

Green protocol for the synthesis of N-oxides from secondary amines using vanadium silicate molecular sieve catalyst

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Received 10 June 2005; received in revised form 6 December 2005; accepted 8 December 2005

Available online 23 January 2006

Abstract

Vanadium silicate molecular sieve catalyst VS-1 was found to promote efficiently the oxidation of α,α' -tetrasubstituted secondary amines with 30% aqueous hydrogen peroxide as oxidant. In comparison to other catalysts reported to date, this heterogeneous catalyst offers a remarkably simple workup procedure and is reusable without any appreciable loss of activity.

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Keywords: VS-1; N-oxide; Hydrogen peroxide; Heterogeneous catalyst; Zeolite

1. Introduction

In the past decades, a shift in emphasis in chemistry is apparent with the desire to develop environmentally benign routes to a variety of materials [1]. Green chemistry approaches hold out significant potential for the reduction of byproducts, waste minimization and lowering of energy cost, which have a great impact on the overall technology development for essential materials. In this regard, use of Zeolite has considerable potential for the development of new methodologies.

In recent years, N-oxides are occupying an important place in the realm of synthetic and biological chemistry because of their unique property to exist as stable free radicals. They are finding applications as probes in materials [2], spin labels in biochemistry [3], magnetic resonance imaging [4], electron spin resonance imaging [5], in polymer synthesis [6] and more widely as metal free oxidant in organic synthesis [7]. Among various methods of the synthesis of N-oxides, amine oxidation is recent and more widely used in recent years, particularly in the preparation of cyclic dialkyl nitroxides. Moreover, metal catalyzed oxidation of amines is of interest because of its relevance to

the enzymatic degradation of nitrogen containing compounds in biological systems. A variety of oxidizing agents have been introduced to prepare N-oxides [8]. Many of these methods have the drawback such as use of homogeneous catalysts, use of toxic metals, tedious workup, low yield of the product, etc. which is not necessarily desirable from the point of *green chemistry*. Development of environmentally benign reaction conditions is always desirable for the purpose of reducing the burden of waste disposal.

The discovery of titanium and vanadium silicate (TS-1 and VS-1, respectively) of MFI structure Zeolites has, in recent years led to remarkable progress in the field of oxidation of organic substrates with H_2O_2 [9,10]. Herein, we report the synthesis of N-oxides from α,α' -tetrasubstituted secondary amines using VS-1 as heterogeneous catalyst (Scheme 1).

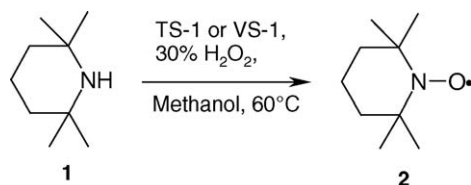
2. Experimental

2.1. Catalyst preparation

The catalyst VS-1 [11] and TS-1 [12] was synthesized according to literature procedure. In a general procedure, the silica source tetraethyl orthosilicate was hydrolysed by adding a solution of tetrapropylammonium hydroxide followed by the addition of tetrabutylorthotitanate (in 2-propanol for TS-1) or vanadyl sulphate (and water for VS-1). The crystallization was

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carried out in stainless still autoclaves at 433–443 K for appropriate time (24 h for TS-1 and 72 h for VS-1) till fully crystalline material is obtained. The samples were mainly characterized by X-ray diffraction (XRD), UV–vis spectroscopy, FTIR spectroscopy and energy dispersive X-ray analysis (EDX) [10,13]. The Spectral data are matching with those reported in the literature. The Si/Ti ratio was found to be 35 for TS-1 and Si/V ratio for VS-1 was found to be 56.

2.2. General procedure for the synthesis of N-oxides

A mixture of 2,2,6,6-tetramethylpiperidine (0.5 g, 3.5 mmol) 30% H_2O_2 (1.6 mL, 14.1 mmol) and 50 mg of VS-1 (or TS-1) were taken in 10 mL of methanol and refluxed for 12 h (TLC). Sodium metabisulfite (0.2 g) was added and stirred for 30 min to destroy excess of hydrogen peroxide. The reaction mixture was then filtered and methanol was evaporated. Thereafter, the reaction mixture was extracted with DCM and the organic layer was washed with brine and dried (Na_2SO_4). Evaporation of solvent and chromatography of the crude product with 10–15% EtOAc–petroleum ether gave 0.47 g of 2,2,6,6-tetramethylpiperidine-1-oxyl (85%).

3. Result and discussion

Oxidations of various $\alpha\alpha'$ -tetrasubstituted secondary amines were performed with 30% H_2O_2 using VS-1 and TS-1 as catalysts. Initially a systematic study was undertaken for catalytic evaluation of VS-1 under different reaction conditions for oxi-

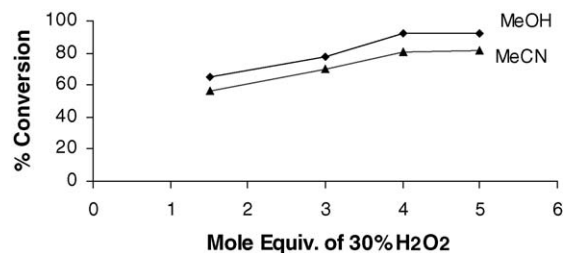


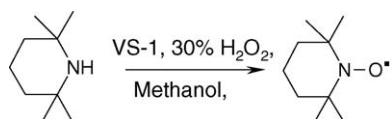
Fig. 1. Effect of concentration of 30% H_2O_2 on oxidation of 2,2,6,6-tetramethylpiperidine.

dation of 2,2,6,6-tetramethylpiperidine using 30% hydrogen peroxide as oxidant as described in the Table 1. The yield of the product increases with increasing amount of hydrogen peroxide (Fig. 1). It is evident from the table that use of 4 mol equivalent of hydrogen peroxide in methanol as solvent at reflux temperature gives the best result. Reaction proceeds with a similar conversion at room temperature also, but the rate of the reaction is slow (30 h). Reduction of the amount of hydrogen peroxide to 1.5 molar equivalent led to low conversion. Use of other solvent like acetonitrile did not produce better result. Encouraged by this result we have extended the procedure for the synthesis of various N-oxides. Results are summarized in Table 2. Different N-oxides are formed in a very effective manner under this condition.

Another catalyst, TS-1 was also used for comparison. Both VS-1 and TS-1 catalyze oxidation of secondary amines efficiently in good yield. TS-1 gives little lower conversion which is not very significant. Oxidation of tertiary amine with the same catalyst system also gave N-oxide. After successful application of the catalyst for various amines we looked for the reusability of the catalyst. The catalyst was recovered by simple filtration was successfully reused three times in case of 2,2,6,6-tetramethylpiperidine without loss of its activity. The recovered catalyst was dried at 120 °C for 24 h prior to use.

Mechanistically, it may be rationalized a peroxo species forms due to the interaction of the metal in the framework and

Table 1
Oxidation of 2,2,6,6-tetramethylpiperidine with H_2O_2 over VS-1 as catalyst

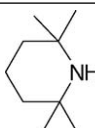
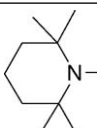
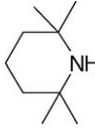
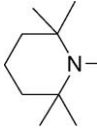
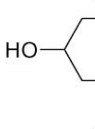
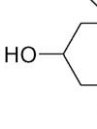
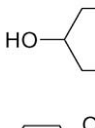
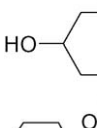

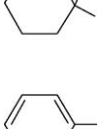
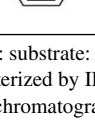
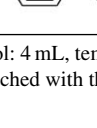


Entry	Amount of 30% H_2O_2^a (mol eq.)	Solvent	Temperature (°C)	Time (h)	%Conv. by GC ^b
1	1.5	Methanol	60	12	65
2	3	Methanol	60	12	78
3	4	Methanol	60	12	92
4	5	Methanol	60	12	92
5	4	Methanol	25	30	90
6	1.5	Acetonitrile	80	12	56
7	3	Acetonitrile	80	12	70
8	4	Acetonitrile	80	12	81
9	5	Acetonitrile	80	12	83

^a Molar equivalent is based on the substrate.

^b Column: CP sil 5B, 0.5 mm i.d.; oven temperature: 60 °C, 4 min and 240 °C, 10 min, ramp rate: 12°/min; inj. temperature 250 °C; detector temperature 275 °C, flow rate: 20 mL/min.

Table 2
Oxidation of $\alpha\alpha'$ -tetrasubstituted secondary amines to corresponding N-oxides^a

Entry	Substrate	Catalyst	Product ^b	Time	Yield ^c
1		VS-1		12	85
2		TS-1		12	82
3		VS-1		18	74
4		TS-1		18	71
5		VS-1		12	78
6		VS-1		8	72

^a Reaction conditions: substrate: 1 mmol, 30% H₂O₂: 4 mmol, catalyst: 10 wt.%, methanol: 4 mL, temp: 60 °C.

^b Products are characterized by IR, ESR (NMR for product 8) mass and mp data and matched with that reported in literature.

^c Isolated yield after chromatographic purifications.

hydrogen peroxide under liquid phase condition [14]. It is well known that hydroxylamines are the intermediate for the formation of N-oxide from an amine [10,13b,15]. Thus, under the present investigation the speculated reaction pathway is the generation of an in situ hydroxylamine which subsequently undergoes further oxidation resulting in the formation of N-oxide.

In conclusion, we have developed an efficient and environmentally benign protocol for the synthesis of N-oxides from the corresponding $\alpha\alpha'$ -tetrasubstituted secondary amines using TS-1 and VS-1 as heterogeneous catalyst and 30% H₂O₂ as oxidant. The catalyst can be and recycled without appreciable loss of its catalytic activity.

Acknowledgement

Financial support from CSIR, India is gratefully acknowledged. The authors are thankful to Dr. S. Sivasanker for the supply of catalyst and Dr. D. Srinivas for the measurements of EPR spectra.

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