nitrogen pressure. The flask was placed in a constant temperature water bath, where the temperature was controlled to ± 0.05°. Acrylonitrile, solvent, and alkoxide solutions were transferred to the reaction flask by syringes, filled under positive nitrogen pressure. The solution of acrylonitrile in alcohol was brought to the required temperature, and catalyst solution was then added. Aliquot portions were removed at various time intervals, into 50-ml. weighed volumetric flasks containing 5 ml. of solution of hydrochloric acid in isopropyl alcohol (1 *M*). Acrylonitrile was determined volumetrically by the *n*-dodecyl mercaptan method.[21]

Acknowledgment.—The authors are pleased to acknowledge partial support of this work by the Israel National Council for Research and Development.

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(21) American Cyanamid Company, "The Chemistry of Acrylonitrile," 1951, p. 69.

Anionic Oxidation of Heterocyclic Nitrogen Bases and the Effect of Solvent on Such Reactions[1a]

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Pyrrole and the three picoline isomers were autoxidized in solutions of strong bases near ambient temperature. Since the oxidation does not take place at measurable rates without base being present, the carbanions formed from these compounds must be attacked by oxygen. Pyrrole is readily oxidized in potassium *t*-butoxide–*t*-butyl alcohol as the base–solvent medium. Complex products are formed in this oxidation which has an apparent energy of activation of 4 kcal./mole. All three picoline isomers are oxidized with practically quantitative selectivity to the potassium salts of the corresponding carboxylic acids using the same base, potassium *t*-butoxide, but changing the solvent to N,N-dimethylformamide. The direct addition of oxygen to the picoline carbanions is proposed as the mechanism accounting for these oxidations.

Molecular oxygen reacts readily with a number of organic compounds in solutions of strong bases, even under mild conditions where the thermal reaction is immeasurably slow in the absence of base. Experimental evidence[1b–5] indicates that these reactions involve the oxidation of anionic species, since only compounds containing relatively acidic hydrogen atoms have been reported to undergo such oxidations. Thus oxygen molecules react with carbanions formed by abstracting a proton from the acidic carbon–hydrogen bonds of compounds such as 2-nitropropane,[2] substituted fluorenes,[4] and *p*-nitrotoluene.[5]

The various mechanisms postulated for the attack of oxygen molecules on carbanions have been reviewed recently by Russell and Moye.[5] According to these reaction schemes, following anion formation *via*

$$RH + B^- \rightleftharpoons R^- + BH \qquad (1)$$

oxygen may add directly to form the anion of a hydroperoxide[1,4]

$$R^- + O_2 \longrightarrow RO_2^- \qquad (2)$$

or the anion may exchange electrons with oxygen[5]:

$$R^- + O_2 \longrightarrow R\cdot + \cdot O_2^- \qquad (3a)$$

$$R^- + \cdot O_2^- \longrightarrow R\cdot + O_2^= \qquad (3b)$$

Finally, an electron-exchange reaction with thermally formed peroxy free radicals has been suggested to explain the anionic oxidation of 2-nitropropane[2]:

$$R^- + RO_2\cdot \longrightarrow R\cdot + RO_2^- \qquad (4)$$

Reaction 4 would then lead to a chain reaction sequence *via*

$$RO_2^- + RH \longleftarrow RO_2H + R^- \qquad (5)$$

According to Russell and Moye, the free radicals formed in step 3 may dimerize or react further with oxygen, depending on the "availability" of oxygen in the system.

The present study reports on the anionic oxidation of heterocyclic nitrogen compounds—pyrrole and the three isomeric picolines. Both pyrrole and pyridine derivatives occur in petroleum oils and are representative of the "nonbasic" and "basic" nitrogen compound types, respectively.[6] While the nitrogen–hydrogen bond of the pyrrole molecule is quite acidic, and therefore proton abstraction may be expected to occur with relative ease, the hydrogen atoms of the methyl groups of the picolines are considerably less acidic so that the latter compounds are likely to be inert under similar conditions of base, solvent, and temperature.

Experimental

Materials.—The oxidation experiments were performed using pyrrole and picoline reagents distilled in an inert atmosphere of nitrogen. The reagents were obtained from Matheson, Coleman & Bell.

The solvent–base systems were all prepared in a drybox under nitrogen atmosphere, using 100 ml. of distilled solvent (*t*-butyl alcohol or N,N-dimethylformamide) and essentially alcohol free potassium *t*-butoxide at various molarities of the base. Potassium *t*-butoxide was obtained from the Mine Safety Appliance Co. and analysis showed it to be above 98.5% pure. The major impurity was potassium carbonate. Half of the required volume of solvent was poured into a glass-stoppered graduated cylinder with the base slowly added under continuous agitation. As the limit of base solubility was approached the remaining portion of solvent was added and the base concentration was adjusted to the required molarity.

For experiments run under atmospheric pressure, weighed amounts of reactants were introduced into a specially adapted heavy-walled 500-ml. Erlenmeyer flask which had been previously flushed with nitrogen. The homogeneous solvent–base solution was then poured into the reactor flask.

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(1)(a) Paper presented at 141st National Meeting of the American Chemical Society, Washington, D. C., March, 1962; (b) W. E. Doering and R. M. Haines, *J. Am. Chem. Soc.*, **76**, 482 (1954).

(2) G. A. Russell, *ibid.*, **76**, 1595 (1954).

(3) C. Walling, "Free Radicals In Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 464–465.

(4) Y. Sprinzak, *J. Am. Chem. Soc.*, **80**, 5449 (1958).

(5) G. A. Russell and A. J. Moye, 137th National Meeting of the American Chemical Society, Division of Petroleum Chemistry Preprints, **5**, C-25, Cleveland, Ohio, 1960.

(6) F. P. Richter, *et al.*, *Ind. Eng. Chem.*, **44**, 2601 (1952).

Apparatus.—The atmospheric oxidation apparatus consisted of the above reactor flask thermostated (within ±0.5°) and stirred magnetically. Oxygen gas was supplied from a partially filled collapsible polyethylene gas balloon of *ca.* 14-l. capacity through a wet-test gas meter connected to a glass column packed with indicating Drierite. The nitrogen atmosphere of the reactor flask was displaced with oxygen from the gas balloon, then the entire reactor mixture was allowed to stand (without agitation) until the gas meter indicated equilibrium. At this time, the magnetic stirrer was set in motion to start the oxidation experiment. As the reaction proceeded, oxygen was metered at the prevailing barometric pressure through an overhead Friedrichs condenser into the reactor flask (details of this experimental arrangement will be published elsewhere). At the completion of an experiment the reaction mixture was immediately poured into 100 g. of ice–water which hydrolyzed any remaining potassium *t*-butoxide.

A number of experiments were carried out using a procedure similar to the above by means of a low pressure Parr apparatus. Starting at total initial pressures of oxygen ranging up to 4 atm. absolute, the rate of oxidation was determined by measuring the pressure drop in the system.

Analytical Procedure.—The heterogeneous mixtures containing pyrrole oxidation products were first distilled. The overhead and bottoms fractions of the distillation were analyzed by infrared absorption and mass spectroscopic methods.

The analytical scheme used for the identification of oxidation products of picolines consisted of multiple extractions with carbon tetrachloride following the addition of 40% aqueous sodium hydroxide solution to the reaction mixture. Unchanged picoline was recovered in the carbon tetrachloride extracts and identified by infrared absorption spectra. The aqueous phase was distilled after acidifying it with aqueous hydrochloric acid to separate water and the solvent from the oxidation products. The distillation residue was eluted with fresh solvent, then filtered in order to separate the insoluble inorganic salts. A final distillation of the filtrate separated the oxidation products from the added solvent.

Results

Oxidation of Pyrrole.—Because of the acidic nature of pyrrole ($pK_a = -0.27$ for the conjugate acid in water),[7] the pyrrolyl anion is formed in the presence of strong base.

In relatively "weak" bases, such as potassium hydroxide in methanol solutions, the oxidation of pyrrole was found to be very slow. For example, even at a 5 *M* base concentration (and base–pyrrole mole ratios of 50:1) the slow uptake of oxygen at room temperature became measurable only after several hours. In contrast, however, pyrrole solutions in potassium *t*-butoxide in *t*-butyl alcohol were oxidized readily under similar experimental conditions. In control experiments using pyrrole solutions in *t*-butyl alcohol, without adding the base, no measurable oxygen absorption could be detected up to reaction times of twenty hours. As shown in Fig. 1, the anionic oxidation of pyrrole appears to follow an over-all stoichiometry of two moles of oxygen absorbed per mole of pyrrole present. However, base must be added in excess over the amount of pyrrole, since at a base–pyrrole mole ratio of 0.7 the absorption of oxygen leveled off after an amount equivalent to 0.7 mole of oxygen/mole of pyrrole.

The exact identification of the oxidation products of pyrrole did not prove to be possible. The literature[8] of the thermal oxidation of pyrrole in neutral media indicates the formation of polymeric products ("pyrrole blacks") of complex structure, probably containing three pyrrole nuclei per monomer unit. Analysis of the oxidation products in basic solutions suggested that structures of similar complexity were present. The infrared spectra showed a strong absorption band at 5.7 μ corresponding to the C=O functional group.

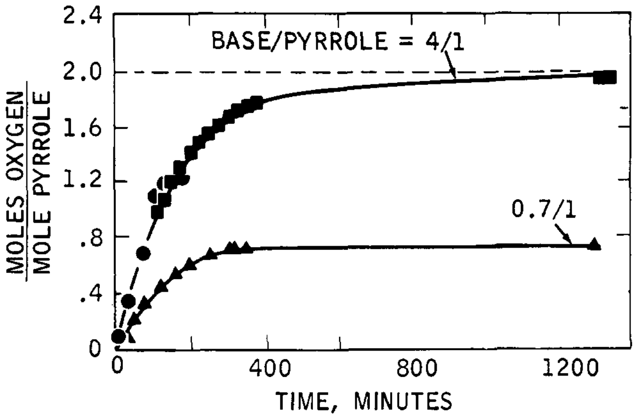

Fig. 1.—Oxidation of pyrrole in potassium *t*-butoxide–*t*-butyl alcohol solution. Temperature = 25°; oxygen pressure = 1 atmosphere (constant).

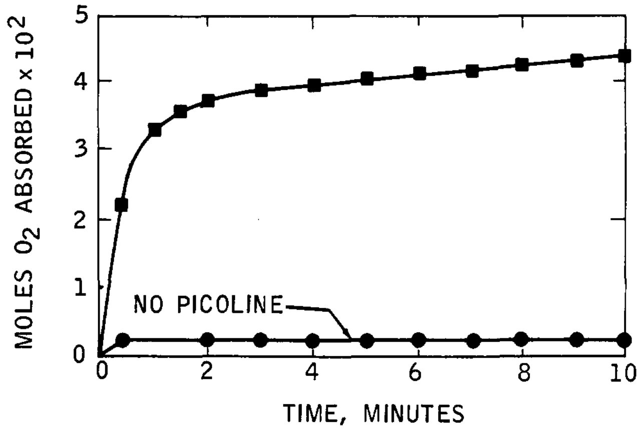

Fig. 2.—Oxidation of 2-picoline in "inhibited" 0.9 *M* potassium *t*-butoxide–N,N-dimethylformamide solution. Solvent: 20 mole % *t*-butyl alcohol/30 mole % dimethylformamide. Temperature = ambient; initial oxygen pressure 4 atmospheres absolute.

Oxidation of Picolines.—As expected, based on the relative acidity of the methyl hydrogen atoms of the isomeric picolines, the ionization and hence, the oxidation of these compounds required stronger base systems than used for pyrrole. Thus, even in experiments lasting twenty-four hours, no measurable oxidation of picolines occurred using the potassium *t*-butoxide–*t*-butyl alcohol base–solvent system. However, when a polar, nonhydroxylic solvent, N,N-dimethylformamide (DMF) was employed instead of *t*-butyl alcohol, all three picoline isomers were oxidized rapidly. This behavior indicates the predominant role of the solvent in these reactions, since the same base at the same concentration levels can be changed from unreactive to highly reactive by changing the nature of the solvent.

The dimethylformamide itself was found to react with oxygen in control experiments. Furthermore, dimethylformamide itself decomposes, probably into dimethylamine in the presence of potassium *t*-butoxide. Both the oxidation and the decomposition of the solvent could be largely reduced by dilution with *t*-butyl alcohol. As illustrated in Fig. 2 for the oxidation of 2-picoline, the addition of 20 mole % *t*-butyl alcohol to dimethylformamide reduced the extent of oxygen attack

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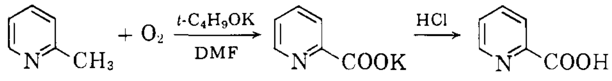
[7] N. Naqui and Q. Fernando, *J. Org. Chem.*, **25**, 551 (1960).

[8] A. A. Oswald and F. Noel, Preprints of General Papers, 137th National Meeting of the American Chemical Society, Division Petroleum Chemistry Preprints, **5**, 57, Cleveland, Ohio, 1960.

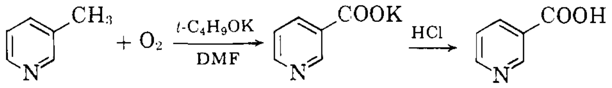
on the solvent to negligible proportions for experiments of ten-minute durations. This method of inhibiting solvent oxidation was successful with the other two isomers also as reactants. In general, the rate of picoline oxidation was reduced less than 50% by inhibiting the oxidation of the solvent.

All three isomers were selectively oxidized to the potassium salts of the corresponding carboxylic acids which could be converted into the acids by neutralization with dilute hydrochloric acid.



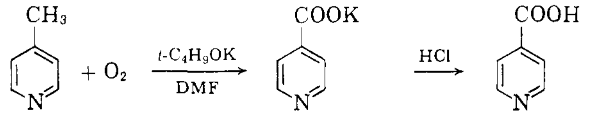
2-Picoline

Picolinic Acid



3 Picoline

Nicotinic Acid



4-Picoline

Isonicotinic Acid

The carboxylic acid products were identified and quantitatively determined by means of the analytical procedure outlined previously. In the case of the 4-picoline, the crystalline isonicotinic acid oxidation product was actually isolated. Only mass spectrometric analyses indicated the presence of an impurity of higher molecular weight which could have been due to the successive reaction of the acid product with the solvent to yield the dimethylamide derivative of the carboxylic acid. However, even the small amounts of such by-products would result only from the acid, and hence, would not affect the primary yield of oxidation itself. In ten-minute oxidation experiments at ambient temperature and four atmospheres absolute oxygen pressure using 2.2 g. of reactant, the following yields were obtained from the three isomers: 1.30 g. of picolinic acid, 1.57 g. of nicotinic acid, and 1.76 g. of isonicotinic acid. The per cent conversion of the three isomers in these experiments was 59% for 2-picoline, 70% for 3-picoline, and 80% for 4-picoline, with essentially 100% selectivity for the respective acid products.

Discussion

A low value of 4 kcal./mole of the activation energy found for the anionic oxidation of pyrrole at 25–55° suggests the possibility of a process controlled by the diffusion of oxygen gas. As another alternative, the possibility of a "slow step" in the reaction sequence such as the transfer of an electron cannot be ruled out altogether, since reactions of this type would be expected to proceed with a small energy of activation. Since base must be employed in excess amounts over that of pyrrole to drive the oxidation to completion, no chain reaction or paths leading to the regeneration of base can be suggested. Rather indirect evidence involving the addition of lead nitrate (a known catalyst for the decomposition of hydrogen peroxide) in small amounts suggests that O_2^{-2} ions may be formed according to reactions 3a and 3b. The absorption of oxygen levels off at a value of 7/4 mole/mole of pyrrole, instead of at a value of 2 as in curve (a) of Fig. 1 when 5 mole % of lead nitrate (based on the amount of pyrrole present) is added. This behavior is similar to that found in the oxidation of *p*-nitrotoluene,[5] suggesting that oxygen is evolved *via*

$$O_2^{=} + t\text{-}C_4H_9OH \longrightarrow OH^- + t\text{-}C_4H_9O^- + 1/2O_2 \qquad (6)$$

In view of the complex nature of the products of pyrrole oxidation, however, a mechanism cannot be suggested at this time.

The marked solvent dependence of anionic oxidation reactions is in agreement with the behavior of carbanion systems reported by others.[9-12] The exact mechanism of solvent action is not known, but the general behavior strongly suggests that the solvation of ionic species may play a role just as important as the polarity of the solvent medium.

Based on the well defined nature of picoline oxidation reactions, it seems likely that all three isomers react following the same mechanisms. This mechanism probably involves ionization (equation 1) followed by either direct oxygen addition (equation 2) or electron transfer (equations 3a and b). This scheme accounts for the leveling off observed in the rate since potassium *t*-butoxide is converted into a weaker base, and the dimethylformamide is further diluted with *t*-butyl alcohol produced in the ionization step. At this time the results are too preliminary to correlate the apparent order of reactivity (4-picoline > 3-picoline > 2-picoline) with structure without further experimentation.

Acknowledgment.—The authors wish to express their appreciation to Mr. H. Pobiner for the analytical work performed in connection with this study.

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(10) T. J. Wallace and A. Schriesheim, Organic Division Preprints, 140th National Meeting of the American Chemical Society, Chicago, Ill., September 8, 1961.

(11) D. J. Cram, *et al.*, *J. Am. Chem. Soc.*, **81**, 5750–85 (1959).

(12) G. A. Russell, 17th National Organic Chemistry Symposium of the American Chemical Society, Bloomington, Ind., June 25–29, 1961.