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Synthesis of β-nitrostyrenes in the Presence of Sulfated Zirconia and Secondary Amines

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A simple and efficient protocol for the synthesis of β-nitrostyrenes has been achieved by the use of sulfated zirconia-secondary amine (piperidine, pyrrolidine, proline or prolinol) cooperative systems. The condensation of different aldehydes and nitromethane demonstrates the efficiency of this process, which does not require high-temperature reactivation for the reuse of the catalytic material.

Introduction

Sulfated zirconia (SO_4^{2-}/ZrO_2, SZ) is a solid super acid[1] that can exist in four crystalline forms: orthorhombic, cubic, tetragonal and monoclinic, depending on the sulfation process and activation temperature.[2] The acidic property of the material ($H_o \leq -14$) has been used to catalyse diverse organic reactions[3] for which the crystal structure was determined to be crucial for obtaining excellent results.[4] The most of the processes described in the literature have focused on the use of monoclinic and tetragonal catalysts that show high activities,[5] owing to their Brønsted and Lewis acid sites.[6] The thermally driven transformation of the tetragonal phase to the monoclinic phase[7] leads to structural modifications that change a solid containing Brønsted and Lewis acids to a solid containing Lewis acids only; it also presents an opportunity to apply this material to different processes, depending on the nature of the catalysis.[8]

With these features in mind, our study focuses on the effect of the crystalline structure of SZ in a condensation process, namely, the Henry reaction, which involves the condensation of an aldehyde with nitromethane to produce β-nitrostyrenes. These organic compounds are useful and versatile building blocks[9] that are generally used as starting materials for the heterocyclic synthesis[10] of compounds such as pyrroles,[11] pyrazoles,[12] 1,2,3-triazoles,[13] nitrochromenes,[14] and allylic alcohols.[15] Furthermore, owing to the presence of a double bond, β-nitrostyrenes are used in asymmetric synthesis,[16] and the versatile nitro group is used to obtain different functional groups.[17] The preparation of β-nitrostyrenes[18] has been achieved using heterogeneous catalysts, such as amino-functionalized MIL-101,[19] nickel hydroxyapatite,[20] amino-functionalized silicas,[21] amine-MCM-41,[22] diamino-functionalized FDU-mesoporous polymers,[23] Envirocat EPZG,[24] and zeolites.[25] In this work, we choose to use SZ in the tetragonal phase to generate a cooperative system that allows us to obtain β-nitrostyrenes via the activation of an aldehyde and nitromethane due to the Brønsted and Lewis acid sites present in the material.

Results and discussion

First, we evaluated the ability of the tetragonal phase SZ (for full characterization, see ESI†) to catalyse the condensation reaction between *p*-tolualdehyde **1a** and nitromethane using microwave heating. The model reaction was carried out at 110 °C in toluene for 30 minutes. Under these reaction conditions, the desired product **2a** was not obtained (Table 1, entry 1). However, when the reaction was performed in the presence of SZ and piperidine as catalysts, the corresponding β-nitrostyrene **2a** was obtained in 85% yield (Table 1, entry 2). This result contrasts with the yield obtained when only piperidine was used as a catalyst (40% yield, Table 1, entry 3). To evaluate other secondary amines and optimize the catalytic SZ/amine system, the reaction was performed in the presence of pyrrolidine, proline, prolinol, morpholine and diisopropylamine. As shown in Table 1 (entries 4 and 5), an excellent yield was obtained using pyrrolidine and proline (90% and 95% yield, respectively). The use of prolinol led to a β-nitrostyrene **2a** yield of 80%, while in the presence of morpholine, the yield decreased significantly (Table 1, entry 7). The product was not obtained when the reaction was carried out using the SZ/diisopropylamine system. It is important to note that the use of minor SZ concentration is reflected in the decrease in the reaction yield.

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Based on the optimized conditions of the condensation process, the scope of the reaction with different aldehydes was studied using the SZ/piperidine system (Table 2). Thus, a variety of aromatic aldehydes with various types of substituents underwent the reaction, leading to moderate to good yields of the desired products **2a-m** in short reaction times. The aldehydes with electron-donating groups provided good yields (Table 2, entries 1-4). The same trend was observed in aldehydes with electron-withdrawing groups, with the products **2h-2l** obtained in 70-85% yield (except for **2k**). The SZ-piperidine system was also efficient for reactions of 6-bromopiperonal and benzaldehyde, which produced the corresponding β-nitrostyrenes **2f**-**2g** in 65%, and 70% yield, respectively (Table 2, entries 5 and 6). Heteroaromatic aldehyde **1m** was also shown to be a good substrate to yield the product **2m** in 90% yield (Table 2, entry 12). The behaviour of SZ-proline catalytic system during the synthesis of the same group of β-nitrostyrenes was also evaluated. In that case, the reactions proceeded with moderate yields with a methoxy substituent in the aromatic ring (Table 2, entries 1-4). The reaction did not evolve the desired product with electron-withdrawing groups (Table 2, entries 7-11). Using heteroaromatic aldehyde, excellent reaction yields were again obtained (Table 2, entry 12). The use of SZ/pyrrolidine system was abandoned because the purification on the chromatographic column was complicated, owing to a complex reaction mixture.

Table 1. Screening of catalysts and the optimization of reaction conditions[a]

Entry	Amine	Yield (%)[b]
1	-	n.r.
2	Piperidine	85
3[c]	Piperidine	40
4	Pyrrolidine	90
5	Proline	95
6	Prolinol	80
7	Morpholine	40
8	Diisopropylamine	n.r.

[a]Reagents: Aldehyde 1a (1 mmol), nitromethane (3 mmol), piperidine (0.1 mmol), SZ (50 mg), and toluene (1 mL). [b]Yield of isolated product after chromatographic purification. [c]The reaction was performed without SZ.

An analysis of SZ after the organic reaction demonstrates that the tetragonal phase is the major crystalline structure. However, it is also possible to identify the formation of the monoclinic phase (Figure 1). The monoclinic phase content increases with the number of reuses of the material without affecting the yield of the organic reaction. The maximum phase transformation was found after the fourth reuse (Figure 1). This behaviour leads us to believe that both crystalline structures participate in the reaction via their respective acid sites. For the tetragonal phase, Lewis and Brønsted acid catalysis is possible, while in the monoclinic phase, only Lewis

acid catalysis takes place. To demonstrate that the monoclinic structure will be able to catalyse the organic reaction, the condensation of *p*-tolualdehyde **1a** and nitromethane was tested in the presence of SZ with the aforementioned structure, and β-nitrostyrene was obtained in 60% yield, confirming that both crystal structures can participate in the reaction process.

Table 2. Synthesis of β-nitrostyrenes catalysed by SZ-piperidine[a]

Entry	R	Product	Yield (%)[b]	
			Pyrrolidine[c]	Proline[d]
1	3-MeOC$_6$H$_4$	**2b**	85	50
2	4-MeOC$_6$H$_4$	**2c**	75	70
3	3,4-(MeO)$_2$C$_6$H$_3$	**2d**	60	65
4	3,4,5-(MeO)$_3$C$_6$H$_2$	**2e**	75	70
5		**2f**	65	50
6	Ph	**2g**	70	45
7	2-BrC$_6$H$_4$	**2h**	85	n.r.
8	4-BrC$_6$H$_4$	**2i**	75	n.r.
9	4-ClC$_6$H$_4$	**2j**	80[d]	n.r.
10	2-NO$_2$C$_6$H$_4$	**2k**	40	n.r.
11	4-NO$_2$C$_6$H$_4$	**2l**	70	n.r.
12		**2m**	90	65

[a]Reagents: Aldehyde (1 mmol), nitromethane (3 mmol), piperidine (0.1 mmol), SZ (50 mg), and toluene (1 mL). [b]Yield of isolated product after chromatographic purification. [c] 30 minutes were necessary for the reaction. [d]4 h were necessary for the reaction.
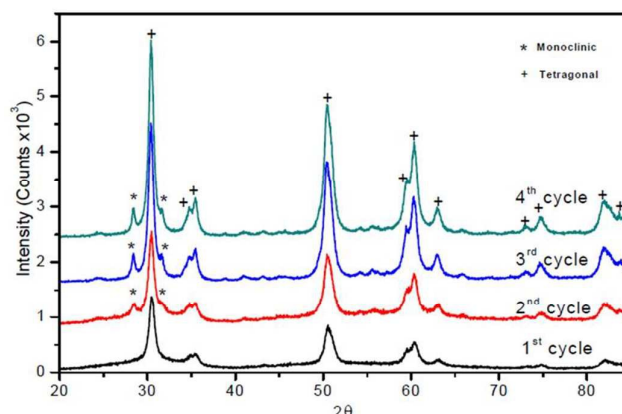

Fig. 1 SZ Powder X-ray diffraction patterns of sulphated zirconia as synthesised and recovered in four cycles
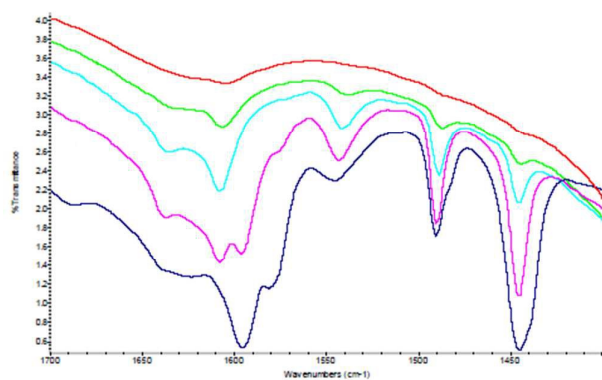
Fig. 2 FT-IR spectra of SZ after pyridine desorption at different temperatures: a) dark blue 50 °C, purple 100 °C, turquoise 200 °C, green 300 °C and red 400 °C.

The identification of the Brønsted and Lewis acid sites present in synthesised SZ was achieved by FT-IR spectra, which exhibited the characteristic bands of pyridinium ion at 1600, 1540 and 1490 cm^{-1} (Brønsted acid sites), and pyridine coordinated over Lewis acid sites at 1490 and 1445 cm^{-1} (Figure 2). The concentration of both types of acid sites could be estimated from the intensities of the bands at 1540 and 1445 cm^{-1}. Those results indicated a major concentration of Lewis acid sites (Table 3).

Table 3. Concentration of acid sites as calculated after pyridine desorption at different temperatures

Entry	Temperature °C	Brønsted $\mu molg^{-1}$	Lewis $\mu molg^{-1}$	Total	B/L Ratio
1	50	101	179	280	0.564
2	100	69	94	143	0.734
3	200	33	52	85	0.634
4	300	14	27	41	0.518

It is known that the monoclinic phase can be formed during the reactivation process of material;[26] however, in this case where there is no reaction process, the monoclinic phase is formed during the reaction as a consequence of the adsorption of oxygen onto defectives sites of the SZ, as previously described.[5b,26] Owing to the X-ray analysis of the different SZ samples after the reaction and without the use of a reactivation process, it was possible to detect the presence of the monoclinic phase in the material (Figure 1).

Adsorption of N_2 (BET method) was used to quantify and compare the surface area and pore size of synthesised and reused (four times) SZ. The recovered sample revealed lower porosity and surface area than the synthesised material (Table 4). It is noteworthy that, the structural change in the recovered sample, does not affect the efficiency of material in the catalysis of the organic reaction.

For the reuse of material, two different reactivation procedures were used. In the first, the material was calcined at 500 °C under O_2 atmosphere during 3 h. In the second procedure, the material was only dried at 100 °C in an oven for 12 h. To our delight, the reaction yield is the same in both cases (85%), implying that it is not necessary to use high temperatures to reactivate the catalyst in this catalytic process. The reaction yield decreased to 80% during the tenth run for the material dried at 100 °C. If this material was calcined at 500 °C under O_2 atmosphere, the yield increased to 85% (Figure 3). These results suggest that the reduced activity of the catalysts during the tenth run is likely due to the presence of organic material on the surface area; this material is eliminated during the calcination process.

Table 4. The nitrogen adsorption–desorption analysis parameters of materials

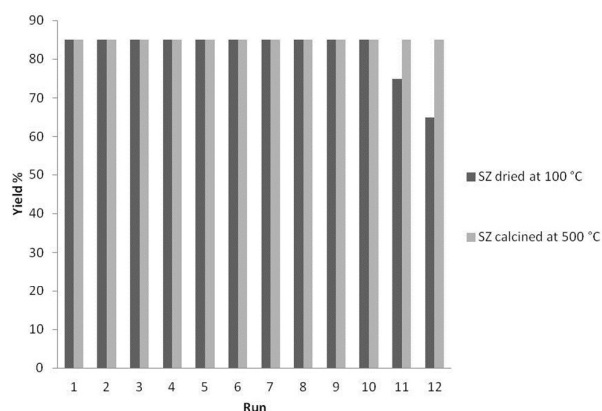| Entry	Parameters	Synthesised SZ	Recovered SZ
1	S_{BET} ($m^2 \cdot g^{-1}$)	90.75	86.15
2	Pore volume ($cm^3 \cdot g^{-1}$)	0.12	0.089
3	Pore size (Å)	52.73	41.62

Fig. 3 Reuse of SZ dried at 100 °C and calcined at 500 °C

The importance of SZ in the catalytic process is demonstrated by the yield of the reaction carried out without the SZ material (40%, Table 1, entry 3). Based on this result and other studies reported in literature, in which piperidine participated in cooperative catalysis,[27] a putative reaction mechanism is shown in Scheme 1. The first step involves the interaction of SZ and the aldehyde to yield an activated intermediate, **I** (immobilised at the solid/liquid interface), which reacts with piperidine to yield the iminium ion **II**. The reaction then proceeds as previously described:[27-28] intermediate **III** is formed by reaction **II** with nitromethane, followed by elimination of the secondary amine in **III**, also catalysed by SZ, leading to the formation of b-nitrostyrene **2g**.

In this putative reaction mechanism, it is considered that the piperidene is not adsorbed on the SZ surface. If that interaction were to occur, the catalytic activity of the secondary amine could be inhibited as consequence of neutralization process between a base and acid. It is true that the interaction of SZ surface with amines is possible under special conditions – a common method to determine the acid

sites in SZ (see ESI†) – however in this case the interaction between SZ and starting materials, aldehyde and nitromethane, is faster than the interaction between the secondary amine and SZ. For these reasons, we consider that the secondary amine is acting as a homogeneous component.

Moreover, it is known that under neutral conditions, the equilibrium constant of the formation of nitronic acid from nitromethane is very small.[29] However, under acidic conditions (SZ), this equilibrium can be shifted to the formation of the nitronic acid,[30] owing to the acid sites of material. These considerations suggest a cooperative role for SZ, in which the material participates in the activation of the carbonyl group and nitromethane.
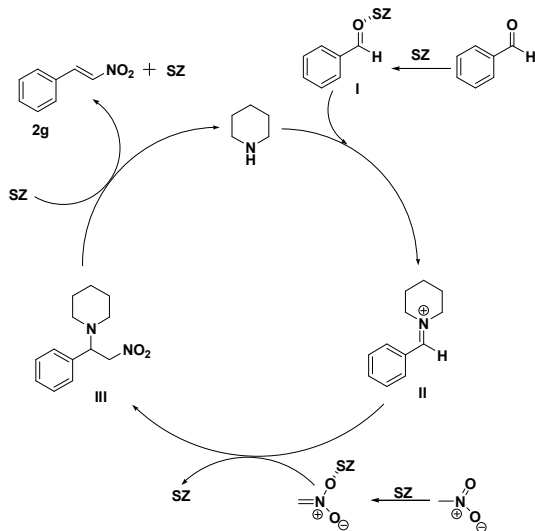
Scheme 1 Proposed mechanism

Conclusions

In conclusion, we have developed a convenient protocol for the synthesis of trans-β-nitrostyrenes through a cooperative catalysis by employing sulfated zirconia with secondary amines that directly influence the condensation process between an aldehyde and nitromethane (Henry reaction). Brønsted and Lewis catalytic acid sites present in the material allowed for the direct activation of carbonyl groups by the formation of an iminium ion. At the same time, SZ allows for the formation of nitronic acid, which is the C-C bond precursor. The efficiency and operational simplicity of this protocol was demonstrated by the reuse of the material (ten times) with very good yields, without the requirement of reactivation at high temperatures.

Acknowledgements

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A simple and efficient protocol for the synthesis of β-nitrostyrenes has been achieved by the use of sulfated zirconia-secondary amine cooperative systems.