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Optimization of process conditions for catalytic alkylation of isomeric cresols with cyclohexene

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Abstract

Alkylation of isomeric cresols with cyclohexene in presence of perchloric acid as catalyst was studied and cyclohexyl cresols obtained in high yield. The effects of the variation of reaction parameters such as temperature, molar ratio of cresol to cyclohexene, amount of perchloric acid and time of reaction were investigated. The yield of the products increased with the increase of each of the above-mentioned parameters. Optimum yield (97.6% for cyclohexyl *m*-cresol; 95.4% for 2-cyclohexyl-4-methylphenol and 91.2% for cyclohexyl *o*-cresol) of the products were obtained under the reaction conditions of a temperature of 140°C; an 8-6:1 molar ratio of cresol to cyclohexene, a 5% by weight perchloric acid of cresol, a 2 h time of addition of cyclohexene and a 2 h time of stirring of the reaction mixture. Considering the yields of cyclohexyl cresols and ease of purifications, the above mentioned conditions were accounted as optimum for the alkylation of isomeric cresols with cyclohexene in the presence of perchloric acid.

Keywords: Alkylation, Cyclohexene, Isomeric cresols, Process optimization.

Introduction

The alkylation of aromatic substrates is important in many sectors of the chemical industry. Alkylation of cresols has earned much interest of the scientists since alkylated cresols may be used as raw materials for the production of resins, durable surface coatings, varnishes, printing inks, surface active agents, antioxidants, fungicides, petroleum additives, and multifunctional stabilizers for fuels, lubricating oils and polymeric materials (Krishnan *et al.,* 2002; Lebedev, 1984; Ravikovich, 1984; Sakthivel *et al.*, 2000; Sato *et al.,* 2001; Subramanian *et al.,* 1997; Zhang *et al.,* 2001). Catalytic alkylations of isomeric cresols with different alcohols and esters have been studied by several research groups (Basak *et al.,* 2004; Devassy *et al.,* 2004; Grabowska *et al.,* 2004; Grabowska and Wrzyszcz, 2001; Saha *et al.,* 2001; Saha and Roy, 1992; Shanmugapriya *et al.,* 2006; Velu and Sivasankar, 1998; Yadav *et al.,* 1999; Yadav and Pathre, 2006). Reports are also available on the alkylation of isomeric cresols with olefins and styrene in presence of different catalysts (Chaudhuri *et al.,* 1990; Kozlikovskii *et al.,* 1986; Sadykhov *et al.,* 1996; Saha *et al.,* 1997; Trocsanyi, 1975; Yadav and Pala, 2000). While alkylation of cresols with alkenes especially cyclohexene was not studied so much. With the best of our knowledge only alkylation of *o*-, *m*-, and *p*- cresols with cyclohexene in the presence of aluminum cresolates have been studied (Kozlikovskii, 1887), but no -

attempt has so far been made to investigate the reaction of isomeric cresols with cyclohexene in the presence of perchloric acid. Perchloric acid is a protic acid catalyst of industrial importance due to the fact that it is stronger in its action, comparatively less corrosive, and causes no undesirable side reaction.

Process optimization is the discipline of adjusting a manufacturing process so as to optimize some specified set of parameters without violating some constraint. The most common goals are minimizing cost, maximizing throughput, and/or efficiency.

The optimization of chemical processes is a major activity in both process development and library production groups within the chemical industry. Chemistry process optimization requires an understanding of which variables are important to the outcome (yield, purity, cost, etc.) and to what level the variables should be set. As in most scientific disciplines, chemists have historically followed the practice of changing one variable at a time (OVAT) during optimization. Each variable is scanned this way, and the combination of their optimum values is accepted as the global optimum.

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In the present work, the reaction of *ortho*-, *meta*- and *para*-cresols with cyclohexene in the presence of perchloric acid as catalyst has been investigated and the yield of cyclohexyl cresols optimized using a set of input variables that included reactant parameters (amount of catalyst and molar ratio of cresol to cyclohexene) and processing variables (temperature, and reaction time).

Materials and Methods

Chemicals used in this work were purchased from Merck Chemicals Co. and were used without further purification unless stated. Perchloric acid was used as catalyst.

The reactions were carried out in a three necked round bottomed flask fitted with a condenser, a thermometer, a dropping funnel and a stirrer. Cresol-catalyst mixture was charged into the flask, heated to the temperature of the experiment, the cyclohexene was introduced into the mixture gradually over 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 addition of the total amount of cyclohexene. The reaction mass was then cooled to room temperature and neutralized with an equivalent amount of 10% KOH solution. The neutralized reaction mass was then dissolved in diethyl ether, washed with distilled water several times and dried with anhydrous magnesium sulfate. Unreacted reactants and solvent were distilled off at atmospheric pressure. The product thus obtained was subjected to fractionation by distillation and characterized by physico-chemical and spectral means.

Results and Discussion

Alkylation of *m*-cresol

Reaction of m-cresol with cyclohexene was investigated in the presence of perchloric acid over the temperature range of 60 to 140ºC. The reaction gave cyclohexyl *m*-cresol (cyclohexyl group substituted the aromatic ring to the *ortho*- or *para*- position with respect to the -OH group). The effect of the variation of temperature, molar ratio of *m*-cresol to cyclohexene, amount of perchloric acid and time of reaction have been shown in Figs. 1-4.

Fig. 1 shows that the yield of the product increased with the rise in temperature. Thus the yield increased from 67.8 to 94.5% when the temperature was raised from 60 to 140ºC.
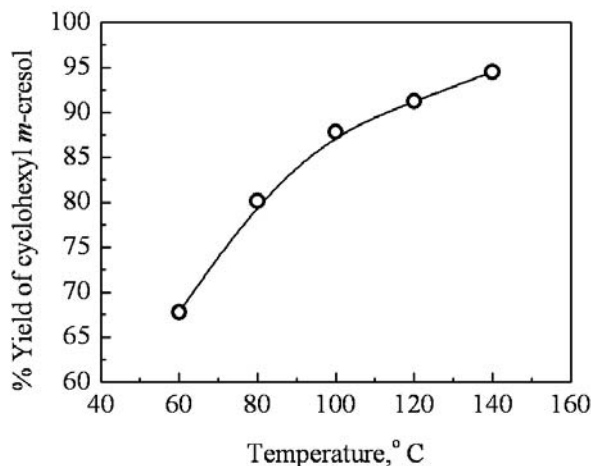

Fig. 1:   **The effect of variation of temperature on the reaction of *m*-cresol with cyclohexene in the presence of perchloric acid (molar ratio of *m*-cresol to cyclohexene = 8:1, amount of catalyst = 5% by wt. of *m*-cresol, time of addition = 2 h and time of stirring = 1 h)**
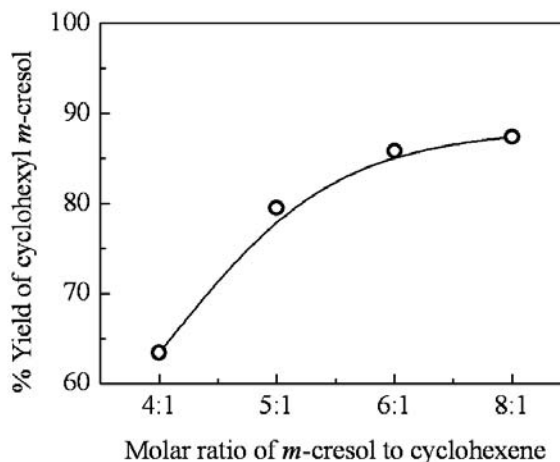

Fig. 2: **The effect of variation of molar ratio of *m*-cresol to cyclohexene on the reaction of *m*-cresol with cyclohexene in the presence of perchloric acid (temperature = 140ºC, amount of catalyst = 5% by wt. of *m*-cresol, time of addition = 2 h and time of stirring = 1 h).**

The yield of the product also depended on the molar ratio of *m*-cresol to cyclohexene (Fig. 2). The yield of cyclohexyl m-cresol increased from 63.4 to 87.4% on increasing the molar ratio of *m*-cresol to cyclohexene from 4:1 to 8:1.

The effect of the variation of the amount of perchloric acid showed that the yield of the product increased with the

increase of the amount of catalyst (Fig. 3). By changing the amount of catalyst from 1 to 5% by wt. of m-cresol, the yield of the product raised from 78.4 to 94.5%. The best yield was obtained when the amount of catalyst was taken in an amount of 5% by wt. of *m*-cresol.
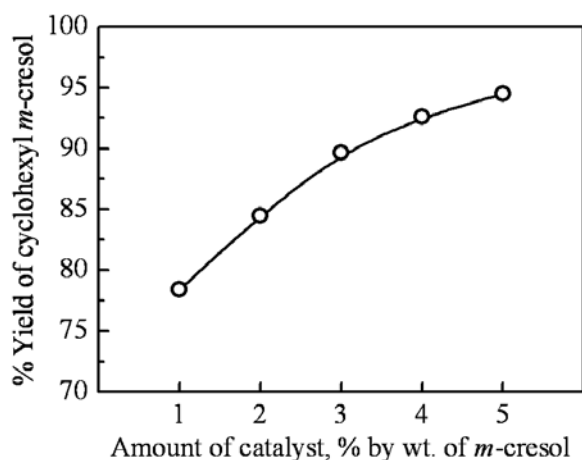

Fig. 3: **The effect of variation of the amount of perchloric acid on the reaction of *m*-cresol with cyclohexene (temperature = 140ºC, molar ratio of *m*-cresol to cyclohexene = 8:1, time of addition = 2 h and time of stirring = 1 h).**
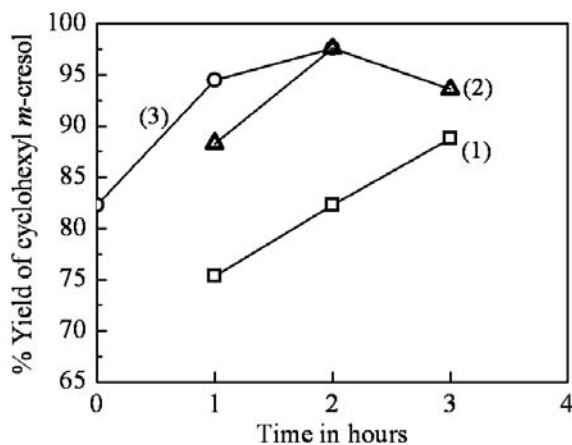

Fig. 4: **The effect of variation of reaction time on the yield of cyclohexyl *m*-cresol (temperature = 140ºC, molar ratio of *m*-cresol to cyclohexene = 8:1 and amount of catalyst = 5% by wt. of *m*-cresol): 1- The effect of variation of time of addition (time of stirring = 0 h); 2- The effect of variation of time of addition (total time of reaction = 4 h) and 3- The effect of variation of time of stirring (time of addition = 2h)**

Fig. 4 shows the effect of the variation of time of reaction on the yield of the product. The yield of the product increased with the increase of time of addition (Fig. 4, curve 1). By increasing the time of addition to a value greater than 2 h, no significant effect on the yield was observed (Fig. 4, curve 2). The yield also increased by additional stirring (Fig. 4, curve 3). The best yield was obtained when the time of stirring was 2 h.

Therefore, the following conditions may be considered as optimum (yield = 97.6%) for the production of cyclohexyl m-cresol: temperature = 140ºC, molar ratio of *m*-cresol to cyclohexene = 8:1, amount of perchloric acid = 5% by wt. of *m*-cresol, time of addition = 2 h and time of stirring = 2 h.

The UV spectrum of cyclohexyl m-cresol in 0.01 M petroleum ether solution showed a strong absorption at $\lambda_{max.}$ = 287.5 nm.

The IR spectrum of cyclohexyl *m*-cresol (Fig. 5) showed the absorption bands at 2850-2920 cm^{-1} for saturated C-H group while band at 775 cm^{-1} accounted for 1,2,3-trisubstituted benzene ring. Bands near 810 cm^{-1} and 855 cm^{-1} indicated the presence of 1, 2, 4-trisubstituted benzene ring and bands at 1570 cm^{-1} and 3400 cm^{-1} were due to aromatic ring and -OH group respectively.
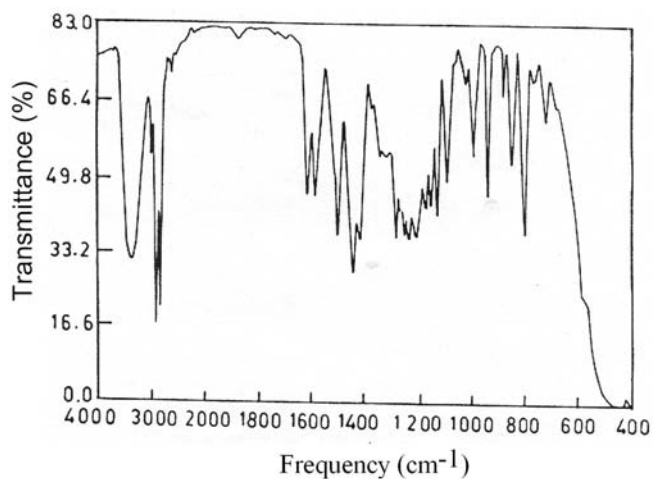

Fig. 5: IR-spectrum of cyclohexyl *m*-cresol

The ^{1}H NMR-spectrum of cyclohexyl *m*-cresol (Fig. 6) showed signal at δ = 6.13-7.17 ppm for aromatic ring protons. Signals for -OH group proton, methyl group protons, all the protons on the cyclohexane ring except one on the α-position relative to the aromatic ring and one proton on the

α-position were observed at δ = 5.0-5.85 ppm, δ = 2.03-2.46 ppm, δ = 0.77-2.03 ppm and δ = 2.46-3.17 respectively.

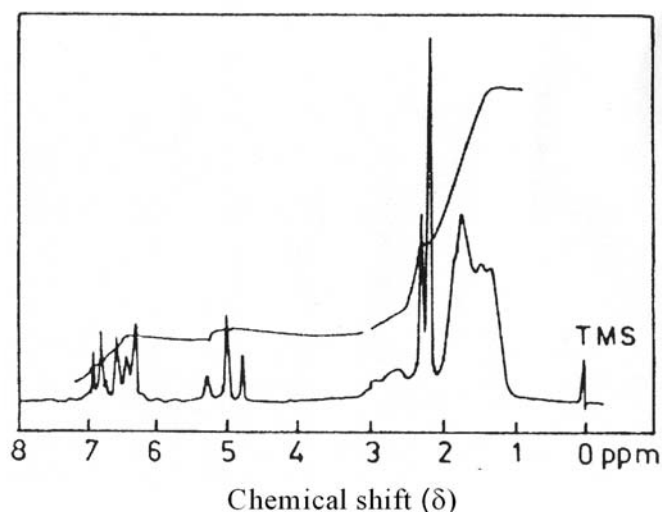Cyclohexyl *m*-cresol had b.p. = 310°C, d_4^{20} = 0.9971 and n_D^{20} = 1.5248.

Fig. 6: ^{1}H NMR-spectrum of cyclohexyl *m*-cresol

Alkylation of *p*-cresol

The results of the reaction of *p*-cresol with cyclohexene in the presence of perchloric acid are presented in the Tables I-IV. The reaction gave 2-cyclohexyl-4-methylphenol. The effects of the variation of temperature, molar ratio of *p*-cresol to cyclohexene, amount of perchloric acid and time of reaction on the yield of the product were investigated.

Like cyclohexyl *m*-cresol, the yield of 2-cyclohexyl-4-methylphenol increased with the increase of temperature (Table I). The yield increased from 51.3 to 74.3% on increasing the temperature from 60 to 140°C.

Table I: The effect of the variation of temperature on the reaction of *p*-cresol with cyclohexene in the presence of perchloric acid (molar ratio of *p*-cresol to cyclohexene = 4:1, amount of catalyst = 5% by wt. of *p*-cresol, time of addition = 2 h and time of stirring = 1 h)

Temp., °C	% Yield of 2-cyclohexyl-4-methylphenol
60	51.3
80	58.6
100	61.2
120	68.8
140	74.3

Table II: The effect of the variation of molar ratio of *p*-cresol to cyclohexene on the reaction of *p*-cresol with cyclohexene in the presence of perchloric acid (temperature = 140°C, amount of catalyst = 5% by wt. of *p*-cresol, time of addition = 2 h and time of stirring = 1 h)

Molar ratio of *p*-cresol to cyclohexene	% Yield of 2-cyclohexyl-4-methylphenol
4:1	74.3
5:1	81.2
6:1	86.8
8:1	93.6

The yield of the product also increased with the increase of the molar ratio of *p*-cresol to cyclohexene (Table II). The yield of the product increased from 74.3 to 93.6% when the molar ratio *p*-cresol to cyclohexene was increased from 4:1 to 8:1.

The effect of the variation of amount of perchloric acid showed that the yield of the product increased with increase of amount of perchloric acid (Table III). Thus the yield increased from 72.1 to 93.6% on increasing the amount of catalyst from 1 to 5%.

Table III: The effect of the variation of amount of perchloric acid on the reaction of *p*-cresol with cyclohexene (temperature = 140°C, molar ratio of *p*-cresol to cyclohexene = 8:1, time of addition = 2 h and time of stirring = 1 h)

Amount of catalyst, % by wt. of *p*-cresol	% Yield of 2-cyclohexyl-4-methylphenol
1	72.1
2	85.2
3	87.8
4	90.3
5	93.6

Table IV shows the effect of the variation of time of reaction on the yield of the product. The yield of the product increased with the increase of time of addition (Set 1). By increasing the time of addition to a value greater than 2 h, no significant effect on the yield was observed (Set 2). However, the yield also increased by additional stirring (Set 3). The best yield was obtained when the time of stirring was 2 h.

Table IV: **The effect of the variation of reaction time on the yield of cyclohexyl *p*-cresol (temperature = 140 ºC, molar ratio of *p*-cresol to cyclohexene = 8:1, amount of catalyst = 5% by wt. of *p*-cresol).**
   **(1)   The effect of variation of time of addition (time of stirring = 0 h).**
    (2)   The effect of variation of time of addition (total time of reaction = 4 h).
    (3)   The effect of variation of time of stirring (time of addition = 2 h).

No.	Time of addition t_a, h	Time of stirring t_s, h	Total time of reaction, $t = (t_a + t_s)$, h	% Yield of 2-cyclohexyl -4-methylphenol
	1	0	1	72.4
1	2	0	2	81.9
	3	0	3	87.4
	1	3	4	86.7
2	2	2	4	95.4
	3	1	4	91.2
	2	0	2	81.9
3	2	1	3	93.6
	2	2	4	95.4

Therefore, the maximum yield (95.4%) of 2-cyclohexyl-4-methylphenol was obtained under the following conditions: temperature = 140ºC, molar ratio of *p*-cresol to cyclohexene = 8:1, amount of perchloric acid = 5% by wt. of *p*-cresol, time of addition = 2 h and time of stirring = 2 h.

The UV spectrum of 2-cyclohexyl-4-methylphenol showed strong absorption at $\lambda_{max.}$ = 295.0 nm in 0.01 M methanol solution.

The IR spectrum of 2-cyclohexyl-4-methylphenol (Fig.7) showed bands at 800-900 for the presence of 1,2,4-trisubstituted benzene ring and band at 3400 cm^{-1} accounted for H-bonded -OH. The spectrum also showed absorption bands at
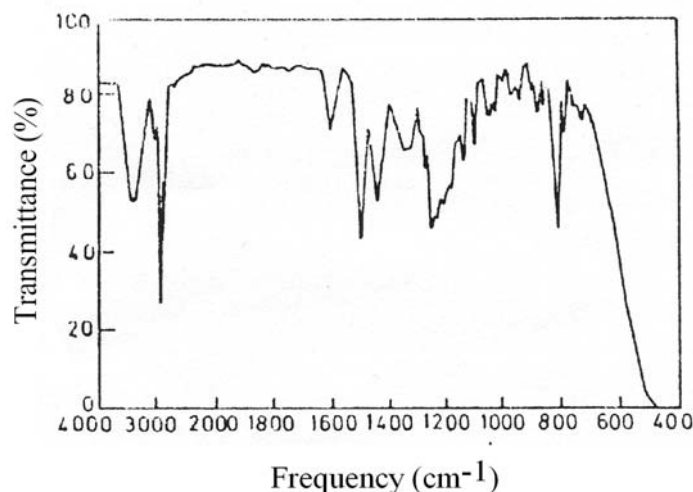
Fig. 7: IR-spectrum of 2-cyclohexyl-4-methyl phenol

2950 cm^{-1} and 3000 cm^{-1} for saturated C-H stretching. Band at 1600 cm^{-1} indicated benzene ring C — C.

Chemical shifts of the protons in the ^1H NMR-spectrum of 2-cyclohexyl-4-methylphenol (Fig. 8) are presented in the Table V.

Table V: ^1H NMR-spectrum of 2-cyclohexyl-4-methylphenol

Observed signals of the protons	Protons	Chemical shift in δ ppm
	a,b,c	6.25-7.00
	d	6.03
	x	2.46-3.13
	y	2.03-2.30
	z	0.50-2.04

2-Cyclohexyl-4-methylphenol had b.p. = 270ºC, d_4^{20} = 0.9917 and n_D^{20} = 1.5218.

Alkylation of *o*-cresol

The influence of the variation of parameters on the reaction of *o*-cresol with cyclohexene in presence of perchloric acid has been shown in Table VI. The reaction of *o*-cresol with cyclohexene under the conditions studied gave cyclohexyl *o*-cresol (cyclohexyl group substituted the aromatic ring to the *ortho*- and *para*- positions with respect to the -OH group).
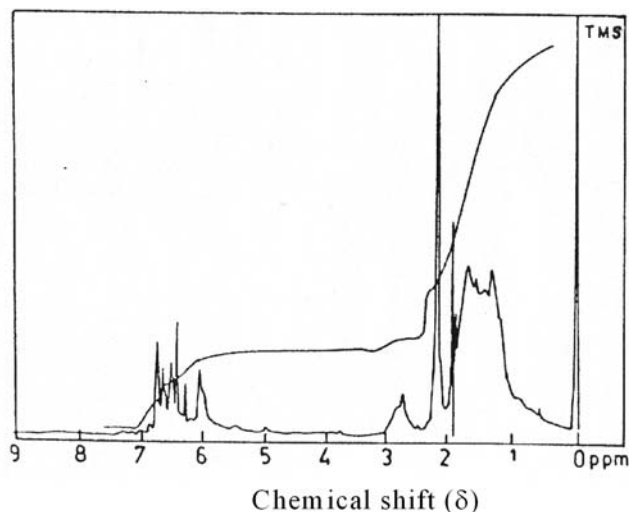
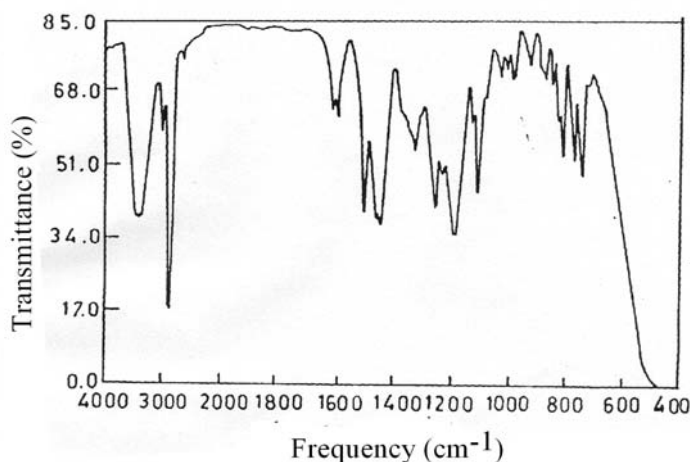**Fig. 8: ^{1}H NMR-spectrum of 2-cyclohexyl-4-methyl phenol**

Fig. 9: IR-spectrum of cyclohexyl o-cresol

Table VI: Alkylation of o-cresol with cyclohexene in the presence of perchloric acid

Expt. No.	Reaction Conditions					% Yield of cyclohexyl o-cresol
	Temp, ^{o}C	Molar ratio of o-cresol to cyclohexene	Amount of catalyst, % by wt. of o-cresol	Time of addition, h	Time of stirring, h	
1	60	4:1	1	2	1	41.2
2	140	4:1	1	2	1	61.2
3	60	6:1	1	2	1	47.8
4	140	6:1	1	2	1	74.4
5	60	4:1	5	2	1	44.8
6	140	4:1	5	2	1	68.6
7	60	6:1	5	2	1	67.4
8	140	6:1	5	2	1	89.5
9	140	6:1	5	2	2	91.2

As can be seen from Table VI, the yield of cyclohexyl o-cresol increased with the increase of temperature (Expt. No. 1, 2; 3, 4; 5, 6 and 7, 8), molar ratio of o-cresol to cyclohexene (Expt. No. 1, 3; 2, 4; 5, 7 and 6, 8), amount of catalyst (Expt. No. 1, 5; 2, 6; 3, 7 and 4, 8) and reaction time (Expt. No. 8, 9)

Thus, the reaction conditions so far studied, the best yield 91.2% of cyclohexyl o-cresol was obtained under the following conditions: temperature = 140°C, molar ratio of o-cresol to cyclohexene = 6:1, amount of perchloric acid = 5% by wt. of o-cresol, time of addition = 2 h and time of stirring = 2 h.

The UV spectrum of cyclohexyl o-cresol showed strong absorption at $\lambda_{max.}$ = 296.0 nm in 0.01 M petroleum ether solution.

In the IR spectrum of product (Fig. 9), absorption band at 775 cm^{-1} accounted for 1,2,3-trisubstituted aromatic ring,

while bands near 805 cm^{-1} and 855 cm^{-1} indicated the presence of 1,2,4-trisubstituted benzene ring. Band at 3400 cm^{-1} indicated the presence of -OH group. Aromatic C $\cdots$ C stretch and saturated C-H stretch were observed at 1570 cm^{-1} and 2850-2910 cm^{-1} respectively.

The ^{1}H NMR-spectrum of cyclohexyl o-cresol (Fig. 10) showed signal at = 6.26-7.1 ppm for aromatic ring protons. Signals for -OH group proton, methyl group protons, all the protons on the cyclohexyl group except one on the -position relative to the aromatic ring and one proton on the α -position were observed at δ = 4.84 ppm, δ = 2.03-2.33 ppm, δ = 0.94-2.03 ppm and δ = 2.33-3.23 respectively.

Cyclohexyl o-cresol had b.p. = 297°C, d_4^{20} = 1.0418 and n_D^{20} = 1.5459.
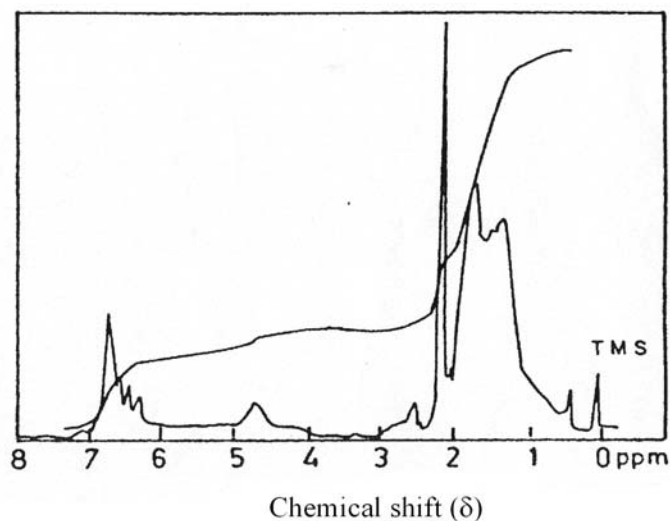
Fig. 10: ^{1}H NMR-spectrum of cyclohexyl *o*-cresol

Conclusion

The yield of alkylation of isomeric cresols with cyclohexene in presence of perchloric acid was optimized and the alkylated products were thoroughly characterized. Results of this study indicated that the effects of temperature, molar ratio of isomeric cresols to cyclohexene, amount of catalyst and time of reaction were significant. All these variables significantly affected the yield of cyclohexyl cresols. Optimum yield (97.6% for cyclohexyl *m*-cresol; 95.4% for 2-cyclohexyl-4-methylphenol and 91.2% for cyclohexyl *o*-cresol) of the products were obtained under the reaction conditions of a temperature of 140ºC; an 8-6:1 molar ratio of cresol to cyclohexene, a 5% by weight perchloric acid of cresol, a 2 h time of addition of cyclohexene and a 2 h time of stirring of the reaction. We hope that elaborated method of catalytic alkylation of isomeric cresols with cyclohexene in presence of perchloric acid would be a convient and an efficient method for the synthesis of alkylated phenol derivatives and results of this study would provide a convenient set of experimental conditions for the production of cyclohexyl cresols.

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