Screening of Reaction Variables Through Plackett-Burman Experimental Design in Alkylation of *p*-Cresol with Cyclohexylchloride

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Abstract

A Plackett-Burman experimental design was used to identify the reaction variables that influence the alkylation of p-cresol with cyclohexylchloride in presence of anhydrous aluminium chloride. Reaction variables such as temperature, molar ratio of p-cresol to cyclohexylchloride, amount of catalyst, addition time, stirring time, speed of stirring were changed at two levels and cyclohexyl p-cresol was evaluated as the response. Statistical analysis in this study reveals that temperature, molar ratio of p-cresol to cyclohexylchloride and amount of anhydrous aluminium chloride were identified as the major variables to influence the alkylation of p-cresol with cyclohexylchloride.

Keywords: Plackett-Burmann Experimental Design, alklylation, *p*-Cresol, Cyclohexylchloride.

1. Introduction

Alkylation of phenol and its derivatives with different alkenes and alcohols has been of interest because of industrial importance of the alkylated phenols [1-5]. Since a large number of factors are involved in any chemical process, a preliminary screening should be performed. Plackett-Burman design helps to identify the most significant variables for a certain system with only few experiments, but it can not give the optimum value for each variable [6-9]. This design has the advantage of limiting the number of experiments that are to be performed. Screening techniques such as factorial designs allow the analyst to select which factors are significant and at what levels. Such techniques are vital in determining initial factor significance for subsequent optimization. The P-B design has been used by several researchers for screening the important variables in pharmaceuticals [10-14], biotechnology research and development [15-20]. Pluckett-Burman experimental design used in this study to screen out the important variables of alkylation of p-cresol is a 2-run design (n = 12) with 11 variables (k). The highest (+) and lowest (−) levels of the variables were chosen based the previous experiments. In this study, P-B experimental design is used for the screening of significant variables of alkylation of *p*-cresol with cyclhexylchloride in presence of aluminium chloride.

2. Experimental

All Alkylation of *p*-cresol with cyclohexylchloride in presence of aluminium chloride was done according to the method described elsewhere [21]. P-B experimental design was used to screen out the significant variables that affect the yield cyclohexyl *p*-cresol.

3. Results and Discussion

Alkylation of *p*-cresol with cyclohexylchloride in presence of anhydrous aluminium chloride was carried out in random manner. Reaction variables such as temperature, molar ratio of *p*-cresol to cyclohexylchloride, amount of catalyst, addition time, stirring time, speed of stirring were changed at two levels and cyclohexyl p-cresol was evaluated as the response. Six potential variables were considered to have an influence on the yield and selected for screening experiments. These factors and the selected experimental levels are listed in Table 1. Since there were six factors, a 12-trial Plackett-Burman design was suitable. This design had a nominal capacity of 11 variables or factors. The five unassigned factors (X_7 through X_{11}) were used in the computation to get some measure of the experimental error.

Data analysis was carried out as described by Akhnazarova and Katarov [22]. The first row in the design matrix was obtained from Akhnazarova and Katarov [22] for $n = 12$ and $K = 11$ and given as + − + − − − + + + − +. The remaining design matrix was generated row (or column)-wise from the first one by moving the elements of the row (or column) to the right

(or down) one position and placing the last element of the first row (or column) in the first position. A third row (or column) was produced from the second similarly and the process continued until row (or column) *K* was generated. A row of minus signs was added to complete the design (18, 19).

Table 1. Experimental range and levels of independent variables

Variable	(+) Level	(-) Level
Temperature, °C, X_1	150	130
PC:CHC, X_2	8:1	6:1
Amount of sulphuric acid, % by wt. of PC, X_3	15	5
Time of addition, t_a, X_4	2	1
Time of stirring, t_s, X_5	2	1
Speed of stirring, X_6 rpm	600	200
X_7 - X_{11}, Unassigned factors used to calculate standard deviation.		
Response, Y: % yield of CMP		

Table 2. Placket-Burman experimental design for screening significant variables.

								Unassigned Factors					
Trial	Mean	X_1	X_2	X_3	X_4	X_5	X_6	UFE X_7	UFE X_8	UFE X_9	UFE X_{10}	UFE X_{11}	Response, yield, %
1	+	+	+	–	+	+	+	–	–	–	+	–	61.5
2	+	+	–	+	+	+	–	–	–	+	–	+	79.8
3	+	–	+	+	+	–	–	–	+	–	+	+	81.7
4	+	+	+	+	–	–	–	+	–	+	+	–	92.5
5	+	+	+	–	–	–	+	–	+	+	–	+	56.2
6	+	+	–	–	–	+	–	+	+	–	+	+	47.3
7	+	–	–	–	+	–	+	+	–	+	+	+	39.6
8	+	–	–	+	–	+	+	–	+	+	+	–	69.7
9	+	–	+	–	+	+	–	+	+	+	–	–	46.5
10	+	+	–	+	+	–	+	+	+	–	–	–	79.8
11	+	–	+	+	–	+	+	+	–	–	–	+	81.7
12	+	–	–	–	–	–	–	–	–	–	–	–	35.2
Sum + 'S	771.5	417.1	420.1	485.2	388.9	386.5	388.5	387.4	381.2	384.3	392.3	386.3	
Sum – 'S	0	354.4	351.4	286.3	382.6	385.0	383.0	384.1	390.3	387.2	379.2	385.2	
Sum + 'S & – 'S	771.5	771.5	771.5	771.5	771.5	771.5	771.5	771.5	771.5	771.5	771.5	771.5	
Difference	771.5	62.7	68.7	198.9	6.3	1.5	5.5	3.3	–91	–2.9	13.1	1.1	
Effect	64.29	10.455*	11.45*	33.15*	1.05	0.25	0.92	0.55	–1.52	–0.48	2.18	0.18	
$(UFE)^2$								0.3025	2.3104	0.2304	4.7524	0.0324	

The experimental design and the calculations are illustrated in Table 2. Each of the 12 trials of the design was listed in horizontal lines. The vertical columns labeled X_1 through X_{11} indicated the label of the factor in each trial. In regard to the design, in the 12 trials each factor was at a high + level for 6 trials and at a low (–) level for 6 trials. The yield for each trial was indicated in the Y column on the right.

The Sum+'s line was then computed by adding the yield values for all lines where the factor was at a + level. (Example: X_1 factor 61.5 + 79.8 + 92.5 + 56.2 + 47.3+79.8 = 417.1). This operation was continued across the table for all factors, including the five unassigned factors. In a similar way, the Sum–'s line was computed. The next line simply totaled the Sum+'s and Sum–'s to check to the arithmetic. The next line was the difference between the Sum+'s and the Sum–'s for each factor. This represented the total difference in yield for the six trials where the factor was at the plus level, from the six trials where the factor was at a minus level. The last line represented the average effects of the factor at the plus level and was computed by dividing the difference by 6, the number of plus signs in the column. The absolute values of the calculated factor effects related to their relative importance. X_3- amount of catalyst was the most important variable.

In order to determine whether a factor effect was significant, experimental error was considered. The minimum value for factor effect to be significant was computed using the five unassigned factor effects X_7 through X_{11}. Each unassigned factor effect was squared, totaled, divided by 5, the number of unassigned factors. The square root of this number multiplied by a magic number gave the minimum significant factor effect MIN. The magic number used in this computation (2.57) came from a table of probability points of the t-distribution corresponding to five degrees of freedom (five unassigned factors) and the 95% confidence level.

The effect of each variable was determined according to the following equation.

$$E_{xi} = (\sum M_{i+} - M_{i-})/N$$

where E_{xi} = variable main effect
M_{i+} and M_{i-} = response of alkylation when the variable was at high level and low level respectively.
N = is the number of trials divided by two.
In every trial except the 12^{th}, 6 variables are at a high level and 5 variables are at low level.

From the analysis it is observed that temperature, molar ratio of *p*-cresol to cyclohexylchloride and amount of catalyst were the most significant variables in the alkylation of p-cresol with cyclohexylchloride. Addition time of cyclohexylchloride to the *p*-cresol-$AlCl_3$ mixture and stirring time after the addition of cyclohexylchloride and stirring speed either had no effect or an effect so small that it was obscured by the experimental error and interaction effects. Thus P-B design provides an efficient and reliable method for screening several reaction variables of alkylation of p-cresol with cyclohexylchloride with the minimum possible number of experiments.

4. Conclusion

In this study alkylation of *p*-cresol with cyclohexylchloride was carried out in presence of aluminium chloride and Plackett-Burman experimental design was used to screen out the significant variables for these alkylations. Three variables: temperature, molar ratio *p*-cresol to cyclohexylchloride and amount of aluminium chloride were identified as significant variables. The highest experimentally yield was found to be 96.9% under the following reaction conditions: temperature 150^0C, molar ratio of *p*-cresol to cyclohexylchloride 8:1, amount of aluminium chloride 15 % by wt. of p-cresol, addition time 2h and stirring time 1h.

10. References

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Dedication

The authors would like to dedicate this research article to the memory of late Professor Manoranjan Saha of Applied Chemistry and Chemical Engineering, University of Dhaka, Bangladesh who was the designer of this research.