Mercedes Muñoz¹, Gustavo Pasquale², Angel Gabriel Sathicq¹, Gustavo Pablo Romanelli^{1,2,*}, Carmen Inés Cabello^{1,4,*} and Delia Gazzoli³

Volcanic ash as reusable catalyst in the green synthesis of 3*H*-1,5-benzodiazepines

https://doi.org/10.1515/gps-2019-0030 Received October 10, 2018; accepted April 16, 2019.

Abstract: The volcanic ash from the Andes mountain range (Puyehue-Cordon Caulle volcanic complex situated in western South America on the Argentinean-Chilean border) was used as heterogeneous acid catalyst in the suitable synthesis of 3*H*-1,5-benzodiazepines. The natural ashes were classified according to their particle size to generate the different catalytic materials. The catalysts were characterized by powder X-ray diffraction (XRD), scanning electron microscopy (SEM) with energy dispersive spectroscopy (EDS), vibrational spectroscopies (FT-IR and Raman), and textural properties were determined by N_2 adsorption (S_{BET}). Potentiometric titration with n-butylamine was used to determine the acidic properties of the catalytic materials. Several 3*H*-1,5-benzodiazepines were obtained by reaction of o-phenylenediamine and substituted 1,3-diphenyl-1,3-propanedione in solvent-free conditions, giving good to excellent yields of a variety benzodiazepines. The method was carried out in environmentally friendly conditions and it was operationally simple. The volcanic ash resulted in a safe and recyclable catalyst.

Carmen Inés Cabello, Centro de Investigación y Desarrollo en Ciencias Aplicadas 'Dr. J. J. Ronco', (CINDECA), CONICET - UNLP 47 N° 257 (1900) La Plata, Argentina; CIC-PBA Researcher - Facultad de Ingeniería, Univ. Nac. de La Plata, Argentina

Mercedes Muñoz, Centro de Investigación y Desarrollo en Ciencias Aplicadas 'Dr. J. J. Ronco', (CINDECA), CONICET - UNLP 47 N° 257 (1900) La Plata, Argentina, e-mail: mmercedes@quimica.unlp.edu.ar Gustavo Pasquale, Centro de Investigación en Sanidad Vegetal, (CISaV), Facultad de Ciencias Agrarias y Forestales, UNLP. Calles 60 y 119 s/n, La Plata, Bs. As., Argentina

Angel Gabriel Sathicq, Centro de Investigación y Desarrollo en Ciencias Aplicadas 'Dr. J. J. Ronco', (CINDECA), CONICET - UNLP 47 N° 257 (1900) La Plata, Argentina

Delia Gazzoli, Dipartimento di Chimica, Università di Roma "La Sapienza", P. le Aldo Moro 5, Roma, Italia **Keywords:** volcanic ash; benzodiazepines; green chemistry; heterogeneous catalysis; solvent-free reaction

1 Introduction

In the last three decades, methods based on the use of heterogeneous catalysts have been widely used in laboratory and industrial processes because they play an important role in the current bid for the development of suitable synthetic processes [1].

The requirement of green procedures leads to the use of different environmentally friendly reaction conditions; among them, the substitution/elimination of toxic organic solvents in organic transformations is one of the most important targets in 'green' chemistry [2,3]. Formerly, it was thought that a reaction could not be carried out without the presence of a solvent; however, this statement is no longer valid. In fact, many reactions occur more efficiently and selectively than those carried out in the presence of a solvent. Such reactions under solvent-free conditions are simple to handle, comparatively easy to operate, reduce pollution, and are especially important in laboratory research and particularly in the industry [4]. In this context, a particularly important area is the development of suitable synthetic processes in the absence of solvents [1]. Many reports show the efficiency of performing solventfree reactions, especially in the heterocyclic chemistry synthesis of indoles [5], coumarins [6,7], 2-arylchromone [8], quinoxalines, dipyridophenazines [9], and many others.

The use of reusable solid acid rather than inorganic or organic liquids, such as hydrochloric, sulfuric, *p*-toluenesulfonic and trichloroacetic acids as catalyst, is another approach to the implementation of green procedures. Numerous inorganic, organic and hybrid materials can catalyze different reactions with several advantages and excellent results [10].

Particularly, the use of clay and related materials as suitable catalysts is a field of increasing worldwide importance. Numerous studies on basic and applied research have been carried out in the last three decades.

^{*} Corresponding authors: Gustavo Pablo Romanelli, Centro de Investigación y Desarrollo en Ciencias Aplicadas 'Dr. J. J. Ronco', (CINDECA), CONICET - UNLP 47 N° 257 (1900) La Plata, Argentina; Centro de Investigación en Sanidad Vegetal, (CISaV), Facultad de Ciencias Agrarias y Forestales, UNLP. Calles 60 y 119 s/n, La Plata, Bs. As., Argentina, e-mail: gpr@quimica.unlp.edu.ar;

The use of clays as solid acid catalysts has aroused great interest because they are noncorrosive, environmentally compatible, inexpensive, nontoxic, and generally allow for simple isolation of reaction products and easy catalyst separation [1,11,12].

There are several reports about the use of clay material in suitable green organic synthesis, e.g., reaction of enaminones, β-ketoesters and ammonium acetate to form pyridines; addition of carbenes to C=N double bonds to produce aziridines; synthesis of methylenedioxyprecocene (MDP), a natural insecticide; solvent-free method for Biginelli reaction under IR irradiation; coumarin-3-carboxylic acids from malonic acid and salicylic aldehydes; furano-/pyrano-quinolines from aryl amines and dihydrofuran/dihydropyran and multicomponent Povarov reaction for the synthesis of quinolones [11]. In this regard, our research group reported the use of bentonite in the benzodiazepine synthesis (acid catalysis) [13] and the selective hydrogenation of cinnamaldehyde [14].

Volcanic ashes particularly amorphous are aluminosilicate materials. They are well known and their applications were reported several years ago. Volcanic ashes can be used in abrasives, cleansers, scouring or polishing compounds, concrete admixtures, glazes for pottery, bricks and tiles, glass wool, enamels, lightweight products, fertilizers, asphalt constituents, acoustical tiles, sweeping compounds, paint fillers, insecticide carriers, absorptive packing material, and in the purification of lard and tallow [15]. Some more recent applications of these materials involve their transformation to zeolites and their use as catalyst in different organic reactions on a laboratory and industrial scale [16].

Benzodiazepines are bicyclic compounds that possess a phenyl group fused with a heptagonal heterocyclic ring with two nitrogen atoms in their structure. These compounds have been previously studied due to their pharmacological properties, such as biological activity as anxiolytic, sedative, antidepressant [17], antifungal, and antibacterial agents [18], as insecticides and herbicides [19], and as light-sensitive fibers in photography [20].

Benzodiazepines have been usually synthesized by the condensation of 1,2-phenyldiamines with β-dicarbonyl compounds using different inorganic or organic acid promoters, e.g., polyphosphoric acid [21], acetic acid [22], HY zeolite [23], p-toluenesulfonic acid [24], N-propylsulfamic acid/nanosilica [25], indium tribromide [26], zinc montmorillonite [27], sulfated zirconia [28], MCM-22 zeolite [29], heteropolyacids [30,31], among others [32,33].

In the present paper, we report the treatment, characterization and application as catalysts of volcanic ashes obtained from the Puvehue-Cordon Caulle volcanic complex (Argentina-Chile), located at 2236 m above sea level, which is part of the southern Andes system. The last volcanic eruption started on June 4 2011. The dominance of regional "westerly" winds has been responsible for the transport, dispersion and accumulation of tephras along the eastern mountain chain, in Argentine territory. In this context, the volcanic eruption produced large deposits of pyroclastic material in northern Patagonia [34,35].

The catalysts made of selected particle size were characterized by Raman and FT-IR spectroscopies, powder X-ray diffraction (XRD), scanning electron microscopy and energy dispersive spectroscopy (SEM-EDS) analysis and textural properties (S_{RET}) . Acidic properties were determined through potentiometric titration with n-butylamine. We studied the application of these recyclable solid catalysts in a simple, convenient, efficient, and ecofriendly process for the preparation of 3*H*-1,5-benzodiazepines in solvent-free conditions.

2 Experimental

2.1 Catalyst pretreatment

Volcanic ashes from the Puyehue-Cordon Caulle volcanic complex (PVA), collected from natural accumulations in S. C. de Bariloche (Río Negro Province, Argentina), were washed with distilled water at room temperature for 72 h, dried and separated according to particle size by sieving. The particle sizes were selected using four mesh sizes: greater than #40 (0.420 mm), #40-60 (0.420-0.250 mm), #60-100 (0.250-0.149 mm) and lower than #100 (0.149 mm).

The systems were named PVA N, where N stands for the mesh size (PVA 40, PVA 40-60, PVA 60-100, and PVA 100). Ashes without any treatment were called natural PVA.

Commercial acid catalysts based on natural montmorillonite modified by hydrothermal treatment (K-10 and K-30 from Fluka, general formula (Al₄(Si₄O₁₀)₂(OH)₄)) were evaluated for comparison.

2.2 Catalyst characterization

The PVA powder X-ray diffraction patterns were collected with Philips PW-1732 equipment (Cu Kα radiation, Ni filter).

The scanning electron microscopy and energydispersive X-ray spectroscopy microanalysis (SEM-EDS) of the materials was performed in a Philips 505 SEM equipped with EDAX 9100.

Textural properties and specific surface area of the PVAs were determined using the Brunauer-Emmett-Teller (BET) multipoint method performed from the N₂ adsorption-desorption isotherms using Micromeritics ASAP 2020 equipment.

Vibrational FT-IR and Raman spectra of the catalysts were performed with a Thermo Bruker IFS 66 FT-IR (using KBr pellets) and with a Renishaw spectrometer, respectively.

The acid strength and number of acid sites of the solids were determined by potentiometric titration with *n*-butylamine in acetonitrile. The titration was conducted with 94 Basic Titrino Metrohm equipment using a double junction electrode.

For further details on experimental data, see Supplementary material.

2.3 Catalytic test

All the reactants were provided by Aldrich and used without further refinement. Melting points were measured in open capillary tubes. Thin layer chromatography (TLC) was performed on UV-active aluminum-backed plates of silica gel. The nuclear magnetic resonance of ¹H and ¹³C (¹H-NMR and ¹³C-NMR) spectra were determined on a Bruker 400 MHz spectrometer.

The synthesis of benzodiazepines was achieved by combination of 1,3-diphenyl-1,3-propanedione with the corresponding o-phenyldiamine added to the solid catalyst (1% mmol with respect to dione). The process was conducted at 130°C under magnetic stirring. The pure benzodiazepines were characterized by TLC and physical constants (comparison with standard samples) and by ¹H-NMR and ¹³C-NMR analysis.

In order to study the catalyst reusability, after the separation from the reaction media, the catalyst was washed with toluene and dried in vacuum at 80°C up to constant weight. For additional experimental and characterization details, see Supplementary material.

3 Results and discussion

3.1 Catalyst characterization

3.1.1 X-ray diffraction

The XRD pattern of the different particle fractions of PVA presented the amorphous phase mainly, with vitreous

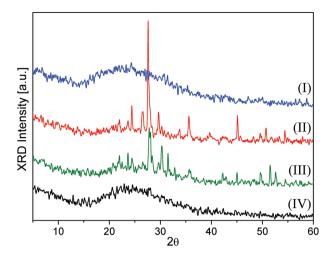


Figure 1: Comparative XRD patterns for catalysts based on volcanic ash materials: (I) PVA 40, (II) PVA 40-60, (III) PVA 60-100, and (IV) PVA 100.

characteristics as shown in Figure 1 (lines I-IV). Fractions of PVA 40-60 and 60-100 (0.420-0.250 mm and 0.250-0.149 mm respectively) also exhibited the characteristic peaks of crystalline phases (Figure 1, lines II and III) [35], which can be ascribed to the presence of iron oxide phases such as magnetite (PDF 80-0390) and hematite (PDF 89-2810). These phases exhibited their main peaks at $2\theta = 30^{\circ}$ and 35°. They also presented crystal phases of quartz (PDF 79-1906), plagioclase (CaAl₂Si₂O₆) and pyroxene (Mg₂Si₂O₆) (PDF 89-1463, 85-1740, 88-2377), with their major intensity peaks located about 26.5°, 28° and 30° of 2θ [36,37].

3.1.2 Scanning electron microscopy and energy dispersive spectroscopy

Figures 2a-d show the SEM images of the volcanic pyroclastic material of different fractions. It can be observed that the major component corresponds to pumiceous-type material, dominated by vesiculated particles (cavity formed by entrapment of a gas bubble during solidification) with few connections among the channels and pores.

SEM-EDS analysis showed the average composition of natural and washed ashes in all systems (Table 1). According to EDS results, the ashes are basically aluminosilicates, the SiO₂/Al₂O₂ ratio in the systems being between 2 and 4. The decrease of Al content can be associated with the enrichment of Si species (crystalline or glassy). Those fractions with a particle size between #40-60 and #60-100 contain about 5% more Fe. This fact suggests the existence of mixed valence iron oxides or related phases (magnetitetype) containing Fe, Mg, Al, and Ti [36,37].

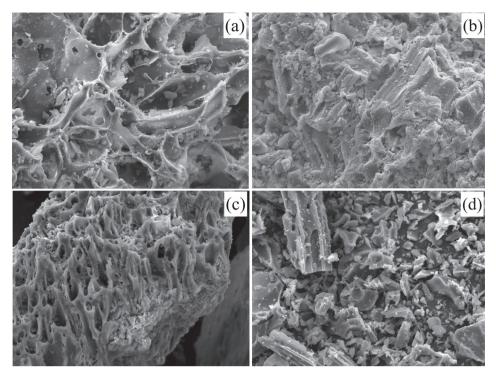


Figure 2: SEM micrographs of the volcanic ash studied (mag. 500x): (a) PVA 40, (b) PVA 40-60, (c) PVA 60-100, and (d) PVA 100.

Table 1: EDS chemical data for the studied ashes and K-materials.

Element (oxide)	PVA40 (% m/m)	PVA40-60	PVA60-100	PVA100	Natural PVA
Na ₂ O	5.4	4.5	4.6	3.8	5.2
MgO	0.2	3.1	2.4	0.4	0.8
Al ₂ O ₃	15.0	14.2	16.7	14.2	14.2
SiO ₂	66.3	67.0	55.3	70.1	73.2
K ₂ O	3.9	1.3	2.5	3.2	1.9
CaO	2.7	2.2	6.1	2.7	1.1
TiO ₂	0.0*	0.4	2.5	0.0*	0.3
Fe ₂ O ₃	6.5	7.2	9.9	5.5	3.6
Si/Al#	3.8	4.0	2.8	4.2	8.7

^{*} not detected by EDS; # in atoms

The K-10 and K-30 systems are commercial aluminosilicates based on natural montmorillonite with the general formula $(Al_4(Si_4O_{10})_2(OH)_4)$. They were obtained by acid hydrothermal treatment. EDS chemical data for K-10 and K-30 systems are listed in Table 1. The ratio SiO₂/Al₂O₂ was around 3-4, similar to those found for ashes. Fe, Ti and Mg traces were also found.

3.1.3 Textural properties

A variability of the textural properties in the different fractions of ashes can be observed (Table 2). It was

Table 2: BET and pore data for different fractions of volcanic ashes.

	S _{BET} (m²/g)	Total pore vol. (cm³/g)	Pore size (Å)
PVA 40	3.7	0.007	75.5
PVA 40-60	1.4	0.005	151.0
PVA 60-100	45.5	0.200	191.8
PVA 100	2.0	0.005	106.3
natural PVA	1.5	0.003	85.1
K-10	225.9	0.280	50.1
K-30	222.9	0.340	60.2

found that the BET area was independent of particle size, except for VPA 60-100 that presented the highest surface area (45 m²/g). The surface area of the rest of the ashes was between 1 and 4 m²/g. In addition, the material presented meso- and macropores (50-500 Å according to IUPAC convention), thus indicating its low overall density [35-38].

3.1.4 Fourier transform infrared spectroscopy

Figure 3 shows the comparative FT-IR spectra of ashes and K systems in the frequency range of 4000 to 400 cm⁻¹. The FT-IR vibrational spectra of PVA systems presented the characteristic signals of aluminosilicates (Figure 3).

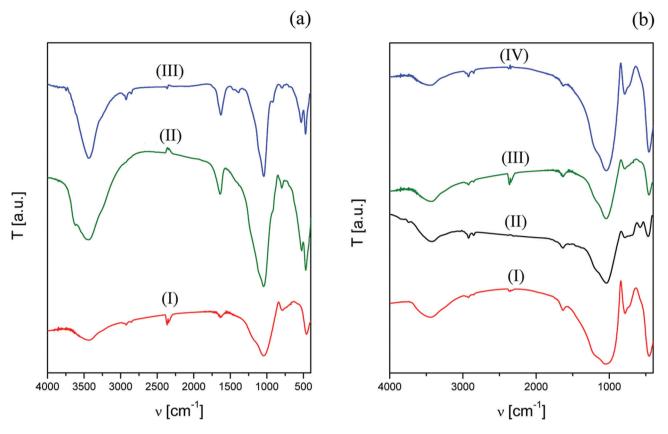


Figure 3: FT-IR comparative spectra of: (a) (l) K-10, (II) K-30, and (III) natural volcanic ashes; (b) (l) PVA 100, (II) PVA 40-100, (III) 40-60, and (IV) PVA 40.

The spectral bands around 3450 cm⁻¹ could be attributed to ν O-H stretching and those around 1630 cm⁻¹ to the δ H-OH; the ν_s and ν_{as} T-O (Si/Al-O) in tetrahedral environment appeared at 1050-1100 and 790 cm⁻¹, respectively, and network stretching modes at 460 cm⁻¹. The broadening of the bands below 1500 cm⁻¹ could be attributed to the coupling between different vibrational modes of the T-O units due to the inherent structural distortion of amorphous systems [37].

The K-10 and K-30 systems also have the characteristic spectrum of aluminosilicates, but in this case the bands are more defined due to their higher crystallinity and more defined structure.

3.1.5 Raman spectroscopy

The presence of microcrystals and vitreous particles in the PVA was determined by Raman microprobe spectroscopy [37]. Raman spectroscopy of vitreous materials gave low resolution spectra due to the structural disorder [37]. In Figure 4, the Raman spectrum

of a part of the PVA selected under optical microscope presents signals at 999, 664, 325 cm⁻¹, characteristic of pyroxene (997, 667 and 322 cm⁻¹) and a line centered at 530 typical of plagioclase (~510 cm⁻¹) [37]. The Raman spectra of the crystal phases were in concordance with those suggested by XRD.

3.1.6 Potentiometric titration

The acidity measurements of the catalysts by means of potentiometric titration with n-butylamine let us estimate the total number of acid sites (where the plateau is reached) and their acid strength ($E_{\rm initial}$), Figure 5. As shown in Figure 5, the PVA systems present weak acid sites ($E_{\rm initial}$ in the range of -70.7 and -25.9 mV). The total number of acid sites is 0.7, 0.55, and 0.65 meq/g of solid for PVA 40, PVA 40-60, and PVA 60-100, respectively, i.e., a small number of acid sites. However, the PVA 100 system presented two types of acid sites: weak and very weak ones corresponding to an $E_{\rm initial}$ of -25.9 and 88.0 mV, respectively [38].

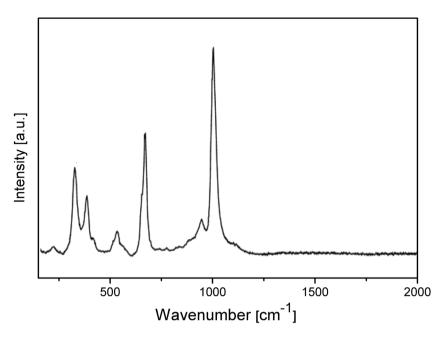


Figure 4: Raman microprobe spectra for natural PVA.

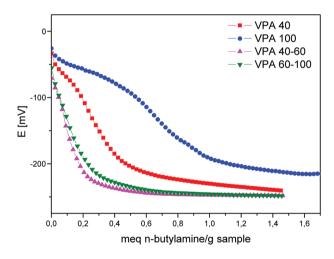


Figure 5: Potentiometric titration of PVA.

3.2 Catalytic test

The condensation reaction was initially studied using 1-phenyl-3(2 hydroxyphenyl)-1,3-propanedione and 1,2-phenylendiamine as substrates (Scheme 1). From this point, different reaction conditions were checked, such as temperature, time, molar ratio of reactants, catalyst amount, and catalyst reusability. The reaction conditions were: 130°C, 10 min, under solvent-free conditions using a 1:1 molar ratio of substrates.

In a blank experiment, without the presence of catalyst, no products were detected by TLC, indicating

that the presence of a catalyst is necessary (Table 3, entry 8). Commercial clays Montmorillonite K-10 and Montmorillonite K-30, tested for comparison purposes (Table 3, entries 1 and 2), yielded conversions of 48% and 55% with a benzodiazepine selectivity of 79% and 84%, respectively. In both cases, the yields of pure benzodiazepine were 38% and 46% respectively.

Results of catalytic tests in solvent-free conditions with different ashes as catalysts are summarized in Table 3 (entries 3-7). There is an apparent increase in the reaction yields for three PVA catalysts compared to the natural PVA (44%, Table 3, entry 3); PVA 40-60 (58%, Table 3, entry 4), PVA 60-100 (64%, Table 3, entry 6), and PVA 100 (58%, Table 3 entry 7). In all cases, benzodiazepine selectivity was high, between 82% and 89% (Table 3, entries 1-7). The system that showed the best catalytic performance was PVA 60-100, that with the highest Fe and Ti content and with the largest pore size (Tables 1 and 2). So, the catalytic activity is related to the Fe and Ti content, which could be ascribed to the larger number of Lewis acid sites given by the presence of Fe and Ti and greater availability of active sites due to larger pore size.

The effect of reaction time on reaction yields at the selected temperature of 130°C was also tested at four different times: 10, 20, 30 and 40 min (Table 4). An excellent yield was obtained at 20 min of reaction (86%, Table 4, entry 2), without any variation at longer reaction times such as 40 min (84%, Table 4, entry 4). In all cases, the selectivity ranged between 83% and 91%.

Scheme 1: Scheme of reaction.

Table 3: Catalyst effect.

Entry	Catalyst	Conv. (%)	Benzodiazepine selectivity (%)	Other selectivity (%)	Yield pure benzodiazepine (%)
1	Montmorillonite K-10	48	79	10	38
2	Montmorillonite K-30	55	84	9	46
3	Natural PVA	57	77	13	44
4	PVA 40	51	80	10	41
5	PVA 40-60	58	83	10	48
6	PVA 60-100	64	86	9	55
7	PVA 100	58	81	11	47
8	No Catalyst	0	_	_	_

Table 4: Time effect for PVA 60-100.

Entry	Time (min)	Conv. (%)	Benzodiazepine selectivity (%)	Other selectivity (%)	Yield pure benzodiazepine (%)
1	10	64	86	9	55
2	20	95	91	9	86
3	30	96	88	12	84
4	40	96	83	17	80

Table 5: Temperature effect for PVA 60-100.

Entry	Temperature (°C)	Conv. (%)	Benzodiazepine selectivity (%)	Other selectivity (%)	Yield pure benzodiazepine (%)
1	80	-	_	_	_
2	100	33	90	10	30
3	130	95	91	9	86
4	140	100	68	32	68

The influence of temperature on the production of benzodiazepine 3a (*3H*-2,4-diphenyl-1,5-benzodiazepine) was investigated with experiments performed at 80, 100, 130 and 140°C (Table 5). The best yield was obtained at 130°C (86%, Table 5, entry 4) with a selectivity of 91%. No reaction was detected when the test was performed at 80°C

(Table 5, entry 1). When the temperature was increased to 140°C, a conversion of 100% was obtained; however, the selectivity was very low, and several unidentified secondary products were detected by TLC.

Another key factor to optimize the reaction conditions is the molar ratio of reactants. Table 6 lists the results

Table 6: Effect of substrate molar ratio for PVA 60-100.

Entry	Molar ratio dione/diamine	Conv. (%)	Benzodiazepine selectivity (%)	Other selectivity (%)	Yield pure benzodiazepine pure (%)
1	1:1	95	91	9	86
2	1:1.5	100	92	8	92
3	1:2	100	89	11	89
4	1:3	100	85	15	85

Table 7: Catalyst amount effect.

Entry	Catalyst amount (mg)	Conv. (%)	Benzodiazepine selectivity (%)	Other selectivity (%)	Yield pure benzodiazepine (%)
1	25	75	93	7	70
2	50	100	92	8	92
3	100	100	90	10	90
4	200	100	90	10	90

obtained with different proportions of the reactants using the previously defined optimal temperature (130°C) and time (20 min). Equimolar quantities gave a good yield; an excess of o-phenyldiamine improved the vield, while a ratio 1:1.5 of o-phenyldiamine/1-phenyl-3-(2-hydroxyphenyl)-1,3-propanedione gave the best performance (92%, Table 6, entry 2), with a selectivity of 92%. An increase of molar ratio to 2:1 or 3:1 decreased the selectivity, and unidentified secondary products were detected by TLC.

Under the optimal conditions determined (solventfree, a reactant molar ratio of 1:1.5 at 130°C for 20 min of reaction) the PVA 60-100 catalyst was tested as a function of its mass. The results listed in Table 7 show that 50 mg of the PVA 60-100 catalyst gives the best yield (92%, Table 7, entry 2), and no additional amount of catalyst is required to improve it.

The catalyst reusability in the reaction was studied in the same conditions and proportions as for natural PVA (in solvent-free conditions, at 130°C, 1:1.5 dione/ diamine ratio and 50 mg of PVA 60-100 catalyst), at five consecutive times of reaction. The used catalyst was separated from the reaction media, washed with toluene and dried in vacuum to recover it. The results showed no considerable variations in the reaction performance (Table 8) when the catalyst was reused five consecutive times.

According to the good results achieved for experiments under solvent-free reaction conditions, involving 50 mg of catalyst at 130°C and 20 min reaction time (hereafter denoted as optimal conditions), several reactions were

Table 8: Catalyst reuse.

Entry	Cycle	Yield pure benzodiazepine (%)
1	Use	92
2	1st Reuse	90
3	2nd Reuse	90
4	3rd Reuse	88

carried out using different 1,3-diones and 1,2-diamines. The corresponding benzodiazepines were obtained in very good yields as indicated in Table 9 (entries a to d and g). However, phenylenediamine containing nitro group or nitrogen in their structure does not react under the established reaction conditions, probably due to the decrease in the nucleophilicity of amino groups present in the reagent.

The workup and catalyst recovery are simple, and all reactions have very high selectivity toward the corresponding benzodiazepines. The TLC analysis shows small amounts of by-products. The products are known compounds and were characterized by ¹H NMR and ¹³C NMR spectroscopy. The NMR characterization details of all compounds are shown in Supplementary material.

4 Conclusion

In this article, we present the treatment and characterization of volcanic ashes obtained from the Puyehue-Cordon Caulle volcanic complex. The volcanic ashes were

 Table 9:
 Yield and Green Metric Parameters for the different substituted 3*H*-1,5-benzodiazepines obtained.

Compounds	Product	-	Yield (%)	Gr	een Metric Parame	ters
				AE %	PMI	E Factor
3a		[39]	61	89.2	2.41	1.41
3b	CH ₃ N	[30]	91	89.6	1.62	0.62
Зс	CI	[30]	82	90.2	1.80	0.80
3d	Br N	[30]	78	91.2	1.90	0.90
3e	O ₂ N N	-	-	89.2	-	-
3f		-	-	90.5	-	-
3g	HO-	[40]	92	89.7	1.57	0.57
3h	HO—CH ₃	[40]	73	90.1	1.96	0.96
3i	HO—CI	[40]	79	90.6	1.78	0.78
3 j	P Z Z	[40]	63	91.0	2.20	1.20
3k	HO N N	[30]	79	91.7	1.71	0.71

characterized by Raman and FT-IR spectroscopy, XRD, SEM, and BET. The acidic strength of the catalysts was determined by potentiometric titration with n-butylamine. Substituted 3H-1,5-benzodiazepines were synthesized 1,3-propanediones and 1,2-phenylendiamine, under solvent-free reaction conditions, using volcanic ashes as catalysts. This procedure allows obtaining good to excellent performance of the derivatives in a short reaction time of approximately 20 min, and a temperature of 130°C. The volcanic ash catalysts are insoluble in organic solvent, which allows easy removal of the reaction products without affecting their catalytic activity.

Different PVA fractions were comparable from the viewpoint of spectroscopic, textural and acidity characteristics. The PVA system that showed the best catalytic performance was that with higher Fe content and larger total number of acid sites.

The applications of these catalysts in oxidation and biomass valorization through multicomponent reaction are in progress in our laboratory.

Acknowledgments: The authors thank G. Valle for FT-IR spectra, M. Theiller for the SEM analysis, E. Soto and Pablo Fetsis for S_{pet} data, and F. Ziarelli for ³¹P-NMR spectra.

Funding sources: This work was supported by "Consejo Nacional de Investigaciones Científicas y Técnicas" (CONICET - PIP 003), "Agencia Nacional de Promoción Científica y Tecnológica" (ANPCyT - PICT 0409), "Comisión de Investigaciones Científicas de la Prov. de Bs. As." (CICPBA - Project 832/14) and Universidad Nacional de La Plata (Project I11/172). MM, AGS, and GPR are members of CONICET. CIC is a member of CIC-PBA and Facultad de Ingeniería, Universidad Nacional de La Plata.

References

- [1] Rocchi D., González J.F., Menéndez J.C., Montmorillonite Clay-Promoted, Solvent-Free Cross-Aldol Condensations under Focused Microwave Irradiation. Molecules, 2014, 19, 7317-7326.
- [2] Capello C., Fischer U., Hungerbühler K., What is a green solvent? A comprehensive framework for the environmental assessment of solvents. Green Chem., 2007, 9, 927-934.
- [3] Kerton F.M., Marriott R., Alternative Solvents for Green Chemistry. Royal Society of Chemistry Publishing, 2013.
- [4] Himaja M., Poppy D., Asif K., Green technique-solvent free synthesis and its advantages. Int. J. Res. Ayurveda Pharm., 2011, 2(4), 1079-1086.

- [5] Sayyed-Alangi S.Z., Hossaini Z., ZnO nanorods as an efficient catalyst for the green synthesis of indole derivatives using isatoic anhydride. Chem. Heterocyc. Compd., 2015, 51, 541-544.
- Zolfigol M., Ayazi-Nasrabadi R., Baghery S., Synthesis and characterization of two novel biological-based nano organo solid acids with urea moiety and their catalytic applications in the synthesis of 4,4'-(arylmethylene)bis(1H-pyrazol-5-ol), coumarin-3-carboxylic acid and cinnamic acid derivatives under mild and green conditions. RSC Adv., 2015, 5(88), 71942-71954.
- Atghia S.V., Beigbaghlou S.S., Use of a highly efficient and [7] recyclable solid-phase catalyst based on nanocrystalline titania for the Pechmann condensation. C. R. Chim., 2014, 17, 1155-1159.
- Perez M., Ruiz D., Autino J., Sathicg A.G., Romanelli G.P., A very simple solvent-free method for the synthesis of 2-arylchromones using KHSO, as a recyclable catalyst. C. R. Chim., 2016, 19, 551-
- [9] Krishnakumar B., Swaminathan M., Solvent free synthesis of quinoxalines, dipyridophenazines and chalcones under microwave irradiation with sulfated Degussa titania as a novel solid acid catalyst. J. Mol. Catal. A-Chem., 2011, 350, 16-25.
- [10] Clark J.H., Solid Acids for Green Chemistry. Acc. Chem. Res., 2002, 35, 791-797.
- [11] Nagendrappa G., Organic synthesis using clay and claysupported catalysts. Appl. Clay Sci., 2011, 53, 106-138 (and the references cited herein).
- [12] Kaur N., Kishore D.V., Montmorillonite: An efficient, heterogeneous and green catalyst for organic synthesis. J. Chem. Pharm. Res., 2012, 4, 991-1015.
- [13] Muñoz M., Sathicq A.G., Romanelli G.P., Hernández S., Cabello C.I., Botto I.L., et.al., Porous modified bentonite as efficient and selective catalyst in the synthesis of 1,5-benzodiazepines. J. Porous Mat., 2013, 20, 65-73.
- [14] Bertolini G.R., Vetere V., Gallo M.A., Muñoz M., Casella M.L., Gambaro L., et al., Composites based on modified clay assembled Rh(III)-heteropolymolybdates as catalysts in the liquid-phase hydrogenation of cinnamaldehyde. C. R. Chim., 2016, 19, 1174-1183.
- [15] Manz O.E., Investigation of pozzolanic properties of the Cretaceous volcanic ash deposit near Linton: North Dakota Geological Survey Report of Investigation. J. W. Acad. Sci., 1962, 38(7), 80.
- [16] Suib Newnes S.L., New and future developments in catalysis: hybrid materials, composites, and organocatal (1st ed.). Elsevier, 2013.
- [17] Abdollahi-Alibeik M., Mohammadpoor-Baltork I., Zaghaghi Z., Yousefi B.H., Efficient synthesis of 1,5-benzodiazepines catalyzed by silica supported 12-tungstophosphoric acid. Catal. Commun., 2008, 9, 2496-2502.
- [18] Jadhav K.P., Ingle D.B., Synthesis of 2,4-diaryl-2,3-dihydro-1,5benzothiazepines and their 1,1-dioxides as antibacterial agents. Indian J. Chem., 1983, B22, 180-182.

- [19] Reddy R.J., Ashok D., Sharma P.N., Synthesis of 4,6-bis(2'substituted-2',3'-dihydro-1,5-benzothiazepin-4'-yl)resorcinols as potential antifeedants. Indian J. Chem., 1993, B32, 404-406.
- [20] Rodriguez R., Insusti B., Abonía R., Quiroga J., Preparation of some light-sensitive 2-nitrophenyl-2,3-dihydro-1Hbenzodiazepines. Arkivoc, 2004, 13, 67-71.
- [21] Jung D., Song J., Kim Y., Lee D., Lee Y., Park Y., et al., Synthesis of 1H-1,5-benzodiazepine derivatives and pyridinylquinoxalines with heterocyclic ketones. B. Korean Chem. Soc., 2007, 28(10), 1877-1880.
- [22] Pozarentzi M., Stephanidou-Stephanatou I., Tsoleridis C.A., An efficient method for the synthesis of 1,5-benzodiazepine derivatives under microwave irradiation without solvent. Tetrahedron Lett., 2002, 43, 1755-1758.
- [23] Jeganathan M., Pitchumani K., Solvent-Free syntheses of 1,5-Benzodiazepines using HY Zeolite as a green solid acid catalyst. ACS Sustain. Chem. Eng., 2014, 2, 1169-1176.
- [24] Pasha M.A, Jayashankara V.P., An expeditious Synthesis of 1,5-benzodiazepine derivatives catalyzed by p-toluensulfonic acid. J. Pharmacol. Toxicol., 2006, 1, 573-578.
- [25] Tarannum S., Siddiqui Z., Nano silica-bonded N-propylsulfamic acid as an efficient and environmentally benign catalyst for the synthesis of 1,5-benzodiazepines. Monatsh Chem., 2017, 148(4), 717-730.
- [26] Yadav J.S., Reddy B.V.S., Praveenkumar S., Nagaiah K., Indium(III) Bromide: A novel and efficient reagent for the rapid synthesis of 1,5-Benzodiazepines under solvent-free conditions. Synth., 2005, 3, 480-484.
- [27] Varala R., Enugala R., Adapa S.R., Zinc montmorillonite as a reusable heterogeneous catalyst for the synthesis of 2,3-dihydro-1H-1,5-benzodiazepine derivatives. Arkivoc, 2006, 13, 171-177.
- [28] Reddy B.M., Sreekanth P.M., An efficient synthesis of 1,5-benzodiazepine derivatives catalyzed by a solid superacid sulfated zirconia. Tetrahedron Lett., 2003, 44, 4447-4449.
- [29] Majid S.A., Khanday W.A., Tomar R., Synthesis of 1,5-benzodiazepine and its derivatives by condensation reaction using H-MCM-22 as catalyst. J. Biomed. Biotechnol., 2012.
- [30] Pasquale G.A., Ruiz D., Jios J.L., Autino J.C., Romanelli G.P., Preyssler catalyst-promoted rapid, clean, and efficient condensation reactions for 3H-1,5-benzodiazepine synthesis in solvent-free conditions. Tetrahedron Lett., 2013, 54(48), 6574-6579.

- [31] Pasquale G., Ruiz D., Baronetti G., Thomas H., Autino J., Romanelli G.P., Wells-Dawson type catalyst: An efficient, recoverable and reusable solid acid catalyst for the solvent-free synthesis of benzodiazepines. Curr. Catal., 2014, 3(2), 229-233.
- [32] Willy B., Dallos T., Rominger F., Schönhaber J., Müller T.J.J., Threecomponent synthesis of cryofluorescent 2,4-disubstituted 3H-1,5-benzodiazepines - conformational control of emission properties. Eur. J. Org. Chem., 2008, 4796-4805.
- [33] Young J., Schäfer C., Solan A., Baldrica A., Belcher M., Nişanci B., et al., Regioselective "hydroamination" of alk-3-ynones with non-symmetrical o-phenylenediamines. Synthesis of diversely substituted 3H-1.5-benzodiazepines via (Z)-3-amino-2-alkenones. RSC Adv., 2016, 6, 107081-107093.
- [34] Special reports of volcanic activity Puyehue-Cordon Caulle volcanic complex. SERNAGEOMIN, 2011, sernageomin.cl/.
- [35] Botto I.L., Barone V., Canafoglia M.E., Rovere E., Violante R., González M.J., et al., Pyroclasts of the first phases of the explosive-effusive PCCVC volcanic eruption: physicochemical analysis. Mater. Phys. Chem., 2015, 5(8), 302-315.
- [36] Canafoglia M.E., Vasallo M., Barone V., Botto I.L., Problems associated to natural phenomena: potential effects of PCCVC eruption on the health and the environment in different zones of Villa La Angostura, Neuquen, Argentina. In: Proceedings of AUGM-DOMUS (2012, La Plata, Argentina). La Plata, Bs. As., Argentina, 2012, 4, 1-11.
- [37] Botto I.L., Canafoglia M.E., Gazzoli D., González M.J., Spectroscopic and microscopic characterization of volcanic ash from Puyehue-(Chile) eruption: Preliminary approach for the application in the arsenic removal. J. Spectrosc., 2013, ID-254517, DOI:10.1155/2013/254517.
- [38] Villabrille P., Vázquez P., Blanco M., Cáceres C., Equilibrium adsorption of molybdosilicic acid solutions on carbon and silica: basic studies for the preparation of ecofriendly acidic catalysts. J. Colloid Interf. Sci., 2002, 251, 151-159.
- [39] Tsoleridis C., Pozarentzi M., Mitkidou S., Stephanidou-Stephanatou J., An experimental and theoretical study on the regioselectivity of successive bromination sites of 7,8-dimethyl-2,4-diphenyl-3H-1,5-benzodiazepine. microwave assisted solventless synthesis of 4-phenyl-3H-1,5benzodiazepines. Arkivoc, 2008, xv, 193-209.
- [40] Ahmad R., Zia-Ul-Haq M., Hameed S., Nadeem H., Duddeck H., Synthesis of 1,5-benzodiazepine nucleosides. J. Chem. Soc. Pakistan, 2000, 22, 302-308.