

Oxidation of p-Anisaldehyde to p-Anisic Acid by Organic Clay as a Novel Method

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Oxidation of p-anisaldehyde by microwave irradiation produces p-anisic acid under solvent-free condition. This oxidation reaction is performed in presence of different red, white and black organic clay as catalyst. This method possess functional group compatability, does not involve cumbersome work-up exhibits chemoselectivity since other functional groups remain intact and proceeds under mild reactions. The structure of the obtained products were analyzed by ¹H and ¹³C NMR(Nuclear Magnetic Resonance) spectral studies and organic clay catalysts were characterized by EDX(Energy dispersion x-ray analysis), XRD (X-ray diffraction) techniques. Elemental composition of red, white and black clay determined by EDX pattern recorded in the binding energy region of 1-10 KeV. XRD studies showed average crystallite size of clay catalyst is in the range of 20 - 30 nm. The resulting product obtained in good yield within reasonable time.

Keywords: Oxidation, p-anisic acid, Organic clay

Oxidation reactions play an important role in modern organic chemistry. Recent advances in the development of selective fundamental transformation in organic synthesis have led to new processes for the production of biologically active compounds.

The oxidation of aldehydes is one of the fundamental reaction. The carboxylic acid moiety is common functional group used extensively as synthetic intermediate in the preparation of a variety of fine or special chemicals, drugs^{1,2} and is usually synthesized through oxidation reactions starting from reduced precursors such as alcohols³, aldehydes⁴, or ketones⁵. The transformation of aldehydes into carboxylic acids is very useful chemical reaction and the most popular and widely used reagents for such transformation are John's reagent⁶⁻¹¹, oxone¹² calcium hypochlorite¹³ 2-hydroxyperoxyhexafluoro-2-propanol.¹⁴ These reactions involved use of superstoichiometric amounts of expensive compounds and use of basic or highly acidic reaction conditions. Substrates with acid-sensitive functionalities may not tolerate such acidity. Recently interesting methodologies have been reported for metal-mediated transformation of aldehydes functionality to carboxylic acid¹⁵⁻²⁶.

Methoxybenzoic acids (o-, m-, p-anisic acids) are derivatives of benzoic acid that possess antibacterial properties and characteristic odors and can be derived through series of chemical extraction processes. It can be synthetically derived from benzene derivatives; such as cresol, benzoic acid and p-hydroxy benzoic acid. It can be obtained by oxidation of anethole²⁷ by using P-bromo anisole (II), n-butyl lithium and carbon dioxide gas²⁸. P-anisic acid was synthesized by using n-hexyl bromide, tri(n-hexyl) amine, para-methoxy toluene with cobalt chloride hexahydrate in about 9 h²⁹ and

also by a catalytic oxidation process using p-methoxy toluene and propionic acid over a catalyst comprising of $\text{CoBr}_2 \cdot 6\text{H}_2\text{O}$ and $\text{MnBr}_2 \cdot 4\text{H}_2\text{O}$ with a reaction time of 20 h.³⁰ After this by changing the mole ratio of cobalt and manganese, p-anisic acid was synthesized by using p-methoxy toluene with oxygen or oxygen containing gas in the presence of acetic acid.³¹ By reduction of p-iodo anisole at mercury pool cathodes in dimethyl formamide saturated with carbon dioxide gas p-anisic acid was synthesized³². Synthesis of p-anisic acid was carried out by a homogenous catalytic reaction using the catalyst mixture of cobalt acetate tetrahydrate and manganese acetate tetrahydrate with co-promoter tungstophosphoric acid bromine / bromide, paramethyl anisol, glacial acetic acid (97%), carbon dioxide and oxygen gas.³³ These methods involved the toxic and hazardous metals as catalysts and also higher temperature, pressure.

P-anisic acid is used as raw material in many pharmaceuticals applications and has a significant role in food and cosmetics industries³⁴. It is a constituent of anise oil (*Oleum anisi*)³⁵ that possess antiseptic, aperients, and vermifuge properties. It is effective in clearing congestion in the lungs and the respiratory tracts in conditions like asthma or bronchitis.³⁶⁻³⁸ In the synthesis of vanillin it is used as intermediate.³⁹ Recently many synthetic methodologies are reported in the literature to prepare corresponding carboxylic acid from alcohols, aldehydes, ketones and nitriles. Synthetic methodology involves the synthesis from p-methoxy benzyl alcohol by insertion of oxygen atom of nitrous oxide into rhodium complex⁴⁰, sodium hypochlorite oxidation in the presence of catalytic amount of oxoammonium salts⁴¹, photo oxidation using N-bromosuccinimide⁴², dehydrogenation using NHC-ruthenium complex⁴³. Synthesis from p-methoxy benzaldehyde involves oxidation using 70% t-butyl hydrogen peroxide in the presence of catalytic amount of 10 mol % of Mohr's salt⁴⁴, sodium chlorite-35% hydrogen peroxide oxidation using oxygen scavengers⁴⁵, diphenyl diselenide oxidation with stoichiometric hydrogen peroxide.⁴⁶ Synthesis from p-methoxy acetophenone involves pH controlled oxidation of p-methoxy acetophenone by sodium hypochlorite^{47,48}, hydrogen peroxide oxidation in the presence of catalyst in ionic liquid⁴⁹, in presence of trifluoro acetic acid by oxone⁵⁰, cobalt carbonyl catalyzed carbonylation of 4-bromo anisole^{51, 52}, carboxylation of 4-bromoanisole by four membered ring disilane⁵³, oxidation of 4-methoxy benzyl amine⁵⁴, debenzoylation of benzyl-4-methoxy benzoate in the presence of silica supported sodium hydrogen sulphate⁵⁵, oxidation of p-methoxy toluene in the presence of a mixture of catalyst⁵⁶. All these reagents require organic solvents dichloromethane, acetone, or dimethyl-formamide, which are hazardous in cases of skin contact, eye contact, ingestion, or inhalation.

Clays are the aluminosilicates with layered structures, they provide several possibilities for synthetic applications and can be used as acid or base catalysts for various types of organic reactions⁵⁷. Due to environmental regulations and safety concern the development of environmentally benign methodologies⁵⁸ are necessary and among the viable alternatives available for green synthetic methods clay have attracted significant attention due to their extremely versatile properties. Microwave assisted synthesis provides clean synthesis with the advantage of enhanced reaction rates, higher yields, greater selectivity and economic for the synthesis of larger number of organic molecules. Microwave heat the compounds directly, therefore usage of solvents in the chemical reaction can be reduced or eliminated. Solvent-free synthesis in which reagent are absorbed on mineral support, has a great potential as it offers an eco-friendly green protocol in synthesis. Natural clays can be applied to catalyze a broad

variety of chemical transformations, thus providing exceptional importance for these materials in the development of new synthetic processes. Selective heating based on the principle that different materials respond differently to microwaves. Due to their physical nature, clays as catalysts absorb microwave energy and are excellent catalysts for microwave-assisted organic synthesis (MAOS).⁵⁹

Clays are layer aluminosilicates catalyze reactions in numerous ways. They stabilize high-energy intermediate. They can store energy in their lattice structures and can release it in the form of chemical energy. They can catalyze redox reactions and can serve as photocatalytic devices. They often exhibit high surface acidity [60].

A mixture of P-anisaldehyde (0.01 mol) and red/white/black clay (0.3g) was microwave irradiated in solvent-free condition for appropriate time. Completion of reaction was monitored by TLC. By ethanol product was separated in pure form and spent catalyst was collected by filtration and washed with hot ethanol. Products were characterized by ¹H NMR and ¹³C NMR.

Analysis of clay: In order to elucidate the mechanisms of the catalytic activities, the surfaces of the clay particles were examined with a scanning electron microscope (SEM), coupled with an energy dispersive x-ray spectroscopy (EDX). The elements present in the mineral structure are partially responsible for the catalytic activities of clays. The oxygen in the clays is almost 47-50% by weight in all three clays as shown in Table 1. Typical EDX spectra recorded for natural red, white and black clay. This shows that sample contains oxygen (O), Sodium (Na), Magnesium (Mg), Aluminium (Al), Silicon (Si), Potassium (K), Titanium (Ti), Iron (Fe).

Table 1. EDX analysis of red, white and black clay (Main Element Composition)

Elements	Red clay (Wt%)	White clay (Wt%)	Black clay (Wt%)
Oxygen(O)	48.19	47.29	50.81
Sodium (Na)	0.37	---	0.16
Magnesium (Mg)	0.84	1.44	2.14
Aluminium (Al)	8.87	3.19	5.59
Silicon (Si)	14.66	23.14	17.74
Potassium (K)	0.37	0.86	0.56
Titanium (Ti)	0.70	0.66	0.52
Iron (Fe)	18.08	7.39	14.78

Basically, clay soil is composed of millions of clay particles which are 0.002 mm in diameter or smaller. We have calculated the 2θ and crystallite size of the red, white and black organic clays by XRD spectra. Results are summarized in **Table 2**.

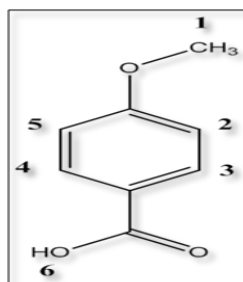
Table 2. XRD spectral analysis

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.1	250	14	48

Table 3. Screening result of the reaction condition for oxidation of P- anisaldehyde by red clay

Clays	2θ	Crystallite Size (nm)
Red Clay	48.783	20.407
White Clay	29.984	30.604
Black clay	26.498	22.373

^1H NMR spectra shows the methyl group peak at 3.83 singlet. **Figure 1** shows two aromatic protons (3, 4) shows peak at 6.95, 6.97 as a doublet and other aromatic protons (2, 5) shows peak at 7.89, 7.91 as a doublet. Acidic proton (6) shows peak at 12.53. ^{13}C NMR spectra shows methoxy group carbon at 55.16 and carboxylic acid carbon at 167.01. Aromatic carbons shows peak at 113.41, 114.21, 122.96, 131.20, 131.59, 162.68. Peaks from 39.90-40.15 and 78.36-79.02 are the CDCl_3 solvent peaks.

**Figure 1 P-anisic acid protons**

Reactions were performed by using different moles of reactant with each of 0.1 g of red, white and black clay as a catalyst. Final optimized results are shown below (**Table 3, 5, and 7**).

1 **Table 4. Optimization of the conditions for the oxidation of P-anisaldehyde with Red clay**

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.05	250	10	38
0.01	0.10	250	14	48
0.01	0.15	250	9	55
0.01	0.20	250	12	59
0.01	0.25	250	15	63
0.01	0.30	250	20	^a88
0.01	0.35	250	18	50

^a88 = 182-184 °C**Table 5. Screening result of the reaction condition for oxidation of P-anisaldehyde by white clay**

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.1	250	17	56

Table 6. Optimization of the conditions for the oxidation of P-anisaldehyde with White clay

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.05	250	13	35
0.01	0.10	250	10	56
0.01	0.15	250	12	49
0.01	0.20	250	16	57
0.01	0.25	250	19	75
0.01	0.30	250	22	^b92
0.01	0.35	250	20	64

^b92 = 181-184 °C

By taking different moles (0.005-0.06 mol) of p-anisaldehyde with 0.1g of organic clay such as red clay, white clay and black clay, reactions were carried out in solvent-free conditions under microwave irradiation (250 watt). Completion of reactions were checked by TLC. With 0.01 mol of p-anisaldehyde and 0.1g red clay yields 48% p-anisic acid in 14 min. When p-anisaldehyde (0.01 mol) reacted with white clay (0.1g) yields 56% p-anisic acid in 17 min while with black clay yields in 54% in 16 min.

From the results, it was clear that with the **0.01 mol** of substrate and **0.1g** of catalyst we got the good yield of p-anisic acid. To optimize the reaction conditions we have carried out the reactions with substrate (0.01 mol) and different amount of red, white and black clay as catalyst (**Table 4, 6 and 8**).

Table 7. Screening result of the reaction condition for oxidation of P-anisaldehyde by Black clay

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.1	250	16	54

Table 8. Optimization of the conditions for the oxidation of P-anisaldehyde by Black Clay

Substrate (mol)	Catalyst (g)	Power (w)	Time (min)	% Yield
0.01	0.05	250	11	36
0.01	0.10	250	16	54
0.01	0.15	250	14	61
0.01	0.20	250	18	64
0.01	0.25	250	15	70
0.01	0.30	250	21	90
0.01	0.35	250	16	83

°90 = 182-184 °C

To optimize the reaction conditions reactions were carried out with p-anisaldehyde (0.01 mol) and different amount of red, white and black organic clay as catalyst. By taking different amount (0.05-0.35g) of organic clay such as red clay, white clay and black organic clay with 0.01 mol of p-anisaldehyde reactions were carried out in solvent-free conditions under microwave irradiation (250 watt) to optimize the reaction conditions. With 0.01 mol of p-anisaldehyde and 0.3g of red clay yields 88% p-anisic acid (X) in 20 min and with the white and black clay as a catalyst yields 92% (Y) in 22 min and 90% (Z) in 21 min p-anisic acid respectively.

Basic mechanism of organic clay: Clay minerals are an important soil component. Organic reactions that take place by using clay catalysts which may function as Bronsted or Lewis acid or both. This property is derived from the mineral's characteristic structures. The lewis acidity is due to Al^{+3} & Fe^{+3} at the crystal edges. The Bronsted acid character of clays arises mainly due to the dissociation of the intercalated water molecules co-ordinated to cations. Surface area and the pore volume in the clay structure also add to the efficiency of the catalyst. Macropores in fine textured soils exist between aggregates. Because fine-textured soils have both macro and micropores **Figure 2** due to this they generally have a greater total porosity than coarse-textured soils.⁶⁰

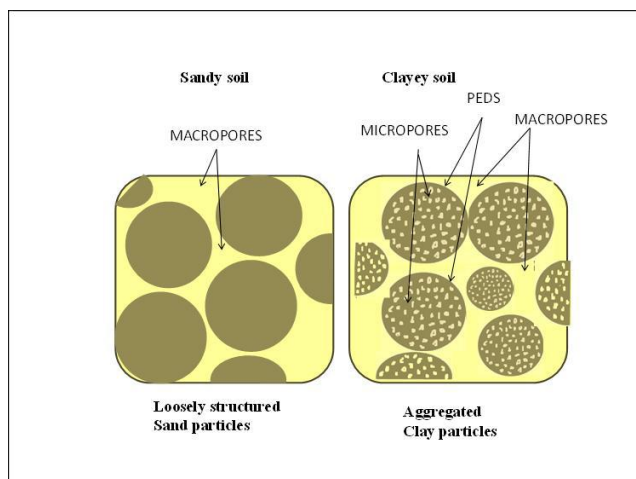


Figure 2 Structure of sandy and clayey soil

In conclusion, a novel method was developed to prepare p-anisic acid from p-anisaldehyde selectively and in good yields using red, white and black natural clay as a catalyst. Crystallite size was calculated from XRD spectra of red clay, white clay and black clays was found to be 20 nm, 30 nm and 22 nm respectively. In soils, clay are generally the most important adsorbents for inorganic metals and often for organic solutes as well. This is because of their very high surface areas. This method was cost effective, simple and less time consuming. The product p-anisic acid has been confirmed by ^1H NMR and ^{13}C NMR spectrum.

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