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Full Paper

Co-Polymeric Nanosponges from Cellulose Biomass as Heterogeneous Catalysts for amine-catalyzed Organic Reactions

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Heterogeneous catalysts prepared from biomass waste sources are attracting increasing interest. The reasons rely on the possibility of combining the virtuous approach of circular economy with the consolidated advantages of heterogeneous catalysis, namely the recycling of the system and the possibility to drive selectivity towards desired products. Herein we report a highly porous cellulose-based nanosponge (CNS) and its use as a recoverable catalyst for Henry and Knoevenagel reactions, two classical amino-catalyzed transformations. The material is obtained

by cross-linking between TEMPO-oxidized cellulose nanofibers (TOCNF) and branched polyethyleneimine 25 kDa (bPEI) in the presence of citric acid. CNS have been developed as sorbent materials for water remediation but their use as heterogeneous catalysts was never investigated. The fully characterized micro- and nano-porous system guarantees a complete penetration of CNS, allowing reagents to diffuse within. Indeed, by modulating reaction conditions (catalyst loading, temperature, solvent, microwave *versus* conventional heating, relative ratio of reagents) it was possible to drive selectivity towards the desired products, while maintaining high efficiency in terms of conversion. The catalyst could be re-used several times without losing in catalytic efficiency. In most cases the products' distribution is quite different from homogeneous conditions, this much more emphasizing the importance of this heterogeneous solution.

Introduction

The advantages of heterogeneous catalysis over homogeneous one are numerous. Among the most evident are certainly the possibility of easily recovering and reusing the catalyst from the reaction medium, and consequently isolating the final products in a simpler way. Other advantages are the duration of the catalyst and a considerable reduction in costs.

Microporous nanomaterials have been widely proposed as heterogeneous catalysts,^[1] due to the remarkable catalytic efficiency of these solutions, often designed to drive selectivity towards desired products. However, in most cases the high energy demand for their synthesis and the end-of-life disposal of these systems, with consequent production of waste, negatively impact on the environment.

Given the raising trend towards the discovery of alternative materials that may be less impacting, greener, more sustainable and renewable, the widespread use of materials derived from natural biomass is increasing also in the field of catalysis. In particular, in the recent literature, biopolymers such as wool,^[2] chitosan,^[3] and lignin^[4] are increasingly taking root as ideal building blocks for the design of heterogeneous catalysts. Despite the improvements in the field of biopolymer-based catalysis, the development of catalytic systems bearing several active sites and capable to drive the selectivity of the processes remain rather rare.

Cellulose represents a source of major interest among those derived from biomass (Figure 1). It is the most ubiquitous structural amphiphilic renewable polymer resource in the biosphere,^[5] with an estimated annual production of 7.5×10^{10} tons. This nearly unlimited supply of sustainable polysaccharide possesses remarkable physical and chemical properties, suggesting its use in a wide range of materials and products.^[6] In recent years, heterogeneous cellulose-based catalytic systems have been developed for promoting different chemical reactions,^[7,8] obtaining excellent yields and very short reaction times. These systems are often reusable, and this fact represents a key point from an industrial application point of view.^[9]

Recently our research group has developed a new class of cellulose-based nanostructured aerogels, obtained by valorizing different biomass waste sources of cellulose, such as beached *Posidonia Oceanica* and recycled paper pulp. These cellulose nanosponges (CNS) are produced by following a two-step protocol. First, cellulose fibers are chemically treated through a well-consolidated TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl radical)-mediated NaClO/NaBr regioselective oxidation.^[10] After ultra-sonication in an alkaline medium, we obtain TEMPO-oxidized cellulose nanofibers (TOCNF), characterized by micrometric length and nanometric diameter, and provided with a high content of carboxylic groups.

In the second step TOCNFs are thermally cross-linked with 25 kDa branched polyethyleneimine (bPEI), promoting the formation of amidic bonds and providing micro- and nano-porous aerogels. These systems were first proposed as efficient sorbent materials for water decontamination from heavy metal ions and organic contaminants.^[11,12,13] In this context, they have also been made eco-safe through an in-depth eco-design study, consisting in a life cycle analysis (LCA)^[14] and in an ecotoxicological evaluation,^[15,16] obtaining an optimized synthetic strategy of the material, which saw the introduction of citric acid as a third component, and ensuring the absence of risks for aquatic biota.

Moreover, their high versatile properties and the possibility to easily functionalize both the polymeric components suggested an extension of their potential application, so that they resulted to be successful drug-delivery systems,^[17] useful templates for organic^[18] and inorganic coatings,^[19] and suitable heterogeneous sensors for specific anions, when functionalized with adequate fluorophores.^[20,21]

By continuing our investigation to completely exploit the potentialities of this material, we envisioned that the combination of the chemical composition and the specific morphology, made of micro and nano-porosity, could make CNS ideal candidates as sustainable heterogeneous solid catalysts. In particular, the presence of bPEI as a structural component makes them suitable for the promotion of amine-catalyzed reactions. Indeed, this polyamine has many primary, secondary, and tertiary amino groups that can act as catalytic sites in reactions usually promoted by conventional bases such as triethylamine or pyridine. Herein we report the role of CNS in promoting two different organic transformations, Henry and Knoevenagel^[22--24] reactions, which were chosen as models of study to understand the efficiency and the behavior of our eco-compatible catalyst. We focused on these aldolic condensations also because they both represent key transformations for the synthesis of bioactive molecules in the pharmaceutical and fragrance industries, where the use of heterogeneous catalysts for base-catalyzed reactions has allowed to overcome some problems related to homogeneous catalysis, first of all the poor recovery of the organo-catalyst from the reaction medium.^[25--27]

Results and Discussion

Synthesis and Characterization of Heterogeneous catalyst

TOCNF were obtained from virgin and renewable sources, including recycled paper pulp and beached *Posidonia Oceanica*, by selective oxidation of the primary alcoholic moieties in C6 position of the glucopyranose units to the corresponding carboxylic acids. At basic pH and under ultrasonication, the electrostatic repulsion between the negatively charged cellulosic chains, due to deprotonation of carboxylic groups, promotes the formation of nanofibers by defibrillation. The sponge-like catalytic material described in this work has been synthesized starting from TOCNF and bPEI 25 kDa. These two building-blocks underwent cross-linking through a thermal process at about 100 °C, *via* formation of amidic bonds between the carboxylic moieties on the cellulosic nanofiber backbone and the primary amines of bPEI polymer. The optimized formulation herein investigated includes the use of citric acid (CA) as co-reticulant. The addition of CA guarantees a higher crosslinking between the two polymers by increasing the overall content of carboxylic units. The same result cannot be obtained by pushing the conversion during oxidative process, as further oxidation leads to the

depolymerization of TOCNF.^[28] This formulation provides CNS with excellent mechanical properties.^[17] Scheme 1 summarizes the synthetic procedure. Each step is essential to attribute specific properties to the material. The addition of polyethyleneimine (which has an estimated amount of primary amines of 7.43 mmol/g)^[21] is of fundamental importance to ensure the presence of a high number of primary, secondary and tertiary amines on the surface of the final material, traceable through elemental analysis^[17] and through titration (see paragraph Experimental Section). With this latter we were able to determine the presence of about 4.5 mmol of amines per gram of nanosponge. The freeze-drying process is crucial for determining the morphology and the porosity of the nanosponge. The final CNS exhibits a classical 2D sheet-like structure, with a porosity close to 70 % of bulk material, as determined by microcomputed tomography,^[14] and which includes both micro-porosity, evidenced by scanning electron microscopy (SEM) technique (Scheme 1), and nano-porosity, previously determined through a detailed small angle neutron scattering (SANS) analysis, which afforded a short-range correlation length in a range between 25 and 35 Å,^[29] and more recently by a combined investigation of the FTIR-ATR spectra of CNS hydrated with H₂O and D₂O.^[30]

The material was grinded in a mortar before use to guarantee a higher contact surface area. Particle sizes resulted to be in a range between 50 and 400 μm, with a maximum distribution at 130 μm.

CNS as catalysts for Henry reaction

The Henry reaction,^[31] is a very versatile C-C bond formation reaction leading to nitro-derivatives, resulting from the coupling of a nucleophilic nitroalkane with an electrophilic aldehyde or ketone. The main product is a β-nitro alcohol (Scheme 2), which can be further transformed into amino-alcohols, useful for the synthesis of many drugs and natural products. The reaction occurs under basic conditions in the presence of bases, such as carbonates, alkali metal hydroxides, alkoxides, or organic nitrogen bases. In the view of a more sustainable approach, environmentally friendly processes using heterogeneous catalysis,^[32] green and non-toxic solvents,^[33] microwave irradiation^[34] have been proposed.

To investigate the catalytic activity of the CNS system for Henry transformation, the reaction of nitromethane with *p*-fluorobenzaldehyde was selected as the model. Methanol was

chosen as a typical solvent for this reaction. Several different parameters as temperature, reaction time, nitromethane equivalents, and catalyst loading were considered. In all the reactions, the products were easily recovered in quantitative amounts by filtering the nanosponge powder and washing with methanol. The crude residue was then submitted to analysis by NMR spectroscopy.

The outcome of the reaction was evaluated in terms of percentage of conversion of the starting aldehyde and in selectivity toward the final product. It is known that three possible products can form in this reaction, namely the expected nitroaldol **1**, the elimination product β -nitrostyrene **2** and the bis-adduct **3** (Scheme 1). Under standard conditions, **1** is the main product but in some cases **2** or **3** can also be obtained.

In a first study, the catalyst loading was fixed to a 20 % molar ratio referred to the free amino groups present on the catalyst, which were determined to be 4,5 mmol/g (see experimental for details). Results are reported in Table 1. At room temperature, after 48 h the main product resulted to be the β -nitrostyrene **2** but with a poor 8 % conversion (*entry 1*). An increase of the temperature from rt to 40 °C allowed to obtain complete selectivity toward **2** after 24 h in 37 % conversion (*entry 2*). By heating the reaction mixture at reflux for 24 h, the conversion increased to a good 98 % (*entry 3*), but the selectivity was decreased. The amount of 1,4 adducts **3** increased and notably, the main product of the reaction was found to be the derivative **4** (Scheme 3) which was obtained in 54 % selectivity.

This product can be explained as the result of a Michael addition of methanol on β -nitrostyrene **2**; similarly, the formation of **3** is the result of reaction between **2** and nitromethane (*vide infra*). In order to optimize these results, we performed the reaction by operating under microwave irradiation instead of conventional heating. We could obtain a complete selectivity toward the formation of **2** with a 97 % conversion after 2 h at 40 °C (*entry 4*). Finally, a further increase of the temperature up to 80 °C produced a good conversion (93 %) but a lower selectivity (*entry 5*).

We then investigated the effect of catalyst loading. Different m/m percentages of catalysts were employed. Results are reported in Table 2. The mol % of catalyst calculated on the amount of *p*-fluorobenzaldehyde is also showed.

Different experiments were run at different times to find out the best balance between yield, selectivity, reaction time and amount of catalyst. The first acceptable 73 % yield was achieved with 5 % m/m of catalyst (2.8 mol%) after 4 h, with a complete selectivity toward **2** (*entry 4*). After the same time and using 20 % m/m (11 mol%) of catalyst, the yield was 91 % (*entry 8*). Finally, when 35 % m/m (20 mol%) of catalyst was employed, the yield was 97 % (100 % selectivity) after only 2 h (*entry 9*). To better evaluate the effectiveness of the CNS catalyst, the two single components of the catalyst, i.e. TOCNF and PEI, were tested separately in the same conditions. With the use of TOCNF, no reaction occurred (*entry 10*). As expected, when pure PEI was used as catalyst at 20 % mol, **2** was obtained with good selectivity but in poor conversion (*entry 11*). At higher concentration of PEI (50 % mol), the conversion increased but the selectivity lowered. These experiments confirm that PEI is the active component of the catalyst, however the TOCNF not only supply the structural properties of the material but also provides the correct environment to drive the reaction toward high conversion and selectivity.

These results showed that the catalyst is very effective and good conversions can be achieved with only 2.8 % mol loading (5 % m/m in the case of *p*-fluorobenzaldehyde). Nevertheless, our main focus was to obtain the highest yield/selectivity in the mildest conditions and in the shortest time possible and this result could be reached with 20 % mol of catalyst. The catalyst herein proposed can be easily prepared in huge amounts from cheap starting materials and with little efforts. Moreover, our catalyst can be easily recovered and recycled without significative loss of activity (*vide infra*). Following these remarks, we decided to use the 20 % mol loading as the optimized condition for our further studies.

Due to the highly hydrophilic nature of the material, we then decided to investigate the effect of using water as the solvent (Table 3). By heating the reaction mixture at 40 °C (MW irradiation) for 2 hours with 2 equivalents of nitromethane, despite a lower conversion of 28 %, it was possible to push the reaction to a complete selectivity for the nitroaldol product **1** (*entry 1*). After some trials, quantitative conversion was achieved with 5 equivalents of nitromethane even if with a lower selectivity (89 % of product **1**, *entry 2*) for the presence of some amounts of product **3**. The formation of this last compound can only result from the addition of nitromethane on the β -nitrostyrene **2**, although no trace of the alkene could be

detected in the mixture. Even in this case, at higher temperatures or with longer reaction times the selectivity decreased and mixtures of products **1**, **2** and **3** were obtained (*entry 3, 4*).

Since we could observe the presence of the unanticipated bis adduct **3**, with the aim to switch the selectivity towards this product, the same reaction was performed using neat nitromethane as solvent, at 80 °C under MW irradiation (Table 4). As expected, **3** was obtained as the major product (70 %) with a good 91 % conversion yield (*entry 1*). Notably, under conventional heating, the major product resulted to be the β -nitrostyrene **b** (*entry 2*).

After these tests, we were able to define three different sets of conditions which allowed to switch the selectivity among the three expected products of the Henry reaction of nitromethane with *p*-fluorobenzaldehyde. In all cases, the amount of catalyst was 20 % mol with respect the aldehyde and the reaction mixtures were heated under microwave irradiation for 2 h at the indicated temperature. The only changes were the solvent and the amount of nitromethane used. The final set of conditions are described in Table 5. To resume, the nitroaldol product **1** can be obtained in water at 40 °C with 5 equiv. of nitromethane (Table 5, cond. **B**) whereas the β -nitrostyrene **2** is achieved in methanol at the same temperature with 5 equiv. of nitromethane (Table 5, cond. **A**). Lastly, in neat nitromethane at 80 °C the 1,3-dinitropropane derivative **3** is the main product (Table 5, cond. **C**).

In a last experiment, to verify the hypothesis on the formation of **4**, we performed an experiment in which the β -nitrostyrene **2** was dissolved in methanol and heated to 80 °C in the presence of 20 % mol of the catalyst. After few hours we could detect the formation of the expected product **4** in 37 % yield. Notably, in the same way, when the β -nitrostyrene **2** was treated in water as solvent at 100°, after 2 h it was converted in 54 % of the nitroaldol **1**. Finally, as expected, the treatment of **2** with neat nitromethane at 80 °C produced the bis-adduct **3** with a selectivity of 66 %. These experiments suggested that the first product of the reaction is probably always the β -nitrostyrene **2**, then a further addition to the double bond occurs from a nucleophile, i.e. the solvent, to produce the main product (Scheme 4). It is worth noting that the addition of oxygen nucleophiles to β -nitrostyrenes is not common and it is usually accomplished by the use of metal catalysis^[35] or with strong alkoxide nucleophiles.^[36]

The reaction of *p*-fluorobenzaldehyde with nitropropane was also investigated (Scheme 5). According to the optimized reaction conditions, product **5**, **6**, and **7** were obtained (Table 6).

In water the nitroaldol **5** was recovered in good yields whereas in methanol the β -nitrostyrene **6** was the main product. In neat nitropropane the principal product was again **6**, together with moderate amounts of the unprecedented bis-adduct **7** which could be isolated as a mixture of diastereoisomers (see SI).

We then explored the scope of this protocol and other aldehydes were employed (Scheme 6). Depending on the reaction conditions used, a main product was obtained, according to the results reported in Table 7.

Results from Table 7 are generally in agreement with the previous achievements. Good yields can be obtained with both electron donating (EDG) and electron withdrawing (EWG) substituents on the aromatic ring, in particular for the formation of compounds **8** and **9**. The formation of the 1,3-dinitropropane derivatives was more difficult. In particular, in the case of the strongly donating methoxy group (*entry* 7, 8), and the methyl group (*entry* 6), the double adduct **10** was obtained in 56--61 % yields, together with the olefin **9** (35 to 40 % yield). The presence of the EDG made the Michael addition to the double bond less effective. Surprisingly, when the highly reactive nitrobenzaldehyde was employed, the only product which we could obtain was the nitroaldol **8** (*entries* 1 and 2) in all the conditions tested. In particular, with methanol as the solvent, the yields were very low for the formation of a complex mixture of products. All the attempts to obtain a different selectivity on these substrates failed.

At the end of the reactions, the catalyst was usually recovered by easy filtration and washing with organic solvent. Recyclability of solid heterogeneous catalysts is of great interest for practical applications. We then decided to test the feasibility to recycle the catalyst. We conducted the test using once again *p*-fluorobenzaldehyde as model substrate to afford product **2**, by operating according to **B** procedure. We could observe that the catalyst could be reused up to five times in the same conditions without significant changes in both selectivity and conversions (Figure 2).

It is also important to highlight how the same results in terms of conversion and selectivity were obtained independently of the cellulosic source of choice. In fact, nanosponges produced with TOCNF derived from waste sources of cellulose (i.e. recycled paper pulp and beached *Posidonia Oceanica*) provided the same catalytic performances obtained by using cotton linters as starting biomass material. Moreover, it is worth noticing that cotton linters itself represent the discharge stock in textile industry.^[37]

CNS as catalyst for Knoevenagel reaction

As a further application, the nanosponges were also tested as basic catalyst in the Knoevenagel reaction. The product of this reaction is an olefin resulting from the condensation of an activated methylene group on a generic aromatic aldehyde, usually with the use of a secondary amine as catalyst. As the methylene component, different malonate ester were used, namely dimethyl (DMM) and diethyl (DEM) (Scheme 7).

According to the previous results, reactions were performed both in methanol and in water using *p*-fluorobenzaldehyde as the reference substrate. In both solvents, the expected condensation product **11 a,b** were obtained as a single product. Again, the use of microwaves as source of heating proved to be more beneficial with respect to classical heating. High conversions could be obtained in water by using 20 % mol of catalyst and after 4 h (see Table 8).

Following these results, the reaction was then repeated with diethylmalonate (DEM) on different aromatic aldehydes using water as solvent and heating at 100 °C under microwave irradiation for 4 h. The Knoevenagel product was obtained in all the cases with moderate to very good yields (Table 9). The product could be easily isolated without further purification after filtering of the catalyst and solvent extraction.

Conclusion

In this work, we reported the use of a nanostructured heterogeneous catalyst easy to prepare starting from waste sources containing cellulose, by combining TOCNFs and bPEI. These nanosponges (CNS) were tested in two typical amine-catalyzed reactions, the Henry nitroaldol and the Knoevenagel condensation. In the first case an unexpected but remarkable

selectivity toward different products could be observed depending on the reaction conditions. In the second case, high yields could be obtained with different substrates. In both the reactions, the use of microwave irradiation was crucial to speed up the reaction still maintaining the catalyst preserved and active for up to five cycles. Notably, this material can be obtained in high amount and short time, making it a good candidate for the scale-up of these reactions. Further investigations on this promising material will be done in order to explore the scale-up feasibility and the application to other reactions.

Experimental Section

The reagents were purchased from Sigma-Aldrich. The starting material (cotton linter) was obtained from Bartoli paper factory (Lucca, Italy). Deionized water was produced within the laboratories with a Millipore Elix® Deionizer with Progard® S2 ion exchange resins. All ¹H-NMR spectra were recorded on a 400 MHz Bruker NMR spectrometer. Microwave reactions were conducted in a Biotage® Initiator+. Other equipment used in the procedures include a Branson SFX250 Sonicator and a SP Scientific BenchTop Pro Lyophilizer. Scanning electron microscopy (SEM) was performed using a variable-pressure instrument (SEM Cambridge Stereoscan 360) at 100/120 Pa with a detector VPSE. The operating voltage was 20 kV with an electron beam current intensity of 150 pA. The focal distance was 8 mm. The specimens were used without any treatment.

Cellulose Oxidation with TEMPO/NaClO/KBr system

In a 1 L beaker, 100 g of cotton linter paper were minced with gradual addition of deionized water. Simultaneously, on a 8 L keg placed on a magnetic stirrer, 2.15 g of tetramethyl-piperidine-N-oxide (TEMPO) and 15.42 g of KBr were dissolved in 2 L of deionized water. Once the paper was homogeneously blended with water, the solution was transferred in the keg and water was added in order to obtain a total volume of 5.7 L. While keeping the solution stirred, a pH meter and two dropping funnels were installed above the keg, one of the funnels containing 437 mL of aqueous solution of NaClO and the other 250 mL of NaOH 4 M. NaClO was then slowly dripped into the solution and pH was monitored to kept it above 10.5--11 by dripping NaOH 4 M. Once consumed the NaClO, some of the residual NaOH 4 M was dripped again to maintain basic pH until stability above 10.5--11, then the solution was left stirring overnight. After 12--16 hours the oxidized cellulose was acidified with concentrated HCl for aggregation of the cellulose fibers and their easy separation from water. The

oxidized cellulose was then filtered on a Buchner funnel and washed with deionized water (2 L, 5÷6 times) until neutrality.

TEMPO-Oxidized Cellulose Nanofibers (TOCNFs) Titration

Estimation of the obtained concentration of carboxylic acids on the cellulose structure was performed with NaOH using phenolphthalein as colorimetric indicator. The change of color happens around pH 9.5, when all the carboxylate groups have gone through base hydrolysis.

NaOH Titration

NaOH solution was first titrated by means of potassium hydrogen phthalate. 218.6 mg were dissolved in water, a drop of phenolphthalein solution 10 mM in acetonitrile was added and then the NaOH solution was dripped in the beaker under continuous stirring. After neutralization of the phthalate with 11.35 mL of NaOH, the molar concentration of the solution was calculated to be 0.0943 M.

TOCNFs Titration

This solution was then used to titrate the oxidized cellulose obtained with the TEMPO/NaClO/KBr system: 616.0 mg of TOCNF were dispersed in water and sonicated to obtain a homogeneous water/cellulose solution. A drop of the same phenolphthalein solution was added and then the NaOH solution previously titrated was dripped in the beaker under continuous stirring: 9,75 mL were required to neutralize the carboxylic acids of the oxidized cellulose. The concentration of the carboxylic groups was calculated by means of the *equation 1* (see Scheme 8).

Synthesis of the Nanosponge (NS)

In a 1 L beaker, 3.5 g of oxidized cellulose were suspended in 140 mL deionized water, in order to obtain a 2.5 % w/v solution. While mixing it, granular NaOH in a stoichiometric quantity was added to the solution to obtain basic pH (evaluated with litmus paper), obtaining a slightly yellow viscous solution. The beaker was placed in an ice bath and the solution was sonicated to further promote the separation of the nanofibers, obtaining a transparent and more homogeneous solution. This latter was then acidified with concentrated HCl and filtered on a Buchner funnel under vacuum, then washed and re-suspended. This procedure was repeated with deionized water until a neutral pH was reached. Wet cellulose was removed from the filter paper and weighted; 3.5 g were assumed to correspond to the starting cellulose, while the remaining mass represented the residual water content. The remaining water necessary to obtain a 2.8-3 % w/v TOCNFs solution for the next phase was split up in three quotas, in order to re-suspend the cellulose and dissolve the cross-linking polymer (branched polyethylenimine,

bPEI 25 kDa) and the co-reticulant agent (citric acid monohydrate), in three separate batches. The amount of the co-reticulant was calculated with the *equation 2* (see Scheme 8).

Once dissolved in water, the cross-linker and the co-reticulant agents were slowly added to the cellulose solution, while continuously stirring until obtaining a white and homogeneous hydrogel, which was placed in 24-wells well-plates (about 15.6 mm diameter, half-filled with about 2 mL each) and quickly frozen at - 35 °C. After a few hours, the well-plates were moved to the freeze-dryer, which allowed water removal by sublimation, thus retaining the internal structure of the freeze hydrogels. At the end of the process, white cylindrical-shaped spongy aerogels were obtained. They were removed from the wells and placed in the laboratory oven, at the initial temperature of 55 °C. The temperature was then slowly raised up to 102 °C in 4 hours, in order to avoid sudden overheating and prevent the risk of burning the material. Above 100 °C the water formed due to the reticulation reactions between carboxylic moieties and amines (formation of amidic bonds) was quickly evaporated, favoring the formation of amidic bonds. The sponges were removed from the oven after 16 hours. Their aspect was yellow and their texture slightly soft but hardened while cooling down. If not kept in an anhydrous atmosphere, they tended to adsorb water and become softer. At the end of the process, nanosponges were washed 6 times with deionized water and the last time with ethanol to eliminate the excess of bPEI.

Nanosponge Titration

Estimation of the obtained concentration of amino groups on the surface of NS was performed with HCl and NaOH using phenolphthalein as colorimetric indicator.

NaOH Titration

NaOH solution was first titrated by means of potassium hydrogen phthalate. 179.7 mg were dissolved in water, a drop of phenolphthalein solution 10 mM in acetonitrile was added and then the NaOH solution was dripped in the beaker under continuous stirring. After neutralization of the phthalate with 7.9 mL of NaOH, the molar concentration of the solution was calculated to be 0.1114 M.

HCl Titration

To 15.0 mL of HCl solution, a drop of phenolphthalein solution 10 mM in acetonitrile was added and then the NaOH solution previously titrated was dripped in the beaker under continuous stirring. After neutralization of the phthalate with 7.9 mL of NaOH, the molar concentration of the solution was calculated to be 0.0962 M.

NS Titration

27 mg of NS were added to 10 mL HCl (0.0962 M). The mixture was shaken for 16 hours in a sealed container and then filtered to remove the solid from the solution. Immediately after filtration, to the solution was added a drop of phenolphthalein solution 10 mM in acetonitrile and then HCl was titrated with NaOH (previously titrated, 0.1114 M), using a seal of parafilm in order to avoid probable HCl evaporation and so change in acid concentration. The consumed HCl by NS was accounted to be equivalent with the amount of amine functions on their surface. Consequently, the difference between initial moles of HCl and moles of HCl consumed by NaOH titration represents the amount of amine functions on the NS. So, this amount was calculated following *equation 3* (see Scheme 8), where C_a , V_a and C_b and V_b were the concentration and volume of the initial acid as well base solution and the sample weight represents the dry weight of NS subjected to the titration.

Catalytic Activity

Henry reaction: 50 mg of the substituted aldehyde, nitromethane (2 or 5 equivalents with methanol or water as solvent), 2.5 mL of the solvent (methanol, water or nitromethane) and the desired amount of powdered nanosponge (CNS) catalyst were added in a 5 mL-microwave vial equipped with a magnetic stirrer. The reaction was heated at the desired temperature (from 40 °C to 105 °C) for the required reaction time. Alternatively, when conventional heating was used, the reaction was performed in a two-neck round-bottom flask equipped with a magnetic stirrer, oil bath, and water condenser. Similar amount of reagents, catalyst (CNS) and solvent were used. The reaction mixture was stirred at different temperature for different reaction times. After the reaction was complete, the catalyst was filtered and washed three times with 5 mL of methanol. The solvent was then removed under reduced pressure and the crude were analyzed by NMR on a Brüker NMR spectrometer, acquiring ^1H -spectra in CDCl_3 (see SI for further information). NMR analytical data for all the known compounds were in agreement with the literature.^[38] A full NMR characterization of compound **7** is reported in the SI.

Knoevenagel reaction: 50 mg of the substituted aldehyde, 1.2 equivalent of diethylmalonate (DEM), 2.5 mL of the solvent (water) and 0.2 molar equivalents of the powdered nanosponge (CNS) catalyst were added in a 5 mL-microwave vial equipped with a magnetic stirrer. The reaction was heated at 100 °C for 4 h. After the reaction was complete, the catalyst was filtered and washed three times with 5 mL of methanol. The solvent was then removed under reduced pressure and the crude were analyzed by NMR on a Brüker NMR spectrometer, acquiring ^1H -spectra in CDCl_3 . NMR analytical data for all the known compounds were in agreement with the literature.^[39]

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Conflict of Interest

The authors declare no conflict of interest.

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Table 1 Results from reaction between nitromethane and *p*-fluorobenzaldehyde in methanol as solvent.

<i>entry</i>	time [h]	T [°C]	CH ₃ NO ₂ equiv.	Conv. [%] ^[a]	4 [%] ^[b]	2 [%] ^[b]	3 [%] ^[b]
1	48	rt	2	8	12	79	10
2	24	40	2	37	0	97	3
3	24	reflux	2	98	54	21	25
4	2	40 ^[c]	2	97	1	98	1
5	2	80 ^[c]	5	93	53	29	18

Reaction conditions: methanol 2.5 mL, aldehyde 0.4 mmol, cat. 20 % mol.

[a] Conversion was measured with ¹H-NMR on the crude with respect to unreacted aldehyde,

[b] Percentage of compound in the mixture of products as obtained by ¹H-NMR on the crude,

[c] Reaction was heated under microwave (MW) irradiation.

Table 2 Results from screening of the CNS catalyst loading in the reaction between nitromethane and *p*-fluorobenzaldehyde.

<i>entry</i>	catalyst [% mol]	catalyst [% m/m]	time [h]	Conv. [%] ^[a]	selectivity [%] ^[b]
1 ^[c]	1.1	2	2	0	n.d
2 ^[c]	1.1	2	4	0	n.d
3 ^[c] ^e	2.8	5	2	32	100
4 ^[c]	2.8	5	4	73	100
5 ^[c]	5.5	10	2	54	100
6 ^[c]	5.5	10	4	74	100
7 ^[c]	11	20	2	60	100
8 ^[c]	11	20	4	91	100
9 ^[c]	20	35	2	97	100
10 ^[d]	n.d.	20	4	0	n.d.
11 ^[e]	20	n.d.	2	36	99
12 ^[e]	50	n.d.	2	56	71

Reaction conditions: methanol 2.5 mL, aldehyde 0.4 mmol, MW heating at 40 °C.

[a] Conversion was measured with ¹H-NMR on the crude with respect to unreacted aldehyde.

[b] Percentage of compound **2** in the mixture of products as obtained by ¹H-NMR on the crude, [c] CNS was used as catalyst, [d] TOCNF was used as catalyst, [e] PEI was used as catalyst.

Table 3 Results from reaction between nitromethane and *p*-fluorobenzaldehyde in water as solvent.

<i>entry</i>	T	T [°C]	CH ₃ NO ₂ equiv.	Conv. [%] ^[a]	1	2	3 [%] ^[b]
	[h]				[%]	[%] ^[b]	
1	2	40	2	28	100	0	0
2	2	40	5	99	89	0	11
3	8	80	5	99	42	0	58
4	2	105	5	65	26	29	45

Reaction conditions: water 2.5 mL, aldehyde 0.4 mmol, cat. 20 % mol, MW heating.

[a] Conversion was measured with ¹H-NMR on the crude with respect unreacted aldehyde,

[b] Percentage of compound in the mixture of products as obtained by ¹H-NMR on the crude.

Table 4 Results from reaction between nitromethane and *p*-fluorobenzaldehyde in neat nitromethane as solvent.

<i>entry</i>	T	T [°C]	Conv. [%] ^[a]	1 [%]	2 [%] ^[b]	3 [%] ^[b]
	[h]					
1	8	80	91	0	30	70
2	2	80 ^c	68	9	71	20

Reaction conditions: nitromethane 2.5 mL, aldehyde 0.4 mmol, cat. 20 % mol, MW heating

[a] Conversion was measured with ¹H-NMR on the crude with respect unreacted aldehyde, [b]

Percentage of compound in the mixture of products as obtained by ¹H-NMR on the crude, [c]

Reaction was heated with conventional heating.

Table 5 Resume of the optimized reaction conditions between nitromethane and *p*-fluorobenzaldehyde

Cond.	Solv.	T [°C]	CH ₃ NO ₂ equiv.	Selectivity	Product
A	CH ₃ OH	40	2	98 %	2
B	Water	40	5	89 %	1
C	CH ₃ NO ₂	80	-	70 %	3

Reaction conditions: solvent 2.5 mL, aldehyde 0.4 mmol, cat. 20 % mol, MW heating for 2 h.

Table 6 Results from reaction between nitropropane and *p*-fluorobenzaldehyde. Only the main product is reported.

entry	Solv.	T [°C]	yield	Product
<i>1</i>	Water	40	84 %	5
<i>2</i>	CH ₃ OH	80	84 %	6
<i>3</i> ^[a]	CH ₃ CH ₂ NO ₂	80	88 %	6

Reaction conditions: solvent 2.5 mL, nitropropane 2 mmol, aldehyde 0.4 mmol, cat. 20 % mol, MW heating for 4 h.

[a] 60 equivalents of nitropropane were used.

Table 7 Results from Henry reaction between nitromethane and different aromatic aldehydes under optimized conditions **A**, **B** and **C**, as described in Table 5<xtabr5>.

entry	Ar.	Conditions		
		A [% of 8] ^[a]	B [% of 9] ^[a]	C [% of 10] ^[a]
1	<i>p</i> -NO ₂ Ph	12 ^b	98	87 ^c
2	<i>o</i> -NO ₂ Ph	traces ^b	96	56 ^c
3	<i>p</i> -BrPh	74	76	81
4	<i>m</i> -BrPh	98	71	76
5	<i>o</i> -BrPh	81	91	86
6	<i>p</i> -MePh	60	88	61
7	<i>p</i> -MeOPh	79	92	58
8	<i>m</i> -MeOPh	84	92	56

[a] Conversion was measured with ¹H-NMR on the crude with respect unreacted aldehyde.

Percentage of compound in the mixture of products as obtained by ¹H-NMR on the crude.

[b] A complex mixture of inseparable products was obtained, [c] The main product was **9**.

Table 8 Results from Knoevenagel reaction between malonate diester and *p*-fluorobenzaldehyde.

<i>entry</i>	Product ^[a]	Yield [%] ^[b]	Yield [%] ^[c]
1	11 a	73	56
2	11 b	72	93

Reaction conditions: solvent 2.5 mL, aldehyde 0.4 mmol, malonate diester 0.48 mmol, cat. 20 % mol.

[a] Conversion was measured with ¹H-NMR on the crude with respect unreacted aldehyde.,

[b] Reaction was performed in methanol at 80 °C under microwave irradiation for 4 h, [c]

Reaction was performed in water at 100 °C under microwave irradiation for 4 h.

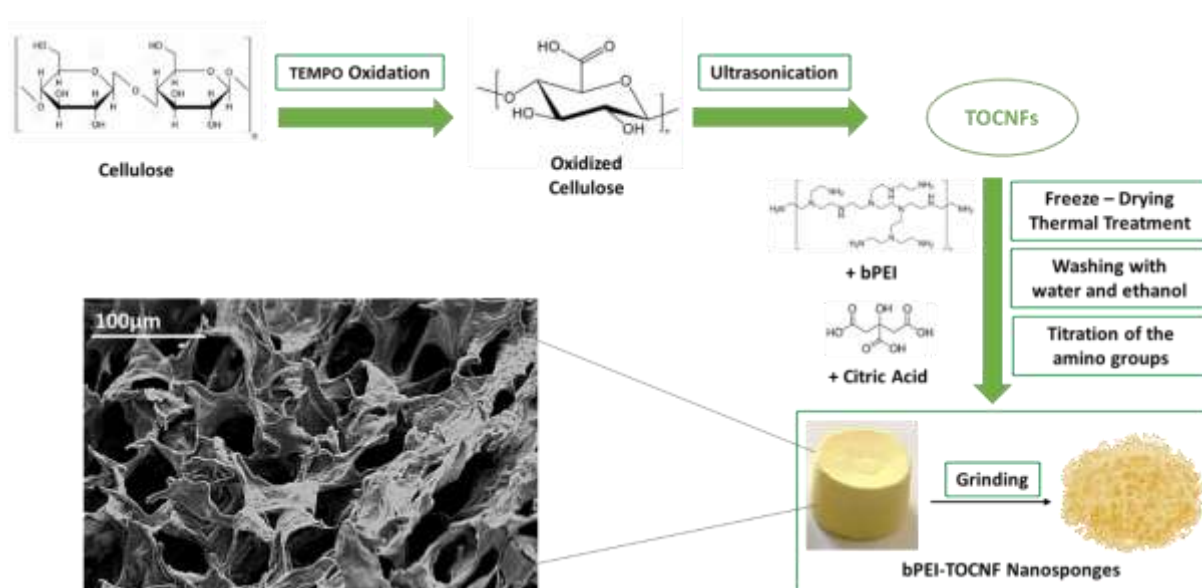
Table 9 Results from Knoevenagel reaction between diethylmalonate (DEM) and different aromatic aldehydes under optimized conditions.

<i>entry</i>	Ar	Yield [%] ^[a]
1	<i>p</i> -BrPh	96
2	<i>m</i> -BrPh	79
3	<i>o</i> -BrPh	97
4	<i>p</i> -MePh	97
5	<i>o</i> -MeOPh	77
6	<i>m</i> -MeOPh	92
7	<i>p</i> -MeOPh	89

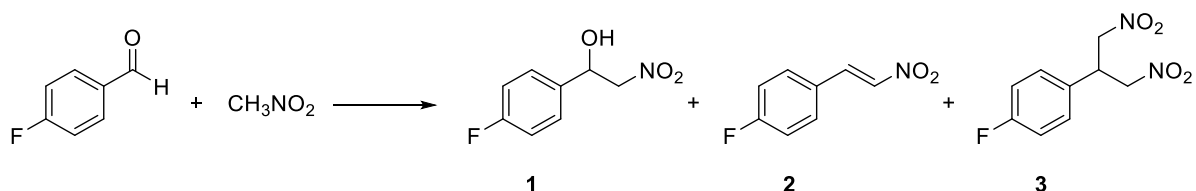
Reaction conditions: water 2.5 mL, aldehyde 0.4 mmol, malonate diester 0.48 mmol, cat. 20 % mol, MW heating (T=100 °C) for 4 h.

[a] Conversion was measured with $^1\text{H-NMR}$ on the crude with respect unreacted aldehyde.

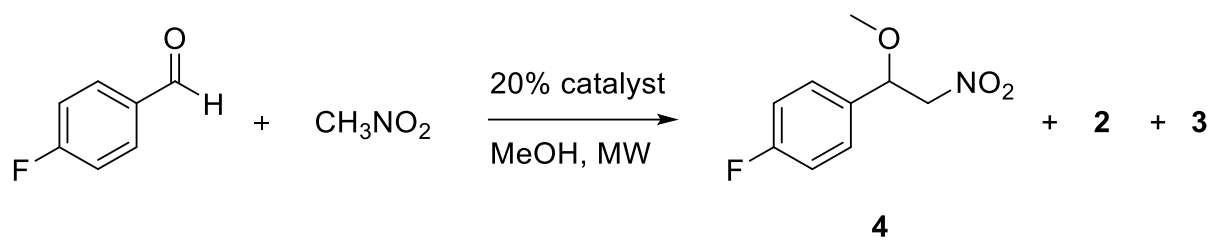
Scheme 1 Scheme of the synthesis of the nanosponge, with a SEM image at 300x magnification showing the micro-pores of the catalytic system



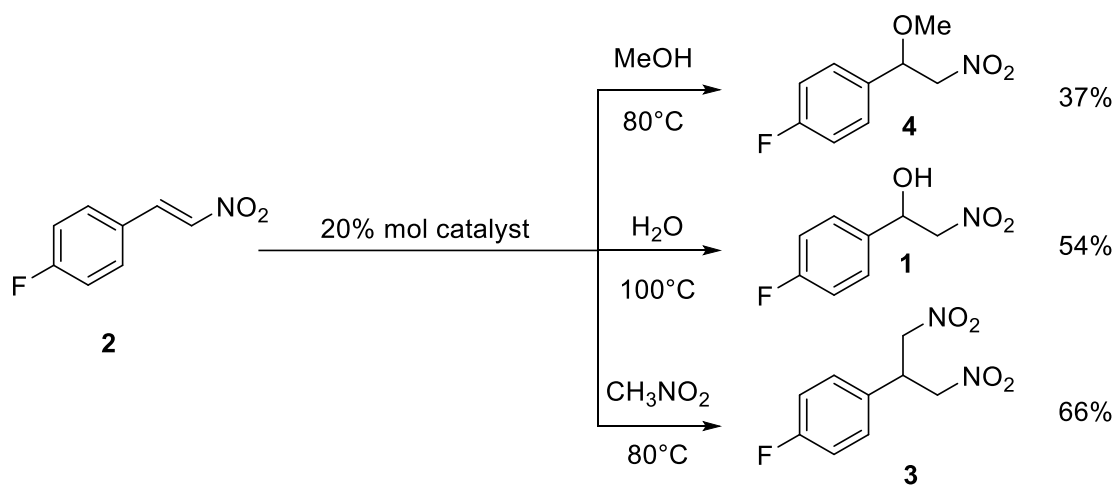
Scheme 2 Possible products resulting from the Henry reaction between nitromethane and *p*-fluorobenzaldehyde.



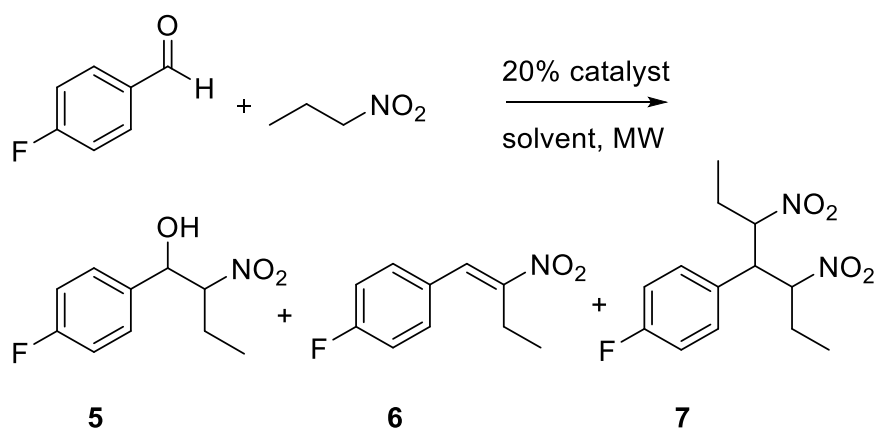
Scheme 3 Products from the Henry reaction between nitromethane and *p*-fluorobenzaldehyde in methanol as solvent.



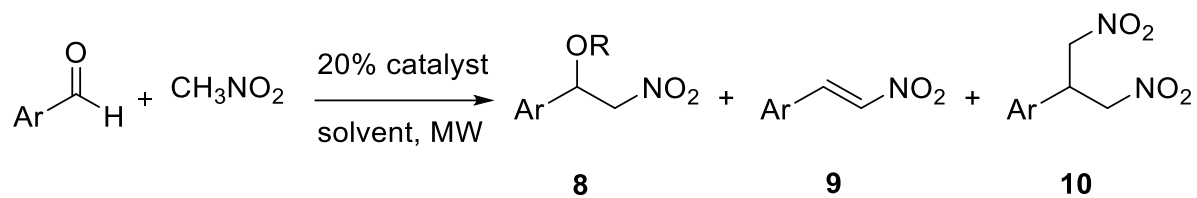
Scheme 4 Reactions of β -nitrostyrene **2** with different nucleophiles.



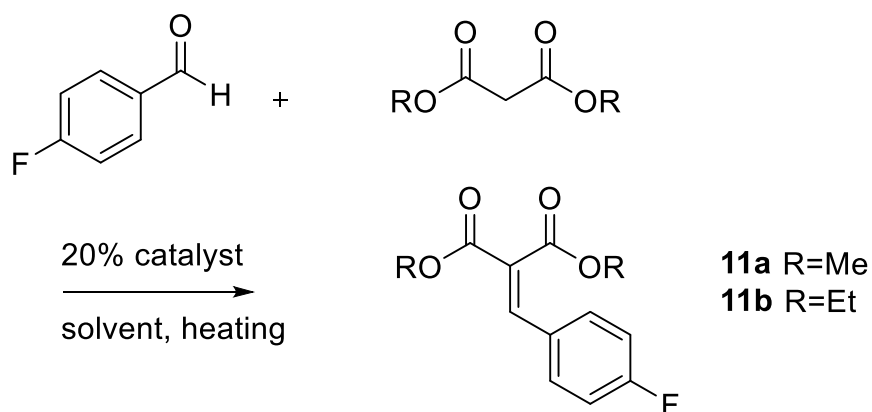
Scheme 5 Products from the Henry reaction between nitropropane and *p*-fluorobenzaldehyde.



Scheme 6 Products from the Henry reaction between nitromethane and various aldehydes.



Scheme 7 The Knoevenagel reaction between DMM and DEM and *p*-fluorobenzaldehyde.



Scheme 8 Scheme of the equations used for the titration of the NS.

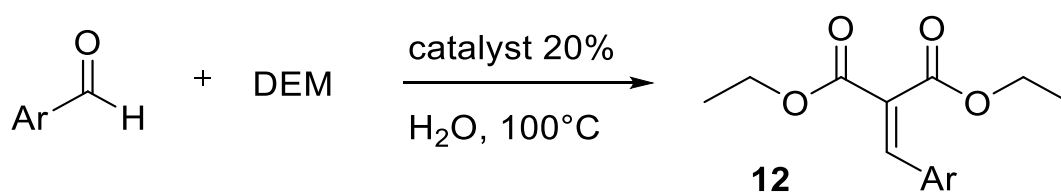


Figure 1 Various applications of nanocellulose obtained from recycled sources.



Figure 2 Results from recycle of the catalyst. Reaction conditions: methanol 2.5 mL, aldehyde 0.4 mmol, catalyst 20 % mol, MW heating at 40 °C for 2 h.

