Michael Additions Catalysed by N,N-dimethyl-3-aminopropyl - Derivatised Amorphous Silica and Hexagonal Mesoporous Silica (HMS)

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Abstract: Solid bases prepared by derivatisation of amorphous silica and hexagonal mesoporous silica with dimethylaminopropyl groups are good catalysts for Michael addition reactions. Of the prepared catalysts, those based on hexagonal mesoporous silica show particularly high activities. The sol-gel method used in preparing the catalysts based on hexagonal mesoporous silica enables loading to be increased to more than twice that of those based on amorphous silica which are prepared by the post-modification method.

The Michael addition is a carbon - carbon bond forming reaction important in synthetic chemistry. Typically, the reaction involves a nucleophilic addition of carbanions to α,β-unsaturated carbonyl compounds. During the course of the reaction, electronic charge migrates from the carbon in the donor molecule to a better acceptor atom, usually oxygen, in the electrophile. A base is used to form the carbanion by abstracting a proton from an activated methylene precursor. The reaction is thus base catalysed and in addition to its synthetic utility, may serve as a useful test reaction for studying the catalytic activity of solid bases.

Traditionally, the Michael reaction is catalysed by mild to moderately strong bases. Bases such as diisopropylamine, potassium *t*-butoxide[1] and tetramethylguanidine[2,3] have been used as homogeneous catalysts. However, production of significant amounts of multiple Michael adducts, other side reactions, difficult product separation and catalyst recovery, have always been problematic. These problems, plus the recent increase in the interest of developing environmentally friendly solid catalysts, has led to the development of heterogeneous catalytic systems for this reaction. Examples of such systems are those based on KF- and CsF-alumina,[4] potassium *t*-butoxide on xonotlite,[5] and Amberlyst A-27,[6] which have been used with different degrees of success. The number of genuinely useful systems however, remains low. As part of a programme aimed at developing heterogeneous base catalysts for use in reactions of synthetic value, we have prepared two catalysts by derivatising amorphous silica and hexagonal mesoporous silica (HMS) with N,N-dimethyl-3-aminopropyl groups. The catalysts were evaluated in the Michael additions of nitroalkanes and α,β-unsaturated carbonyl compounds.

The first catalyst (N,N-dimethyl-3-aminopropyl-silica) **1**, was prepared according to a known post-modification method[7] using N,N-dimethyl-3-aminopropyltrimethoxysilane (Fluorochem, Derbys, 95%) and silica gel (Kieselgel 100, Merck). Titration with dil. HCl showed a loading of about 0.85 mmol g^{-1}. Increasing the amount of N,N-dimethyl-3-aminopropylsilane did not increase the loading of the catalyst beyond 1 mmol g^{-1}, suggesting that this is the maximum loading with this type of preparation method. Thermogravimetric analysis revealed the material to be thermally stable and it does not lose the organic functions until temperatures above 350 ^{o}C. Surface area and pore size distribution were determined by N_2 physisorption. The material has a specific surface area of 245 m^2 g^{-1} and a broad pore size distribution centred at 10 nm which was essentially the same as for the parent silica. The Diffuse Reflectance FTIR (DRIFT) spectrum of **1** displayed the expected peaks at 2960 cm^{-1} ($C\text{-}H_{st.}$), 2760 cm^{-1} [$\text{-}N\text{-}(CH_3)_{st.}$] and 1480 cm^{-1} ($C\text{-}H_{def.}$). A value of 0.74 for the surface $\mathbf{E}_N^T$ (Dimroth's parameter measured using Reichardt's dye) has also been measured indicative of reduced polarity compared to underivatised silica (0.967).[8]

Two novel catalysts based on HMS and N,N-dimethyl-3-aminopropylsilane were prepared using a templated sol-gel method[9,10] by varying the ratios of the amine to the silane. Catalysts **2** and **3**, with tetraethoxysilane : N,N-dimethyl-3-aminopropylsilane ratios of 9:1 and 4:1, respectively, were obtained. The products were characterised by thermogravimetric analysis and showed good thermal stability. Both materials lose the organic groups between 400 ^{o}C and 650 ^{o}C. N_2 physisorption and acid titration analyses gave surface areas of 925 m^2 g^{-1} and 370 m^2 g^{-1} and loadings of 1.2 mmol g^{-1} and 2.2 mol g^{-1} for catalyst **2** and **3**, respectively. The pore diameter of **2** was 5.6 nm with some larger pores of > 10 nm also being evident which are possibly due to interparticle voids. **3** was predominantly amorphous (pore diameter > 10 nm) with a small amount of templated structure with a pore diameter of 4 nm. Diffuse Reflectance FTIR (DRIFT) gave peaks at 2960 cm^{-1} ($C\text{-}H_{st.}$), 2890 cm^{-1} [$\text{-}N\text{-}(CH_3)_{st.}$], and 1480 cm^{-1} ($C\text{-}H_{def.}$). The surface $\mathbf{E}_N^T$ values were 0.75 and 0.68 for material **2** and **3**, respectively.

All three materials were evaluated as catalysts in the reactions of nitroalkanes with α,β-unsaturated carbonyl compounds.[10] The results are given in Table 1.

Generally, the catalysts based on hexagonal mesoporous silica show higher activities than those prepared from amorphous silica, rates being about 3 times faster on comparing catalysts with similar loadings (Fig. 1).

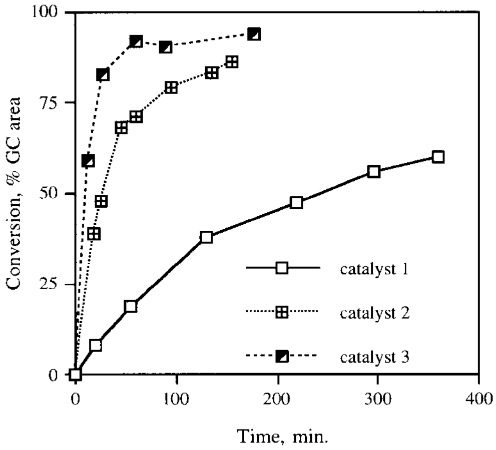
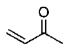
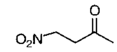
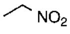
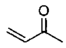
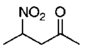
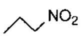
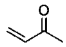
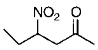
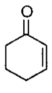
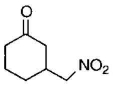
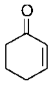
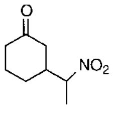
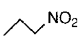
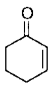
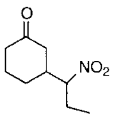


Fig. 1. The rate curves for the reaction between but-3-en-2-one and nitroethane using catalysts **1**, **2** and **3**

The HMS based catalysts do, however, have much higher surface areas although when the amine loading was increased from 1.2 to about 2.2 mmol g^{-1} on the HMS, the rate increased correspondingly despite the fact that the surface area is much reduced and the catalyst structure is essentially amorphous. The polarities of catalysts **1** and **2** as measured

Table 1. Michael reactions catalysed by solid bases

Entry	Michael donor	Michael acceptor	Product	Catalyst	Yield[a] (%)	Time (h)
1	$MeNO_2$			**1**	58(53)[b]	7
2				**2**	70	3
3				**3**	80	4
4				**1**	72[c]	7.5
5				**2**	92 (89)	2
6				**3**	94	1.2
7				**1**	76[c]	6.5
8				**2**	90	2
9				**3**	95 (93)	1.5
10	$MeNO_2$			**1**	58[d]	13
11				**2**	62	6
12				**3**	90 (86)	4
13				**1**	65[c]	5
14				**2**	72	4.5
15				**3**	88 (87)	1.5
16				**1**	82[e]	8
17				**2**	86 (83)	5
18				**3**	93	2.5

[a] Yield of products quoted as % GC area (isolated yields in brackets) characterised by ^1H NMR, GC-MS and IR. [b]The ^1H NMR spectra of these compounds are identical to those reported in ref. 6. [c]The ^1H NMR spectrum of this compound is identical to that reported in ref. 11. [d]The ^1H NMR spectrum of this compound is identical to that reported in ref. 12. [e]We were unable to locate this compound in the literature. Analytical data is given elsewhere.[13]

by their surface E_N^T values are similar and higher than that of catalyst **3**. All three catalysts show high reaction selectivities especially in the reactions between nitroalkanes and but-3-en-2-one. In the reaction between 2-cyclohexen-1-one and the nitroalkanes, nitroethane and nitropropane, two diastereoisomers were obtained as products in a 1:1 ratio in both cases. In neither reactions, however, were any Knoevenagel type products observed.

No leaching of the catalysts was observed in the reaction mixtures, and the reactions did not proceed when they were interrupted before their completion by removing the catalyst. This observation has also been noted in Knoevenagel reactions catalysed by aminopropyl-silica catalyst.[7a] The reuse of the catalysts after decantation of the supernatant and recharging with fresh substrate mixtures has been studied. The two groups of catalysts, *i.e.*, those based on amorphous silica and those based on HMS, showed different results. Catalysts **2** and **3** continued to catalyse the reactions close to completion, though after progressively longer times. Effective reuse of the catalysts for up to 3 and 5 times, for catalyst **2** and **3**, respectively, was possible. Catalyst **1**, on the other hand, showed an induction period of about 3 h on reuse before any product was observed. The rate started to pick up when additional but-3-en-2-one was introduced. High yields were obtained even on the second or third re-use of the catalyst but again only if additional but-3-ene-2-one was introduced. Our catalysts show good activity and stability in relatively small amounts, and outperform other known catalysts such as Amberlyst A-27[14] which is used in relatively large amounts, requires longer reaction periods and suffers from limited thermal stability. Basic alumina has also been used for such reactions,[15] but again is required in large amounts to ensure good rates. KF-Alumina, a very active catalyst in these reactions[4] suffers from lack of reproducibility, and is therefore unreliable.

Our results show that solid bases derived from chemically modified mesoporous silicas are effective catalysts for Michael reactions. The HMS-based materials are especially active. There is no simple correlation between activities and any of the material properties of surface area, surface polarities or loading.

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7. a) Macquarrie, D. J.; Clark, J. H.; Lambert, A.; Mdoe, J. E. G. and Priest, A. *React. Funct. Polym.* **1997**, *35*, 153.
   b) Haginaka, J.; Yasuda, N.; Wakai,. J.; Matsunaga, H.; Yasuda, Y. and Kimura, Y. *Anal. Chem.* **1989**, *61*, 2445.
8. Tavener, S. J.; Clark, J. H.; Gray, G. W.; Heath, P. A. and Macquarrie, D. J. *Chem. Commun.* **1997**, 1147.
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10. *Typical procedure for catalyst preparation*: In a typical preparation of catalyst **2**; 18.75 g of tetraethoxysilane and 2.08 g N,N-dimethyl-3-aminopropyltrimethoxysilane were added simultaneously over a few seconds to a stirred mixture of n-dodecylamine (5.09 g) in ethanol (52 g) and distilled water (53 g) at room temperature. The reaction was allowed to continue for 18 h. The resulting white solid was filtered and washed with ethanol (50 cm^3). The powder was then refluxed in 3 x 100 cm^3 ethanol to remove the template, drying initially at room temperature overnight, then at 110 °C.
    Typical procedure for the Michael reaction: To a 100 ml two-necked round-bottomed flask was added 0.5 g catalyst **2**, 25 ml nitroethane, 20 mmol of but-3-en-2-one and 0.3 ml n-dodecane (GC internal standard). The reaction mixture was stirred, refluxed and monitored continuously by GC. When no significant increase in product was observed, the reaction was stopped and the reaction mixture filtered and evaporated at reduced pressure to give the crude product. The crude product was purified by chromatography over silica gel with ethyl acetate/n-hexane (1:4) as eluent giving 2.58 g (89%) of pure product. ^1H NMR ($CDCl_3$): δ 1.6 (d, 3H), 2.2 (s, 3H superimposed on m, 2H), 2.6 (t, 2H), and 4.7 (m, 1H). GC-MS: *m/z* (%) 146 ($M^{+\cdot}$, 4), 115(8), 99(100), 83(5), 76(3), 55(12). IR: 1730 (υ_{CO}), 1560 cm^{-1} (υNO_2).
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13. The analytical data for **3-(1-nitropropyl)cyclohexanone**: ^1H NMR ($CDCl_3$) δ 1.1 (t, 3H), 1.25 - 2.6 (m, 11H), 4.5 (m 1H). ^{13}C NMR ($CDCl_3$) δ 208.6 ($\underline{C}O$), 94.1 ($\underline{C}HNO_2$), 43.6, 43.2, 41.2,

40.7, 27.4, 27.3, 24.2, 23.9, 10.1 ($-CH_2\underline{C}H_3$). IR: 1730 (υ_{CO}), 1560 cm-1 (υNO_2); and GC-MS: m/z (%) 186 ($M^{+\cdot}$, 28), 168(5), 155(10), 139(80), 121(65), 109(10), 97(90), 81(25), 69(55), 55(100).

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