical-pair process. Evidence in favor of
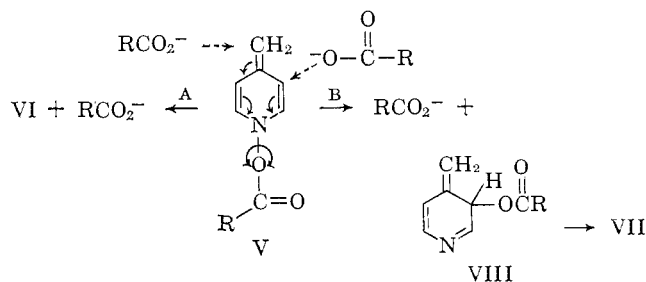
(1) Grateful acknowledgment is made to the National Science Foundation for a research grant (NSF-G-13154) in partial support of this work.

(2) For paper IV in this series, see V. J. Traynelis and P. L. Pacini, *J. Am. Chem. Soc.*, 86, 4917 (1964).

(3) (a) Department of Chemistry, West Virginia University, Morgantown, W. Va.; (b) abstracted from the Ph.D. dissertation of A. I. G. submitted Oct. 1964.

(4) S. Oae, T. Kitao, and Y. Kitaoka, *J. Am. Chem. Soc.*, 84, 3362 (1962).

(5) V. J. Traynelis and A. I. Gallagher, unpublished results.

the intramolecular rearrangement of V was obtained from experiments in the presence of foreign anions (other acid anions[6] and aryl oxide ions[7]) which were not incorporated in the products. On the other hand, Oae and co-workers[4,8,9] studied the reaction of 4-picoline N-oxide with acetic and with butyric anhydride enriched with oxygen-18 and found that all oxygens in the system including the unlabeled N-oxide oxygen became equilibrated and completely scrambled in the two ester products. Oae concluded that these results are best explained by an intermolecular reaction. The present paper offers data which can be accommodated by radical pairs generated from the anhydro base V.

In a previous report[6] we have described the appearance of gaseous products and a number of alkylpyridines in addition to esters VI and VII from the reaction of 4-picoline N-oxide with acetic anhydride and with butyric anhydride. Among the gaseous products was carbon dioxide, and interestingly the amount of carbon dioxide increased from 4.7 to 42.5% in changing from acetic to butyric anhydride and a simultaneous increase of 3.7 to 18.5% was observed for the alkylpyridine mixture. In contrast the yield of esters decreased 65 to 38% in going from acetic to butyric anhydride. We have now reinvestigated the reaction of 4-picoline N-oxide with acetic anhydride and extended this study to isobutyric and pivalic anhydrides.

The products from the reaction of 4-picoline N-oxide with various anhydrides are combined into three categories: carbon dioxide, esters, and alkylpyridines. The results are reported in Table I.

Table I. Product Distribution from the Reactions of 4-Picoline N-Oxide with Acid Anhydrides

Anhydride	Reaction time, hr.	% carbon dioxide	% esters[a]	% alkylpyridines[b]
Acetic	3	4.7	60	4.3
Acetic[c]	2.2	4.7	65	3.7
Butyric[c]	1.5	42.5	38	18.5
Isobutyric	3	38.7[d]	11.4	25.2
Isobutyric	5	53.4	12.2	25.8
Pivalic	5	51.5	7.3	35.2

[a] The ester mixture was composed of 4-acyloxymethylpyridine and 3-acyloxy-4-methylpyridine. A composition analysis for those ester mixtures described in this work can be found in the Experimental Section. [b] The distribution of alkylpyridines is listed in Table II. [c] See ref. 6. [d] The reaction time in this experiment consisted of addition of reactants over 1 hr. with a 2-hr. heating period while the following experiment had a 3-hr. addition time and 2-hr. heating period. The lower value for carbon dioxide in this experiment may be a result of incomplete absorption of carbon dioxide owing to a more rapid evolution of gas. The similarity in the yields of ester and alkylpyridines for these two reactions suggests that both reactions have progressed to the same degree.

Analysis of carbon dioxide was based on the procedure of Willard and Diehl[10a] and van Nieuwenberg and

(6) V. J. Traynelis and R. F. Martello, *J. Am. Chem. Soc.*, **82**, 2744 (1960).
(7) V. J. Traynelis, A. I. Gallagher, and R. F. Martello, *J. Org. Chem.*, **26**, 4365 (1961).
(8) S. Oae, Y. Kitaoka, and T. Kitao, *Tetrahedron*, **20**, 2677 (1964).
(9) S. Oae, Y. Kitaoka, and T. Kitao, *ibid.*, **20**, 2685 (1964).
(10) (a) H. H. Willard and H. Diehl, "Advanced Quantitative Analysis," D. van Nostrand Co., Inc., New York, N. Y., 1943, p. 212; (b) G. J. van Nieuwenberg and L. A. Hegge, *Anal. Chim. Acta*, **5**, 68 (1951). This procedure for trapping carbon dioxide was tested with calcium carbonate plus acid and found to be at least 95% effective.

Hegge[10b] and consisted of trapping the evolved carbon dioxide in excess standard barium hydroxide. The results by this method for the reaction of 4-picoline N-oxide with acetic anhydride were in excellent agreement with those obtained in previous work by measurement of the gas volume and mass spectrometric analysis of the gas mixture.[6]

Identification of the esters formed in the reactions was accomplished by comparison of physical constants, infrared spectra and/or n.m.r. spectra with authentic samples. These authentic esters, except 3-pivaloxy-4-methylpyridine, were prepared by esterification of the corresponding hydroxy compounds with the appropriate anhydrides and derivatized in the usual manner. Good separation of the ester components by g.l.c. was not achieved and peak distortion made the analysis at best approximate; however, pure samples of the ester mixtures were obtained by preparative g.l.c. and composition analysis was determined by n.m.r.
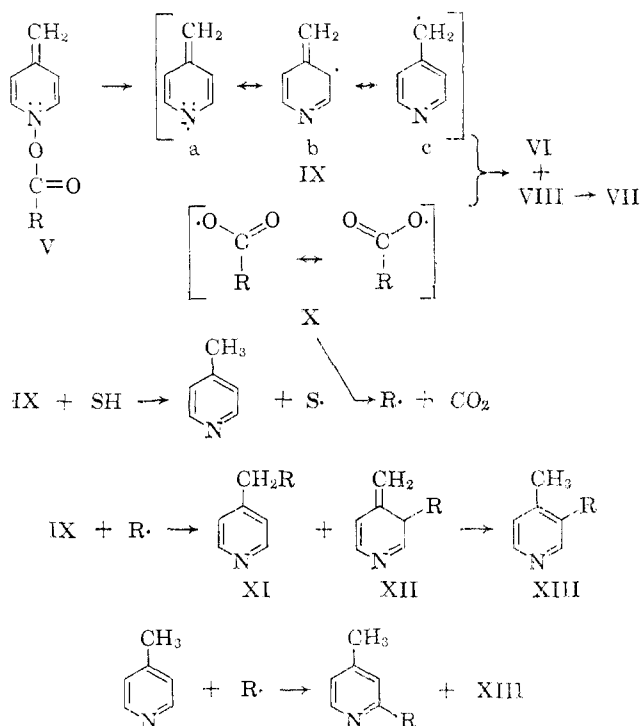
G.l.c. provided a convenient method of analysis and separation of the mixture of alkylpyridines. A number of authentic alkylpyridines were used to determine retention times, peak enhancement, and detector response (area/mole ratios). The individual components were isolated and identified by comparison of physical constants and infrared spectra with those of authentic material. Structures for the new pyridine derivatives were established on the basis of elemental analysis of the picrate and infrared and n.m.r. spectra of the alkylpyridine. N.m.r. spectroscopy proved to be a particularly useful tool in the elucidation of the structures of these alkylpyridines which gave unambiguously unique n.m.r. spectra (see Experimental Section).

The complex mixture of products obtained in these studies may result from contributions from several reactions. Carbon dioxide and 4-picoline could arise in part from a reaction analogous to the oxidative decarboxylation of anhydrides with pyridine N-oxides[11]; however, the extent to which this reaction occurs is probably small. Cohen and co-workers[11] showed that pivalic anhydride and pyridine N-oxide produced very little carbon dioxide at temperatures comparable to those used in this work. In addition the ratio of reactants and experimental conditions in this report differ considerably from those of Cohen. The ester products formed in this reaction are best rationalized through the anhydro base V intermediate which also appears as an attractive precursor for the alkylpyridines and carbon dioxide. The simultaneous decrease in the yield of ester and increase in the yield of alkylpyridines and carbon dioxide as one progresses from acetic to pivalic anhydride (see Table I) is consistent with the designation of a common precursor for these products. Since 1-acyloxy-4-methylpyridinium perchlorates have been isolated as stable salts, the decomposition of these cations does not present an attractive explanation for the origin of alkylpyridines and carbon dioxide.

Although the anhydrobase may proceed to the esters by one path and to the alkylpyridines and carbon dioxide by another, a single rationalization for all products is possible. Homolytic cleavage of the an-

(11) T. Cohen, I. H. Song, and J. F. Fager, *Tetrahedron Letters*, **4**, 237 (1965); C. Ruchardt, S. Eichler, and O. Kratz, *ibid.*, **4**, 233 (1965). No attempt was made to isolate and identify the oxidative products from the anhydrides used in this work.

hydro base V at the N–O bond would lead to the picolyl radical (IX) and an acyloxy radical (X). Recombina-

$$IX + SH \rightarrow \text{[4-methylpyridine]} + S\cdot \qquad R\cdot + CO_2$$

$$IX + R\cdot \rightarrow \underset{XI}{\text{CH}_2R} + \underset{XII}{\text{CH}_2, R} \rightarrow \underset{XIII}{\text{CH}_3, R}$$

$$\text{[4-picoline]} + R\cdot \rightarrow \text{[product]} + XIII$$

tion of IX and X can produce the ester VI and the intermediate VIII which upon allylic rearrangement forms ester VII. In view of the very short lifetime of the acyloxy radicals,[12] where R is alkyl, such a radical-pair recombination requires holding the generated radicals in a solvent cage. Decomposition of the acyloxy radical leads to the observed carbon dioxide and an alkyl radical R· which may recombine with IX while still in a solvent cage, or R· may diffuse away from its original partner and recombine with another IX. The combination of R· and IX would produce the 4-alkylpyridine XI or the intermediate XII which upon allylic rearrangement provides the 3,4-dialkyl-pyridine XIII. Separation of the original radical pair IX and X would lead to decomposition of X to carbon dioxide and R· and would provide an opportunity for IX and R· to abstract a hydrogen atom producing 4-picoline and the alkane RH. Such alkanes have been observed in previous work[6] and in the pivalic anhydride experiment; however, no serious attempt to study the presence of these alkanes was made in this work. The 2,4-dialkylpyridines observed can be explained by the free-radical alkylation[13] of 4-picoline or the 4-alkylpyridine XI. This pathway may also account for some 3,4-dialkylpyridine (XIII).

Qualitative evidence in support of the radical explanation for the origin of the alkylpyridines can be extracted from the product trends listed in Table I. As one proceeds from acetic to the more branched anhydrides, the amount of alkylpyridines and carbon dioxide increases.[14] This product increase is in the

(12) L. Herk, N. Feld, and M. Szwarc, J. Am. Chem. Soc., 83, 2998 (1961), and preceding and subsequent papers by Szwarc; H. J. Shine, J. A. Waters, and D. M. Hoffman, ibid., 85, 3613 (1963).

(13) Such a free-radical alkylation may also be expected for the esters VI and VII; however, none of these products have been observed. The alkylated esters may have been formed in very small amount and escaped detection.

same qualitative[15] order as the ease of decomposition of the acyloxy radicals [$(CH_3)_3CCOO\cdot > (CH_3)_2CHCOO\cdot > CH_3COO\cdot$] and in the same general order as the stability of the resulting alkyl radicals [$(CH_3)_3C\cdot > (CH_3)_2CH\cdot > CH_3\cdot$]. Szwarc[16] has summarized the studies of the decomposition of diacyl peroxides, from which the above stability pattern of acyloxy radicals is obtained. Thus, the general similarity between the results of this study and those for the diacyl peroxide decomposition suggests a radical process for anhydro base V decomposition comparable to the diacyl peroxide system.

A few alternatives are available to rationalize the decline of ester yield as the alkyl group on the anhydro base V is varied from methyl to t-butyl. One explanation requires two different modes of decomposition of the anhydro base: one reaction proceeding by a radical path to produce alkylpyridines and sensitive to the imposed structure change, while the alternate reaction, which forms ester, proceeding by a pathway not appreciably influenced by the structure variation. A second explanation involves a single reaction, namely, the rupture of the N–O bond of the anhydro base to produce radical pairs. Recombination of these radical pairs form esters while separation and subsequent reactions of the radical pairs produce alkanes, carbon dioxide, and the alkylpyridines. The influence of the above structural changes on the radical-pair processes should favor decomposition of the acyloxy radicals over the migration of these radicals to the other end of the picolyl radical and recombination to esters.

The one difficulty encountered with the intramolecular radical-pair mechanism is an interpretation of Oae's[4,8,9] reported equilibration of the N-oxide oxygen with all other oxygens in the system. Under certain conditions Oae's results conform with an intramolecular radical-pair process; however, upon increasing the quantity of carboxylic acid in the reaction medium, one rapidly reaches equilibration of the N-oxide oxygen with the system. An explanation for this latter result is still required. One interpretation offered by Oae, that equilibration of the fragmented components of the anhydro base V occurs with the shell of solvating molecules prior to recombination, is worthy of further exploration. The control experiments did not appear to clearly exclude this possibility.

Experimental Section[17]

Isobutyric Anhydride. The procedure of Gerrad and Thursh[18] was employed to convert isobutyric acid

(14) In each experiment the yield of carbon dioxide exceeds that of the alkylpyridines. This reflects the complex nature of the reactions of the alkyl radicals, some of which produce alkylpyridines, as compared to the decomposition of the acyloxy radical to carbon dioxide and an alkyl radical.

(15) The experimental conditions of solvent, temperature, time, etc., were not identical for each reaction of 4-picoline N-oxide with the various anhydrides.

(16) M. Szwarc, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience, Division of John Wiley and Sons, Inc., New York, N. Y., 1961, p. 164.

(17) All melting points and boiling points are uncorrected. The microanalysis were carried out by Midwest Microlab, Inc., Indianapolis, Ind., or Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer and their n.m.r. spectra were determined by D. Schifferl or W. E. Hunter with a Varian Associates 60-Mc. high resolution n.m.r. spectrometer, Model V-4300 B.

(18) W. Gerrad and A. M. Thursh, J. Chem. Soc., 741 (1952).

(44 g., 0.5 mole) to 30.9 g. (78%) of isobutyric anhydride, b.p. 60–70° (11 mm.), $n^{20.5}$D 1.4057, which when redistilled gave 20.6 g. (53%) of pure isobutyric anhydride, b.p. 68–70° (11 mm.), n^{21}D 1.4050 (lit.[19] b.p. 73–75° (18 mm.)).

Pivalic Anhydride. Employing the method of Ansell, *et al.*,[20] pivalic acid (50 g., 0.49 mole) and acetic anhydride (90 g., 0.88 mole) produced 24.9 g. (57%) of pivalic anhydride, b.p. 78° (12 mm.), n^{20}D 1.4089 (lit.[20] b.p. 78° (12 mm.), n^{20}D 1.4089).

4-Pyridylmethyl Acetate. After a mixture of 4-pyridylmethanol[21] (3.0 g., 0.03 mole) and acetic anhydride (4.0 g., 0.04 mole) was warmed for 4 hr., distillation of reaction mixture gave 1.62 g. (40%) of 4-pyridylmethyl acetate, b.p. 119–121° (11 mm.), n^{20}D 1.5030 (lit.[6] b.p. 110–112° (12 mm.), n^{20}D 1.5035). The n.m.r. spectrum[24] showed the following peaks: singlet τ 7.94, wt. of 3 (methyl protons); singlet τ 4.93, wt. of 2 (methylene protons); doublet τ 2.81 ($J = 6$ c.p.s.), wt. of 2 (C-3 and C-5 pyridine protons); poorly resolved broad peak τ 1.46, wt. of 2 (C-2 and C-6 pyridine protons).

3-Acetoxy-4-methylpyridine. A sample available from the previous study[6] had the following n.m.r. spectrum[24]: singlet τ 7.96, wt. of 3 (acetoxy methyl protons); singlet τ 7.86, wt. of 3 (C-4 methyl protons); doublet τ 2.98 ($J = 6$ c.p.s.), wt. of 1 (C-5 pyridine proton); and broad peak τ 1.74, wt. of 2 (C-2 and C-6 pyridine protons).

4-Pyridylmethyl Isobutyrate. From the reaction of 4-pyridylmethanol[21] (3.88 g., 0.035 mole) and isobutyric anhydride (6.32 g., 0.040 mole) the highest boiling fraction upon redistillation gave 2.61 g. (41%) of 4-pyridylmethyl isobutyrate, b.p. 112° (3.75 mm.), n^{20}D 1.4917.

Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31. Found: C, 67.19; H, 7.27.

The n.m.r. spectrum[24] displayed a doublet at τ 8.85 ($J = 7$ c.p.s.), wt. of 6 (isobutyrate methyl protons); heptet τ 7.45 ($J = 6.9$ c.p.s.), wt. of 1 (isobutyrate methine proton); singlet τ 4.93, wt. of 2 (methylene protons); doublet τ 2.80 ($J = 6$ c.p.s.), wt. of 2 (C-3 and C-5 pyridine protons); and doublet τ 1.45 ($J = 6$ c.p.s.), wt. of 2 (C-2 and C-6 pyridine protons).

A picrate was prepared in the usual manner and obtained from ethanol as bright yellow needles, m.p. 127°.

Anal. Calcd. for $C_{16}H_{16}N_4O_9$: C, 47.09; H, 3.95. Found: C, 47.20; H, 4.09.

3-Isobutyroxy-4-methylpyridine. The reaction of 3-hydroxy-4-methylpyridine[21] (0.5 g., 0.004 mole) and isobutyric anhydride (0.73 g., 0.005 mole) gave 0.40 g. (55%) of 3-isobutyroxy-4-methylpyridine, b.p. 97–99°

(7 mm.). The n.m.r. spectrum[24] had a doublet τ 8.68 ($J = 7.3$ c.p.s.), wt. of 6 (isobutyrate methyl protons); singlet τ 7.84, wt., of 3 (C-4 methyl protons); heptet τ 7.21 ($J = 7.3$ c.p.s.), wt. of 1 (isobutyrate methine proton); doublet τ 2.87 ($J = 5$ c.p.s.), wt. of 1 (C-5 pyridine protons); poorly shaped peak τ 1.73, wt. of 2 (C-2 and C-6 pyridine protons).

A picrate was prepared for analysis. Two recrystallizations from ethyl acetate gave an analytical sample, m.p. 148–149°, as green-yellow needles.

Anal. Calcd. for $C_{16}H_{16}N_4O_9$: C, 47.09; H, 3.95. Found: C, 46.82; H, 4.05.

4-Pyridylmethyl Pivalate. Distillation of the mixture resulting from the reaction of 4-pyridylmethanol[21] (3.88 g., 0.035 mole) and pivalic anhydride (7.45 g., 0.040 mole) gave a fraction which on redistillation afforded 4.55 g. (67%) of 4-pyridylmethyl pivalate, b.p. 132° (12 mm.), n^{20}D 1.4862. The n.m.r. spectrum[24] had a singlet τ 8.82, wt. of 9 (t-butyl protons); singlet τ 4.95, wt. of 2 (methylene protons); doublet τ 2.85 ($J = 6$ c.p.s.), wt. of 2 (C-3 and C-5 pyridine protons); and a doublet τ 1.51 ($J = 6$ c.p.s.), wt. of 2 (C-2 and C-6 pyridine protons).

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82. Found: C, 68.42; H, 7.98.

A picrate was prepared in the usual manner; an analytical sample was obtained by recrystallization from water, m.p. 142–143°, as green-yellow needles.

Anal. Calcd. for $C_{17}H_{18}N_4O_9$: C, 48.34; H, 4.29. Found: C, 48.38; H, 4.30.

4-Neopentylpyridine, b.p. 87–88° (13 mm.), n^{20}D 1.4920 (lit.[25] b.p. 134° (101 mm.), $n^{25.5}$D 1.4902) was prepared by the procedure of Osuch and Levine[26] and had the following n.m.r. spectrum[24]: singlet τ 9.09, wt. of 9 (t-butyl protons); singlet τ 7.58, wt. of 2 (methylene protons); doublet τ 2.98 ($J = 6.5$ c.p.s.), wt. of 2 (C-3 and C-5 pyridine protons); and doublet τ 1.55, ($J = 6.5$ c.p.s.), wt. of 2 (C-2 and C-6 pyridine protons).

The Reaction of 4-Picoline N-Oxide with Acid Anhydrides. Apparatus. A three-necked, round-bottom flask was fitted with a nitrogen inlet tube, an addition funnel with a pressure equalizer side arm, and a reflux condenser. To the condenser was attached the following series of traps: an acetone–Dry Ice trap, a large balast bottle, four traps, the first three fitted with Ostwald bubblers and the fourth with a sintered glass bubbler and each flask containing standard barium hydroxide, and a mercury trap. The apparatus and gas analysis train were flushed with dry nitrogen before the reactants were added, during the reaction period, and during the cooling period.

General Procedure. 4-Picoline N-oxide[27] dissolved in the acid corresponding to the anhydride was added dropwise to the refluxing anhydride over the specified period of time and the reaction mixture heated for the additional period indicated. After cooling the reaction mixture to room temperature, the amount of carbon dioxide collected in the barium hydroxide traps was

(19) M. H. Fournier, *Bull. soc. chim.*, 7, 839 (1910).

(20) M. F. Ansell, M. A. Davies, J. W. Hancock, W. J. Hickenbottom, P. G. Holton, and A. A. Hyatt, *J. Chem. Soc.*, 2705 (1955).
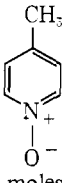
(21) 4-Pyridylmethanol was obtained by saponification of the ester mixture resulting from the reaction of 4-picoline N-oxide and acetic anhydride.[22] 4-Pyridylmethanol, m.p. 53–54°, was isolated by chloroform extraction of the alkaline saponification mixture. From the acidified reaction mixture, 3-hydroxy-4-methylpyridine, m.p.119°, was isolated by extraction and purified by the procedure of Berson and Cohen.[23]

(22) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, 76, 1286(1954).

(23) J. A. Berson and T. Cohen, *ibid.*, 77, 1281 (1955).

(24) The n.m.r. spectrum was determined with a 15 or 20% solution in deuteriochloroform with tetramethylsilane as an internal standard.

(25) W. M. Schubert and J. Robins, *J. Am. Chem. Soc.*, 80, 559 (1958).

(26) C. Osuch and R. Levine, *ibid.*, 78, 1725 (1956).

(27) The authors wish to thank Dr. F. E. Cislak, Reilly Tar Chemical Co., Indianapolis, Ind., for a generous supply of 4-picoline N-oxide and for authentic samples of 2,4-lutidine, 3,4-lutidine, 4-ethylpyridine, and 4-isobutylpyridine.

Table II. Reaction of 4-Picoline N-Oxide with Various Anhydrides

O $\|$ $(RC)_2$—O R, moles	N-oxide moles	Addition time, hr.	Reflux time, hr.	% yield of CO_2	% yield of total	Esters—Composition CH_2OCR	CH_3 OCR	Alkylpyridines, % yield CH_3	CH_2R	CH_3 R	CH_3 R	CH_2R R	Total
CH_3, 0.412	0.400	1	2	4.7	60	89	11	3.3	0.63	0.40	0.02	...	4.35
$(CH_3)_2$ CH, 0.102	0.100	1	2	38.7	11.4	90	10	10.7	9.8	2.8	1.85	...	25.15
$(CH_3)_2$CH, 0.102	0.100	3	2	53.4	12.2			9.9	10.4	3.25	2.25	...	25.8
$(CH_3)_3$C, 0.239[a]	0.230[a]	2	3	51.5[b]	7.4	36	64	9.8	15.0	3.7	3.7	3.0	35.2

[a] This reaction was performed without the gas analysis train and provided all the data listed except the per cent yield of carbon dioxide. [b] The experiment which provided the per cent yield of carbon dioxide was carried out with 0.100 mole of 4-picoline N-oxide and 0.102 mole of pivalic anhydride with a 1-hr. addition period followed by a 4-hr. heating period.

determined by the volumetric procedure of Willard and Diehl.[10] The reaction mixture was distilled (except in the case of the pivalic anhydride reaction) under reduced pressure; after the bulk of the carboxylic acid was removed, three or four fractions of crude product were collected. Fraction III from the acetic anhydride reaction was composed of esters and analyzed by g.l.c., while with isobutyric anhydride fractions III and IV were redistilled and the distillate (ester products) analyzed by g.l.c.. Fractions I and II from the acetic and isobutyric anhydride reactions were treated with 50% sodium hydroxide and the mixture was extracted with chloroform. After the extract was dried over anhydrous potassium carbonate, the chloroform was removed and the composition of the residue (alkylpyridine) was determined by g.l.c.[28]

In the pivalic anhydride experiment the reaction mixture was treated with 25% sodium hydroxide for 24 hr.[29] and the alkaline solution extracted with chloroform. The extract was dried over anhydrous sodium sulfate; after the solvent was removed, the residue was distilled under reduced pressure and gave three fractions. Since no separation of esters and alkylpyridines was effected, the three fractions were combined and the composition was determined by g.l.c.[28]

The results of these experiments are summarized in Table II.

Identification of Products. Acetic Anhydride. Fraction III from the distillation of the reaction mixture was a mixture of 4-pyridylmethyl acetate and 3-acetoxy-4-methylpyridine, b.p. 116–125° (14 mm.), $n^{24}D$ 1.4990 (lit.[6] b.p. 100–101° (5 mm.), $n^{20}D$ 1.5021). A sample of the ester mixture was purified by preparative g.l.c.[30] and the composition of the mixture was estimated

(28) The g.l.c. analyses were performed with a Wilkens Aerograph A-90 B instrument. A 6-ft. column, packed with 20% Apiezon N on Chromsorb W, methyl silicone treated 60–80 mesh, was used at 90° and a flow rate of 10 p.s.i. helium for the acetic anhydride products, at 125° and 10 p.s.i. helium for the isobutyric anhydride products, and 138° and 15 p.s.i. for the pivalic anhydride products. The analysis of the mixture was made on the basis that the area under each peak was proportional to the molar concentration of each component. This was verified for 4-picoline, 4-ethylpyridine, 2,4-lutidine, and 4-isobutylpyridine and assumed for the other components.

(29) In a preliminary experiment the reaction mixture was exposed to 50% sodium hydroxide for 48 hr. and some saponification of the esters was noted. 4-Pyridylmethanol was detected in g.l.c. analysis but was present in small amount. The alcohol was not detected in the above described experiment; however, we cannot completely exclude the possibility that some was present but not detected.

(30) A Wilkens "Autoprep" Model A-700 was used for preparative g.l.c. using a 10-ft. × ³/₈-in. column packed with 20% Apiezon N on Chromsorb W.

from the n.m.r. spectrum using the ratio of integrated areas of the peaks at τ 4.95 and 7.88 (4-CH_2/4-CH_3).

Fractions of all alkylpyridines, except 3,4-lutidine, were collected and their infrared spectra were identical with those of authentic samples. Peak enhancement without distortion was observed in all cases when samples of the mixture were enriched individually with authentic samples.

Isobutyric Anhydride. The redistilled mixture of crude esters, b.p. 110–135° (13 mm.), $n^{20}D$ 1.4995, was analyzed by g.l.c.[28] The n.m.r. spectrum[24] of a sample purified by preparative g.l.c.[30] ($n^{20}D$ 1.4912) was identical with those of authentic samples of 4-pyridylmethyl isobutyrate and 3-isobutyroxy-4-methyl-pyridine. The ester composition was estimated from the relative areas of the peak at τ 4.88 and 7.86 (4-CH_2/4-CH_3).

A 30-g. mixture of alkylpyridines was distilled *in vacuo* through an 18-in. spinning-band column and 17 fractions were collected and analyzed by g.l.c.[28] Samples so obtained were characterized by physical constants and derivatives. These data are summarized in Table III. In addition the n.m.r. spectrum[24] was consistent with the assigned structures. 4-Isobutyl-pyridine: doublet τ 9.10 ($J = 6.4$ c.p.s.), wt. of 6 (isopropyl methyl protons); heptet τ 8.18 ($J = 6.4$ c.p.s.), wt. of 1 (isopropyl methine proton); doublet τ 7.57 ($J = 6.4$ c.p.s.), wt. of 2 (methylene protons); doublet τ 2.98 ($J = 5.3$ c.p.s.), wt. of 2 (C-3 and C-5 pyridine protons); and doublet τ 1.62 ($J = 5.3$ c.p.s.), wt. of 2 (C-2 and C-6 pyridine protons). 4-Methyl-2-isopropylpyridine: doublet τ 8.68 ($J = 6.8$ c.p.s.), wt. of 6 (isopropyl methyl protons); singlet τ 7.68, wt. of 3 (4-methyl protons); heptet τ 7.01 ($J = 6.8$ c.p.s.), wt. of 1 (isopropyl methine proton); doublet τ 3.20 ($J = 6.2$ c.p.s.) (C-5 pyridine proton); singlet τ 3.08 superimposed on one-half of doublet (C-3 pyridine proton), combined wt. of 2; and doublet τ 1.63 ($J = 6.2$ c.p.s.), wt. of 1 (C-6 pyridine protons). 4-Methyl-3-isopropylpyridine: doublet τ 8.73 ($J = 6.8$ c.p.s.), wt. of 6 (isopropyl methyl protons); singlet τ 7.71, wt. of 3 (4-methyl protons); heptet τ 6.90 ($J = 6.8$ c.p.s.), wt. of 1 (isopropyl methine proton); doublet τ 3.12 ($J = 5.5$ c.p.s.), wt. of 1 (C-5 pyridine proton); doublet τ 1.85 ($J = 5.5$ c.p.s.), wt. of 1 (C-6 pyridine proton); and singlet τ 1.71, wt. of 1 (C-2 pyridine proton).

Pivalic Anhydride. The liquid material collected in the acetone–Dry Ice trap was allowed to warm to

Table III. Alkylpyridines from 4-Picoline N-Oxide–Isobutyric Anhydride Reaction

Alkylpyridine	B.p., °C. (mm.).	Lit. b.p., °C. (mm.)	n^{20}D	Lit. n^{20}D	Picrate m.p., °C.	Lit. m.p., °C.
4-Picoline	46.5–47 (20)	145.1[a]	1.5049	1.5064[a]	162–165	166–167[b]
2-Isopropyl-4-methylpyridine	77–78 (21)[c]	81–82 (23)[d]	1.4910	1.4908[d]	117–119	118.5–119.5
3-Isopropyl-4-methylpyridine	87.5 (16)[e]	...	1.5016[f]	...	173–174[g]	...
4-Isobutypyridine	85–86.5 (14)[h]	63–66 (8.5)[i] 93–95 (23)[j]	1.4904[f]	1.4902[i]	120–121	122[k]

[a] O. Flaschner, *J. Chem. Soc.*, **95**, 670 (1909). [b] G. R. Clemo and W. M. Gourlay, *ibid.*, 478 (1938). [c] 96% pure determined by g.l.c.[28] [d] H. F. Lockte, P. F. Krause, Jr., and E. N. Wheeler, *J. Am. Chem. Soc.*, **75**, 4477 (1953). [e] 80% pure determined by g.l.c.[28] [f] Determined after preparative g.l.c.[30] purification. [g] Crystallized from ethanol as lustrous charteuse needles. *Anal.* Calcd. for $C_{15}H_6N_4O_7$: C, 49.45; H, 4.43. Found: C, 49.64, H, 4.55. [h] 99% pure determined by g.l.c.[28] [i] H. Pines and D. Wunderlick. *J. Am. Chem. Soc.*, **81**, 2569 (1959). [j] See ref. 26. [k] A. E. Chichibabin, *Bull. soc. chim. France*, **3**, 1623 (1936).

room temperature and the volatile material collected in another acetone–Dry Ice trap. This liquid condensate (*ca.* 2% yield) was composed of 51% isobutane and 49% isobutylene identified by comparison of g.l.c. retention time and peak enhancement with authentic material. In a subsequent experiment the isobutylene was converted to 1,2-dibromo-2-methylpropane (5% based on N-oxide), b.p. 140–145°, n^{20}D 1.5188 (lit.[31] b.p. 143–145°, n^{20}D 1.5072), and a mixture of 1,2-dibromo-2-methylpropane and 1,2,3-tribromo-2-methylpropane.

Preparative g.l.c.[30] was used to obtain samples of the alkylpyridines and ester mixture for identification. 4-Neopentylpyridine, n^{20}D 1.4910 (lit.[25] $n^{25.5}$D 1.4902), had infrared and n.m.r. spectra identical with those of an authentic sample. The structure of 2-*t*-butyl-4-methylpyridine was assigned on the basis of its n.m.r. spectrum[24]: singlet τ 8.64, wt. of 9 (2-*t*-butyl methyl protons); singlet τ 7.69, wt. of 3 (4-methylprotons); doublet τ 3.12 (J = 5.2 c.p.s.), wt. of 1 (C-5 pyridine proton); singlet τ 2.96, wt. of 1 (C-3 pyridine proton); and doublet τ 1.59 (J = 5.2 c.p.s.), wt. of 1 (C-6 pyridine proton).

The *picrate* of 2-*t*-butyl-4-methylpyridine, m.p. 145°, was obtained as light green-yellow fern-like plates from ethyl acetate ("Skelly B").

Anal. Calcd. for $C_{16}H_{18}N_4O_7$: C, 50.79; H, 4.80. Found: C, 50.64, 50.88; H, 4.79, 4.84.

The n.m.r. spectrum[24] of 3-*t*-butyl-4-methylpyridine consisted of a singlet τ 8.54, wt. of 9 (3-*t*-butyl methyl protons); singlet τ 7.49, wt. of 3 (4-methyl protons); doublet τ 3.05 (J = 5.2 c.p.s.), wt. of 1 (C-5 pyridine

(31) S. Searles and M. J. Gortatowski, *J. Am. Chem. Soc.*, **75**, 2639 (1953).

proton); doublet τ 1.67 (J = 5.2 c.p.s.), wt. of 1 (C-6 pyridine proton); and a singlet τ 1.38, wt. of 1 (C-2 pyridine proton).

The *picrate* of 3-*t*-butyl-4-methylpyridine, m.p. 162–163°, was obtained as green-yellow needles from ethanol.

Anal. Calcd. for $C_{16}H_{18}N_4O_7$: C, 50.79; H, 4.80. Found: C, 51.09; H, 4.90.

The last alkylpyridine overlapped with the esters and was collected with the esters. After recycling this mixture through preparative g.l.c.[30] an impure sample of material was obtained which was assigned the structure of 2-*t*-butyl-4-neopentylpyridine on the basis of its n.m.r. spectrum[24]: singlet τ 9.09 (4-neopentyl methyl protons), singlet τ 8.63 (2-*t*-butyl methyl protons), singlet τ 7.54 (4-neopentyl methylene protons), doublet τ 3.14 (J = 5.9 c.p.s.) (C-5 pyridine proton), singlet τ 2.93 (C-3 pyridine protons), and a doublet τ 1.57 (J = 5.3 c.p.s.) (C-6 pyridine proton). Impurity peaks at τ 7.86, 7.83, and 1.35 indicated a minor component.

The infrared spectra of the alkylpyridines were consistent with the assigned structures.

Structural assignment of the mixture of 4-pyridylmethyl pivalate and 3-pivaloxy-4-methylpyridine, isolated by preparative g.l.c.,[30] n^{20}D 1.4808, was based on comparison of the infrared and the n.m.r. spectra of the mixture with that of authentic 4-pyridylmethyl pivalate. The n.m.r. spectrum[24] of the mixture indicated 36% 4-pyridylmethyl pivalate and 64% 3-pivaloxy-4-methylpyridine determined from a ratio of the signals at τ 4.97 and 7.97 (4-CH$_2$/4-CH$_3$), as well as τ 1.48 and 1.74 (C-2 proton of 4-ester/C-2 proton of the 3-ester).