A Mathematical Model for the Benzylation of
p-Cresol with Benzyl Alcohol

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Abstract

The reaction of *p*-cresol with benzyl alcohol in the presence of perchloric acid produces only 2-benzyl-4-methylphenol in high yield. A mathematical model has been developed for the process by Yates pattern experimental design.

Introduction

Benzylated phenols can be used as antioxidants in synthetic rubber, polypropylene, lubricating oil, wax, paper and lard (Filbey *et al.* 1985; Ravikovich, 1964). Some of the phenol derivatives are strong herbicides, bactericides and insecticides (Melinikov *et al.* 1954; Nemetkin *et al.* 1951). Isomeric cresols have been alkylated with different alcohols in the presence of different catalyst by several authors (Abdurasulev *et al.* 1965; Abdurasulev *et al.* 1969; Rana *et al.* 2003; Saha and Roy 1989; Saha and Badruzzaman, 1990; Saha *et al.* 1996 and Saha *et al.* 1997). Reports are also available on the benzylation of phenol, cresols, xylenols, chlorophenol and 2,4,6-tribromophenol (Fukumoto *et al.* 1996; Saha *et al.* 2001; Saha *et al.* 2005 and Wang and Ming 1993). But no attempt yet has so far been made to investigate reaction of *p*-cresol with benzyl alcohol in the presence of perchloric acid as a catalyst.

In the present work, the reaction of *p*-cresol with benzyl alcohol in the presence of perchloric acid has been investigated and a mathematical model of the reaction has been developed.

Materials and Methods

Chemicals used in the present work were of reagent grade. The reactions were carried out in a three necked round bottomed flask fitted with a condenser, a thermometer, a dropping funnel and a magnetic stirrer. *p*-Cresol (30g) and perchloric acid (0.3-1.5g) were charged into the flask and heated to the desired temperature and benzyl alcohol (7.5-10g) was introduced into the mixture gradually for a certain period of time (time of addition) with constant stirring. The reaction mixture was stirred for another period of time (time of stirring) at the same temperature after the complete addition of total amount of benzyl

alcohol. The reaction mass was then cooled to room temperature, dissolved in petroleum ether, neutralized, washed with distilled water several times and subjected to distillation. Unreacted reactants and solvent were distilled off at atmospheric pressure. The residual product was finally distilled (b.p. 308$^\text{O}$ C) and the yield (based on benzyl alcohol) was expressed as percentage of theory. Structure of the product was elucidated by spectral means.

Results and Discussion

p-Cresol with benzyl alcohol in the presence of 60 % perchloric acid (aqueous) as catalyst gave 2-benzyl-4-methylphenol. Three parameters viz. temperature, molar ratio of *p*-cresol to benzylalcohol and amount of perchloric acid were considered in the development of the mathematical model of the reaction of *p*-cresol with benzyl alcohol in the presence of perchloric acid using Yates pattern experimental design (Clausen, 1978).

The experimental ranges of the variables are listed in Table I. The critical response of

interest was yield of 2-benzyl-4-methylphenol. Time of addition of benzyl alcohol to cresol-catalyst mixture was 2h and time of stirring after the addition of benzyl alcohol was 1h.

The experimental design used was Yates pattern, 3 factor two level factorial; there were 2^3 i.e. eight trials. Since the basic 2^3 factorial design involves eight trials, each was run in duplicate yielding 16 trials. In order to check the lack of fit due to curvature, additional trial was made at the midpoint level of each factor. The difference between the average centre point value and the overall average of the design points indicated the severity of curvature.

Table II illustrates the two level 3-factor design with the factors in coded form. The experimental runs for trial 1 through 8 were run in duplicate; trial 9, the centre point trial was run four times, interspersed throughout the experimental run.

The results of these experiments are listed in the Table III. The average yield $\bar{Y}$, the range

Table I. Process variables and response

Variable	Range		
	Low (-)	Mid (0)	High (+)
X_1 , Temperature ($^\text{O}$ C)	70	100	130
X_2 , Molar ratio of *p*-cresol to benzyl alcohol	3:1	3.5:1	4:1
X_3 , Amount of catalyst, % by wt. of *p*-cresol	1.0	3.0	5.0
Y, Response : Yield of 2-benzyl-4-methylphenol			

Table II. Experimental design

Trial no.	Replicates	Design		
		Temperature, X_1	Molar ratio, X_2	Amount of catalyst, X_3
1	2	-	-	-
2	2	+	-	-
3	2	-	+	-
4	2	+	+	-
5	2	-	-	+
6	2	+	-	+
7	2	-	+	+
8	2	+	+	+
9	4	0	0	0

Table III. Results of three-factor experiment

Trial no.	Results				
	Yield, %				
	Y_1	Y_2	$\overline{Y}$	Range	Variances
1	30.4	31.2	30.8	1	0.32
2	46.9	48.1	47.5	1	0.72
3	37.4	38.4	37.9	1	0.50
4	50.6	51.8	51.2	1	0.72
5	70.6	72.0	71.3	1	0.98
6	85.0	86.8	85.9	2	1.62
7	77.4	79.0	78.2	2	1.28
8	90.1	92.3	91.2	2	2.42
9	60.2 60.7	61.5 62.0	61.1	2	0.647

and the variance were calculated for each trial. The variance, which is an estimate of dispersion of data, was calculated by the following formula :

Variance = S^2 =

$$\frac{\left(Y_1 - \overline{Y}\right)^2 + \left(Y_2 - \overline{Y}\right)^2 + ... + \left(Y_n - \overline{Y}\right)^2}{n-1}$$

where Y = response value, $\overline{Y}$ = average or mean of response values, n = number of observations

For example, for trial 1,

Variance = $S_1^2 = \dfrac{\left(30.4 - 30.8\right)^2 + \left(31.2 - 30.8\right)^2}{2-1}$

$= 0.16 + 0.16 = 0.32$

and for trial 9,

Variance $= S_9^2 =$

$$\frac{(60.2-61.1)^2+(60.7-61.1)^2+(61.5-61.1)^2+(62.0-61.1)^2}{4-1}$$
$$= 0.647$$

The variances calculated for each trial were then used in the calculation of a weighted average of the individual variances for each trial.

Pooled variance $= S^2_{pooled} =$

$$\frac{(n_1-1)(S_1^2)+(n_2-1)(S_2^2)+.......+(n_K-1)(S_K^2)}{(n_1-1)+(n_2-1)+...............+(n_K-1)}$$

$$= \frac{0.32+0.72+0.50+0.72+0.98+1.62+1.28}{1+1+1+1+1+1+1+1+3}$$

$$\frac{+2.42+3\times0.647}{} = 0.955$$

The pooled standard deviation is the square root of the pooled variance :

Standard deviation $_{pooled} = \sqrt{S^2_{pooled}}$
$$= \sqrt{0.955} = 0.977$$

The pooled standard deviation used to calculate the minimum observed effect that was statistically significant.

The computation analysis for this experiment is shown in the Table IV. The design matrix was supplemented with a computation matrix, which was used to detect any interaction effect. This computation matrix was generated by simple algebraic multiplication of the coded factor levels. In trial 1, X_1 was minus, X_2 was minus, therefore, X_1X_2 was

plus; in trial 2, X_1 was plus, X_2 was minus, therefore X_1X_2 was minus. The column at the far right of the table is the average yield for each trial. The sum +'s row was generated by totaling the response values on each row with a plus for each column. For X_1 factor, 47.5 + 51.2 + 85.9 + 91.2 = 275.8. In the similar manner the sum —'s row was generated. The sum of these two rows should equal the sum of all the average responses and was included as a check on the calculations. The difference row represented the difference between the responses in the four trials when the factor was at a high level and the responses in the four trials when the factor was at a low level. The effect was then calculated by dividing the difference by the number of plus signs in the column.

In the first column, labeled mean, the effect row value was the mean or average of all data points. The average of the centre point runs, Trial 9, was then subtracted from the mean effect to give a measure of curvature.

The minimum significant factor effect [MIN] and the minimum significant curvature effect [MINC] were again derived from t-test significance criteria. The relationships are:

$$[MIN] = t.s\sqrt{\frac{2}{m.k}}$$

$$[MINC] = t.s\sqrt{\frac{1}{m.k}+\frac{1}{c}}$$

where t = appropriate value from "t- table", s = pooled standard deviation, m = number of

plus signs in column, k = number of replicates in each trial, c = number of centre points. The t value of 2.20 is from the student's "t" table for the 95 % confidence level and 11 degrees of freedom (Davies, 1979). The degrees of freedom result from eight trials with two replicates and one trial with four replicates.

Degrees of freedom = $8(2-1) + 1(4-1) = 11$

The calculations for the minimum significant effects are as follows:

$[MIN] = 2.20 \times 0.977 \times \sqrt{\frac{2}{4\times 2}} = 1.075$

$[MINC] = 2.20 \times 0.977 \times \sqrt{\frac{2}{8\times 2} + \frac{1}{4}} = 1.202$

Applying these criteria to the calculated effects, it was seen that the effects of temperature (X_1), molar ratio of p-cresol to benzyl alcohol (X_2), amount of perchloric acid (X_3) and interaction between temperature and molar ratio of p-cresol to benzyl alcohol (X_1X_2) were significant. There was no significant curvature effect. These results were expressed as a mathematical model using a first order polynomial. The values for the co-efficient were one half the factor effects listed in the Table IV. Since these were based upon coded levels +1 and –1 that differed by two units.

$Y=61.75+7.2X_1+2.875X_2+19.9X_3-0.625X_1X_2$

Table IV. Computation matrix for three factor experiment

Trial	Mean	Design			Computation				Response
		X_1	X_2	X_3	X_1X_2	X_1X_3	X_2X_3	$X_1X_2X_3$	
1	+	-	-	-	+	+	+	-	30.8
2	+	+	-	-	-	-	+	+	47.5
3	+	-	+	-	-	+	-	+	37.9
4	+	+	+	-	+	-	-	-	51.2
5	+	-	-	+	+	-	-	+	71.3
6	+	+	-	+	-	+	-	-	85.9
7	+	-	+	+	-	-	+	-	78.2
8	+	+	+	+	+	+	+	+	91.2
Sum +'s	494.0	275.8	258.5	326.6	244.5	245.8	247.7	247.9	
Sum -'s	0.0	218.2	235.5	167.4	249.5	248.2	246.3	246.1	
Sum	494.0	494.0	494.0	494.0	494.0	494.0	494.0	494.0	
Diff.	494.0	57.6	23.0	159.2	-5.0	-2.40	1.40	1.80	
Effect	61.75	14.40*	5.75*	39.8*	-1.25*	-0.60	0.35	0.45	

Curvature = $61.75 - 61.10 = 0.65$

[Curvature = Mean effect–Average of central point runs $\overline{Y}$]

In this equation, the factors were expressed in coded units. These were converted into real units by substituting:

for temperature T (^{O}C),

$$X_1 = \frac{T - \frac{130+70}{2}}{\frac{130-70}{2}}$$

$$= \frac{T-100}{30}$$

for molar ratio (m:1),

$$X_2 = \frac{m - \frac{4+3}{2}}{\frac{4-3}{2}} = \frac{m-3.5}{0.5}$$

for the amount of catalyst (y),

$$X_3 = \frac{y - \frac{5+1}{2}}{\frac{5-1}{2}}$$

$$= \frac{y-3}{2}$$

These substitutions yielded the following final expression :

$$Y = 61.75 + 7.2\times(\tfrac{T-100}{30}) + 2.875 \times (\tfrac{m-3.5}{0.5})$$
$$+ 19.9 \times (\tfrac{y-3}{2}) - 0.625 \times (\tfrac{T-100}{30})(\tfrac{m-3.5}{0.5})$$

$$= -26.925 + 0.387 + 9.95m + 9.95y - 0.042Tm$$

For trial 1, temperature (T) = 70° C, molar ratio of *p*-cresol to benzyl alcohol (m:1) = 3:1 and the amount of catalyst (y) = 1 % by wt. of *p*-cresol. Therefore, yield calculated from the derived model,

$$Y_{(cal.)} = -26.925 + 0.387 \ 70 + 9.95 \ 3 + 9.95$$
$$1 - 0.042 \ 70 \ 3 \ = 31.1$$

Experimental average yield of the trial 1, $Y_{(exp.)}$ = 30.8

Hence, deviation = 0.3 and percentage deviation = 0.97

All the values of the experimental average yield and the calculated yield from the derived equation are shown in the Table V.

Table V. Experimental average yield and calculated yield

Trial	Y (exp.)	Y (cal.)	Deviation	Percentage deviation
1	30.8	31.1	0.3	0.97
2	47.5	46.8	0.7	1.47
3	37.9	38.2	0.3	0.79
4	51.2	51.3	0.1	0.20
5	71.3	70.9	0.4	0.56
6	85.9	86.6	0.7	0.81
7	78.2	78.0	0.2	0.25
8	91.2	91.1	0.1	0.11

The discrepancies between the experimental and calculated values did not exceed 1.47 %.

Formation of 2-benzyl- 4-methylphenol can be shown by the following mechanism :
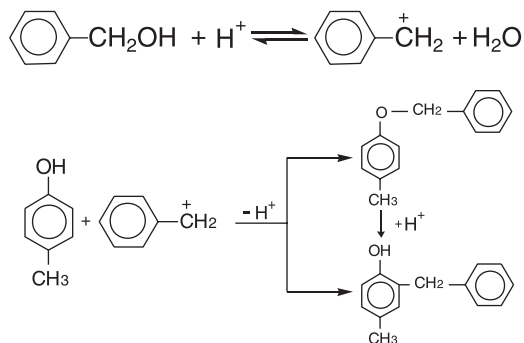
The product showed strong absorption at λ_{max} = 291.0 nm in 0.01M methanol solution in the UV- spectrum.

The IR spectrum of the product showed absorption bands at 810 cm^{-1} and 880 cm^{-1} for the 1, 2, 4- trisubstituted benzene ring. Absorption bands at 3510 cm^{-1}, 3020 cm^{-1}, 2900 cm^{-1} and 1595cm^{-1} indicated the presence of −OH group, aromatic =C−H, saturated C−H and benzene ring C ⋯ C stretch, respectively.

The ^{1}H NMR spectrum of 2-benzyl-4-methyl phenol showed in the Table VI.

Table VI   The ^{1}H NMR spectrum of 2-benzyl- 4-methyl phenol

Observed signals of the protons	Chemical shift in δ ppm
Three −CH$_3$ group protons	2.00
Two protons of −CH$_2$- on benzyl group	3.60 - 3.90
One proton on the −OH group	5.25
Eight protons on the two aromatic rings	6.20 - 7.20

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