The Oxidation of Oxygen-Labeled Phenylacetic Anhydride by Pyridine N-Oxide. The Relative Nucleophilicities of Pyridine and Pyridine N-Oxide[1a]

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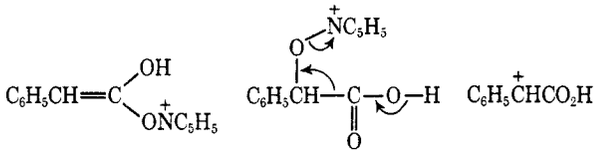
The reaction of pyridine N-oxide with phenylacetic anhydride, uniformly labeled with ^{18}O, produces unlabeled benzaldehyde, indicating that the oxygen atom of the product is derived from the amine oxide. When this reaction is conducted in a large excess of pyridine, the ratio of benzaldehyde to N-benzylpyridinium ion produced is 0.12–0.23, indicating that pyridine N-oxide is substantially more nucleophilic than pyridine toward the intermediate. By the use of competition experiments, it was determined that the ratios of nucleophilic attack of pyridine to that of the N-oxide on methyl iodide, benzhydryl bromide, and *p*-methoxybenzhydryl bromide are 8–15, 5.7, and 3.8, respectively. It is concluded that attack by pyridine N-oxide becomes relatively more favorable as the positive charge on the electrophile increases. This implies that the carbon atom of the intermediate which is to become bonded to the N-oxide group in the oxidative decarboxylation bears a high positive charge. It is suggested that the α-carboxybenzyl cation (**3**) or its conjugate base is the intermediate which is directly attacked by pyridine N-oxide.

The oxidation of phenylacetic anhydride by pyridine N-oxide produces benzaldehyde and proceeds with the given stoichiometry.[2-5] The suggestion has been

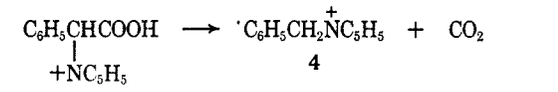
$$(C_6H_5CH_2CO)_2O + 2C_5H_5NO \longrightarrow C_6H_5CHO + 2C_5H_5N + CO_2 + C_6H_5CH_2CO_2H$$

made[2,4,5] that the reaction involves acylation of pyridine N-oxide followed by nucleophilic displacement of pyridine by a second pyridine N-oxide molecule from the enol (**1**) (or the corresponding enolate) of the acylation product to produce the cation (**2**) (or the corresponding carboxylate species). Loss of a proton, carbon dioxide, and pyridine from **2** would lead to the major observed products.[6] The attack of pyridine N-oxide on **1** could be S_N2' or S_N1' in nature; in the latter case, the cation **3** or its conjugate base would be an intermediate.



1 **2** **3**

Some such electrophilic intermediate has been trapped by acetic acid and by pyridine, each utilized as a solvent.[5] In the latter case, it has now been found that a significant quantity of benzaldehyde (0.05–0.10 mol per mole of carbon dioxide generated) is produced in addition to the N-benzylpyridinium ion, **4** (0.43 mol per mole of carbon dioxide), which is thought to be formed by the known[7] decarboxylation shown. It is



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very likely that even more benzaldehyde than that isolated is produced in the reaction since this product is known to be partially destroyed under similar conditions even in the absence of excess pyridine, probably by a Perkin-type condensation with phenylacetic anhydride.[8] In view of the large molar excess (49:1) of pyridine over pyridine N-oxide in this experiment, the considerable degree of capture of the intermediate by pyridine N-oxide would require the latter to be substantially more nucleophilic than pyridine toward the electrophilic intermediate in order for the above mechanism to be acceptable. Such a nucleophilicity order is *a priori* unexpected since pyridine is almost 10^5 times more basic than pyridine N-oxide.[9a] Of course, nucleophilicity does not always correlate well with basicity[10] but we have found (see below) that pyridine is more nucleophilic than pyridine N-oxide toward several substrates and it therefore became necessary to consider the possibility of a mechanistic alternative in which a direct competitive attack of the nucleophiles on the benzylic carbon atom is not required.

One such mechanism, which seems reasonable in a solution containing phenylacetic anhydride and pyridine, involves acylation of the hydroxyl group of **1** prior to the loss of pyridine. The acyloxy group would be expected to stabilize the positive charge of **3** to yield the cation **5**. Attack of pyridine at the partially positive carbon atom or at the carbonyl group might be reversible whereas attack by pyridine N-oxide might lead irreversibly to product **6**, which upon hydrolysis or loss of an anhydride molecule would yield benzaldehyde (only the attack at the carbonyl group is shown in Scheme I).

In order to distinguish between the attack of pyridine N-oxide directly on the α position as required by all previously suggested mechanisms[2-5] and any other mechanism such as the one outlined above, the reaction of pyridine N-oxide with phenylacetic anhydride which was uniformly labeled with ^{18}O (1.4%) was performed. The anhydride was prepared by hydrolysis of phenylacetonitrile with water enriched to the extent of 1.4%

(1) (a) We wish to thank the donors of the Petroleum Research Fund, Administered by the American Chemical Society, for support of this work. (b) NASA Predoctoral Fellow.

(2) T. Cohen and J. H. Fager, Abstracts, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan 1964, p 36 C; T. Cohen, I. H. Song, and J. H. Fager, *Tetrahedron Lett.*, 237 (1965).

(3) C. Rüchardt, S. Eichler, and O. Krätz, *ibid.*, 233 (1965); C. Rüchardt and O. Krätz, *ibid.*, 5915 (1966).

(4) T. Koenig, *ibid.*, 3127 (1965); 2751 (1967).

(5) T. Cohen, I. H. Song, J. H. Fager, and G. L. Deets, *J. Amer. Chem. Soc.*, **89**, 4968 (1967).

(6) T. Cohen and I. H. Song, *J. Org. Chem.*, **31**, 3058 (1966).

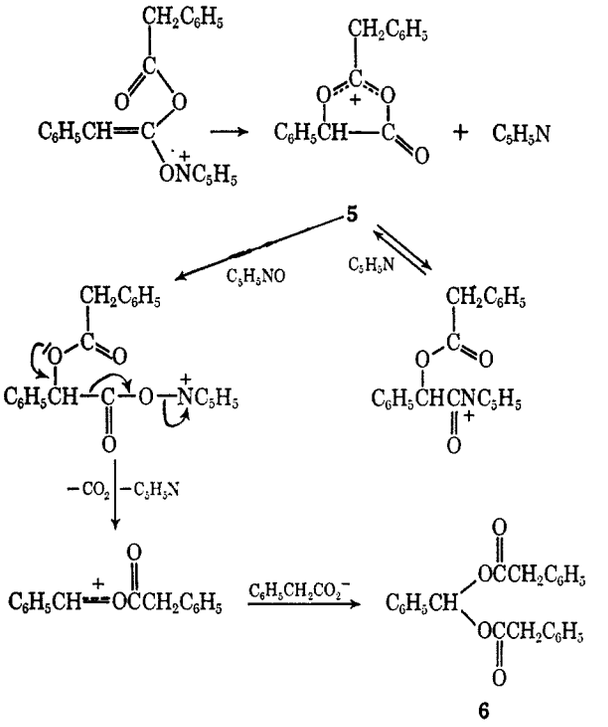
(7) T. Cohen and I. H. Song, *J. Amer. Chem. Soc.*, **87**, 3780 (1965).

(8) T. Cohen and J. H. Fager, *ibid.*, **87**, 5701 (1965).

(9) (a) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., New York, N. Y., 1967, p 97; (b) p 153.

(10) R. Gompper, *Angew. Chem. Intern. Ed. Engl.*, **3**, 560 (1964), and references cited there.

SCHEME I



with ^{18}O. Since commercial samples of such water are also highly enriched with deuterium, it became necessary to convert it into protium water in order to avoid the introduction of deuterium into the benzylic position during the hydrolysis; this would seriously complicate the mass spectrometric analysis of the benzaldehyde produced. The exchange was accomplished very effectively by extended ebullition of the enriched water with hydrogen sulfide.

The resulting benzaldehyde, which was analyzed on the LKB 9000 combined gas chromatograph–mass spectrometer equipped with an accelerating voltage alternator, was found to contain 0.23% ^{18}O, the same as that found for unlabeled benzaldehyde. It is thus clear that pyridine N-oxide does indeed attack the carbon atom which is originally α to the carboxylic acid function as suggested earlier.[2-5]

In order to determine whether a mechanism involving attack of pyridine N-oxide on the α-carbon atom is consistent with the finding that pyridine N-oxide is more nucleophilic than pyridine toward the intermediate, a study of the comparative nucleophilicities of these two bases was undertaken next. An equimolar mixture of the two nucleophiles was allowed to react with each of the following substrates: methyl iodide, benzhydryl bromide, and *p*-methoxybenzhydryl bromide. Methyl iodide was chosen as the prototype of an SN2 substrate; the reaction in this case was performed in acetonitrile since this solvent, unlike several others, allowed a resolution of the nmr peaks used for the product analysis (see below). The experiments with the other two substrates were performed in dimethylformamide in order to maximize the SN1 contribution.

In the case of methyl iodide, the products were N-methylpyridinium iodide and N-methoxypyridinium iodide. Control tests showed that the former is stable under the reaction conditions but that the latter is slowly converted into the former by the action of pyridine. However, without carrying out an extensive kinetic investigation, it is possible with a knowledge of the approximate rate of this conversion to arrive at a minimum (8) and a maximum (15) figure for the ratio of attack of pyridine to that of pyridine N-oxide (see Table I).

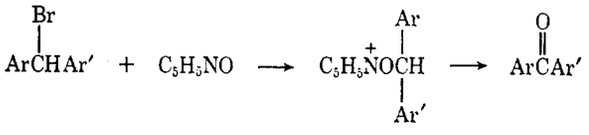
TABLE I

RATIO OF ATTACK OF PYRIDINE TO THAT OF PYRIDINE N-OXIDE ON ALKYL HALIDES

RX	Pyridine attack/ pyridine N-oxide attack	Total yield, %
CH_3I	8–15,[a,b] 9–15[a,c]	*d*
$(C_6H_5)_2CHBr$[e]	5.5, 6.0	97
CH_3O–$C_6H_4(C_6H_5)CHBr$[f]	3.7, 3.9	93

[a] See Experimental Section for method of calculation of minimum and maximum values. [b] Thirteen millimoles of each nucleophile and 11 mmol of methyl iodide in 10 ml of acetonitrile. [c] Thirty-four millimoles of each nucleophile and 8.5 mmol of methyl iodide in 20 ml of acetonitrile. [d] Not determined. [e] Fifty-seven millimoles of each nucleophile and 50 mmol of alkyl halide in 45 ml of DMF. Results are for duplicate experiments. [f] Twenty-five millimoles of each nucleophile and 22 mmol of alkyl halide in 25 ml of DMF. Results are for duplicate experiments.

Attack of pyridine on either of the benzhydryl bromides (7) produces the corresponding N-benzhydrylpyridinium bromide which is stable under the reaction conditions and which was gravimetrically determined as the picrate. Attack of pyridine N-oxide on either bromide produces the unstable salt 8 which, as expected,[11] is rapidly converted into the corresponding benzophenone (9); the latter was determined by gas chromatography.



The results in the table indicate that as the SN1 character of the displacement increases the nucleophilicity of the pyridine N-oxide increases relative to that of pyridine.[12] This is quite understandable on the basis of current knowledge of nucleophilicity, particularly with regard to ambident anions,[10] and of the structure of pyridine N-oxide, the oxygen atom of which has a substantially greater negative charge than the nitrogen atom of pyridine.[9b] A fairly good analogy would be the competition between oxygen and nitrogen attack in the displacement of bromide ion from substituted benzyl bromides by nitrite ion, supplied as the silver salt. The ratio of attack of the formally neutral nitrogen atom to that of the negatively charged oxygen atom decreases from 5.3 to 0.64 in proceeding from the *p*-nitro to the *p*-methoxy substituent.[13] The increased ability of the negative oxygen atom to attack as the positive charge on the target carbon atom is increased is presumably a result of favorable electrostatic interactions in the transition state.

From an extrapolation of the results in Table I, it seems likely that a very high positive charge on the car-

(11) W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957).

(12) Strictly speaking, the ratios of nucleophilic attack in the table are not relative nucleophilicities since a large excess of the nucleophiles was not used. The actual nucleophilicity ratios and also the spread between the two benzhydryl cases would be expected to be somewhat larger.

(13) N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Amer. Chem. Soc.*, **77**, 6269 (1955).

bon atom which is to become bonded to the N-oxide function would be required in order for pyridine N-oxide to be substantially more nucleophilic than pyridine toward the intermediate. Thus, attack of pyridine N-oxide on the cation **3** (or possibly its conjugate base), rather than directly on the enol **1**, is probably indicated. This conclusion is consistent with, but not demanded by, the kinetic study of Koenig[4] which shows that the reaction rate is dependent on the first power of the concentration of pyridine N-oxide.[14]

Further evidence for the intermediate **3** is being sought and the synthetic implications of such cations are under investigation.

Experimental Section

^{18}O-Enriched Phenylacetic Anhydride.—All glassware used throughout the ^{18}O experimental work was oven dried overnight at 180°.

^{18}O-Enriched sodium phenylacetate was prepared as follows. To a solution of 18.9 g (1.05 mol) of ^{18}O-enriched protium water (see below) and 82 ml of absolute ethanol in a flask equipped with a condenser and magnetic stirrer was added piece by piece 8.0 g (0.35 g-atom) of freshly cleaned metallic sodium. Then 41 g (0.35 mol) of phenylacetonitrile, which had been dried over 3-A molecular sieve, was added and the solution was stirred and heated at reflux (78°) for 68 hr. Throughout this period the reaction solution was swept with dry nitrogen to remove ammonia. Evaporation of the solvent left a white solid. The crude solid was dissolved in 200 ml of water and the basic solution extracted with ether to clearness. Evaporation of the water yielded 56.2 g (97%) of pure white material after being dried in a vacuum desiccator ($CaSO_4$).

To a suspension of 10.0 g (0.0633 mol) of ^{18}O-enriched sodium phenylacetate and 40 ml of acetonitrile (refluxed over calcium hydride overnight and distilled at 81°) was added dropwise and with stirring a solution of 6.02 g (0.0317 mol) of pure *p*-toluenesulfonyl chloride in 20 ml of acetonitrile. The reaction mixture was heated at reflux (81°) for 2.5 hr. Evaporation of the solvent left a white solid which was added to 150 ml of ether and the suspension filtered. The solid salt was further washed with ether (three 20-ml portions) and the combined filtrates were washed with 50 ml of 10% sodium carbonate and two 25-ml portions of water. Evaporation of the ether afforded the crude pale yellow product. The material was then dissolved in a minimum amount of ether. Cooling in powdered Dry Ice gave a white crystalline solid which was removed by filtration and dried in a vacuum desiccator ($CaSO_4$) to yield 5.3 g (66%) of pure product, mp 72.0–72.5° (lit.[8] mp 72.5–73.0°).

Analysis of ^{18}O-Enriched Phenylacetic Anhydride.—To determine the per cent enrichment of the labeled anhydride, a derivative, ^{18}O-enriched N,N-diethylphenylacetamide, was prepared by adding 100 mg of the labeled anhydride to 3 ml of diethylamine and heating at reflux for 1 hr. Isotopic analysis, performed on the LKB 9000 combined gas chromatograph–mass spectrometer equipped with an accelerating voltage alternator (Carbowax 20M column at 235°), indicated 1.4 atom % ^{18}O enrichment.

Reaction of ^{18}O-Enriched Phenylacetic Anhydride with Pyridine N-Oxide.—It is essential that anhydrous conditions prevail throughout this reaction. To the extent that water is present, any enriched benzaldehyde produced would be diluted by a hydration–dehydration exchange reaction. The pyridine N-oxide was freshly distilled at 125–130° (0.4 mm). Benzene was refluxed over calcium hydride overnight and distilled (80°) into a 3-A molecular sieve. The pyridine N-oxide, ^{18}O-enriched phenylacetic anhydride, benzene, balance, and appropriate equipment were placed in a glove bag containing phosphorus pentoxide as a desiccant. The bag was filled with nitrogen and then pumped down, the cycle being repeated four times. All weighings and transfers were performed in the dry bag. The flasks were securely stoppered before bringing them out. The reaction was performed in duplicate. Both flasks contained 1.12 g (0.0118 mol) of pyridine N-oxide, 1.50 g (0.0059 mol) of ^{18}O-enriched phenylacetic anhydride, and approximately 35 ml of benzene. The flasks were equipped with dry reflux condensers and the reaction solutions were heated at reflux over nitrogen (dried by passing through Drierite) for 24 hr. After being cooled to room temperature, the flasks were stoppered, sealed with Teflon tape, and stored in a desiccator ($CaSO_4$).

Analysis of Benzaldehyde for ^{18}O-Enrichment.—Combined gas chromatograph–mass spectrometer analysis (Carbowax 20M column at 130°) of the product benzaldehyde indicated an ^{18}O content of 0.23 atom %. An authentic sample of unlabeled benzaldehyde was found to contain 0.2 atom % ^{18}O.

***Normalization of* ^{18}O-Enriched Deuterium Oxide.**—The 1.6 atom % ^{18}O-enriched deuterium oxide was obtained from Bio-Rad Laboratories. Baker CP grade (99.6%) hydrogen sulfide was used. The molecular sieve pellets (3 A,[15] Linde) were activated by drying in an oven at 180° for a minimum of 2 days. The exchange system was assembled as follows. Hydrogen sulfide was passed through a pancake-type single-stage regulator into the activated molecular sieve, then through a three-way stopcock and gas dispersion tube of porosity C into the labeled heavy water. Finally, it was allowed to exit through a spiral condenser and a one-way exit valve. The three-way stopcock, connecting the entrance of the gas dispersion tube to the exit of the condenser, served as a pressure-equalizing system to prevent the labeled water from backing up into the frit and tubing whenever ebullition of hydrogen sulfide was ceased. All line connections in the Tygon tubing were sealed with Teflon tape. The dispersion tube and condenser were likewise sealed onto the flask containing the water. At no time was the system exposed to air. Tubing connectors allowed the molecular sieve to be replaced with freshly activated sieve at least once a week. An ice–water bath was maintained at all times during ebullition to prevent loss of water vapor to the passing hydrogen sulfide. Initially, the temperature was held at 5–6° (deuterium oxide freezes at 4°). After 4 days of exchange, the flask could be immersed in ice without freezing. Thereafter the temperature was held at 1–5°. Through 88 g (4.4 mol) of the ^{18}O-enriched deuterium oxide, 3.9 pounds (53 mol) of dry hydrogen sulfide was slowly bubbled for approximately 660 hr. The water remained clear throughout the exchange. Virtually no free sulfur appeared. After completion of the ebullition, the system was disconnected and the normalized ^{18}O-enriched water was heated at reflux for 2 hr in order to remove dissolved hydrogen sulfide. The labeled water was then distilled at 100°. A recovery of 61.0 g (77%) was obtained. The absence of deuterium in the water was indicated by the lack of deuterium incorporation into the benzaldehyde product of the above reaction; this was clear from the mass spectrogram.

Reactivity of Pyridine and Pyridine N-Oxide toward Methyl Iodide. A.—A solution of 1.25 g (0.013 mol) of pyridine N-oxide, 1.06 g (0.013 mol) of pyridine, and 1.54 g (0.011 mol) of methyl iodide in 10 ml of acetonitrile was stirred for 1 hr at room temperature. The solution was then diluted with acetonitrile[16] and analyzed by comparing the areas of the N-methyl and N-methoxy signals on a Varian A-60 nmr spectrometer. This analysis indicated the presence of 6.2% of N-methoxypyridinium iodide and 93.8% of N-methylpyridinium iodide. However, the control reaction described below showed that under conditions similar to those in this reaction 45% of N-methoxypyridinium iodide is converted into N-methylpyridiniun iodide. This figure is an absolute maximum since (1) the pyridine concentration in the control was greater than that in the reaction itself at all times and (2) in the control, N-methoxypyridinium ion was exposed to the pyridine during the whole hour, whereas in the reaction this ion is generated at an unknown rate as the reaction progresses. A maximum ratio of pyridine attack to that of pyridine N-oxide (93.8/6.2 = 15) can be calculated assuming such slow formation of N-methoxypyridinium iodide that essentially none of it is attacked by pyridine. A minimum value (89/11 = 8) can be calculated assuming that all of the salt produced was exposed to pyridine during the whole hour.

B.—A solution of 3.20 g (0.0337 mol) of pyridine N-oxide, 2.73 g (0.034 mol) of pyridine, and 1.20 g (0.0085 mol) of methyl iodide

(14) If the enolization is rate determining rather than an equilibrium step, this dependence on pyridine N-oxide concentration would be found regardless of the S_N1' or S_N2' nature of the attack of pyridine N-oxide on the enol **1**.

(15) Selective adsorption of water from hydrogen sulfide occurs with a 3-A molecular sieve. With 4-A or greater hydrogen sulfide itself is absorbed.

(16) Such dilution was necessary in order to separate the N-OMe and N-Me signals.

in 20 ml of acetonitrile was allowed to react as described above. The yields of N-methoxypyridinium iodide and N-methylpyridinium iodide were 6 and 94%, respectively. The maximum and minimum ratios are calculated to be 15 and 9, respectively.

C. Control Tests.—A solution of 0.308 g (0.0013 mol) of N-methoxypyridinium iodide and 1.03 g (0.013 g mol) of pyridine in 7.15 ml of acetonitrile was stirred for 1 hr, at room temperature. At the end of this period the nmr spectrum showed that 45% of the N-methoxypyridinium ion had been converted into the N-methylpyridinium ion. This experiment indicates that the rate of attack of pyridine on the methyl group of the methoxy compound is sufficiently slow so that this mechanism can not account for the much greater apparent nucleophilicity of pyridine. However, this conclusion would be invalid if the iodide ion displaced the O-methyl group, since the concentration of iodide ion in the control test was considerably below that in the competition reaction. The resulting methyl iodide could then methylate pyridine.

Therefore, another test was performed in order to determine whether methylation of the pyridine N-oxide is reversible under the reaction conditions. A solution of 0.320 g (0.00138 mol) of N-trideuteriomethoxypyridinium iodide and 0.184 g (0.00138 mol) of undeuterated methyl iodide in 3.25 ml of acetonitrile was stirred at room temperature for 1 hr. The nmr spectrum indicated that exchange of the methyl groups is negligible.

Another control test showed that N-methylpyridinium iodide is stable toward pyridine N-oxide under the reaction conditions.

Reaction of Pyridine N-Oxide and Benzhydryl Bromide.—Equivalent quantities of pyridine N-oxide and benzhydryl bromide were dissolved in benzene and the solution heated at reflux for 2 hr. Comparison of glpc retention times with those of an authentic sample of benzophenone indicated the presence of this ketone in the reaction mixture.

Reactivity of Pyridine and Pyridine N-Oxide toward Benzhydryl Bromide.—To a solution of 5.417 g (0.0569 mol) of pyridine N-oxide and 4.500 g (0.0569 mol) of pyridine in 45 ml of dimethylformamide (dried over calcium sulfate and distilled under reduced pressure at 60°) was added 12.4 g (0.050 mol) of benzhydryl bromide, which had been purified by recrystallization from hexane. The solution was heated at 80° for 2 hr. Gas chromatograph comparison with an authentic sample indicated that benzophenone was present: Carbowax 20M column at 237°, retention time 12.6 min; Hi-Eff-8BP column at 210°, retention time 14.0 min. By glpc examination the yield of benzophenone was calculated to be 15%. The N-benzhydrylpyridinium bromide product was analyzed as the picrate which was prepared as follows. An aliquot (11.81 g) of the reaction solution was made basic with concentrated ammonium hydroxide. The resulting cloudy solution was extracted with three 10-ml portions of ether. The aqueous solution was then treated with 50 ml of basic ammonium picrate solution and stored in a refrigerator for 3 hr. The yellow crystalline picrate was collected in a Büchner funnel and 100 ml more of ammonium picrate solution was added to the filtrate which was then stored in a refrigerator for 3 hr. The additional picrate was similarly collected and washed with ice water. Treating the filtrate with ammonium picrate solution produced no more precipitate. The product was oven dried at 90° until a constant weight was obtained to yield 3.46 g (82%), mp 171–171.5° (lit.[17] mp 172°). In a duplicate run, the yields were 14% benzophenone and 84% N-benzhydrylpyridinium picrate.

A control test showed that N-benzhydrylpyridinium bromide is stable toward pyridine N-oxide under the reaction conditions.

(17) A. E. Chichibabin, *J. Russ. Phys. Chem. Soc.*, **34**, 133 (1902).

4-Methoxybenzhydryl Bromide.—4-Methoxybenzophenone was prepared in 87% yield by the method of Gattermann, *et al.*[18] The ketone was reduced to 4-methoxybenzhydrol as follows. To a slurry of 2.70 g (0.071 mol) of lithium aluminum hydride and 150 ml of anhydrous ether in a flask equipped with a reflux condenser and magnetic stirrer was added a solution of 30.0 g (0.142 mol) of 4-methoxybenzophenone in 150 ml of anhydrous ether at such a rate as to maintain gentle reflux (addition time, 20 min). The gray slurry was stirred overnight. Excess lithium aluminum hydride was destroyed by slowly adding water through an addition funnel until all hydrogen evolution ceased. The resulting gel was poured onto ice and acidified with 10% aqueous hydrogen chloride. After separation of the ether layer the aqueous layer was extracted to clearness with ether. The combined extract was washed with saturated sodium carbonate solution, water, and dried over Drierite. The solution was concentrated on a rotatory evaporator to approximately 150 ml and stored in a freezer overnight. The white crystalline product was collected on a sintered-glass funnel and air dried to yield 24.5 g (81%), mp 65–66° (lit.[19] mp 65–66°). Recrystallization from hexane afforded white silky needles, mp 66.5–67.0°. An ir spectrum showed an O–H band present at 2.75 μ (s) and no carbonyl band at 5.90 μ.

To a solution of 11.0 g (0.047 mol) of the pure alcohol in 125 ml of spectroscopic grade chloroform was added 10 g of calcium sulfate. Dry hydrogen bromide gas was bubbled through a gas dispersion tube into the solution for 20 min. The light orange solution was flushed with nitrogen and filtered, and the filtrate stripped to yield a deep red oil. The oil was extracted with hot hexane. Concentration and cooling of the extract afforded the product as white crystals rapidly turning to light pink. An ir spectrum showed no O–H band present at 2.75–3.00 μ and no carbonyl band at 5.90 μ. The yield was 9.8 g (75%).

Reactivity of Pyridine and Pyridine N-Oxide toward 4-Methoxybenzhydryl Bromide.—To a solution of 2.34 g (0.0246 mol) of pyridine N-oxide and 1.95 g (0.0246 mol) of pyridine in 25 ml of purified dimethylformamide was added 6.21 g (0.0224 mol) of 4-methoxybenzhydryl bromide. The solution was heated at 80° for 2 hr. Gas chromatographic comparison with an authentic sample indicated that 4-methoxybenzophenone was present: OV-17 column at 210°, retention time 15.7 min. By glpc examination the yield of 4-methoxybenzophenone was calculated to be 20%. The N-(4-methoxybenzhydryl)pyridinium bromide was analyzed as the picrate as in the above procedure. The yield was 73%. The picrate, recrystallized from benzene, melted at 141–141.5°.

Anal. Calcd for $C_{25}H_{20}N_4O_8$: C, 59.52; H, 4.00. Found: C, 59.32, 59.22; H, 4.01, 4.09.

A duplicate reaction yielded 19% 4-methoxybenzophenone and 75% N-(4-methoxybenzhydryl)pyridinium picrate.

Registry No.—Phenylacetic anhydride, 1555-80-2; pyridine N-oxide, 694-59-7; pyridine, 110-86-1; N-(4-methoxybenzhydryl)pyridinium picrate, 20104-04-5.

Acknowledgments.—We wish to thank the National Institutes of Health for providing the LKB 9000 combined gas chromatograph–mass spectrometer which was used for the isotopic analyses. We also thank Mr. John Naworal for recording the mass spectra.

(18) L. Gattermann, R. Ehrhardt, and H. Maisch, *Ber.*, **23**, 1199 (1890).
(19) R. F. Tietz and W. E. McEwen, *J. Amer. Chem. Soc.*, **77**, 4007 (1955).