

[Regular Paper]

Halogen-free Friedel–Crafts Acylation of Toluene with Benzoic Anhydride over Insoluble Heteropoly Acid Catalyst

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Friedel–Crafts acylation of toluene with benzoic anhydride to produce phenyl tolyl ketone was studied over various ion exchanged heteropoly acids (HPA). Metal chloride such as AlCl_3 was not used as a catalyst. Acid chloride was not used as an acylating agent. Therefore, this reaction could provide a halogen-free fine chemical synthesis process. The effect of partial ion exchange with Na, Rb, K, Cs, Ca, Mg and Fe on HPA was tested at atmospheric pressure. Insoluble $\text{H}_{0.5}\text{CS}_{2.5}\text{PW}_{12}\text{O}_{40}$ catalyst showed the highest yield of 60%. The limited value of maximum yield was attributed to the side reaction. The effect of temperature showed that higher temperatures above the boiling point of toluene were desirable to reduce the side reaction. Then, the reaction was conducted in a sealed stainless autoclave reactor under pressurized conditions. Almost complete conversion without the side reaction was observed with this system above 410 K. The distribution of isomers of phenyl tolyl ketone at high temperatures was the same as that at low temperatures, suggesting that the reaction mechanism was independent of temperature. After washing the used catalyst with toluene, the catalyst was active for the second run but the activity gradually decreased after the third run.

Keywords

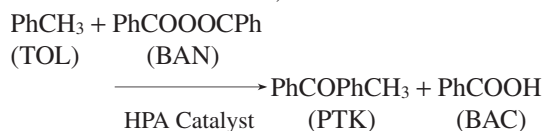
Friedel–Crafts acylation, Phenyl tolyl ketone, Chlorine free process, Heteropoly acid catalyst, Ion exchange

1. Introduction

The Friedel–Crafts acylation of aromatic compounds is an important method to produce aromatic ketones as useful intermediates for synthetic chemistry¹⁾. Conventionally, the Friedel–Crafts acylation of aromatic hydrocarbon is carried out in a homogeneous phase using acid halides as the acylating agents with acid catalysts such as AlCl_3 , BF_3 , ZnCl_2 , TiCl_4 , FeCl_3 or various Brønsted acids. These catalysts pose several problems, such as high toxicity, corrosion, spent acid disposal, and the necessity of more than stoichiometric amounts of acid catalysts. The acid halides are also decomposed to waste the halogen ion.

At present, considerable efforts are being made to find recyclable and environment-friendly catalysts. Nafion-H²⁾, zeolites^{3)–6)}, heteropoly acids (HPA) and their salts^{6)–9)}, clays^{10),11)}, and sulfate-doped metal oxides^{12),13)} are all useful catalysts. Heteropoly acids have attracted considerable attention because of their high surface area, high acidity and insolubility of their cesium salts^{14)–16)}. These characteristics suggest the possibility of using heterogeneous strong acid catalysts

in a liquid phase¹⁷⁾. Izumi *et al.*⁸⁾ and Castro *et al.*^{6),9)} conducted catalytic acylation using organic acid as acylating agents over heteropoly acids and suggested the possibility of chlorine free acylation. Goto *et al.*¹²⁾ also studied acylation of toluene with benzoic anhydride over SO_4/ZrO_2 . In our previous studies, insoluble cesium salts of heteropoly acids were used as heterogeneous catalysts for MTBE synthesis¹⁸⁾ and acylation of toluene¹⁹⁾. The acid strength correlated with the acylation activity of toluene with benzoic anhydride. In this study, the acylation of toluene (TOL) with benzoic anhydride (BAN) to produce phenyl tolyl ketone (PTK) with benzoic acid (BAC) over various heteropoly acid (HPA) catalysts was investigated under various reaction conditions;



Metal chloride such as AlCl_3 was not used as the catalyst. Acid chloride was not used as the acylating agent. Therefore, this reaction system provides a halogen-free Friedel–Crafts acylation process.

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2. Experimental

2.1. Catalysts

Heteropoly acids were purchased (Wako Pure Chemical Ind., Ltd., "Wako Special Grade") and used without further purification. Alkaline ion exchanged heteropoly acids were prepared by the reaction between an aqueous solution of the heteropoly acid and an aqueous solution of alkaline carbonate¹⁹. Other ion exchanged samples were also prepared in a similar procedure. Incorporation of iron ions was also examined according to the reported preparation procedure²⁰. The obtained samples were calcined at 573 K under flow of air for 3 h and kept in sealed glass ampoules.

Fine powders of ion exchanged HPA catalysts were dispersed in toluene during the reaction but the solubility of these samples in toluene was not determined. The colloidal characteristics made it difficult to recover the catalysts from the reaction mixtures by filtration method. The centrifugal method was used in this study to stop the reaction and to recover the catalyst.

2.2. Reaction Procedure

The acylation reaction was carried out in the following two modes.

- (1) Reaction at low temperature in an all-glass apparatus equipped with a condenser was carried out under reflux conditions at atmospheric pressure. The reaction was started by adding catalyst to the mixture of TOL and BAN under the desired reaction conditions.
- (2) Reaction at high temperature in a sealed stainless autoclave was carried out under pressurized conditions. The reaction was started by adding BAN solution to the mixture of TOL and the catalyst under the desired conditions. Although the total reaction pressure depended on the vapor pressure of TOL at the reaction temperature, it did not exceed 0.6 MPa in this experiment.

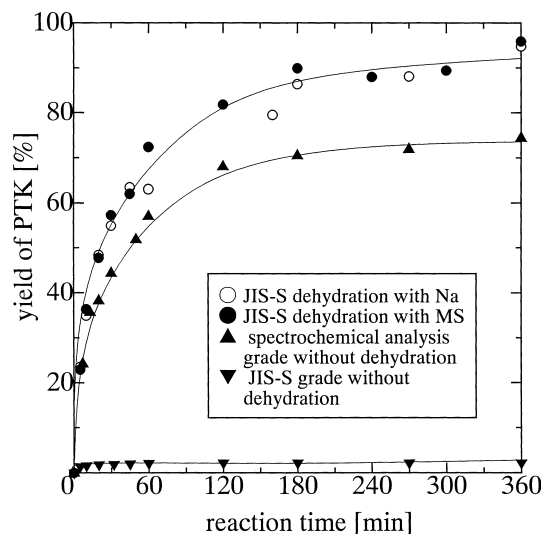
Standard reaction conditions were as follows:

TOL 1.17 mol (excess amount was used as a solvent), BAN 6.6 mmol, catalyst 0.33 mmol, tetradecane, 2.53 mmol (internal standard), rotation speed 200 rpm. Small samples of the reaction mixture were taken at adequate intervals. After immediate centrifugal removal of the catalyst, the sample was analyzed by gas chromatography. FID (hydrogen-flame ionization detector) gas chromatography (GL Science: GC353B) was used with a CHROMPACK CP-Sil 8CB column (0.25 mm × 25 m) at 463 K.

3. Results and Discussion

3.1. Effect of Moisture in TOL

The Friedel-Crafts reaction is a typical acid catalyzed reaction, so moisture in the reactants and solvents should be removed. The addition of water strongly decreases the catalytic activity of heteropoly acid in Friedel-Crafts reaction¹⁹. The effect of dehy-



TOL (JIS Special Grade, JIS-S) was dehydrated with molecular sieves (MS) or metallic sodium (Na).

Fig. 1 Effect of Dehydration Treatment of TOL on $H_{0.5}Cs_{2.5}PW_{12}O_{40}$ Catalyst (0.33 mmol) with BAN (6.6 mmol) at 383 K

dration of TOL on the yield of PTK is shown in **Fig. 1**. Without dehydration treatment of the "JIS Special Grade" of TOL (abbreviated as JIS-S TOL), the yield of PTK was very low. The "Spectrochemical Analysis Grade" of TOL without dehydration provided higher yield of PTK. Further increases in PTK yield was observed after the dehydration treatment of JIS-S TOL with molecular sieve zeolite (MS). The effect of dehydration of JIS-S TOL with sodium (Na) was almost the same as dehydration with MS. Based on these results, JIS-S TOL was used after dehydration with MS.

3.2. Screening of Catalysts

Figure 2 shows the results of the screening test under standard conditions at 373 K. Various ions were introduced into $H_3PW_{12}O_{40}$ catalyst. The promotion effects of partial ion exchange are indicated in **Fig. 2**. The yield of PTK depended on the type of exchanged ions and decreased in the order Cs > K > Rb > Na > without ion exchange. The yield of PTK reached to the maximum and never exceeded 60% in the case of the Cs derivative. Ion exchange with Ca and Mg resulted in loss of activity. Promotion with Fe ion was reported in the case of SO_4/ZrO_2 catalyst¹³, so the effect of Fe incorporated into $H_3PW_{12}O_{40}$ catalyst was tested. However, catalytic activities were lost in the cases of $H_{0.5}FePW_{12}O_{40}$ and $H_7PW_9Fe_3O_{37}$. In the following study, details of catalytic behavior of $H_{0.5}Cs_{2.5}PW_{12}O_{40}$ were reported because this catalyst showed the highest yield in this screening test.

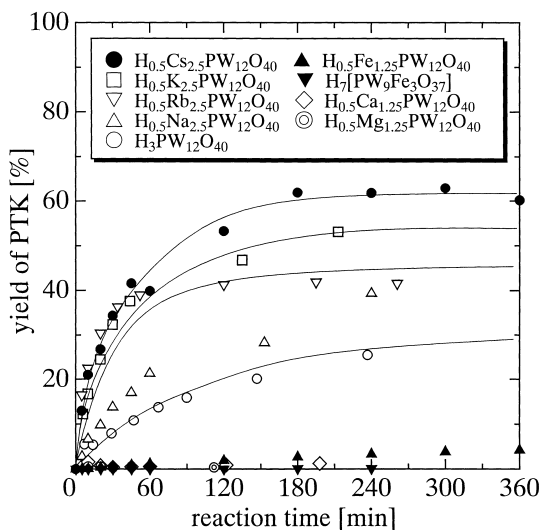


Fig. 2 Screening of Catalyst at 373 K under Standard Conditions with a Refluxing Glass Reactor

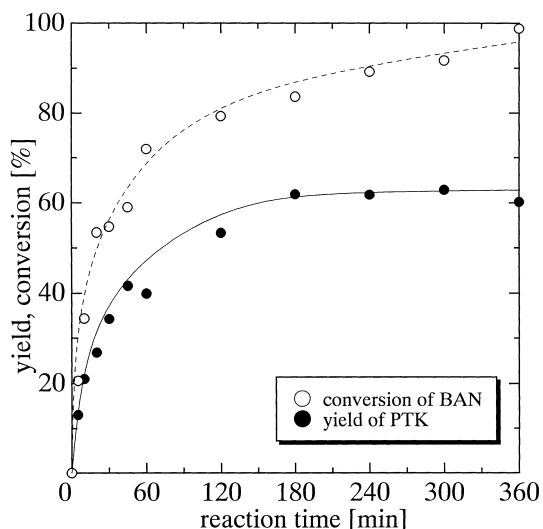
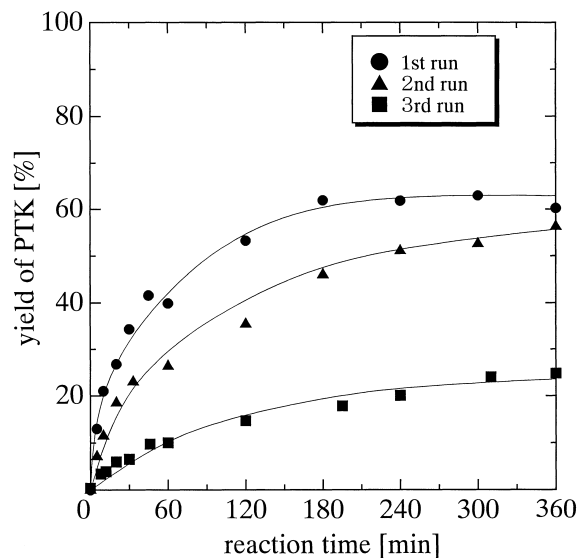


Fig. 3 Conversion and Yield at 373 K over $H_{0.5}CS_{2.5}PW_{12}O_{40}$ Catalyst under Standard Conditions

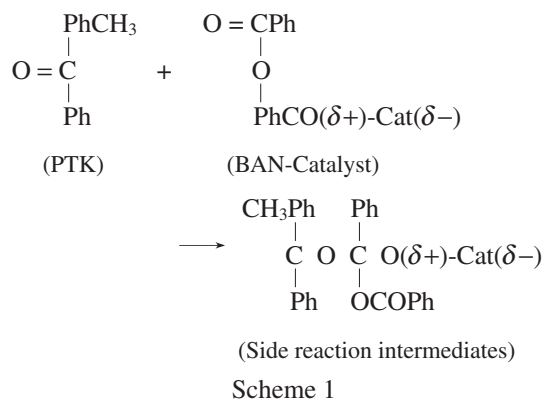
3.3. Time Course of Yield and Conversion

The time course of the yield of PTK and the conversion of BAN over $H_{0.5}CS_{2.5}PW_{12}O_{40}$ is shown in Fig. 3. Almost all BAN was consumed after 360 min but the yield of PTK was constant at about 60% after 180 min. The difference between the conversion and the yield could be attributed to by-products formed through side reactions. Although by-products could not be detected by GC (gas chromatography) analysis, GC-MS (mass spectroscopy) suggested the following intermediates of BAN-catalyst complex were formed with the product PTK¹⁹⁾.



Used catalyst was collected, washed with TOL and then used in the next run without calcination.

Fig. 4 Repeated Use of $H_{0.5}CS_{2.5}PW_{12}O_{40}$ Catalyst at 373 K under Standard Conditions



The intermediates would be decomposed into by-products and the regenerated catalyst. This assumption indicates that the constant yield of PTK after 180 min may not be caused by deactivation of the catalyst. The details of the reaction mechanism were discussed in the previous study¹⁹⁾.

3.4. Repeated Use of the Catalyst at Low Temperature

Figure 4 shows the results of repeated use of the catalyst. In this experiment, the used catalyst was washed with TOL three times and used for another run. Calcination pre-treatment of the used catalyst was not performed to avoid deactivation¹⁹⁾. The catalyst activity in the second run provided a similar yield to the first run although the rate of reaction decreased to some extent. In our previous paper¹⁹⁾, we reported that addition of reactant in the steady state of first run caused further formation of PTK. These results showed that the limited conversion at the first run was not caused by

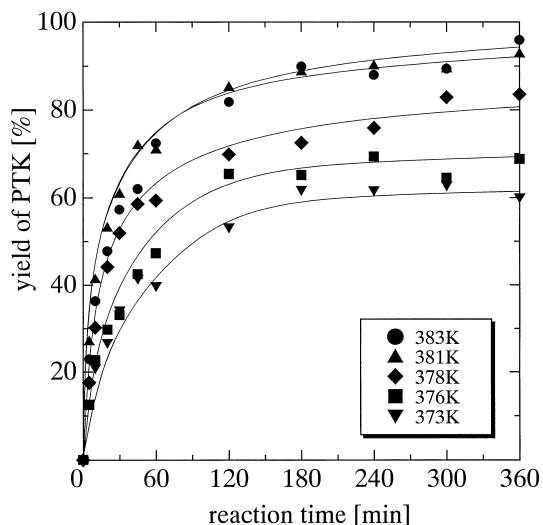


Fig. 5 Effect of Reaction Temperature in the Refluxing Glass Apparatus under Standard Reaction Conditions over $H_{0.5}Cs_{2.5}PW_{12}O_{40}$

intrinsic loss of catalytic activity. Gradual decrease in the activity was observed with repeated use. This suggests that part of the products adsorbed on the catalyst cannot be removed by washing with TOL.

3. 5. Effect of Reaction Temperature on the Yield

Assuming that the side reaction proceeds *via* Scheme 1, a catalyst-BAN complex attacks the adsorbed PTK to form a bulky “catalyst-BAN-PTK” intermediate, so high temperature operation of this reaction should prevent formation of such a bulky intermediate.

Figure 5 shows the results at higher temperatures under atmospheric pressure. In the range of 373–383 K, the yield of PTK reached a constant value, but the value increased with temperature to reach above 90% at 381 K and 383 K. The difference between the conversion of BAN and the yield of total PTK at 360 min in this experiment is plotted against the reaction temperature in Fig. 6. As shown in Fig. 3, the difference between the conversion and the yield suggests the amount of by-products. The results in Fig. 6 show that the formation of by-products decreases with increased reaction temperature, which supports the above assumption that high temperature operation will prevent the formation of the bulky intermediate complex formed in the side reaction.

Figure 7 shows the results at higher temperatures above boiling point using the autoclave reactor. In this case, the reaction pressure was greater than atmospheric pressure depending on the vapor pressure of TOL at the operation temperature. The total reaction pressure in this study was always below 0.6 MPa. With increased reaction temperature, the yield of PTK increased and reached almost 100% at 423 K within 60 min. In this case, the conversion of BAN and the

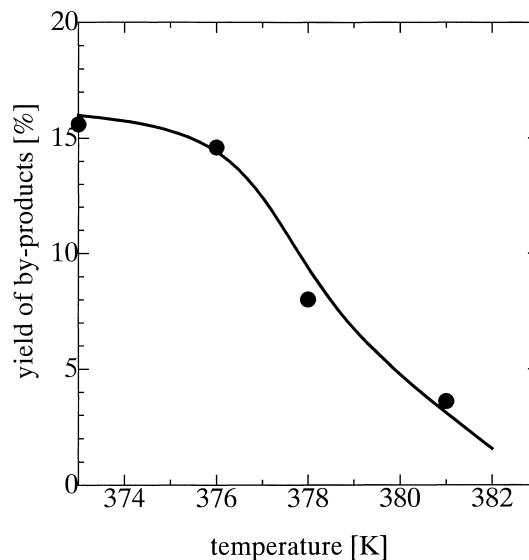


Fig. 6 Effect of Reaction Temperature on the Yield of By-products as Estimated by the Difference between Conversion of BAN and Yield of PTK

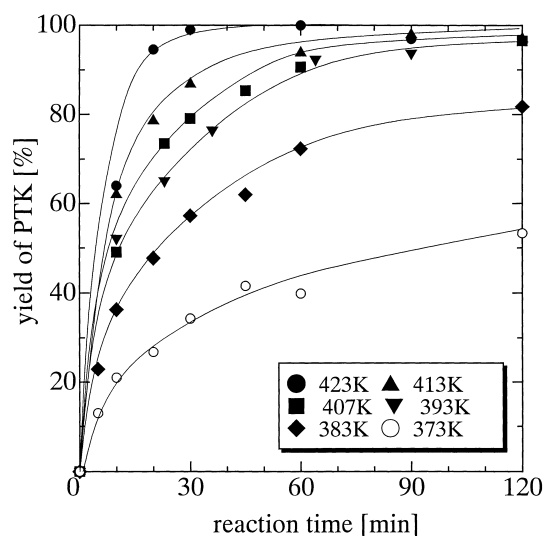


Fig. 7 Effect of Reaction Temperature in the Autoclave Reactor under Standard Reaction Conditions over $H_{0.5}Cs_{2.5}PW_{12}O_{40}$

yield of PTK agreed completely. These results also support the conclusion of the previous section about the side reaction.

3. 6. Effect of Reaction Temperature on the Selectivity

PTK has *o*-, *m*-, *p*-isomers, the product distribution of which is plotted against the reaction temperature in Fig. 8. The product distribution of PTK isomers was almost independent of the reaction temperature, suggesting that the reaction mechanism was not changed by the increase of reaction temperature and a typical

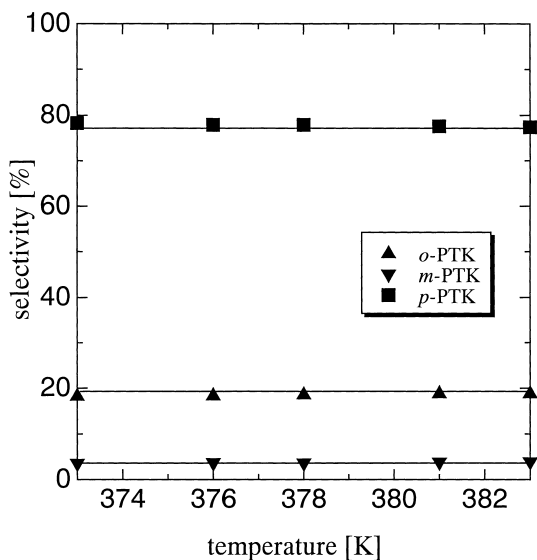
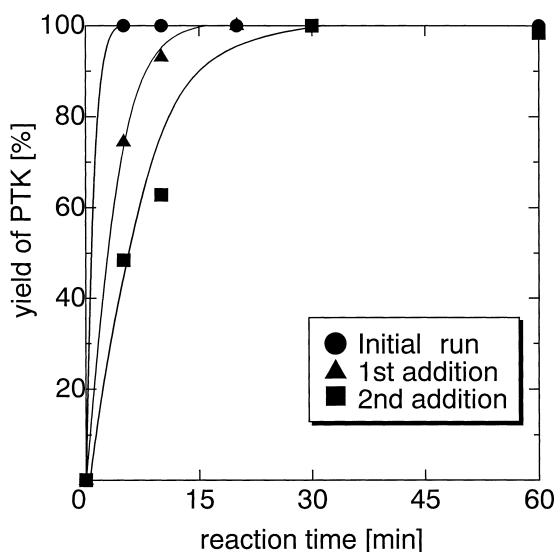


Fig. 8 Effect of Reaction Temperature on the Selectivity of PTK Isomers under Standard Reaction Conditions over $\text{H}_{0.5}\text{Cs}_{2.5}\text{PW}_{12}\text{O}_{40}$



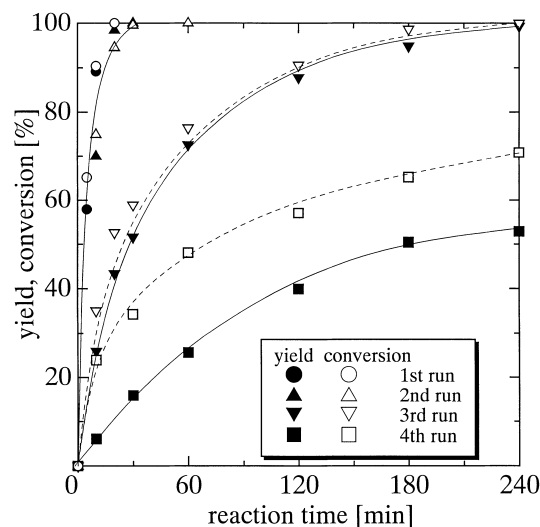
6.6 mmol of BAN was added repeatedly after 60 min intervals.

Fig. 9 Addition of Reactant at 423 K over $\text{H}_{0.5}\text{Cs}_{2.5}\text{PW}_{12}\text{O}_{40}$

acid catalyzed reaction was suggested from the *o*- and *p*- orientation of PTK isomers.

3.7. Addition of BAN at High Temperature

Figure 9 shows the effect of addition of BAN during the reaction at 427 K. In this experiment, BAN was added repeatedly after the yield of PTK reached the constant value. The time courses after each BAN addition are plotted in Fig. 9. The yield was calculated on the basis of the amount of BAN after each addition. Although complete conversions were observed repeatedly, a gradual decrease in the initial rate was



Used catalyst was collected, washed with TOL and then used in the next run without calcination.

Fig. 10 Repeated Use of $\text{H}_{0.5}\text{Cs}_{2.5}\text{PW}_{12}\text{O}_{40}$ Catalyst at 423 K under Standard Conditions

observed during this high temperature operation. The accumulation of products on the catalyst surface might cause this decrease in the initial rate.

3.8. Repeated Use of the Catalyst at High Temperature

Figure 10 shows the results of repeated use of catalyst at 423 K. After each run, the catalyst was recovered, washed with TOL three times and then used in the next run. The initial run and the second run showed almost the same time course and the total material balance indicated that by-products were not produced. The initial rate of the reaction decreased in the third run but by-products were not formed because the conversion and the yield agreed. In the fourth run, the initial rate further decreased. The difference between the conversion and the yield was significant at the fourth run, suggesting the formation of by-products.

These results suggest that the adsorbed products are not washed out completely by the washing procedure and that the accumulation of surface species causes the side reaction. In order to avoid deactivation, alternate methods to regenerate catalyst are required. Another possibility¹⁹⁾ is the deactivation shown in Fig. 10 which may occur during the recovery and regeneration procedure of the used catalyst. This suggests that the deactivation may be avoided by continuous operation on a fixed solid catalyst. For such a reaction system, colloidal $\text{H}_{0.5}\text{Cs}_{2.5}\text{PW}_{12}\text{O}_{40}$ catalyst should be fixed into a particle catalyst. Thus, further developments of heterogeneous HPA catalysts are needed.

4. Conclusions

Friedel-Crafts acylation of toluene (TOL) with benzoic anhydride (BAN) was conducted over various heteropoly acids as a model of the halogen free process. Among tested catalysts, insoluble $H_{0.5}Cs_{2.5}PW_{12}O_{40}$ showed the highest activity. Higher temperatures above the boiling point of TOL were desirable to reduce the side reaction. Reaction under pressurized conditions in a stainless steel autoclave reactor achieved complete conversion without by-products and repeated use of catalyst was possible by washing the used catalyst with TOL. However, the activity gradually decreased after the third run.

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要 旨

不溶性ヘテロポリ酸触媒を用いたハロゲンフリーでのトルエンの無水安息香酸によるフリーデル・クラフツ型アシル化反応

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トルエンと無水安息香酸からフェニルトリルケトンを誘導するフリーデル・クラフツ型アシル化反応を様々なイオン交換ヘテロポリ酸触媒存在下で試みた。塩化アルミニウム触媒やアシル化剤としての酸塩化物を使用しないのでハロゲンフリーのファインケミカルズ合成プロセスの一例と考えられる。Na, Rb, K, Cs, Ca, Mg, Fe 等によるヘテロポリ酸の部分交換を行いその促進効果を検討した。不溶性の $H_{0.5}Cs_{2.5}PW_{12}O_{40}$ 触媒が 60% という最高収率を示した。収率が上がらないのは副反応

によるものと考えた。副反応の抑制にトルエンの沸点以上の高温が適していることが分かったため、反応を密閉型のステンレスオートクレーブ反応器を用いて行った。410 K 以上で、完全転化が得られ、副反応も生じなかった。フェニルトリルケトンの異性体の分布は高温と低温で変化なく、反応機構は温度に依存しないことが示された。使用済み触媒をトルエンで洗浄することで、触媒は 2 回目の使用が可能であった。しかし、3 回目の反応から活性が低下した。