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Friedel–Crafts alkylations on nanoscopic inorganic fluorides

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ABSTRACT

The catalytic potential of nanoscopic MF_x (M = Mg, Al; x = 2, 3) has been investigated using batch Friedel–Crafts alkylation of aromatic compounds, including benzene, ethylbenzene, trimethylhydroquinone (TMHQ), and menadiol (MDL), with isophytol and benzyl alcohol. The conversion of isophytol was 100% in the reactions with trimethylhydroquinone (TMHQ), menadiol (MDL) and benzene while the highest selectivity in alkylated compounds was achieved with TMHQ (>99%). The different reaction rates of the alkylation reactions are due to the different nucleophylicities of the substrates, and therefore, due to their ability to delocalize the positive charge in the Wheland intermediate by inductive and resonance effects. The conversions of benzyl alcohol varied between 10 and 84% as a function of the catalyst nature and reaction conditions while the highest selectivity to monobenzyl derived compounds (25%) was achieved with ethylbenzene. The formation of high amounts of dibenzyl ether was also observed, indicating the presence of high amounts of Brønsted acid sites in this type of catalysts.

1. Introduction

Nowadays most of the fine chemicals are synthesized under acid–base catalysis conditions. Traditionally, the syntheses carried out in liquid-phase follow either a stoichiometric chemistry or use homogeneous acid and base catalysis. The commonly encountered drawbacks of such syntheses include salt formation and problems of waste disposal. Among these syntheses, the Friedel–Crafts alkylation is widely used in the large-scale production of petrochemicals and in a great variety of fine chemicals and intermediates processes.

Literature reported many examples of such syntheses. Thus, an important example of fine chemicals is the synthesis of (all-*rac*)-[α]-tocopherol (Vitamin E) which displays important antioxidant properties and shows promising results in the prevention and treatment of heart disease, cancer and Alzheimer's disease [1–4]. As it is also used in high amounts in other important industrial markets the demand of (all-*rac*)-[α]-tocopherol is constantly increasing from year to year [1]. The synthesis of this valuable compound, made via the condensation of 2,3,6-trimethylhydroquinone (TMHQ) with isophytol (IP), possibly proceeds through Friedel–Crafts alkylation–cyclization [5–12] or through an ortho-Claisen rearrangement of an intermediary allyl ether [13,14].

Another example is the synthesis of vitamin K_1, an important compound in the control of blood clotting, which involves as a key-step the Friedel–Crafts alkylation of menadiol acetate (MDA) with isophytol [15].

The industrial-scale synthesis of both products comes up against corrosion caused by acidic media, contamination of the wastewater with acids, and the difficult purification of the main product [16]. In line with the need for more environmentally acceptable processes, the search for highly efficient, heterogeneous catalysts for these syntheses, which might replace presently used homogeneous catalysts, is a challenging task.

Recently, we have developed novel nanoscopic, partly hydroxylated metal fluorides with bi-acidic (Lewis/Brønsted) properties [17]. We have shown that hydroxylated nanoscopic fluorides (MgF_2 and AlF_3) can be successfully applied as highly active catalysts in the synthesis of both vitamins [18,19]. With the aim to extend the applicability of this promising new class of catalytic materials we applied them in the synthesis of diphenylmethane (DPM) and its derivatives which are generally prepared via Friedel–Crafts alkylation (benzylation) reaction. Diphenylmethane and its derivatives are industrially important compounds used as pharmaceutical intermediates [20] and fine chemicals [21]. In the fragrance industry diphenylmethane has been used as both a fixative and a scenting soap, as a synergist in some insecticides and as a plastisizer for dyes [22]. Their synthesis is traditionally performed using H_2SO_4, HF, $AlCl_3$, $FeCl_3$, or $ZnCl_2$ [23] as acid catalysts. To overcome the derivate problems, Lewis acids have been supported by different solids, such as MCM-41 [24], hydroxyapatite (HAP) [25], and fluorapatite (FAP) and have been used as heterogeneous catalysts for

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the Friedel–Crafts reaction of benzyl chloride with benzene and its derivatives, respectively. Such heterogeneous catalysts gave rise to good yields of monoalkylated products and reduced isolation problems. In spite of the above-mentioned advantages for the use of supported acids, the preparation of these catalysts is commonly tedious, furthermore, these catalysts deactivate rapidly due to coke formation. Moreover, the use of benzyl chloride as the alkylating agent is undesirable from the green chemistry point of view, generating hydrogen chloride as by-product. More appropriate is the use of benzylic alcohol, which generates only benign water as by-product. Hence, there is still a need to develop an easy-clean technology more suitable for the synthesis of diphenylmethane and its derivatives.

Here we will show that, partly hydroxylated, nanoscopic fluorides (MgF_2 and AlF_3) can also be applied in the synthesis of diphenylmethane and its derivatives, using benzyl alcohol as alkylating agent in free solvent conditions. The successful application of Friedel–Crafts alkylation reactions is strongly influenced by the main features of the reaction system as the catalyst nature, the substrate and alkylating agent reactivities; an optimal combination of them being essential.

2. Experimental

2.1. Catalyst preparation

All the synthesis reagents were analytically pure, and were used as received from Aldrich. The catalysts were synthesized as reported elsewhere [17,26]. Nanoscopic partly hydroxylated aluminum fluoride was prepared from aluminum *iso*-propoxide (Aldrich, 98%) using a one-pot fluorolytic sol–gel synthesis [18]. The obtained sample was named as AlF_3-50, where 50 indicates the concentration of the aqueous HF solution used in the synthesis. In a similar way, other five MgF_2-based samples were obtained from dissolving metallic Mg (Aldrich, 99.98%) [17] in methanol followed by the sol–gel-fluorination. The prepared catalysts were referred to hereafter as MgF_2-40, MgF_2-57, MgF_2-71 and MgF_2-87, where the numbers indicate the different concentrations of aqueous HF solutions used.

2.2. Catalyst characterization

XRD, CP-MAS-NMR, TEM, thermal analysis, and elemental analysis have been applied to study the structure, composition, and thermal behavior of the bulk materials. XPS measurements, FTIR with probe molecules, NH_3-TPD, and the determination of N_2/Ar adsorption–desorption isotherms have been carried out to investigate the surface properties. All characterization procedures were described elsewhere [17,18,27,28].

2.3. Catalytic tests

2.3.1. The synthesis of vitamin E

Trimethylhydroquinone (TMHQ) (97 wt.%) and isophytol (IP) (95 wt.%) were purchased from Across Organics. The other reagents (analytical grade) were obtained from Merck. In a typical procedure, 152–304 mg (1–2 mmol) TMHQ was dissolved in 6 cm^3 of solvent (heptane:propylene carbonate (50:50, vol:vol)) in a glass vial (standard capacity of 8 cm^3) equipped with a magnetic stirrer. To this mixture 0.4 cm^3 (1 mmol) of IP and 50 mg of catalyst were added. After that the vial was closed, immersed in an oil bath with a temperature of 100 °C, and the charged mixture was stirred (1250 rpm) for 5–60 min. After reaction the catalyst was separated from the two-phase solvent mixture, the heptane phase (containing the tocopherol) was separated from the propylencarbonate phase and the solvent removed under vacuum to give a crude product. The crude product was analysed by HPLC (column – EC 125/4.6 NUCLEOSIL 120-5 C18; eluent: acetonitrile; flow rate: 0.8 cm^3/min; wavelength: 280 nm; volume sample: 15 μL) chromatography and ^1H, ^{13}C NMR (Bruker AV 400 spectrometer, in $CDCl_3$ solvent and Me_4Si as internal standard) spectroscopy.

2.3.2. The synthesis of vitamin K_1

In a typical procedure, 174 mg (1 mmol) menadiol (MDL) were dissolved in 6 cm^3 of the solvent (propylene carbonate:heptane (50:50, vol:vol)) in a glass vial equipped with a magnetic stirrer. To this mixture 0.4 cm^3 (1 mmol) of IP and 50 mg of the catalyst were added. After that, the vial was closed, immersed in an oil bath with a temperature of 100 °C, and the charged mixture was stirred (1.250 rpm) for 1–5 h. The resulting reaction mixture was cooled down to room temperature and the catalyst was removed by filtration from the two phase solvent mixture, the heptane phase (containing the reaction product) was separated from the propylene carbonate phase and the solvent was removed under vacuum to give a crude product. The crude product was analysed by UPLC chromatography (Ultrahigh Pressure Liquid Chromatography) Thermo Scientific (column – EC 125/4.6 NUCLEOSIL 120-5 C18; eluent: acetonitrile; flow rate: 0.5 μL/min; wavelength: 280 nm; volume of sample: 1 μL) and ^1H, ^{13}C NMR spectroscopy (Bruker AV 400 spectrometer, in DMSO-d_6 or $CDCl_3$ solvent and Me_4Si as internal standard).

2.3.3. The synthesis of biphenylmethane

In a typical procedure, to a solution of 0.40–1.56 mg of benzene and 0.54–1.08 mg of benzyl alcohol (corresponding to a molar ratio of 1/2 and 4/1), 100 mg of catalyst were added. The obtained mixture was kept to a reaction temperature of 100–120 °C, for 4–24 h. The same experiments were performed using ethylbenzene instead of benzene. After the reaction, the catalyst was separated by filtration and the reaction products were analyzed by gas-chromatography GC (Shimadzu instrument with FID detection, TR-WAX-TR1MS column of 60 m length and 0.32 mm inner) and identified by GC–MS (TERMO Electron Corporation instrument, Treace GC Ultra and DSQ).

3. Results and discussion

The synthesis and characteristic properties of the nanoscopic metal fluoride catalysts were presented in more detail recently [17,28]. In brief, when a metal alkoxide is reacted with stoichiometric amounts of aqueous HF, a competition between fluorolysis (reaction with HF) and hydrolysis (reaction with water) occurs resulting in the formation of hydroxofluorides. The F/OH ratio in the products formed this way depends on the free Gibbs enthalpy of each reaction and on the reaction rate. In fact both, the thermodynamic data as well as the reaction rate (the fluorolysis rate higher than the hydrolysis rate) let expect the dominant formation of the metal fluoride [28]. However, by varying the H_2O to HF-ratio in the hydrofluoric acid differently hydroxylated metal fluoride phases can be obtained. This competitive reaction system is schematically illustrated in Eq. (1). Thus, the simultaneous fluorolysis and hydrolysis reaction leads to partly hydroxylated aluminium or magnesium fluorides, respectively, as has been already demonstrated [17,18].

$$M(OR)_n + nHF + xH_2O \overset{\text{fluorolysis}}{\underset{\text{hydrolysis}}{\longrightarrow}} MF_{n-x}(OH)_x + nROH + n - xHF \quad (1)$$

Based on TEM, MAS NMR, and XPS results, we showed that adjusting the HF-stoichiometry HF: Mg to 2 but varying the water content results in shell-like nanoparticles of $MgF_{2-x}(OH)_x$ phases, the inner cores (bulk) of which mainly consist of essentially pure MgF_2. In their outer shells (surface), they become increasingly hydroxylated (with x still <0.1), as evidenced by XPS and FTIR results. This is

because the competing hydrolysis reaction becomes increasingly relevant after the fluorolysis reaction has consumed the HF in the reaction system [17]. These materials possess medium-strong Lewis acid sites and, by increasing the amount of water, Brønsted acid sites as well [28]. Therefore, using different amounts of water during the sol–gel synthesis the Lewis/Brønsted acid site ratio can be tuned very precisely.

Since a long time it has been established that acidic halides, which are typically Lewis acids, have little or no activity for alkylation when used in a pure state. They can be activated by the addition of low concentrations of co-catalysts which interact with the Lewis acids to generate actual or potential Brønsted sites [29]. Thus, against any expectation, partly hydroxylated MgF_2 was found to carry Brønsted acidic instead of basic OH groups. The unexpected results obtained in the synthesis of vitamins E and K_1 clearly indicate that the high activity in combination with an exciting high selectivity to the main product is due to the synergistic effect of the presence of both Brønsted and Lewis sites on the surface of the nanoscopic hydroxylated fluorides [17]. Therefore, the best catalyst for the target product can be obtained through a very simple tuning of the acidic properties of the material [19].

The general mechanism of alkylation involves first the interaction of the alkylating agent with the acid catalyst to form an activated electrophile, E^+, which adds to the aromatic ring acting as a nucleophile, followed by proton elimination (Eq. (2)):

$$E^+ + ArH \rightarrow \underset{\mathbf{1}}{[E - Ar - H^+]} \rightarrow E - Ar + H^+ \quad (2)$$

where **1** is known as a Wheland intermediate [29]. The nature of the catalyst has a considerable influence on the reactivity and selectivity of the alkylating agent, the activated specie (E^+) existing as a more or less tight ion pair with a considerable degree of covalent bonding between the carbocation and the catalyst macroanion. In these conditions, its relative stability is very important for determining the rate of alkylation.

On the other hand the substrate selectivity is governed by its nucleophilicity and its ability to delocalize the positive charge in the Wheland intermediate **1** by inductive and resonance effects [29].

Therefore, the successful application of Friedel–Crafts alkylation reactions is strongly influenced by several features of the reaction system as the catalyst nature, the substrate and alkylating agent reactivities, and the reaction parameters, an optimal combination of these features being essential.

As we have already shown the nature of the catalyst (i.e., the Brønsted/Lewis acid site ratio) is crucial in the synthesis of two important vitamins: vitamin E and K_1, both involving as first step the Friedel–Crafts alkylation of an aromatic ring (e.g., trimethylhydroquinone (TMHQ) and menadiol (MDL), respectively) with isophytol (IP) as alkylating agent (Scheme 1) [19]. Therefore, taking this into account for the synthesis of vitamin E, the overall rate of the synthesis seems to be dictated by the rate of the chromane ring closure step (Fig. 1A–D). The first alkylation step of TMHQ to phytilhydroquinone (PHQ) is much faster than the chromane ring closure of the phytil-hydroquinone (PHQ) step and is dictated both by the acid strength and the Brønsted/Lewis acid site ratio of the catalysts. Moreover, the same catalytic features influence the overall selectivity to the main product (vitamin E).

The time dependent analysis of the reaction products (Fig. 1A–D) shows that the acid strength has a positive influence both on the reaction rate and the selectivity to vitamin E (VE). The alkylation intermediate (PHQ) is formed in a high degree with a maximum of 69.6% in only 5 min (Fig. 1A). A decrease in the acid strength slowed down the rate of the alkylation step, the maximum of alkylated intermediate being obtained after 10 min (Fig. 1B). Increasing the density of Brønsted sites in disfavour of the Lewis sites slowers even more the rate of the alkylation step down (Fig. 1C and D).

At the moment, it is not entirely clear as to whether the total number of acidic sites has an influence upon the synthesis, but it is obvious that the presence of Brønsted acid sites is essential to promote the first alkylation synthesis step, while for the general synthesis the Lewis/Brønsted acid site ratio is a critical feature. It seems that the optimal combination of Lewis/Brønsted acid sites was generated in the sample MgF_2-71, while an optimal acidic strength was characteristic for AlF_3-50. Moreover, the decreasing alkylation rate is accompanied by an increasing of the selectivity to phytadienes, formed through the dehydration of the isophytol.

By replacing the TMHQ with MDL (Scheme 1) the reaction rate of the Friedel–Crafts alkylation became slower, conversions of 100% of MDL being obtained only after 5 h. Such behaviour is due to the lower nucleophilicity of MDL as compared with TMHQ and, as a consequence, due to its lower ability to interact with the activated electrophile.

The overall yields to the alkylated intermediates in the synthesis of Vitamin E and Vitamin K_1, as a function of the catalyst's characteristics, are presented in Table 1.

As Table 1 shows, in terms of overall yield to the alkylated intermediates, the differences from one catalyst to another one are, apparently, insignificantly, the values varying in a narrow domain. Generally speaking, in both cases, the MgF_2-40 sample, with a high amount of Brønsted acidity is less selective to alkylated intermediates than the other samples due to the increasing amount of phytadienes in the reaction products. Therefore, although the catalyst is able to generate the activated electrophile through its interaction with the alkylating agent, the Friedel–Crafts alkylation takes place to a lower degree. Comparing the results obtained in the presence of MgF_2 samples, this behaviour seems to be more a consequence of the Lewis/Brønsted acid sites ratio and not of the acidic sites density (Table 1).

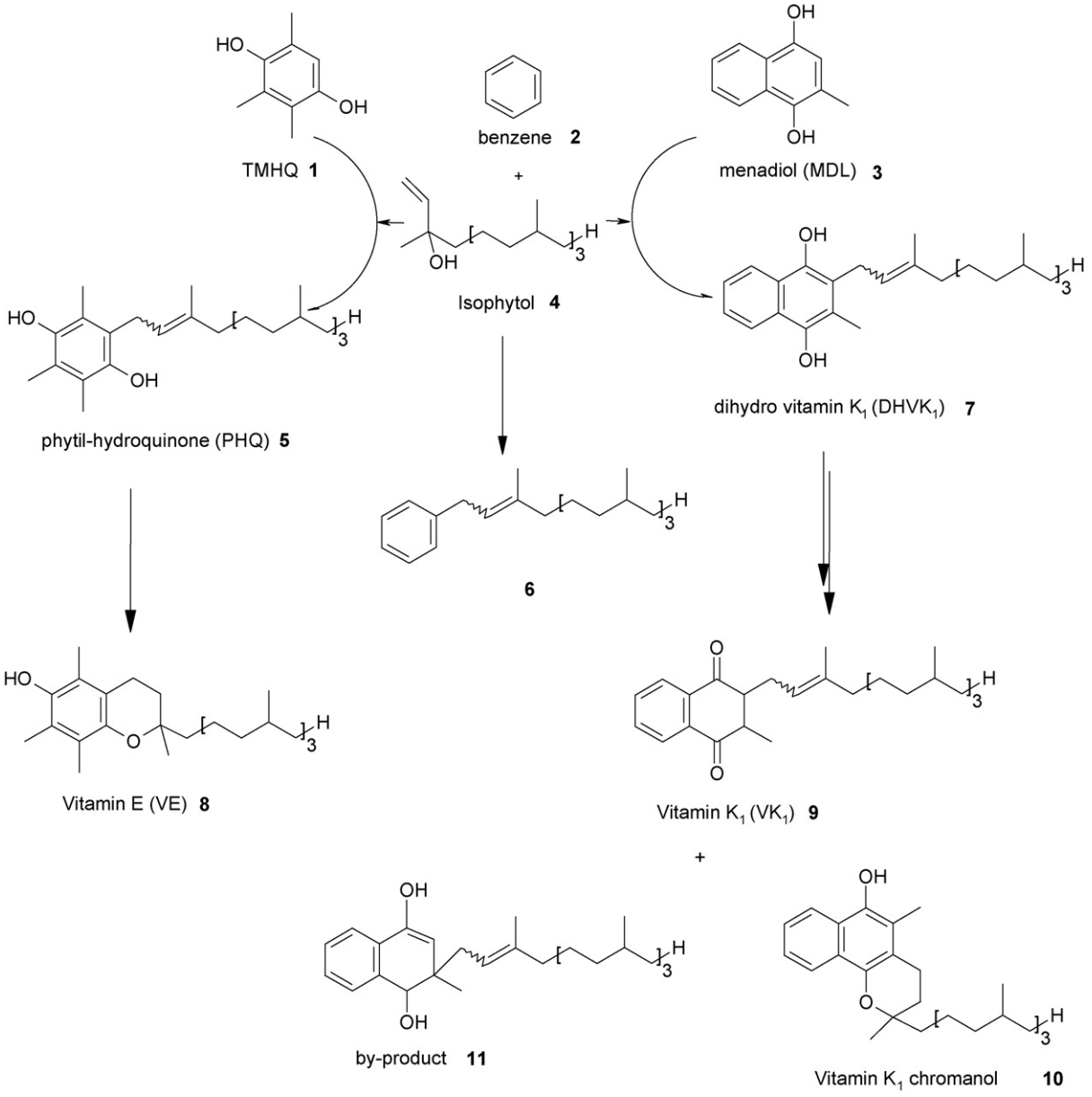
In the case of benzene (Scheme 1) the only detected reaction products were phytadienes formed by the dehydration of isophytol, because of the very low nucleophilicity of the substrate.

Furthermore, the catalysts were re-used in the benzylation of benzene and ethyl benzene. Obviously, the benzylic alcohol is a less reactive alkylating agent than isophytol (IP), taking into account the higher stability of the former. Even alkylation with benzylic alcohol (instead of isophytol) as alkylation agent was not expected as long as the alkylation conditions were the same. Therefore, the Friedel–Crafts alkylation of benzene (**1a**) and ethylbenzene (**1b**) with benzyl alcohol (**2**) (Scheme 2) were made in solvent-free conditions under autogenic pressure. The best results obtained in the alkylation of benzene are summarized in Table 2. TOF values are given as the number of benzylic alcohol molecules transformed in time at the acidic sites, calculated from NH_3-TPD and N_2-sorption isotherms measurements (Table 1).

As Table 2 shows, the highest activity in the benzylation of benzene with benzylic alcohol is obtained by the MgF_2-71 sample (Table 2, entries 4–6). A higher amount of benzylic alcohol led to a faster transformation but, unfortunately, predominantly results into the benzylic ether by-product. In this case, nor the Brønsted/Lewis acid sites ratio neither the acidic strength increases the selectivity to DPM, the highest values being below 15%, irrespective of the catalyst nature or of the reaction conditions.

It is clear that, under these conditions, the etherification reaction is much faster than the benzylation due to the low reactivity of the substrate.

Replacing benzene by ethyl benzene, that exhibits a stronger ability to delocalize the positive charge in the Wheland intermediate **1** by inductive and resonance effects, the results are somehow better (Table 3).



Scheme 1. The Friedel–Crafts alkylation of various aromatic substrates with different nucleophilicities.

Comparing the results obtained in the alkylation of ethyl benzene (Table 3) with those obtained in the alkylation of benzene (Table 2) with benzylic alcohol, it is clear that the increase of the TOF's and, more important, of the selectivities to the main product (PDPM *versus* DPM) is a result of the substrate nucleophilicity.

These results show that the electron donating $-C_2H_5$ group enhances the benzylation reaction because the transition state is

Table 1
Textural and chemical characterization of the catalysts.

Entry	Catalyst	BET surface[a] ($m^2\ g^{-1}$)	Pore size[a] (nm)	Amount of acid sites[b] (mmol g^{-1})	Overall yield	
					(**5**+**8**)[c] (wt.%)	(**7**+**10**+**11**)[d] (wt.%)
1	MgF_2-40	180	2.3	0.168	85.9	85.9
2	MgF_2-57	235	2.5	0.262	87.8	89.1
3	MgF_2-71	276	2.4	0.163	91.1	91.2
4	AlF_3-50	187	6.5	0.624	99.9	90.8

[a] Determined from N_2-sorption isotherms measurements.
[b] Determined from NH_3-TPD measurements.
[c] Reaction conditions: conversion: 100%; 50 mg catalyst, 304 mg TMHQ + 0.4 mL IP (2/1 molar ratio), 6 mL solvent (propylencarbonate/heptane = 50/50, vol/vol), 100 °C, reaction time = 0–1 h.
[d] Reaction conditions: conversion: 100%; catalyst amount: 50 mg; reaction temperature: 100 °C, MDL/IP molar ratio: 1/1, solvent: propylene carbonate/heptane (50/50, vol/vol), reaction time 5 h. The differences to 100% represent the phytadiene by-products.

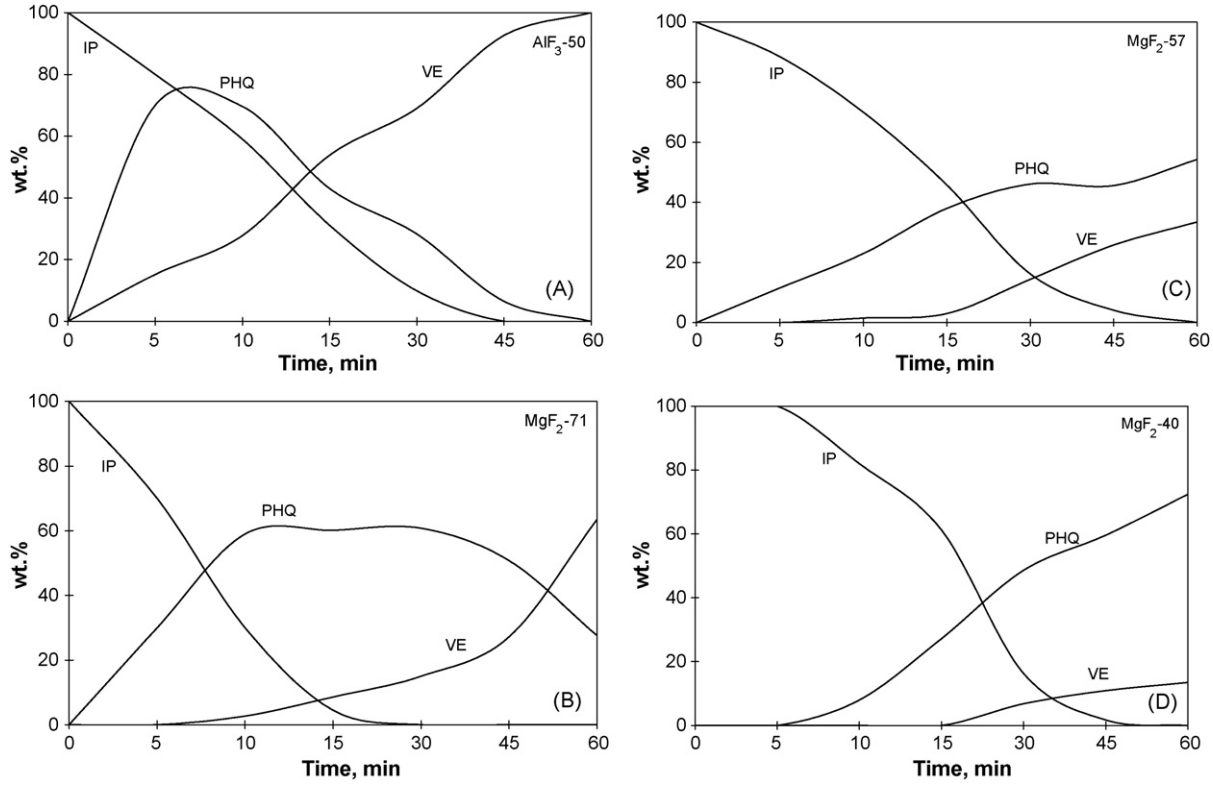


Fig. 1. The distribution of the reaction products in the synthesis of Vitamin E as a function of the catalyst's nature (reaction conditions: 50 mg catalyst, 304 mg TMHQ + 0.4 cm^3 IP (2/1 molar ratio), 6 cm^3 solvent (propylencarbonate/heptane = 50/50, vol/vol), 100 °C, reaction time = 0–60 min). IP, isophytol; VE, vitamin E; PHQ, phytil-hydroquinone.

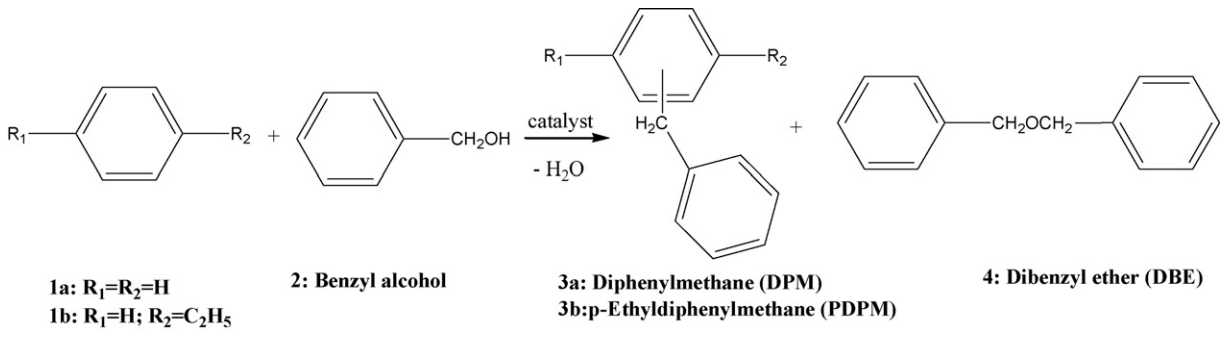
Table 2
The conversion of benzylic alcohol and selectivity to diphenylmethane under different reaction conditions as a function of the catalyst nature and reaction conditions.

Entry	Catalyst	T (°C)	**1a/2** molar ratio	C (wt.%)	TOF (h^{-1})	S (wt.%)	
						3a, DPM	**4**
1	MgF_2-57	100	1/2	11.1	1.8	3.5	96.5
2	MgF_2-57	100	4/1	12.6	1.0	11.7	88.3
3	MgF_2-57	120	4/1	38.2	3.1	14.5	85.5
4	MgF_2-71	100	1/2	17.5	4.5	2.7	97.3
5	MgF_2-71	100	4/1	18.4	2.35	10.1	89.9
6	MgF_2-71	120	4/1	42.0	5.4	13.2	86.8
7	AlF_3-50	100	1/2	14.1	0.9	7.1	92.9
8	AlF_3-50	100	4/1	15.4	0.5	10.3	89.7
9	AlF_3-50	120	4/1	52.3	1.7	12.7	87.3

Reaction conditions: 100 mg catalyst, 24 h.

stabilized by the electron donating groups both on benzene and benzyl alcohol. The order in the activity of the samples was the same, the most active being the MgF_2-71 sample, followed by MgF_2-57 and AlF_3-50 samples. Although not in a spectacular way, the selectivity to PDPM increases, the highest value reaching almost 25% at 120 °C and a **1b/2** molar ratio of 4/1.

The formation of ether, observed for these reactions (Tables 2 and 3), was also reported for other catalysts [30–32],



Scheme 2. Friedel–Crafts reaction of benzene and ethylbenzene with benzyl alcohol.

Table 3
The conversion of benzylic alcohol and selectivity to *p*-ethyldiphenylmethane (PDPM) under different reaction conditions as a function of the catalyst nature and reaction conditions.

Entry	Catalyst	T (°C)	**1b/2** molar ratio	C (wt.%)	TOF (h^{-1})	S (wt.%)	
						3b, PDPM (*ortho* + *para*)	**4**
1	MgF_2-57	100	1/2	12.8	2.0	4.0	96.0
2	MgF_2-57	100	4/1	45.6	3.6	9.6	90.4
3	MgF_2-57	120	4/1	64.0	5.1	22.5	77.5
4	MgF_2-71	100	1/2	20.7	5.3	5.2	94.8
5	MgF_2-71	100	4/1	51.0	6.5	11.4	88.6
6	MgF_2-71	120	4/1	70.3	9.0	22.7	77.3
7	AlF_3-50	100	1/2	16.0	0.5	7.8	92.2
8	AlF_3-50	100	4/1	64.2	2.1	21.8	78.2
9	AlF_3-50	120	4/1	84.6	2.8	24.3	75.7

Reaction conditions: 100 mg catalyst, 24 h.

the authors associating its formation to both, Brønsted and Lewis acid sites. On the other hand, Deshpande et al. [31] reported that in the benzylation with benzyl alcohol the etherification is faster than the alkylation reaction, and the generated dibenzyl ether can act as alkylating agent. Moreover, Lachter and co-workers [32] showed that the rate of dibenzyl ether formation is the same for the toluene, ethylbenzene and propylbenzene.

The interesting feature of the benzylation in the presence of nanoscopic fluorides is the isomer composition of the reaction products: In accordance with a typical electrophilic aromatic substitution pathway, benzylation products obtained from aromatic alkylation should predominantly consist of *ortho*–*para* substituted compounds. While in the presence of MgF_2-71 and AlF_3-50 samples, the percentage of *ortho*-isomer represent 33–40% from the total *ortho*–*para* DPM, in the presence of MgF_2-57 fluoride (S_{sp} = 235 m^2/g; D_p = 2.5 nm; amount of acid sites = 0.262 mmol/g), the main benzylation product is the *para*-isomer, *ortho*-isomer being formed by less than <1%. Such behavior may by an effect both of the catalyst's porosity (shape-selectivity) and of the density of the acid sites onto the surface.

The recovered catalysts showed consistent activity. The catalytic activity and selectivity were maintained even after the third re-use. Hydroxilated AlF_3 and MgF_2 materials exhibit very low solubility because of their high lattice energy. Moreover, these fluorides are hydrolysis resistant as is commonly known [18]. Consequently, the leaching test carried out showed that, indeed, the nanoscopic metal fluorides correspond to the stable catalysts. After the separation of the catalyst from the liquid solution, neither the level of the IP conversion nor the products distribution was changed for another 1 h. It can be concluded that these catalysts are stable under the reaction conditions, and the reaction takes place under heterogeneous conditions.

4. Conclusions

The nanoscopic fluorides catalyze the alkylation of trimethylhydroquinone (TMHQ), and menadiol (MDL) with total conversion and high selectivity to the alkylated product. The difference in the reaction rate (e.g., few minutes in the case of TMHQ *versus* few hours for MDL) is due to the lower nucleophilicity of MDL as compared with TMHQ and, as a consequence, due to its lower ability to interact with the activated electrophile of the alkylating agent. The very low nucleophilicity of benzene is responsible for the formation of only phytadienes in its alkylation reaction with isophytol.

The benzylation of aromatic hydrocarbons with benzyl alcohol in the liquid-phase proceeded under relative mild conditions, with moderate activities and selectivities to diphenylmethane (DPM) and its derivatives. The etherification of benzyl alcohol to dibenzylether (DBE) was much faster than the benzylation of the substrate. The selectivity to the main benzylation product could not be improved above 25% irrespective of the catalyst's nature (e.g., the Brønsted/Lewis acid sites ratio and acidity strength) suggesting a limitation of the catalyst's ability for this kind of reactions. Nevertheless, the MgF_2-57 catalyst's porosity and the density of the acid sites enabled selectivity to the *para*-isomer as the almost quantitatively formed reaction product of the benzylation.

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