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Statistical optimization of process variables in batch alkylation of *p*-cresol with *tert*-butyl alcohol using ionic liquid catalyst by response surface methodology

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ABSTRACT

Alkylation of *p*-cresol with *tert*-butyl alcohol was studied using ionic liquid catalyst prepared from N-(1,4-sulfonic acid) butyl triethylammonium hydrogen sulfate. An experimental design using response surface methodology (RSM) is used to optimize the process parameters in this batch alkylation to minimize rigorous experimental procedures and conserve the catalyst. The parameters, namely, temperature, reactant mole ratio, catalyst (IL) to *p*-cresol mole ratio and time of reaction on the conversion of *p*-cresol and yield of 2-*tert*-butyl-*p*-cresol (TBC) were optimized using Box–Behnken design. Low temperature, low *p*-cresol to alcohol ratio and low catalyst (IL) to *p*-cresol ratio in a batch reactor were found to maximize conversion of *p*-cresol and yield of TBC.

1. Introduction

Alkylated phenols are important antioxidants and used in petroleum products to improve octane number and as anti-gumming agents. Alkylation of *p*-cresol with *tert*-butyl alcohol (TBA) gives 2-*tert*-butyl-*p*-cresol (TBC) and 2,6-di-*tert*-butyl-*p*-cresol (DTBC) called butylated hydroxytoluene (BHT). Butylated *p*-cresol is used as an additive in food industry and also as an additive in jet fuels, petroleum products, cosmetics, pharmaceuticals, rubber and as antiseptic, polymerization inhibitor and UV-absorber [1–3]. Earlier researchers reported the use of both homogeneous and heterogeneous catalysts for the production of butylated *p*-cresol [4–9]. However, all these catalysts and processes have one or more problems related to product selectivity, spent catalyst disposal, environmental safety and catalyst recyclability. Recently, there has been an increasing interest in developing catalytic processes with minimum environmental threats and maximum economic benefits. Ionic liquids (ILs) have growing potential applications as environmentally benign alternative reaction media in organic transformations [10–12]. They possess attractive properties such as negligible vapor pressure, excellent chemical and thermal stability, potential recoverability and recyclability [13–16]. Before they can be used commercially on an industrial scale, the process variables need to be optimized in the laboratory, both in batch, and continuous reactor systems, for maximum reactant conversion and product yield. In order to minimize the wastage of the laboratory prepared catalyst by rigorous experimental procedures, statistical techniques are used for parameter optimization. Hence, the present work was taken up to establish the optimum conditions for the alkylation of *p*-cresol with *tert*-butyl alcohol in a laboratory prepared Bronsted acid functionalized ionic liquid catalyst using the response surface methodology (RSM).

2. Experimental

2.1. Materials and reagents

The experiments were conducted using commercially available solvent and chemicals and are used without further purification. Triethylamine and 1,4-butane-sultone are supplied by M/s Sigma–Aldrich Chemicals Pvt. Ltd., India. *p*-Cresol and *tert*-butanol are supplied by M/s Merck & CDH., New Delhi, India.

2.2. Preparation of ionic liquids

In a typical ionic liquid (N-(1,4-sulfonic acid) butyl triethylammonium hydrogen sulfate) preparation procedure [16–18], triethylamine (0.1 mol) was mixed with 1,4-butane-sultone (0.1 mol) stirring continuously for about 6–12 h at 353 K. After solidification, the zwitterion mass was washed with ethyl ether and then dried under vacuum. A stoichiometric amount of sulfuric acid (0.1 mol) was then added to the precursor zwitterion. The mixture was stirred at 353 K for 8 h to obtain the ionic liquid.

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Table 1
Parameter levels and coded values used in the experimental design.

Factors	Symbol	Range and level		
		−1	0	+1
Time (min)	X_1	30	300	570
Temperature (°C)	X_2	50	70	90
Reactant ratio	X_3	0.5	1	1.5
Catalyst (IL) to *p*-cresol ratio	X_4	0.5	0.75	1

2.3. Batch alkylation

The alkylation using the ionic liquid catalysts was carried out in sealed glass tube equipped with a magnetic stirrer under autogeneous pressure. Typical batch reactions consist of 10 mmol of *p*-cresol, TBA and ionic liquids. The reaction temperature was maintained at 343 K and the reaction mixture was stirred for 570 min. At the end of the reaction, the mixture was cooled and the products were extracted by toluene. The value of 343 K for the reaction temperature is a particular value, only for some of the different experiments carried out, and other values of 323 and 363 (the low and high levels for this parameter) have been used according to Tables 1 and 2. The value of 570 min is typical in some of the experiments and the other values 30 and 300 (the low and medium levels of this parameter) have been used according to Tables 1 and 2. Similarly, the values of *p*-cresol to TBA mole ratio are varied from 0.5 to 1.5 and the values of *p*-cresol to ionic liquid mole ratio 0.5–1.5 have been used.

A qualitative product analysis was conducted with a GC–MS and quantitative analyses were conducted with a NUCON GC supplied by AIMIL India Ltd. in a CHROMSORB-WHP (2 m × 3.175 mm × 2 mm) column using a flame ionization detector.

2.4. Experimental design using response surface methodology (RSM)

Response surface methodology is a compilation of statistical and mathematical methods that are useful for modeling and analyzing engineering problems [19]. The various process parameters can be optimized using one of the surface response techniques. Response surface methodology computes the relationship between the convenient input parameters and the achieved response surfaces [20–22].

The objective of the present research was to study the combined effects of time, temperature, reactant ratio and amount of ionic liquid on the phenol conversion and selective yield of TBC. This is a complex response under various combinations of these factors. Generally, 2 factorial design with 2 levels is used for such experimental design. This problem involves 4 factors and 3 levels design for multiresponse (i.e., two in this case). For this, Box–Behnken method has better accuracy since it is a spherical, revolving and linear trend free design. It generates the second order model from the experimental responses by response surface methodology in central composite design (CCD). Moreover, this method is used for all the systems with effective curvature in the response. Box–Behnken design requires a number of experimental runs according to $N = K^2 + K + \text{Cp}$, where K is the factor number and Cp is the replicate number of central point. This design involves studying the effects of 3 levels and 4 factors in a single block of 27 sets of test conditions and 4 central points (i.e., four experiments). Time (X_1), temperature (X_2), reactant ratio of *p*-cresol to TBA (X_3) and catalyst (ionic liquids) to *p*-cresol ratio (X_4) were independent variables studied to predict the response. The selection of assigned values for the low and high levels was based on values given in literature for alkylation of *m*-cresol by TBA using similar ionic liquid catalysts [15] as well as initial experiments of alkylation of *p*-cresol by TBA in ionic catalysts. The speed of the stirrer in

Table 2
Experimental design and response value.

Run no.	X_1	X_2	X_3	X_4	Conversion of *p*-cresol (Y_C)	Yield of TBC (Y_Y)
1	−1	−1	0	0	18.5	13.6
2	1	−1	0	0	68.4	51.2
3	−1	1	0	0	41.3	37.6
4	1	1	0	0	72.1	65.7
5	0	0	−1	−1	36.8	27.6
6	0	0	1	−1	66.4	51.2
7	0	0	−1	1	40.5	34.9
8	0	0	1	1	76.4	63.8
9	−1	0	0	−1	22.6	18.6
10	1	0	0	−1	65.3	57.1
11	−1	0	0	1	46.8	40.3
12	1	0	0	1	82.3	71.7
13	0	−1	−1	0	39.2	30.6
14	0	1	−1	0	37.8	35.4
15	0	−1	1	0	61.4	47.1
16	0	1	1	0	76.3	69.5
17	−1	0	−1	0	16.4	13.6
18	1	0	−1	0	41.6	36.3
19	−1	0	1	0	39.4	32.6
20	1	0	1	0	77.6	65.3
21	0	−1	0	−1	61.3	44.8
22	0	1	0	−1	68.8	49.9
23	0	−1	0	1	64.7	49.6
24	0	1	0	1	74.6	66.4
25	0	0	0	0	81.6	69.6
26	0	0	0	0	80.4	68.9
27	0	0	0	0	81.2	69.1

Table 3
Estimated regression coefficients and corresponding statistical *t*- and *P*-values for conversion of *p*-cresol (Y_C).

Term	Coefficient factor	*t*	*P*
Constant	60.141	−4.187	0.001
X_1	0.054	5.765	0.001
X_2	0.963	3.402	0.005
X_3	31.711	4.277	0.001
X_4	71.957	2.286	0.041
X_1^2	0.0001	−8.870	0
X_2^2	0.006	−3.923	0.002
X_3^2	9.308	−7.984	0.001
X_4^2	37.234	−2.790	0.016
$X_1 \times X_2$	0.001	−2.149	0.053
$X_1 \times X_3$	0.020	1.209	0.250
$X_1 \times X_4$	0.040	−0.670	0.516
$X_2 \times X_3$	0.269	1.517	0.155
$X_2 \times X_4$	0.537	0.223	0.827
$X_3 \times X_4$	21.497	0.493	0.631

Table 4
Estimated regression coefficients and corresponding statistical *t*- and *P*-values for yield of TBC (Y_Y).

Term	Coefficient factor	*t*	*P*
Constant	39.043	−5.674	0.001
X_1	0.035	6.465	0.001
X_2	0.625	4.538	0.001
X_3	20.587	5.242	0.001
X_4	46.714	3.410	0.005
X_1^2	0.0001	−10.867	0.001
X_2^2	0.004	−6.084	0.001
X_3^2	6.043	−10.511	0.001
X_4^2	24.172	−4.884	0.001
$X_1 \times X_2$	0.000	−1.361	0.198
$X_1 \times X_3$	0.013	1.433	0.177
$X_1 \times X_4$	0.026	−1.018	0.329
$X_2 \times X_3$	0.174	2.522	0.027
$X_2 \times X_4$	0.349	1.677	0.119
$X_3 \times X_4$	13.956	0.760	0.462

Table 5
Experimental and predicted values of conversion of *p*-cresol and yield of TBC.

Run no.	Experimental conversion	Predicted conversion	Residual in conversion	Experimental yield	Predicted yield	Residual in yield
1	14.5	21.55	−7.05	13.6	18.0	−4.40
2	68.4	70.81	−2.41	51.2	54.6	−3.38
3	41.3	43.33	−2.03	37.6	37.4	0.25
4	72.1	69.50	2.60	65.7	64.4	1.27
5	36.8	37.05	−0.25	27.6	28.2	−0.62
6	66.4	65.10	1.30	51.2	50.8	0.45
7	38.5	44.25	−5.75	34.9	38.5	−3.58
8	73.4	77.60	−4.20	63.8	66.3	−2.52
9	22.6	28.35	−5.75	18.6	21.3	−2.65
10	65.3	69.67	−4.37	57.1	56.6	0.46
11	46.8	41.80	5.00	40.3	37.7	2.58
12	82.3	75.92	6.38	71.7	66.0	5.70
13	39.2	36.97	2.23	30.6	28.6	1.96
14	37.8	39.05	−1.25	35.4	34.4	0.96
15	61.4	59.52	1.88	47.1	45.0	2.08
16	76.3	77.90	−1.60	69.5	68.4	1.08
17	16.4	10.89	5.51	13.6	10.9	2.70
18	41.6	42.10	−0.50	36.3	37.7	−1.43
19	39.4	35.09	4.31	32.6	31.1	1.52
20	77.6	79.30	−1.70	65.3	67.9	−2.61
21	61.3	56.00	5.30	44.8	41.8	3.00
22	68.8	65.04	3.76	49.9	50.5	−0.65
23	64.7	64.65	0.05	49.6	48.9	0.74
24	74.6	76.09	−1.49	66.4	69.3	−2.91
25	81.6	81.07	0.53	69.6	69.2	0.40
26	80.4	81.07	−0.67	68.9	69.2	−0.30
27	81.2	81.07	0.13	69.1	69.2	−0.10

the reactor system was maintained constant and the reaction was conducted under autogeneous pressure, therefore, these effects are not considered in this model. The order of the experiments is fully randomized. In this study, the Box–Behnken experimental design is chosen to estimate the relationship between conversion of *p*-cresol and yield of TBC with temperature, ionic liquid to *p*-cresol ratio and molar ratio of *p*-cresol to *tert*-butyl alcohol. A 3^4 full-factorial central composite design with three coded levels leading to 27 sets of experiments was performed. Four variables were tested at levels by associated plus signs (+1) with high levels, zero (0) indicating centre value and minus signs (−1) with low levels. For statistical computation, the variables were coded according to Eq. (1) below:

$$X_i = \frac{U_i - U_0}{\Delta U_i} \quad (1)$$

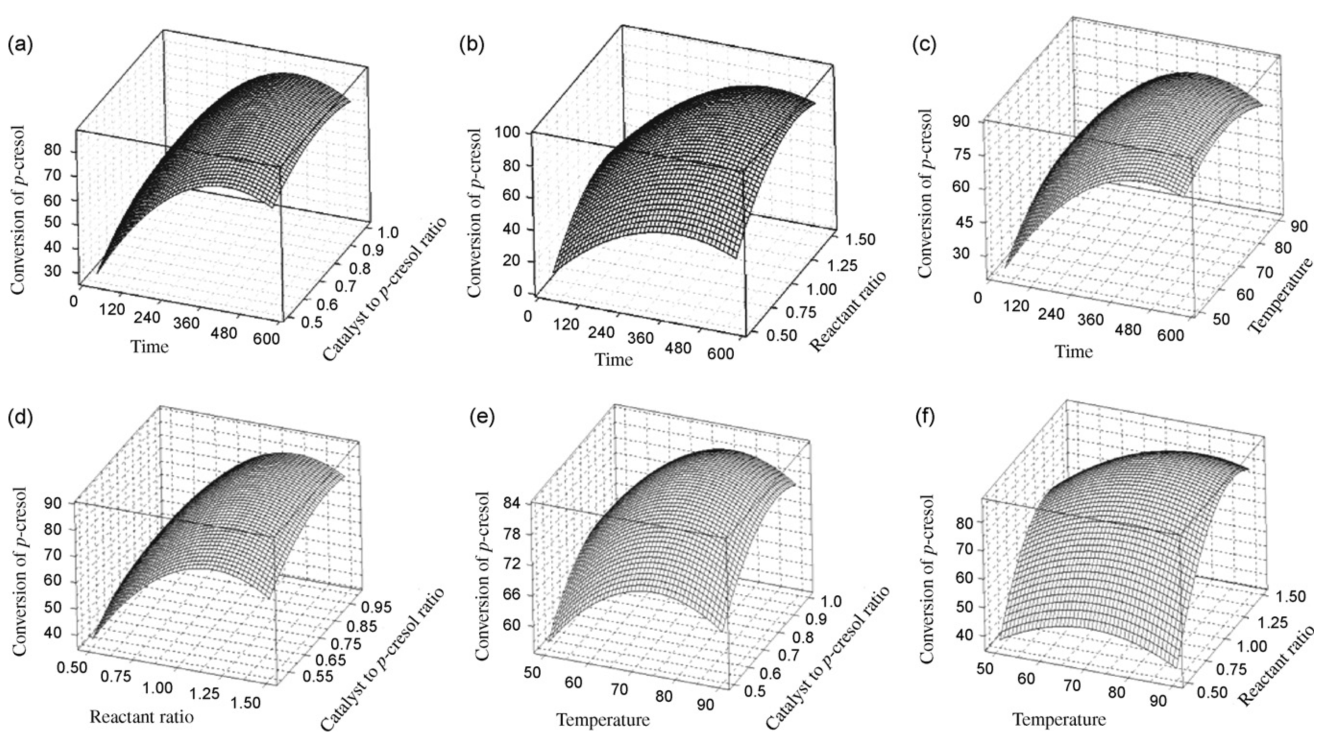

Fig. 1. Response surface plot showing the predicted values of *p*-cresol conversion: effect of time and catalyst *p*-cresol ratio (a), time and reactant ratio (b), time and temperature (c), reactant ratio and catalyst to *p*-cresol ratio (d), temperature and catalyst to *p*-cresol ratio (e) and temperature and reactant ratio (f) on *p*-cresol conversion. Other variables are held at constant level.

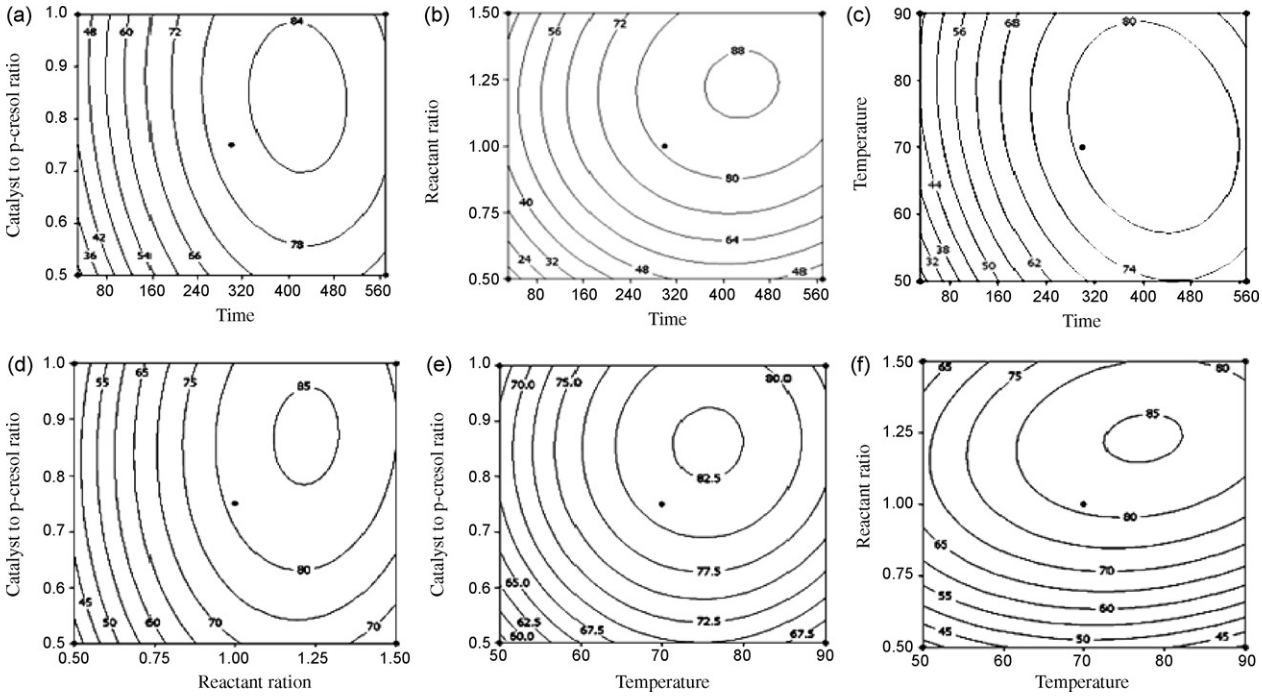

Fig. 2. Contour plot showing the predicted *p*-cresol conversion: effect of time and catalyst *p*-cresol ratio (a), time and reactant ratio (b), time and temperature (c), reactant ratio and catalyst to *p*-cresol ratio (d), temperature and catalyst to *p*-cresol ratio (e) and temperature and reactant ratio (f) on *p*-cresol conversion. Other variables are held at constant level.

where X_i is the independent variable coded value; U_i is the independent variable real value; U_0 is the independent variable real value on the centre point; and ΔU_i, step change value.

The mathematical relationship among the three variables and response is approximated by the second order polynomial Eq. (2) [23]:

$$Y_c = a_0 + \sum a_i x_i + \sum a_{ii} x_i^2 + \sum a_{ij} x_i x_j \tag{2}$$

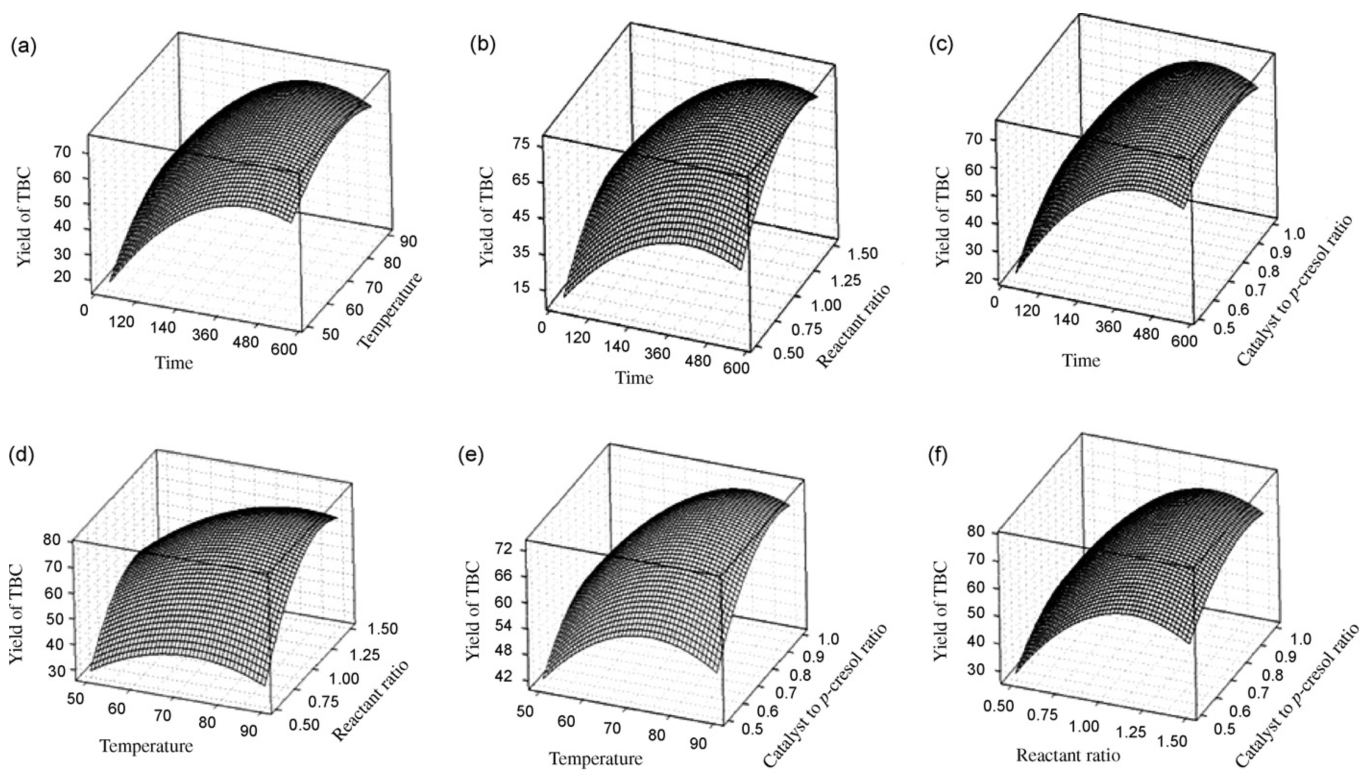

Fig. 3. Response surface plot showing the predicted yield of TBC (*tert*-butyl *p*-cresol): effect of time and temperature (a), time and reactant ratio (b), time and catalyst *p*-cresol ratio (c), temperature and reactant ratio (d), temperature and catalyst to *p*-cresol ratio (e) and reactant ratio and catalyst to *p*-cresol ratio (f) on yield of TBC. Other variables are held at constant level.

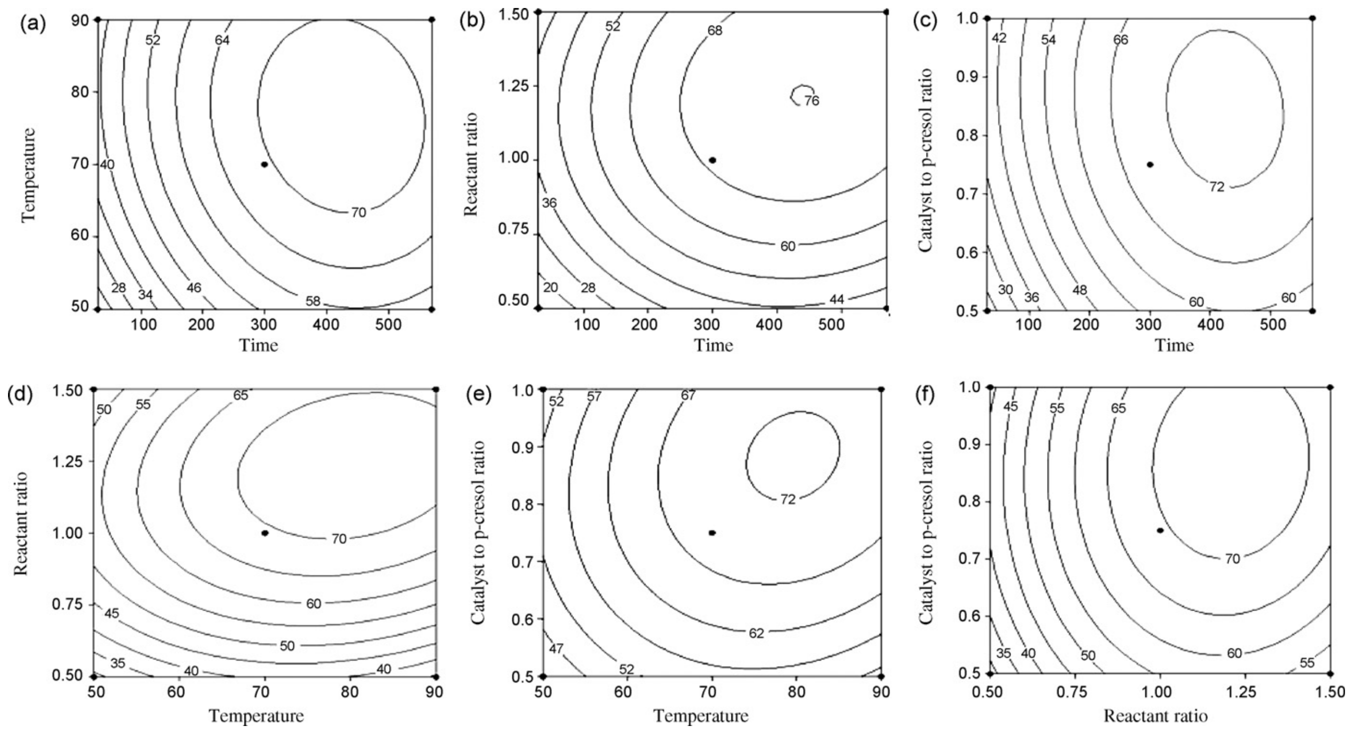

Fig. 4. Contour plot showing the predicted yield of TBC (*tert*-butyl *p*-cresol): effect of time and temperature (a), time and reactant ratio (b), time and catalyst *p*-cresol ratio (c), temperature and reactant ratio (d), temperature and catalyst to *p*-cresol ratio (e) and reactant ratio and catalyst to *p*-cresol ratio (f) on yield of TBC. Other variables are held at constant level.

where Y_c is the predicted response by the model; X_1, X_2, X_3 are independent variables; a_0 is equation constant; a_i, a_{ii}, a_{ij} are regression coefficients of the model. The accuracy and general ability of the second order multiple regression models could be evaluated by the coefficient of determination (R^2). The coefficients, a_i and two interaction factors a_{ii} and a_{ij} have been estimated from the experimental results. The 'MINITAB^{TM}' (version 15) software is used for regression analysis of the experimental data and the response. The quality of the multiple regression model fit are expressed by the coefficient of regression R^2 and *F*-test used for checking its statistical significance. The significance of the regression coefficient was tested by a Student's *t*-test. The confidence levels of the experimental values are about 95% [22].

3. Results and discussion

The fractional factorial experimental design was chosen for the optimization due to the reduced number of cumbersome experiments without significant loss of information [24]. Independent variables and their levels for the Box–Behnken design used in this study are shown in Table 1. By the relationship in Table 1, the actual level of the variables for all experiments in the design matrix were determined and experimental results achieved as given in Table 2. The relationship between *p*-cresol conversion, yield of TBC and the process variables were obtained for the coded units using Eq. (2) and the coefficients are presented in Tables 3 and 4.

The Student's *t*-test was used to determine the significance of the regression coefficients of the parameters. The *P* values were used as a tool to check the significance of each of the interactions among the variables. In general, the Fischer's '*F*-test' value with a low probability *P* value indicates high significance of the regression model. The larger the value of *t* and smaller the value of *P*, the more significant is the corresponding coefficient term. Tables 3 and 4 list the regression coefficients, *t* and *P* values for all the linear, quadratic and interaction effects of the parameters. From these tables, the coefficients for the linear and quadratic effect of time, temperature, reactant ratio and catalyst to *p*-cresol ratio ($P < 0.05$) were highly significant. The coefficients of interactive effects were least significant as compared to linear and quadratic coefficients. The experimental and predicted values of conversion of *p*-cresol (Y_C) and yield of TBC (Y_Y) are given in Table 5.

The analysis of variance (ANOVA) table was used to test the statistical significance of the ratio of mean square due to regression and mean square due to residual error. The result of this in the form of analysis of variance (ANOVA) is given in Tables 6 and 7. From this table it is evident that, the *F*-statistical values of linear and squared regression were higher. Generally, *P* values lower than 0.05 indicate that the model is considered to be statistically significant at the 95% confidence level. The *F*-test values for all regressions were higher; the large value of *F* indicates that nearly all of the variation in the response can be clarified by the regression model equation [25]. The *F*-test value of *p*-cresol conversion and yield of TBC is greater than tabulated $F_{0.05}$ (9, 5)-test (2.64) which indicates that the second order polynomial equation is highly significant and adequate to represent the actual relationship between the response and the

Table 6
Analysis of variance model regression on conversion of *p*-cresol.

Source	DF	Seq. SS	Adj. SS	MS	F	P
Regression	14	11,127.70	11,127.67	794.834	27.520	0.000
Linear	4	7,700.30	1,362.68	340.670	11.800	0.000
Square	4	3,163.80	3,163.83	790.958	27.390	0.000
Interaction	6	263.50	263.50	43.916	1.520	0.252
Residual error	12	346.60	346.590	28.882	28.882	
Lack-of-fit	10	345.80	345.840	34.584	92.640	0.011
Pure error	2	0.700	0.750	0.373		
Total	26	11,474.3				

R^2 = 96.98%, R^2 (adj.) = 93.46%, $F_{0.05}$ (9, 5) = 2.64.
DF, degree of freedom; SS, sum of squares; MS, mean of squares; *F*, *F*-value; *P*, significance level of *P*-value (a significance level <0.05).

Table 7
Analysis of variance model regression on yield of TBC.

Source	DF	Seq. SS	Adj. SS	MS	*F*	*P*
Regression	14	8362.35	8362.35	597.31	49.07	0.000
Linear	4	6082.68	794.84	198.71	16.32	0.000
Square	4	2100.81	2100.81	525.20	43.15	0.000
Interaction	6	178.85	178.85	29.81	2.45	0.088
Residual error	12	146.07	146.07	12.17		
Lack-of-fit	10	145.81	145.81	14.58	112.16	0.009
Pure	2	0.26	0.26	0.13		
Total	26	8508.42				

R^2 = 98.28%, R^2 (adj.) = 96.28%, $F_{0.05}$ (9, 5) = 2.64.
DF, degree of freedom; SS, sum of squares; MS, mean of squares; F, *F*-value; *P*, significance level of *P*-value (a significance level <0.05).

variables. Predicted values of *p*-cresol conversion and TBC yield are presented in Figs. 1–4. Predicted values match with the experimental data points, indicating a good fitness (R^2 value of 0.97 for conversion of *p*-cresol and R^2 value of 0.96 for yield of TBC). The three dimensional response plots and contour plots obtained from the predicted models are presented in Figs. 1 and 3 and Figs. 2 and 4, respectively. The response surfaces of mutual interactions among the variables were found to be elliptical. The response surface and contour plots given in Figs. 1–4 show the relative effects of any two variables when the other variables are kept constant.

4. Conclusion

Liquid phase batch alkylation of *p*-cresol with *tert*-butyl alcohol was performed, in an attempt to optimize and study the linear, square and interactive effects of process parameters namely, time, temperature, reactant mole ratio and catalyst (ionic liquid) to *p*-cresol mole ratio on the conversion of *p*-cresol and yield of TBC. Graphical response surface method is used to locate the optimum point. A fractional factorial design and central composite design were applied to establish second order model relating to the alkylation of *p*-cresol with *tert*-butyl alcohol. *F*-test and *P* values show the parameters have very significant influence on the *p*-cresol conversion and the TBC yield. The optimum parameters for the batch alkylation of *p*-cresol with TBA using sulfonic acid functionalized ionic liquid catalyst are, a temperature of 348 K, *p*-cresol to alcohol ratio of 1:1.25, catalyst (IL) to *p*-cresol ratio of 1:0.85 and 420 min reaction time. This set of optimum parameters gives a maximum of 89.4% conversion of *p*-cresol and a maximum 78.6% yield of TBC.

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