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ANODIC OXIDATION OF 2-PICOLINE

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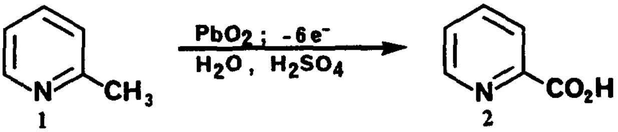
Summary: Concentrations, temperature, and current density for anodic oxidation of 2-picoline were optimized by using three statistically-designed experiments. Criteria for optimization were chemical yield, current efficiency, space-time-yield and rate of anode corrosion.

Introduction

Optimizing anodic oxidation of 2-picoline 1 (Scheme 1) required study of as many as twelve possible experimental parameters.[1] Such multivariate studies are most efficiently done with statistically designed experiments.[2] Prior reports of 1 oxidation did not disclose complete effects of parameters like changes in concentrations, temperature, and current density.[3]

In this paper, effects of these variable changes on yield, current efficiency, space-time-yield, and rate of anode loss are reported.

Scheme 1



Results and Discussion

Simplex study of anolyte composition

First statistically-designed experiment was a Simplex series for three components of anolyte.[4] Triangular experimental space was normalized so that variation in each weight assumed values between 0.0 and +1.0. Dependent variable was chemical yield as determined by UV analysis. Independent variables were 1 weight (5-30 g), sodium bisulfate weight (12-48 g), and water weight (180-300 g). Certain combinations (Table 1) of *independent variables* produced electrolytes *with* a ratio of equivalents of acid to equivalents of 1 greater than unity and some combinations produced ones with ratios less than unity. As a result, initial electrolyte pH varied considerably. Figure 1 shows yield results for ten experimental points. No modelling equation was developed. All electrolytes with initial pH >5 gave poor yields (<20%); some electrolytes with pH <2 gave good yields (>65%), but not all of them. In general, best yields were obtained at lowest weight of 1, higher weight of sodium bisulfate, and highest weight of water. Optimization required dilute, highly-acidic solutions for yields over 70%.

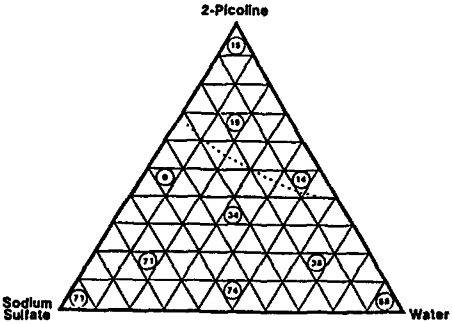


Figure 1. Results of Simplex Design on Anolyte Composition. Numbers in parenthases are molar yield of 2.

Factorial study of current density and temperature

Next, a factorial design series was done to explore effect of current density (X_1; 5-55 mA/cm^2), and temperature (X_2; 25-55 deg C) on yield (Y_1). Anolyte concentrations were held at levels where >70% yield was obtained in Simplex design. Independent variables (Table 2) were normalized to a range of -1.0 to +1.0. At the 99% confidence limit, the Taylor Series in *Eqn 1* described results. Negative coefficient of X_1 denoted decreasing yield on increasing current density. Positive coefficient of X_2 denoted mild increase in yield with rising temperature. Lack of cross-term in *Eqn 1* meant those relationships held over all experimental space studied.

$$Y_1 = 67.6 - 15.8(X_1) + 3.4(X_2). \qquad \textit{Eqn 1}$$

Table 1. Simplex design, variable levels and results.

Real variable			Normalized variable[a]			Initial	Yield[b]
1 (g)	Na_2SO_4 (g)	H_2O (g)	1	Na_2SO_4	H_2O	pH	(%)
30.00	13.08	178.20	1	0	0	6.4	14.7
9.17	20.71	257.30	1/6	1/6	2/3	1.6	37.7
5.00	55.23	172.80	0	1	0	0.3	70.7
21.67	20.71	197.30	2/3	1/6	1/6	5.9	19.0
17.50	34.52	175.50	1/2	1/2	0	1.7	0.0
5.00	13.08	298.20	0	0	1	1.7	68.4
17.50	13.08	238.20	1/2	0	1/2	6.2	13.8
9.17	41.42	194.60	1/6	2/3	1/6	1.0	70.9
13.33	27.62	216.40	1/3	1/3	1/3	1.7	34.1
5.00	34.52	235.50	0	1/2	1/2	0.8	74.4

[a] Real variable range was normalized from 0.0 to +1.0

[b] Molar yield of 2 based on 1 added into the electrolyte at 100% theoretical charge passage for a 6 e^- process

Table 2. Factorial design, variable levels and results for current density and temperature.

X_1	X_2	Y_1[b]
- 1	- 1	81.8
+1	- 1	48.8
- 1	+1	87.2
+1	+1	57.0
0	0	67.6

[a] Real variable range was normalized from -1.0 to +1.0.

[b] Molar yield of 2 based on 1 added into the electrolyte at 100% theoretical charge passage for a 6 e^- process, average of duplicates.

Factorial study of anolyte composition

Results of Simplex design were disappointing since operating in dilute, highly-acidic electrolytes would tend to maximize resourses put into synthesizing 2. That is, the synthesis would not be optimized. Therefore, another series of experiments was done to explore concentration changes, but this time using a factorial design rather than a Simplex one. Results of Simplex work were valid and correctly described results to be expected within space studied, but not all available experimental space had been explored. Simplex designs are triangular slices through multi-dimensional experimental space. A three-variable factorial would effectively explore missing volume.

For this series, independent variables were 1 weight (X_3; 20-110 g), sodium sulfate weight (X_4; 5-50 g), and water weight (X_5; 300-600 g). Weight of sulfuric acid, fourth component of anolyte, was held constant (90 g). All experimental space was within an equivalent ratio of 1 to sulfuric acid >1. Dependent variables were current efficiency (Y_2) for formation of 2 at 100% theoretical charge passed, space-time-yield (Y_3; expressed as g/hr/cell), and rate of loss of PbO_2 from anode (Y_4; expressed as mg/hr/cell). Independent variables (Table 3) were normalized to a range of -1.0 to +1.0, as before. For these systems, previous Simplex series had shown a direct correlation between yield and current efficiency.

Model for current efficiency at 95% confidence limits is shown in ***Eqn 2*** Lack of measurable variation on X_3 was unexpected. However, cross-terms in ***Eqn 2*** indicated interesting behavior for variation of Y_2 with changes in X_3.

$$Y_2 = 74.9 - 3.2(X_4) - 2.5(X_5) + 1.2(X_3X_4) - 3.6(X_4X_5) - 1.8(X_3X_4X_5). \qquad \textit{Eqn 2}$$

Table 3. Factorial design, variable levels and results for anolyte concentrations.

X_3	X_4	X_5	Y_2[a]	Y_3[b]	Y_4[c]
-1	-1	-1	81.3	1.56	25
+1	-1	-1	72.7	1.39	13
-1	+1	-1	76.1	1.46	18
+1	+1	-1	79.5	1.52	5
-1	-1	+1	78.1	1.50	22
+1	-1	+1	80.0	1.53	10
-1	+1	+1	65.8	1.26	25
+1	+1	+1	65.5	1.25	11
0	0	0	86.1	1.65	14

[a] Current efficiency for formation of 2 based on passage of 100% theoretical charge, average of duplicates.

[b] Space-time yield expressed as grams of 2 per hour per cell.

[c] Rate of loss of PbO_2 expressed as mg lost per hour per cell.

This behavior is best seen in Figure 2, where variation is shown as a "saddle" plot of lines of constant current efficiency. The important result was, for certain combinations of independent variables, increased picoline concentration gave rise to increased efficiency; in particular, when X_5 was held at high level and X_4 was held constant at -1.0, increased X_3 led to increased efficiency (or 2 yield). This meant there were regions of experimental space that did allow high loading of 1 in anolyte and which also gave good yields and current efficiencies. Taylor Series ***(Eqn 3)*** described space-time-yield. Inspection of terms showed a saddle plot similar to Figure 2, which meant space-time-yield was optimized at same point as current efficiency.

$$Y_3 = 1.43 - 0.06(X_4) - 0.05(X_5) + 0.03(X_3X_4) - 0.07(X_4X_5) - 0.04(X_3X_4X_5) \qquad \textit{Eqn 3}$$

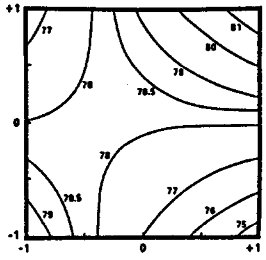


Figure 2. Results of Factorial Design on Anolyte Composition. Lines of constant current efficiency are shown.

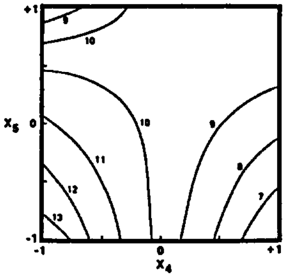


Figure 3. Results of Factorial Design on Current Density and Temperature. Lines of constant rate of anode loss are shown (mg/hr/cell)

Finally, rate of corrosion was modelled from results *(Eqn 4)*. Again, there was a significant cross-term denoting interesting behavior of corrosion with independent variables. This is shown in Figure 3. Optimum results were at high 1, high sodium sulfate, and high water concentrations.

$$Y_4 = 16.1 - 6.4(X_3) - 1.4(X_4) + 2.4(X_4X_5) \qquad \textit{Eqn 4}$$

This last factorial study gave one result similar to Simplex design (water weight "high" for best efficiency), but other two relationships were seemingly opposed to Simplex results. This only meant that, within restricted variance of Simplex design, effects of variable changes were always in the same direction. Within wider variance of last factorial, effects of variable changes were seen to invert direction depending on where, within experimental space, one started.

Verification of predictions

When larger scale oxidations (1 kg) were done, 2 yield (85% isolated), current efficiency (89% at 133% theoretical charge), space-time yield (1.68 g/hr/cell), and lead dioxide loss (12 mg/hr/cell) were all very close to predictions of *Eqn 1-4*. Operating at much lower current densities (2 mA/cm^2) gave even better isolated yields (98%). In comparison to the best process known before these studies, using the optimum process reduced sulfuric acid consumption by one-third, sodium sulfate usage by two-thirds, and increased loading of 1 more than double. Optimization with this kind of experimental strategy made significant improvements in the process for 2.

Experimental

All reactions were carried out under a nitrogen purge. Deionized water was used throughout. 2-Picoline was commercial-grade of >98% purity by GC. Sulfuric acid was iron-free electronic-grade. Sodium bisulfate was Baker reagent-grade used as the monohydrate. Power supply was an Amel model 555B run in the potentiostatic mode (10A, 32V compliance). Pumps were March centrifugal ones with magnetic drives capable of at least 0.75 GPM and 15 psig output. All pipework, reservoirs, cell plates, and valving were polypropylene. Cells were filter-press design (Figure 4) having high-surface-area anode and cathode, each composed of hardened, commercially-available, lead shot used for reloading shotgun shells (3-6% antimony alloy, average diameter 3.2 mm). Membranes were Ionac cation-exchange type MC 3470. Sealing of the cell was accomplished with fluorocarbon elastomer O-rings. The experimental apparatus is shown in Figure 5. Analysis for 2 was done by UV spectroscopy.

Simplex and factorial designs were accomplished and analysed according to established procedures.[2,4] Taylor Series equations were calculated for factorial designs.

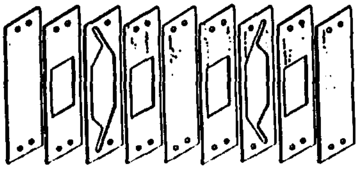


Figure 4. Filter-press Cell Design (US 4,589,968).

Typical electrolysis of 2-picoline (1)

Anolyte was prepared by slowly adding required amount of either sulfuric acid or sodium bisulfate to water with adequate stirring and cooling. If sodium sulfate was used, it was added at this point. Then the requisite amount of 2-picoline was carefully added with good stirring and cooling. Cooled electrolyte was added to anolyte reservoir.

Catholyte was prepared identically to anolyte except an equal volume of water was substituted for picoline. Cooled catholyte was transferred to catholyte reservoir.

Pumps were started and pressures at cell inlet were equalized between the two streams at about 6 psig each. This normally gave flow rates through the cell of 800-1,000 ml/min. Heat was supplied by steam running through a coil of polyethylene tubing inside reservoirs. Temperature in electrolytes was increased to desired level. Power supply was turned on and current adjusted to required amperage based on geometric anode area of 1,000 cm^3.

Charge was passed until desired quantity of charge had been passed based on quantity of picoline charged into anolyte. Power supply and pumps were turned off, and anolyte was sampled for UV analysis.

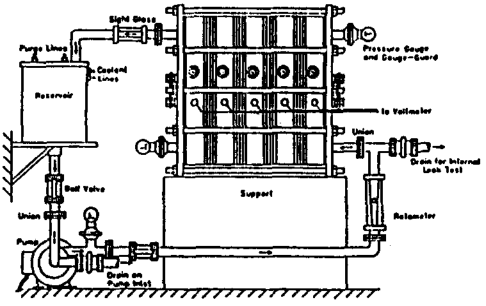


Figure 5. Experimental Apparatus.

Typical isolation of picolinic acid from the electrolyte

Electrolyte was neutralized to isolelectric point of picolinic acid with sodium hydroxide. The solution was concentrated by distillation. Then an aliquot of toluene was added to concentrate and last of the water was azeotropically distilled using Dean-Stark trap to return toluene. When toluene was dry, hot filtration was used to separate soluble picolinic acid from insoluble sodium sulfate. A second extraction of the filter cake was done with fresh, hot toluene. Filtrate was concentrated, cooled and crystallized product filtered in a Buchner funnel. Dried product could be analysed by titration with sodium hydroxide, or by UV analysis.

Conclusions

Contrary to experience with a more restricted Simplex design, factorial designs showed increased concentration of **1** did not always lead to lower yield and current efficiency for **2**. There were regions of experimental space where increasing **1** actually led to increasing yield. Exploration of as wide a range of experimental space as possible was critical to ability to see the whole effect each variable had on process results.

Obtaining high loading of electroactive substance in anolyte maximized reactor space-time-yield and optimized the process. Increased current density always resulted in lowered current efficiency for **2**. Therefore, any increase in rate of synthesis needs to be balanced against a reduced efficiency. Increased temperature increased efficiency slightly under all conditions.

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