

C-alkylation reactions catalyzed by silica-supported Keggin heteropolyacids

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Abstract

Aromatic alkylation reactions were studied using molybdophosphoric and tungstophosphoric acids supported on silica as catalysts. Benzene and toluene alkylation was carried out with benzyl chloride or benzyl alcohol. Also, cyclohexene and cyclohexanol were used as alkylating agents of toluene. These catalysts allow quantitative conversions in short times, with very good yields in monoalkylation products and minimal formation of polyalkylation products. Regioselectivity in these reactions is similar to that described in literature for different catalysts but the latter are markedly less efficient. In the reaction of formal [3 + 2] cycloaddition with benzyl alcohols catalyzed by silica-supported molybdophosphoric acid, the results are similar to those previously obtained using SnCl₄ as catalyst.

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1. Introduction

Electrophilic aromatic substitution and in particular Friedel–Crafts reactions are among the prevailing reactions in organic and industrial chemistry, and they are also reactions that require catalysis [1]. In the course of more than 100 years, Lewis acid catalysts have gained wide recognition despite some unfavorable properties such as decomposition, operating corrosion problems, difficulties in the separation of the catalyst, the need to use large catalyst

amounts [2], not to mention the isomerization they often cause.

For such reasons, and also because of an easier setup and workup, solid catalysts are useful for industrial processes and have awakened much interest. They include resins such as Nafion-H [3], the graphite–aluminum–chloride intercalate [4], modified alumina [5], a number of phyllosilicates [6] and montmorillonite doped with transition-metal cations [7], among others.

The use of catalytic processes with Keggin-type heteropolycompounds has been widely studied in recent decades. Due to their strong Brønsted acidity, Keggin heteropolyacids (HPA) can be used instead of conventional acid catalysts, such as sulfuric acid [8]. Besides, they can present a Lewis acidity, depending on the constituent elements of the heteropolycompounds, and can be used in

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another group of reactions, in replacement of classical catalysts, such as aluminum chloride [9]. In both cases, higher conversions than those obtained with usual catalysts are expected to be achieved, with the consequent energy and cost saving. Other advantages comprise the environmental benefit of decreasing the amount of acid effluents that the conventional technologies produce and the easy recovery and reuse of the catalysts.

Taking into account these statements, our research group has worked in the preparation, the physicochemical and catalytic characterization of catalysts based on Keggin heteropolycompounds. Most studies have been carried out by supporting Keggin HPA on different carriers. The purpose is to overcome the probable disadvantage that the bulk compounds could have, due to their low surface area. Detailed studies of the nature of the supported species were performed [10–15] in order to ensure that any effect on the primary structure of the catalytic species occurs due to the interaction between the compound and the support. This interaction takes place during the catalyst preparation and is strongly dependent on the support characteristics, the preparation method and some of the operative variables.

The supported heteropolycompounds can be used as catalysts in gas–solid as well as in liquid–solid reactions. For the latter, the main task is to ensure that solubilization of the active component in the reaction medium takes place, in order to achieve an easier product separation and catalyst recovery.

In previous papers we have reported that molybdophosphoric (MPA) and tungstophosphoric (TPA) acids supported on silica (MPA/S and TPA/S, respectively) are efficient catalysts for reactions that proceed through a carbocation intermediate, such as dehydration of alcohols [16,17] or cyclodimerization of alkenes [18].

Bearing in mind our experience in the use of supported Keggin-type heteropolyacids, a detailed examination of the scope and limitations of such catalysts for aromatic alkylation in liquid phase is now undertaken. A comparison with the results already published with other solid catalysts [7] and the improvements achieved are also reported. To further evaluate these catalysts, their use in formal [3 + 2] cycloaddition reactions is also studied.

2. Experimental

2.1. Catalyst preparation

The catalysts, MPA/S and TPA/S, were prepared by the equilibrium impregnation technique starting from impregnating solutions of $\text{H}_3\text{PMo}_{12}\text{O}_{40}\cdot n\text{H}_2\text{O}$ (Merck) or $\text{H}_3\text{PW}_{12}\text{O}_{40}\cdot n\text{H}_2\text{O}$ (Fluka). The solvent was a mixture of demineralized water and 96% ethanol (Soria), in a 1:1 volumetric ratio. The concentration of the solution used was 120 g Mo(W)/l. The support was SiO_2 (Grace) with a specific surface area of 311 m^2/g and a mean pore diameter

of 3.4 nm. Solids thus obtained were washed with solvent in order to avoid HPA solubilization during the reaction. Further details on the preparation technique are described in a previous paper [16].

2.2. Catalyst characterization

Catalyst characterization was carried out by means of fourier transform infrared (FT-IR), diffuse reflectance spectroscopy (DRS), X-ray diffraction (XRD) and acidity measurement determined by potentiometric titration with *n*-butylamine, as described in a previous paper [16].

2.3. Alkylation reactions

Reactions were carried out in a glass batch reactor at atmospheric pressure. The alkylating reagents used were benzyl alcohol (Fluka), benzyl chloride (Mallinckrodt), cyclohexanol (Fluka) and cyclohexene (Fluka).

The alkylating reagent (0.48 mmol) with benzene or toluene (2 ml) and MPA/S or TPA/S (0.016 mmol HPA) were heated to reflux. Once the reaction time was reached, the catalyst was removed by filtration, the solvent evaporated and the compounds characterized by ^1H NMR. The catalyst amount was varied in some experiments.

The conversion of the alkylating reagents at different reaction times was determined by gas chromatography. A Konic KNK-300 chromatograph was used, with FID detector and OB-1 capillary column. The experimental conditions for benzyl alcohol and benzyl chloride with benzene or toluene were as follows: initial temperature, 70 °C; final temperature, 180 °C; retention times: benzyl chloride, 5.50 min; benzyl alcohol, 5.78 min; diphenylmethane, 9.23 min; and phenyltoluylmethanes, 10.05 min. The experimental conditions for cyclohexanol or cyclohexene with toluene were as follows: initial temperature, 50 °C; final temperature, 180 °C; retention times: cyclohexene, 2.75 min; cyclohexanol, 7.90 min; and cyclohexyltoluene, 16.70 min.

Conversion was calculated as mmol of alkylating reagent transformed by 100 mmol of initial reagent and the yield for each product as mmol of the product by 100 mmol of initial reagent.

2.4. Formal [3 + 2] cycloaddition reactions

The cycloaddition of benzyl alcohols and benzohydrols with alkenes was studied. The reactions were carried out in a reactor similar to the above-mentioned. MPA/S (0.015 mmol) was added to a solution of alcohol (0.464 mmol) and alkene (0.464 mmol) in solvent (10 ml). Once the reaction was completed, the catalyst was removed by filtration, the solvent evaporated, and the compounds purified and characterized by ^1H NMR. The yield for each product was calculated as mmol of product per mmol of initial reactive.

3. Results and discussion

3.1. Catalyst characterization

The HPA content of the catalysts after leaching with solvent was 0.22 or 0.13 mmol MPA (TPA)/g catalyst, respectively. It may be pointed out that HPA amount in the washing solutions was negligible, due to the insolubility of the HPA in solvents of low polarity [16].

The catalyst characterization by means of DRS and FT-IR spectroscopies showed that the intact Keggin-type heteropolyanions are the species mainly present. After their use in the reaction, the catalysts were also characterized by DRS and FT-IR. DRS spectra showed features similar to those of the original catalysts, although they present an absorbance increase in the 600 nm zone, indicative of partial Mo or W reduction. In the FT-IR spectra heteropolyanion bands are observed.

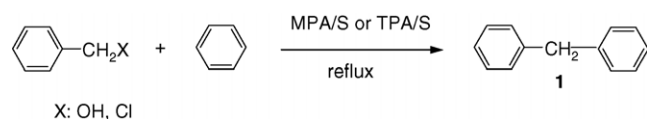
XRD patterns of the catalysts were similar to that of the support, lacking the diffraction lines corresponding to heteropolyanions. This indicates that the acids are highly dispersed on the support surface or present as non-crystalline species.

The acidity measurements of the catalysts were carried out by potentiometric titration with *n*-butylamine. The catalysts presented very strong acid sites, the initial electrode potential *E* in the range 600–700 mV, having an acid strength considerably higher than that of the support (–72 mV). Also, the number of acid sites present in the catalysts was higher. The differences between the acidic characteristics of the obtained catalysts were not appreciable, since *E* as well as the number of meq/mmol Mo(W) have similar values.

Further details about catalyst characterization may be found in a previous report [16].

3.2. Aromatic alkylation reactions

To explore the catalytic activity of MPA/S and TPA/S in aromatic alkylation reactions, benzene benzylation to obtain diphenylmethane (**1**) was firstly chosen as a test reaction, using benzyl alcohol or benzyl chloride as alkylating agents (Scheme 1). These alkylating reagents lead to stable carbocations, without possibility of dehydration. Then toluene alkylation with the same alkylating agents was studied to observe the regioselectivity of the reaction. Afterwards, the study was extended to other type of alcohol, cyclohexanol, and also the behavior of cyclohexene as alkylating agent was studied.



Scheme 1. Benzene alkylation with benzyl alcohol or benzyl chloride.

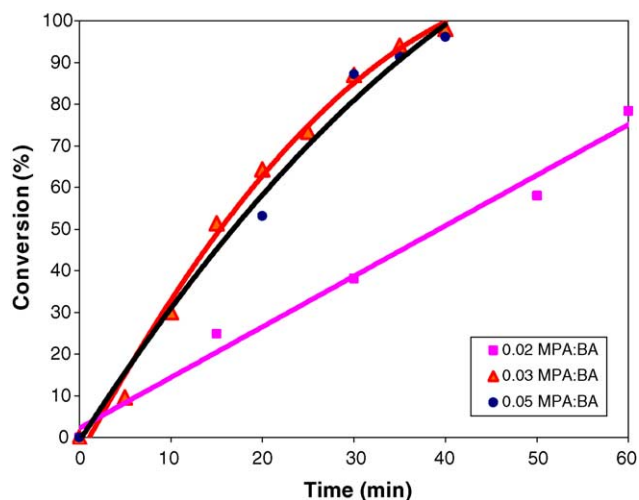


Fig. 1. Percentage conversion of benzyl alcohol as a function of time for benzene alkylation in presence of MPA/S catalyst with different catalyst:benzyl alcohol molar ratio (MPA:BA).

3.2.1. Benzene benzylation with benzyl alcohol

The effect of the catalyst:benzyl alcohol molar ratio on the alkylating reagent conversion was studied. The best molar ratio found was 0.03:1, when MPA/S was used as catalyst (Fig. 1). An increase in the catalyst amount improved the conversion when the molar ratio was increased from 0.02 to 0.03. However, the conversion did not change when the molar ratio was increased from 0.03 to 0.05. Similar results were obtained using the TPA/S catalyst.

Using this best molar ratio, the percentage conversion change with time was followed for the benzene benzylation with benzyl alcohol as alkylating agent in the presence of

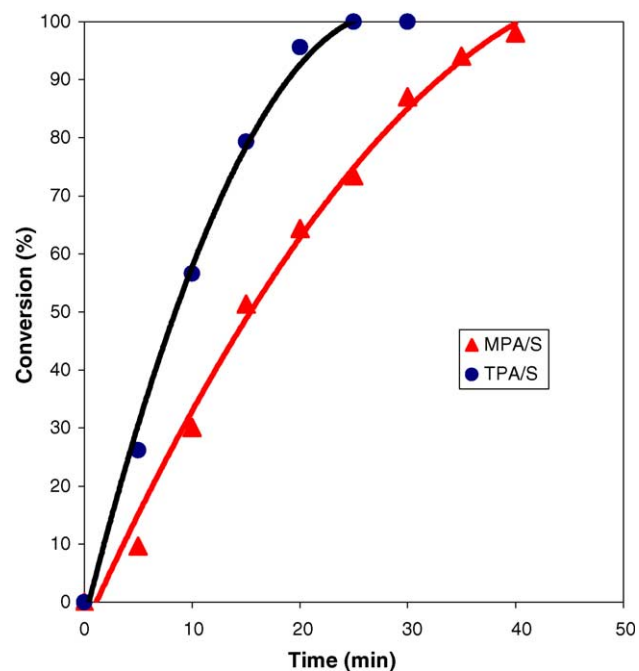


Fig. 2. Percentage conversion of benzyl alcohol as a function of time for benzene alkylation in presence of MPA/S and TPA/S catalysts.

Table 1
Diphenylmethane yield using different catalysts for benzene alkylation with benzyl alcohol

Catalyst	Reaction time (h)	Yield (%)
K-10Ti (IV) ^a	0.5	54
K-10Ti (IV) ^a	1	40
K-10Ta (V) ^a	1.2	43
AlCl ₃ ^{a,b}	48	50
AlCl ₃ ^{a,b}	120	55
MPA/S ^c	0.66	85
TPA/S ^c	0.40	87

^a From reference [7].

^b 0.004 mol catalyst per 0.1 mol alcohol.

^c 0.003 mol catalyst per 0.1 mol alcohol.

MPA/S or TPA/S as catalysts. High conversion of the benzyl alcohol (>99%) was observed at 25 min reaction time when TPA/S was used as catalyst, and 40 min in the case of MPA/S (Fig. 2).

In a previous paper [16], similar results were obtained for alcohol dehydration reactions using these catalysts. Since the HPA were structurally stable, as it was determined by FT-IR and DRS, and the acidity of MPA/S and TPA/S catalysts after leaching with the solvent was similar, the lower reaction time for the TPA/S catalyst could be due to the fact that the MPA amount adsorbed on the surface was higher than that of TPA. It is worth noting that the HPA fraction adsorbed on the surface of the support may be interacting strongly and so there are fewer available protons.

The better performance of MPA/S and TPA/S catalysts for this reaction compared to other catalysts described in the literature [7] should be highlighted (Table 1). Remarkably higher yields of monoalkylated products are obtained with MPA/S and TPA/S (85–87%), as compared with the catalysts based on montmorillonite K-10 (40–54%) and with AlCl₃ (43–55%). The reaction times to obtain maximum conversion (0.66–0.40 h) were lower than those of catalysts based on K-10 (0.50–1.20 h), but they are much lower than those indicated when AlCl₃ is used (48–120 h). On the other hand, the required catalyst:alkylating agent molar ratio is lower than that with AlCl₃, the usual Lewis acid catalyst [7]. The catalysts based on heteropolyacids also give rise to a lower amount of dialkylation products.

The reutilization of both MPA/S and TPA/S catalysts was investigated in this reaction. When MPA/S fresh catalyst is

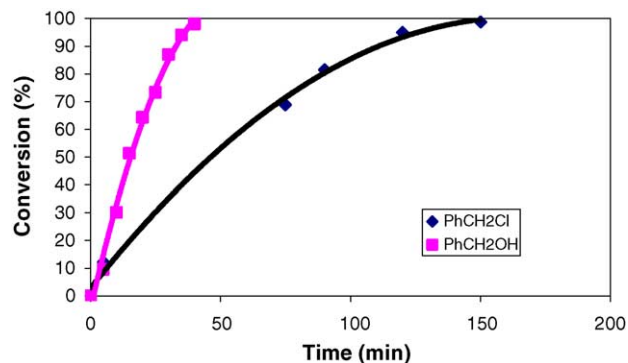


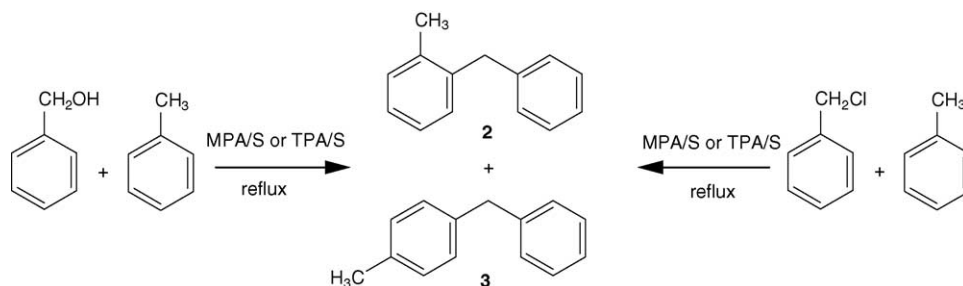
Fig. 3. Percentage conversion of alkylating agent as a function of time for benzene alkylation with benzyl alcohol and benzyl chloride using MPA/S.

used, 98% conversion is achieved at 40 min, whereas for the used catalyst, 96% conversion is obtained at 1 h. A similar behavior was observed for the TPA/S catalyst. These results cannot be ascribed to the HPA leaching because the leaching stability during the liquid–solid reaction was proved. As above-mentioned during the washing, HPA in the solutions were not detected. On the other hand, no further conversion was observed in the resulting solution after the catalyst filtration at reaction temperature [16]. However, in spite of the activity loss, as high conversions were obtained at not very long time (1 h), the catalysts were reusable again.

3.2.2. Benzene benzylation with benzyl chloride

The alkylation reaction of benzene with benzyl chloride using MPA/S as catalysts showed 98% conversion and 88% yield to obtain diphenylmethane. However, as is observed in Fig. 3, the reaction time for maximum conversion was shorter for benzyl alcohol (40 min) than for benzyl chloride (150 min). The catalyst:reagent ratio for alkylation with benzyl chloride was the same used for the reaction with benzyl alcohol.

The benzyl alcohol was more active than benzyl chloride for benzene alkylation, probably due to the higher Brønsted acidity than Lewis character of the HPA. Lewis acids and proton acids, especially H₂SO₄, are often used to catalyze alkylation reaction with alcohols. When a Lewis acid catalyst is used, more catalyst is required, since the catalyst is complexed with the OH group. Lewis acids are the catalysts used in the alkylation reaction with alkyl halides.



Scheme 2. Toluene alkylation with benzyl alcohol and benzyl chloride.

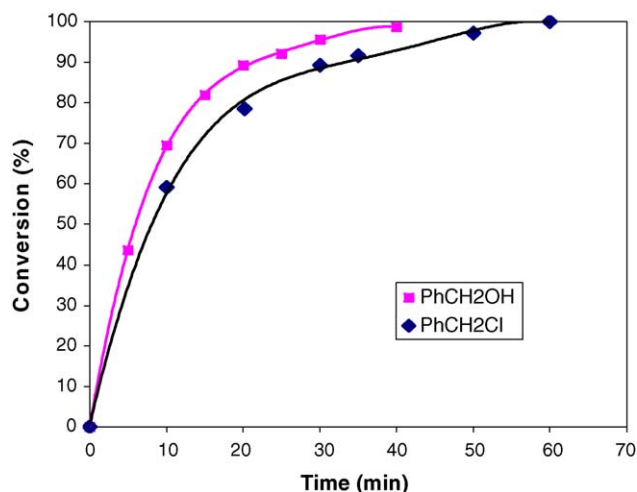


Fig. 4. Percentage conversion of alkylating agent as a function of time for toluene alkylation with benzyl alcohol and benzyl chloride using MPA/S.

Table 2
Toluyphenylmethane yield using different catalysts for toluene alkylation

Alkylating reagent	Catalyst	Reaction time (min)	Yield (%) ^a	3:2 isomer distribution
PhCH ₂ OH	MPA/S	40	98	57:43
PhCH ₂ OH	TPA/S	30	98	60:40
PhCH ₂ OH	K-10Ti(IV) ^b	12	60	62:38
PhCH ₂ Cl	MPA/S	60	99	57:43
PhCH ₂ Cl	TPA/S	50	99	61:39
PhCH ₂ Cl	K-10Fe(III) ^b	15	70	59:41

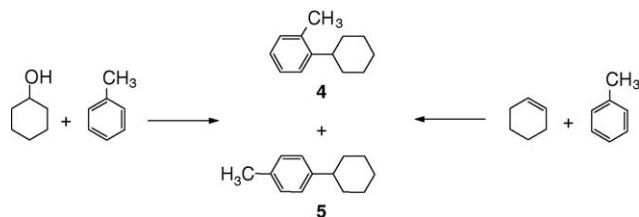
^a Monoalkylation products.

^b From reference [7].

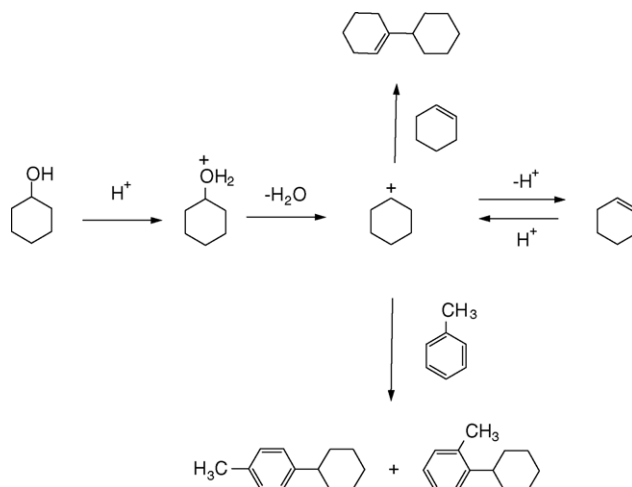
3.2.3. Toluene alkylation with benzyl chloride or benzyl alcohol

The behavior of TPA/S and MPA/S catalysts in toluene alkylation was investigated. The same alkylating agents and the same catalyst:reagent ratio than for benzene alkylation were used. The use of a mono-substituted benzene compound allowed discerning the regioselectivity of the reaction (Scheme 2).

Conversion of alkylating agents as a function of time for toluene benzylation with benzyl chloride and with benzyl alcohol using MPA/S as catalyst is shown in Fig. 4. On the other hand, the yield of *o*- and *p*-toluyphenylmethanes (2 and 3), the 3:2 ratio and the comparison of results obtained with other catalysts described in the literature [7] are presented in Table 2. The isomeric ratio was established by



Scheme 3. Toluene alkylation with cyclohexanol and cyclohexene.



Scheme 4. Competition among dehydration, dimerization and C-alkylation in the reaction of cyclohexanol and toluene.

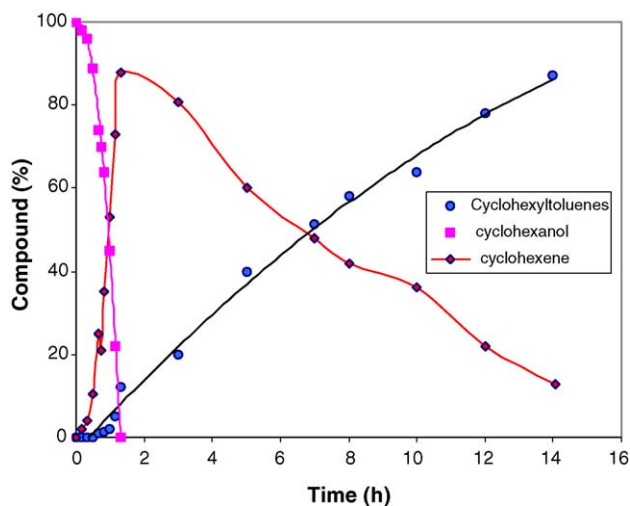


Fig. 5. Percentage of cyclohexanol, cyclohexene and cyclohexyltoluenes as a function of time for toluene alkylation with cyclohexanol using MPA/S catalyst.

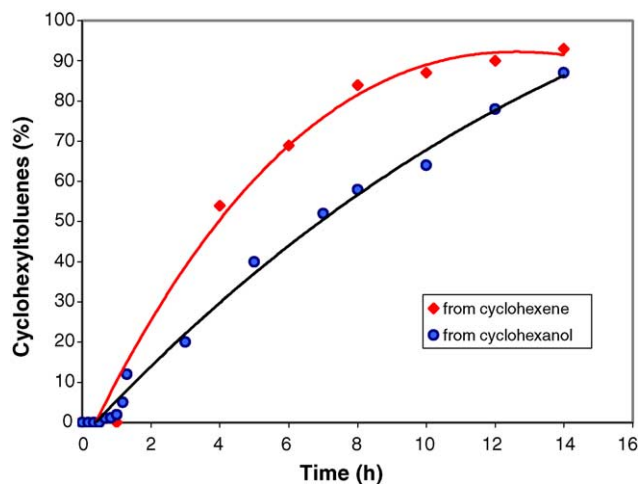
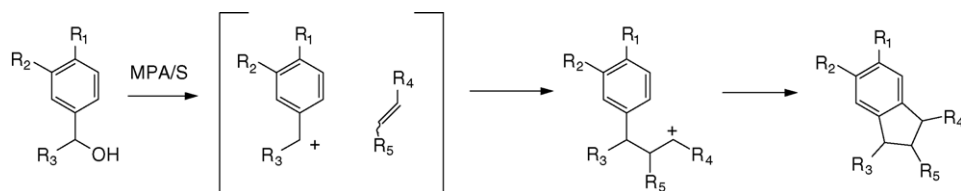


Fig. 6. Percentage yields as a function of time for cyclohexyltoluenes from toluene alkylation with cyclohexanol and cyclohexene.



Scheme 5. Proposed mechanism for the formal [3 + 2] cycloaddition.

comparison of integrated signals corresponding to CH_3 and CH_2 groups in the ^1H NMR spectrum.

Yields and regioselectivity achieved were similar for both catalysts (MPA/S and TPA/S) and no substantial differences were observed between the two alkylating reagents. In this case, the similarity in conversion rate of both alkylating agents may be attributed to the higher activation of toluene for aromatic electrophilic substitution.

The yields of monoalkylation products (**2** and **3**) indicate the higher catalytic selectivity of MPA/S and TPA/S with

regard to K-10-based catalysts, when the conversion is 100% in all cases. Then, the almost total absence of dialkylation products is the main advantage of the HPA/S catalysts, though the reaction time to obtain maximum conversion is higher. The regioselectivity of the reaction depends slightly on the catalyst, since no significant differences among the catalysts were observed.

The catalytic performance of MPA/S and TPA/S in aromatic alkylation reactions allows using alcohols as well as halides for this reaction under similar conditions.

Table 3
Formal [3 + 2] cycloaddition reactions

Alcohols	Alkenes	Products	SnCl_4 yield ^a (%) (a:b)	MPA/S yield (%) (a:b)
			66 ^b (1:2)	46 ^c (1:1.8)
			40 ^b	22 ^d
			55 ^e (14:1)	75 ^f (14:1)
			45 ^e (4.5:1)	60 ^g (4.5:1)

Comparison of yield using MPA/S and SnCl_4 as catalysts.

^a From references [21,22].

^b Cl_2CH_2 , 0 °C, 30 min and then room temperature (r.t.), 180 min.

^c Toluene, reflux, 120 min.

^d Cl_3CH , reflux, 120 min.

^e Cl_2CH_2 , 0 °C, 30 min.

^f Cl_3CH , r.t., ultrasonic, 20 min.

^g Cl_3CH , r.t., ultrasonic, 10 min.

3.2.4. Toluene alkylation with cyclohexene and cyclohexanol

The reaction of toluene with cyclohexanol or cyclohexene was carried out using the MPA/S catalyst. This reaction may lead to the possible products depicted below (Scheme 3).

In a previous paper, we reported the dehydration of alcohols [16,17] and the dimerization of alkenes [18] using MPA/S and TPA/S catalysts. Then, it is interesting to study the reaction of cyclohexanol and toluene to discern the competition among dehydration, dimerization, and C-alkylation, as shown in Scheme 4.

During the first minutes of reaction, the dehydration of cyclohexanol produced cyclohexene, with no evidence of alkylation products. At 40 min, the presence of *p*- and *o*-cyclohexyltoluene (**4** and **5**) began to be recorded. At 90 min, the conversion of cyclohexanol was complete. The yield of cyclohexyltoluenes was 12% and cyclohexene production reached its maximum level (88%), to diminish gradually thereafter, with 87% cyclohexyltoluene yield at 14 h (Fig. 5). Formation of dimerization products of cyclohexene was not observed.

Using cyclohexene as alkylating agent, the yield of **4** and **5** is 90% at 12 h of reaction (Fig. 6), with 50% yield reached before 4 h. The reaction rate is higher for cyclohexene than for cyclohexanol, indicating that in the latter case alkylation proceeds mainly through the cyclohexene formed in situ.

The catalyst:reagent molar ratio was the same (0.03:1) when either cyclohexanol or cyclohexene was employed. In both cases the *p*- and *o*-cyclohexyltoluene ratio (**5**:**4** ratio) was 8:3 and there was no formation of cyclohexene dimerization products.

3.3. Formal [3 + 2] cycloaddition reactions

Benzyl alcohols and benzohydrols in the presence of alkenes rendered formal [3 + 2] cycloaddition reactions [19]. Unlike dimerization, this type of reactions lead to aromatic products with different substituents, thus a large increase in molecular complexity can be obtained by means of a one-pot reaction. These reactions are usually catalyzed by a Lewis acid. The cation generated starting from the alcohol reacts with the alkene to form a new benzyl cation, which then cyclizes to give an aryindane (Scheme 5). There are many synthetic compounds possessing the dihydroindene skeleton that show significant biological activity [20]. On account of the importance of the compounds possessing this skeleton, a large number of methods were developed for their synthesis, nevertheless the [3 + 2] cycloadditions render a stereoselective method for the preparation of highly substituted indanes.

In previous papers, numerous examples of this type of reaction using SnCl₄ as catalyst were published [21,22]. Here, the results obtained using MPA/S as catalyst and the better reaction conditions for each pair of reactants are presented (Table 3).

For instance, the reactivity of the benzyl alcohol 4-(hydroxyphenylmethyl)-2-methoxyphenol (**6**) was tested with cyclic alkenes, styrenes systems in a rigid environment such as indene (**7**) and 1-phenyl-3,4-dihydronaphthalene (**9**). With alkene **7**, epimeric tetracyclic compounds **8a** and **8b** are obtained, while with alkene **9** only compound **10** is produced.

On the other hand, the benzyl alcohols 1-(3,4-dimethoxyphenyl)propanol (**11**) and 1-(3,4-methylenedioxyphenyl)propanol (**12**) react with styrenes 4-methoxystyrene (**13**) and 2,4,5-trimethoxystyrene (**15**) to render two pairs of stereoisomeric indanes **14a**, **14b** and **16a**, **16b**, respectively, with identical stereoselectivity to that obtained with SnCl₄ [22] but in a shorter time and with higher yield.

It is worth pointing out that MPA/S is an efficient catalyst in reactions catalyzed by Brønsted acids as well as by Lewis acids.

4. Conclusions

The obtained results in C-alkylation reactions are outstanding since the supported-heteropolyacids, MPA/S and TPA/S, afforded quantitative conversions in short times with very good yields in monoalkylation products and minimal formation of polyalkylation products. The catalyst:substrate molar ratio required is low in the case of the alcohols, compared to those employed with Lewis catalysts such as metal-doped montmorillonite K-10 and Cl₃Al. Regioselectivity in these reactions is similar to that described for other catalysts but the latter are markedly less efficient.

The results in the reaction of formal [3 + 2] cycloaddition, catalyzed by MPA/S, are indeed promising compared to those achieved in reactions carried out using SnCl₄ with benzyl alcohols.

Besides, in all the reactions, the workup is simple and the isolation of the final products consists of a single filtration to remove the catalyst, followed by solvent evaporation.

In other words, with these catalysts C-alkylation reactions are not only faster but also cleaner from the environmental point of view, and the catalysts may also be used again.

Acknowledgments

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References

- [1] G.A. Olah, D. Meidar, 3rd ed., Friedel–Crafts Chemistry Kirk–Othmer Encycl. Chem. Technol., 11, Wiley, New York, 1980, p. 269.
- [2] G.A. Olah, Friedel–Crafts Chemistry, vol. III, Wiley, New York, 1973.
- [3] G.A. Olah, J.A. Olah, T. Ohyama, J. Am. Chem. Soc. 106 (1984) 5284.
- [4] J.M. Lalancette, US Patent 3,880,994 (1975).
- [5] H. Schmall, W. Schunack, Sci. Pharm. 42 (1974) 248.

- [6] E. Herdieckerhoff, W. Sutter, German Patent 1.051.864 (1959).
- [7] P. Laszlo, A. Mathy, *Helvet. Chim. Acta* 70 (1987) 577.
- [8] I. Kozhevnikov, *Chem. Rev.* 90 (1998) 171.
- [9] M. Misono, *Chem. Commun.* (2001) 1141.
- [10] M.A. Castillo, P.G. Vázquez, M.N. Blanco, C.V. Cáceres, *J. Chem. Soc., Faraday Trans.* 92 (1996) 3239.
- [11] L.R. Pizzio, C.V. Cáceres, M.N. Blanco, *J. Colloid Interf. Sci.* 190 (1997) 318.
- [12] L.R. Pizzio, C.V. Cáceres, M.N. Blanco, *Appl. Catal. A: Gen.* 167 (1998) 283.
- [13] A. Concellón, P. Vázquez, M. Blanco, C. Cáceres, *J. Colloid Interf. Sci.* 204 (1998) 256.
- [14] P.G. Vázquez, M.N. Blanco, C.V. Cáceres, *Catal. Lett.* 60 (1999) 205.
- [15] M. Chimienti, L. Pizzio, C. Cáceres, M. Blanco, *Appl. Catal. A: Gen.* 208 (2001) 7.
- [16] P. Vázquez, L. Pizzio, C. Cáceres, M. Blanco, H. Thomas, E. Alesso, L. Finkielstein, B. Lantaño, G. Moltrasio, J. Aguirre, *J. Mol. Catal. A: Chem.* 161 (2000) 223.
- [17] E. Alesso, R. Torviso, L. Finkielstein, B. Lantaño, G. Moltrasio, J. Aguirre, P. Vázquez, L. Pizzio, C. Cáceres, M. Blanco, H. Thomas, *J. Chem. Res. (S)* 508 (2001) 1232 (M).
- [18] E. Alesso, R. Torviso, M. Erlich, L. Finkielstein, B. Lantaño, G. Moltrasio, J. Aguirre, P. Vázquez, L. Pizzio, C. Cáceres, M. Blanco, H. Thomas, *Synth. Commun.* 32 (24) (2002) 3803.
- [19] S. Angle, D. Arnaiz, *J. Org. Chem.* 57 (1992) 5937.
- [20] R. Xunstmann, U. Lerch, H. Gerhards, M. Leven, U. Schacht, *J. Med. Chem.* 27 (1984) 432.
- [21] B. Lantaño, J. Aguirre, L. Finkielstein, E. Alesso, E. Brunet, G. Moltrasio, *Synth. Commun.* 34 (2004) 607.
- [22] E. Alesso, R. Torviso, B. Lantaño, M. Erlich, L. Finkielstein, G. Moltrasio, J. Aguirre, E. Brunet, *Arkivoc* (2003) 283.