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Graphical Abstract

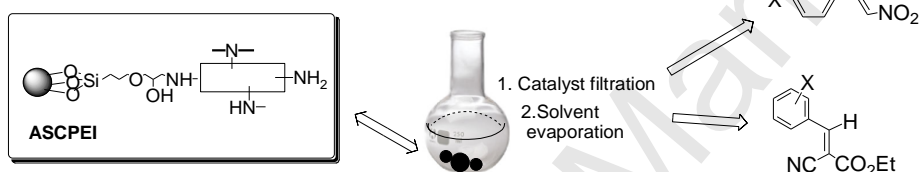
Silica graphped polyethylenimine as heterogeneous catalyst for condensation reactions

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Research highlights

- A heterenogeneous material with poliethylenimine graphted in a silica matrix (ASCPEI) can be easily synthesized;
- ASCPEI catalyzes nitroaldol condensations;
- ASCPEI is an efficient catalyst for Knoevenagel condensation reactions with ethyl cyanoacetate;

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Abstract

Primary amine groups were attached to a silica surface by using α,ω -diamines derivatives and (3-glycidyloxypropyl)-trimethoxysilane activation. The same activation was used to graft polyethylenimine, which also contains secondary and tertiary amine groups. These silica aminated structures were tested as heterogeneous catalysts in nitroaldol condensation with nitromethane, the derivative with the polyethylenimine moiety being the more active catalyst. This catalyst also showed efficiency in the Knoevenagel condensation of benzaldehydes with ethyl cyanoacetate under very mild reaction conditions and showed much the same efficiency when used in consecutive reaction runs. A reaction mechanism with participation of the several amine groups of the catalysts is discussed.

Keywords:

Polyethylenimine, silica, heterogeneous catalysts, Knoevenagel condensation.

1. Introduction

The search for green chemical processes [1] with high efficiency but at the same time with reduced uses of energy and materials, as well as the lowest generation of waste has increased the interest for supported catalytic processes. Also, the cost associated with product isolation from the reaction mixture is an important feature in the choice of a heterogeneous process [2-5]. Supported catalytic processes are therefore attractive to answer the above requirements. Searching for a catalytic process can be tricky if the reaction requires an acid-base activation. **General homogeneous conditions make** difficult

the compatibilization between acid and basic sites but this can be circumvented using ionic liquids [6]. In this particular case, heterogeneous supports with acid and base groups located separately can work cooperatively and be an advantageous solution [7]. This acid-base cooperativity which is common in enzymatic systems [8] can also be achieved using heterogeneous organic-inorganic bifunctional catalysts [9, 10]. Silica is an inexpensive, easily available and resistant material that can be superficially modified with organic groups in order to modify the acid-base properties or covalently anchor different catalysts [7-12]. An analogous **more developed** approach is the use of synthesized mesoporous silica incorporating different organic functionalities [13, 14]. An interesting capacity of these silica functionalizations is the placement of amino groups near silanols in order to get efficient acid-base activation processes.

The Knoevenagel condensation [15] and the nitroalkene synthesis from nitroaldol condensation [16] are carbon-carbon forming reactions that originate valuable compounds with biological activity [17-21]. Both reactions can be catalyzed by homogeneous catalysts [22-31] but heterogeneous catalysts have been also successfully used [32-39].

In this work various aminofunctionalized silica materials were prepared with a terminal amine group separated from the silica structure by a carbon chain of variable length. The effect of this separation on the catalytic activity of the material as a heterogeneous catalyst for carbon-carbon condensations was studied. In addition, grafting a polyethylenimine structure at the silica surface originates a much more active heterogeneous catalyst.

2. Experimental Section

All solvents were purified before use according to the literature procedures. Ethyl cyanoacetate (98% purity, Fluka), ninhydrin (95% purity, Fluka), anisaldehyde (98% purity, Riedel-de Haën), 4-chlorobenzaldehyde (98% purity, Fluka), benzaldehyde (98% purity, Merck), cinnamaldehyde (98%, BDH), 4-methylbenzaldehyde (97% purity), 4-nitrobenzaldehyde (98% purity), 4-hydroxybenzaldehyde (98% purity), 3,4-dimethoxybenzaldehyde (99% purity), 2-furfuraldehyde (99% purity, freshly distilled), pyrrole-2-carboxaldehyde (98% purity), 1-naphthaldehyde (97% purity), cyclohexanone,

3-aminopropyltrimethoxysilane (97% purity), (3-glycidyloxypropyl)-trimethoxysilane (98% purity), 1,12-diaminododecane (98% purity), 1,6-diaminohexane, polyethyleneimine (low molecular weight typical M_w -800) were used as purchased from Aldrich. Silica gel type 60, 35-70 mesh, with particle size of 0.2–0.5 mm was purchased from Fluka.

2.1 Catalysts Preparation

Synthesis of the aminoalkylated silica derivatives

ASC3: To a stirred solution of 70 ml dry toluene containing 10% of 3-aminopropyltrimethoxysilane was added 45 g of SiO_2 (silica gel type 60, 35–70 mesh) activated as described at 120 °C. The resulting mixture was refluxed overnight. The amine functionalized silica **ASC3** was isolated by filtration and washed with tetrahydrofuran and methanol, then dried under vacuum for several days [40].

ASC6.6, ASC6.12 and ASCPEI [41]: To a stirred solution of 80 ml dry toluene containing 3.0 mmol of diamine (1,6-diaminohexane for **ASC6.6**, 1,12 –diaminododecane for **ASC6.12**, **polyethylenimine** for **ASCPEI**); 1.0 mmol of (3-glycidyloxypropyl)-trimethoxysilane was added. The resulting mixture was allowed to react at 80 °C for 24 h. After this time, 1.5 g of activated SiO_2 (Silica gel type 60, 35-70 mesh) and 5 ml of ethanol were added to that stirred solution and was maintained at 80 °C for 24 h. The amine functionalized silicas were isolated by filtration and washed with methanol and ethanol. Then, they were refluxed with ethanol during 1 h, filtered again and dried at 40 °C for several days.

SilPEI: To a stirred solution of 80 ml dry toluene, containing 3.0 mmol of **polyethylenimine**, 1.5 g of activated SiO_2 (Silica gel type 60, 35-70 mesh) and 5 ml of ethanol were added and was maintained at 80 °C for 24 h. The silica product obtained was isolated by filtration and washed with methanol and ethanol. Then, it was refluxed with ethanol during 1 h, filtered again and dried at 40 °C for several days.

2.2 Catalysts Characterization

2.2.1 Measurement of total nitrogen content

Total nitrogen content was determined using a Fisons Instruments EA1108-CHNS-0 apparatus.

2.2.2 Quantification of amines group by ninhydrin test

The procedure employed followed a previously report for amine-functionalized silica material [42, 43]. Typically, 50 mg of the catalyst samples was mixed with 5 mL of ethanolic ninhydrin solution (0,175 M). The solution was stirred at 90°C for 25 min. It was cooled and centrifuged for 10 min. The absorbance of the supernatant solution was monitored and the amount of aminogroups estimated from a calibration curve made with different concentrations of 3-aminopropyltrimethoxysilane.

2.2.3 N₂ adsorption/desorption isotherms

The N₂ adsorption/desorption isotherms were obtained in an ASAP 2000 (Micrometrics Instrument Corporation) using liquid nitrogen for analysis gas. The samples were pre-treated in situ under vacuum at 295/296 K until vacuum stabilization at a pressure below 10 micrometers of mercury. The surface area was calculated by the BET method. The pore volume was measured using the adsorption curve. The pore size distribution (PSD) were determined from the desorption isotherm using BJH model.

2.3 Catalytic tests

2.3.1 General procedure for aldehyde /nitroalkane condensations

In a typical experiment, a mixture of the aldehyde (5 mmol) and catalyst (50 mg) in the nitroalkane (2 mL) was stirred at 95°C. The reaction was monitored by gas chromatography. The gas chromatography with flame ionization detector (gc-fid) was carried out using a Supelcowax (30 m x 0.25 mm) capillary column on a Hewlett-Packard 5890A instrument with a Hewlett-Packard 3396A integrator. GC analysis was run at 100 °C (2 min)/20 °C min⁻¹/220 °C (20 min); detector temperature 250 °C, injector temperature 220 °C. After completion, the catalyst was filtered off and washed with chloroform. The filtrate was evaporated and the residue was washed with cold hexane. The product was analysed by NMR, IR spectroscopy and mass spectrometry. NMR spectra were recorded on a 400 MHz Bruker spectrometer. J values are given in Hertz. The IR spectra were obtained at room temperature in transmission mode using Thermo

Nicolet 6700 FTIR spectrometer. Mass spectra were obtained on a HP 5973 MSD apparatus by electronic impact at 70 eV.

The structure of the products was established by comparison with data shown in the literature and the product characteristics are identical to that previously reported. The conversion and selectivity were determined by ^1H NMR (for the dinitro and nitroalcohol derivatives see ref. 44,45):

(E)-1-(4-Methoxyphenyl)-2-nitroethene (**3a**) [46]; *(E)*-1-(4-Chlorophenyl)-2-nitroethene (**3b**) [47]; *(E)*-1-phenyl-2-nitroethene (**3c**) [23]; *(E)*-1-(4-Methylphenyl)-2-nitroethene (**3d**) [48]; *(E)*-1-(4-Hydroxyphenyl)-2-nitroethene (**3e**) [48].

2.3.2 General procedure for the Knoevenagel condensation reaction

In a typical experiment, a mixture of the aldehyde (5,23 mmol), ethyl cyanoacetate (5,23 mmol) and 50 mg of catalyst in ethanol (6 mL) was stirred at 43 °C. The reaction was monitored by GC or TLC. After completion of the reaction, the catalyst was filtered off and washed with chloroform. The filtrate was evaporated and the residue was washed with cold hexane. The product was analysed by NMR, IR and mass spectroscopy. The structure of the products was established by comparison with data described in the literature.

Ethyl (E)-2-Cyano-3-(4-methoxyphenyl)-2-propenoate (**8a**); *Ethyl (E)*-3-(4-Chlorophenyl)-2-cyano-2-propenoate (**8b**); *Ethyl (E)*-2-Cyano-3-phenyl-2-propenoate (**8c**); *Ethyl (E)*-2-Cyano-3-(4-methylphenyl)-2-propenoate (**8d**); *Ethyl (E)*-2-Cyano-3-(4-nitrophenyl)-2-propenoate (**8f**); *Ethyl (E)*-2-Cyano-3-(1-naphthyl)-2-propenoate (**8g**); *Ethyl (E)*-2-Cyano-3-(2-furyl)-2-propenoate (**8i**); *Ethyl (E)*-2-Cyano-3-(1H-pyrrol-2-yl)-2-propenoate (**8j**); *Ethyl (2E,4E)*-2-Cyano-5-phenyl-2,4-pentadienoate (**8k**) [30].

Ethyl (E)-2-Cyano-3-(3,4-dimethoxyphenyl)-2-propenoate (**8h**) [49] : ^1H NMR (400 MHz, CDCl_3) δ (ppm): δ 1.40 (t, $J=7$ Hz, 3 H), 3.96 (s, 6 H), 4.37 (q, $J=7$ Hz, 2 H), 6.94(d, $J=8.2$ Hz, 1 H), 7.47(d, $J=8.2$ Hz, 1 H), 7.80 (s, 1 H), 8.15 (s, 1 H). ^{13}C NMR (100.613 MHz, CDCl_3) δ (ppm): 14.21, 56.05, 56.15, 62.44, 99.43, 110.96, 111.67, 116.35, 124.63, 127.87, 149.29, 153.68, 154.65, 163.08.

Ethyl cyano (cyclohexylidene) acetate (10c) [27]: ^1H NMR (400 MHz, CDCl_3) δ (ppm): 1.33 (t, $J=7.2$ Hz, 3 H), 1.66-1.80 (m, 6 H), 2.66 (t, $J=6$ Hz, 2 H), 2.98 (t, $J=6$ Hz, 2 H),

4.27 (q, $J = 7.2.0$ Hz, 2 H); ^{13}C NMR (100.613 MHz, CDCl_3) δ (ppm): 13.95, 25.49, 28.16, 28.49, 31.45, 36.74, 61.15, 101.88, 161.83, 179.84. EI-MS: m/z (%) 193 (58, M^+), 165 (75), 148 (62), 137 (100), 121 (81), 109 (27), 93 (37), 80 (17), 65 (12).

3. Results and discussion

3.1 Catalyst Preparation

Siliceous materials with supported amines have been largely tested as heterogeneous catalysts for carbon-carbon condensation reactions. Several kinds of silica supports can be used to incorporate the amine functionalities, such as synthesized mesoporous silica [50-54] or MCM-41 silica structures [55-60]. However an easier approach is to use commercial silica and incorporate the amine functionality by reaction of the silanol groups with aminotriethoxysilane derivatives. First works with aminopropyl groups showed activity for Knoevenagel reactions [61, 62]. More recently the same approach was followed using silica-alumina supports and catalysts proved to be efficient in Michael additions and nitroaldol condensations. The incorporation of only diethylamino groups or these in the presence of primary amine groups modulates the activity of the heterogeneous catalyst [63-66]. The effect of the structure of the amine groups grafted into silica materials has been studied for mesoporous silica materials [67-71] in which the catalytic process occurs at the surface, but also within pores and channels. These different catalytic environments can originate misleading contributions of the amine groups to the catalytic process. In a different previous work, we prepared a series of silica based photosensitizers with different chain spacers and studied the contribution of the silica structure to reaction efficiency [41]. Taking into account this experience and to enlighten the cooperative effect of the amine groups and silica surface on catalytic activity we decided to graft into the silica surface several kinds of aminoalkyl groups in which the amine functionality is increasingly separated from the silica silanol groups. For the smaller carbon chain catalyst **ASC3** we reacted commercial silica (Kieselgel 60) with 3-aminopropyltrimethoxysilane following a described procedure [40]. To increase the carbon chain length it was necessary to use the silica activation with (3-glycidyloxypropyl)-trimethoxysilane [72] followed by reaction with 1,6-hexanediamine or 1,12-dodecanediamine giving the corresponding aminated silica catalysts **ASC6.6**, and

ASC6.12. As pointed out in other works with mesoporous silicas as catalysts, the type of amine group (primary, secondary or tertiary) can influence the catalytic activity. The literature describes simultaneous grafting of primary and tertiary amine groups in silica structures using the silane activation approach [64]. We envisaged another strategy by grafting in the silica surface a polyamine, such as **polyethylenimine** [73], which presents the three kinds of amine groups and proved to be efficient catalysts for hydrolysis reactions [74-76] (Scheme 1). The presence of these different amine groups, with different acid-base behavior, could originate interesting catalytic effects. The possibility of simple **polyethylenimine** adsorption to silica surface was taken into consideration by treating polyethylenimine with activated silica gel in the same conditions used in the case of amine grafted samples and the corresponding catalyst was also prepared (SilPEI).

Scheme 1

Evidence for the presence of the amine groups in the silica structures is obtained by IR spectra evidence (Fig. 1). The reduction in intensity of the broad band around 3500 cm^{-1} (O-H stretching) can be due to decrease of the silica hydrophilicity by reaction of the silanols with trimethoxysilyl groups [58] which is more evident in the **ASC6.12** catalyst. Also, reduction of absorbed water due to increased hydrophobicity can explain this behavior [77]. The existence of bands around 2940 cm^{-1} and 2850 cm^{-1} due to C-H stretching, visible in the ASC catalysts shows the presence of the amine carbon chain bonded to silica.

Fig. 1

The total amine **groups were** assessed by elemental analysis and those groups which are accessible to catalysis were estimated by the ninhydrin tests (Table 1).

Table 1

Elemental analysis of the aminated silica catalysts shows that **ASCPEI** shows the highest nitrogen content, as expected due to the polyamine incorporation. The **SilPEI** catalyst shows also high nitrogen content and evidences the adsorption ability of **polyethylenimine** to silica surface. The values for the nitrogen content for the other

catalysts show that amine incorporation is lower and inversely related to the length of the carbon chain. The ninhydrin test is a measured of the active amine groups mainly the primary ones [42]. Despite having moderate value for amine incorporation, **ASC6.6** and **ASC6.12** catalysts show very low values for the active amine groups, which can be explained by the double reaction of the two terminal amino groups with two siloxane activated surface places creating diamine bridges [42, 43]. Nitrogen adsorption-desorption isotherms for the **ASC3** and **ASCPEI** and catalyst characteristics are presented in Fig. 2.

Relatively to the characteristics of the commercial silica-gel used as starting reagent [78] the catalysts **ASC3** and **ASCPEI** shows low values for surface area and pore diameter as expected for the introduction of the aminated structures [79]. Between the two catalysts **ASCPEI** presents lower values for surface area due to its higher value of amine bonding.

3.2 Nitroaldol condensation

The activity of the different aminated silica catalysts was first tried in the reaction of *p*-methoxybenzaldehyde (**1a**) with nitromethane (**2**) (Table 2). For all the experiments the isolation process consists of the catalyst isolation by filtration and evaporation of the excess of nitroalkane. The **ASC3** catalysts showed good selectivity for the nitroalkene product (**3**) with high yields. Pre-activation of the catalysts seems to be important to promote a faster reaction. A reaction with aldehyde **1a** catalysed by a sample of **ASC3**, without heating activation, only gives sluggish conversion after 19h. Analysis of the effect of the carbon chain on the activity of the catalysts shows that the catalyst with the smaller carbon chain, **ASC3**, is the most active. Catalysts **ASC6.6** and **ASC6.12** shows low conversion values even after 24 hours reaction. These results and the observation of a better catalyst activity observed with pre-activated samples confirm the involvement of the silanol groups in the catalytic process as suggested by others [10, 54, 56, 65, 68, 80]. The catalysts with the primary amine group, which are involved in catalytic process, apart from the silica surface (**ASC6.6** and **ASC6.12**) gives much slower catalysis probably due to the more difficult involvement of surface silanol groups in catalytic

process. Another explanation is the reaction of the terminal primary amino groups of the carbon chain with siloxane surface groups forming bridges [42] and blocking the participation of these groups in catalytic process. The low value for the ninhydrin test for **ASC6.6** and **ASC6.12** may confirm this hypothesis. **Catalyst ASCPEI** with the polyamine grafted at silica surface is the most active with aldehyde **1a** and was tried with other aldehydes (**1b-1e**). The main product is the nitroalkene with variable amounts of dinitro derivative **4** and nitroalcohol **5**. The higher values from the ninhydrin test for **ASCPEI** means a larger number of active amine groups and explain the higher catalytic efficiency relatively to **ASC3**. The reason for the catalytic success of **ASCPEI** can also be related to the organoamine functionality of **ASCPEI** which is probably flexible enough to allow proximity between amine and silanol groups and cooperativity between groups is working [69]. Relatively to selectivity and comparatively to **ASC3**, **ASCPEI** presents a lower selectivity for the product **3** and originates a greater amount of the dinitro derivative **4**. This difference can be explained by the existence of tertiary amine groups in the structure of **ASCPEI** which helps the proton abstraction in nitromethane (**2**) favoring the Michael addition to the formed nitroalkene molecule [64].

Table 2

Catalytic activity of **ASCPEI** was further explored using anisaldehyde and the less active nitroethane [50]. In this case the catalyst also showed activity, the nitroalkene product with *E* geometry [81, 82] being isolated in 89% yield. Recyclability of the catalyst was tried in consecutive runs using *p*-anysaldehyde as substrate and nitromethane.

Unfortunately the first reutilization showed only 29% of conversion indicating that some catalyst deactivation occurred. The IR spectrum of this material shows new sharp bands at 1384 and 1558 cm^{-1} probably due to the presence of a nitro groups.

3.3 Knoevenagel condensation

The Knoevenagel condensation requires the same kind of acid-base activation but mechanistically the involved species are quite different and the products formed are less reactive than nitro alkenes. This prompted us to try the **ASCPEI** catalyst on the

condensation of ethyl cyanoacetate (**7**) with several aromatic aldehydes as showed in Table 3.

Table 3

The **ASCPEI** catalyst was found to be a very efficient catalyst for the synthesis of α -cyanocinnamates (**8**). The reaction goes fast in very mild conditions and in some cases the product soon begins to precipitate from the reaction media. The great advantage of this catalytic system is that products are obtained by simply evaporation of the solvent after filtering the catalyst. Purity of the obtained products is relatively high, based on NMR spectra and melting point values. A blank experiment without catalyst and aldehyde **1c** gives 21% of conversion after 4 hours.

Even at room temperature reactions go to completion, albeit slightly slower (entry 3). Analysis of the products shows that the reaction occurs in a stereoselective manner originating the exclusively the *E* isomer. Changing the solvent to non polar toluene gives slower reaction (entry 2) relatively to that in ethanol which can be indicative of a stabilization of the transition states by the more polar solvent [54]. Another advantage of this catalyst is that reutilization can be done without losing the catalytic activity (entry 4 and 5). Using the best reaction conditions, the catalytic efficiency of **ACSPEI** was also observed for other substituted aromatic aldehydes (entry 6-11). Heteroaromatic aldehydes give the corresponding products in good yields (entry 12 and 13). With cinnamaldehyde (entry 14) the reaction stops after 4 hours and the product with *E,E* stereochemistry [30] is isolated with a small amount of the starting reagent. Looking at the IR spectrum of the recovered catalyst new bands of medium intensity appear at 1743 and 702 cm^{-1} which can not be related to the described deactivation process by amide formation between amine groups of the catalyst and ethyl cyanoacetate which correspond to a band at lower frequency (1690 cm^{-1}) [62,67,83]. This deactivation is caused by the reaction product since a new sample of catalyst left in contact with the product **8k** originates new IR bands at 1741 and 702 cm^{-1} . The value obtained by the deactivated catalyst (1743 cm^{-1}) is closer to the carbonyl frequency of the ethyl cyanoacetate, 1755 cm^{-1} [83] which may indicate that this molecule participates in the deactivation process.

The possibility of some catalytic effect by the adsorbed polyethylenimine was analyzed using **SilPEI** catalyst giving 97 % of product 3c after 7 hours of reaction. This is a reduced catalytic activity compared with **ASCPEI**. The difference is more evident from the reutilization experiment in which **SilPEI** originates 97% of the same product but in 13,5 hours.

Simple comparisons with others silica based systems namely mesoporous materials can be misleading since differences in reaction conditions as solvent and temperature can originate incorrect conclusions. However taking into account the same substrate and analyzing the conversion of substrate versus reaction time, **ASCPEI** can be more active than silica grafted 1,8-bis(dimethylaminonaphthalene) [54], aminopropyl-functionalized mesoporous SBA-15 [58] or amine functionalized MCM-41 [59] but seems less active than aminopropyl functionalized AIMCM-41 [71].

As expected for steric reasons, the Knoevenagel condensation with ketones is much slower [27, 35]. With **ASCPEI** catalyst no reaction was observed after 24 h under conditions of Table 2. However at higher temperature no conversion for acetophenone is observed, sluggish conversion occurs for methyl isobutylketone and there is a reasonable conversion for cyclohexanone (Table 4).

Table 4

The mechanism of the catalyzed reaction, in which the silanol groups and the different amine groups of the catalyst work cooperatively, can be visualized in Fig. 3 [71, 84-86].

Fig. 3

At the catalyst surface the aldehyde group is activated by silanol groups favoring the NH_2 group attack forming the corresponding imine. It is also possible that the presence of secondary amine groups in the catalyst gives the possibility of iminium ion activation. Catalyst structure with tertiary amine groups promotes the abstraction of a proton from ethyl cyanoacetate. Attack of the anion to the imine, followed by proton elimination, originates the product and regenerates the catalyst. Besides stereochemical reasons, ketones which do not form the imine do not suffer this kind of activation, also contributing to a much slower reaction.

4. Conclusion

In nitroaldol condensations the catalytic activity of primary amine groups grafted onto silica surfaces by carbon chain spacers is dependent on the length of the chain. The catalyst with amine groups near the silica surface is more efficient than catalysts with amine groups far-off.

Grafting a polyethylenimine polymer onto the silica structure by 3-(glycidyloxypropyl)-trimethoxysilane activation originates an active catalyst showing great efficiency in the Knoevenagel condensation, originating α -cyanocinnamates in good yields under mild reaction conditions. Reutilization of this catalyst showed no loss of activity. The increased activity of this catalyst can be related to the presence, on the polymer structure, of primary amine and other amine groups that can work in cooperation.

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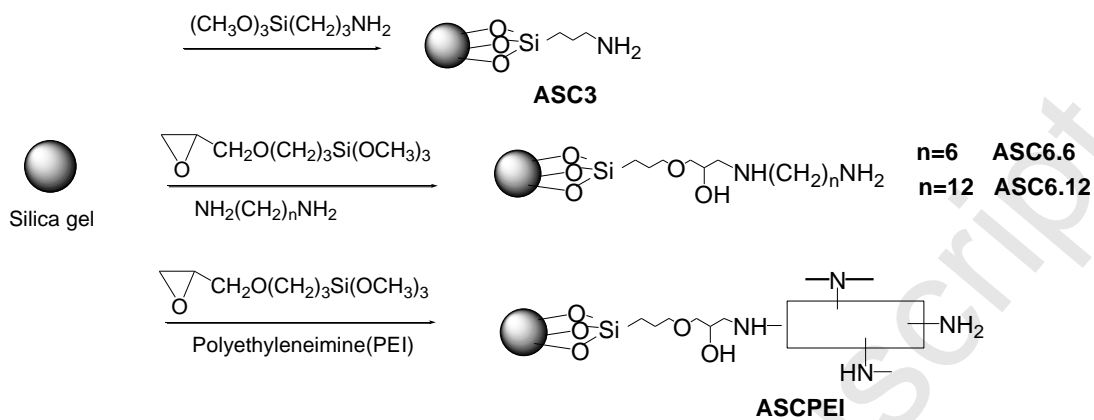
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Scheme 1. Strategies for grafting aminoderivatives into silica structures

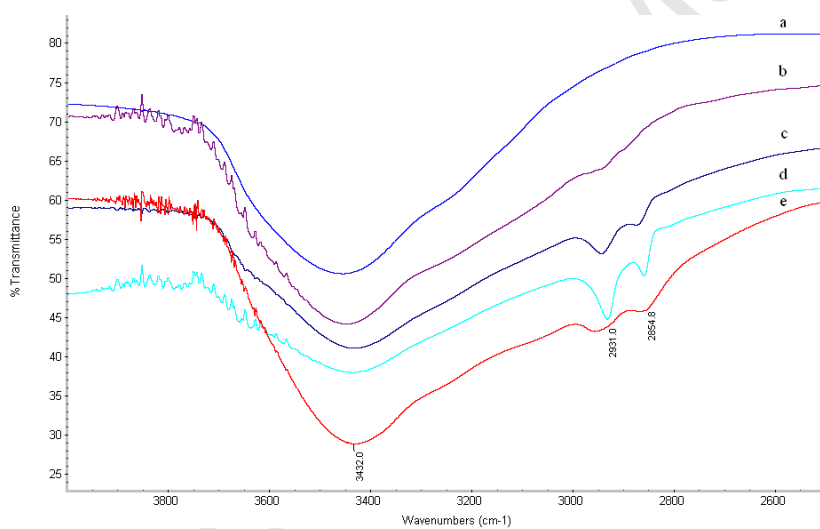
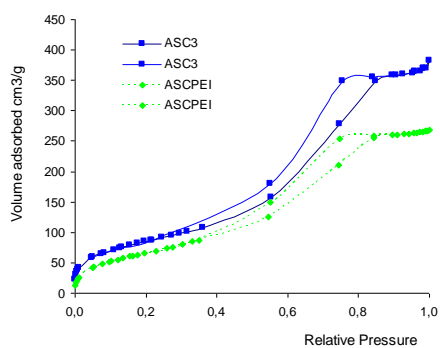


Fig. 1. IR region corresponding to C-H stretching vibrations. a) silica; b) **ASC3**; c) **ASC6.6**; d) **ASC6.12** and e) **ASCPEI**



Catalyst	Surface area BET(m ² /g)	Average pore diameter (nm)	Mesopore volume ^a (cm ³ /g)
ASC3	312	3.9	0.599
ASCPEI	256	3.9	0.420

^a From BJH adsorption

Fig. 2. Nitrogen adsorption/desorption isotherms and surface characteristics for **ASC3** and **ASCPEI** catalysts.

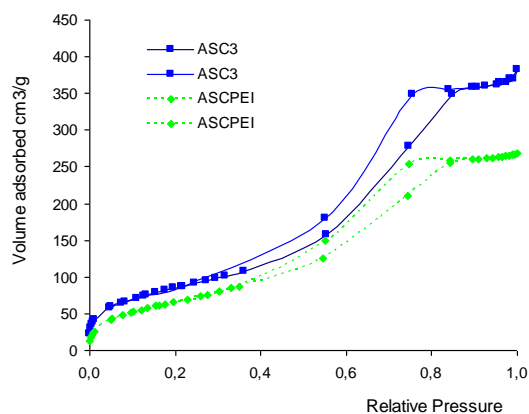


Table 1. Total nitrogen and active amine groups (by ninhydrin test) of the catalysts

Catalysts	% N by elemental analysis	% N by ninhydrin test
ASC3	1.29	0.540
ASC6.6	1.07	0.068
ASC6.12	0.880	0.048
ASCPEI	4.80	0.702
SiIPEI	3.45	1.36

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Table 2. Results for the catalytic activity of amine silica catalysts in nitroaldol condensation^a

$$\text{X-C}_6\text{H}_4\text{-CHO} \xrightarrow[\text{CH}_3\text{NO}_2]{\text{Catalyst}} \text{X-C}_6\text{H}_4\text{-CH=CH-NO}_2 + \text{X-C}_6\text{H}_4\text{-CH(OH)-CH}_2\text{-NO}_2 + \text{X-C}_6\text{H}_4\text{-CH}_2\text{-CH}_2\text{-NO}_2$$

(1) (2) (3) (4) (5)

X=OCH₃ (**1a**) X=CH₃ (**1d**)
 X=Cl (**1b**) X=OH (**1e**)
 X=H (**1c**)

Entry	Aldehyde	Catalyst	Time (h)	Conversion (%)	Relative yield of Products (%) ^b		
					3	4	5
1	1a	-----	24	0	-	-	-
2	1a	ASC3	8	97	99	1	-
3	1b	ASC3	7	98	98	1	1
4	1c	ASC3	7	99	98	1	1
5	1d	ASC3	7	99	95	4	1
6	1a	ASC6.6	24	16	98	1	1
7	1b	ASC6.6	24	69	87	3	10
8	1a	ASC6.12	24	12	99	-	1
9	1b	ASC6.12	24	59	75	7	18
10	1a	ASCPEI	4	95	85	12	3
11	1b	ASCPEI	6	95	87	7	6
12	1c	ASCPEI	3	99	86	11	3
13	1d	ASCPEI	5	95	84	11	5
14	1e	ASCPEI	4	93	81	16	3

^a Reaction conditions: **1a** to **1e** (5 mmol), **2** (2 ml), catalyst (50mg), 95°C.

^b Determined by ¹H NMR spectroscopy, based on **1**.

Table 3. Results for the catalytic activity of ASCPEI catalyst in Knoevenagel condensation of aldehydes^a.

Reaction scheme: Aldehyde (1) + NC-CH₂-CO₂Et (7) $\xrightarrow[\text{Ethanol}]{\text{ASCPEI}}$ Knoevenagel adduct (8)

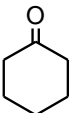
Entry	Aldehyde	Time (h)	Yield (%) ^b	m.p. (lit.)
1	1c	1,5	97	46-47°C (49-50°C) ^c
2 ^d	1c	5	96	45-47 °C
3 ^e	1c	4	96	46-48 °C
4 ^f	1c	2	98	45-48 °C
5 ^g	1c	2	98	45-48 °C
6	1a	1,5	95	79-80°C (79-81°C) ^c
7	1b	2,5	96	87-88°C (89-90 °C) ^c
8	1d	3	99	89-91 °C (90-92 °C) ^c
9	1f	1	99	166-167°C (170-171 °C) ^c
10	1g	3	98	73-76 °C (73-74 °C) ^c
11	1h	2	98	152-153°C (155-157 °C) ^h
12	1i	1	97	91°C (89-91°C) ^c
13	1j	3	98	138-138°C(135-137°C) ^c
14	1k	4	84	-----

^a Reaction conditions: Aldehyde (5,2 mmol), ethyl cyanoacetate (5,2 mmol), ethanol (6 mL), **ASCPEI** (50mg), 43°C.

^b isolated yield; ^c see ref 29; ^d toluene as solvent; ^e room temperature; ^f 1st reutilization of the catalyst of entry 2; ^g; 2nd reutilization of the catalyst; ^h see ref. 72.

Table 4. Results for the catalytic activity of ASCPEI catalyst in Knoevenagel condensation of ketones^a.

$$\begin{array}{c} R_1 \\ \diagdown \\ C=O \\ \diagup \\ R_2 \end{array} \text{ (9)} + \text{NC-CH}_2\text{-CO}_2\text{Et (7)} \xrightarrow[\text{Ethanol}]{\text{ASCPEI}} \begin{array}{c} R_1 \quad R_2 \\ \diagdown \quad \diagup \\ C=C \\ \diagup \quad \diagdown \\ \text{NC} \quad \text{CO}_2\text{Et} \end{array} \text{ (10)}$$

Entry	Ketone (9)	Reaction Temperature (°C)	Time (h)	Conversion ^b %
1	9a R ₁ =CH ₃ R ₂ =isobutyl	43	24	17
2	9a R ₁ =CH ₃ R ₂ =isobutyl	78	24	12
3	9b R ₁ =CH ₃ R ₂ =Phenyl	43	24	0
4	9b R ₁ =CH ₃ R ₂ =Phenyl	78	24	0
5	9c 	78	24	75

^a Reaction conditions: ketone (5,2 mmol), ethyl cyanoacetate (5,2), ethanol (6mL), **ASCPEI** (50mg).^b Determined by ¹H NMR spectroscopy.

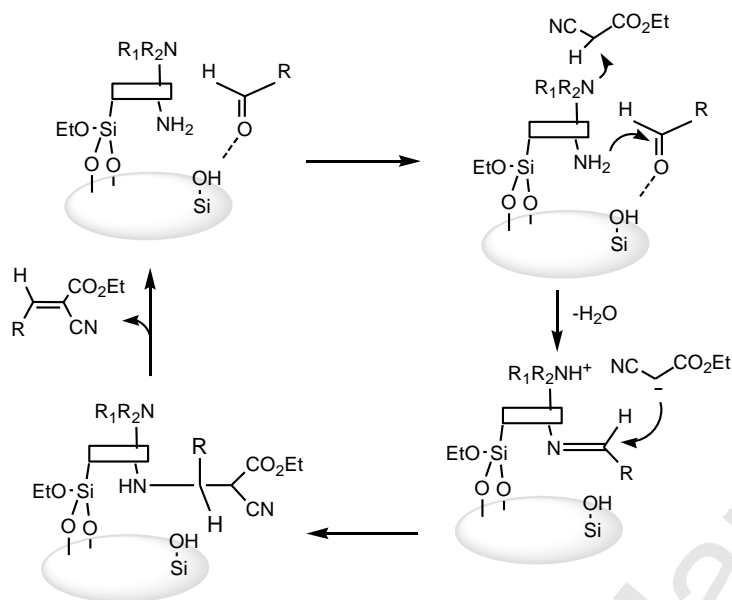


Fig. 3. Proposed reaction mechanism for the Knoevenagel condensation reaction involving the different amine groups of the ASCPEI catalyst.

Scheme 1. Strategies for grafting aminoderivatives into silica structures.

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(1) **(2)** **(3)** **(4)** **(5)**

X=OCH₃ (**1a**) X=CH₃ (**1d**)
 X=Cl (**1b**) X=OH (**1e**)
 X=H (**1c**)

Entry	Aldehyde	Catalyst	Time (h)	Conversion (%)	Relative yield of Products (%) ^b		
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1	1a	-----	24	0	-	-	-
2	1a	ASC3	8	97	99	1	-
3	1b	ASC3	7	98	98	1	1
4	1c	ASC3	7	99	98	1	1
5	1d	ASC3	7	99	95	4	1
6	1a	ASC6.6	24	16	98	1	1
7	1b	ASC6.6	24	69	87	3	10
8	1a	ASC6.12	24	12	99	-	1
9	1b	ASC6.12	24	59	75	7	18
10	1a	ASCPEI	4	95	85	12	3
11	1b	ASCPEI	6	95	87	7	6
12	1c	ASCPEI	3	99	86	11	3
13	1d	ASCPEI	5	95	84	11	5
14	1e	ASCPEI	4	93	81	16	3

^a Reaction conditions: **1a** to **1e** (5 mmol), **2** (2 ml), catalyst (50mg), 95°C.^b Determined by ¹H NMR spectroscopy, based on **1**.

Table 3. Results for the catalytic activity of ASCPEI catalyst in Knoevenagel condensation of aldehydes^a.

Reaction scheme: $\text{X-C}_6\text{H}_4\text{-CHO (1)} + \text{NC-CH}_2\text{-CO}_2\text{Et (7)} \xrightarrow[\text{Ethanol}]{\text{ASCPEI}} \text{X-C}_6\text{H}_4\text{-CH=C(NC)-CO}_2\text{Et (8)}$

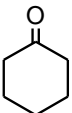
Entry	Aldehyde	Time (h)	Yield (%) ^b	m.p. (lit.)
1	1c	1,5	97	46-47°C (49-50°C) ^c
2 ^d	1c	5	96	45-47 °C
3 ^e	1c	4	96	46-48 °C
4 ^f	1c	2	98	45-48 °C
5 ^g	1c	2	98	45-48 °C
6	1a	1,5	95	79-80°C (79-81°C) ^c
7	1b	2,5	96	87-88°C (89-90 °C) ^c
8	1d	3	99	89-91 °C (90-92 °C) ^c
9	1f	1	99	166-167°C (170-171 °C) ^c
10	1g	3	98	73-76 °C (73-74 °C) ^c
11	1h	2	98	152-153°C (155-157 °C) ^h
12	1i	1	97	91°C (89-91°C) ^c
13	1j	3	98	138-138°C(135-137°C) ^c
14	1k	4	84	-----

^a Reaction conditions: Aldehyde (5,2 mmol), ethyl cyanoacetate (5,2 mmol), ethanol (6 mL), **ASCPEI** (50mg), 43°C.

^b isolated yield; ^c see ref 30; ^d toluene as solvent; ^e room temperature; ^f 1st reutilization of the catalyst of entry 2; ^g; 2nd reutilization of the catalyst; ^h see ref. 87.

Table 4. Results for the catalytic activity of **ASCPEI** catalyst in Knoevenagel condensation of ketones^a.

$$\begin{array}{c}
 R_1 \\
 \diagdown \\
 C=O \\
 \diagup \\
 R_2 \\
 \text{(9)}
 \end{array}
 + \text{NC-CH}_2\text{-CO}_2\text{Et} \text{ (7)}
 \xrightarrow[\text{Ethanol}]{\text{ASCPEI}}
 \begin{array}{c}
 R_1 \quad R_2 \\
 \diagdown \quad \diagup \\
 C=C \\
 \diagup \quad \diagdown \\
 \text{NC} \quad \text{CO}_2\text{Et} \\
 \text{(10)}
 \end{array}$$

Entry	Ketone (9)	Reaction Temperature (°C)	Time (h)	Conversion ^b %
1	9a R ₁ =CH ₃ R ₂ =isobutyl	43	24	17
2	9a R ₁ =CH ₃ R ₂ =isobutyl	78	24	12
3	9b R ₁ =CH ₃ R ₂ =Phenyl	43	24	0
4	9b R ₁ =CH ₃ R ₂ =Phenyl	78	24	0
5	9c 	78	24	75

^a Reaction conditions: ketone (5,2 mmol), ethyl cyanoacetate (5,2), ethanol (6mL), **ASCPEI** (50mg).

^b Determined by ¹H NMR spectroscopy.