Friedel–Crafts reactions induced by heteropoly acids. Regioselective adamantyl substitution of aromatic compounds

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Heteropoly acid catalyzed adamantylation of aromatic compounds (toluene, anisole, fluoro- and bromobenzene) was studied. The catalysts applied were various dodecaheteropoly acids of Keggin-type ($H_n[XM_{12}O_{40}]$; $n = 3, 4$; X = Si, P; M = Mo, W) and some of their derivatives ($Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$ and heat-treated $H_4[SiMo_{12}O_{40}]/SiO_2$). The reaction in each case took place in excellent yield, however, the selectivity strongly depended on the experimental conditions applied. The para-isomer was shown to be formed under kinetic control, whereas para to meta isomerization occurred in the presence of acids with high acid strength ($H_0 \leqslant -13$) during longer reaction time. As a rule, strong acidity dependence was observed for the regioselectivity: the Mo-containing acids yield the para-substituted isomers with high selectivity, whereas the W-containing catalysts result in high meta/para ratios. In addition, using halobenzenes as reactants the formation of adamantane was observed as a product of reductive side reaction. This transformation was found to be significant in the presence of Mo-containing acids due to the redox character of these compounds.

Keywords: heteropoly acids, regioselective adamantylation, para-selectivity, acidity dependence, adamantane formation

1. Introduction

There has recently been strong driving force to use solid catalysts as replacements for homogeneous ones in industrial and laboratory processes [1]. Among solid catalysts, solid acids have particular importance in electrophilic transformations. As a result of the extensive research solid acids became widely used in synthetic organic chemistry as well [2,3]. A new class of inorganic materials called heteropoly acids (HPA) are good candidates for this purpose due to their stability, environmentally friendly character etc. [4]. According to their unique structural properties they exhibit bifunctional catalytic behavior [5]. They can be applied in reactions requiring electrophilic catalysis (alkylation, acylation, isomerization, hydration and dehydration), and also promote oxidations both in homogeneous and heterogeneous phase [6–10]. Heteropoly acids have recently been introduced, mainly in Japan, as a new class of catalytic materials into several petrochemical processes [1,8]. As a consequence of some unique properties (multifunctional character, homogeneous, heterogeneous, pseudoliquid and phase-transfer catalysis) and favorable technological features (easy recovery and environmentally safer handling), there is still a growing interest in widening the application possibilities.

One of these possible new applications is the use of heteropoly acids in the Friedel–Crafts alkylation of aromatics. As reviewed earlier these reactions were carried out predominantly in homogeneous reactions [11]. However, due to the striking advantages of using solid acids such as easy workup and recovery, formation of no complex product mixture etc., these catalysts have become particularly important and widely used in solid–liquid phase organic reactions [12–14]. As an important topic in Friedel–Crafts chemistry, the protection of certain positions of the benzene ring can provide methods for selective preparation of disubstituted aromatics. The two methods described for this purpose are the introduction of a tert-butyl group [15] and the adamantyl substitution [16]. The adamantylation was found to be more convenient and economical since the corresponding alkene (adamantene) is highly unstable and as a result, the adamantyl cation is recyclable through transalkylation processes. In a recent paper [16] we described the regioselective adamantylation of substituted benzenes in good yield and excellent para-selectivity using Amberlyst cross-linked ion exchange resin as catalyst. The only problem with this procedure is the relatively low thermal stability (~ 100–120°C) of the Amberlyst resin.

As a result, a systematic study was carried out with thermally stable heteropoly acids [17] and here we present our results concerning a heteropoly acid catalyzed adamantylation of substituted benzenes. The study is focused on the regioselectivity of the substitution, how-

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ever, the effect of acid strength on the alkylation is also discussed. The four heteropoly acids used as catalysts were $H_4[SiMo_{12}O_{40}]$, $H_3[PMo_{12}O_{40}]$, $H_4[SiW_{12}O_{40}]$ and $H_3[PW_{12}O_{40}]$. Although a wide variety of heteropoly acids is described, these four acids are commercially available and commonly used as acid catalysts for organic synthesis. In addition, the recently described $Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$ and a heat-treated acid supported on silica were also applied.

2. Experimental

Materials. $H_4[SiMo_{12}O_{40}]\cdot \sim 14H_2O$ (denoted as $SiMo_{12}$) and $H_3[PMo_{12}O_{40}]\cdot \sim 26H_2O$ (PMo_{12}) were purchased from Aldrich, $H_4[SiW_{12}O_{40}]\cdot \sim 26H_2O$ (SiW_{12}) from Riedel–de-Haen, while $H_3[PW_{12}O_{40}]\cdot \sim 19H_2O$ (PW_{12}) was a Serva product. A supported, heat-treated catalyst ($SiMo_{12}/SiO_2$) was prepared on the basis of a literature method [18] by heating 10% $H_4[SiMo_{12}O_{40}]$ supported on silica at 300°C for 3 h in a continuous argon flow. $Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$ was synthesized from the as-received PW_{12} and $CsNO_3$ (Aldrich). The PW_{12} was dissolved in deionized water and the solution with calculated amount of $CsNO_3$ was then added. The white powder precipitated was separated by centrifugation, washed several times with deionized water and air-dried. 1-bromoadamantane, anisole, fluoro- and bromobenzenes were available from Aldrich (minimum purity $> 99\%$), while toluene (99% purity by GC) was purchased from Reanal.

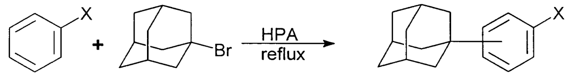
Analysis. The products were identified on the basis of their ^1H-, ^{13}C-NMR- (Bruker AM 400) and mass spectra (an HP-5890 GC coupled with an HP-5970 mass spectrometer). The detailed spectral characterization of the individual products were published earlier [16]. Product distributions were determined by gas chromatographic analyses with a HP-5890 GC coupled with flame ionization detector on a 30 m long DB-5 capillary column, with helium as carrier gas.

General method for adamantylation of aromatics in the presence of heteropoly acids. The reactions were carried out in a 10 ml round-bottomed flask equipped with a reflux condenser and magnetic stirrer. A mixture of 100 mg (0.46 mmol) of 1-bromoadamantane and 100 mg of catalyst ($\sim 10^{-5}$ mol depending on the individual HPA) was introduced into the flask then 2.0 ml substituted aromatic compound was added. The reaction mixture was heated up to reflux temperature and stirred at that temperature for 2 h. The workup consisted of the removal of acid traces by contacting the reaction mixture with a basic alumina column using ether as a solvent. The exact conditions related to individual reactions are detailed in tables.

Kinetic studies. The adamantylation of toluene was carried out in a larger scale (all quantities doubled) with 0.2 ml samples withdrawn at appropriate time intervals. The workup procedure and analysis were identical with those applied in preparative studies.

3. Results and discussion

According to the general rule for the Friedel–Crafts reaction the adamantylation of monosubstituted aromatic compounds using electrophilic reagents theoretically can produce three isomeric products:



X= CH_3, OCH_3, F, Br

However, it was pointed out that in solid acid (superacid) catalyzed adamantylation reactions only *m*- and *p*-products were formed accompanied by the formation of certain amount of adamantane as byproduct [16].

In order to determine the activity and selectivity of the heteropoly acids chosen and those of their derivatives the adamantylation reactions were carried out at reflux temperature in the presence of the catalysts. These were dodecaheteropoly acids of Keggin type with Si, P, Mo and W as heteroions, a heat-treated $SiMo_{12}/SiO_2$ and the $Cs_{2.5}$ salt of PW_{12}. The experimental results including activity and selectivity data are summarized in tables 1–4.

As the results show the reactions took place with complete (100%) conversion during a short reflux period. However, the chemo- and regioselectivity data strongly depend on the experimental conditions applied. The three most important experimental variables are the acidity of the catalysts, the temperature and the redox character of metal ion in the acids. It is important to point out, that the near exclusive *p*-isomer formation with anisole ($m/p = 0.8/99.2$) and fluorobenzene (adamantane/$m/p = 2/0/98$) in the presence of $SiMo_{12}$ is of significance from a synthetic point of view.

To attain a better understanding of the phenomena observed the time dependence of the changes in activity and selectivity of the adamantylation of toluene was

Table 1

Adamantylation of toluene with 1-bromoadamantane using various heteropolyoxometalate catalysts (reaction time = 2 h, conversion is 100%)

Catalyst	*T* (°C)	Adamantane (%)	*m* (%)	*p* (%)
$H_4[SiMo_{12}O_{40}]$	111	–	6.8	93.2
$H_3[PMo_{12}O_{40}]$	111	–	13.3	86.7
$H_4[SiW_{12}O_{40}]$	111	–	60.1	39.9
$H_3[PW_{12}O_{40}]$	111	–	66.6	33.4
$SiMo_{12}/SiO_2$	111	–	28.8	71.2
$Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$	111	–	65.8	34.2

Table 2
Adamantylation of anisole with 1-bromoadamantane using various heteropolyoxometalate catalysts (reaction time = 2 h, conversion is 100%)

Catalyst	T (°C)	Adamantane (%)	m (%)	p (%)
$H_4[SiMo_{12}O_{40}]$	152	–	0.8	99.2
$H_3[PMo_{12}O_{40}]$	152	–	3.3	96.7
$H_4[SiW_{12}O_{40}]$	152	–	6.0	94.0
$H_3[PW_{12}O_{40}]$	152	–	6.1	93.9
$SiMo_{12}/SiO_2$	152	–	12.0	88.0
$Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$	152	–	56.3	43.7

Table 4
Adamantylation of bromobenzene with 1-bromoadamantane using various heteropolyoxometalate catalysts (reaction time = 2 h, conversion is 100%)

Catalyst	T (°C)	Adamantane (%)	m (%)	p (%)
$H_4[SiMo_{12}O_{40}]$	155	25.1	–	74.9
$H_3[PMo_{12}O_{40}]$	155	35.2	0.5	64.3
$H_4[SiW_{12}O_{40}]$	155	0.2	25.0	74.8
$H_3[PW_{12}O_{40}]$	155	–	26.0	74.0
$SiMo_{12}/SiO_2$	155	66	6.9	27.1
$Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$	155	–	26.1	73.9

studied and the results are presented in figures 1 and 2. As figure 1 indicates, complete conversions are achieved in relatively short reflux periods in the presence of any of the catalysts. Slight activity differences can, however, be observed. It appears that about a 10 min reflux is sufficient to attain complete conversion by using the supported sample $SiMo_{12}/SiO_2$ and $Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$. All four neat heteropoly acids, in contrast, exhibit a slightly lower activity. This difference can be accounted for by the vastly different surface areas of the various catalysts. Heteropoly acids have very low surface areas (adamantylation is mostly a heterogeneous catalytic process due to the negligible solubility of heteropoly acids in aromatic solvents), whereas the surface area of $SiMo_{12}/SiO_2$ and $Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$ are about two orders of magnitude higher.

Changes in selectivities are given in figure 2. It is seen that in all cases the para isomer is formed with high selectivity in the early stages of the transformation. Once the reagent 1-bromoadamantane is completely consumed a sudden increase in the meta to para ratio occurs in the presence of the tungsten-containing catalysts. These data indicate that kinetic control prevails in the formation of the para isomer, then the adamantylated isomers approach thermodynamic equilibrium as duration increases. The acid strength of the catalysts, however, clearly plays a determining role in selectivity.

The determination of the acid strength of heteropoly acids was the subject of extended research. It was pointed out that the acid strength of the PW_{12} in the solid state is $H_0 < -13.16$ which means that it is a solid superacid [19]. Izumi and coworkers determined the relative acid strength of a series of heteropoly acids based on the hydrogen bonding with chloral hydrate and the order was found to be $PW_{12} > PMo_{12} > SiW_{12} > SiMo_{12}$ [20]. However, on the basis of NH_3 temperature programmed desorption experiments the sequence $PW_{12} > SiW_{12} > PMo_{12} > SiMo_{12}$ [21] was observed. The same order was proposed by a more recent investigation [10] and it was proven at least with tungsten-containing acids in homogeneous solutions as well [22]. No data are available for the acidity of $Cs_{2.5}PW_{12}$ and the heat-treated $SiMo_{12}/SiO_2$ catalysts. However, Chang pointed out by MAS NMR studies, that the high temperature treatment of silica-supported HPAs produces increased acid strength through stronger surface bonding [18]. In summary, according to the literature data, these catalysts exhibit superacidic properties in the solid state and the estimated values cover the lower region of the Hammett scale ($-H_0 = 12.3$–13.2).

In the light of the data mentioned above, the strong influence of the catalytic acids on the regioselectivity can be interpreted as acidity dependence. The weak Mo-containing acids produce the smallest amount of *m*-isomer, independently from the reactant used. The stronger W-containing acids ($H_0 \leqslant -13$), in contrast, are able to induce the para to meta isomerization at a sufficient rate to reach, ultimately, the thermodynamic equilibrium. Fluorobenzene, a deactivated compound seems to be an exception. It exhibits such a low reactivity at its boiling point that high para selectivites are observed even in the presence of the strongly acidic W-containing catalysts.

The additional experimental variables like the temperature and the acid–reactant relationship are determining factors influencing the chemoselectivity of the reactions. A comparison of the product distribution of the adamantylation of toluene and anisole to that of halobenzenes indicates, that in the latter case adamantane formation became more significant. The main reasons for these observations are the increased

Table 3
Adamantylation of fluorobenzene with 1-bromoadamantane using various heteropolyoxometalate catalysts (reaction time = 2 h, conversion is 100%)

Catalyst	T (°C)	Adamantane (%)	m (%)	p (%)
$H_4[SiMo_{12}O_{40}]$	85	2.0	–	98.0
$H_3[PMo_{12}O_{40}]$	85	6.1	1.8	92.1
$H_4[SiW_{12}O_{40}]$	85	–	2.2	97.8
$H_3[PW_{12}O_{40}]$	85	traces	4.1	95.9
$SiMo_{12}/SiO_2$	85	1.2	2.1	96.7
$Cs_{2.5}H_{0.5}[PW_{12}O_{40}]$	85	traces	3.1	96.9

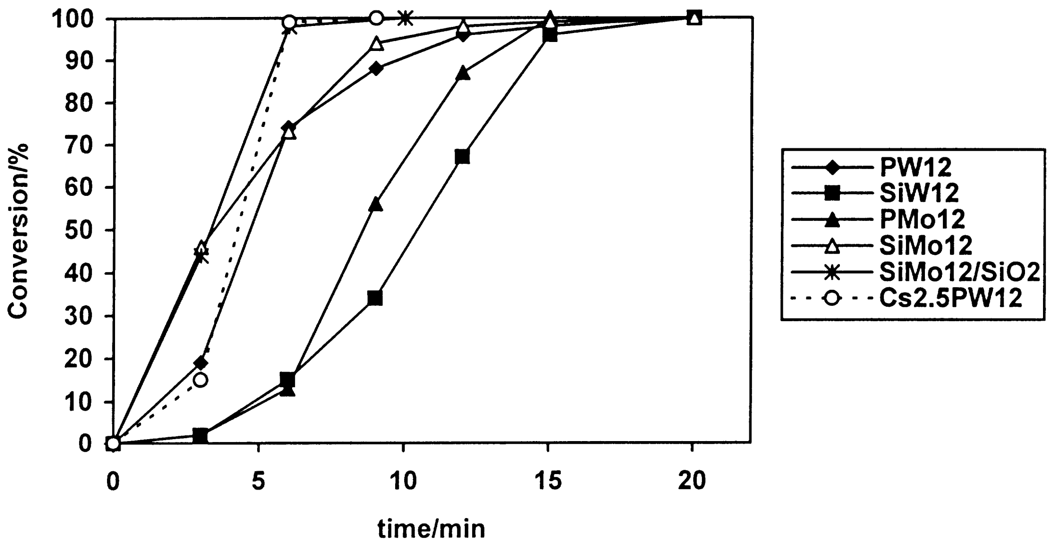


Figure 1. Product accumulation vs. time curves in heteropoly acid catalyzed adamantylation of toluene.

intermolecular isomerization (disproportionation) and the more pronounced decomposition of the solvents producing suitable hydrogen source for transfer ionic hydrogenation of 1-bromoadamantane. Since it is well-known that the Mo(VI) → Mo(V) one-electron transfer takes place very easily [4] the formation of the large amount of adamantane in the presence of molybdenum containing acids is not surprising.

4. Conclusion

In conclusion, heteropoly acids and a $Cs_{2.5}$ salt were found to efficiently catalyze the Friedel–Crafts adamantylation of substituted benzenes. It was pointed out that the regioselectivity of the substitution has a strong acidity dependence, increasing acid strength (W-containing catalysts) prefers the formation of *m*-isomer. Adamantylation of aromatics, consequently, is a kinetically controlled process, but the final isomer distribution is influenced by subsequent isomerization. The selectivity of the reaction can be used in assessing acid strength of catalysts provided appropriate substrates and reaction time are chosen. The weakest acid (neat $H_4[SiMo_{12}O_{40}]$) can be considered as an excellent catalyst to synthesize potentially important *p*-protected aromatics.

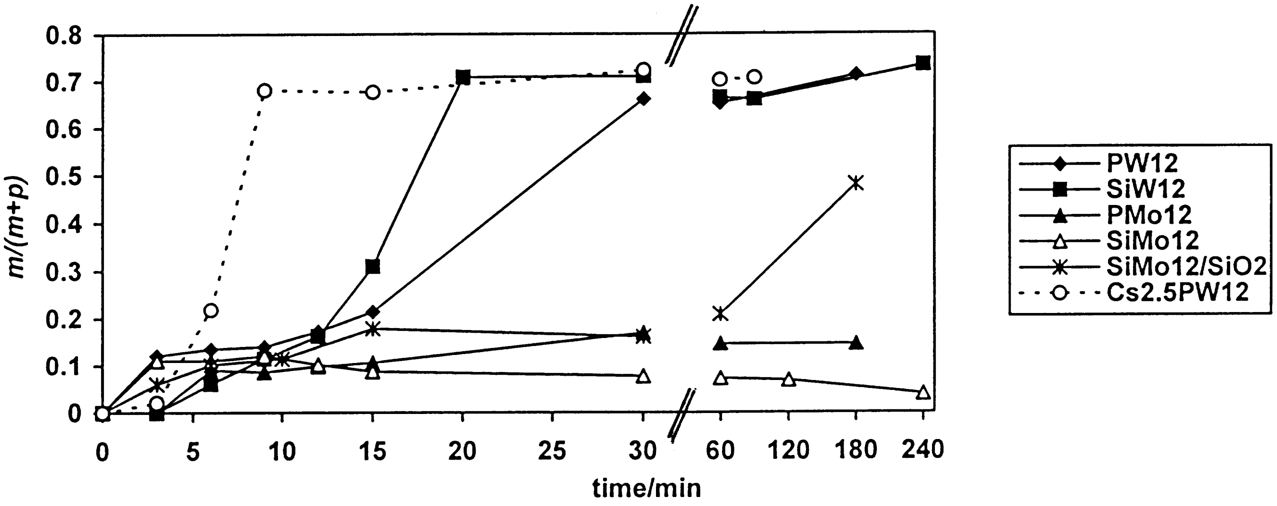


Figure 2. Change in selectivities as a function of time in heteropoly acid catalyzed adamantylation of toluene.

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