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Effect of catalyst thermal treatment

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Sulfated zirconia as an efficient catalyst for sulfonylamidomethylation of benzylsulfonamides and 2-phenylethanesulfonamides. Effect of catalyst thermal treatment

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Abstract: The synthesis of 3,4-dihydro-1H-2,3-benzothiazine 2,2-dioxides and 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxides is studied using sulfated zirconia as catalyst. The sulfated zirconia calcined at 550^oC achieved a high selectivity which is attributed to the formation of a tetragonal phase. In addition, the catalyst can be reused up to three times without loss of its catalytic activity.

Keywords: sulfated zirconia, sulfonylamidomethylation, benzylsulfonamides, 2-phenylethanesulfonamides, 2,3-benzothiazine 2,2-dioxides, 3,2-benzothiazepine 3,3-dioxides.

1. Introduction

Benzothiazine and benzothiazepine derivatives are interesting compounds due to their pharmacological properties. Among them, 1,2-benzothiazine 1,1-dioxide derivatives are well known for their analgesic and anti-inflammatory activities [1,2], while 1,4-benzothiazines generally possess significant antifungal activity [3,4]. Recently it has been found that 3,4-dihydro-1,2-benzothiazine-3-carboxylate 1,1-dioxide acts as potent calpain I inhibitors [5,6]. On the other hand, 1,2-, 1,4- and 1,5-benzothiazepines have shown activity as endogenous natriuretic factors, enzyme inhibitors, anticonvulsants, sedatives, and hypnotics [7-9]. Therefore, active studies for the synthetic development of benzothiazine and benzothiazepine derivatives have been carried out.

Despite this, at the present time biological activity of 3,4-dihydro-1H-2,3-benzothiazine 2,2-dioxides **2** and 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxides **4** has been unexplored.

Synthetic approaches for 3,4-dihydro-1H-2,3-benzothiazine 2,2-dioxides **2** include intramolecular vicarious nucleophilic substitution of hydrogen of m-nitrochloromethylsulfonamides [10] and sulfonylamidomethylation of benzylsulfonamides [11].

In the last methodology, we have prepared these compounds by treatment of benzylsulfonamides **1** and formaldehyde with an acid catalyst followed by intramolecular cyclization of imine intermediate via electrophilic aromatic substitution. Homogeneous catalysts such as methanesulfonic acid (MSA), trifluoroacetic acid (TFA) and trifluoromethanesulfonic acid (TFMSA) have been used with good yield for several substituents R^1 and R^2[11]. (Scheme 1)
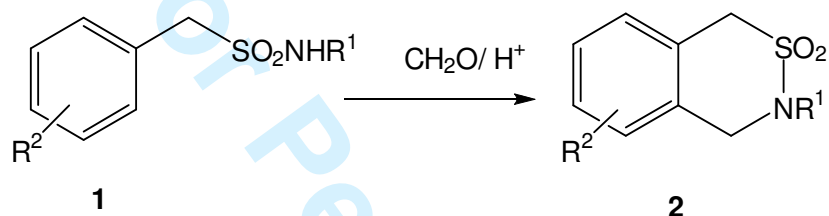
Scheme 1

A similar approach was subsequently applied for the construction of 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxides **4** from 2-phenylethanesulfonamides **3** using methanesulfonic acid and trifluoroacetic acid as catalyst with good yield (Scheme 2) [12]. Up to now, no other method was found for the preparation of 3,2-benzothiazepine 3,3-dioxide with the exception of 1-ethoxy-2,4,5-trihydro-3,2-benzothiazepine 3,3-dioxide, which was prepared in several steps [13].
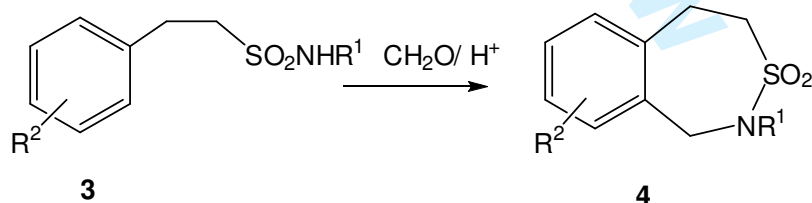
Scheme 2

The use of homogeneous catalysts has several disadvantages since they are toxic, corrosive, and produce a large amount of by-products which are difficult to separate from the reaction medium.

Heterogeneous catalysts offer several advantages such as mild reaction conditions, high selectivity, high yields and easy work-up procedures. In addition, solid catalysts can be

regenerated and are environmentally benign, allowing their multiple reuses with little waste released to the environment [14-16].

For these reasons various studies about the sulfonylamidomethylation of benzylsulfonamides **1** and 2-phenylethanesulfonamides **3** were made using heterogeneous catalysts.

We have employed Amberlyst 15 resins and more recently heteropolyacids H_3PWO_{40} and H_3PMoO_{40} supported on silica as a heterogeneous catalyst in the synthesis of 3,4-dihydro-1H-2,3-benzothiazine 2,2-dioxides **2** with good yields [17,18]. Also, Amberlyst resins were used in the efficient synthesis of 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxides **4** [19].

As continuation of our work on the development of useful synthetic methodologies, we have studied a mild and suitable method for the preparation of 3,4-dihydro-1H-2,3-benzothiazine 2,2-dioxides **2** and 1,2,4,5-tetrahydro-3,2-benzothiazepine 3,3-dioxides **4** by sulfonylamidomethylation of benzylsulfonamides and 2-phenylethanesulfonamides in the presence of a heterogeneous catalyst.

Among several solid acid catalysts investigated, sulfated zirconia has attracted much attention in the recent years because of its good catalytic activity, super-acidity, non-toxicity and low cost [20]. Among other reactions, it has been used in Friedel-Crafts acylation [21], stereocontrolled glycosidation [22], synthesis of coumarins by Pechmann reaction [23] and synthesis of 1,5-benzodiazepines [24].

Sulfated zirconia is a useful catalyst in many reactions under simple conditions, in the liquid phase as well as in the vapor phase, and it offers several advantages such as short reaction times, high selectivity and the easiness of work-up procedure.

Herein, we report a high yield sulfonylamidomethylation of benzylsulfonamides **1** and 2-phenylethanesulfonamides **3** catalyzed by sulfated zirconia. The influence of the thermal treatment of sulfated zirconia on the activity and selectivity in the synthesis of benzothiazine **2** and benzothiazepine **4** derivatives is also reported in the present work.

2. Experimental

2.1. Materials

Melting points were determined with a Buchi apparatus. ^{1}H-NMR spectra were obtained on a Varian-Mercury (200 MHz) spectrometer. Thin layer chromatography was performed on silica gel sheets 60 F_{254} (Merck). Silica gel 60 (70-230 Mesh) (Fluka) was used for column chromatography. Reagent grade s-trioxane was used. Reagent grade

solvents were used; 1,1,2-trichloroethane and 1,1,2,2-tetrachloroethane were distilled over phosphorous pentoxide and stored over 4 Å Molecular Sieves. The purity of the isolated compounds was checked by comparison with authentic samples prepared according to known procedures (^{1}HRMN spectra, m.p., TLC) [11,12,19]. The known reaction products were characterized by melting point and ^{1}HNMR spectra. The identification of a new compound was made through ^{1}HNMR, ^{13}CNMR spectra and elemental analysis.

The benzylsulfonamides **1** and 2-phenylethanesulfonamides **3** were prepared from the corresponding benzyl and 2-phenylethyl halides following a general method [11,12]. Commercial SO_4^{2-}/ZrO_2 from Mel Chemical Co was dried at 110 ºC for 2 h in air and was subsequently calcined for 5 h in air atmosphere between 250 ºC and 800 ºC. It was used in the reaction without calcined, and calcined at the indicated temperatures.

2.2. Catalyst characterization

The samples were characterized by Raman microprobe, X Ray Diffraction and superficial acidity. Textural parameters, specific surface and pore volume, were determined by nitrogen adsorption at 77 K, in an Accusorb 2100E Micrometrics equipment (Table 1). Samples were outgassed at 100 ºC during 12 h before adsorption. The specific surface area was determined by the BET method. X-ray diffractograms were obtained in a Philips PW 1732/10 equipment using Cu Kα radiation Ni filter; 30mA and 40 kV, scanning angle between 5 and 60 ºC and scanning rate 1º/min. Raman spectra were obtained in a Lab RAM Infinity spectrometer (Jobin Yvon) equipped with a liquid nitrogen detector with spectral resolution of 3 cm^{-1}. The spectrometer was calibrated using the Si line at 521 cm^{-1} and MoO_3 lines at 818 and 996 cm^{-1}. The support was taken as reference.

The catalytic superficial acidity was measured by potentiometric titration with n-butylamine. A known mass of catalyst was suspended in acetonitrile (Baker) with stirring. Then, the suspension was titrated with a 0.05-N-acetonitrile solution of n-butylamine (carlo Erba), at a flow rate of 0,05 ml/min. The electrode potential variation was measured with a digital Instrumentalia pH-meter, using a Ag/AgCl electrode.

The initial electrode potential is considered indicative of the maximun strength of the acid sites, and the value (mEq amine/g catalyst) from which the plateau is reached as indicative of the total number of acid sites of the solid. The strength of the sites was

considered according the following scale: E > 100 mV (very strong sites); 0<E<100 mV (strong sites);-100<E<0 (weak sites), and E<-100 mV (very weak sites).

2.3. Reaction study

The reactions were performed in a batch reactor, by stirring a solution of sulfonamides **1** or **3** (1.0 mmol) and s-trioxane (0.33 mmol) in 1,1,2-trichloroethane or 1,1,2,2-tetrachloroethane and the catalyst for the specified time (Tables 2 and 3). The reactions were carried out at four different temperatures (35, 80, 115 and 140 ºC). The catalyst was removed of reaction mixture by filtration and the solvent evaporated. The crude products were purified by crystallization or by chromatography column on silica gel. The known reaction products were characterized by melting point and ^{1}HNMR spectra. The identification of the new compound (2d) was made through ^{1}HNMR, ^{13}CNMR spectra and elemental analysis.

The used catalysts were washed with fresh solvent followed by drying in air at 120 °C and reused in following experiments.

3. Results and discussion

3.1. Catalyst characterization

Typical powder X-ray diffractograms of catalysts without calcination, calcined at different temperatures, without use and after being used are shown in Fig.1. The crystallographic changes during calcination were monitored.

The samples before calcination and calcined at 250 ºC (A) were observed to be predominantly amorphous in nature. Whereas the fresh sample calcined at 550 ºC (B) contained only tetragonal (2θ = 30.24, 35.30 and 50.70) phases. For reused samples calcined at 550 ºC (C, D) the predominant phase is the tetragonal phase. With the increase in calcination temperature, the tetragonal phase diminishes while the monoclinic phase increases. In the samples calcined at 800 °C (E) only the monoclinic phase is present. As it was reported by Song and Sayari, it is evident that the calcination temperature of the amorphous zirconia has a significant influence on the crystallographic phase formed [25].
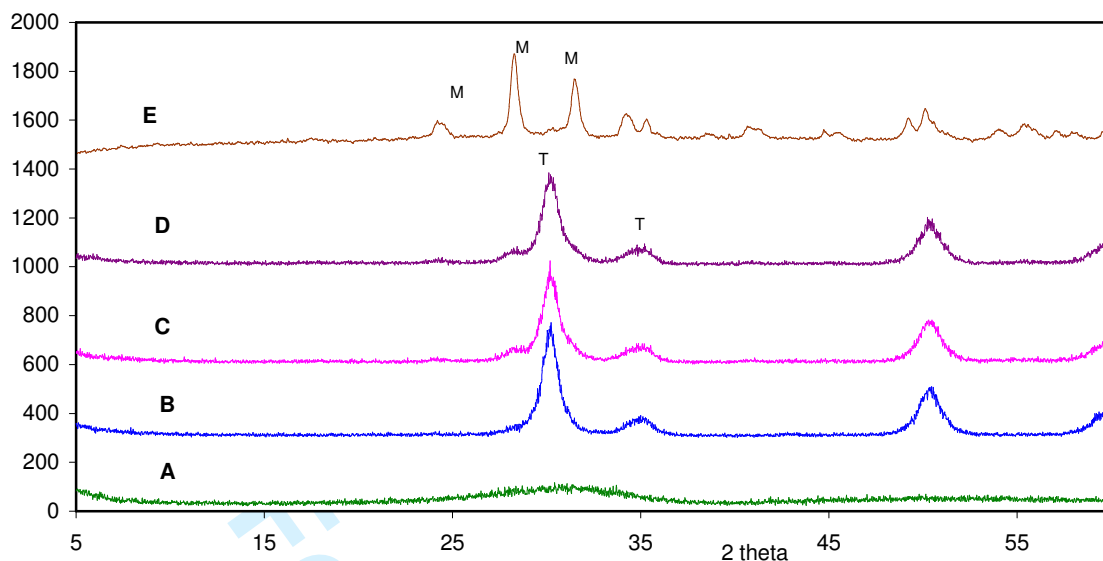
Figure 1. XRD patterns of sulfated zirconia. A) calcined at 250 ºC, B) fresh sample calcined at 550 ºC, C) used sample calcined at 550 ºC, D) reused sample calcined at 550 ºC, E) fresh sample calcined at 800 ºC.

According with XRD data, the Raman spectra of sample calcined at 550 ºC revealed bands pertaining to a tetragonal phase (149, 272, 316, 462 and 646 cm^{-1}) (Fig. 2). In the region 800-1400 cm^{-1}, bands of the surface sulfates are visible. Also, the region at 1146 and 1266 cm^{-1} corresponding to S=O stretching suggests the presence of different surface sulfate species.
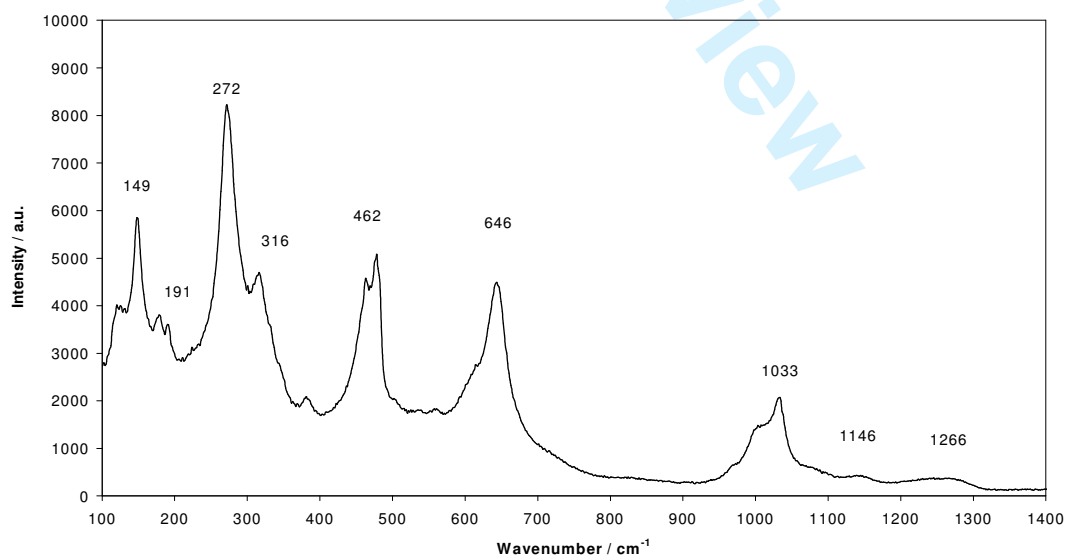

Figure 2. Raman spectra of sulfated zirconia calcined at 550 ºC.

3.2. Textural properties

In order to analyze the calcination temperature effect over textural properties, the specific surface and the pore volume of the catalysts was determined by N_2 adsorption. Table 1 shows the specific surface, pore volume and average pore radius content for sulfated zirconia without calcination, calcined at 250, 550 and 800 ºC, fresh and used in reaction.

Table 1. Textural properties of the catalyst at different conditions

SO_4^{2-}/ZrO_2	S_{BET} (m^2/g)	Vp (cm^3/g)	Average pore radius (Å)
without calcination	473	0.450	30.8
calcined at 250 ºC, fresh	384	0.370	29.7
calcined at 250 ºC, used	290	0.260	28.6
calcined at 550 ºC, fresh	349	0.300	29.5
calcined at 550 ºC, used	132	0,150	34.5
calcined at 550 ºC, reused	118	0.117	33.1
calcined at 800 ºC, fresh	15	0.034	71.0
calcined at 800 ºC, used	13	0.050	105.0

As shown in Table 1, the most important changes in the specific surface area and pore volume are produced during the calcination and catalytic reaction, especially in the samples calcined at 550 ºC. For the catalysts calcined at 800 ºC a high area loss was observed, which has been attributed to the elimination of surface sulfates from the zirconia, according to the S% content determined by TGA.

3.3. Reaction studies

Effect of calcination temperature

The SO_4^{2-}/ZrO_2 samples were used without calcination and calcined at 250, 550, 650 and 800 ºC. The effect of calcination temperature on the yield for the obtain products **2b** and **4b** was studied. The results are shown in Fig. 3. The best catalytic performance was obtained on the sulfated zirconia calcined at 550 ºC, which shows tetragonal structure and an important specific surface area. No changes were observed with further increase in calcination temperature to 650 ºC and low activity was developed with catalyst calcined at 800 ºC. According with the bibliography [26] the catalytic activity of sulfated zirconia could be associated with the formation of the tetragonal phase at 550 ºC.

Consequently, structural changes of the support and the lower specific area could be responsible for the deactivation of the catalyst calcined at 800 ºC. The change of

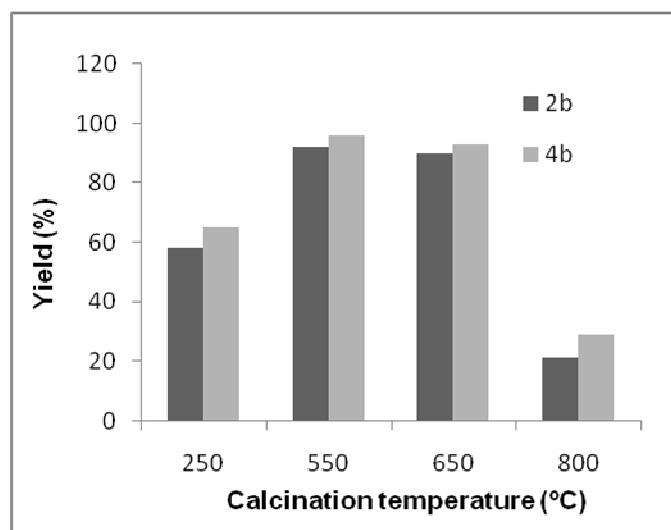zirconia phase modifies the support acid properties involving specific area loss of the material [27].

Fig. 3. Yield for **2b** and **4b** using catalysts calcined at 250, 550, 650 and 800 ºC

In order to estimate the maxima acidity of the catalysts, the potentiometric method with NBTA was used. The potentiometric titration curves in Fig 4 show how the calcination temperature can modify the acidity of catalyst. It can be observed that the initial electrode potential E is 430 and 80 mV for the SO_4^{2-}/ZrO_2 calcined at 550 and 800 ºC, respectively . Therefore, the catalyst calcined at 550 ºC presents very strong acid sites and the acidity decreases strongly when the sample is calcined at 800 ºC, which would explain the deactivation.
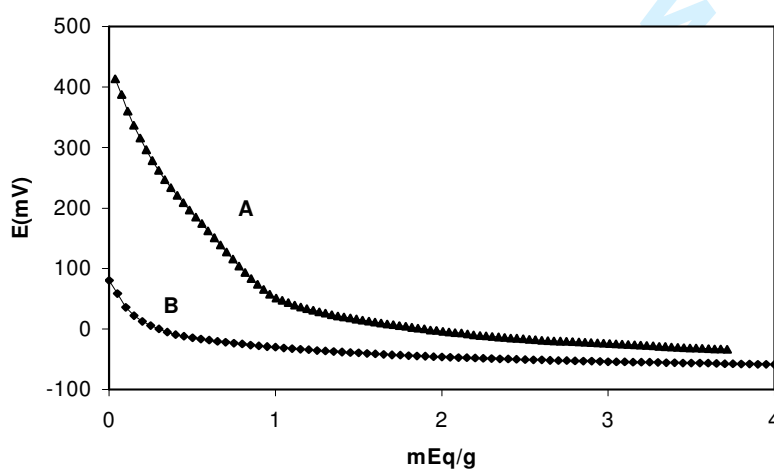

Fig.4. Potentiometric titration curves of the SO_4^{2-}/ZrO_2 calcined. A) 550 ºC, B) 800 ºC

Xu et al. [28] suggested that the sulfate removal from the surface catalysts eliminates the Brønsted acidity and decreases Lewis acid sites. On the other hand, Bravo et al. reported that the reaction mechanism involves Brønsted acids [11], which suggests a decrease in catalytic activity for zirconia calcined at 800 ℃.

Effect of reaction temperature

The catalytic activity of the SO_4^{2-}/ZrO_2 was highly dependent on the reaction temperature. Lower conversion was observed when the reaction was carried out at 35 ℃. When the reaction was performed at 115 ℃ (using 1,1,2-trichloroethane as solvent), the highest yields were obtained. Further increase in temperature to 140 ℃ using 1,1,2,2-tetrachloroethane as solvent did not have much effect on the reaction yield. In general, all the reactions were completed with high selectivity within 3 and 24 h, depending mainly on the sulfonamide employed. Lower times (between 3 and 6 h) are necessary in reactions for substrates with aliphatic substituents; in contrast, with bulky substituents the reaction time was extended to 24 h. In order to compare the effectiveness of this catalyst, the yields using SO_4^{2-}/ZrO_2 were compared with those obtained in previous studies using Amberlyst 15 resin and heteropolyacids H_3PXO_{40} supported on silica [17, 18, 19] (Tables 2 and 3). A good performance with high conversion was shown using sulfated zirconia and Amberlyst 15 resin [17,19]. However, the use of SO_4^{2-}/ZrO_2 offers comparative advantages respect to the Amberlyst 15 as higher stability at high temperatures, major resistance to magnetic stirring, high selectivity and lower retention of products on the active sites of catalyst.

Table 2. Cyclization of benzylsulfonamides **1** at 115 ℃ to give 2,3-benzothiazine 2,2-dioxides **2** using sulfated zirconia

Entry	R^1	R^2	Time (h)	Yield SO_4^{2-}/ZrO_2	Yield homogeneous acid[a]	Yield A-15[b]	Yield HPAs W and Mo[c]	Mp (℃) Found/Lit.
1a	H	H	6	82	68	100	68	75-76/74-75[a]
1b	Et	H	3	96	88	100	88	71-72/70-71[a]
1c	*i*-Pr	H	6	57	90	92	90	91-92/90-91[a]
1d	*n*-Bu	H	3	98	-	-	-	96-97
1e	$CH_2C_6H_4$	H	24	55	58	50	40	84-85/84-85[a]
1f	H	3-Cl	24	95	49	90	45	119-120/118-119[a]

[a]Using homogeneous acids [11]; [b]Using Amberlyst resins [17]; [c] Using heteropolyacids $H_3PW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ supported on SiO_2 [18].

Spectral data of new product, N-Butyl-3,4-dihydro-1H -2,3-benzothiazine 2,2-dioxide **2d** : [1]H nmr (200 MHz): δ 0.97 (t, 3H, J= 7.5 Hz, (N(CH$_2$)$_3$C$\underline{H}_3$); 1.39 (sex, 2H, J= 7.5

Hz, N(CH$_2$)$_2$C$\underline{H}_2$CH$_3$); 1.59 (m, 2H, NCH$_2$C$\underline{H}_2$CH$_2$CH$_3$); 3.19 (t, 3H, J= 7.3 Hz NC$\underline{H}_2$CH$_2$CH$_2$CH$_3$); 4.23 (s, 2H, PhC$\underline{H}_2$S); 4.49 (t, 3H, Ph-C$\underline{H}_2$N); 7.01-7.39 (m, 4H, Ph); ^{13}C nmr (62.9 MHz): δ 13.8 (N(CH$_2$)$_3$C$\underline{H}_3$); 19.8 (N(CH$_2$)$_2$C$\underline{H}_2$CH$_3$) ; 30.3 (NCH$_2$C$\underline{H}_2$CH$_2$CH$_3$);   48.1 (NC$\underline{H}_2$CH$_2$CH$_2$CH$_3$); 49.0 (Ph-C$\underline{H}_2$N); 52.5 (PhC$\underline{H}_2$S) 127.3; 127.7; 128.2; 129.8, 130.0; 130.8 (C-5, C-6, C-7, C-8, C-9, C-10) Anal calculated for C$_{12}$H$_{19}$NO$_2$S (239.11): C, 61.63; H, 7.56; N, 5.53; O, 12.63; S, 12.66; found: C, 61.60; H, 7.62; N, 5.47; O, 12.63; S, 12.97.

Table3. Cyclization of 2-phenylethanesulfonamides **3** at 115ºC to give 3,2-benzothiazepine 3,3-dioxides **4** using sulfated zirconia

Entry	R^1	Time (h)	Yield SO$_4^{2-}$/ZrO$_2$	Yield homogeneous acid[a]	Yield A-15[b]	Mp (ºC) Found/Lit.
3a	H	9	92	89	92	163-164/163-164[a]
3b	Et	3	92	-	92	94-95/95-96[b]
3c	*i*-Pr	7	42	-	42	92-93/91-92[b]
3d	*n*-Pr	9	49	-	53	78-79/78-79[b]
3e	*n*-Bu	3	84	-	84	79-78/78-79[b]
3f	C$_6$H$_{11}$	24	-	82	-	159-160[a]
3g	CH$_2$C$_6$H$_4$	24	85	73	85	137-138/137-138[a]

[a]Using homogeneous acids [12]; [b] Using Amberlyst resins [19]

Effect of different catalyst loading

The effect of catalyst loading using sulfated zirconia calcined at 550 ºC was studied to obtain product **2b** at 115 ºC in the range 20 to 120 wt%. The conversion of reactant increased with the increase in the amount of catalyst as shown in Fig. 5. The best results were obtained with 100 wt% of catalyst loading. Therefore, further reactions were carried out in this condition.
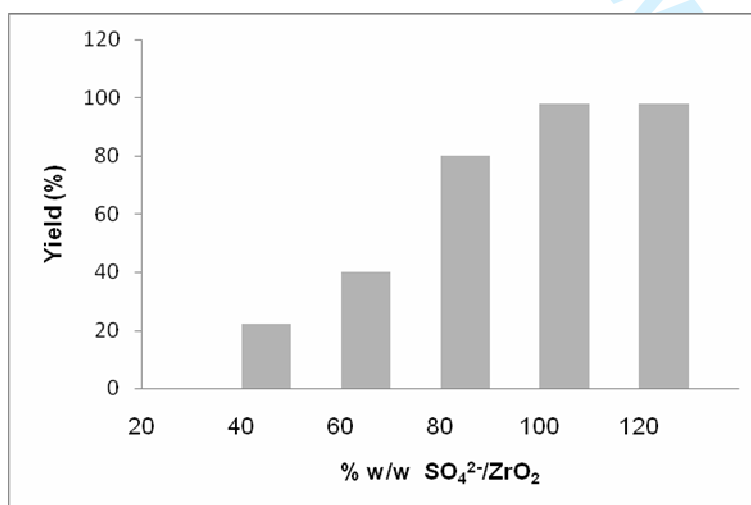

Fig. 5. Yield for **2b** using different catalyst loading at 115 ºC.

Reuse of the catalyst

The recovered catalyst was reused three times consecutively with a negligible change of its activity. For example, compound **2b** was obtained in a 96 % yield using fresh catalyst. With recovered sulfated zirconia the yields decrease by 2-5% (Fig. 6)
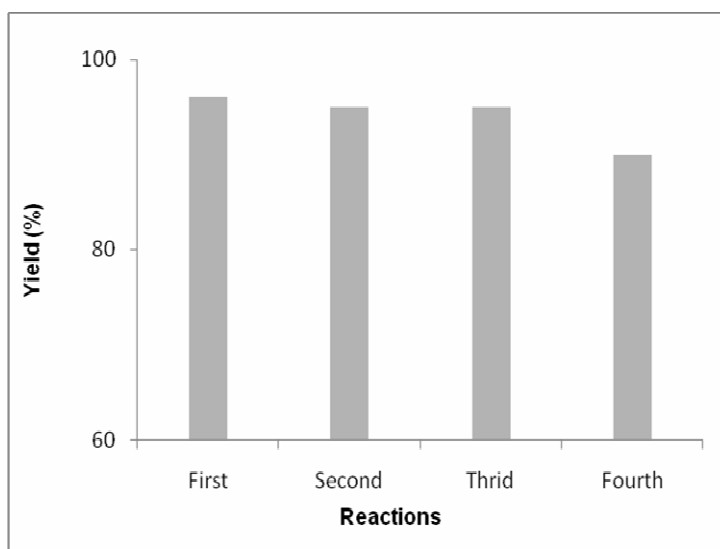

Fig. 6. Recycling SO_4^{2-}/ZrO_2 in reactions for **2b** after activation by calcination at 550 ºC.

4. Conclusion

In conclusion, sulfated zirconia is an efficient catalyst for the synthesis of 2,3-benzothiazines **2** and 3,2-benzothiazepine **4** by sulfonylamidomethylation of benzylsulfonamides **1** and 2-phenylethane sulfonamides **3**. The catalytic activity of SO_4^{2-}/ZrO_2 is influenced by the calcination temperature, being the sample calcined at 550 ºC the most effective for the reaction, which is attributed to the formation of the tetragonal structure and a higher specific area on catalyst.

The SO_4^{2-}/ZrO_2 offers comparative advantages respect to the other catalysts as higher stability at high temperatures, major resistance to magnetic stirring, high selectivity and lower retention of products on the active sites of the catalyst. It shows good yields, high selectivity and operational simplicity. It is important to mention that the catalyst was recovered and reused up to three times without any noticeable loss of activity.

Compared with the use of homogeneous acids, a notable advantage of this heterogeneous catalyst is that decreases the production of chemical waste.
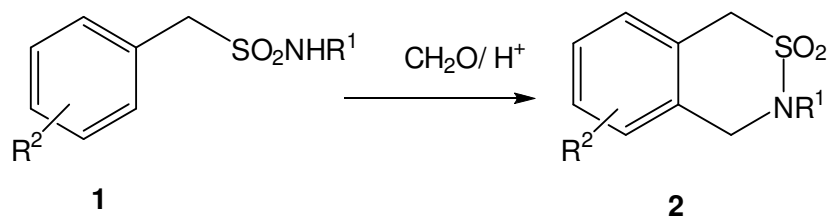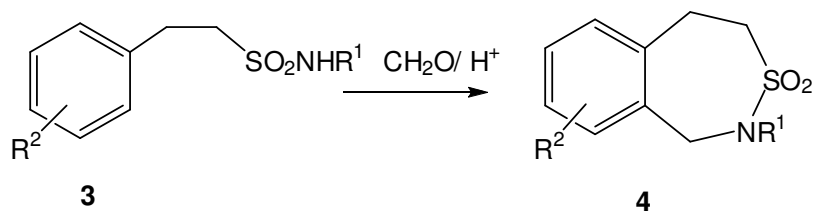
References

1. J. G. Lombardino, E. H. Wiseman, W. Mclamore (1971) J. Med. Chem. 14:1171.

2. D. Turck, U. Busch, G. Heinzel , H. Narjes , G. Nehmiz (1996) Clin. Pharmacol. 36:79.

3. A. Baruffini, G. Pagani, L. Amoretti (1967) Il Farmaco 22:528.

4. R. Fringuelli, F. Schiaffella , A. Vecchiarelli (2001) J. Chemother. 13:9.

5. G. J. Wells, M. Tao, K. A. Josef, R. Bihovsky (2001) J. Med. Chem. 44:3488.

6. R. Bihovsky, M. Tao, J. P. Mallamo, G. J. Wells (2004) Bioorg. Med. Chem. Lett. 14:1035.

7. M. B. Tollefson, S. A. Kolodziej, T. R. Fletcher, W. F. Vernier, J. A. Beaudry, B. T. Keller , D. B., Reitz (2003) Bioorg. Med. Chem. Lett. 13:3727.

8. C. Root, C.D.Smith, S.S. Sundseth, H.M. Pink, J.G. Wilson, M.C. Lewis (2000) J. Lipid Research 43:1320.

9. G. De Sarro, A. Chimirri, A. De Sarro, R. Gitto, S. Grasso, M. Zappalà (1995) Eur. J. Med. Chem. 30:925.

10. M. Makosza, K. Wojciechowski (1992) Synthesis 571.

11. O. Orazi, R. A. Corral, R. D. Bravo (1986) J. Heterocycl. Chem. 23:1701.

12. J. Zinczuk, J.I. H. Sorokin, O. Orazi, R.A. Corral (1992) J. Heterocycl. Chem. 29:859.

13. H. Bohme, F. Ziegler (1974) Liebigs Ann. Chem. 734.

14. T. Peters, N. Benes, A. Holmen, A. Keurentjes (2006) J. Appl. Catal. A: Gen. 297:182.

15. B. Das, K. Damodar, N. Chowdhury, R. Kumar (2007) J. Mol. Catal. A: Chem. 274:148.

16. A. Wolfson, O. Shokin, D. Tavor, J. Mol. Catal. A: Chem. 226 (2005) 69.

17. A. S. Cánepa, R. D. Bravo, Synth. Commun. 32 (2002) 3675.

18. A. S. Cánepa, L. D. Sasiambarrena, R. D. Bravo, Synth. Commun. 38(15) (2008) 2655.

19. A. S. Cánepa, L. D. Sasiambarrena, R. D. Bravo, Synth. Commun. (in press)

20. B. M. Reddy, P. M. Sreekanth, P. Lakhsmanan, J. Mol. Catal. A: Chem. 237 (2005) 93.

21. Deutsch, H.A. Prescott, D. Muller, E. Kemnitz, H. Lieske, J. Catal. 231 (2005) 269.

22. K. Toshima, H. Nagai, K. Kasumi, K. Kawahara, S. Matsumura, Tetrahedron 60 (2004) 5331.

23. T. Beena, K. M. Mishra, R. V. Jasra, J. Mol. Catal. A: Chem. 276 (2007) 47.

24. B. M. Reddy, P. M. Sreekanth, Tetrahedron Lett. 44 (2003) 4447.

25. X. Song, A. Sayari, Catal. Rev.-Sci.Eng. 38 (1996) 329.

26. C. Morterra, G. Cerrato, F. Pinna, M. Signoretto, J. Catal. 157 (1995) 109.

27. Y. Zhao, W. Li, M. Zhang, K. Tao, Catal. Commun. 3 (2002) 239.

28. B. Xu, W.M.H. Sachtler, J. Catal. 167 (1997) 224.
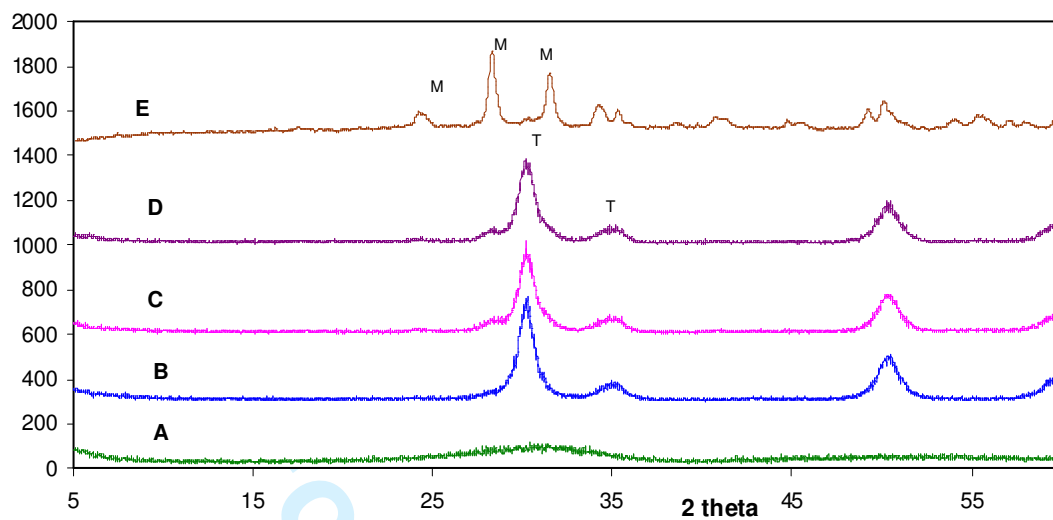
Scheme 1

Scheme 2

Figure 1. XRD patterns of sulfated zirconia A) calcined at 250ºC, B) fresh sample calcined at 550ºC, C) used sample calcined at 550ºC D) reused sample calcined at 550ºC, E) fresh sample calcined at 800ºC.
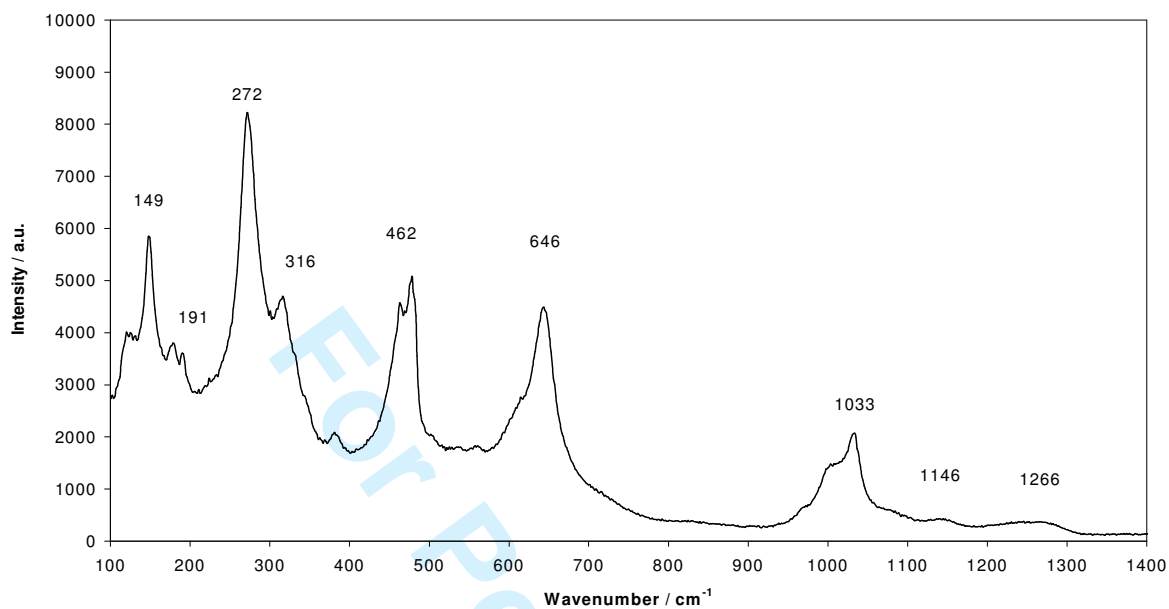
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Figure 2. Raman spectra of sulfated zirconia calcined at 550 ºC.

Table 1. Textural properties of the catalyst at different conditions

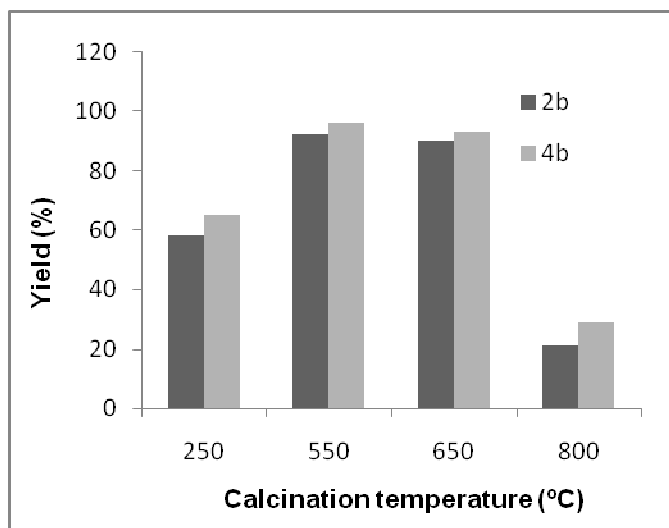| SO_4^{2-}/ZrO_2	S_{BET} (m^2/g)	Vp (cm^3/g)	Average pore radius (Å)
without calcination	473	0.450	30.8
calcined at 250 ºC, fresh	384	0.370	29.7
calcined at 250 ºC, used	290	0.260	28.6
calcined at 550 ºC,fresh	349	0.300	29.5
calcined at 550 ºC, used	132	0,150	34.5
calcined at 550 ºC, reused	118	0.117	33.1
calcined at 800 ºC,fresh	15	0.034	71.0
calcined at 800 ºC, used	13	0.050	105.0

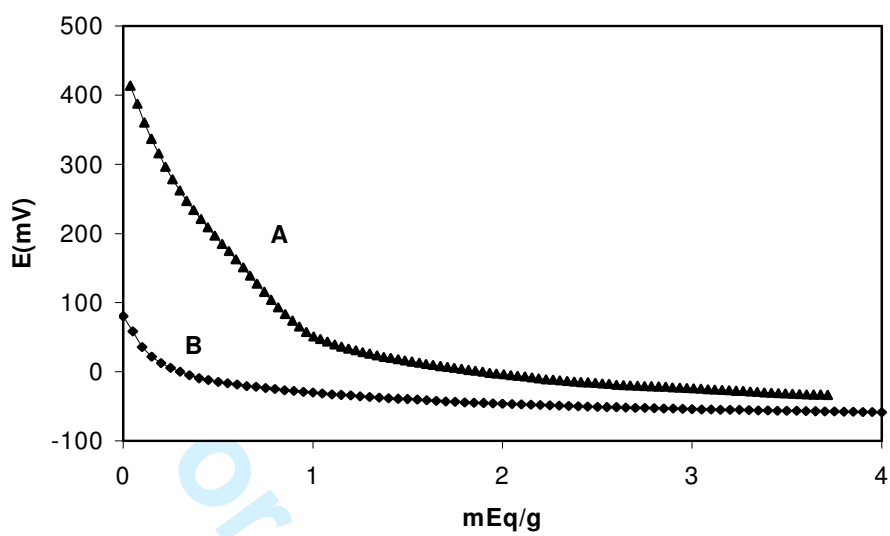**Fig. 3.** Yield for **2b** and **4b** using catalyst calcined at 250, 550, 650 and 800 ºC

Fig.4. Potentiometric titration curves of the SO_4^{2-}/ZrO_2 calcined. A) 550 ºC, B) 800 ºC

Table 2. Cyclization of benzylsulfonamides **1** at 115 ºC to give 2,3-benzothiazine 2,2-dioxides **2** using
sulfated zirconia

Entry	R^1	R^2	Time (h)	Yield SO_4^{2-}/ZrO_2	Yield homogeneous acid[a]	Yield A-15[b]	Yield HPAs W and Mo[c]	Mp (ºC) Found/Lit.
1a	H	H	6	82	68	100	68	75-76/74-75[a]
1b	Et	H	3	96	88	100	88	71-72/70-71[a]
1c	i-Pr	H	6	57	90	92	90	91-92/90-91[a]
1d	n-Bu	H	3	98	-	-	-	96-97
1e	$CH_2C_6H_4$	H	24	55	58	50	40	84-85/84-85[a]
1f	H	3-Cl	24	95	49	90	45	119-120/118-119[a]

[a]Using homogeneous acids [11]; [b]Using Amberlyst resins [17]; [c] Using heteropolyacids $H_3PW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ supported on SiO_2 [18].

Table3. Cyclization of 2-phenylethanesulfonamides **3** at 115ºC to give 3,2-benzothiazepine 3,3-dioxides

4 using sulfated zirconia

Entry	R^1	Time (h)	Yield SO_4^{2-}/ZrO_2	Yield homogeneous acid[a]	Yield A-15[b]	Mp (ºC) Found/Lit.
3a	H	9	92	89	92	163-164/163-164[a]
3b	Et	3	92	-	92	94-95/95-96[b]
3c	i-Pr	7	42	-	42	92-93/91-92[b]
3d	n-Pr	9	49	-	53	78-79/78-79[b]
3e	n-Bu	3	84	-	84	79-78/78-79[b]
3f	C_6H_{11}	24	-	82	-	159-160[a]
3g	$CH_2C_6H_4$	24	85	73	85	137-138/137-138[a]

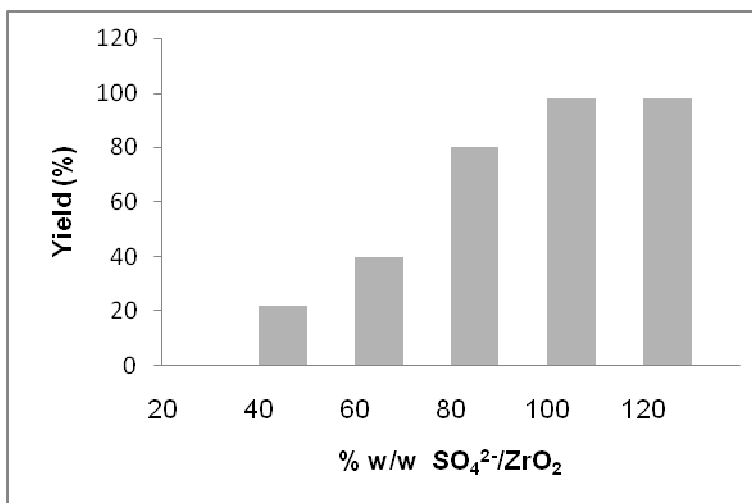[a]Using homogeneous acids [12]; [b] Using Amberlyst resins [19]

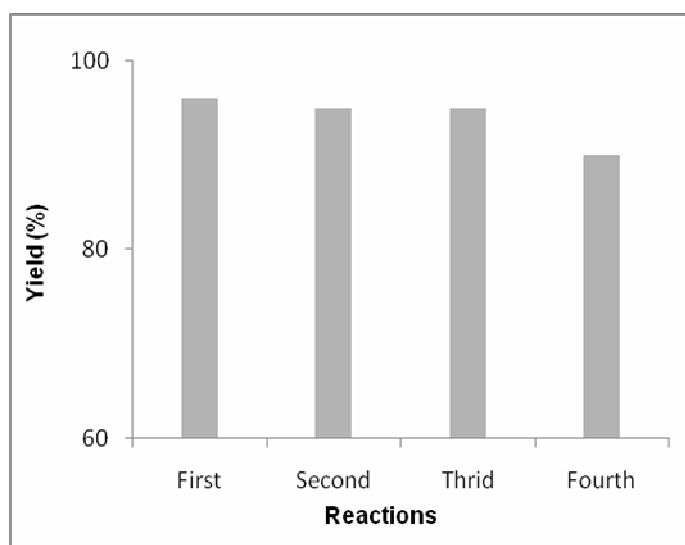**Fig. 5.** Yield for **2b** using different catalyst loading at 115 ºC.

Fig. 6. Recycling SO_4^{2-}/ZrO_2 in reactions for **2b** after activation by calcination at 550 ºC.