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Process Optimization of Vapor Phase Pyridine Synthesis Using Response Surface Methodology[1]

K. Suresh Kumar Reddy[a], C. Srinivasakannan[a], and K. V. Raghavan[b]

[a] *Chemical Engineering Department, the Petroleum Institute, Abu Dhabi, U.A.E*

[b] *Chemical Engineering Division, Indian Institute of Chemical Technology, Hyderabad, India*

e-mail: skuppireddy@pi.ac.ae

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Abstract—The vapor phase pyridine synthesis from acetaldehyde, formaldehyde and ammonia over HZSM-5 catalyst was studied. The process parameters like temperature, aldehyde ratio, and Si/Al ratio in HZSM-5 was investigated and the process conditions were optimized using surface response methodology (*RSM*) based on Box–Behnken design. The influence of process parameters investigated using analysis of variance (ANOVA), to identify the significant parameters. The optimum conditions for high yield of pyridine were identified to be a reaction temperature 400°C, aldehyde ratio 1 : 1 and Si/Al ratio 106.7. A maximum of 55% yield of pyridine formed under the optimum experimental conditions. The proposed model equation using RSM has shown good agreement with the experimental data, with a correlation coefficient $R^2 = 0.99$.

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Pyridine and picolines are useful intermediates in the synthesis of herbicides, pharmaceuticals and surfactants [1]. Their synthetic production from easily available Feedstock like acetaldehyde, formaldehyde and ammonia has provided the best prospect for meeting their growing user demand. The global market favors pyridine and 3-picoline in comparison with other bases. The catalytic vapor phase aminocyclization has enough flexibility to tailor the catalyst and process parameters to achieve a market friendly product distribution. Vapor phase pyridine synthesis from aldehydes and ammonia was reported first by Chichibabin [2] in 1924. The first commercial production of pyridine began in 1953 in the USA based on a patented process [3]. Subsequently ICI, Rutgerwerk, Nepara, Koei Chemicals and others [4–12] patented processes employing SiO_2–Al_2O_3, ZSM-5 and Ti-ZSM-5 as catalysts in which several by-products were produced with rapid catalyst deactivation due to coking. A range of carbonyl-containing precursors like acrolein and acetone employing zeolite catalysts were tried in fixed and fluid bed reactors. Solid acid-catalysed vapor phase pyridine synthesis has established the total benefits of high yield, selectivity and environmental cleanliness. The pyridine synthesis is a multi-step reaction involving condensation, cyclization and hydrogen transfer. Reported studies [1, 13–15] have established that HA, HX, HY and HM zeolites and solid acids such as SiO_2–Al_2O_3 have moderate effect on selectivity towards pyridine formation, whereas the pentasil type of zeolites such as HZSM-5 and silicalites with medium SiO_2/Al_2O_3 ratios 30–120, which are ion-exchanged with metal cations such as Ti(I), Zn(II) or Co(II), have more pronounced effects on pyridine formation. It is interesting that the latter imparts dehydrogenation activity to the catalyst with a mild drop in its acidity. The pore diameters of Pentasil zeolite (HZSM-5) as well as silicalites are almost identical to that of pyridine molecular diameter. In the present work, HZSM-5 is accordingly employed as the catalyst.

The catalyst acidity has been reported [1, 14–17] to have significant influence on product distribution as evidenced by: (a) presence of both Lewis and Brønsted acid sites existing in a thermodynamic equilibrium with the latter promoting carbonium ion formation, (b) high catalyst acidity retarding pyridine synthesis due to predominance of unreactive adsorbed ammonium ions and enhanced catalyst coking ability, (c) the need for an optimum level of catalyst acidity and (d) Pentasil structure of HZSM-5 and silicalite catalysts promoting selective formation of pyridine under medium acidity.

Optimizing refers to improving the performance of a system, a process, or a production in order to obtain the maximum benefit from it. Traditionally, optimization has been carried out by monitoring the influence of one factor at a time on an experimental response. While only one parameter is changed, others are kept at a constant level. This optimization technique is called one-variable-at-a-time. Its major disadvantage is that it does not include the interactive effects among the variables studied. Another disadvantage of the one-factor optimization is the increase in the number of experiments necessary to conduct the research,

[1] The article is published in the original.

Table 1. High and low levels of factors

Factor	Low level (−1)	Center point (0)	High level (+1)
Temperature, °C (X_1)	250	325	400
Aldehyde ratio (X_2)	0.5	0.75	1.0
Catalyst Si/Al ratio (X_3)	40	140	240

which leads to an increase of time and expenses as well as an increase in the consumption of reagents and materials. In order to overcome this problem, the optimization of process objective functions has been carried out by using multivariate statistic techniques. Among the most relevant multivariate techniques used in analytical optimization is response surface methodology (**RSM**). Experimental design technique is a very useful tool for this purpose as it provides stastical models which help in understanding the interactions among the parameters that have been optimized [18].

The process optimization by designing the experiments using RSM discussed in detail. RSM is a collection of mathematical and statistical techniques based on the fit of polynomial equation to the experimental data, and also one of the multivariate techniques which can deal with multivariate [19] experimental design strategy, statistical modeling and process optimization. It is used to examine the relationship between variables or factors. This method is often employed after indentifying the controllable variables and to optimize variables to attain best system response.

Vapor phase aminocyclization requires proper selection of catalyst and standardization of process parameters to achieve a market friendly product distribution and reactor operation. In the present study using design of experiments the process optimization studies were carried out as reaction temperature (X_1), aldehyde ratio (formaldehyde/acetaldehyde, X_2) and silica/alumina ratio (X_3) as process variables and yield of pyridine as an objective function, and these results were compared with experimental results. Nobody earlier reports available elsewhere using design of experiments for particularly such a commercially important process in fine chemical industries.

EXPERIMENTAL

The vapor phase pyridine synthesis is carried out in a continuous tubular downflow Pyrex reactor (20 mm inner diameter and 450 mm length) at atmospheric pressure. The catalyst bed temperature is maintained at reaction temperature using a PID controller with ±0.5°C accuracy. 4 g of the HZM-5 catalyst loaded for each experiment, and aldehyde mixture fed from the top of the reactor using a syringe pump (Be Braun, USA) and ammonia is fed from a pressurized cylinder. The condensed product collected from bottom of the reactor was analyzed by GC (Shimadzu-14B) using internal standard method [20]. The detail experimental setup [21] and product analysis [22] were reported by the same authors.

Design of Experiments

RSM is a stastical method that uses quantitative data from appropriate experiments to determine regression model equations and operating conditions [23]. It can be used for studying the effect of several factors at different level and their influence on each other. In the present study, a Box–Behnken design [24] was chosen to evaluate the combined effect of three independent variables. The independent variables selected in the present study are X_1, X_2 and X_3.

The chosen independent variables used in process optimization were coded (−1, +1), where "−1" coded as low level and "+1" coded as high level, respectively. The center point coded as (0, 0, 0). The center points are used to determine the experimental error and the reproducibility of the data. The axial points are (±1, 0, 0), (0, ±1, 0) and (0, 0, ±1), it makes the design rotatable. The minimum and maximum ranges of variables were investigated and the full experimental plan with respect to their values in actual and coded form is

Table 2. Experimental data

Run	X_1	X_2	X_3	Yield, % (Y)
1	250	0.75	240	4.2
2	250	0.75	40	6.6
3	325	0.75	140	21.2
4	325	0.75	140	22.0
5	325	1.0	40	23.5
6	325	1.0	240	25.0
7	400	0.5	140	28.2
8	250	1.0	140	9.6
9	325	0.75	140	21.0
10	325	0.5	240	10.5
11	250	0.5	140	7.8
12	400	0.75	40	43.6
13	325	0.5	40	15.5
14	400	0.75	240	32.0
15	400	1.0	140	56.0

Table 3. Estimated coefficients using RSM for pyridine yield

Term	Coefficient	t	P
Constant	21.4	18.03	0.001
X_1	16.45	22.63	0.000
X_2	6.51	8.96	0.000
X_3	−2.19	−3.01	0.030
X_1^2	3.49	3.26	0.022
X_2^2	0.51	0.479	0.652
X_3^2	−3.29	−3.072	0.028
X_1X_2	6.50	6.322	0.001
X_1X_3	−2.30	−2.237	0.075
X_2X_3	1.63	1.580	0.175

Note: $R^2 = 0.9926$.

listed in Table 1. The actual values of three independent variables together with the responses are shown in Table 2. The experimental sequence was randomized in order to minimize the effects of the uncontrolled factor. The response considering in this study was yield of pyridine (Y). This response was used to develop an empirical model which correlated the response to the preparation variables using a second-degree polynomial equation as given by

$$Y = b_0\sum_{i=1}^{n} b_iX_i\sum_{i=1}^{n} b_{ii}X_i^2 + \sum_{i=1}^{n-1}\sum_{j=i+1}^{n} b_{ij}X_iX_j,$$

where Y is the predicted response (pyridine yield), b_0 is the value for the fixed response at the central point of the experiment, and b_i, b_{ii}, b_{ij} are the linear, quadratic and cross product coefficients, respectively. The analyses of variance (**ANOVA**) and response surfaces were processed using the Minitab-15 software. The optimized pyridine yield was estimated using the software's numerical and graphical optimization tools.

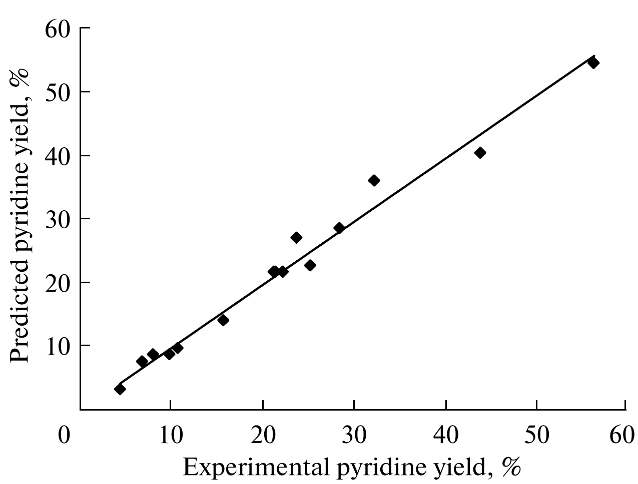

Fig. 1. Predicted *vs.* experimental yield of pyridine.

RESULTS AND DISCUSSION

Development of Regression Model Equation

Central Composite Design (CCD) was used to develop a polynomial regression equation in order to analyze the correlation between the independent variables to the pyridine yield. Table 2 shows the complete design matrices together with response values obtained in the experimental work. Total 15 experimental runs conducted, among them 3 are at center point to determine the experimental error and the reproducibility of the data. The pyridine yield varies from 4.2 to 56.0%. The design together with the response values from the experiments are shown in Table 3. The objective function based on pyridine yield utilized the quadratic model according to the propositions of the software. The final empirical models in terms of coded factors for pyridine yield are shown in below equation as

$$Y = 21.72 + 16.45X_1 + 6.513X_2 - 2.187X_3 + 3.448X_1^2 - 3.327X_3^2 + 6.5X_1X_2. \quad (1)$$

The quality of the model developed was evaluated based on the correlation coefficients R^2. In fact, the models developed seems to be the best at low standard deviation and high R^2 statistics which is closer to unity as it will give predicted value closer to the actual value for the responses [25]. The R^2 value for Eq. (1) was found to be 0.993 close to unity, indicating a good agreement between experimental data and the model predicted data, which do not show any significant non-linear pattern (S-shaped curve) indicating non-normality in the error term.

Figure 1 shows an approximate linearity confirming normality of the data [26] and also model parameters interaction shown in Fig. 2. Each pair of parameters is showing different effects on the objective function at different levels.

Analysis of Variance

The significance and adequacy of the models were further justified through ANOVA, the quadratic model is presented in Tables 3 and 4. The Student t-test was used to determine the significance of the regression coefficients of the parameters, and the P values are used as tool to check the significance of each interaction among the variables. In general the larger the magnitude of t and smaller value of P, the more significant is the corresponding coefficient term [27]. The reaction temperature has the greatest effect on pyridine yield with highest t value of 22.63 whereas alde-

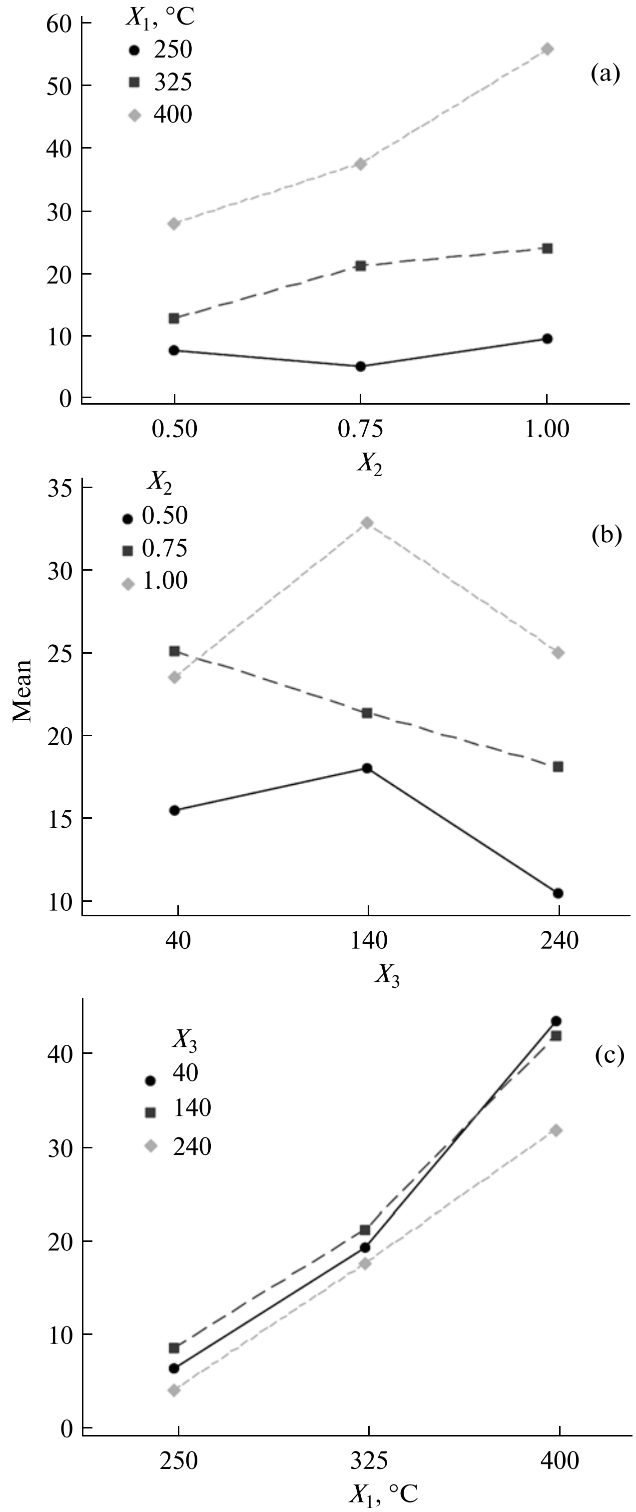

Fig. 2. Interaction plots of X_1 (a), X_2 (b), and X_3 (c).

hyde ratio and silica/alumina ratio were found to be less significant. The model with *F* value of 74.52 and *P* value 0.001 implies the significance of the model. The influence of all the variables can be estimated using *P*

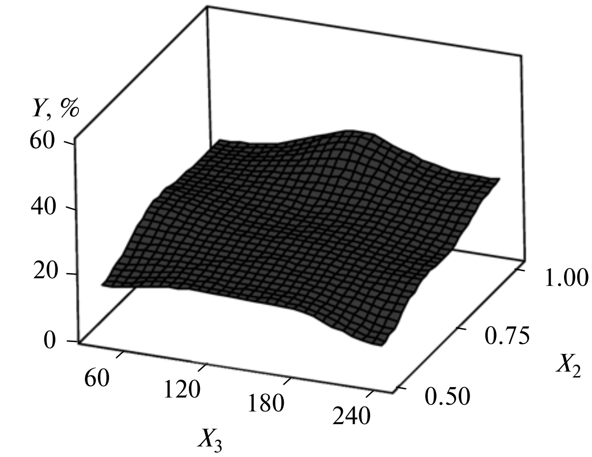

Fig. 3. Surface plot for X_2 and X_3 (X_1 = 325°C).

value shown in Table 3. The *P* values less than 0.05 indicate that the model terms are significant in formulating the objective function (pyridine yield in %). In this case X_1, X_2, X_3 and the interaction terms X_1^2, X_3^2, X_1X_2 were significant and others are non-significant. In order to enhance the model remove insignificant terms and formulate with significant terms as shown in Eq. (1).

Process Optimization

Pyridine formation involves typical series-parallel reactions in vapor phase. The reaction temperature, aldehyde ratio and Si/Al ratio has been reported to have a significant influence on pyridine yield [21, 22, 28]. The imines are building blocks in formation of cyclic pyridine compounds, these imines formation depends on acidity type (Brønsted or Lewis), and this acidity type will depend on Si/AI ratio of HZSM-5. Brønsted and Lewis acid sites are in equilibrium and change from one state to other as reaction temperature changes, so reaction temperature, Si/Al ratio and aldehyde ratio are vital process parameters in obtaining high yield of pyridine.

After finding a suitable model, the process independent variables interaction and its effect on objective variable (pyridine yield) is shown in Fig. 3. Here each plot represents the effect of two variables at their studied range. The trends of lines can interpret the interactions between two variables in all various combinations. The interaction between temperature, aldehyde ratio and temperature, catalyst Si/Al ratio follows similar trend but the interaction between aldehyde ratio and catalyst ratio at high temperatures (>325°C) has a very close interaction. This may be due to changes in catalyst nature at high temperatures and favors the high yields of pyridine synthesis by predominant demethylation of picolnes taken place [28, 29].

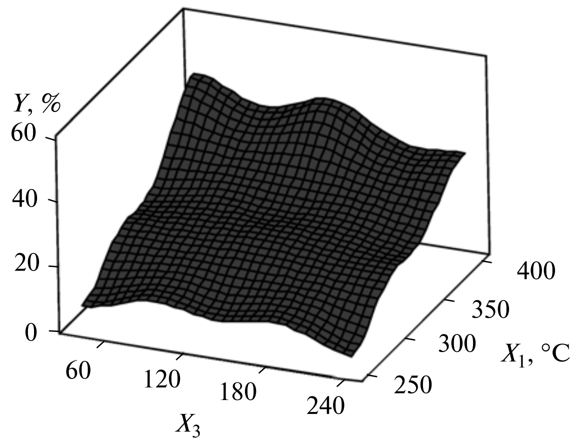

Fig. 4. Surface plot for X_1 and X_3 ($X_2 = 0.75$).

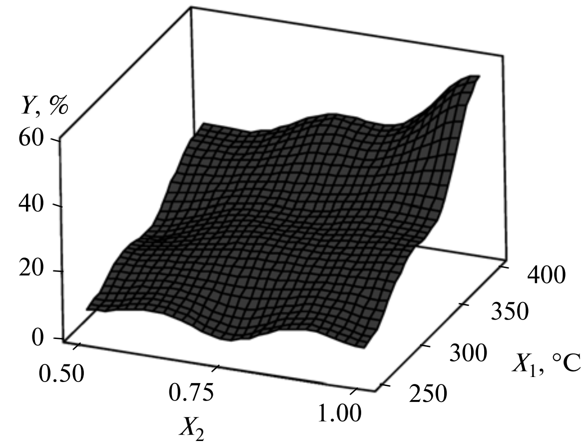

Fig. 5. Surface plot for X_1 and X_2 ($X_3 = 140$).

Figure 3 shows the three dimensional plot of effect aldehyde ratio and catalyst ratio on pyridine yield. As catalyst Si/Al ratio increases from 40 to 140 the pyridine yields increases and then decreases from 140 to 240. From this it is infer that high aldehyde ratio and optimum acidity of the catalyst gives high yield of pyridine [28, 29]. Figure 4 shows the three dimensional plot of effect temperature and catalyst ratio on pyridine yield. As temperature increases the yield of pyridine increases, and among temperature, catalyst Si/Al ratio the effect of temperature is substantial. This can also infer from Table 3, with high t value. Figure 5 shows the three dimensional plot of effect of aldehyde ratio and temperature on pyridine yield. Here also among these parameters temperature has more influencing parameter than aldehyde ratio with respect to pyridine yield. This can confirm from Table 3, with high t value of 22.63. Aldehyde ratio also has positive effect on pyridine yield with t value of 8.96.

With the objective being to maximize the pyridine yield the optimum conditions were identified using Minitab-15 software. It reports that temperature $X_1 = 400°C$, aldehyde ratio $X_2 = 1$ and Si/Al ratio $X_3 = 106.7$ are optimum conditions with 54.99% predicted yield of pyridine (experimental yield 55.6%). These results are fall under similar range as the authors [20–22, 28, 29] reported elsewhere.

So, the RSM technique is used to optimize the process conditions, for the high yield of pyridine synthesis. The influence of temperature, aldehyde ratio and Si/Al ratio on pyridine yield was investigated using ANOVA, to identify the significant parameters. The experimental data and model predicted data are satisfactory coincided. Beyond 400°C and aldehyde ratio greater than 1 gives decrease in pyridine yield (due to high coke formation and decreasing available acid sites for pyridine formation). It is apparent that Brønsted sites promote the creation of carbonium ions, whereas Lewis sites facilitate the formation of labile adsorbed ammonia. At high temperatures Brønsted sites will decrease by releasing water molecule and convert into Lewis sites; this is not suitable conditions for high yields of pyridine. That's why we are not considered the experimental conditions beyond temperature

Table 4. Analysis of variance for the RSM model

Source	Degree of freedom	Sum of squares	Mean squares	F	P
<u>Model</u>	9	2835.92	315.10	74.52	0.001
Linear	3	2542.40	847.47	200.42	0.000
Square	3	92.80	30.93	7.32	0.028
Interaction	3	200.72	66.91	15.82	0.006
<u>Error</u>	5	21.14	4.23	–	–
Lack of fit	3	20.58	6.86	24.50	0.039
Pure error	3	0.56	0.28	–	–
<u>Total</u>	14	2857.06			

400°C and aldehyde ratio 1 in these studies. The optimum conditions for high yield of vapor phase pyridine synthesis to be a reaction temperature 400°C, aldehyde ratio 1 and Si/Al ratio 106.7. The optimum pyridine experimental yield obtained in this study was 55.0%.

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