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Catalysis

Efficient Preparation of Alkyl Benzoates by Heteropolyacid-Catalysed Esterification of Benzoic Acid under Solvent-Free Condition

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This study reports a high-yielding, solvent-free, and scalable synthesis of alkyl benzoates from benzoic acid and its derivatives using heteropolyacids (HPA) as efficient and recyclable acid catalysts. The alkyl benzoates were obtained in excellent isolated yields (>85%) within 4 h at 120 °C using 1.5 equivalent of the alcohol reagent and only 0.4 mol% of the phosphotungstic acid (PTA) catalyst. The PTA catalyst was conveniently recovered and reused for three consecutive cycles without significant loss in mass or activity.

Introduction

Acid-catalysed esterification of carboxylic acids is one of the most versatile chemical transformations in the arsenal of synthetic organic chemistry, making products of significant commercial interests.[1] The presence of carboxylate esters is ubiquitous in the chemical literature with applications as a solvent,[2] surfactant,[3] biodiesel,[4] food additive,[5] plasticizers,[6] monomer for polymers,[7] agrochemicals,[8] and pharmaceuticals.[9] Esters of benzoic acid have significant commercial markets. For example, the esters of terephthalic acid are used as a monomer for terephthalate polymers,[10] and the diesters of phthalic acid are commercial plasticizers.[11] Esterification of benzoic acid is routinely carried out by Fischer esterification in the presence of an acid catalyst.[12] Alternatively, benzoate esters can be synthesized by transesterification of a readily available ester like methyl benzoate.[13] The catalytic activity, stability, and reusability are some of the essential parameters in selecting acid catalysts for the esterification reaction. Various classes of acid catalysts such as mineral acids, Lewis acids, and ion-exchange resins have been used for the esterification of benzoic acid and its derivatives.[14] The alcohol reagent is generally used in excess to favor the equilibrium towards ester formation and also to compensate for evaporative loss during the reaction. However, the use of excess alcohol introduces additional steps in product purification and catalyst recovery. Moreover, prolonged reaction time and higher loading of the acid-catalyst are often required for the esterification reactions. Some major challenges associated with the acid catalysts used in the esterification reaction include corrosive nature of the catalyst, high volatility and toxicity, formation of undesired side products, and difficulty in recycling. In this regard, HPAs are well-structured metal-oxide clusters that have strong Brönsted acidity, low volatility, low-toxicity, tunable solubility, and less corrosiveness.[15] HPA-based homogeneous and heterogeneous catalysts have been used over the past several years as efficient and environment-friendly catalysts for various organic transformations such as esterification, etherification, condensation, and hydrolysis.[16] Interestingly, HPA on a heterogeneous support has been used as catalyst for the preparation of alkyl benzoates.[17] Heterogeneous catalysts are relatively easy to recover from the reaction media, but they generally require more stringent reaction conditions. Leaching of the active catalyst from the supporting material is often encountered. On the other hand, homogeneous catalysts work under milder conditions, but their isolation and recycling are more challenging.[18] Hereby, we report the use of commercially-available HPA catalysts for the esterification of benzoic acid derivatives under homogeneous condition within a batch-type glass pressure reactor. After the reaction, the HPA catalysts are made heterogeneous by precipitating them in a non-polar solvent and recycled. We envisaged that using a sealed vessel for the reaction would allow achieving reaction temperatures higher than the boiling point of alcohol and help reach the equilibrium faster. The setup would also help to stop evaporative loss of the volatile reagent and allow less equivalent of the alcohol to be used. Use of only slight excess of the alcohol reagent helps to lower the amount of catalyst required, making the product separation straightforward, and easing the catalyst recyclability. In this work, a solvent-free, scalable, and high-yielding preparation of alkyl benzoates from benzoic acid and its derivatives is reported using commercially-available Keggin-type HPA catalysts (Scheme 1).

The reaction was optimized on the type and loading of HPA catalyst, the temperature of the reaction, and the molar ratio of the reagents (*i.e.*, benzoic acid and alkyl alcohol). The catalyst was separated from the reaction mixture by simple precipita-

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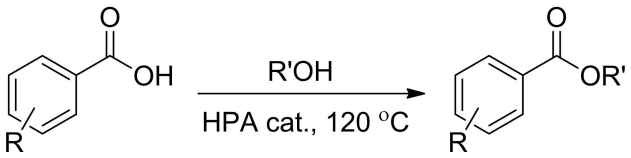


Scheme 1. Preparation of alkyl benzoates from benzoic acid and its derivatives using HPA catalyst.

tion, recovered by filtration and successfully reused for three consecutive cycles without significant loss in mass or catalytic activity.

Esterification of benzoic acid and its derivatives were carried out within a glass pressure reactor fitted with a Teflon screw top. The reactor was heated conventionally in an oil-bath while stirred continuously during the reaction. The HPA catalyst behaved as a homogenous catalyst since it got dissolved in hot alcohol. However, after the reaction, the catalyst was conveniently precipitated from the reaction medium by adding a non-polar solvent like petroleum ether. The reaction was optimized on the temperature of the reaction, type, and loading of catalyst, molar ratio of reagents, and duration of the reaction. Butyl benzoate was chosen as the substrate for the optimization. The catalyst was successfully recycled for three consecutive cycles without significant loss in mass or activity of the catalyst.

Results and discussion

To investigate the efficiency of various HPA catalysts, the esterification reaction was carried out using commercial phosphotungstic acid (PTA), phosphomolybdic acid (PMA), silicotungstic acid (STA), and silicomolybdic acid (SMA) catalyst. The catalysts were pre-dried at 110 °C overnight prior use. The esterification of benzoic acid (**1**) with 1-butanol was carried out at 120 °C for 4 h using 0.4 mol% of HPA catalysts. Among the four HPAs examined, PTA was found to be the most effective catalyst (Figure 1). Use of PTA as catalyst afforded butyl

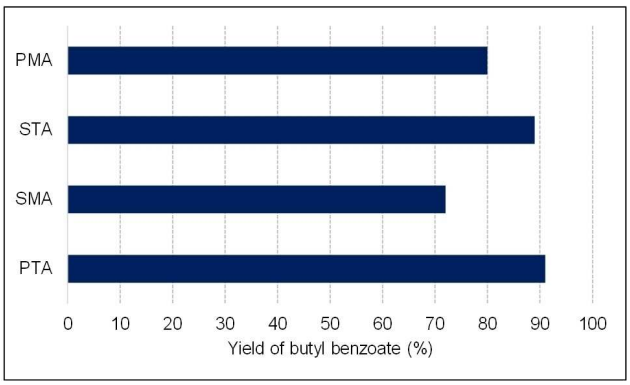


Figure 1. The efficiency of various HPAs on the yield of butyl benzoate (**1d**). Reaction conditions: benzoic acid (**1**) (1.00 g, 8.19 mmol): 1-butanol (0.910 g, 12.30 mmol, 1.5 eq.), 120 °C, 4 h, HPA (0.4 mol%).

benzoate (**1d**) in 91% isolated yield. STA was found to be nearly as efficient as PTA and provided **1d** in 89% yield. SMA and PMA produced **1d** in 72% and 80% yield, respectively, under identical conditions. The results may be explained by the highest acidity of PTA among the HPA catalysts examined.[19]

Since PTA was found to be the most active catalyst, the effect of loading of PTA on the isolated yield of **1d** was investigated while keeping the other reaction parameters unaltered. When the loading of the PTA catalyst was lowered to 0.2 mol%, the yield of **1d** dropped to 75% after 4 h at 120 °C. However, the loading of PTA catalyst more than 0.4 mol% did not increase the yield of **1d** appreciably (Figure 2).

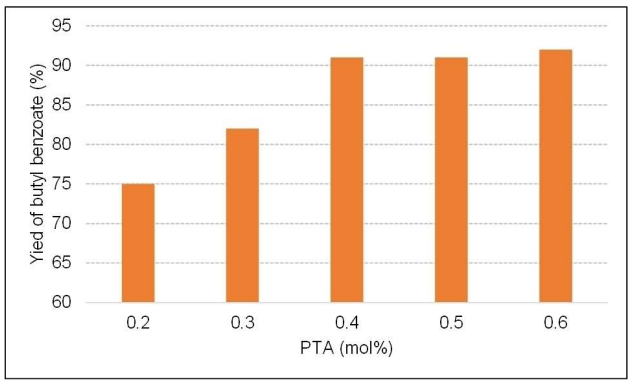


Figure 2. Effect of loading of PTA catalyst on the isolated yield of butyl benzoate (1d). Reaction conditions: benzoic acid (**1**) (1.00 g, 8.19 mmol): 1-butanol (0.910 g, 12.30 mmol, 1.5 eq.), 120 °C, 4 h, PTA.

The acid-catalysed esterification of benzoic acid (**1**) is reversible, and the maximum yield of butyl benzoate (**1d**) can be obtained if the reaction reaches equilibrium. The effect of reaction temperature on the conversion of **1** and yield of **1d** was studied using PTA as the acid catalyst. The reaction was conducted for 4 h at the chosen temperature using 1.5 equivalent of 1-butanol and 0.4 mol% PTA catalyst. After the reaction, the PTA catalyst was precipitated by adding petroleum ether. The product was purified by column chromatography using silica gel as adsorbent. Reaction temperatures below 100 °C provided **1d** in poor yields (Figure 3) after 4 h of reaction. When the temperature was increased further, the yield of **1d** increased significantly from 70% at 100 °C to 88% at 110 °C. When the temperature was increased to 120 °C, the yield of **1d** improved marginally to 91%. There was virtually no side product, and the mass balance was essentially unreacted benzoic acid.

The yield of esters in the acid-catalysed esterification reaction generally improves if excess alcohol is used since it favors the equilibrium towards the product (*i.e.*, ester) side. However, the use of excess alcohol complicates the product purification and catalyst recovery. Additionally, the use of excess alcohol increases the process cost, and the recycling of unreacted alcohol is energy-intensive. Synthesis of **1d** was attempted at a temperature of 120 °C, duration of 4 h, and

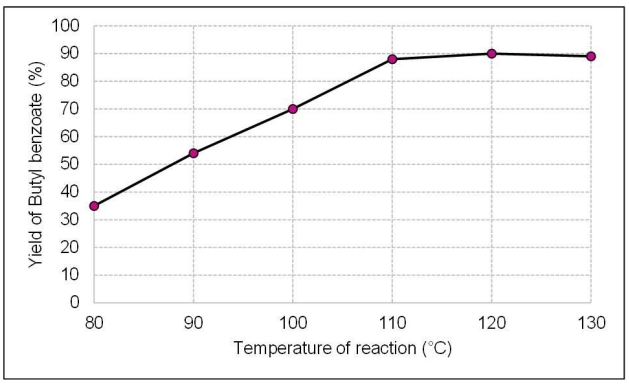


Figure 3. Effect of reaction temperature on the yield of butyl benzoate (**1d**). Reaction conditions: benzoic acid (**1**) (1.00 g, 8.19 mmol): 1-butanol (0.910 g, 12.30 mmol, 1.5 eq.), 4 h, PTA (0.4 mol%).

0.4 mol% of PTA catalyst. The molar ratio of benzoic acid to 1-butanol was varied between 1:1 and 1:2. The results show that the yield of **1d** at ratios above 1:1.5 is nearly constant (Figure 4). However, using molar ratios lower than 1:1.5

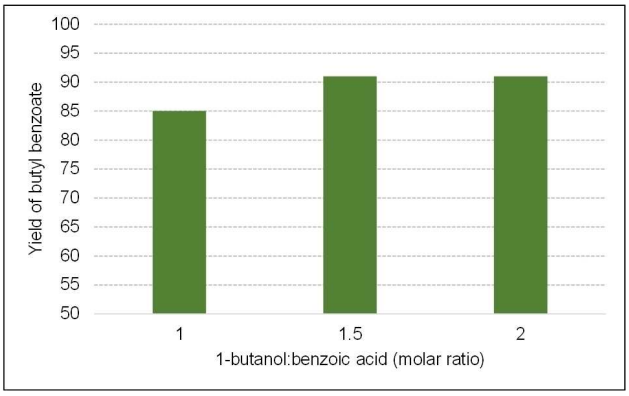
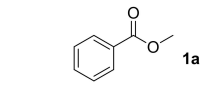
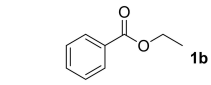
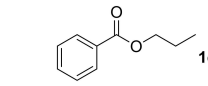
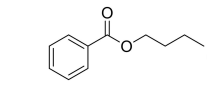
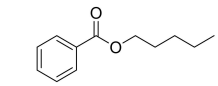
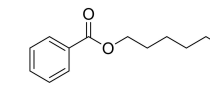
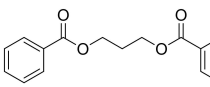


Figure 4. Effect of 1-butanol: benzoic acid molar ratio on the isolated yield of butyl benzoate (1d). Reaction conditions: benzoic acid (1) (1.00 g, 8.19 mmol), 120 °C, 4 h, PTA (0.4 mol%).

decreased the yield of **1d** due to incomplete reaction and unfavorable equilibrium towards the formation of ester. However, even with an equivalent amount of 1-butanol, **1d** was isolated in 85% yield. Increasing the equivalence of 1-butanol from 1 to 1.5 (with respect to benzoic acid) increased the yield incrementally and reached 91% at 1.5 equivalent of 1-butanol.

The optimized reaction for **1d** was adopted for the production of a homologous series of alkyl benzoates using straight-chain primary alcohols of different alkyl chain length. Methyl- to hexyl benzoates (**1a**–**1f**) were prepared in excellent isolated yields. In the case of methyl benzoate (**1a**) and ethyl benzoate (**1b**), higher alcohol amount (5 mL), and PTA loading (0.8 mol%) were required to obtain good yields within 4 h of reaction time. Notably, an overnight reaction allowed a lower amount of alcohol and PTA catalyst to be used. The yield of alkyl benzoate was found to increase marginally with increasing alkyl chain length in the alcohol reagent. The result may be explained by a lower rate of hydrolysis of the ester and easier phase separation of the water byproduct. While butyl benzoate (**1d**) was isolated in 91% yield, hexyl benzoate (**1f**) was obtained in 96% yield (Table 1, entry 4&6). Use of propane-1,3-diol as the alcohol provided propane-1,3-diyl dibenzoate (**1g**) in 40% yield. For the synthesis of **1g**, toluene was added as a solvent that helps to dissolve benzoic acid that otherwise sublimes and collect at the neck of the reactor.

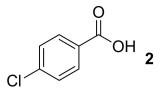
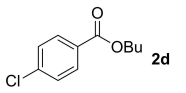
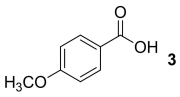
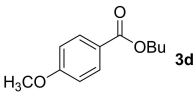
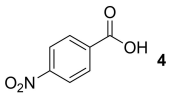
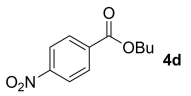
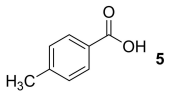
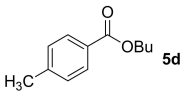
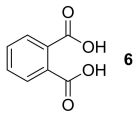
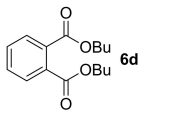
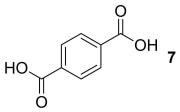
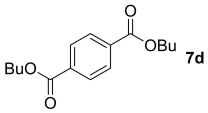
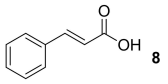
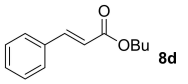
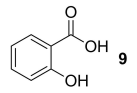
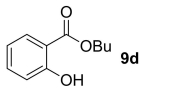
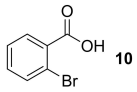
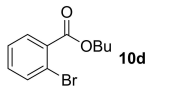
Table 1. Esterification of benzoic acid (**1**) with alkyl alcohols using the PTA catalyst.

Entry	Product	Reaction conditions	Yield (%)[b]
1[a]	 **1a**	120 °C, 4 h, methanol (5 mL), PTA (0.8 mol%)	84
2[a]	 **1b**	120 °C, 4 h, ethanol (5 mL), PTA (0.8 mol%)	86
3	 **1c**	120 °C, 4 h, 1-propanol (1.5 eq.), 0.4 mol% PTA	83
4	 **1d**	120 °C, 4 h, 1-butanol (1.5 eq.), 0.4 mol% PTA	91[d]
5	 **1e**	120 °C, 4 h, 1-pentanol (1.5 eq.), 0.4 mol% PTA	92
6	 **1f**	120 °C, 4 h, 1-hexanol (1.5 eq.), 0.4 mol% PTA	96
7[c]	 **1g**	120 °C, 12 h, 1,3-propanediol (0.5 eq.), toluene (5 mL)	40

[a] With 0.4 mol% PTA, **1a** and **1b** were obtained in 70% and 78% yield, respectively. [b] Isolated yield. [c] Toluene was added to avoid sublimation of benzoic acid in the reactor. [d] Turnover number of the PTA catalyst was calculated to be 229.

Butyl ester of various substituted benzoic acids was also synthesized using the PTA catalyst. The electron-donating and electron-withdrawing groups attached to the benzene moiety did not seem to affect the yield of butyl ester. Whereas butyl 4-chlorobenzoate (**2d**) was obtained in 93% yield, butyl 4-methyl benzoate (**5d**) was isolated in 89% yield. With strong electron-donating and electron-withdrawing group at the *para* position, butyl 4-methoxybenzoate (**3d**) and butyl 4-nitrobenzoate (**4d**) were isolated in 84% and 86% yield, respectively (Table 2, entry 2&3). Dibutyl phthalate (**6d**) was isolated in 45% yield. The mass balance is the monoester and unreacted phthalic acid. Dibutyl terephthalate (**7d**) provided a similar yield (40%) under the same reaction condition. Esterification of cinnamic acid afforded butyl cinnamate (**8d**) in 88% yield. Butyl 2-hydroxybenzoate (**9d**) was obtained in 83% isolated yield starting from 2-hydroxybenzoic acid or salicylic acid.

Table 2. Esterification of various benzoic acid derivatives using the PTA catalyst.

Entry	Starting material	Product	Yield (%)
1	 2	 2d	93
2	 3	 3d	84
3	 4	 4d	86
4	 5	 5d	89
5	 6	 6d	45
6	 7	 7d	40
7	 8	 8d	88
8	 9	 9d	83
9	 10	 10d	87

The products were purified by column chromatography. Alternatively, the crude reaction mixture (after separating the PTA catalyst) can be washed with saturated sodium bicarbonate solution and dissolve the unreacted benzoic acid.

Recyclability of the catalyst is one of the most important parameters for the green indices and process economics. Although the esterification reaction worked with a relatively small quantity of PTA catalyst (*i.e.*, 0.4 mol%), efficient recovery of the PTA catalyst was undertaken. The PTA catalyst used in the preparation of butyl benzoate (**1d**) was successfully recovered and recycled for three consecutive runs. After the reaction, the crude mixture of **1d** was diluted with petroleum ether, and the precipitated PTA catalyst was separated by decantation or centrifugation. The precipitated recovered catalyst was then dried in a hot-air oven at 110 °C for 12 h before submitting it for the subsequent esterification reaction. The mass loss of PTA catalyst was minimized by merely transferring the organic reaction mixture into another flask while drying the catalyst in the reaction vessel itself. A typical mass loss of 1–2% was observed between consecutive runs. The yield of **1d** decreased to 86% in the second run and 78% in the 3rd run (Figure 5). The amounts of benzoic acid and 1-butanol were adjusted in each trial based on the mass of PTA recovered.

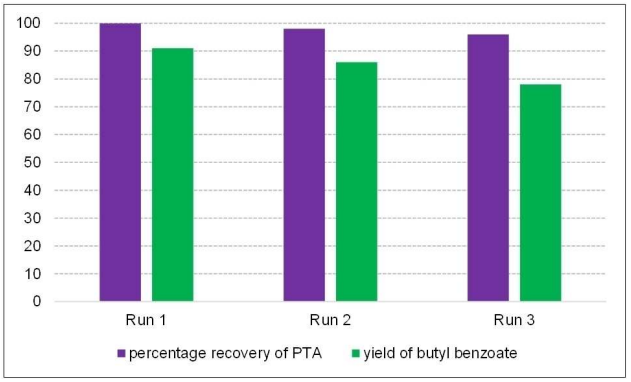


Figure 5. Recovery and reuse of PTA catalyst in the preparation of butyl benzoate (**1d**).

After each cycle, the dried PTA catalyst was characterized by FTIR spectroscopy to ensure that the structural integrity remained intact. The peak at 1077 cm^{-1} is the characteristic peak for the P–O stretching frequency, whereas the peak at 972 cm^{-1} corresponds to W=O stretching. The peaks at 884 cm^{-1} and 776 cm^{-1} correspond to W-O-W bridges (Figure 6).[20]

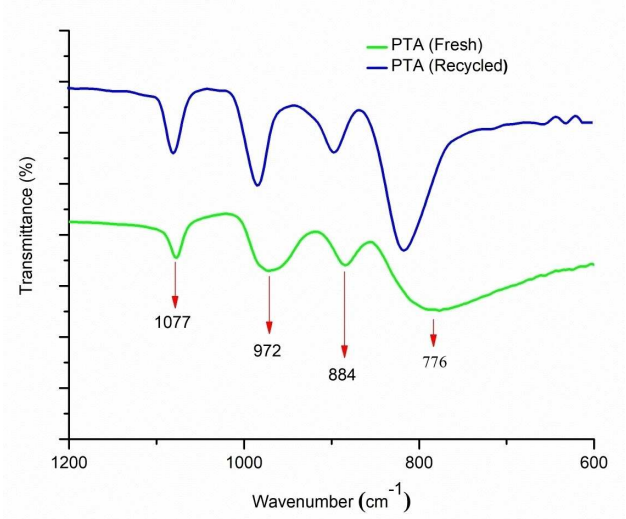


Figure 6. FTIR spectra of the fresh PTA and recycled (3rd cycle) PTA.

In addition, the recovered catalyst after the third cycle was characterized by ^{31}P-NMR spectroscopy and thermogravimetric (TGA) analysis.[21]

In conclusion, a solvent-free and gram-scale synthetic protocol for the esterification of benzoic acid has been developed using PTA as an efficient and green catalyst. The reactions were performed at 120 °C for 4 h in a glass pressure reactor that provided excellent isolated yields of benzoates using only slight excess of the alcohol reagent and 0.4 mol% of the PTA catalyst. Esterification of several substituted benzoic

acid molecules bearing electron-donating and electron-withdrawing groups have been reported. The PTA catalyst was successfully recovered from the reaction mixture by manipulating its solubility. The physical mass loss of the PTA catalyst in subsequent runs was minimal, and the catalyst activity remained nearly the same even after the third run.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: alkyl benzoate · benzoic acid · catalysis · esterification · heteropolyacid

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[21] The ^{31}P-NMR spectra and TGA thermograms of fresh and recycled PTA catalyst are provided in the supplementary information file (Figure S49 and Figure S50).

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