Silica gel-immobilized 1,2-benzenedisulfonimide: a new and versatile Brønsted acid heterogeneous catalyst

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Silica gel-immobilized 1,2-benzenedisulfonimide: a new and versatile Brønsted acid heterogeneous catalyst

Margherita Barbero[a], Giuseppina Cerrato[a], Enzo Laurenti[a], Sebastiano Zanol[a] and Stefano Dughera*[a]

Abstract: a derivative of 1,2-benzenedisulfonimide, a strong and versatile Brønsted acid catalyst, has been immobilized on 3-aminopropil silica gel, by means of an amide bond, to afford a new heterogeneous catalyst. Its structure has been confirmed using IR and NMR spectroscopy. This new catalyst has been employed in five different organic reactions giving excellent results. At the end of the processes, it was recovered by easy filtration and reused without loss in its catalytic activity.

Introduction

Organocatalysis has become a highly dynamic chemical research area.[1] There are essentially four categories of organocatalysts: Lewis acids, Lewis bases, Brønsted bases and Brønsted acids. This last group, Brønsted acids, are powerful catalysts that present a range of benefits, including a lack of sensitivity to moisture and oxygen, ready availability, low cost and low toxicity.[2] This combination confers large and direct benefits over metal catalysis and does so to a great number of synthetic protocols.

A widespread tendency in catalysis is to convert a successful homogeneous organocatalyst into a heterogeneous catalytic system. This is, furthermore, becoming ever more common in sustainable and eco-compatible procedures.[3]

The reasons that make the immobilization of an organic catalyst useful include the easy procurement of the reaction products and the ready and simple recovery of the catalyst from the reaction mixture. It must be stressed that its recovery and recycling are very important in light of recent pressing requests for sustainable and eco-compatible methodologies.

Moreover, homogeneous organic catalysts are prone to decomposing and thus releasing traces of by-products into the reaction mixtures. Catalyst immobilization can resolve this problem since decomposed materials are also supported and can therefore be easily removed. Immobilization is obviously convenient if a catalyst is expensive, or has been obtained after a complex synthesis, or is employed in a relatively large amounts. Ultimately, supported organic catalysis is a multidisciplinary research field that is undergoing rapid expansion bringing together organic and materials chemists and allowing them to combine their skills and knowledge.[3]

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Our previous researches have seen 1,2-benzenedisulfonimide (**1**; Figure 1)[4] and its chiral derivatives[5] frequently used as Brønsted acid catalysts; its high acidity[4d] means that it lends itself well to the large number of homogeneous catalysis synthetic protocol that we have used it in.
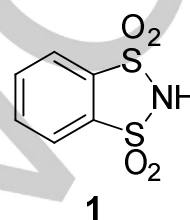

Figure 1. 1,2-Benzenedisulfonimide (**1**).

All synthetic methods generally aim to achieve mild reaction conditions, short reaction times, good selectivity and either absence or minimal formation of by-products, all of which are observed herein. Furthermore, 1,2-benzenedisulfonimide's easy and almost complete recovery from reaction mixtures, thanks to its complete solubility in water, is to be highlighted. This permits its reuse in other reactions, without the loss of catalytic activity, which brings both with economic and ecological advantages. Indeed, 1,2-benzenedisulfonimide can boast of being a non-volatile, non-corrosive, easy-to-handle, highly stable and slightly sensitive to external agents, while also having a long shelf-life. Since it has already proven itself to be an excellent catalyst under homogeneous catalysis conditions, we planned to immobilize it onto the surface of a suitable support and use it under heterogeneous catalysis conditions; the hope being that its particular stability and reactivity characteristics remain unchanged.

A number of approaches have been reported for the immobilization of organocatalysts onto a huge variety of organic and inorganic supports.[3,6] Of these approaches, the most widely used is immobilizing the catalyst via a covalent bond giving it higher stability and applicability. However, it is often necessary to modify the structure of both support and catalyst in order to create this new covalent bond. Another important and fundamental factor to be considered is the fact that the connection must be created far from the catalytic active site in order to prevent harmful interactions with the support. The choice of supports is obviously also a very important point. In fact, a good support should bear some important features including no solubility both in water and organic solvents, commercial availability and low cost, a high degree of functionalization and no involvement in the reaction.

In the light of these considerations, we decided to immobilize **1** on a functionalized silica gel. Silica gel is a clear choice as it is a mesoporous, inexpensive, commercially available and

nontoxic solid. It displays excellent chemical stability in various media and in different reaction conditions, even under acidic conditions, so it should be inert in the reactions in which the immobilized catalyst is used. Moreover, silica gel has high thermal and mechanical robustness. Its surface also presents high chemical reactivity due to the presence of silanol groups, meaning that it can be easily functionalized with organic groups.[7a,b]

Among all commercial functionalized silica gels, we chose 3-aminopropyl functionalized silica gel (**2**) as the support.[7c,d] The presence of the amino groups allows properly-functionalized **1** to be linked onto support **2** via a strong covalent bond, namely an amide bond. Physical characteristics of **2** (e.g. particle size, pore size, surface area) are known and, very importantly, the extent of labeling (1 mmol/g NH_2 loading) is also known
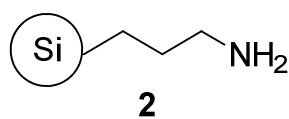

Figure 2. 3-Aminopropyl functionalized silica gel (**2**).

Results and Discussion

Synthesis of 3-(1,2-benzenedisulfonimide-4-yl)propionic acid

Firstly, a derivative of **1** bearing a carboxyl group that can react with the 3-aminopropyl group of the silica gel **2** was designed. In order to keep the sulfonimide group (responsible for the acidity) as far as possible from silica support, the carboxyl group was connected to the aromatic ring of **1** along with a branch of two carbon atoms.

The Heck reaction can be used to insert this group. This reaction takes place between an aromatic halide (or triflate) and an alkene, in a basic environment and in the presence of Pd(0) as a catalyst.[8] It was therefore necessary to synthesize a derivative of **1** (or one of its precursors) that bears a iodine (or bromine) atom on the aromatic ring. As shown in Scheme 1, according to what we have previously reported,[4e] 1,2-benzenedisulfonimide derivative **9** was obtained from the corresponding anthranilic acid **3**.[4e]

Initially, we had to carefully consider which of the various intermediates would be the most suitable for the Heck reaction. The best candidate was adduct **4** from which Heck derivative **5** was obtained in a satisfactory yield (90%). Since the double bond may be an undesired reactive site, it was thought wise to reduce it to a single bond with CuCl and $NaBH_4$.[9] The reduced adduct **6** (obtained in almost quantitative yield) was easily transformed to the corresponding sulfonyl chloride **7** (100% yield) and finally, to the desired ethyl 3-(1,2-benzenedisulfonimide-4-yl)propionate (**8**; 100 % yield).[4e] It must be stressed that the sulfonimide **8** spontaneously (due to the high acidity of sulfonimide NH) tended to hydrolyse to 3-[(1,2-

benzenedisulfonimide-4-yl)]propionic acid (**9**; 100% yield); the overall yield (from **3**) of this protocol was 75%.
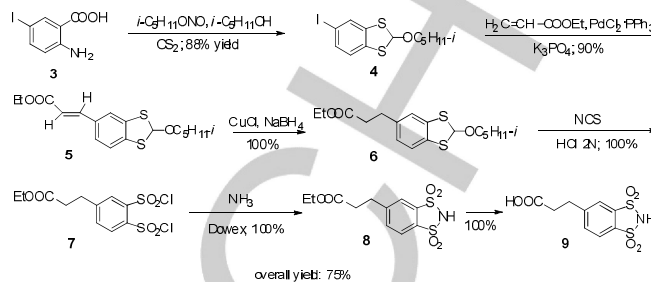
Scheme 1. Synthesis of 3-(1,2-benzenedisulfonimide-4-yl)propionic acid (**9**)

Immobilization of 3-(1,2-benzenedisulfonimide-4-yl)propionic acid (9)

With adduct **9** in hand, our next goal was to immobilize it by means of a covalent bond on the silica support. Its strength and high stability meant that the amide bond would be the best link to irreversibly anchor the imide to silica, even during the various catalytic runs. In the light of this, 3-aminopropyl functionalized silica (**2**) was reacted with **9**. The condensation reaction between the NH_2 and COOH groups was promoted by N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride (EDC; Scheme 2).
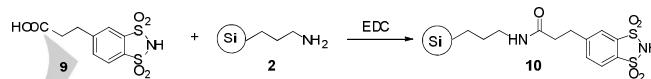
Scheme 2. Immobilization of **9** on silica gel.

The use of carbodiimides for the formation of amide bonds was introduced in 1955 by Sheetan and Hess and is currently a widespread method, both in organic synthesis and in the bioconjugation of proteins.[10a,b,c] In particular, EDC is a very useful tool in the formation of amide bonds (peptide bonds) in an aqueous medium.[10d] Moreover, its byproduct (an urea derivative) is water soluble and can be easily separated from the functionalized silica.

The obtained material was simply isolated via filtration over buchner funnel. The solid was washed firstly with dilute hydrochloric acid in order to fully restore the acid function of the sulfonimide and then with acetone in order to remove any possible organic residue. Both the initially obtained solid and the washed solid were subjected to IR analyses and their IR spectra were compared with the IR spectra of silica **2** and parent sulfonimide **9** (Figure 3).

At first sight, the residual free OH groups of silica (stretching vibration at 3730 cm^{-1}) and CH group (stretching vibration just under 3000 cm^{-1}) were clearly visible. However, it must be stressed that the described spectral zone is dominated by the stretching vibration of the OH species interacting for hydrogen

bonds and normally present at the surface of silica system. For this reason, the NH stretching vibration at about 3400 cm^{-1} is not visible. Furthermore, the overtone band of silica was clearly visible in the spectral region between 2000-1400 cm^{-1} (Figure 4). However, the most important bands, typical of secondary amides, are those located at 1640 and 1540 cm^{-1}. More precisely, the band at 1640 cm^{-1} is associated with the CO stretching vibration, while the band at 1540 cm^{-1} is associated to NH bending vibration of secondary ammides.[11] Differential spectra were therefore processed, by subtracting the contribution of functionalized silica **2** in order to better highlight these components (Figure 4). The weak band observed at 1595 cm^{-1} may be due to the residual unreacted NH$_2$ groups of **2** (NH bending vibration of primary amines) or, more likely, the NH bending vibration of sulfonimide NH (see IR spectrum of **9**). It is interesting to note that the IR spectra of initially isolated and washed material were the same.
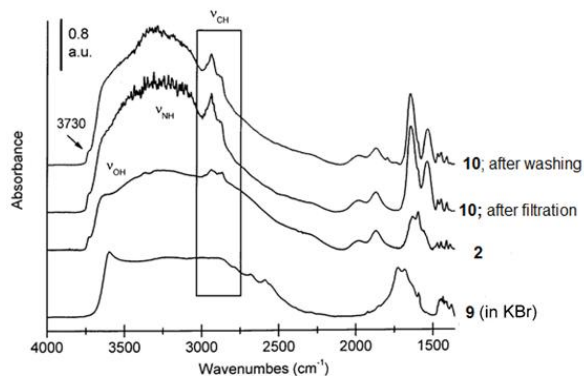

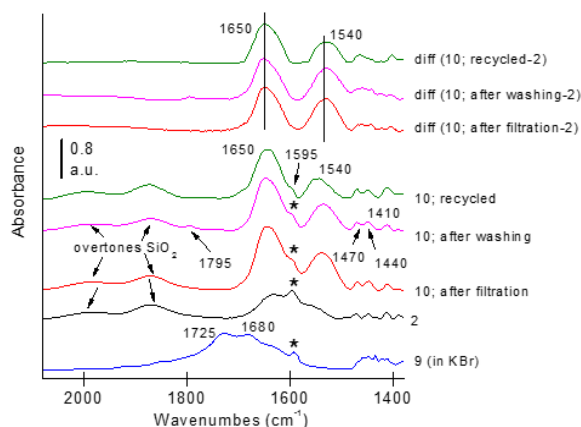**Figure 3.** IR spectra of **2**, **9** and **10**.

Figure 4. Expansion of IR spectra of Figure 3

10 was virtually insoluble in water and in any organic solvent (see Experimental Section). However, an NMR spectra of a suspension of **10** in D$_2$O, registered on a Jeol ECZR spectrometer with an appropriate number of scans (over 250 for ^{1}H-NMR and over 10.000 for ^{13}C-NMR) allowed its structure to be confirmed (Figure 5 and 6).
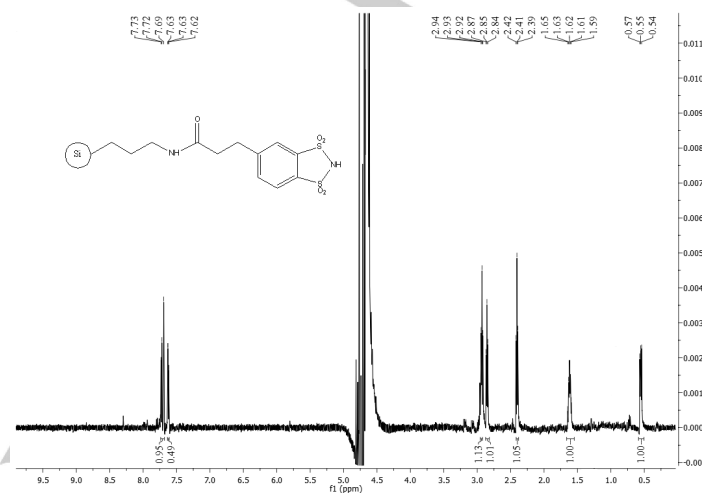
Figure 5. ^{1}H-NMR spectrum of **10**.
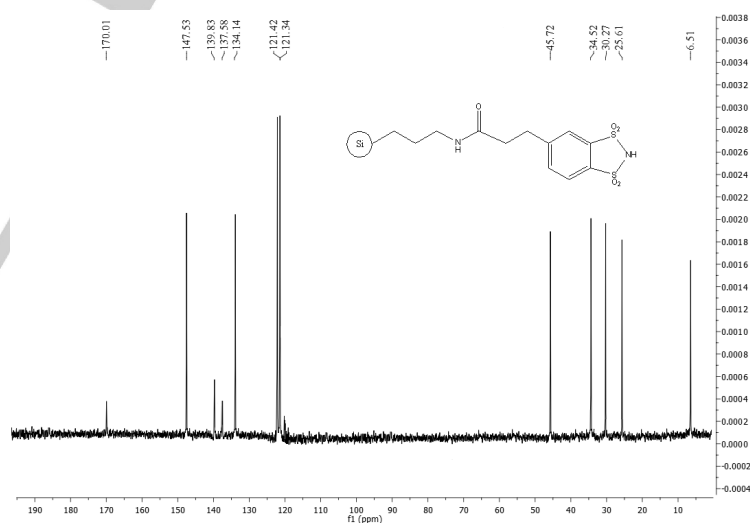
Figure 6. ^{13}C-NMR spectrum of **10**.

In fact, the ^{1}H-NMR spectrum (Figure 5) shows five triplets that are attributable to the five CH$_2$ groups and a multiplet that is attributable to the aromatic hydrogens of the sulfonimide ring. Interestingly, the integrations of the peak areas shows that almost all the NH$_2$ groups of silica **2** reacted with **9**. In the ^{13}C-NMR (Figure 6) spectrum, the five signals of the aliphatic carbons and the six signals of the aromatic carbons are clearly visible. Interestingly, the chemical shift of the carboxyl group was 170 ppm, in the typical position of CONH$_2$, whilst in **9** this

signal was in the typical COOH position, at 176 ppm. As a result, we can state with a reasonable level of certainty that the immobilization of sulfonimmide **9** was successful.

The IR spectrum of a diisopropylalkylamide silica is reported in the literature.[12] (Figure 2 of Supporting Information). Interestingly, bands at 1650 cm^{-1} (stretching CO) and 1542 cm^{-1} (bending NH of secondary amide) appear to be almost identically to those in the IR spectrum of **10**. In order to further confirm that the reaction had taken place, and to exclude the formation of ammonium salt **11** (Figure 7), the reaction between silica **2** and **9** was also carried out in the absence of EDC. The IR spectrum of the obtained product (most probably ammonium salt **11**) is shown in Figure 3 of the Supporting Information and it is clearly different from that of **10** as it is, most importantly, lacking the characteristic bands of the amide bond.
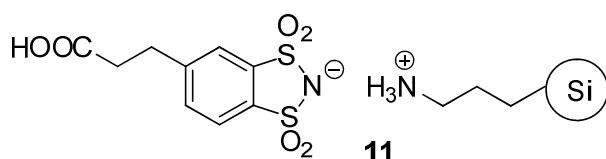

Figure 7. Ammonium salt **11**.

Catalytic activity and recovery of catalyst 10

This new heterogeneous catalyst **10** was tested over five different reactions that require acid catalysis and that had advantageously already been catalyzed by parent immide **1**. More precisely catalyst **10** was used in a Ritter reaction [4b,13] (Scheme 3; Table 1, entry 1), a Strecker reaction[4d,14] (Scheme 3; Table 1, entry 2), a Fischer esterification[4a] (Scheme 3; Table 1, entry 3), a Mannich reaction[5b,15] (Scheme 3; Table 1, entry 4) and a Biginelli reaction[5c,16] (Scheme 3; Table 1, entry 5). Results were generally excellent and very similar to those obtained using **1** as catalyst. (Table 1). It must also be stressed that the same reactions failed in the presence of **2** as a catalyst (Table 1). Catalyst **10** was easily and almost completely recovered via filtration over a folded filter; the recovered catalyst **10** was reused in Ritter reaction for a further four consecutive runs. Results are listed in Table 2 and it can be seen that the yields of target product **14** and the recovery of **10** were consistently excellent over the various runs. In a alternative procedure, instead of recovering **10** by filtration at the end of the reaction, **14** was completely removed via washings with dichloromethane. Fresh **12** and **13** were then added to the same environment and the reaction was repeated several times. The catalyst was efficient up until the tenth consecutive run. The results are reported in Table 3. The IR (Figure 4) and ^{1}H-NMR spectra (Fig.1 in Supporting Information) of the recovered catalyst, were almost identical, at the end of the tenth run, to those of the initial catalyst. In particular, about IR spectrum, no peculiar spectral component is either added or missing if compared to the plain

10 material observed after filtration or washing, indicating that the system is very stable.
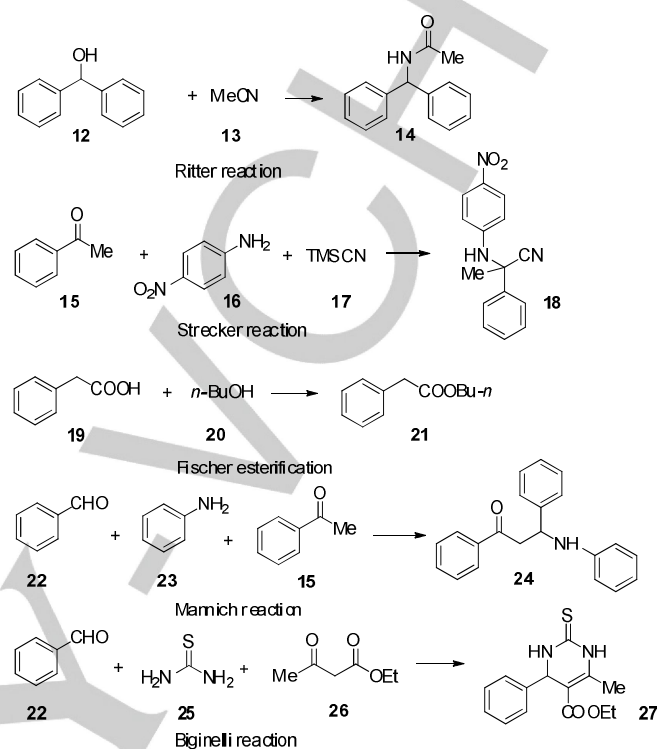
Scheme 3. Reactions carried out in the presence of **10** as a catalyst.

Table 1. Selected reaction catalyzed by **1** and **10**.

Entry	Reaction	Catalysts (mol-%)	Temp (°C)	Time (h)	Products and yields (%)[a]
1	Ritter	**1** (10)	reflux	8	**14**; 89[4b]
		10 (20)[b]	reflux	10	**14**; 95[c]
		2 (20)[d]	reflux	24	-
2	Strecker	**1** (5)	r.t	1	**18**; 81[4d]
		10 (10)[b]	r.t	1.5	**18**; 84[e]
		2 (10)[d]	r.t	24	-
3	Fischer	**1** (25)	90	1.5	**21**; 90[4a]
		10 (20)[b]	90	3	**21**; 94[f]
		2 (20)[d]	90	24	-
4	Mannich	**1** (5)	r.t.	24	**24**; 97[5b]
		10 (10)[b]	r.t.	24	**23**; 94[g]
		2 (10)[d]	r.t.	48	-
5	Biginelli	**1** (5)	50	4	**27**; 97[5c]
		10 (10)[b]	50	6	**27**; 94[h]
		2 (10)[d]	50	24	-

[a] Yields refer to the pure and isolated products. The physical and spectroscopic data of the obtained products are in accordance with those previously reported by us. [b] With lower amounts of catalyst the reaction was not complete. [c] MeCN was both the reactant and the solvent. The recovery of **10** was 100%. [d] The reaction did not occur: only starting reagents were

recovered. [e] The reaction was carried out in neat conditions and reagent ratio (**15**:**16**:**17**) was 1:1:1.1. The recovery of **10** was 100%. [f] Toluene was the solvent and reagent ratio (**19**:**20**) was 1:1.1. The recovery of **10** was 92%. [g] The reaction was carried out in neat conditions and the reactants (**22**,**23**,**15**) were in equimolar amount. The recovery of **10** was 94%. [h] The reaction was carried out in neat conditions and the reactants (**22**,**25**,**26**) were in equimolar amount. The recovery of **10** was 97%.

In a alternative catalytic test, in the Strecker protocol, the reaction was carried out in a vertical double-jacket glass column. The column was charged with **10** and the reagent mixture flowed through the catalytic bed, with toluene as eluent; about 100 ml of solvent are used for the complete recovery of the product at the column outlet. The catalyst remained in the column and the product **18** was obtained firstly by evaporating the solvent and then by a column chromatography of the crude residue (68% yield). The catalyst was also active after two further, consecutive runs.

Table 2. Consecutive runs with recovered **10**

Entry	Time (h)	Yield (%) of **14** [a],[b]	Recovery (%) of **10**
1	10	95	100, 0.64 g[c]
2	10	92	100, 0.64 g[d]
3	12	93	98, 0.63 g[e]
4	12	91	97, 0.61 g[f]
5	12	92	97, 0.59 g

[a] Yields refer to the pure and isolated product. [b] The reaction was carried out at reflux with 2.5 mmol of **12** in 5 ml of **13** and 20 mol-% of **10** (0.64 g equivalent to 0.5 mmol of immobilized acid **9**). [c] Recovered **10** was used as a catalyst in run 2. [d] Recovered **10** was used as a catalyst in run 3. [e] Recovered 10 was used as a catalyst in run 4. [f] Recovered **10** was used as a catalyst in run 5.

Table 3. Consecutive runs without isolating **10**

Entry	Time (h)	Yield (%) of **14** [a],[b]
1	10	95[c]
2	10	92[c]
3	10	94[c]
4	11	95[c]
5	11	93[e]
6	13	92[c]
7	13	91[c]
8	13	93[c]
9	12	92[c]
10	12	94[c]

[a] Yields refer to the pure and isolated product. [b] The reaction was performed at reflux with 2.5 mmol of **12** in 5 ml of **13** and 20 mol-% of **10** (0.64 g equivalent to 0.5 mmol of immobilized acid **9**). [c] **14** was completely removed by washings with CH_2Cl_2; fresh **12** and **13** were then added.

Conclusions

We have herein proposed the preparation and the use of a new Brønsted acid heterogeneous catalyst obtained by anchoring, through an amide bond, an appropriately functionalized derivative of 1,2-benzenedisolfonimmide (**1**), namely (1,2-benzenedisulfonimide-4-yl)propionic acid (**9**), to a 3-aminopropyl functionalized silica gel (**2**) support. This new material **10** possesses several features which make it an excellent and versatile heterogeneous catalyst. In particular, it maintains the same strong acidity of the parent 1,2-benzenedisulfonimide (**1**), it is insoluble both in water and in organic solvents, it has a strong and stable, even to heating link (amide bond) between silica and the 1,2-benzenesulfonimide derivative, its spacer branch is enough long (7 atoms) to keep the catalytic site far from the silica support

This new catalyst has been tested and has given excellent results in five different organic reactions, while it was easily recovered and reused without losing its catalytic activity.

We believe that **10** can take its rightful place in the toolbox of heterogeneous catalysis, as it is an excellent and versatile candidate for efficient, simple and ecofriendly protocols whose use can be expanded to virtually any organic reaction that requires Brønsted acid catalysis.

Experimental Section

General

Analytical grade reagents were used and reactions were monitored by GC, GC-MS. Column chromatography were performed on Merck silica gel 60 (70-230 mesh ASTM). Petroleum ether (PE) refers to the fraction boiling in the range 40–70 °C. Mass spectra were recorded on an HP5989B mass selective detector connected to an HP 5890 GC with a cross-linked methyl silicone capillary column. ^{1}H NMR and ^{13}C NMR

spectra were recorded on a Brucker Avance 200 spectrometer at 200 and 50 MHz respectively. ^{1}H NMR and ^{13}C NMR spectra of **2** and **10** were recorded on Jeol ECZR spectrometer at 600 and 150 MHz respectively. IR spectra were recorded on a IR Perkin-Elmer UATR-two spectrometer. Alternatively, IR spectra of **2**, **9**, **10** and **11** were recorded in the form of self supporting pellets (using the powders either as such or in KBr dispersion) by means of a Bruker IFS Vector 22 spectrophotometer (resolution 4 cm^{-1}), equipped with a MCT cryodetector. All reagents were purchased from Sigma-Aldrich or Alfa-Aesar. Structures and purity of all the products obtained in this research were confirmed by their spectral (NMR, MS, IR) data. Satisfactory microanalyses were obtained for all new compounds

Synthesis of catalyst 10

4-Iodo-2-(3-methylbutoxy)-1,3-benzodithiole (4)

As reported by us,[4e] 3-methylbutyl nitrite (24 mmol, 2.8 g), 3-methylbutan-1-ol (20 mmol, 1.8 g) and CS$_2$ (166 mmol, 12.6 g) were dissolved in 1,2-dichloroethane (50 mL) and heated to reflux at 82 °C. 2-Ammino-5-iodobenzoic acid (**3**; 20 mmol, 5.26 g) dissolved in 1,4-dioxane (12 mL) was added dropwise to the previously prepared mixture. The resulting mixture was initially stirred at reflux for 45 min and then at room temperature for 1 h. The reaction mixture was poured into Et$_2$O/H$_2$O (100 ml, 1:1). The aqueous layer was separated and extracted with Et$_2$O (2 x 50 mL). The combined organic extracts were washed with H$_2$O (2 x 50 mL) and a saturated solution of Na$_2$CO$_3$ (50 mL), dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The crude residue, purified by column chromatography (PE/Et$_2$O 9.5:0.5), afforded the pure 4-iodo-2-(3-methylbutoxy)-1,3-benzodithiole (**4**; 6.55 g, 88% yield). Pale yellow viscous oil; R_f = 0.88 (PE/Et$_2$O 9.5:0.5); ^{1}H NMR (200 MHz, CDCl$_3$, 20°C, TMS): δ = 7.59 (d, J = 1.6 Hz, 1H), 7.34 and 7.30 (dd, ^1J(H,H) = 8.2 Hz, ^2J(H,H) = 1.6 Hz, 1H) 7.02 (d, J = 8.2 Hz, 1H), 6.69 (s, 1H), 3.36 (t, J = 6.5 Hz, 2H), 1.65–1.48 (m, 1H), 1.40–1.30 (m, 2H), 0.79 ppm (d, J = 6.5 Hz, 6H); ^{13}C NMR (50 MHz, CDCl$_3$, 20°C, TMS): 139.1, 136.6, 134.3, 130.3, 123.4, 90.6, 88.9, 63.1, 37.9, 25.0, 22.6 ppm; IR (neat): ν = 3155, 2982, 2241, 1810, 1750, 1610, 1200, 1074, 790 cm^{-1}; MS (70 eV, EI): m/z (%): 366 (35) [M$^+$], 294 (35), 279 (100), 266 (55); elemental analysis: calcd (%) for C$_{12}$H$_{15}$IOS$_2$ (366.3): C 39.35, H 4.13, I 34.65, S 17.51; found: C 39.39, H 4.15, I 34.61, S 17.48.

Trans ethyl 3-[2-(3-methylbutoxy)-1,3-benzodithiol-5-yl]acrilate (5)

4-Iodo-2-(3-methylbutoxy)-1,3-benzodithiole (**4**; 10 mmol, 3.66 g), ethyl acrilate (30 mmol, 3 g), K$_3$PO$_4$ (40 mmol, 8.49 g) PdCl$_2$·PPh$_3$ (5% mol, 0.35 g) and anhydrous toluene (20 mL) were added in a three necked flask. The mixture was heated at reflux for 9 h under nitrogen flow (during the heating the colour of the solution turned black) until the GC and GC-MS analyses showed the complete disappearance of starting compounds and the complete formation of title compound **5**. Then, the reaction mixture was poured into Et$_2$O/H$_2$O (100 mL, 1:1). The aqueous layer was separated and extracted with Et$_2$O (50 mL). The combined organic extracts were washed with H$_2$O (50 mL), dried with Na$_2$SO$_4$ and evaporated under reduced pressure. GC-MS analyses of the crude residue showed title compound (**5**; MS: m/z = 338 [M]$^+$) as the major product, besides traces of 2-(3-methylbutoxy)-1,3-benzodithiole (MS: m/z = 240 [M]$^+$). The crude residue was chromatographed on a short column, eluting with PE/Et$_2$O (9.5:0.5). The first eluted product was 2-(3-methylbutoxy)-1,3-benzodithiole [0.04 g; R$_f$ = 0.84 (PE/Et$_2$O 9.5:0.5)]. The second eluted product was the title compound *trans* ethyl 3-[2-(3-methylbutoxy)-1,3-benzodithiol-5-yl]acrilate (**5**; 3.02 g, 90% yield). Pale yellow viscous oil; R_f = 0.78 (PE/Et$_2$O 9.5:0.5); ^{1}H NMR (200 MHz, CDCl$_3$, 20°C, TMS): δ = 7.54 (d, J = 16 Hz, 1H), 7.44 (d, J = 1.4 Hz, 1H) 7.38–7.17 (m, 2H) 6.75 (s, 1H), 6.32 (d, J = 16 Hz, 1H), 4.19 (q, J = 7.0 Hz,

2H) 3.38 (t, J = 6.5 Hz, 2H), 1.64–1.48 (m, 1H), 1.40–1.23 (m, 5H), 0.78 ppm (d, J = 6.5 Hz, 6H); ^{13}C NMR (50 MHz, CDCl$_3$, 20°C, TMS): δ = 167.0, 143.6, 139.2, 137.8, 132.2, 125.5, 122.2, 121.1, 118.1, 90.6, 63.1, 60.7, 37.9, 25.0, 22.8, 22.6, 14.5 ppm; IR (neat): ν = 3150, 3000, 2988, 2247, 1820, 1740, 1680, 1610, 1225, 1074, 985, 770 cm^{-1}; MS (70 eV, EI): m/z (%): 338 (25) [M$^+$], 251 (100); elemental analysis: calcd (%) for C$_{17}$H$_{22}$O$_3$S$_2$ (338.5): C 60.32, H 6.55, S 18.95; found: C 60.29, H 6.55, S 18.91.

Ethyl 3-[2-(3-methylbutoxy)-1,3-benzodithiol-5-yl]propionate (6)

CuCl (10 mmol, 0.99 g) and then NaBH$_4$ (100 mmol, 3.30 g; in three consecutive portions at 0.5 h distance from each other) were added to a MeOH (10 mL) stirred solution of *trans* ethyl 3-[2-(3-methylbutoxy)-1,3-benzodithiol-5-yl]acrilate (**5**; 10 mmol, 3.38 g). GC and GC-MS analyses showed the complete disappearance of starting compounds **5** and the complete formation of title compound **6**. Then, the reaction mixture was poured into Et$_2$O/H$_2$O (100 mL, 1:1). The aqueous layer was separated and extracted with Et$_2$O (50 mL). The combined organic extracts were washed with water (50 mL), dried with Na$_2$SO$_4$ and evaporated under reduced pressure. Pure ethyl 3-[2-(3-methylbutoxy)-1,3-benzodithiol-5-yl]propionate (**6**; 3.20 g, 94% yield) title compound was obtained. Colourless viscous oil; R_f = 0.78 (PE/Et$_2$O 9.5:0.5); ^{1}H NMR (200 MHz, CDCl$_3$, 20°C, TMS): δ = 7.18 (d, J = 8.2 Hz, 1H), 7.13 (J = 1.4 Hz, 1H), 6.87 and 6.85 (dd, J_1 = 8.0 Hz, J_2 = 1.4 Hz, 1H) 6.68 (s, 1H), 4.06 (q, J = 7.2 Hz, 2H) 3.37 (t, J = 6.5 Hz, 2H), 2.84 (t, J = 7.2 Hz, 2H), 2.52 (t, J = 7.2 Hz, 2H), 1.64–1.48 (m, 1H), 1.39–1.29 (m, 2H), 1.23 (t, J = 7.2 Hz, 3H), 0.78 ppm (d, J = 6.5 Hz, 6H); ^{13}C NMR (50 MHz, CDCl$_3$, 20°C, TMS): δ = 166.8, 143.6, 141.8, 125.5, 122.2, 121.1, 118.1, 90.6, 63.2, 60.7, 48.9, 38.8, 37.9, 25.0, 22.6, 14.5 ppm; IR (neat): ν = 3180, 2974, 2240, 1840, 1730, 1672, 1620, 1215, 1094, 777 cm^{-1}; MS (70 e, EI): m/z (%): 340 (25) [M$^+$], 253 (100); elemental analysis: calcd (%) for C$_{17}$H$_{24}$O$_3$S$_2$ (340.5): C 59.97, H 7.10, S 18.83; found: C 60.00, H 7.13, S 18.77.

Ethyl 3-[(3,4-bischlorosulfonyl)phenyl]propionate (7)

Adduct **6** (10 mmol, 3.40 g) was dissolved in MeCN (10 mL). HCl 2N (2 ml) and then *N*-chlorosuccinimide were added (80 mmol, 10.67 g). The reaction mixture was vigorously stirred at room temperature and was monitored using TLC (PE-EtOAc 7:3). After 1 h, the reaction was complete when the spot of **6** disappeared and there was only one other spot. The reaction mixture was poured into Et$_2$O/H$_2$O (100 mL, 1:1) The aqueous layer was separated and extracted with CH$_2$Cl$_2$ (2 x 50 ml). The combined organic extracts were washed first with a 5% NaOH solution (2 x 50 ml), then with water (4 x 50 ml), dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The crude residue was the pure title compound ethyl 3-[(3,4-bischlorosulfonyl)phenyl]propionate (**7**; 3.75 g, 100% yield). White waxy solid; 3.75 g (100% yield); R_f = 0.38 (PE/EtOAc 7:3); ^{1}H NMR (200 MHz, CDCl$_3$, 20°C, TMS): δ = 8.27 (d, J = 8.2 Hz, 1H), 8.18 (d, J = 1.4 Hz, 1H), 7.78 (d J = 8.2 Hz, 1H), 4.07 (q, J = 7.2 Hz, 2H), 3.13 (t, J = 7.2 Hz, 2H), 2.69 (t, J = 7.2 Hz, 2H), 1.18 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (50 MHz, CDCl$_3$, 20°C, TMS): δ = 165.2, 142.8, 142.1, 139.0, 134.3, 133.3, 130.9, 61,7, 48.9, 38.8, 14.5 ppm; IR (neat): ν = 3013, 3000, 2995, 1685, 1340, 1252, 1210, 804 cm^{-1}; elemental analysis: calcd (%) for C$_{11}$H$_{12}$Cl$_2$O$_6$S$_2$ (375.3): C 35.21, H 3.22, Cl 18.90, S 17.09; found: C 35.27, H 3.18, Cl 18.84, S 17.04.

3-(1,2-Benzenedisulfonimide-4-yl)propionic acid (9)

As reported by us[4e] adduct **7** (10 mmol, 3.75 g) was dissolved in toluene (10 mL) and EtOH (15 mL). The resulting mixture was cooled to 0-5 °C. Ammonia was bubbled through while the temperature was maintained at

0-5 °C and the reaction mixture was vigorously stirred. The reaction was monitored by TLC (PE/EtOAc 7: 3). After 30 min, the reaction was complete when the spot of **7** disappeared. The mixture was first filtered in order to eliminate NH_4Cl and then the solvent was evaporated under reduced pressure. The crude residue was dissolved in H_2O and passed through a Dowex (HCR–W2) column (eluent: H_2O) to afford ethyl 3-(1,2-benzenedisulfonimide-4-yl)propionate (**8**). Brown waxy solid; 3.18 g (100% yield); ^{1}H NMR (200 MHz, D_2O, 20°C, TMS): δ = 7.49– 7.42 (m, 2H), 7.34– 7.28 (m, 1H), 3.69 (q, J = 7.2 Hz, 2H), 2.69 (t, J = 7.2 Hz, 2H), 2.35 (t, J = 7.2 Hz, 2H), 0.77 ppm (t, J = 7.2 Hz, 3H). Spontaneously and in about 8 hours, **8** hydrolyzed to the title compound 3-(1,2-benzenedisulfonimide-4-yl)propionic acid (**9**). It was dried in a oven at 90°C for 1 h and 2.91 g (100% yield) were obtained. Brown waxy solid; ^{1}H NMR (200 MHz, D_2O, 20°C, TMS): δ = 7.80–7.53 (m, 3H), 2.91 (t, J = 7.2 Hz, 2H), 2.57 ppm (t, J = 7.2 Hz, 2H). ^{13}C NMR (50 MHz, D_2O, 20°C, TMS): δ = 176.5, 147.8, 139.9, 137.5, 134,1, 121.2, 120.7, 34.1, 29.7 ppm; IR (neat): v = 2915, 1690, 1615, 1395, 1310, 1225, 800 cm^{-1}; elemental analysis: calcd (%) for $C_9H_9NO_6S_2$ (291.3): C 37.11, H 3.11, N 4.81, S 22.02; found: C 37.07, H 3.12, N 4.85, S 22.06.

3-(1,2-Benzenedisulfonimide-4-yl)propionic acid immobilized on 3-aminopropyl functionalized silica gel (10)

Imide **9** (1.1 mmol, 0.32 g) and *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimmide hydrochloride (EDC, 1.1 mmol, 0.21 g) were added to a stirred suspension of 3-aminopropyl functionalized silica gel **2** (1 g; 1 mmol/g NH_2) in H_2O (5 mL). The reaction mixture was vigorously stirred at r.t. for 5 h. The resulting white solid was filtered over buchner funnel. Firstly was washed with 10 mL of 2 N HCl (in order to fully restore the sulfonimide acidity) and then with 10 mL of acetone (in order to remove eventual organic residues arising from **9**); lastly, it was dried in oven at 70°C overnight. After this treatment, 1.16 g of was obtained (91% yield). IR and NMR spectra reported in Figures 3, 4, 5, 6 in Result and Discussion section confirmed the hypothesized structure **10**. ^{1}H NMR (600 MHz, D_2O, 20°C, TMS): δ = 7.73–7.69 (m, 2H), 7.63–7.62 (m, 1H), 2.93 (t, J = 7.8 Hz, 2H), 2.93 (t, J = 7.8 Hz, 2H), 2.85 (t, J = 7.8 Hz, 2H), 2.41 (t, J = 7.8 Hz, 2H), 1.65–1.59 (m, 2H), 0.55 ppm (t, J = 7.8 Hz, 2H). ^{13}C NMR (150 MHz, D_2O, 20°C, TMS): δ = 170.0, 147.6, 139.8, 137.6, 134.1, 121.4, 121.3, 45.7, 34.5, 30.3, 25.6, 6.5. For the IR description, see Result and Discussion section. Aqueous and acetone washings were collected and evaporated under reduced pressure. No traces of possible unreacted immide **9** were detected. In a collateral proof **2** (1 g) and immide **9** (1.1 mmol, 0.32 g) were reacted without EDC. IR spectrum of the obtained solid (0.94 g), included in Supporting Information (Fig. 3), was markedly different from that of **10** and the characteristic bands of the amide bond were not present.

Catalytic tests

Ritter reaction; recovery and reuse of catalyst 10

In Table 1, entry 1, heterogeneous catalyst **10** (20 mol%; 0.64 g equivalent to 0.5 mmol of immobilized acid) was added to a solution of diphenyl methanol (**12**; 2.5 mmol, 0.46 g) in MeCN (**13**; 5 mL); the mixture was stirred at reflux for 10 hours until the complete disappearance of **12** (GC and GC-MS); in order to recover the catalyst, the reaction mixture was filtered on a folded filter and washed with of H_2O. The resulting filtered solution was poured into CH_2Cl_2/H_2O (100 ml, 1:1). The aqueous layer was separated and extracted with CH_2Cl_2 (2 x 50 ml). The combined organic extracts were washed with H_2O (2 x 50 ml), dried over Na_2SO_4 and evaporated under reduced pressure. The crude residue was chromatographed on a short flash-column, eluting with PE/EtOAc (9:1) to provide pure *N*-(diphenylmethyl)acetamide (**14**; 0.54 g, 100% yield). White solid; mp 147–148 °C (MeOH, lit.[13]147–149 °C), ^{1}H NMR

(200 MHz, CDCl$_3$, 20°C, TMS): *δ* = 7.21–7.17 (m, 10H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.13 (d, *J* = 7.8 Hz, 1H), 1.91 ppm (s, 3H); ^{13}C NMR (50 MHz, CDCl$_3$, 20°C, TMS) : *δ* = 170.3, 141.5, 128.8, 127.7, 127.5, 57.5, 23.0 ppm; MS (70 eV, EI): *m/z* (%): 225 (100) [M+], 182 (65), 165 (45); IR (neat) v (cm^{-1}): 3315 (NH), 1650 (CONH$_2$), 1549 (CONH$_2$). The folded filter with recovered catalyst was dried in oven at 70°C. After this treatment the recovered catalyst (0.32 g, 100% of recovery) was reused in other four consecutive catalytic runs as reported in Table 2. The yield of **14** and the recovery of **10** were always consistently good.

As an alternative, at the end of the reaction, instead of recovering the catalyst by filtration, it was left in the reaction flask. Firstly the reaction mixture was centrifuged and *N*-(diphenylmethyl)acetamide was removed via three successive washings with CH_2Cl_2 (3 x 10 ml). At this point it was possible to perform a new reaction by adding fresh **12** and **13**. Until the tenth consecutive run, the catalyst was still active and, as reported in Table 3, the yields of **14** were always very good. The IR and ^{1}HNMR spectra of the recovered catalyst were almost identical to the initial catalyst.

The details of other catalytic tests are reported in Supporting Information.

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Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

New, efficient and versatile heterogeneous acid catalyst. It has been tested and has given excellent results in five different organic reactions; it was easily recovered and reused without losing its catalytic activity.
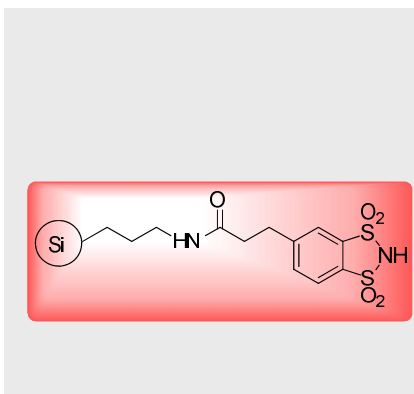
Margherita Barbero, Giuseppina Cerrato, Enzo Laurenti, Sebastiano Zanol and Stefano Dughera*

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Title Silica gel-immobilized 1,2-benzenedisulfonimmide: a new and versatile Brønsted acid heterogeneous catalyst