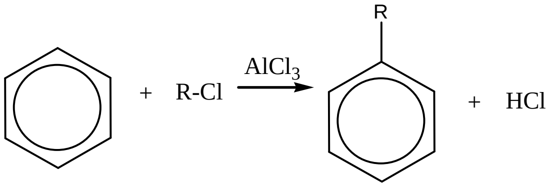
5.1 FRIEDEL-CRAFTS ALKYLATION AND ACYLATION (PART-I)

Charles Friedel and James Crafts in 1877 developed a set of reactions popularly known today as Friedel-Crafts reactions, involving electrophilic aromatic substitution of two types, acylation and alkylation.

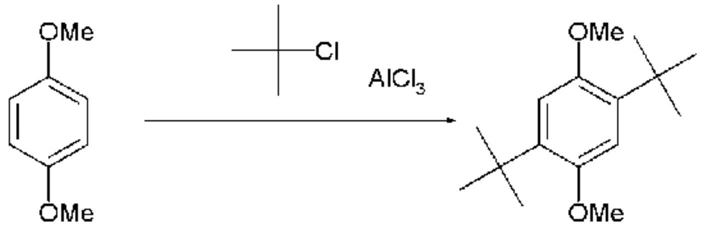
Friedel-Crafts alkylation

Friedel-Crafts alkylation (Scheme 5.1) involves the reaction between an aromatic ring and an alkyl halide using a strong Lewis acid (anhydrous aluminium chloride) as a catalyst in which, the alkyl group substitutes the chloride ion.

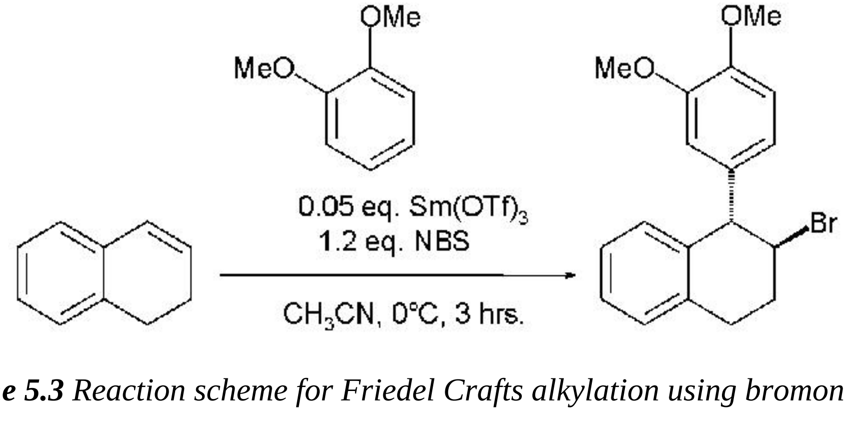


Scheme 5.1 *Reaction scheme for Friedel Crafts alkylation*

In this reaction, the product is more nucleophilic than the reactant due to the electron donating effect of alkyl-chain, therefore, another hydrogen is substituted with an alkyl-chain, which leads to over alkylation of the molecule. Further, if the chlorine is not on a tertiary carbon, carbocation rearrangement reaction occurs, attributed to the relative stability of the tertiary carbocation over the secondary and primary carbocations. Steric hindrance can be exploited to limit the number of alkylations, as in the tertiary butylation of 1,4-dimethoxybenzene (Scheme 5.2).



Scheme 5.2 *Reaction scheme for t-butylation of 1,4-dimethoxybenzene.*



Scheme 5.3 *Reaction scheme for Friedel Crafts alkylation using bromonium ion*

Alkylations are not limited to alkyl halides. Friedel-Crafts alkylation is possible with any carbocationic intermediate such as those derived from alkenes and a protic acid or lewis acid, enones and epoxides. In one study, the electrophile is a bromonium ion derived from an alkene and N-bromosuccinimide(NBS). In this reaction samarium(III) triflate is believed to activate the NBS halogen donor in halonium ion formation (Scheme 5.3).

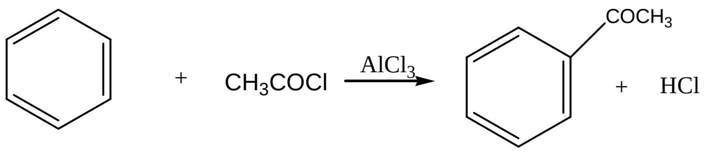
The liquid phase benzylation of benzene and other aromatic compounds by benzyl chloride is important for the production of diphenylmethane and substituted diphenylmethanes which are industrially important compounds used as pharmaceutical intermediates and fine chemicals [1-5].

The use of acyl halides or anhydrides as acetylating agents and soluble Lewis acids as catalysts is polluting, expensive and difficult to work with. In normal practice, strong mineral acids, such as H_2SO_4, HF, or supported Lewis-acid catalysts like anhydrous $AlCl_3/SiO_2$ and BF_3/SiO_2 are used for such reactions. However, these Lewis acids are consumed in more than stoichiometric amounts due to the formation of 1:1 molar adduct with aromatic ketones and further, the subsequent separation of the product by hydrolysis is cumbersome and generates a large amount of environmentally hazardous and corrosive waste.

Friedel-Crafts alkylation reactions catalyzed by homogeneous Lewis acid catalysts generally give complex reaction mixtures. The formation of reactant (and product) catalyst complexes, the increased tendency of alkylated products towards further alkylation and isomerization, coupled with the long contact of the reactant with the catalyst, result in decreased product selectivity.

Friedel-Crafts acylation

Friedel-Crafts acylation (Scheme 5.4) involves the reaction of an acyl chloride or acid anhydride with aromatic compounds in presence of a strong Lewis acid catalyst. Due to the electron-withdrawing effect of the carbonyl group, the ketone product is always less reactive than the original molecule, therefore multiple acylations do not occur, which is an advantage over the alkylation reaction. Also, there are no carbocation rearrangements, as the carbonium ion is stabilized by a resonance structure in which the positive charge is on the oxygen, inhibiting intra molecular reactions.



Scheme 5.4 *Reaction scheme for Friedel Crafts acylation*

The viability of the Friedel-Crafts acylation depends on the stability of the acyl chloride reagent. For example, in synthesis of benzaldehyde via the Friedel-Crafts pathway using formyl chloride as an acylating agent, since formyl chloride is too unstable to be isolated, formyl chloride has to be synthesized in situ. This is accomplished via the Gattermann-Koch reaction, accomplished by reacting benzene with carbon monoxide and hydrogen chloride under high pressure, catalyzed by a mixture of aluminium chloride and cuprous chloride.

Friedel–Crafts acylation of aromatic compounds and aromatic heterocyclic compounds is a ubiquitous reaction in the production of aromatic ketones, largely used as intermediates in the synthesis of pharmaceuticals, naproxen, dextromethorphan, ibuprofen and dyes, fragrances, and agrochemicals [6-11]. In particular, the synthesis of substituted acetophenones employing acylation is an important step for the production of a variety of precursors which find application in the production of pharmaceuticals, paint additives, photo initiators, fragrances, plasticizers, dyes and other commercial products [12-15].

5.2 LITERATURE SURVEY IN THE CURRENT AREA OF STUDY (PART - I)

Acylation/alkylation of aromatic compounds have been reported using several solid acid catalysts in recent years. Kantam et al [5] have reported Friedel–Crafts acylation of aromatics and heteroaromatics using micro crystalline β-zeolites with different acid anhydrides.The micronized β-zeolite shows manifold activity over normal zeolite in acylation reactions of aromatics. Deutsch et al [16] have reported acylation and benzoylation of various aromatics on sulfated zirconia and observed that the rate of acylation reactions is dependent on the nature of the respective aromatic compound. The application of sulfated zirconia as a catalyst for the acetylation of aromatics was only successful in case of anisole amongst various aromatic compounds used. Kaur et al [17] have reported Friedel–Crafts acylation of anisole and toluene with acetic anhydride using HPA supported on silica as catalyst as well as H-β Zeolite. In contrast to anisole, the acylation of toluene with HPA is far less efficient than that with H-β. The inhibited activity of HPA for toluene could be attributed to preferential adsorption of acetic anhydride on the catalyst.

Beers et al [18] have reported use of dealuminated β-zeolites as solid acid catalyst for acylation of anisole with octanoic acid and proposed a structure–activity relation for the same. After dealumination, increased activity and selectivity were found in the acylation of anisole with octanoic acid. The enhanced activity is suggested to result from higher accessibility of the active sites associated with framework-connected aluminum atoms. Bachiller-Baeza et al [19] have studied and compared the behaviours of HPA catalysts supported on commercial silica and on a silica–zirconia mixed oxide for the acylation of anisole with acetic anhydride. The yields of p-methoxyacetophenone were highest for HPA/SiO_2. Castro et al [20] have reported a mechanistic overview on the acylation reactions of anisole using α, β-unsaturated organic acids as acylating agents and solid acids as catalysts. The mechanism of acylation of anisole with α, β - unsaturated acids, i.e. acrylic, crotonic and methylcrotonic acid, have been investigated using 12-PTA, supported on SiO_2 and in the form of cesium salts as catalysts. Since α, β - unsaturated acid can either alkylate and/or acylate the aromatic compound, the influence of the catalyst on the selectivity for these two competing reactions was studied. Analysis of products obtained on the acylation of aromatic compounds with α, β - unsaturated acids shows that all the catalysts are more active for acylation than alkylation. Secondary products coming from intermolecular reactions of the acylated product with anisole as well as tertiary products coming from its further decomposition and recombination with another anisole molecule were observed.

Heteropolyacids supported on silica were found to be more active and selective towards acylation reactions than zeolites HY and H-β. Melero et al [21] have reported Friedel Crafts acylation of aromatic compounds over arene sulfonic acid containing mesostructured SBA-15 materials. Arene sulfonic acid centers anchored on the pore surface of a mesostructured SBA-15 material show greater activity (normalised to the concentration of sulfonic groups) as compared to other homogeneous and heterogeneous sulfonated catalysts and even in solvent free conditions. This high activity is accompanied with a remarkable thermal stability of the acid centers, without leaching of sulfur species during the reaction.

Cardoso et al [22] have reported silica supported HPA catalyst for acylation of anisole using acetic anhydride as acylating agent. High conversions and very high *p*-selectivity were attained in the temperature range of 61–110°C. However, deactivation was observed due to strong adsorption of the products. Ma et al [23] have reported Friedel-Crafts acylation of anisole over Y-zeolite catalyst with alkanoic acids, anhydrides and substituted benzoic acids. When carboxylic acids were used as acylating agents, the activity of the Y-zeolite increased with its Lewis acidity, showing that the Lewis acid sites were more active than the Bronsted acid sites. Further, the reaction mechanism was found to be similar to the homogeneous catalysis, that is, the electrophilic intermediate formed from the acylating agent over zeolite acid sites attacked the aromatic ring of anisole. Gaare et al [24] have reported effect of lanthanum ion exchange and Si/Al ratio of Y-zeolite on the Friedel-Crafts acylation of anisole by acetyl chloride and acetic anhydride. For the rare-earth modified zeolites, the activity was found to be dependent on the lanthanum content, and the yield increased with the level of lanthanum, even up to 93% exchange. De-alunminated Y-zeolites were also found to be very active, and an almost linear increase in the yield with decreasing aluminium fraction was found attributed to the increased hydrophobicity of dealuminated zeolites.

Heidekum et al [25] have reported use of Nafion/Silica composite materials as solid acid catalysts for acylation reactions and claimed that entrapping nanosized Nafion particles in a silica-matrix, effectively enhances the accessibility of the acid sites in comparison to the original material, Nafion resin. Chaudhari et al [26] have reported $AlCl_3$-grafted Si-MCM-41 prepared by reacting anhydrous $AlCl_3$ with terminal Si–OH groups as an active and a reusable (if not exposed to atmosphere) mesoporous solid catalyst for the Friedel–Crafts benzylation and acylation reactions. However, like anhydrous $AlCl_3$, it is highly moisture sensitive and loses its activity on exposure to moist atmosphere. The active species on the catalyst are $(\text{–Si-O})_nAlCl_{3-n}$ (n = 1–3). Cseri et al [27] have reported alkylation of benzene and toluene with benzyl chloride and benzyl alcohol over a series of clays obtained by exchanging the original cations of K10 by Ti^{4+}, Fe^{3+}, Zr^{4+}, Cu^{2+}, Zn^{2+}, Ce^{3+}, Cr^{3+} and Sn^{2+} cations. The acidity of these solids has been determined by infra red spectrometry using pyridine as molecular probe. The acidity of K-10 clays can be changed to a great extent by cation exchange and by the thermal treatments applied to the solids. The rate of alkylation is roughly related to acidity when the substrate is benzyl alcohol, but not when benzyl chloride is used. In that case, the catalysts containing reducible cations (Fe^{3+}, Sn^{4+}, Cu^{2+}) exhibit high activities in spite of their low number of acid sites. Bachari et al [28-30] have investigated benzylation of benzene and substituted benzenes, employing benzyl chloride as the alkylating agent over mesoporous silica with different Sn, Cu and Ga contents. The mechanism involves a redox step at the reaction initiation. The large pores of the mesoporous catalyst do not limit the size of the molecules that could be reacted.

Chaudhary et al [31] have investigated benzylation of benzene by benzyl chloride to diphenyl methane over $InCl_3$, $GaCl_3$, $FeCl_3$ and $ZnCl_2$ supported on commercial clays (viz. Montmorillonite-K10, Montmorillonite-KSF and Kaolin) or on high silica mesoporous MCM-41. The redox function created due to the impregnation of the clays or Si-MCM-41 by $InCl_3$, $GaCl_3$, $FeCl_3$ or $ZnCl_2$ seems to play a very important role in the benzylation process. Kinetics of the benzene benzylation (using excess of benzene) over the supported metal chloride catalysts has also been investigated and a plausible reaction mechanism for the benzylation over the supported metal chloride catalysts is proposed. Silva et al [32] have evaluated catalytic activity of gel and macroreticular ion-exchange resins (Lewatit and Amberlyst-15) for the reaction of benzene with benzyl alcohol and benzyl chloride at 80°C in the liquid phase. With benzylchloride, the monobenzylation product, diphenylmethane, was obtained in low yield, both with the gel and the macroreticular resins. Better results were obtained with benzyl alcohol as benzylation agent and the most active resin was Amberlyst-15, the conversion of benzyl alcohol being proportional to the concentration of acid sites on the resin.

Mantri et al [33] have investigated Friedel–Crafts alkylation of aromatics with benzyl alcohol as alkylating agent over rare earth metal triflates, $Sc(OTf)_3$,$Hf(OTf)_4$, $La(OTf)_3$, and $Yb(OTf)_3$ supported on MCM-41.The catalytic activity of triflates, was enhanced after being loaded onto MCM-41 due to increased dispersion, and gave the benzylated product in high yield. The rate of the benzylation of benzene was accelerated by electron donating groups and retarded by electron withdrawing groups. Narender et al [34] have studied benzylation of benzene and toluene with benzyl alcohol over a series of zeolites and metal modified β-zeolites. A reaction mechanism has been proposed for formation of diphenylmethane and benzyl ether. Benzyl ether formation from benzyl alcohol is explained on the basis of the intermolecular reaction pathway, involving Bronsted acid sites of the zeolite.

Bachari et al [35] have reported benzylation of benzene by benzyl chloride to diphenylmethane over $FeCl_3$, $InCl_3$, $GaCl_3$, $ZnCl_2$, $CuCl_2$ and $NiCl_2$ supported on mesoporous SBA-15. Further it is claimed that the redox property due to the impregnation of the SBA-15 by transition metal chloride, seems to play a very important role in the benzene benzylation process. Zhou et al [36] have reported silica-supported polytrifluoro methanesulfosiloxane (SiO_2–Si–SCF_3) catalyzed Friedel–Crafts benzylation of benzene and substituted benzenes. It was found that SiO_2–Si–SCF_3could catalyze Friedel–Crafts benzylation of benzene and substituted benzenes with benzyl alcohol under relatively mild experimental conditions. Reactions are very clean and water is the only by-product of the reaction. The yields amounted to 97–100%.

Vinu et al [37] have reported benzylation of benzene and other aromatics by benzyl chloride over mesoporous Al-SBA-15 catalysts. Sugi et al [38] have reported Friedel–Crafts benzylation of aromatics with benzyl alcohols catalyzed by heteropoly acids such as 12-TPA ($H_3PW_{12}O_{40}\cdot xH2O$)(HPW), molybdophosphoric acid ($H_3PMo_{12}O_{40}\cdot xH2O$) (HPMo) and tungstosilicic acid ($H_4SiW_{12}O_{40}\cdot xH_2O$) (HSiW) supported on mesoporous silica such as MCM-41, FSM-16 and SBA-15 by the impregnation method to enhance the catalytic activity of these solid acids by their dispersion on the support with high surface area. They also have used rare earth metal triflates supported on MCM-41 mesoporous silica. Donghao et al [39] have successfully prepared mesoporous silica materials, SBA-15, functionalized with strong (-SO_3H), moderate (-PO_3H_2) and weak (-COOH) acid groups and these mesoporous acid catalysts have been applied to the alkylation of phenol with tert-butanol. Subramaniam et al [40] have reported synthesis and characterization of HPA catalysts and their cesium salts. The catalysts have been evaluated for the alkylation of isobutane with 1-butene. Angelis et al [41] have reported solid acid catalysts based on HPAs supported on different oxides that catalyze the alkylation of isobutane with *n*-butenes to yield high-octane gasoline components. Ramos-Galvan et al [42] have reported alkylation of benzene with propylene over 12-TPA supported on MCM-41 and 48 type mesoporous materials. Chaudhari et al [43] have reported highly active Si-MCM-41 supported Ga_2O_3 and In_2O_3 catalysts for Friedel-Crafts-type benzylation and acylation reactions in presence or absence of moisture. Mohammed et al [44] have reported benzylation of benzene over sulfated zirconia supported on MCM-41 using a single source precursor. Kalabasi et al. have reported vapor phase alkylation of toluene using various alcohols over H_3PO_4/MCM-41 catalyst and studied influence of reaction parameters on selectivity and conversion. Selvaraj at al [45] have reported synthesis of 2-acetyl-6-methoxynaphthalene using mesoporous SO_4^{2-}/Al-MCM-41 molecular sieves.

Murugesan et al [46] have reported synthesis, characterization and catalytic activity of Al-MCM-41, Fe,Al-MCM-41 and Zn,Al-MCM-41 in the vapor phase alkylation and acylation of ethylbenzene with ethyl acetate in the temperature range between 250°C and 400°C. Endud et al [47] have reported cubic aluminated mesoporous materials, Al-MCM-48 as highly effective catalysts for Friedel-Crafts acylation of 2-methoxynaphthalene and 2-acetyl-6-methoxynaphthalene. Iwamoto et al [48] have reported Friedel-Crafts acylation of anisole with carboxylic anhydrides of large molecular sizes on mesoporous silica MCM-41 catalyst. Halligudi et al [49] have reported 12-TPA supported over zirconia in mesoporous channels of MCM-41 as catalyst in veratrole acetylation. Liquid-phase Friedel–Crafts alkylation and acylation reactions have been reported using aluminosilicate MCM-41 [50-53].

5.3 OBJECTIVES OF THE PRESENT WORK (PART - I)

In the present chapter, the potential utility of M(IV)PWs (Type-I Inherent SACs) and 12-TPA/M(IV)O_2 (Type-II Induced SACs) has been explored by studying Friedel-Crafts alkylation of toluene with benzyl chloride and acylation of anisole/veratrole with acetyl chloride. Reaction parameters, reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been optimized. Catalytic performance of Type-I and Type-II catalysts have been compared at optimized condition and correlated with acid properties of the materials. The performance ability of the catalysts have also been assessed for regenerated/reactivated catalysts. A reaction mechanism has been proposed and discussed for solid acid catalyzed Friedel – Crafts alkylation and acylation.

5.4 EXPERIMENTAL (PART - I)

Catalyst Synthesis and Characterization

The synthesis and characterization of Type-I catalysts ZrPW, TiPW, SnPW [Inherent SACs - M(IV)PWs] and Type – II catalysts 12-TPA/ZrO_2-20, 12-TPA/TiO_2-20, 12-TPA/SnO_2-20 [Induced SACs - 12-TPA/M(IV)O_2-20] have been discussed in Chapter 2.

Materials and Methods

Anisole, veratrole, acetyl chloride, benzyl chloride and toluene were procured from Merck India. % yields of products were determined by GC performed on Chemito 800 plus, equipped with flame-ionization detector (FID), oven temperature: 150°C, injector temperature: 200°C, detector temperature: 220°C and split ratio is 1:2. EDX analysis for catalysts (fresh and spent) has been performed on Jeol JSM-5610-SLV scanning electron microscope.

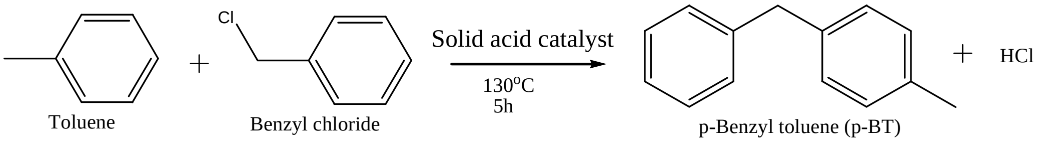
Experimental setup

The reactions were carried out in a two necked 50 ml round bottomed flask equipped with a magnetic stirrer under heating in an oil bath. In a typical set up, a mixture of substituted benzene [toluene (T), anisole (A) and veratrole (V)] (10-20 mmol), benzyl chloride (BC) / acetyl chloride (AC) (10-25 mmol) and catalyst (0.15-0.35g) was taken in a round bottomed flask and stirred at particular temperature (110^{o}C-140^{o}C) for particular time (2-7h). The reactions were monitored by GC. % yields were calculated on the basis of conversion of substituted benzenes used. Reaction parameters, reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been varied and reaction conditions optimized.

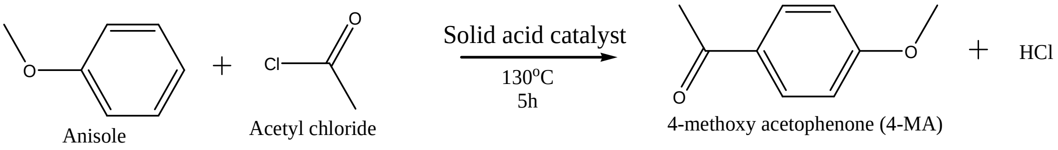
After separation of catalyst from reaction mixture by decantation/filtration, it is first refluxed in ethanol for 30 minutes to solubilise and remove adsorbed molecules, followed by drying at room temperature (~30^{o}C) and then regenerated/reactivated as described in Chapter 3. The regenerated/reactivated catalysts were used to assess the performance ability at optimized condition in subsequent run.

5.5 RESULTS AND DISCUSSION (PART - I)

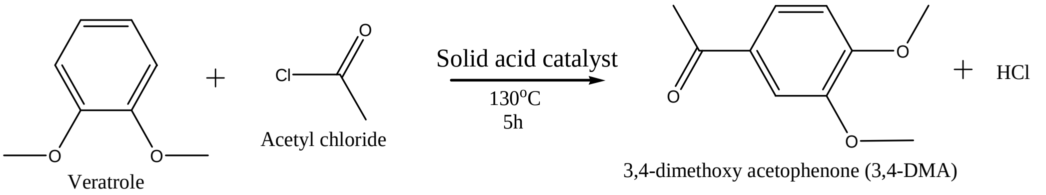
In the present study Friedel–Crafts alkylation and acylation reactions have been performed as described in experimental section which have been presented in schemes 5.5 – 5.7.



Scheme 5.5 *Friedel-Crafts alkylation of toluene with benzyl chloride*



Scheme 5.6 *Friedel-Crafts acylation of anisole with acetyl chloride*



Scheme 5.7 *Friedel-Crafts acylation of veratrole with acetyl chloride*

In the present study substrates toluene, anisole and veratrole have been used both as substrates and solvent. It has been reported earlier that there is no significant effect of solvents in the acylation of anisole and veratrole and best results were obtained when aromatic ethers were used as self solvents [5]. Thus, the Green Chemistry principle 5 which states that the "*use of solvents should be made unnecessary whenever possible and when used, innocuous*" is implemented.

Firstly, reaction conditions were optimized using ZrPW and 12-TPA/ZrO_2-20 as solid acid catalyst for Friedel–Crafts alkylation of T with BC by varying parameters such as reaction time, reaction temperature, catalyst amount and mole ratio of the reactants. The optimized reaction conditions are presented in Table 5.1.

For both catalysts, the effect of reaction time (2 h – 7 h) on the % yield of p-benzyl toluene (p-BT) was studied at 110˚C temperature with 1:1 mole ratio of T:BC and 0.15 g of catalyst. The reaction reached equilibrium within 5 h (Figure 5.1). When reaction temperature is varied (110˚C-140˚C), there is significant increase in yield upto 130°C, after which decrease in yield is observed (Figure 5.2). With increasing catalyst amount (0.15-0.35g), yield increases probably due to increase in the number of acid sites. In both cases, optimum catalyst amount used is 0.25 g (Figure 5.3). The influence of mole ratio of reactants on product yield was studied using 0.25 g of catalyst, at 130^{o}C and at optimized reaction time (5h). The mole ratio of T:BC was varied as 1:1, 1:1.5, 1:2, 1.5:1 and 2:1 (Figure 5.4). In the present study, highest yields were obtained with 1:1.5.

At optimum condition [Table 5.1; reaction time: 5 h, reaction temperature: 130^{o}C, catalyst amount: 0.25 g, mole ratio of substituted benzene (T, A, V) : BC/AC = 1:1.5], Friedel–Crafts alkylation of T with BC and acylation of A/V with AC have been performed using ZrPW, TiPW, SnPW, 12-TPA/ZrO_2-20, 12-TPA/TiO_2-20 and 12-TPA/SnO_2-20 (Tables 5.2-5.4; Figures 5.5-5.7).

Friedel–Crafts alkylation of T with BC gave selectively p-BT and acylation of A and V with AC gave selectively 4-methoxy acetophenone (4-MA) and 3,4-dimethoxy acetophenone (3,4-DMA) respectively.

It is observed that, % yields of 3,4-DMA > 4-MA. The rate-determining step of the Friedel-Crafts acylation is the formation of the electrophilic intermediate. The presence of an additional electron donating methoxy group in veratrole makes it a more active compound for electrophilic substitution of acyl group at para position, due to an increased electron density and resultant increased susceptibility for attack by the electrophile than anisole.

Number and nature of surface acid sites play a predominant role in evaluating and correlating catalytic activity. Amongst M(IV)PWs performance of catalyst in terms of % yields/TONs is found to be TiPW > SnPW > ZrPW whereas, amongst 12-TPA/M(IV)O_2-20, the order is found to be 12-TPA/TiO_2-20 > 12-TPA/SnO_2-20 > 12-TPA/ZrO_2-20 which could be attributed to increased surface acidity of these materials (Tables 2.5-2.10). Comparing performance of M(IV)PWs (Type-I catalysts) and 12-TPA/M(IV)O_2-20 (Type-II catalysts), M(IV)PWs scores over 12-TPA/M(IV)O_2-20 in terms of % yields/TON of p-BT, 4-MA and 3,4-DMA formed.

Regeneration/reactivation and reuse of catalysts

After each catalytic run, there is change in colour of the catalysts [light brown in case of 12-TPA/M(IV)O_2-20 and dark brown/black in case of M(IV)PWs]. This is probably due to the fact that reactant molecules come onto surface of catalyst and enter into reaction to give the product, while a few of them get adsorbed on surface.

After each subsequent run, the acid sites were regenerated in case of type – I catalysts [M(IV)PWs] and reactivated in case of type – II catalysts [12-TPA/M(IV)O_2-20] as described in experimental section. All subsequent catalytic runs were performed at optimized conditions (Tables 5.2 – 5.4; Figures 5.5 – 5.7).

It is observed that, on regeneration M(IV)PWs exhibited only a marginal decrease in % yields in each subsequent run, probably due to regeneration of the acid sites. However, a reactivation in case of 12-TPA/M(IV)O_2-20 exhibited a much higher decrease in % yields. In case of synthesis of p-BT, EDX analysis for both fresh and spent catalysts (ZrPW and 12-TPA/ZrO_2-20) has been performed after first catalytic run (Table 5.5; Figure 5.8 – 5.11). Decrease in atomic wt. % of Zr in ZrPW and Zr and W in 12-TPA/ZrO_2-20 is observed, indicating leaching of ions, which could be the probable reason for decrease in % yields.

When M(IV)PWs were used as such after each subsequent run (i.e. without regeneration), the decrease in % yields are much higher compared to regenerated M(IV)PWs, which is probably attributed to the deactivation of catalysts, due to substrate molecules getting adsorbed on surface or also entering interstices of the catalyst material [54].

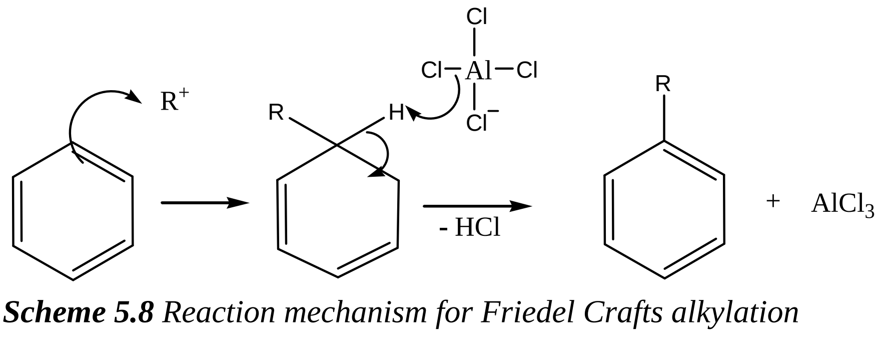
Reaction mechanism for solid acid catalyzed Friedel - Crafts alkylation and acylation

Mechanism for Friedel-Crafts alkylation using conventional catalyst:

In this reaction, first step involves dissociation of a chlorine atom to form an alkyl cation followed by nucleophilic attack of the arene towards the alkyl group. Finally, a chlorine atom reacts to form HCl, and the $AlCl_3$ catalyst is regenerated (Scheme 5.8).

(i) $\text{R-Cl} + AlCl_3 \longrightarrow R^+ + AlCl_4^-$

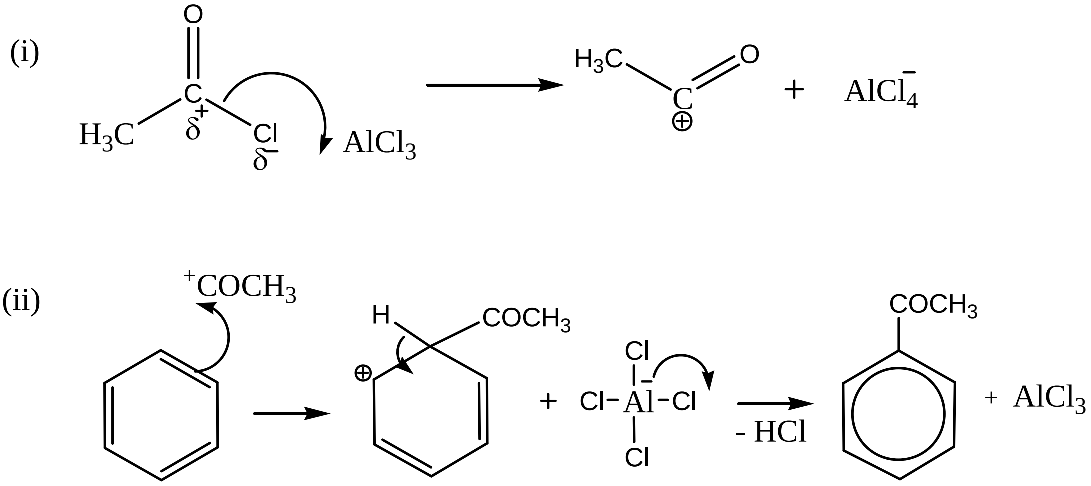
(ii)



Scheme 5.8 *Reaction mechanism for Friedel Crafts alkylation*

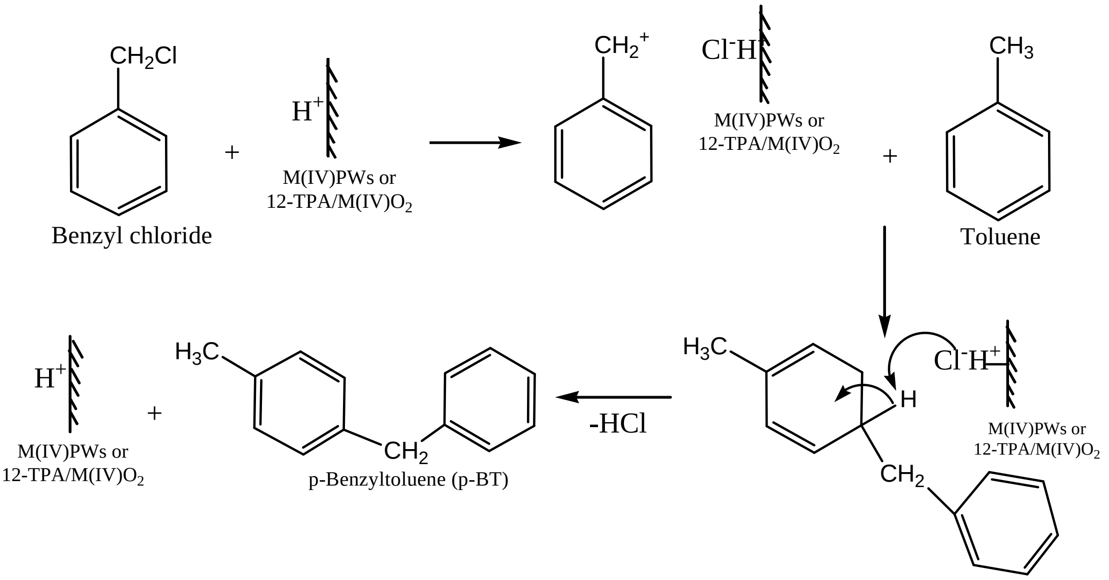
Mechanism for Friedel-Crafts acylation using conventional catalyst:

In this reaction, first step involves dissociation of a chlorine atom to form an acyl cation. This is followed by nucleophilic attack of the arene towards the acyl group. Finally, a chlorine atom reacts to form HCl, and the $AlCl_3$ catalyst is regenerated (Scheme 5.9).



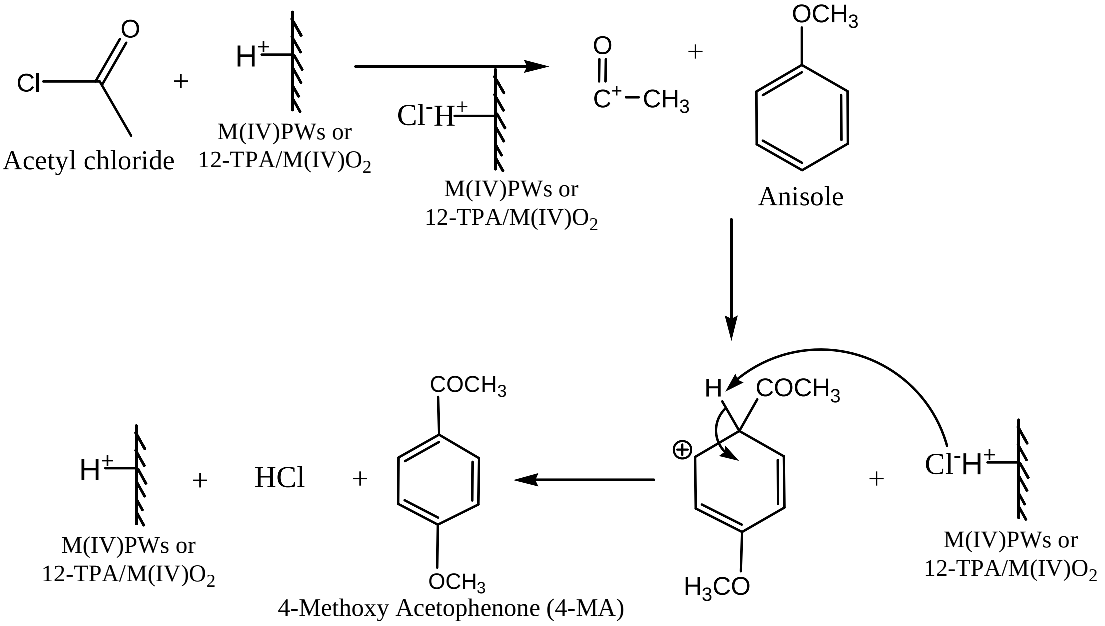
Scheme 5.9 *Reaction mechanism for Friedel Crafts acylation*

It is reported that the mechanism for Friedel-Crafts alkylation and acylation over solid acid catalysts is the same as in case of homogeneous system where Lewis acid catalysts are used [23,28,29].



Scheme 5.10 *Proposed mechanism of Friedel Crafts alkylation of toluene using M(IV)PWs and 12-TPA/M(IV)O_2*

The proposed mechanism for the acylation and alkylation reaction (Scheme 5.10 and 5.11) on solid acid catalyst implies the formation of an adsorbed species by interaction of the acylating/alkylating agent with a Brønsted acid site [28,29] (acyl/alkyl cation). The Brønsted acid site generates an acyl carbonium ion, which in turn affects the electrophilic substitution. A higher density of acid sites increases number of acyl cations enhancing activity of the reaction.



***Scheme 5.11** Proposed mechanism of Friedel Crafts acylation of anisole using M(IV)PWs and 12-TPA/M(IV)O_2*

Table 5.1 *Optimization of reaction conditions for alkylation of toluene with benzyl chloride using ZrPW and 12-TPA/ZrO_2-20.*

Set No.	**Reactants with their mole ratio**	**Reaction time (h)**	**Reaction temperature (^oC)**	**Catalyst amount (g)**	**% Yield of p-BT**	
					ZrPW	**12-TPA/ ZrO_2-20**
(A) Optimization of reaction time						
1	T:BC (1:1)	2	110	0.15	16.82	10.91
2	T:BC (1:1)	4	110	0.15	38.06	27.45
3	T:BC (1:1)	**5**	110	0.15	**46.97**	**41.68**
4	T:BC (1:1)	6	110	0.15	47.19	41.82
5	T:BC (1:1)	7	110	0.15	47.50	42.00
(B) Optimization of reaction temperature						
6	T:BC (1:1)	5	120	0.15	49.95	44.00
7	T:BC (1:1)	5	**130**	0.15	**51.71**	**49.18**
8	T:BC (1:1)	5	140	0.15	48.26	38.96
(C)Optimization of catalyst amount						
9	T:BC (1:1)	5	130	0.20	53.98	50.14
10	T:BC (1:1)	5	130	**0.25**	**55.69**	**51.74**
11	T:BC (1:1)	5	130	0.30	55.94	52.06
12	T:BC (1:1)	5	130	0.35	56.26	52.24
(D)Optimization of mole ratio of reactants						
13*	**T:BC (1:1.5)**	**5**	**130**	**0.25**	**59.68**	**54.26**
14	T:BC (1:2)	5	130	0.25	59.00	53.55
15	T:BC (1:2.5)	5	130	0.25	55.36	47.91
16	T:BC (1.5:1)	5	130	0.25	40.05	39.63
17	T:BC (2:1)	5	130	0.25	32.90	31.06

*(T: toluene; BC: benzyl chloride; *Optimum condition)*

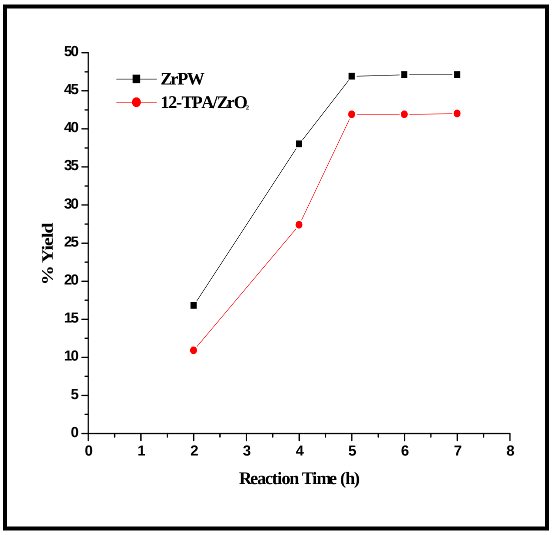


Figure 5.1 *Optimization of reaction time for synthesis of p-BT*

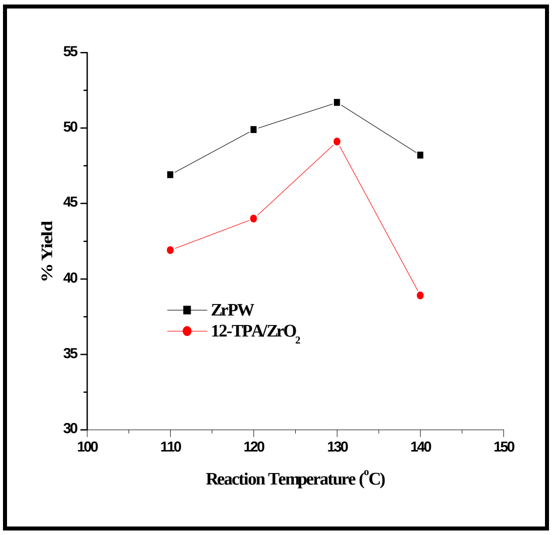


Figure 5.2 *Optimization of reaction temperature for synthesis of p-BT*

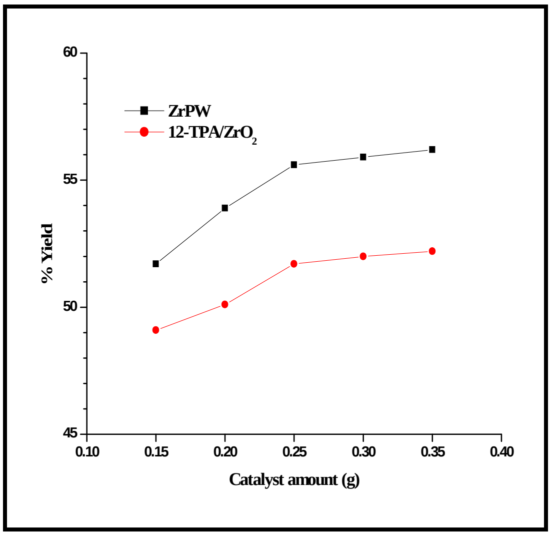


Figure 5.3 *Optimization of catalyst amount for synthesis of p-BT*

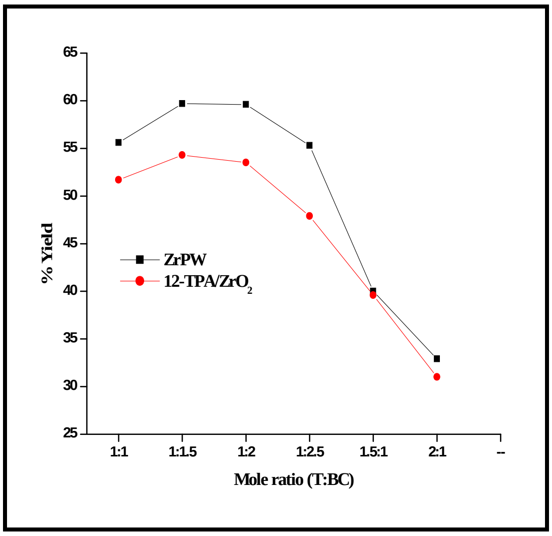


Figure 5.4 *Optimization of mole ratio of reactants for synthesis of p-BT*

Table 5.2 *Friedel-Crafts alkylation of toluene with benzyl chloride at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Catalyst	**% Yield (TON) of p-BT**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	59.68 (6.70) *(F)*	58.32 (6.55) *(Rg)*	56.81 (6.38) *(Rg)*
TiPW	70.38 (7.91) *(F)*	69.00 (7.75) *(Rg)*	67.54 (7.59) *(Rg)*
SnPW	63.27 (7.11) *(F)*	60.08 (6.75) *(Rg)*	58.44 (6.56) *(Rg)*
ZrPW	59.68 (6.70) *(F)*	51.00 (5.73) *(Ru)*	40.84 (4.59) *(Ru)*
TiPW	70.38 (7.91) *(F)*	62.44 (7.01) *(Ru)*	54.12 (6.08) *(Ru)*
SnPW	63.27 (7.11) *(F)*	55.47 (6.23) *(Ru)*	44.56 (5.00) *(Ru)*
12-TPA/ ZrO_2-20	54.26 (6.09) *(F)*	42.18 (4.74) *(Ra)*	30.69 (3.44) *(Ra)*
12-TPA/ TiO_2-20	56.31 (6.32) *(F)*	44.01 (4.94) *(Ra)*	37.89 (4.25) *(Ra)*
12-TPA/ SnO_2-20	55.47 (6.23) *(F)*	43.00 (4.83) *(Ra)*	35.74 (4.01) *(Ra)*

[Reaction time: 5 h, Reaction temperature: 130°C, Catalyst amount: 0.25 g, Mole ratio - Toluene:Benzyl chloride = 1:1.5; F: Fresh catalyst; Rg: Regenerated catalyst; Ru: Reused catalyst (used as such, without regeneration); Ra: Reactivated catalyst]

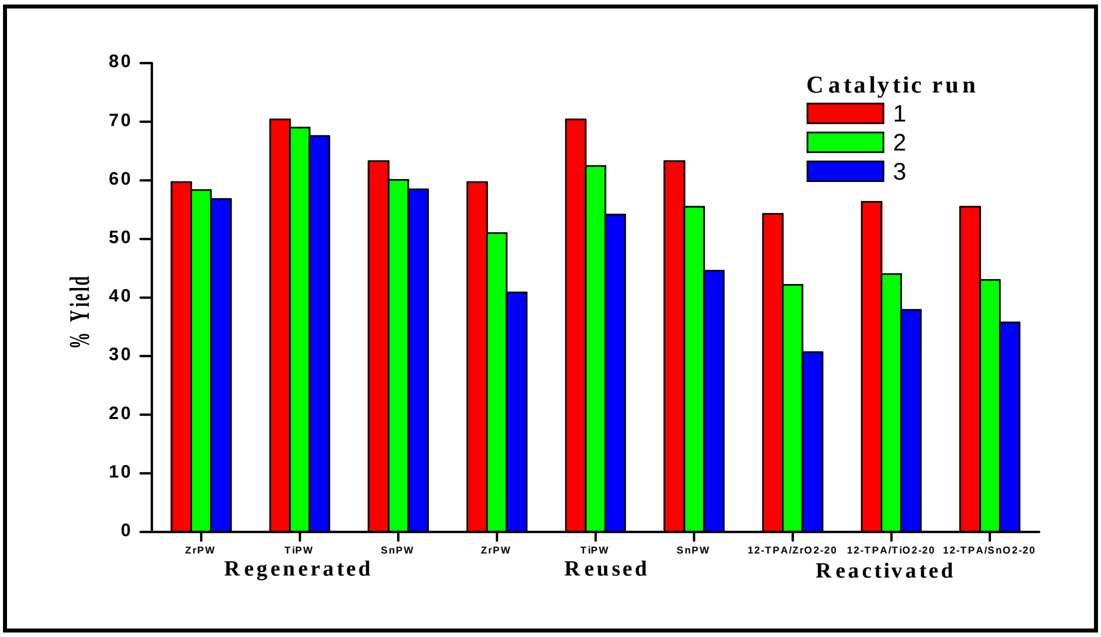


Figure 5.5 *Comparison of % yields of p-BT at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.3 *Friedel-Crafts acylation of anisole with acetyl chloride at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Catalyst	**% Yield (TON) of 4-MA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	50.16 (4.51) *(F)*	48.99 (4.40) *(Rg)*	47.36 (4.26) *(Rg)*
TiPW	56.81 (5.11) *(F)*	55.08 (4.95) *(Rg)*	53.47 (4.81) *(Rg)*
SnPW	52.00 (4.68) *(F)*	50.76 (4.56) *(Rg)*	49.66 (4.46) *(Rg)*
12-TPA/ ZrO_2-20	44.19 (3.97) *(F)*	38.08 (3.42) *(Ra)*	29.46 (2.65) *(Ra)*
12-TPA/ TiO_2-20	48.87 (4.39) *(F)*	40.33 (3.62) *(Ra)*	31.88 (2.86) *(Ra)*
12-TPA/ SnO_2-20	46.00 (4.14) *(F)*	39.10 (3.51) *(Ra)*	30.69 (2.76) *(Ra)*

(Reaction time: 5 h, Reaction temperature: 130°C, Catalyst amount: 0.25 g, Mole ratio - Anisole:Acetyl chloride = 1:1.5; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst)

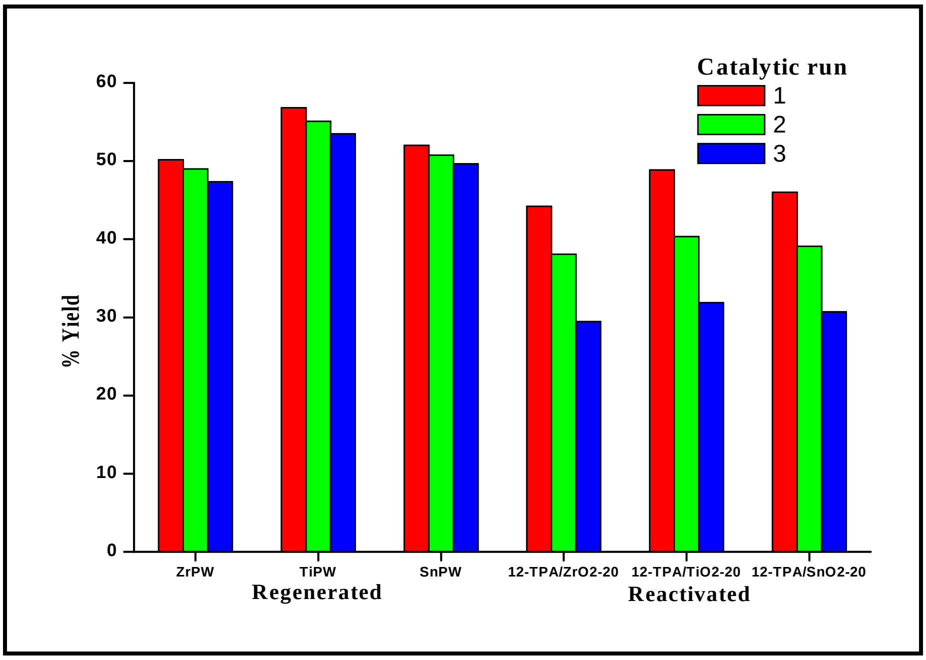


Figure 5.6 *Comparison of % yields of 4-MA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.4 *Friedel-Crafts acylation of veratrole with acetyl chloride at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Catalyst	**% Yield (TON) of 3,4-DMA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	54.89 (5.59) *(F)*	53.00 (5.40) *(Rg)*	52.04 (5.30) *(Rg)*
TiPW	62.38 (6.36) *(F)*	61.46 (6.26) *(Rg)*	60.00 (6.12) *(Rg)*
SnPW	57.70 (5.88) *(F)*	55.00 (5.61) *(Rg)*	53.69 (5.47) *(Rg)*
12-TPA/ ZrO_2-20	48.43 (4.93) *(F)*	40.98 (4.17) *(Ra)*	31.13 (3.17) *(Ra)*
12-TPA/ TiO_2-20	52.89 (5.39) *(F)*	44.11 (4.49) *(Ra)*	35.00 (3.57) *(Ra)*
12-TPA/ SnO_2-20	50.17 (5.11) *(F)*	40.06 (4.08) *(Ra)*	32.63 (3.52) *(Ra)*

(Reaction time: 5 h, Reaction temperature: 130˚C, Catalyst amount: 0.25 g, Mole ratio - Veratrole:Acetyl chloride = 1:1.5; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst)

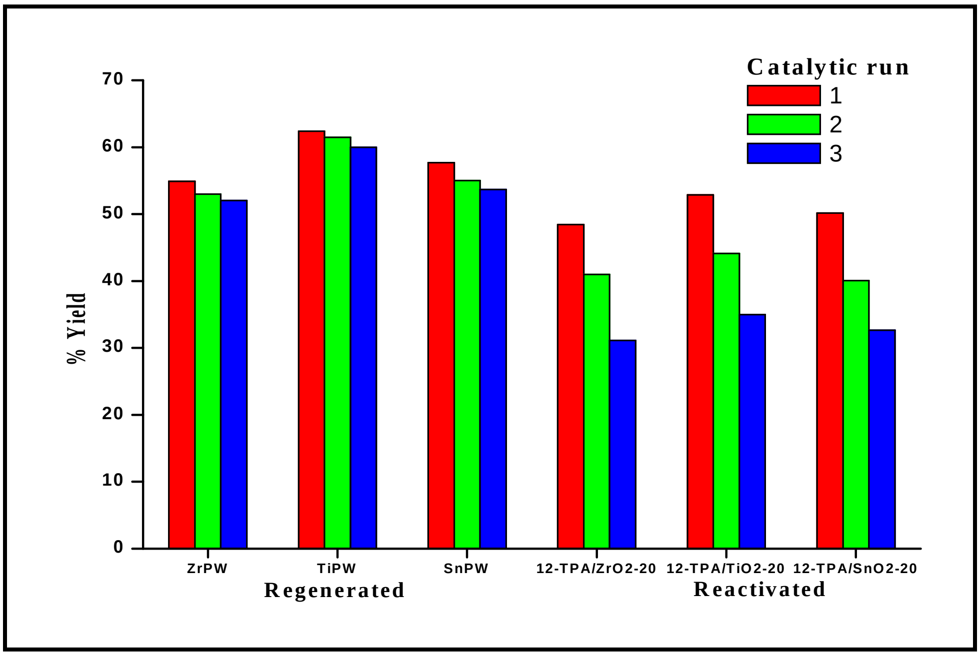


Figure 5.7 *Comparison of % yields of 3,4-DMA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.5 *Elemental analysis by EDX for both fresh and spent ZrPW and 12-TPA/ZrO_2-20 in alkylation of toluene with benzyl chloride at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Materials	**% by EDX analysis**			
	Zr	**P**	**W**	**O**
ZrPW (Fresh)	60.79	18.53	20.67	-
ZrPW (Spent)	50.56	27.06	22.38	-
12-TPA/ZrO_2-20 (Fresh)	28.75	0.11	3.44	67.70
12-TPA/ZrO_2-20 (Spent)	19.21	1.72	2.06	77.01

(Mole ratio of Toluene : Benzyl chloride -1:1.5; Catalyst amount - 0.25g; Reaction temperature - 130 °C; Reaction Time- 5h)

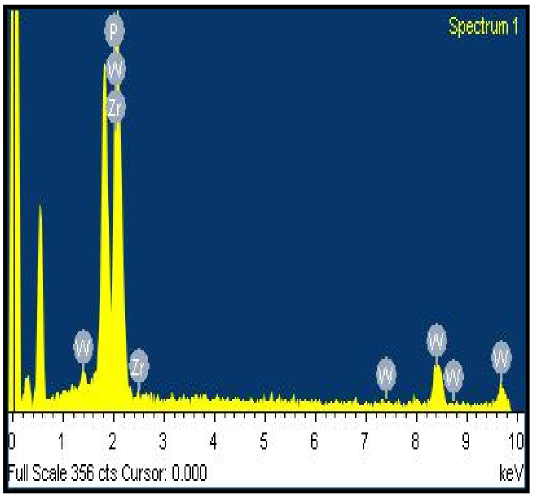


Figure 5.8 *EDX of fresh ZrPW*

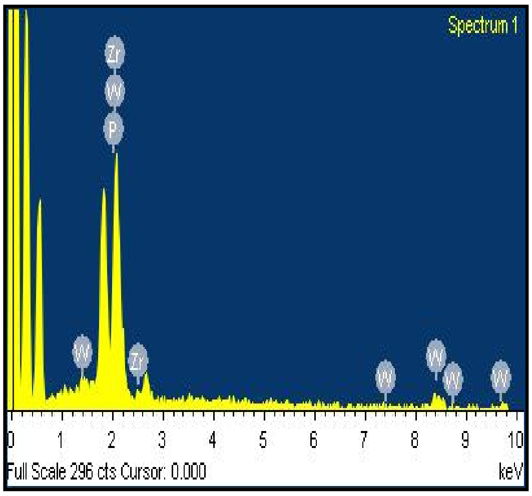


Figure 5.9 *EDX of spent ZrPW in synthesis of p-BT*

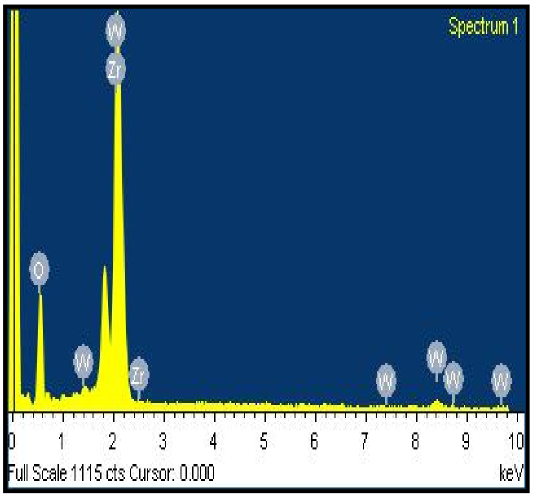


Figure 5.10 *EDX of fresh 12-TPA/ZrO_2-20*

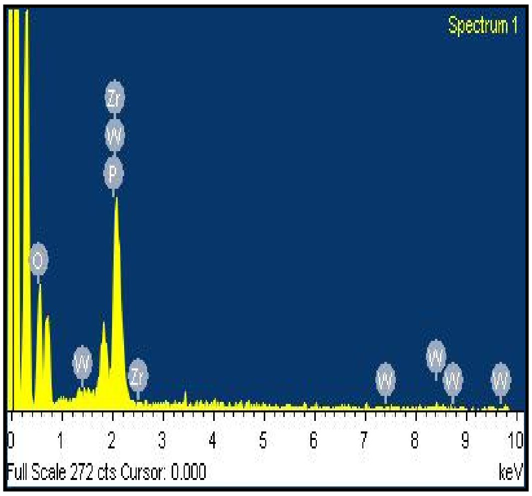
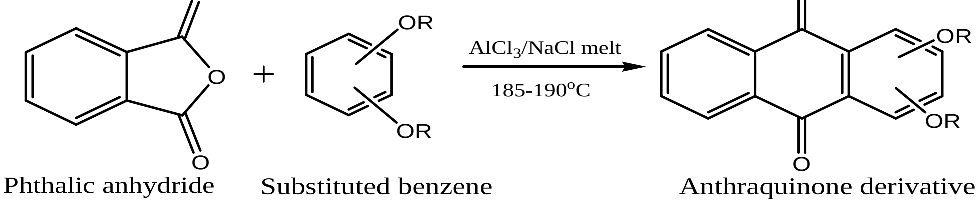


Figure 5.11 *EDX of spent 12-TPA/ZrO_2-20 in synthesis of p-BT*

5.6 SYNTHESIS OF ANTHRAQUINONE DERIVATIVES (PART-II)

Anthraquinones are important members of the organic family. The chemistry of quinones is largely dependent on the substitution being either on the quinonic or on adjacent rings. This is reflected in their chemical reactivity, especially in heterocyclic quinines. Their structure is observed in some synthetic dyes and in many naturally occurring substances such as pigments, vitamins, and enzymes. The quinone compounds occupy an important place among the different classes of *anti*tumor agents. The hydroxylated 9,10-anthraquinones exists widely in nature and are known to display various pharmacological activities. Furthermore, the anthraquinones of the Rubiaceae family exhibit some interesting in vivo biological activities, such as *anti*-microbial, *anti*-fungal, analgesic, *anti*-malarial, *anti*-oxidant, *anti*-leukemic and mutagenic functions. Anthraquinone and its hydroxy and amino derivatives are of considerable practical significance in pharmacology, biochemistry, and dye industry [55].

In synthesis methods, the intramolecular condensation of *o*-aroylbenzoic acids produces anthraquinone derivatives. The dehydrating agents used are fuming sulfuric acid, polyphosphoric acid, benzoyl chloride & concentrated sulfuric acid/zinc chloride. It has been found that Friedel–Crafts reactions between phthalic anhydride and substituted benzenes in the presence of a eutectic mixture of aluminum chloride and sodium chloride melt (2:1) have been used for the preparation of various anthraquinones (Scheme 5.12) [56,57]. These methods suffer from some disadvantages such as long reaction time, use of toxic solvent, the reaction conditions are usually quite severe and the desired products were afforded from two steps with low yields. However, there still remains the need for a simple and efficient process for the synthesis. To overcome the difficulties, some modifications have been made for the synthesis of anthraquinones *via* Friedel–Crafts reaction under solvent free conditions.



***Scheme 5.12** Friedel–Crafts reaction between phthalic anhydride and substituted benzenes*

As indicated earlier in the text owing to stringent and growing environmental regulations worldwide, there is a global effort to replace the conventional liquid acid catalysts by solid acids, which are less toxic, easily regenerable from the product, easy to handle and reusable. In this context, the focus has been towards design of processes to replace homogeneous Lewis acid catalysts with environmentally benign heterogeneous catalysts. The acid sites in solid acids being milder than the conventional Lewis acids, would also inhibit side reactions such as polyalkylation, isomerization, transalkylation, dealkylation and polymerization that occur in traditional procedure. There is, therefore, substantial interest to carry out Friedel-Crafts reactions with solid acid catalysts which decrease these side reactions.

5.7 LITERATURE SURVEY IN THE CURRENT AREA OF STUDY (PART-II)

Madje et al have reported boron sulphonic acid - $B(HSO_4)_3$ catalyzed synthesis of anthraquinone derivatives from phthalic anhydride and substituted benzenes under solvent free condition [55]. This method provides several advantages such as environmental friendly simple procedure, mild reaction conditions and short reaction time (60-120 min). Guo et al have reported dehydration of 2-(4′-ethylbenzoyl) benzoic acid for the synthesis of 2-ethylanthraquinone (2-EAQ) over H-beta zeolites catalyst and achieved high selectivity for 2-EAQ by modifying the acidity of the H-beta zeolite catalyst and varying reaction conditions [58,59]. Hossein et al have reported one pot synthesis of anthraquinone derivatives from the reaction of an aromatic compounds with phthalic anhydride using $AlCl_3/H_2SO_4$ as catalyst under heterogeneous conditions [60]. Singh et al have reported synthesis of anthraquinones and related compounds of *Rubia cordifolia* using montmorillonite clays under solvent-free condition [61].

5.8 OBJECTIVES OF THE PRESENT WORK (PART-II)

In the present study, the potential utility of M(IV)PWs (Type-I Inherent SACs) and 12-TPA/M(IV)O_2 (Type-II Induced SACs) has been explored by studying synthesis of anthraquinone derivatives *via* Friedel–Crafts reaction wherein substituted benzenes (toluene, resorcinol, hydroquinone and nitrobenzene) are treated with phthalic anhydride to give corresponding anthraquinone derivative. Reaction parameters, reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been optimized. Catalytic performance of Type-I and Type-II catalysts have been compared at optimized condition and correlated with acid properties of the materials. The performance ability of the catalysts have also been assessed for regenerated/reactivated catalysts. A reaction mechanism has been proposed and discussed for solid acid catalyzed Friedel – Crafts synthesis of anthraquinones.

5.9 EXPERIMENTAL (PART-II)

Catalyst Synthesis and Characterization

The synthesis and characterization of Type-I catalysts ZrPW, TiPW, SnPW [Inherent SACs - M(IV)PWs] and Type – II catalysts 12-TPA/ZrO_2-20, 12-TPA/TiO_2-20, 12-TPA/SnO_2-20 [Induced SACs - 12-TPA/M(IV)O_2-20] have been discussed in Chapter 2.

Materials and Methods

Resorcinol, hydroquinone, toluene, nitrobenzene, phthalic anhydride, ethyl acetate, anhydrous Na_2SO_4, silica gel (for TLC) and petroleum ether were procured from Loba Chemicals (India). The synthesized anthraquinone derivatives were scanned for FTIR spectra on Shimadzu (Model 8400S) using KBr pellet and ^{1}H-NMR spectra on Bruker 400 MHz instrument using tetramethylsilane (TMS) as internal standard in $CDCl_3$ (solvent). EDX analysis for catalysts (fresh and spent) has been performed on Jeol JSM-5610-SLV scanning electron microscope.

Experimental setup

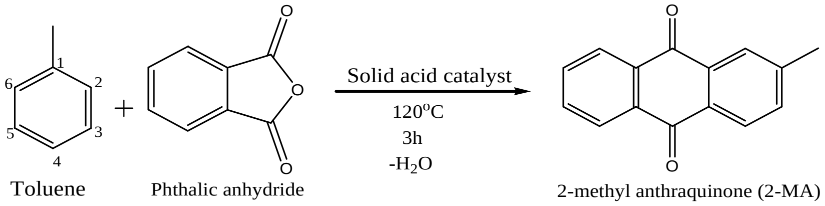
In a typical reaction, a 25 ml round bottomed flask attached to a reflux condenser was charged with phthalic anhydride (PA) (10-12 mmol), substituted benzene [toluene (T), nitrobenzene (Nbz), Resorcinol (R), Hydroquinone (Hq)] (10-12 mmol), water (2-5 ml) and catalyst (0.15-0.35 g). The reaction mixture was stirred at particular temperature (110^{o}C-140°C) in an oil bath for the appropriate time (0.5-4.0 h) and the progress of the reaction monitored by TLC. Reaction parameters reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been varied and reaction conditions optimized.

After completion of the reaction, the mixture was extracted with ethyl acetate (2×20 ml) and the catalyst was separated by decantation/filtration. The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure and the crude product obtained was purified by recrystallization. All synthesized anthraquinone derivatives were characterized for IR spectroscopy, ^{1}H-NMR spectroscopy and melting point. % yields were calculated on the basis of conversion of phthalic anhydride.

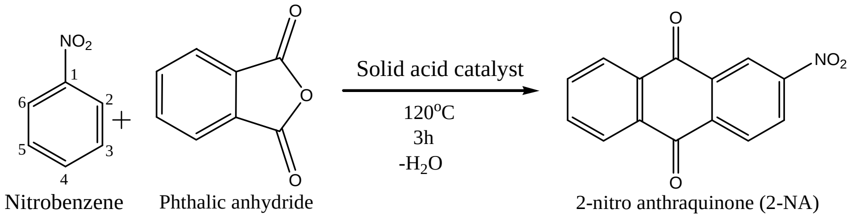
After separation of catalyst from reaction mixture by decantation/filtration, it is first refluxed in ethanol for 30 minutes to solubilise and remove adsorbed molecules, followed by drying at room temperature (~30^{o}C) and then regenerated/reactivated as described in Chapter 3. The regenerated/reactivated catalysts were used to assess the performance ability at optimized condition in subsequent run.

5.10 RESULTS AND DISCUSSION (PART-II)

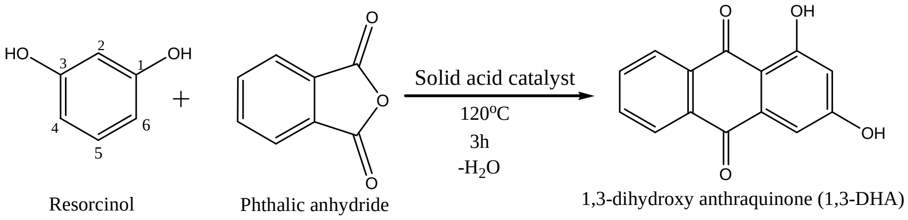
In the present study synthesis of anthraquinone derivatives via Friedel–Crafts reaction has been performed as described in experimental section which have been presented in schemes 5.13 – 5.16.



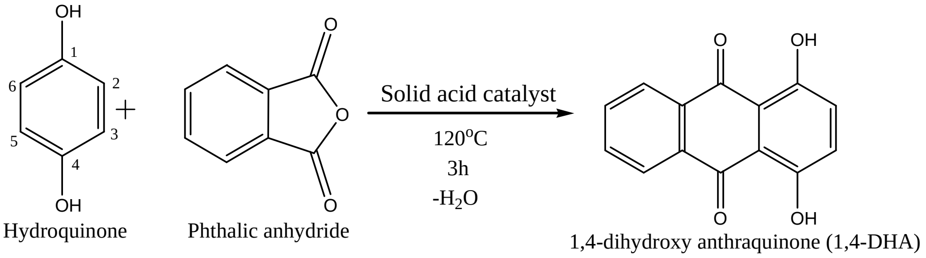
Scheme 5.13 *Friedel-Crafts reaction of toluene with phthalic anhydride to prepare 2-methyl anthraquinone (2-MA)*



Scheme 5.14 *Friedel-Crafts reaction of nitrobenzene with phthalic anhydride to prepare 2-nitro anthraquinone (2-NA)*



Scheme 5.15 *Friedel-Crafts reaction of resorcinol with phthalic anhydride to prepare 1,3-dihydroxy anthraquinone (1,3-DHA)*



Scheme 5.16 *Friedel-Crafts reaction of hydroquinone with phthalic anhydride to prepare 1,4-dihydroxy anthraquinone (1,4-DHA)*

Firstly, reaction conditions were optimized using ZrPW and 12-TPA/ZrO_2-20 as solid acid catalyst for preparation of 2-methyl anthraquinone (2-MA) from T and PA by varying parameters such as reaction time, reaction temperature, catalyst amount and mole ratio of the reactants. The optimized reaction conditions are presented in Table 5.6.

The effect of reaction time (0.5 - 4.0 h) on the product yield (2-MA) for both the catalysts (ZrPW and 12-TPA/ZrO_2-20) was studied at 120˚C temperature with 1:1 mole ratio of T:PA and 0.15 g of catalyst. The reaction reaches equilibrium within 3 h (Figure 5.12). When reaction temperature is varied (110˚C-140˚C), there is significant increase in % yield upto 120^{o}C, after which decrease in yield is observed (Figure 5.13). With increasing catalyst amount, (0.15g-0.35g), % yield increases probably due to increase in the number of acid sites. Optimum catalyst amount was used as 0.3 g (Figure 5.14). The influence of mole ratio of reactants on product yield was studied using 0.3 g of catalyst at 120^{o}C for 3h. The mole ratio T:PA was varied as 1:1, 1.2:1 and 1:1.2 (Figure 5.15). In the present study, highest % yield was observed with 1:1 mole ratio.

At optimized conditions (Table 5.6; reaction time: 3 h, reaction temperature: 120˚C, catalyst amount: 0.3 g and mole ratio of substituted benzene: PA = 1:1), reactions of T, Nbz, R and Hq with PA have been performed using ZrPW, TiPW, SnPW, 12-TPA/ZrO_2-20, 12-TPA/TiO_2-20 and 12-TPA/SnO_2-20 (Table 5.7-5.10; Figure 5.16-5.19).

Friedel–Crafts reactions of T, Nbz, R and Hq with PA gave selectively 2-methyl anthraquinone (2-MA), 2-nitro anthraquinone (2-NA), 1,3-dihydroxy anthraquinone (1,3-DHA) and 1,4-dihydroxy anthraquinone (1,4-DHA), respectively.

For all catalysts (Type – I and Type - II), order of % yield of anthraquinone derivatives formed is 1,4-DHA > 1,3-DHA > 2-MA > 2-NA. % yields are higher for 1,4-DHA compared to 1,3-DHA, which can be explained with reference to the mechanism (Scheme 5.17). During the formation of 1,4-DHA, first electrophilic substitution takes place at "2" or "6" position and second electrophilic substitution takes place at "3" or "5" position of Hq moiety (Scheme 5.16). However, in the formation of 1,3-DHA, first electrophilic substitution takes place at "4" or "6" position followed by second electrophilic substitution at position "5" only (Scheme 5.15). Electrophilic substitution at "2" position is restricted due to steric hindrance of – OH groups present at "1" and "3" positions in R. Due to the presence of more available sites for electrophilic substitution in Hq compared to R, yields are higher for 1,4-DHA compared to 1,3-DHA. % yields of 2-MA is less compared to 1,4-DHA and 1,3-DHA, is due to the presence of an additional e^- releasing (-OH) group in case of R and Hq, compared to T (having only one e^- releasing group – CH_3). Lowest yields of 2-NA is attributed to the presence of electron withdrawing (-NO_2) group in Nbz.

Number and nature of surface acid sites play a predominant role in evaluating and correlating catalytic activity. Amongst M(IV)PWs performance of catalyst in terms of % yields/TON is found to be TiPW > SnPW > ZrPW whereas, amongst 12-TPA/M(IV)O_2-20, the order is found to be 12-TPA/TiO_2-20 > 12-TPA/SnO_2-20 > 12-TPA/ZrO_2-20 which could be attributed to increased surface acidity of these materials (Table 2.5 – 2.10). Comparing performance of M(IV)PWs (Type – I catalysts) and 12-TPA/M(IV)O_2-20 (Type – II catalysts), M(IV)PWs scores over 12-TPA/M(IV)O_2-20 in terms of % yields/TON of anthraquinone derivatives formed.

Regeneration/reactivation and reuse of catalysts

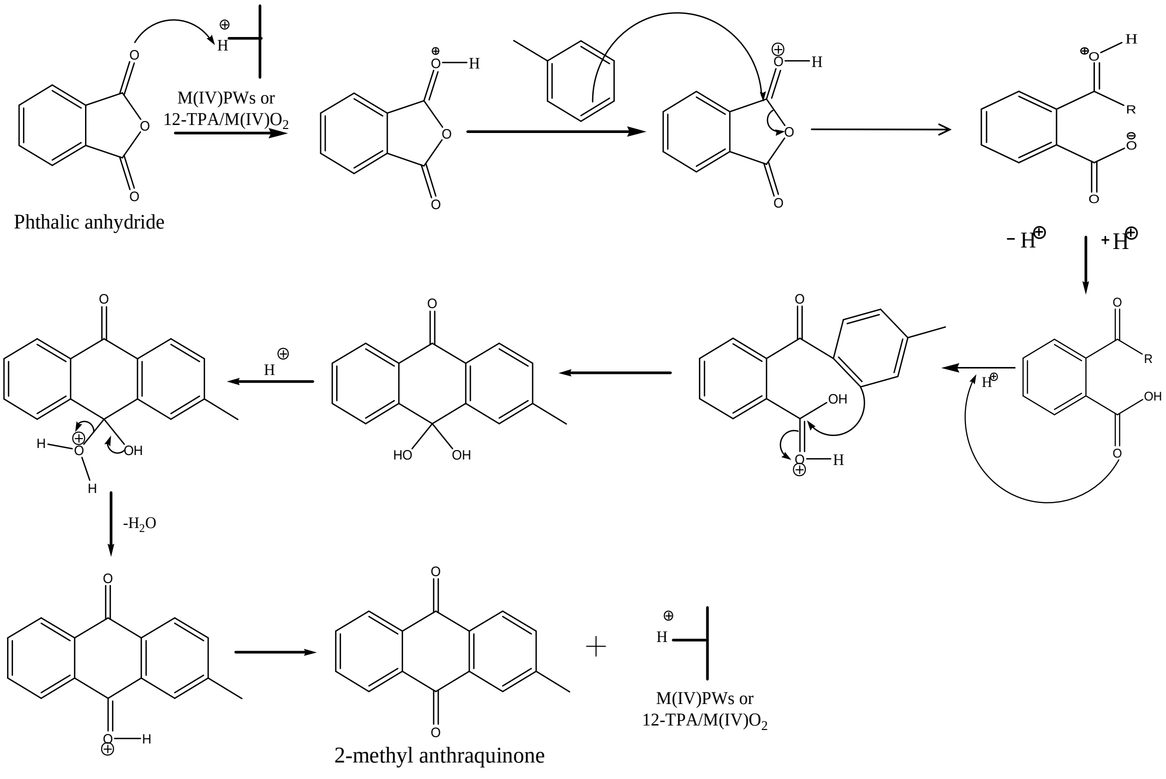
After each catalytic run, there is change in colour of the catalysts [pale yellow in case of 12-TPA/M(IV)O_2-20 and dark grey in case of M(IV)PWs]. This is probably due to the fact that reactant molecules come onto surface of catalyst and enter into reaction to give the product, while a few of them get adsorbed on surface. After each subsequent run, the acid sites were regenerated in case of type – I catalysts [M(IV)PWs] and reactivated in case of type – II catalysts [12-TPA/M(IV)O_2-20] as described in experimental section. All subsequent catalytic runs were performed at optimized conditions (Table 5.7 – 5.10).

It is observed that, on regeneration M(IV)PWs exhibited only a marginal decrease in % yields in each subsequent run, probably due to regeneration of the acid sites. However, a reactivation in case of 12-TPA/M(IV)O_2-20 exhibited a much higher decrease in % yields. In case of synthesis of 2-MA, EDX analysis for both fresh and spent catalysts (ZrPW and 12-TPA/ZrO_2-20) has been performed after first catalytic run (Table 5.11; Figure 5.20 - 5.23). Decrease in atomic wt. % of Zr in ZrPW and Zr and W in 12-TPA/ZrO_2-20 is observed, indicating leaching of ions, which could be the probable reason for decrease in % yields.

When M(IV)PWs were used as such after each subsequent run (i.e. without regeneration), the decrease in % yields are much higher compared to regenerated M(IV)PWs, which is probably attributed to the deactivation of catalysts, due to substrate molecules getting adsorbed on surface or also entering interstices of the catalyst material [54].

Reaction mechanism for solid acid catalyzed synthesis of anthraquinone derivatives

A probable mechanism for the Friedel-Crafts reaction for synthesis of 2-methyl anthraquinone using solid acid catalysts is presented in scheme 5.17.



***Scheme 5.17** Proposed mechanism for synthesis of 2-methyl anthraquinone using solid acid catalyst.*

Table 5.6 *Optimization of reaction conditions for preparation of anthraquinone derivative from toluene and phthalic anhydride by using ZrPW and 12-TPA/ZrO_2-20.*

Set No.	**Reactants with their mole ratio**	**Catalyst amount (g)**	**Reaction time (h)**	**Reaction temperature (°C)**	**% Yield of 2-MA**	
					ZrPW	**12-TPA/ ZrO_2-20**
(A)Reaction time variation						
1	T:PA (1:1)	0.15	0.5	120°C	8.77	6.50
2	T:PA (1:1)	0.15	1.0	120°C	14.81	11.07
3	T:PA (1:1)	0.15	1.5	120°C	27.32	25.60
4	T:PA (1:1)	0.15	2.0	120°C	40.90	37.28
5	T:PA (1:1)	0.15	2.5	120°C	51.77	46.10
6	T:PA (1:1)	0.15	**3.0**	120°C	**61.00**	**55.80**
7	T:PA (1:1)	0.15	3.5	120°C	61.13	55.84
8	T:PA (1:1)	0.15	4.0	120°C	61.20	55.91
(B)Reaction temperature variation						
9	T:PA (1:1)	0.15	3.0	110°C	50.38	41.19
10	T:PA (1:1)	0.15	3.0	**120°C**	**61.00**	**55.80**
11	T:PA (1:1)	0.15	3.0	130°C	57.84	50.45
12	T:PA (1:1)	0.15	3.0	140°C	50.13	38.12
(C)Catalyst amount variation						
13	T:PA (1:1)	0.15	3.0	120°C	61.00	55.80
14	T:PA (1:1)	0.20	3.0	120°C	62.85	57.71
15	T:PA (1:1)	0.25	3.0	120°C	64.99	60.00
16*	**T:PA (1:1)**	**0.30**	**3.0**	**120°C**	**67.74**	**61.11**
17	T:PA (1:1)	0.35	3.0	120°C	67.81	61.19
(D)Mole ratio variation						
18	T:PA (1.2:1)	0.30	3.0	120°C	63.11	57.22
19	T:PA (1:1.2)	0.30	3.0	120°C	40.34	35.16

*(T: toluene; PA: phthalic anhydride; * Optimum condition)*

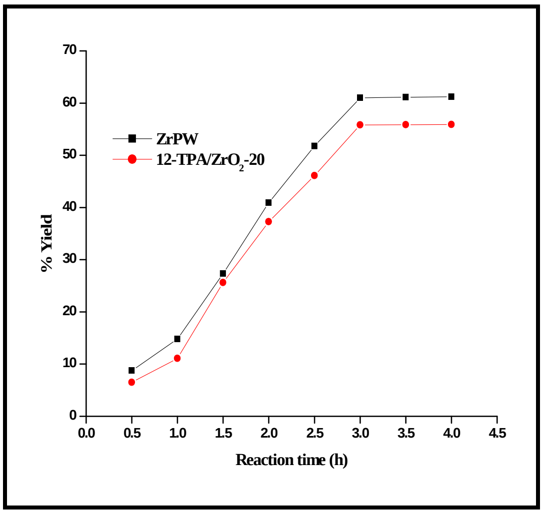


Figure 5.12 Optimization of reaction time for synthesis of 2-MA

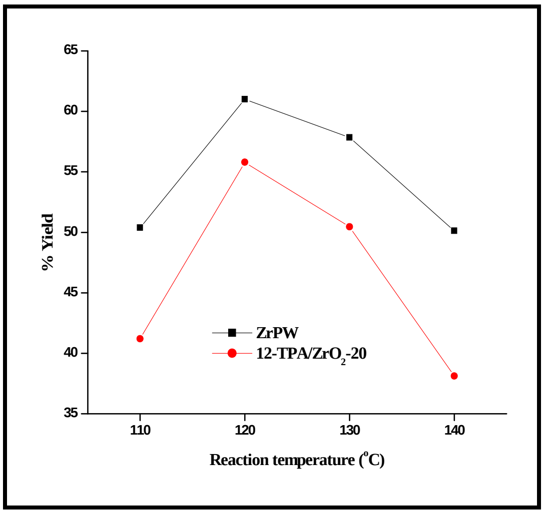


Figure 5.13 Optimization of reaction temperature for synthesis of 2-MA

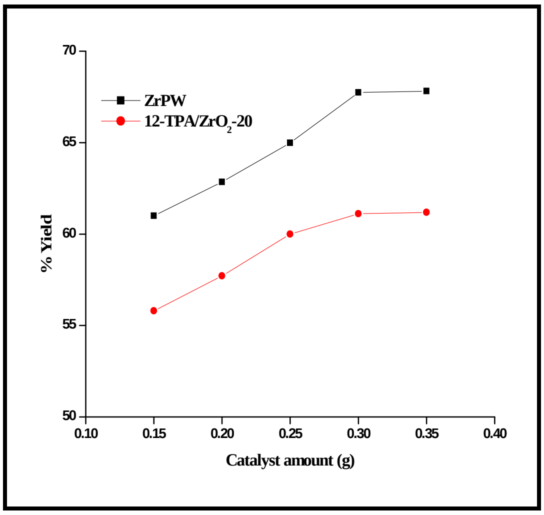


Figure 5.14 Optimization of catalyst amount for synthesis of 2-MA

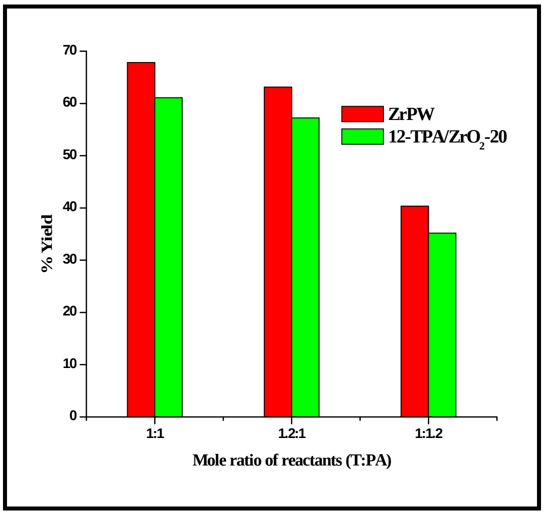


Figure 5.15 Optimization of mole ratio of reactants for synthesis of 2-MA

Table 5.7 *Synthesis of anthraquinone derivative from toluene and phthalic anhydride by using M(IV)PWs and 12-TPA/M(IV)O$_2$-20 at optimized condition.*

Catalyst	**% Yield (TON) of 2-MA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	67.74 (5.41) *(F)*	66.00 (5.28) *(Rg)*	64.07 (5.12) *(Rg)*
TiPW	71.84 (5.74) *(F)*	70.11 (5.60) *(Rg)*	67.95 (5.43) *(Rg)*
SnPW	68.30 (5.46) *(F)*	67.08 (5.36) *(Rg)*	65.17 (5.21) *(Rg)*
ZrPW	67.74 (5.41) *(F)*	59.81 (4.78) *(Ru)*	49.12 (3.92) *(Ru)*
TiPW	71.84 (5.74) *(F)*	60.52 (4.84) *(Ru)*	52.16 (4.17) *(Ru)*
SnPW	68.30 (5.46) *(F)*	55.87 (4.46) *(Ru)*	43.49 (3.47) *(Ru)*
12-TPA/ ZrO$_2$-20	61.11 (4.88) *(F)*	49.65 (3.97) *(Ra)*	37.54 (3.00) *(Ra)*
12-TPA/ TiO$_2$-20	66.40 (5.31) *(F)*	54.22 (4.33) *(Ra)*	42.93 (3.43) *(Ra)*
12-TPA/ SnO$_2$-20	62.90 (5.03) *(F)*	50.19 (4.01) *(Ra)*	37.71 (3.01) *(Ra)*

[Mole ratio of toluene:phthalic anhydride-1:1; Catalyst amount-0.3g; reaction temperature-120°C; reaction Time-3h; F: Fresh catalyst; Rg: Regenerated catalyst; Ru: Reused catalyst (used as such, without regeneration); Ra: Reactivated catalyst; Yields refer to the isolated pure products]

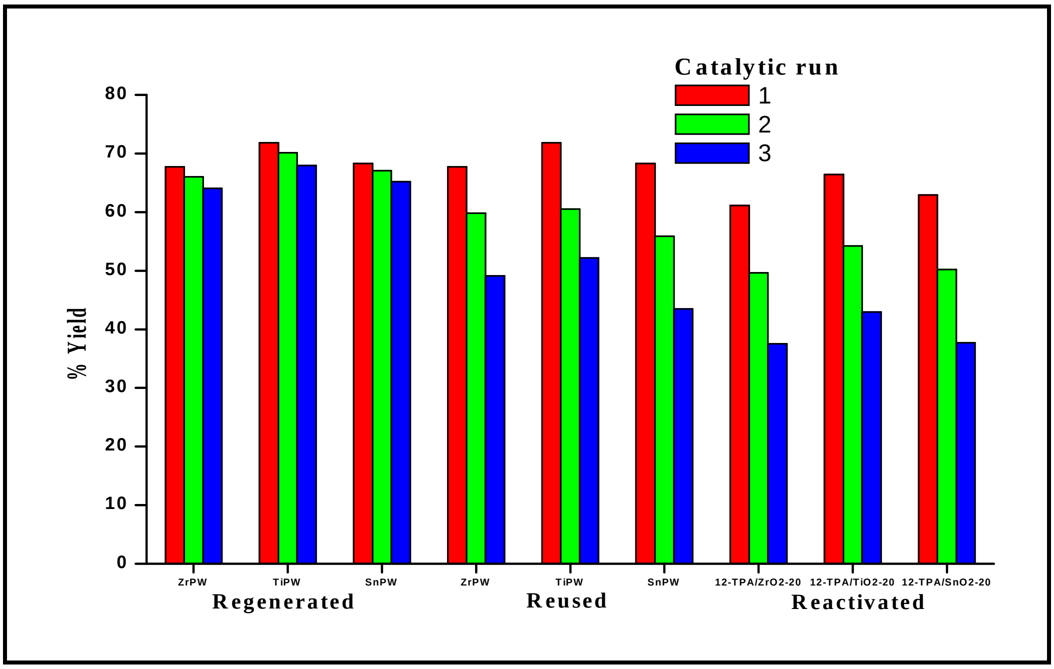


Figure 5.16 *Comparison of % yields of 2-MA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O$_2$-20.*

Table 5.8 *Synthesis of anthraquinone derivative from nitrobenzene and phthalic anhydride by using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimized condition.*

Catalyst	**% Yield (TON) of 2-NA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	48.07 (4.34) *(F)*	46.32 (4.18) *(Rg)*	43.61 (3.93) *(Rg)*
TiPW	54.67 (4.93) *(F)*	53.90 (4.86) *(Rg)*	52.00 (4.69) *(Rg)*
SnPW	53.10 (4.79) *(F)*	52.23 (4.71) *(Rg)*	50.99 (4.60) *(Rg)*
12-TPA/ ZrO_2-20	40.08 (3.61) *(F)*	29.11 (2.62) *(Ra)*	17.80 (1.60) *(Ra)*
12-TPA/ TiO_2-20	42.38 (3.82) *(F)*	33.40 (3.01) *(Ra)*	21.00 (1.89) *(Ra)*
12-TPA/ SnO_2-20	40.54 (3.66) *(F)*	31.70 (2.86) *(Ra)*	20.51 (1.85) *(Ra)*

(Mole ratio of nitrobenzene:phthalic anhydride-1:1; Catalyst amount-0.3g; reaction temperature-120°C; reaction Time-3h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

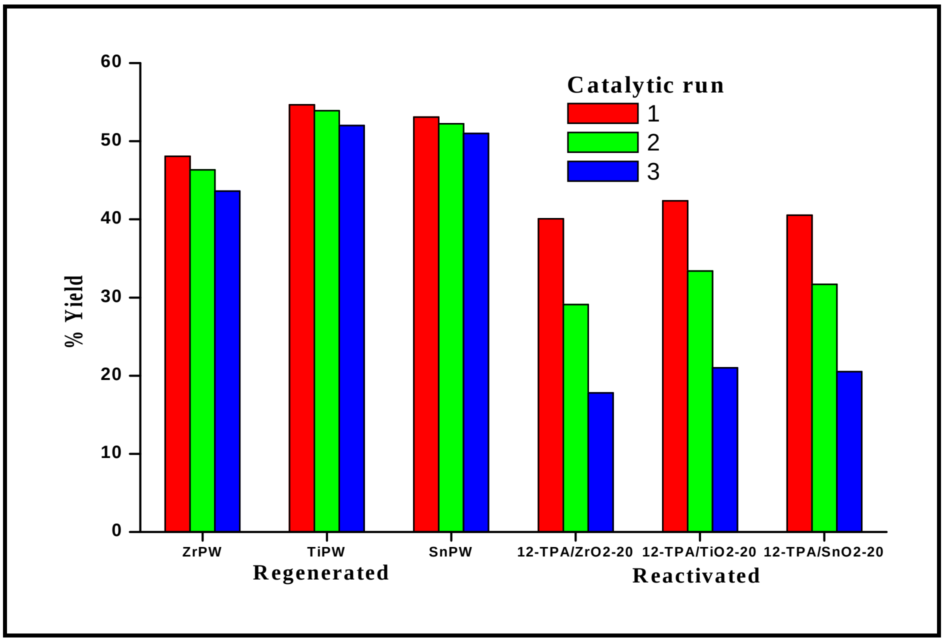


Figure 5.17 *Comparison of % yields of 2-NA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.9 *Synthesis of anthraquinone derivative from resorcinol and phthalic anhydride by using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimized condition.*

Catalyst	**% Yield (TON) of 1,3-DHA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	72.29 (6.21) *(F)*	71.37 (6.13) *(Rg)*	68.19 (5.86) *(Rg)*
TiPW	77.21 (6.64) *(F)*	76.03 (6.53) *(Rg)*	75.30 (6.47) *(Rg)*
SnPW	73.70 (6.33) *(F)*	71.84 (6.17) *(Rg)*	70.00 (6.02) *(Rg)*
12-TPA/ ZrO_2-20	67.17 (5.77) *(F)*	51.48 (4.42) *(Ra)*	40.33 (3.46) *(Ra)*
12-TPA/ TiO_2-20	70.77 (6.08) *(F)*	62.22 (5.35) *(Ra)*	48.51 (4.17) *(Ra)*
12-TPA/ SnO_2-20	68.44 (5.88) *(F)*	55.50 (4.77) *(Ra)*	41.17 (3.54) *(Ra)*

(Mole ratio of resorcinol:phthalic anhydride-1:1; catalyst amount-0.3g; reaction temperature-120°C; reaction Time-3h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

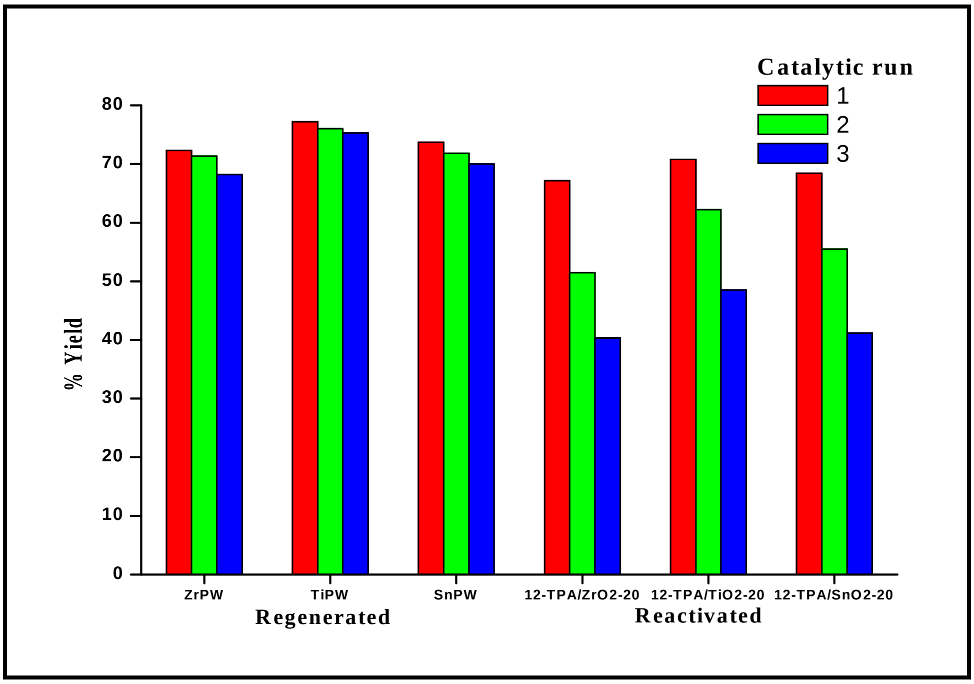


Figure 5.18 *Comparison of % yields of 1,3-DHA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.10 *Synthesis of anthraquinone derivative from hydroquinone and phthalic anhydride by using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimized condition.*

Catalyst	**% Yield (TON) of 1,4-DHA**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	74.00 (6.36) *(F)*	72.85 (6.26) *(Rg)*	69.33 (5.96) *(Rg)*
TiPW	79.11 (6.80) *(F)*	78.00 (6.70) *(Rg)*	75.42 (6.48) *(Rg)*
SnPW	77.09 (6.62) *(F)*	75.53 (6.49) *(Rg)*	72.67 (6.24) *(Rg)*
12-TPA/ ZrO_2-20	68.90 (5.92) *(F)*	54.00 (4.64) *(Ra)*	41.08 (3.53) *(Ra)*
12-TPA/ TiO_2-20	73.12 (6.28) *(F)*	63.09 (5.42) *(Ra)*	50.19 (4.31) *(Ra)*
12-TPA/ SnO_2-20	70.00 (6.02) *(F)*	58.29 (5.01) *(Ra)*	45.66 (3.92) *(Ra)*

(Mole ratio of hydroquinone:phthalic anhydride-1:1; catalyst amount-0.3g; reaction temperature-120°C; reaction Time-3h; F: Fresh catalyst; Rg: Regenerated catalyst; Ru: Ra: Reactivated catalyst; Yields refer to the isolated pure products)

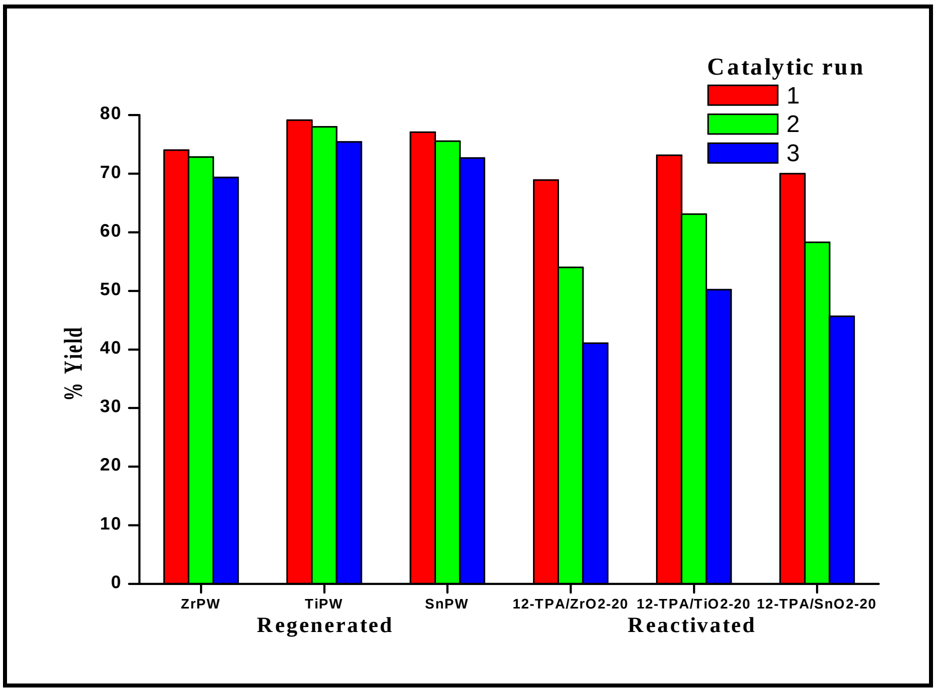


Figure 5.19 *Comparison of % yields of 1,4-DHA at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20.*

Table 5.11 *Elemental analysis by EDX for both fresh and spent ZrPW and 12-TPA/ZrO_2-20 in the synthesis of 2-MA.*

Reactants	**Materials**	**% by EDX analysis**			
		Zr	**P**	**W**	**O**
Toluene: Phthalic Anhydride	ZrPW (Fresh)	60.79	18.53	20.67	-
	ZrPW (Spent)	55.14	22.94	21.92	-
	12-TPA/ZrO_2-20 (Fresh)	28.75	0.11	3.44	67.70
	12-TPA/ZrO_2-20 (Spent)	17.09	1.58	0.51	80.82

(Mole ratio of Toluene: Phthalic anhydride -1:1; Catalyst amount - 0.3 g; Reaction temperature - 120 °C; Reaction Time- 4h)

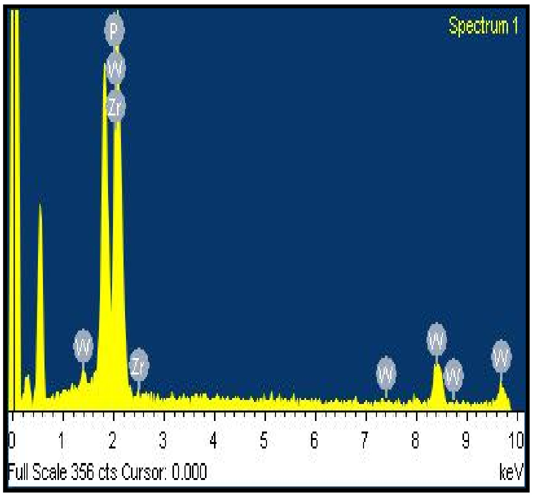


Figure 5.20 *EDX of fresh ZrPW*

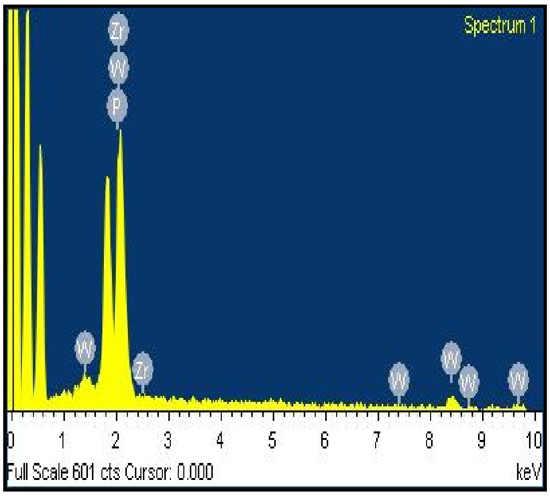


Figure 5.21 *EDX of spent ZrPW in synthesis of 2-MA*

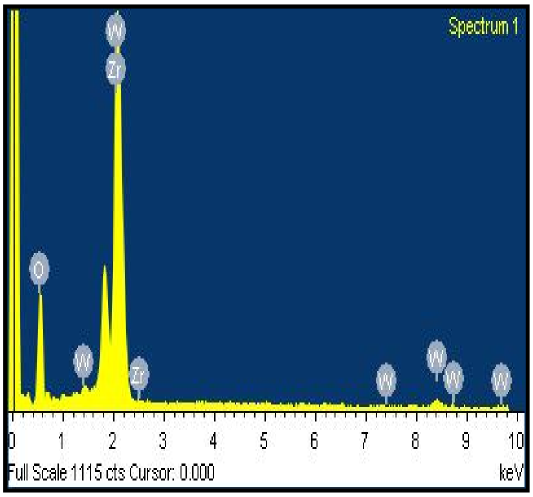


Figure 5.22 *EDX of fresh 12-TPA/ZrO_2-20*

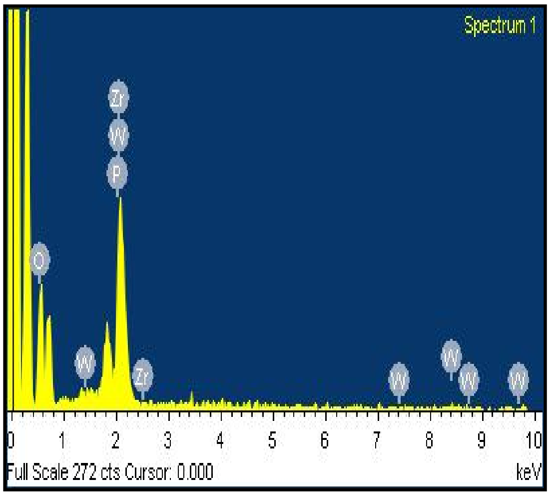
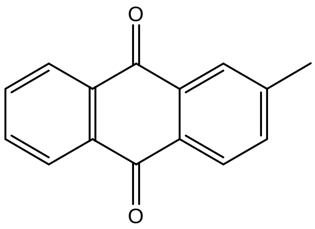
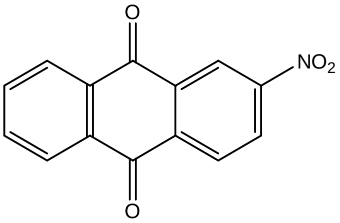
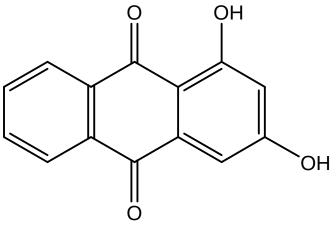
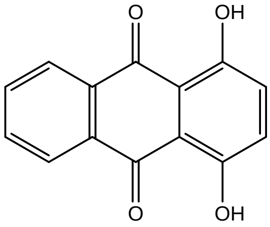


Figure 5.23 *EDX of spent 12-TPA/ZrO_2-20 in synthesis of 2-MA*

Characterization of the products

The isolated products were characterized by FTIR and ^{1}H-NMR spectroscopy. Melting points are in good agreement with reported values [55] (Table 5.12).

Table 5.12 *Characterization of anthraquinone derivatives.*

Product formed	***Characterizations***	
 2-methyl anthraquinone	**M.P. (^{o}C)**	177-178
	IR *(υ_{max}/cm^{-1})*	2950 (w), 2900 (w), 1669 (s), 1593 (s)
	^{1}H-NMR *(δH: 400 MHz; $CDCl_3$)*	2.4 (3H,s), 7.4 – 7.8 (7H,m).
 2-nitro anthraquinone	**M.P. (^{o}C)**	231-232
	IR *(υ_{max}/cm^{-1})*	1670 (m), 1510 (s), 1390 (s)
	^{1}H-NMR *(δH: 400 MHz; $CDCl_3$)*	7.3-7.8 (7H, m)
 1,3-dihydroxy anthraquinone	**M.P. (^{o}C)**	267-268
	IR *(υ_{max}/cm^{-1})*	3216 (s), 1660 (s), 1529 (s); 1434 (s)
	^{1}H-NMR *(δH: 400 MHz; $CDCl_3$)*	6.6 (1H, s), 6.8 (1H, s), 7.5 (2H, m), 7.7 (2H, m), 8.8 (2H, bs).
 1,4-dihydroxy anthraquinone	**M.P. (^{o}C)**	195-196
	IR *(υ_{max}/cm^{-1})*	2920 (w), 1630 (m), 1585 (m), 1450 (m)
	^{1}H-NMR *(δH: 400 MHz; $CDCl_3$)*	6.8 (2H, d), 7.5 (2H, m), 7.7 (2H, m), 9.3 (2H, bs).

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