The Reaction of 2-Picoline N-Oxide with Substituted Acetic Anhydrides

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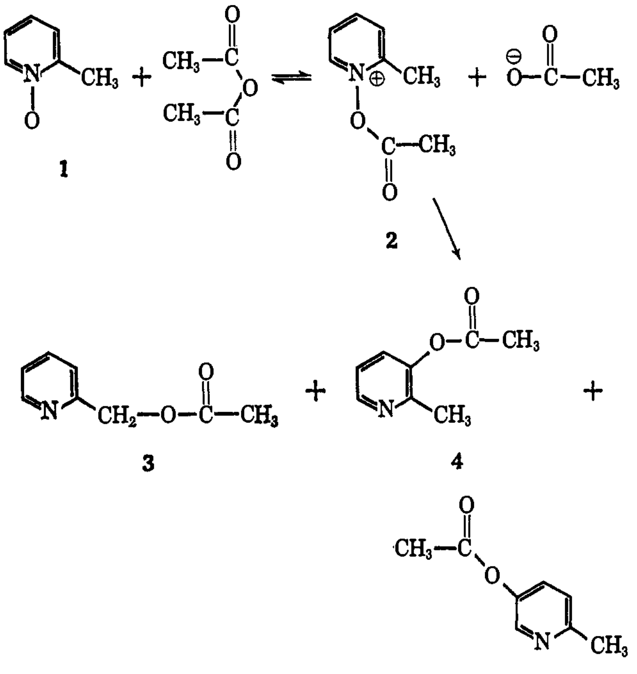
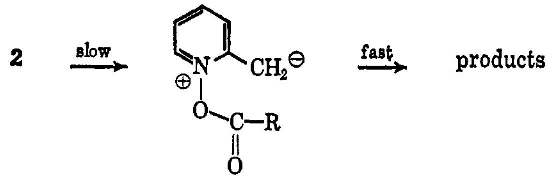
Abstract: The products of the reaction of 2-picoline N-oxide with phenylacetic, trichloroacetic, and trifluoroacetic anhydrides have been determined. The results obtained argue against the radical-pair mechanism for the rearrangement step and are interpreted as favoring an ion-pair mechanism. The details of the ionization step are discussed.

The mechanisms of the reactions of aromatic amine N-oxides with carboxylic acid anhydrides and acid chlorides have received much recent attention.[1] The reaction of 2-picoline N-oxide with acetic anhydride[2] gives a mixture of 2-(α-acetoxymethyl)pyridine (**3**), 3-acetoxy-2-picoline (**4**), and 5-acetoxy-2-picoline (**5**) in high yield.[3]



Picrate[4] and perchlorate[5] salts of the N-acetoxy-2-picolinium ions (**2**) can be isolated and have been shown to give products similar to those observed in the anhydride reaction on treatment with base.[4] These observations strongly suggest that the first step of the reaction is as shown. Studies of the reaction of 1-acetoxy-2-(α,α-dideuteriobenzyl)pyridinium perchlorate with sodium acetate in the presence of acetic acid showed proton transfer to be irreversible and thus rate determining.[6]



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Mechanisms which have been considered to account for product formation from the anhydrobase intermediate **6** include a concerted cyclic process,[7–9] an addition–elimination sequence,[7–9] ion-pair formation,[9,10] and radical-pair formation with efficient cage recombination.[8,9] The addition–elimination sequence was ruled out by the observation that the reaction with butyric anhydride with added acetate or chloride gives no products incorporating the external anion.[9]

Studies of the reaction with oxygen-18-labeled acid anhydrides[8,11] confirmed the rearrangement to be intramolecular, and further showed that equilibration of the two oxygen atoms of the N-acyloxy group occurs in the process. If it is assumed that no other mechanism for this oxygen atom equilibration exists,[12] then these labeling studies effectively rule against the concerted cyclic process. The remaining alternatives appear to be the radical-pair pathway which has been strongly advanced by Oae[8,11] or an ion-pair process.[9,10]

That radicals are formed during the reactions cannot be seriously doubted. However, the fact that several acyl peroxides[13] are known to undergo O–O bond cleavage by competitive homolytic and heterolytic mechanisms makes the mere presence of radical intermediates equivocal.

The lifetime of the acetoxyl radical has been estimated to be *ca.* 10^{-9} sec.[14,15] If this value is correct, then a

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(1) V. J. Traynelis and A. Gallagher, *J. Am. Chem. Soc.*, **87**, 5710 (1965); J. H. Markgraf and M. Ahn, *ibid.*, **86**, 2699 (1964); J. H. Markgraf, H. B. Brown, S. C. Mohr, and R. G. Peterson, *ibid.*, **85**, 958 (1963); S. Oae and S. Kozuka, *Tetrahedron*, **20**, 2671, 2691 (1964).

(2) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954); G. Kobayashi and S. Furukawa, *Pharm. Bull.* (Tokyo), **1**, 347 (1953).

(3) P. W. Ford and J. M. Swan, *Australian J. Chem.*, **18**, 867 (1965).

(4) V. J. Traynelis and R. F. Martello, *J. Org. Chem.*, **26**, 4365 (1961).

(5) C. W. Muth and R. S. Darlak, Abstracts, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1962, p 97Q.

(6) V. J. Traynelis and P. T. Pacini, *J. Am. Chem. Soc.*, **86**, 4917 (1964).

(7) I. J. Pachter, *ibid.*, **75**, 3026 (1953).

(8) S. Oae, T. Kitao, and Y. Kitaoka, *ibid.*, **84**, 3362 (1962).

(9) V. J. Traynelis and R. F. Martello, *ibid.*, **80**, 6590 (1958).

(10) T. Cohen and J. Fager, *J. Am. Chem. Soc.*, **87**, 5701 (1965).

(11) S. Oae, *Tetrahedron*, **20**, 2677 (1964).

(12) Control experiments which rule out other mechanisms for oxygen-18 equilibration have not yet been reported.

(13) T. Koenig and W. Brewer, *J. Am. Chem. Soc.*, **86**, 2728 (1964); J. E. Leffler, *ibid.*, **72**, 67 (1950).

(14) M. Szwarc, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., John Wiley and Sons, Inc., New York, N. Y., 1962, pp 156–174.

(15) The postulate that acetyl peroxide decomposes by concerted three-bond cleavage[16] to give directly methyl radicals and carbon dioxide has been not been supported by studies[17] of the secondary deuterium isotope effects on this reaction.

radical-pair process could conceivably compete with both diffusion and decarboxylation within the cage. There is evidence[18] that acetoxyl radicals are formed reversibly in the decomposition of acetyl peroxide.

The postulate that the decomposition of *t*-butyl phenylperacetate is a concerted process[19] is supported by the α-secondary deuterium kinetic isotope effects observed for the reaction.[17] The decomposition of *t*-butyl trichloroperacetate is also thought to be concerted while that of *t*-butyl trifluoroperacetate is not.[19] Thus, whereas the radical-pair hypothesis for ester formation is a possibility with the acetoxyl radical intermediate, the products of the reaction with phenylacetic or trichloroacetic anhydrides should change to quantitative carbon dioxide if the same mechanism is operative. With this in mind, an investigation of these reactions was initiated. Another group has recently reported[10] a study of the phenylacetic anhydride reaction under different conditions from those employed here.

Results

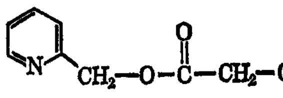
The products of the reactions of 2-picoline N-oxide with phenylacetic, trichloroacetic, and trifluoroacetic anhydrides are summarized in Table I. The carbon dioxide was identified by its infrared and mass spectra and was determined by volume. The yields of other products were determined by a quantitative nmr technique or by glpc after calibrating detector response with known compounds. The ester mixture, obtained in the phenylacetic anhydride reaction by distillation, was shown to give the same glpc response as pure 2-pyridylmethyl phenylacetate. The yields obtained by glpc were generally lower than those obtained using the nmr method but they were in acceptable agreement.

Table I. Products (mole/mole) of 2-Picoline N-Oxide with RCOOCOR

Run	R	Solvent	Initial acid, *M*	Esters	C_6H_5-CHO	CO_2	Other
1	$C_6H_5CH_2$	CH_3CN^a	0	0.49^b	0.25	0.36	0.06^c
2	. . .	CH_3CN^a	0.05	0.56	0.16	0.28	*c*
3	. . .	CH_3CN^a	0.49	0.62	0.13	0.25	*c*
4	CCl_3	$CHCl_3{}^a$	*d*	0.74^e	. . .	0.02	
5	CF_3	$CH_2Cl_2{}^f$	*d*	0.81^e	. . .	None	

[a] Reflux temperatures. [b] The nmr analysis of this mixture indicates 2-pyridylmethyl phenylacetate (**7**, 65%), 5-phenylacetoxy-2-picoline (**8**, 21%), and 3-phenylacetoxy-2-picoline (**9**, 14%). [c] Bibenzyl; picoline dimers were present but not determined. [d] Runs in excess anhydride which did contain some of the acid by infrared spectroscpoy. [e] Yields of 2-pyridylmethyl acetates by nmr. The isolated product was 2-pyridylcarbinol after hydrolysis. [f] 0°, 1 hr.

The nmr spectrum of the major distillation fraction from the phenylacetic anhydride reaction indicated a mixture containing 2-pyridylmethyl phenylacetate as the major component (**7**, methylene singlets at δ 3.66 and 5.16, 6-pyridyl proton multiplet at δ 8.68). Combustion analysis of this fraction was correct for a mixture of isomers. The infrared spectrum showed broad carbonyl absorption between 1770 and 1740 cm^{-1}, suggesting the presence of ring-substituted pyridyl phenylacetates. The presence of two closely spaced peaks at δ 3.78 and 3.81 and two singlets at δ 2.27 and 2.44 in the nmr spectrum supports this assignment (methylene of the phenylacetates and pyridyl methyl groups, respectively). The presence of a second multiplet in the 6-pyridyl proton region (δ 8.38 besides that of **7**, δ 8.68) with a relative area of one-third the sum of the areas of the two methyl group peaks (δ 2.27 and 2.44) indicates that ring substitution is not at the 6 position.



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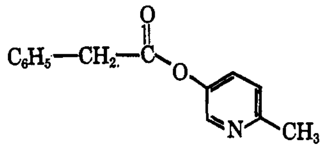

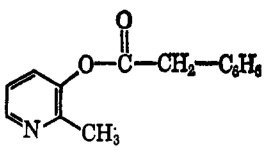

8 **9**

By analogy with the products of the reaction of 2-picoline N-oxide with acetic anhydride (**3**, **4**, and **5**), the components of the present mixture are assigned as **7**, **8**, and **9**. Since the position of the methyl group absorption of **5** is at a lower field than that of **6** (δ 2.52 and 2.38, respectively),[3] the peak at δ 2.44 in the spectrum of the mixture obtained here is assigned to **8** while the peak at δ 2.27 is assigned to **9**. With these assignments, the composition of this mixture of esters is **7** (65%), **8** (21%), and **9** (14%) which is very close to that for the corresponding mixture obtained in the acetic anhydride reaction.[3]

The bibenzyl was isolated by glpc of one of the distillation fractions. It was identified by its retention time on glpc and by spectral comparisons with authentic material. The same distillation fraction contained several other components by glpc and nmr. That these were α-picoline dimers is suggested by the fact that they were extracted from the bibenzyl with acid. No attempt was made to isolate or identify them. The yields of 2-pyridylmethyl trichloroacetate and trifluoroacetate were determined by the nmr techniques. Spectra of product solutions in these cases were nearly identical with those obtained from treatment of 2-pyridylcarbinol with the corresponding anhydrides in the corresponding solvents. The N-oxide product mixtures were subjected to basic hydrolysis, and the overall yield of 2-pyridylcarbinol from N-oxide was greater than 60% in both cases.

Discussion

The initial experiments of this study led to the discovery of an oxidative decarboxylation of phenylacetic anhydride which gives benzaldehyde as a major product. It was found that this reaction is favored with both pyridine N-oxide and 4-picoline N-oxide, and that the stoichiometry involves 2 moles of N-oxide to 1 mole of anhydride. Preliminary studies of the mechanism of this reaction have been reported elsewhere.[20,21]

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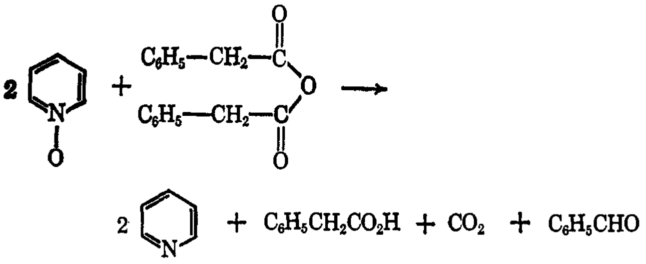
(16) M. J. Goldstein, *Tetrahedron Letters*, No. 24, 1601 (1964).

(17) T. Koenig and W. Brewer, *Tetrahedron Letters*, No. 32, 2773 (1965).

(18) W. Braun, L. Rajenbach, and F. R. Eirich, *J. Phys. Chem.*, **66**, 1591 (1962).

(19) P. D. Bartlett and R. R. Hiatt, *J. Am. Chem. Soc.*, 80, 1398 (1958).

(20) T. Cohen, I. H. Song, and J. H. Fager, *Tetrahedron Letters*, No. 4, 237 (1965); C. Ruchardt, S. Eichler, and O. Krätz, *ibid.*, No. 4, 233 (1965).



The yield of benzaldehyde (Table I) found in the reaction of 2-picoline N-oxide with this anhydride indicates that this path is the less favored one in this case. It has been shown[21] that the rate of benzaldehyde formation with 4-picoline N-oxide is greatly retarded by added phenylacetic acid. Since the deuterium-labeling studies on the reaction of 1-acetoxy-2-benzylpyridinium perchlorate[6] with acetate ion indicate that proton transfer (**2** to **6**) is irreversible, it would be expected that the ester-forming reaction would not be subject to the same retardation by added acid. Thus the aldehyde-forming reaction might be expected to be removed as a kinetically important path by initial addition of phenylacetic acid.

The runs which contained added acid did show changes in product composition in the expected direction but not of the expected magnitude. The rate of the reaction as judged qualitatively by gas evolution was also not greatly affected by the added acid (50% gas after 30-min reaction in all cases). These observations may indicate that the aldehyde can be formed by more than one mechanism.[22]

The present test of the radical pair hypothesis involves the assumption that the concerted decomposition of *t*-butyl phenylperacetate can be extrapolated to the cleavage of an N–O bond in the N-oxide reaction. The experimentally observable criterion is the ratio of the yield of benzyl radicals to esters which can be attributed to this cleavage. A maximum estimate of the benzyl radical yield can be obtained by subtracting the benzaldehyde yield from the carbon dioxide yield. In run 1, the amount arrived at in this way (11%) agrees favorably with twice the yield of bibenzyl (12%).

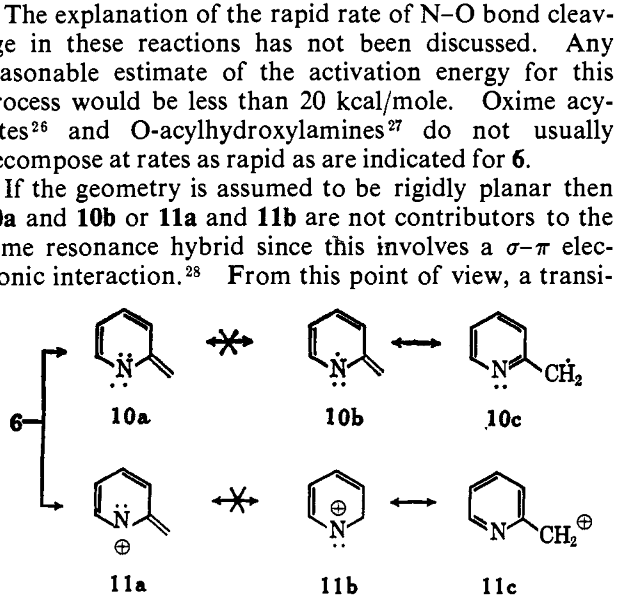
The yield of esters obtained here is quite comparable with that found with acetic anhydride itself when correction is made for the aldehyde reaction. The magnitude of the increase in the relative importance of decarboxylated radical intermediate is small and more compatible with a dual mechanism than with the radical-pair possibility. This interpretation is reinforced by the results of the study of the reaction with trichloroacetic anhydride. In this case, less than 2% gas is evolved while the ester yield is very high. Thus the radical-pair hypothesis is not attractive as a general mechanism for these reactions.

The alternative which can accommodate both the oxygen-18 results and the present results is ion-pair formation. The ratio of ester to benzyl radical products from the phenyl acetic anhydride reaction in the present study is higher than that found by Cohen and Fager in benzene at comparable temperature (4 compared to 1.5). This change is in the direction expected for a dual mechanism considering the difference in solvent polarity. The change in viscosity between the two solvents is not great enough to account for this change in product ratio, assuming a radical cage reaction were operative. The great increase in the rate of the reaction with trifluoroacetic anhydride, as judged by the very mild conditions under which the reaction occurs and the high yield of ester obtained, is also in accord with 2-picolinium acylate ion-pair formation though it does not demand such a mechanism.[23]

Simple Hückel MO calculations also suggest that an ion-pair intermediate from **6** is more favorable than a radical pair. The highest bonding level of the 2-picolyl π system is only stabilized by 0.33β even when the Coulomb integral of the nitrogen atom is given the extreme value $\alpha + 5\beta$.[25] The highest bonding level of the carboxy π system remains at the value given for the Coulomb integral of the oxygen atoms, and most values for this parameter are greater in magnitude than $\alpha + 0.5\beta$.

The explanation of the rapid rate of N–O bond cleavage in these reactions has not been discussed. Any reasonable estimate of the activation energy for this process would be less than 20 kcal/mole. Oxime acylates[26] and O-acylhydroxylamines[27] do not usually decompose at rates as rapid as are indicated for **6**.

If the geometry is assumed to be rigidly planar then **10a** and **10b** or **11a** and **11b** are not contributors to the same resonance hybrid since this involves a σ–π electronic interaction.[28] From this point of view, a transition state for this rearrangement (from **6**) which involves only stretching of the N–O bond in the σ plane should not be very sensitive to the presence of the π-electron system.



On the other hand, the main driving force for the formation of the 2-picolyl radical or cation intermediate must be the transfer of an electron or electrons from the highest occupied π molecular orbital to the rela-

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[21] T. Koenig, *Tetrahedron Letters*, No. 35, 3127 (1965).

[22] Tests for this possibility are presently underway.

[23] The increased acidity of the α protons of the N-trifluoroacetoxy-2-picolinium ion (**2**) and its higher equilibrium concentration would adequately explain the rapid rate of reaction if the cleavage of the N–O bond of the N-trifluoroacetoxy anhydrobase (**6**) is heterolytic. The rates of O–O bond homolyses are usually retarded[24] by electron-withdrawing substituents. Thus, extrapolating to N–O bond homolysis, the cleavage of the N-trifluoroacetoxy anhydrobase might become the slow step and the rate of reaction would not necessarily be so rapid.

[24] C. G. Swain, W. H. Stockmayer, and J. T. Clark, *J. Am. Chem. Soc.*, **72**, 5426 (1950); A. T. Bloomquist, A. F. Ferris, and I. A. Bernstein, *ibid.*, **73**, 5446 (1951).

[25] A more reasonable value for $\alpha_N = \alpha + 1.5\beta$ gives the highest bonding level in the π system at $\alpha + 0.18\beta$.

[26] C. A. Grob, H. Fisher, W. Raudenbusch, and J. Zergenyi, *Helv. Chim. Acta*, **47**, 1003 (1963).

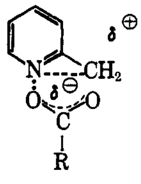
[27] F. Klages, R. Heinle, H. Sitz, and E. Specht, *Ber.*, **96**, 2387 (1963).

[28] For example, the amino ($NH_2\cdot$) radical[29] has a nonlinear ground state with a σ pair and a p vacancy (which corresponds to **10b**). The first excited state has a σ vacancy and a p pair (which corresponds to **10a**). Each state has been observed and has independent existence.

[29] D. A. Ramsay, *Ann. N. Y. Acad. Sci.*, **67**, 485 (1957); H. C. Longuet-Higgins and P. C. Jordan, *Mol. Phys.*, **5**, 121 (1962).

tively more stable σ vacancy on the nitrogen atom.[30] A transition state which might allow such a π–σ electron transfer to occur directly in such planar systems must involve both bending and stretching of the N–O bond and would lead directly to intermediates represented by **10b** and **10c** or **11b** and **11c** but not **10a** or **11a**.

The electron transfer could also occur through σ overlap between the nitrogen atom and the α, 3, or 5 carbon atoms. A transition state for such a process might resemble **12** or **13**. The reported successful detection of the anhydrobase corresponding to 4-picoline N-oxide as well as the differences in labeling pattern observed for the reaction of the latter N-oxide with oxygen-18-labeled acetic anhydride compared to 2-picoline N-oxide both indicate the rearrangement for the 2 isomer to be more rapid.[31] It should be mentioned that the present view of these reactions as net two electron transfer from the α-carbon atom of the anhydrobase (**6**) to the nitrogen atom of the 2-picolyl cation makes the rearrangement formally identical with the oxidative decarboxylation reaction[21,32] which gives benzaldehyde as a side product in the present case if the proposed α-lactone mechanism for the latter process is correct. The difference in the rearrangement and the oxidation reaction is the position of proton removal from the N-acyloxypyridinium ions (**2**). However, the same ambiguities as to mode of electron transfer (π–σ or bond formation) apply, at the present, to all of these reactions.



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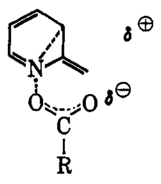

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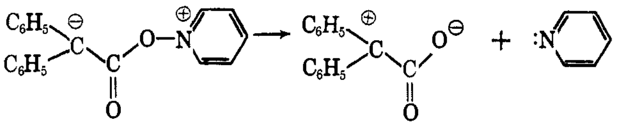

Experimental Section

Acetonitrile was distilled from phosphorus pentoxide. 2-Picoline N-oxide was obtained from Aldrich Chemical Co. and was distilled immediately before use. Trichloroacetic anhydride was obtained from K and K Laboratories, Inc., and was distilled before use, bp 107–111° (10 mm). Trifluoroacetic anhydride was obtained from Matheson Coleman and Bell and was used directly. Infrared spectra were obtained using a Beckman IR-5 spectrophotometer. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Glpc analyses were done using a HyFi Model 600-D with columns containing either 5% SE-30 on Chromosorb W or 20% Carbowax on firebrick and with an Aerograph Model 90-P using a 10 ft × 0.25 in. column with 5% SE-30 on Chromosorb-P. Quantitative glpc analyses were done by calibration of the instrument response using known samples. Quantitative nmr analyses were done by adding a weighed amount of an internal standard (usually dioxane) to weighed amounts of unknowns and measuring relative peak intensities.

Phenylacetic anhydride was prepared by refluxing phenylacetic acid with five times its weight of acetic anhydride for 2 hr. The acetic acid and acetic anhydride were removed under vacuum, and the residue was recrystallized twice from carbon tetrachloride eventually giving 40% yield of material, mp 72–73° (lit.[33] 72.5°).

2-Pyridylmethyl phenylacetate was prepared by warming 2-pyridylcarbinol (2.0 g, 0.018 mole) and phenylacetic anhydride (6.2 g, 0.024 mole) in 10 ml of chloroform for 1 hr. After washing with saturated sodium carbonate solution, the chloroform was removed, and the residue was distilled giving 1.70 g (37%) of the product, bp 135–140° (1 mm).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.98; H, 5.76; N, 6.16. Found: C, 73.77; H, 5.47; N, 6.42.

Phenylacetic Anhydride Reaction. (A). Product Isolation. The anhydride (20.5 g, 0.080 mole) and 180 ml of dried acetonitrile were brought to reflux in a closed system in which the condenser was attached to a U tube containing calcium chloride. The U tube was attached to a gas buret filled with 1% hydrochloric acid solution. The system was equilibrated for 30 min after which the 2-picoline N-oxide (17.6 g, 0.16 mole) in 20 ml of acetonitrile was added from a pressure-equalizing addition funnel. The addition took 5 min, and evolution of gas began almost immediately. After 90 min, the volume of gas evolved was 710 cc (0.029 mole, 36%). That the evolved gas was carbon dioxide was established subsequently when the reaction was carried out in a breakseal flask which allowed collection of the gaseous product and examination of its infrared and mass spectra.

The solvent was removed under vacuum, and examination of the nmr spectrum of this distillate showed only acetonitrile. Bulb-to-bulb distillation of residue at aspirator pressure on the steam bath gave 2-picoline and trace amounts of toluene. Carbon tetrachloride (150 ml) was added to the residue, and the resulting solution was extracted with three 100-ml portions of saturated sodium carbonate. The aqueous phase was extracted with two 100-ml portions of carbon tetrachloride. The combined carbon tetrachloride extracts were dried over calcium chloride, and the solvent was removed. The residue was distilled at reduced pressure and separated into five fractions: I, 0.633 g, bp 30–35° (2 mm); II, 1.224 g, bp 35–135° (1 mm); III, 4.442 g, bp 135–143° (1 mm); IV, 3.260 g, bp 143–145° (1 mm); V, 0.601 g, bp 145–160° (0.6 mm).

Fraction I was shown by nmr to contain 75 mole % benzaldehyde and 25 mole % ester mixture.

Examination of the nmr spectrum of fraction II showed that its major component had a sharp singlet absorption (δ 3.08) in the methylene region. This fraction was passed through a 10 ft × 0.25 in. 5% silicone gum rubber on Chromosorb P glpc column at 140°. The major peak was collected and its nmr spectrum showed two singlets (δ 7.20 and 3.08). It was shown to be bibenzyl by comparison of infrared and nmr spectra and glpc retention times of both an authentic sample as well as mixtures. When fraction II was dissolved in carbon tetrachloride and washed with dilute hydrochloric acid only benzaldehyde and bibenzyl of the original complex mixture remained in the organic phase.

Fractions III and IV gave similar nmr spectra which indicated the major component to be 2-pyridylmethyl phenylacetate by comparison with an authentic sample. The presence of two 2-picolyl phenylacetates was also indicated by two closely spaced absorptions at δ 3.81, two singlets at δ 2.27 and 2.44, and a multiplet typical of 6-pyridyl proton centered at δ 8.38. Combustion analysis on this narrow boiling range mixture was correct for $C_{14}H_{13}NO_2$. *Anal.* Calcd: C, 73.98; H, 5.76; N, 6.16. Found: C, 73.82; H, 5.44; N, 6.39.

Glpc analysis using a HyFi 600-D with a 6 ft × $^1/_8$ in. column packed with 5% SE-30 on Chromosorb P indicated the presence of 2-pyridylmethyl phenylacetate and another component or components which were incompletely resolved from the main peak. It was shown that this mixture gave the same total detector response as pure 2-pyridylmethyl phenylacetate. The infrared spectrum of the mixture showed unresolved carbonyl absorptions between 1740 and 1770 cm^{-1}.

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(30) The heat of reaction for homolytic cleavage of the N–O bond in **6** to give **10a** would be the σ N–O bond energy (DE_σ). The heat of reaction for going from **6** to the π radical represented by **10b** and **10c** would be lowered by the difference in stabilization energy of the highest occupied π molecular orbital (*ca.* $\alpha + 0.2\beta$) and that of the σ orbital on nitrogen (*ca.* $\alpha + 1.5\beta$) or $DE_\sigma - 1.3\beta$. The electron transfer from the picolyl π radical to the carboxyl radical to give the ion pair would be a further stabilization as mentioned earlier.

(31) These reactions could also be nonadiabatic and involve crossing between potential energy surfaces.

(32) Evidence for a corresponding process with acetyl peroxide and acetate anion has been obtained in these laboratories: unpublished work of R. Wielesek.

(33) R. Anshütz and W. Berns, *Ber.*, **20**, 1389 (1887).

Fraction V was found to be composed of 2-pyridylmethyl phenylacetate and phenylacetic acid in a mole ratio of 3:1 by nmr.

Acidification of the basic aqueous washings of the original product mixture and extraction with methylene chloride gave phenylacetic acid contaminated with unreacted 2-picoline N-oxide. The yield of phenylacetic acid was 80.0 mmoles (100%).

(B). **Quantitative Analysis.** Subsequent procedures for quantitative analysis of the products of the reaction were similar to that just described except that a small aliquot of the anhydride solution was removed after refluxing in acetonitrile for a few minutes but before the N-oxide was added and analyzed for hydrolysis by nmr. Small amounts of hydrolysis did occur in some cases, and the yields reported are corrected for the hydrolysis as determined in this way. After gas evolution ceased, the solvent was distilled at reduced pressure, and the residue was dissolved in carbon disulfide and extracted with saturated sodium carbonate solution. The remaining carbon disulfide solution was dried and analyzed directly for benzaldehyde and the ester mixture by the glpc and nmr methods. Control experiments showed all of the 2-picoline N-oxide remained in the aqueous phase, and no more benzaldehyde or esters were extracted from the aqueous phase on washing with methylene chloride.

An alternative procedure was mixing the two reactants in a flask with a breakseal side arm. The system was degassed, sealed under vacuum, and heated at 70° for 10 hr. The gaseous product was measured on a calibrated vacuum line and identified by its infrared spectrum. The solution was then treated as above.

Trifluoroacetic anhydride reactions were carried out in methylene chloride solution in a closed system attached through a drying tube to a gas buret. The 2-picoline N-oxide (10.5 g, 0.10 mole) was dissolved in 75 ml of spectral grade methylene chloride, and the system equilibrated at 0° in an ice bath. The trifluoroacetic anhydride (25 g, 0.12 mole) was added slowly over 15 min. No gas evolution occured in 1 hr at 0°. The solution was allowed to warm to room temperature. Nmr analysis indicated an 80% yield of 2-pyridylmethyl trifluoroacetate. An aliquot of the product solution was extracted with cold 5% sodium bicarbonate and dried over calcium chloride. The nmr and infrared spectra of the resulting solution were nearly identical with those obtained from a methylene chloride solution of 2-pyridylcarbinol treated with trifluoroacetic anhydride and worked up in a similar manner.

The solvent was evaporated from the total product mixture, and the residue was warmed with 10% sodium hydroxide solution. The resulting red liquid was continuously extracted with methylene chloride for 12 hr. Crude 2-pyridylcarbinol (6.50 g, 60% yield) was obtained after solvent evaporation and was identified by spectral and glpc retention time comparison with an authentic sample. A picrate was obtained which had a melting point of 154–156° (undepressed when mixed with known material).

Trichloroacetic anhydride reactions were carried out in refluxing spectral quality chloroform as outlined above. The anhydride (15 g, 0.05 mole) was added to the refluxing solution of 2-picoline N-oxide (2.20 g, 0.020 mole) in 25 ml of solvent. Less than 10 cc of gas was evolved during the 1-hr reflux period, and direct nmr analysis indicated 74% 2-pyridylmethyl trichloroacetate formation. The spectra of an aliquot of this solution after washing with cold sodium bicarbonate solution were nearly identical with those of a solution obtained from 2-pyridylcarbinol which had been treated with trichloroacetic anhydride and worked up in a similar manner. The solvent was evaporated from the total product solution, and the residual dark oil was treated with 10% sodium hydroxide on a steam bath for 10 min. The 2-pyridylcarbinol was obtained and identified as outlined above (1.44 g, 65% yield).

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Mass Spectrometry in Structural and Stereochemical Problems. CXIV.[1] Electron Impact Induced Rearrangement of Thiocarbonates, Carbamates, and Thiocarbamates[2]

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Abstract: The mass spectra of all possible methyl phenyl, and diphenyl mono-, di-, and trithiocarbonates and of a number of methyl- and phenyl-substituted carbamates and mono- and dithiocarbamates have been examined in order to compare the possible elimination of CS, COS, or CS_2 with the well-documented one of CO and CO_2. Rearrangement, with elimination of the central portion of the molecule, is insignificant in the case of the carbamates and thiocarbamates. In the case of the thiocarbonates, loss of CS or of CS_2 is negligible. Significant loss of COS requires the presence of the group $CSOCH_3$ while expulsion of CO_2 is important in the presence of the group $COOCH_3$. In C_6H_5XCOYR ($X = O$ or S; $Y = O$ or S; $R = CH_3$ or C_6H_5) CO_2 is lost when $X = Y = O$ or when $Y = O$ and $R = CH_3$; otherwise CO is eliminated. A preliminary rearrangement of the molecular ion of compounds with the group C_6H_5OCS, to C_6H_5SCO, is observed.

Electron impact induced rearrangements of species other than hydrogen may involve a 1,2-alkyl shift or elimination of a neutral molecule from a nonterminal site. Two examples of a 1,2-methyl migration have been reported[4] recently. Elimination of a neutral molecule, by fragmentation of the type $[A\text{–}B\text{–}C]\cdot^+ \rightarrow [A\text{–}C]\cdot^+ + B$ has been observed with a variety of structures: for example, elimination of carbon mon-

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[1] Paper CXIII: D. Goldsmith and C. Djerassi, *J. Org. Chem.* (in press).

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[4] F. Komitsky, J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1398 (1965); C. Djerassi, A. M. Duffield, F. Komitsky, and L. Tökès, *ibid.*, **88**, 860 (1966).