Organic Process Research & Development **1999**, *3,* 227–231

Kinetics and Process Parameter Studies in Highly Selective Air Oxidation of Side-Chain Alkyl Groups in Picolines, 2-Methylnaphthalene, and Pseudocumene

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Abstract:

Picolines, *2*-methylnaphthalene, and pseudocumene were oxidized by air in acetic acid medium. Process parameters and kinetics of the reaction were studied from the viewpoint of proces research and development. Use of lithium chloride as the promoter was worth considering for this oxidation to obtain a higher rate of reaction. At 170 °C and at a reactant concentration of 15% w/v, 52% conversion of β-picoline with a selectivity of 97% was achieved in 8 h.

Introduction

Pyridine carboxylic acids, naphthalene carboxylic acids, and trimellitic acid have great relevance in organic process industries as intermediates for pharmaceuticals and fine chemicals. In general, these are synthesized by air oxidation of picolines,[1−3] methylnaphthalenes,[4−6] and pseudocumenes[7,8] using different transition metal catalysts and bromide salts as promoters.

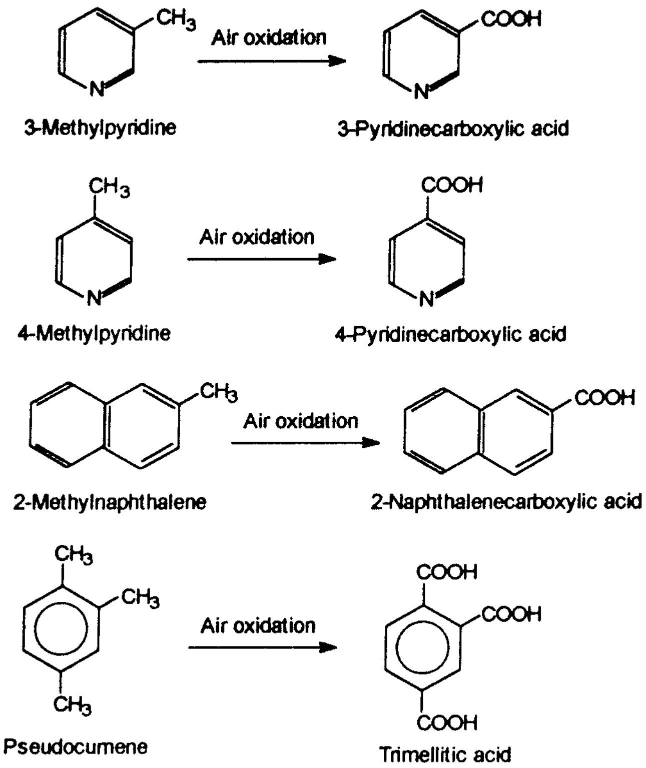
There is little information regarding these air oxidations, and what is available is mostly confined to the patent literature. Thus, this work is an attempt to study the process parameters to establish the most suitable process conditions and a more realastic kinetic interpretation in the air oxidation of picolines, methylnaphthalenes, and pseudocumenes using cobalt and manganese acetates as the catalyst and LiCl as a promoter to synthesize the respective carboxylic acids (Scheme 1).

Experimental Section

Materials. The materials used and their technical grade are tabulated below:

material used	technical grade	material used	technical grade
α-picoline	L.R.	diglyme	technical grade
β-picoline	L.R.	1,4-dioxane	L.R.
γ-picoline	L.R.	cobalt(II) acetate	L.R.
pseudocumene	L.R.	manganese(II) acetate	L.R.
2-methylnaphthalene	Fluka	sodium bromide	L.R.
acetic acid	A.R.	lithium chloride	L.R.

Scheme 1. **Air oxidation of picolines, 2-methylnaphthalene, and pseudocumene**



Experimental Procedure. Predetermined amounts of the catalyst, promoter, and reactant were mixed with solvent, and the solution was shaken thoroughly to make it homogeneous. The reactor was pressurized with air to the desired pressure. The reactor was then heated to the desired temperature, and flow of air was started. After the reaction was allowed to proceed for the predetermined period, the reactor was allowed to cool to the room temperature, and the pressure was released. A complete diagram of the bubble column reactor is shown in Figure 1.

Analytical Details. The reaction mixture was filtered and distilled under vacuum to remove acetic acid and then diluted with water, and organic compounds were extracted in toluene or benzene. The organic layer, after thorough washing with water, was taken for analysis.

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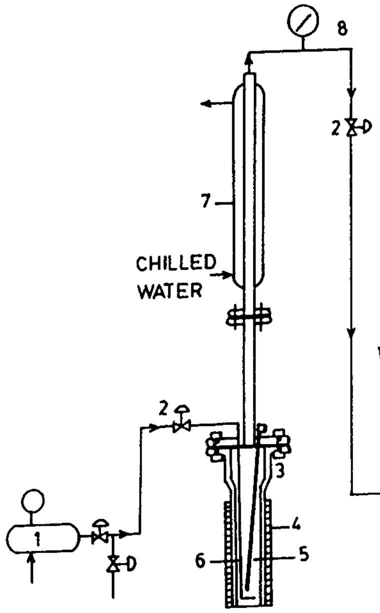

Figure 1. **Experimental setup for liquid phase oxidation by air: 1, compressor; 2, needle valves; 3, reactor; 4, heating element; 5, thermometer pocket; 6, sparger; 7, condenser; 8, pressure gauge; and 9, rotameter.**

Estimation of Unreacted Substrate. The unreacted substrate was analyzed by GC. The conditions are given below:

column used	stainless steel column
column dimensions	3.2 mm × i.d. × 2 m (10% OV-17 on Chromosorb-W)
carrier gas	nitrogen (flow rate, 30 mL/min)
detector	FID
oven temperature	250 °C
injector temperature	300 °C
detector temperature	300 °C

Estimation of Acid. A measured volume of the organic extract was washed with sodium hydroxide to extract the carboxylic acid as sodium salts. The acid layer was neutralized with mineral acid to precipitate the carboxylic acid. The latter was dried and weighed. The organic extract was directly titrated with standard sodium hydroxide to estimate the amounts of carboxylic acids when solvents other than acetic acid were used.

Estimation of Aldehyde. Estimation of aldehyde was done by oximation reaction. In a typical procedure, an accurately measured organic layer was diluted with methanol, and the pH of the solution was adjusted to 3.0. A solution of hydroxyl amine hydrochloride in 90% methanol was made, and the pH was adjusted to 3.0 separately. Both of the solutions were mixed and kept at 45 °C for 1 h.

The liberated HCl was titrated potentiometricaly to pH 3.0 using 0.1 N sodium hydroxide solution. The amount of the aldehyde present in the sample was calculated as follows:

$$\text{grams of aldehyde} = \frac{VNM}{1000}$$

where V is the volume of sodium hydroxide solution required (in mL), N is the normality of the sodium hydroxide solution, and M is the molecular weight of the aldehyde.

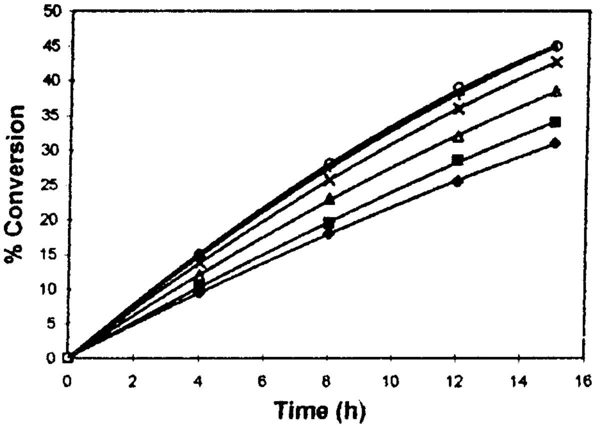

Figure 2. **Effect of air flow rate on overall conversion. Reaction conditions: reactant concentration, 15% w/v; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (L/min): ◆, 0.6; ■, 1.2; △, 1.8; ×, 2.4; +, 3.0; and ○, 3.36.**

The carboxylic acid present in the reaction mixture was analyzed by taking a measured volume of the extracted organic layer. The extract was titrated with standard methanolic sodium hydroxide to estimate the amount of carboxylic acid.

Results and Discussions

The oxidation of the alkyl heterocyclics in acetic acid media using cobalt acetate as catalyst and a promoter such as sodium bromide is fairly well established and is practiced on a large scale. Though the technology has matured, the information is mostly confined to the patent literature. From the limited information available, it is not easy to appraise the relative merits of using one or the other promoter, solvent, substrate concentration, etc. A significant part of the work was carried out in order to study the reaction parameters, using β-picoline as a model compound.

Material Balance. In a typical study, a flow rate of 50 mL/cm^3 was maintained. To ascertain whether mass-transfer effects have been eliminated, air flow was increased from 3.0 to 3.36 L/min; there was almost no change in the conversion obtained. At air flow rates less than 3.0 mL/min (Figure 2), the conversion was relatively poor, presumably because of the effects of the mass transfer. Therefore, in all the subsequent runs, air flow rate was maintained at 3.0 L/min so that effects of mass transfer were eliminated, and the results obtained represent the kinetics of the process (Table 1.

Effect of Air Pressure. In a liquid phase oxidation by air, usually the reaction is carried out at a high pressure. Such a high pressure is required in order to keep reactants in the liquid phase and to maintain a sufficient partial pressure of oxygen.

In this work, the pressure was varied from 6 to 18 atm (Figure 3). At a pressure of 6 atm, the rate of reaction was too slow, and only 17% conversion of β-picoline was obtained. When pressure was increased to 16 atm, marked improvement in the rate of reaction was noticed. However, with a further increase in pressure to 18 atm, the conversion remained more or less the same. Hence, a pressure of about 16 atm was suitable for the process.

Table 1. **Material balance**[a]

material	gmol	% β-picoline accounted for
β-picoline (taken)	0.4838	100
aldehyde	0.0053	1.09
acid	0.1160	23.97
unreacted β-picoline	0.3479	71.92
unaccounted β-picoline	0.0140	2.9
total	0.4833	99.89

[a] Reaction conditions: substrate concentration, 15% w/v; air flow rate, 3.0 L/min; air pressure, 16 atm; cobalt acetate, 0.033 gmol/L; manganese acetate, 0.033 gmol/L; sodium bromide, 0.05 gmol/L; reaction time, 8 h; reaction temperature, 170 °C; solvent, acetic acid; reaction volume, 300 mL.

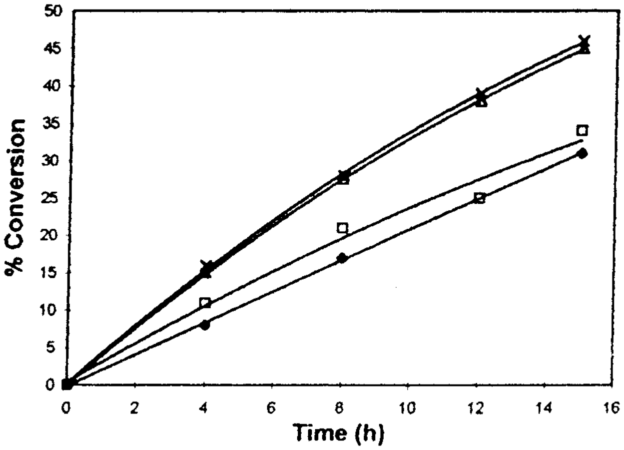

Figure 3. **Effect of air pressure on overall conversion. Reaction conditions: reactant concentration, 15% w/v; air pressure, 16 atm; reaction temperature, 170 °C; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (atm): ◆, 8; □, 12; △, 16; and ×, 18.**

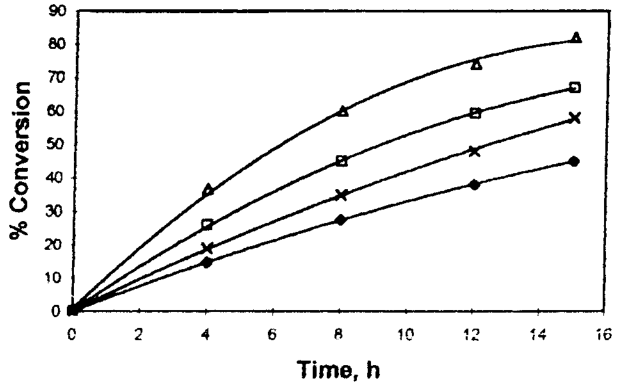

Figure 4. **Effect of period of reaction on overall conversion. Reaction conditions: reactant concentration, 15% w/v; temperature, 170 °C; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL. Key to symbols: ◆, *β*-picoline; □, *γ*-picoline; △, methyl-2-naphthalene; and ×, pseudocumene.**

Effect of Period of Reaction. The reaction was studied for different times. It was observed that, with an increase in the period of reaction, the conversion also increased (Figure 4). The rate of reaction for different starting material was in the following order:

2-methylnaphthalene > γ-picoline > pseudocumene > β-picoline

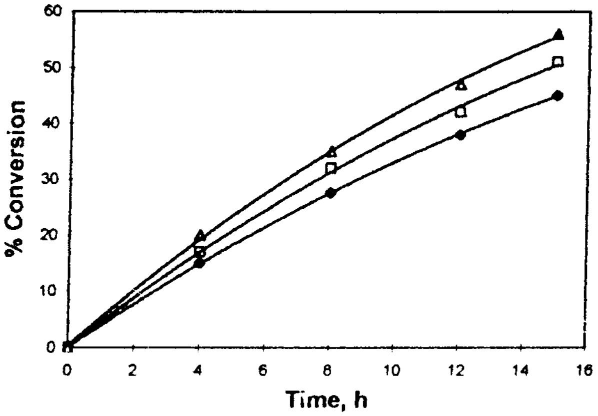

Figure 5. **Effect of initial concentration of reactant on overall conversion. Reaction conditions: reaction temperature, 170 °C; air flow rate, 3.0 L/min; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (% w/v): ◆, 15; □, 30; and △, 45.**

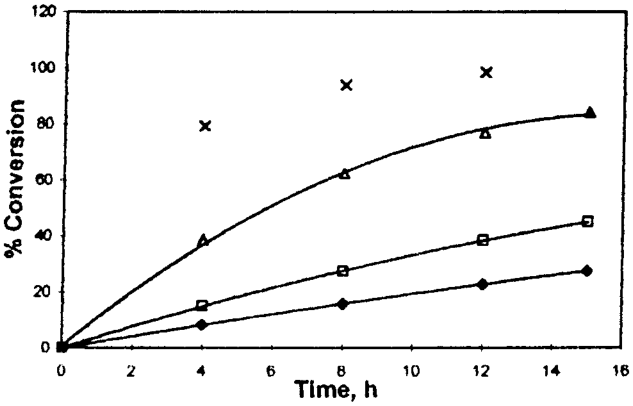

Figure 6. **Effect of temperature on overall conversion. Reaction conditions: reactant concentration, 15% w/v; air flow rate, 3.0 L/min; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (°C): ◆, 140; □, 170; △, 190; and ×, 210.**

Subsequent reactions were carried out by taking β-picoline as the starting material.

Effect of Initial Reactant Concentration. The concentration of the β-picoline was varied from 15 to 45% w/v. It was observed that changing the concentration had very little influence on the rate of reaction of β-picoline (Figure 5). All the reactions were thus carried out at a substrate concentration of 15% w/v.

Effect of Temperature. The reaction temperature was varied from 140 to 210 °C. The reaction temperature was found to have a significant effect on the reaction rate (Figure 6). At 140 °C, the rate of oxidation of β-picoline was very poor, and in 8 h, the conversion to acid was 10.78%. When the temperature was increased to 170 °C, there was a marked improvement in the reaction rate, and the conversion to acid increased to 24%. A further increase in temperature increased the conversion, but the fact that the selectivity was as little as 47% may be due to decomposition of the heterocyclic ring (Figure 7). At higher temperatures, corrosion due to sodium bromide, the promoter, was significant. In view of this, a reaction temperature of 170 °C appeared to be the most suitable for this process.

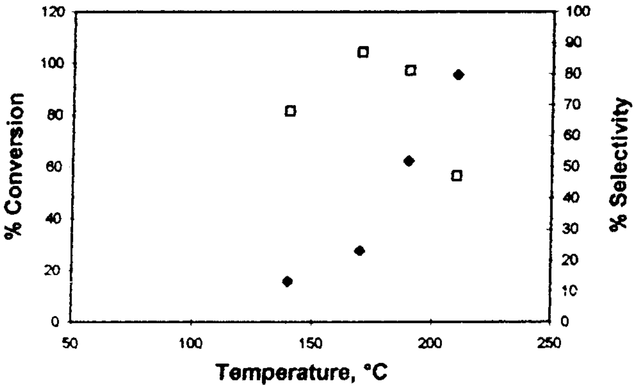

Figure 7. **Effect of temperature on overall conversion and selectivity. Reaction conditions: reactant concentration, 15% w/v; air flow rate, 3.0 L/min; air pressure, 16 atm; time, 8 h; solvent, acetic acid; reaction volume, 300 mL. Key to symbols: ◆, conversion; and □, selectivity.**

Table 2. **Effect of solvent**

name of solvent	% overall conversion of β-picoline	% conversion to aldehyde	% conversion to acid	% selectivity with respect to acid formed
acetic acid	27.59	1.1	24	87
diglyme	14	1.4	11.62	83
1,4-dioxane	17	1.3	13.77	81

[a] Reaction conditions: reaction temperature, 170 °C; air flow rate, 3.0 L/min; air pressure, 16 atm; cobalt acetate, 0.033 gmol/L; manganese acetate, 0.033 gmol/L; sodium bromide, 0.05 gmol/L; reaction time, 8 h; reaction volume, 300 mL.

Table 3. **Effect of promoters**

name of promoter	% overall conversion	% selectivity with respect to acid
no promoter	8	83
paraldehyde	12	85
sodium bromide	27.59	87
lithium chloride	52	97
sodium bromide (50% w/w) + lithium chloride (50% w/w)	46	96

[a] Reaction conditions: reaction temperature, 170 °C; air flow rate, 3.0 L/min; air pressure, 16 atm; cobalt acetate, 0.033 gmol/L; manganese acetate, 0.033 gmol/L; sodium bromide, 0.05 gmol/L; reaction time, 8 h; reaction volume, 300 mL.

Effect of Solvent. With a view toward using the catalyst system under consideration with cobalt acetate, manganese acetate, and sodium bromide with solvents other than acetic acid as the medium, the use of diglyme and 1,4-dioxane was considered. In all cases, the results obtained were somewhat satisfactory (Table 2).

Effect of Promoters. Different type of promoters, such as sodium bromide, lithium chloride, and paraldehyde, were used. It was observed that, under the reaction conditions, lithium chloride was the best promoter. But lithium chloride is costlier than sodium bromide, so a 50/50 (% w/v) mixture of sodium bromide and lithium chloride was proved to be the best to achieve a fast reaction rate. Sodium bromide and lithium chloride are known to be corrosive. To avoid the use of a titanium-lined reactor, paraldehyde was tried as the promoter, but the conversion of β-picoline was as low as 12%, as compared to 52% (Table 3) when lithium chloride was used.

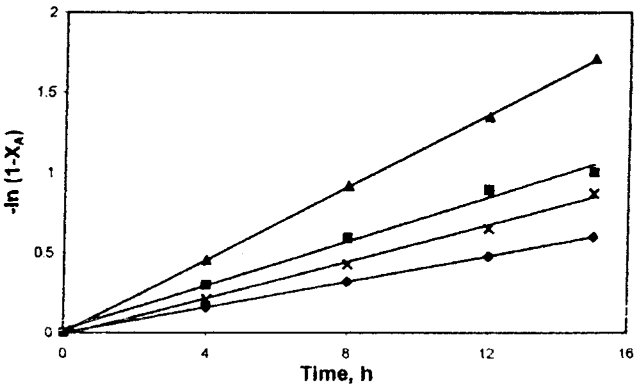

Figure 8. **$-\ln(1 - X_A)$ vs t for different substrates. Reaction conditions: reactant concentration, 15% w/v; air flow rate, 3.0 L/min; air pressure, 16 atm; temperature, 170 °C; solvent, acetic acid; reaction volume, 300 mL. Key to symbols: ◆, β-picoline; ■, pseudocumene; ▲, γ-picoline; and ×, methyl-2-naphthalene.**

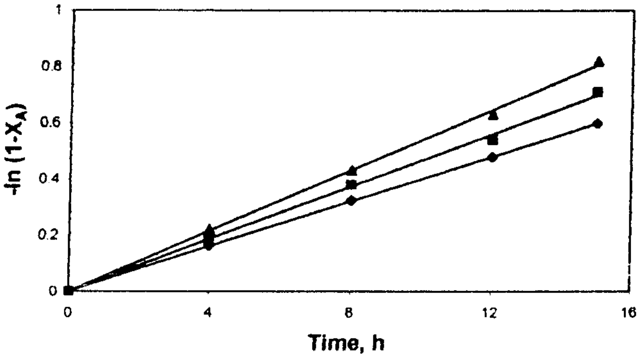

Figure 9. **$-\ln(1 - X_A)$ vs t at different substrate concentrations. Reaction conditions: air flow rate, 3.0 L/min; air pressure, 16 atm; temperature, 170 °C; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (% w/v): ◆, 15; ■, 30; and ▲, 45.**

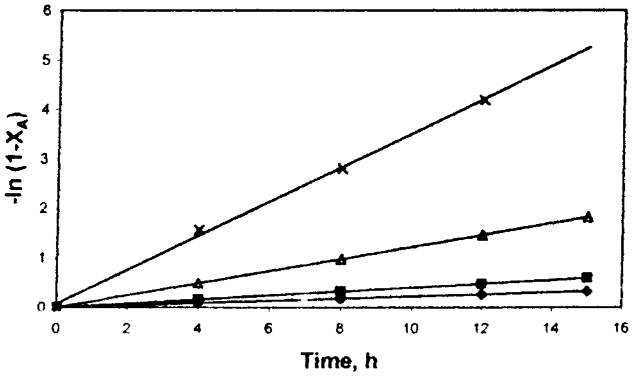

Figure 10. **$-\ln(1 - X_A)$ vs t at different temperatures. Reaction conditions: reactant concentration, 15% w/v; air flow rate, 3.0 L/min; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL. Key to symbols (°C): ◆, 140; ■, 170; △, 190; and ×, 210.**

Optimum Conditions for β-Picoline Oxidation. The following conditions were found to be optimal: air flow rate, 3 L/min; air pressure, 16 atm; cobalt acetate, 0.033 gmol/L; manganese acetate, 0.033 gmol/L; promoter, LiCl; temperature, 170 °C; time, 8 h. These conditions resulted in 52% conversion of β-picoline, with 97% selectivity.

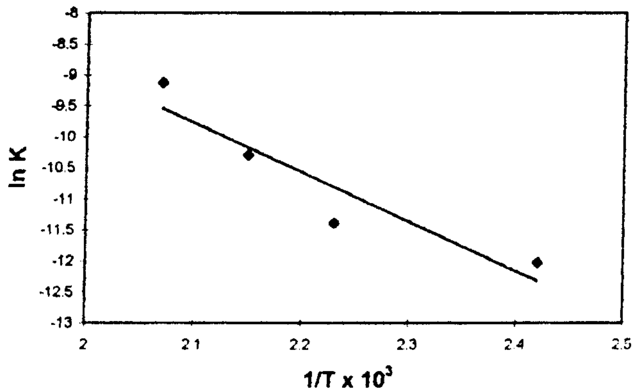

Figure 11. **Arrhenius plot. Reaction conditions: air flow rate, 3.0 L/min; air pressure, 16 atm; solvent, acetic acid; reaction volume, 300 mL.**

Kinetic Interpretation. The reactions were carried out at a high air flow rate and air pressure to ensure that the mass transfer has been eliminated completely.

A plot of -ln(1 − X_A) vs t for different substrates (Figure 8) shows that these oxidation reactions are first order with respect to the substrate. A plot of −ln(1 − X_A) vs t) for different concentrations of β-picoline (Figure 9 further supports the fact that it is a first-order kinetics.

At different temperatures, −ln(1 − X_A) vs t is plotted (Figure 10), and from the slopes, k values at different temperatures are found to be 6.0×10^{-6}, 1.1×10^{-5}, 3.39×10^{-5}, and 9.6×10^{-5} s^{-1} for a particular air flow rate, air pressure, and catalyst loading.

From the Arrhenius plot, the activation energy was found to be 15.9 kcal/mol (Figure 11).

Conclusions

β- and γ-picoline can be readily oxidized to the corresponding acids, but not α-picoline, since at this temperature α-picolinic acid is susceptible to decarboxylation.

Pseudocumene. which is difficult to oxidize, can be oxidized to trimellitic acid with a sizable yield. Lithium chloride seems to be the best promoter under the reaction conditions.

One can produce *2*-naphthanoic acid by this process scheme. The rate of reaction of *2*-methylnaphthalene is higher than those of picolines and pseudocumenes under the same reaction conditions.

The reaction follows a first-order kinetics.

Acknowledgment

S.M. is grateful to the University Grants Commissions, New Delhi, for the award of a senior research fellowship.

Received for review June 1, 1998.

OP980047T