R.S. Walmsley and Z.R. Tshentu,
S. Afr. J. Chem., 2010, **63**, 95–104,
<http://journals.sabinet.co.za/sajchem/>.

Imidazole-based Vanadium Complexes as Haloperoxidase Models for Oxidation Reactions

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Received 14 May 2010, revised 7 July 2010, accepted14 July 2010.

ABSTRACT

Four imidazole-bound oxovanadium(IV) haloperoxidase model complexes were prepared. Two heterogeneous catalysts were prepared by first linking imidazole-4-carboxylic acid or 1-methylimidazole-2-carboxylic acid to chloromethylated polystyrene and subsequently reacting these polymer-anchored ligands with vanadyl sulphate. Two homogeneous catalysts were prepared by reaction vanadyl sulphate with the free ligands. The activity of the catalysts was evaluated for the hydrogen peroxide facilitated oxidation of styrene and ethylbenzene and thioanisole. A maximum conversion of 99.9 % for styrene and 10.6 % for ethylbenzene was achieved. Excellent conversions of thioanisole (100 %) were obtained under mild room temperature conditions. The heterogeneous catalysts also proved to be recyclable for this reaction, with no appreciable loss in activity even after three catalytic cycles. The haloperoxidase activity was evaluated spectrophotometrically by following the bromination of phenol red to bromophenol blue. All four catalysts proved effective in catalysing this process.

KEYWORDS

Oxovanadium, imidazole, catalysis, oxidation.

1. Introduction

Vanadium-dependant haloperoxidases (VHPOs) have been found in several marine organisms including the marine algae *Ascophyllum nodosum* and *Corallina officinalis,* the lichen *Xanthoria parietina* and the fungus *Curvularia inaequalis.*[1] They are capable of catalyzing halogenation reactions by the oxidative addition of halides to organic substrates using hydrogen peroxide.[2] These halogenated products may then act as defence chemicals for these organisms. As the name suggests, the enzymes contain a vanadium atom located in the active site which adopts five-coordinated trigonal bipyramidal geometry. This centre is coordinated to four oxygens – three hydroxyl oxygens in equitorial positions and an oxo group in an axial position. Interestingly, all VHPOs show an imidazole group of a histidine residue coordinated to the remaining axial position *trans* to the oxo group in the trigonal bypyramid.[1,3]

The discovery of these enzymes has inspired the development of structural and functional VHPO model complexes.[4] Many of these complexes contain imidazole[5,6] and benzimidazole-based ligands,[7,8] and all have shown promising catalytic activity. Despite this, there is still a need for further perfection of these complexes in terms of geometrical similarity and activity.[9] The activity of these VHPO models is not limited to halogenation reactions, but encompasses numerous oxidation reactions, including that of sulphides, alkanes, alkenes and alcohols.[5,6,10,11] Hydrogen peroxide, the oxidant typically used in the aforementioned reactions generates water as the only by-product, making the system an 'environmentally friendly' alternative to toxic chromium and permanganate-based oxidising agents.[10] Furthermore, anchoring of the vanadium complexes to a solid support allows for the simple separation and recyclability of the catalyst.[12]

Herein, we describe the preparation, characterisation and catalytic evaluation of two heterogeneous oxovanadium(IV) catalysts and their homogeneous counterparts. The ligands imidazole-4-carboxylic acid and 1-methylimidazole-2-carboxylic acid were covalently linked to chloromethylated polystyrene and subsequently reacted with vanadyl sulphate to form the polymer-bound oxovanadium catalysts. The resultant heterogeneous catalysts were characterised by microanalysis, scanning electron microscopy (SEM) and infrared spectroscopy. The neat oxovanadium(IV) complexes were prepared by reacting the free ligands with vanadyl sulphate. The activity of the catalysts was thoroughly investigated for the oxidation of styrene, thioanisole and ethylbenzene, and the oxidative bromination of phenol red.

2. Experimental

2.1. Materials

Thioanisole, ethylbenzene, styrene, vanadyl sulphate hydrate, imidazole-4-carboxylic acid (Im4COOH), 10 % tetramethylammonium hydroxide (TMAOH), phenol red and Merrifield polymer crosslinked with divinylbenzene (5.5 % crosslinked, ~5.5 mmol Cl/g resin and 16–50 mesh) were purchased from Sigma-Aldrich and used without further purification. All other chemicals and solvents were reagent grade. Hydrogen peroxide was standardised by titration with potassium permanganate.[13]

2.2. Instrumentation

The infrared spectra were recorded on a Perkin Elmer 400 FTIR spectrophotometer in the mid-IR range (4000–400 cm^{-1}) as KBr pellets or as neat solids using a Perkin Elmer 100 ATR-FTIR. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 NMR MHz spectrometer and reported relative to tetramethylsilane (δ 0.00). Electronic spectra were recorded on a Perkin Elmer Lambda 25 UV-Vis spectrophotometer using 1 cm quartz cells. The vanadium content of beads was determined using a Thermo Electron (iCAP 6000 Series) inductively coupled plasma (ICP)

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spectrometer equipped with OES detector. Wavelengths with minimum interferences were chosen (290.88 nm, 292.40 nm, 309.31 nm, 311.07 nm) and three repeats were performed at each wavelength. Catalyzed reactions were monitored using the Agilent 6820 gas chromatograph (GC), fitted with a flame ionisation detector (FID) and a Zebron, ZB-5MSi, capillary column (30 m × 0.25 mm × 0.25 μm). Mass spectra were obtained using a Thermo-Finnigan GC-MS fitted with an electron impact ionisation mass selective detector. Microanalysis was carried out using a Vario Elementar Microcube ELIII. The polymer beads were imaged using a TESCAN Vega TS 5136LM scanning electron microscope (SEM).

2.3. Preparative Work

2.3.1. *1-Methylimidazole-2-carboxylic acid (MeIm2COOH)* (**1**)

Firstly, 1-methylimidazole-2-carboxaldehyde was prepared according to the literature procedure.[14] Aqueous 30 % H_2O_2 (10 g) was then added dropwise to a stirred solution of 1-methylimidazole-2-carboxaldehyde (3.31 g 0.030 mol) in water (10 mL). The reaction was allowed to proceed at room temperature for 72 h, following which the water was removed *in vacuo* at room temperature to afford a white crystalline solid. Yield: 100 %. Note. heating causes decarboxylation. δ_H (400 MHz, D_2O): 7.42, 7.39 (2H, s, Im-H) and 4.08 ppm (3H, s, NCH_3); δ_C (100 MHz, D_2O): 158.7, 139.7, 125.8, 118.5, 36.7 ppm. IR ν (KBr): 3510, 1655, 1517, 1464, 1407, 1353, 1313, 1276, 1028, 993, 824 cm^{-1}. (Found: C, 41.28; H, 5.23; N, 19.12 %. Calc. for $C_5H_8N_2O_3$ (144.12); C, 41.67; H, 5.59; N, 19.44 %).

2.3.2 *VO(Im4COO)$_2$.H$_2$O* (**2a**)

This complex was prepared according to a literature method but with slight modifications.[15] To a stirred aqueous solution of Im4COOH (0.254 g, 2.26 mmol), was added 10 % TMAOH (1.13 mmol). To this solution was added aqueous $VOCl_2$ (1.13 mmol), prepared by the reaction of $VOSO_4$ with $BaCl_2$. The reaction was allowed to stir overnight, following which the light blue precipitate was collected, washed with methanol and ether and dried in an oven (100 °C). Yield: 64.6 %. IR ν (neat): 3129, 2990, 1605, 1574, 1500, 1439, 1356, 1209, 1081, 1012, 981, 877, 819, 780 cm^{-1}. (Found: C, 31.20; H, 2.67; N, 18.14 %. Calc. for $C_8H_8N_4O_6V$ (307.11); C, 31.29; H, 2.63; N, 18.24 %).

2.3.3. *VO(MeIm2COO)$_2$.H$_2$O* (**2b**)

This complex was prepared similarly to **2a**. To a stirred solution of MeIm2COOH (0.285 g, 2.26 mmol) in 5 mL H_2O, was added 10 % TMAOH (1.13 mmol). To this solution was added $VOCl_2$ (1.13 mmol) in 15 mL H_2O. The reaction was stirred overnight and then allowed to stand for 24 h. A light blue precipitate formed, which was filtered and washed with methanol and then ether and dried in an oven (100 °C). Yield 62.3 %. IR ν (neat): 3136, 1631, 1493, 1429, 1329, 1286, 1184, 1168, 972, 839, 800, 771 cm^{-1}. (Found: C, 36.01; H, 3.47; N, 16.67 %. Calc. for $C_{10}H_{12}N_4O_6V$ (335.17); C, 35.83; H, 3.61; N, 16.72 %).

2.3.4. *PS-Im4COO* (**3a**)

Chloromethylated polystyrene (1.0 g, 5.5 mmol Cl) was allowed to swell in DMF (15 mL) for 2 h. To this was added Im4COOH (0.63 g, 5.7 mmol) in 5 mL H_2O followed by triethylamine (0.58 g, 5.7 mmol). The reaction mixture was warmed to 40 °C and stirred overnight. The resultant white beads were filtered, washed several times with DMF and then methanol. The beads were dried in an oven at 60 °C. IR ν (KBr): 3377, 3103, 2929, 1711, 1634, 1543, 1512, 1446, 1423, 1378, 1352, 1333, 1218, 1151, 1105, 976, 817, 767 cm^{-1}. (Found: C, 66.77; H, 6.88; N, 8.14 %).

2.3.5. *PS-MeIm2COO* (**3b**)

This polymer was prepared in a manner similar to **3a** except that MeIm2COOH (0.71 g, 5.7 mmol) was used. IR ν (KBr): 3426, 1711, 1604, 1574, 1512, 1465, 1427, 1334, 1262, 1160, 1019, 814 cm^{-1}. (Found: C, 56.7; H, 7.37; N, 9.48 %).

2.3.6. *PS-[VO(Im4COO)$_x$]* (**4a**)

The ligand-anchored beads **3a** (0.5 g) were allowed to swell in DMF (10 mL) for 2 h. A DMF solution of vanadyl sulphate (0.6 g, 2.75 mmol) was added to the above mixture. This mixture was stirred overnight at 60 °C. The blue-green beads were collected by filtration and washed with DMF and methanol and then dried in an oven at 60 °C. IR ν (KBr): 3124, 2923, 1721, 1652, 1512, 1451, 1385, 1332, 1259, 1160, 1114, 1039, 1020, 972, 822 cm^{-1}. (Found: C, 56.9; H, 5.89; N, 7.47; S, 2.62; V, 4.11 %).

2.3.7. *PS-[VO(MeIm2COO)$_x$]* (**4b**)

This polymer was prepared as for **4a** except that **3b** (0.5 g) was used. IR ν (KBr): 3431, 1631, 1572, 1512, 1451, 1424, 1261, 1159, 1110, 983, 806 cm^{-1}. (Found: C, 49.31; H, 6.60; N, 6.99; S, 4.20; V, 4.60 %).

2.4. Catalytic Activity Studies

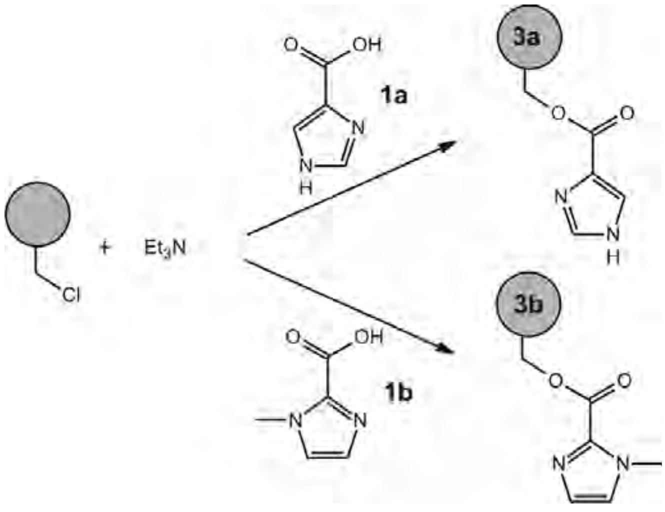
The experiments for the catalytic oxidation of styrene, ethylbenzene and thioanisole were carried out as previously.[10] Acetonitrile (20 mL) was added to a 100 mL round-bottom flask fitted with a glass condenser. The temperature of the oil bath was regulated to ±1 °C using an external temperature probe. The stirring was kept constant for all reactions at 300 rpm. The substrate was then added (10 mmol) followed by hydrogen peroxide (amount varied) and then the catalyst (amount varied). The reaction progress was monitored by gas chromatography over the period of 6 h. The amount of vanadium in the **4a** and **4b** was determined by ICP-OES as before.[10] The amount of **2a** and **2b** used in the homogeneous reactions was equivalent to the number of moles of vanadium in 0.025 g of the corresponding heterogeneous catalyst **4a** and **4b**.

The oxidative bromination reactions were carried out in 25 mL of a pH 5.5 phosphate buffer (50 mM). Phenol red (20 μM) and H_2O_2 (10 mM) were added to KBr (1.0 M). The reaction was initiated by addition of solid catalyst. The temperature during the reaction was maintained at ~20 °C and the stirring rate was kept constant at 700 rpm. The reaction progress was monitored spectrophotometrically. Phenol red shows two weak absorption maxima at 268 nm and 557 nm and a strong absorption maximum at 436 nm.[16] The bromination of phenol red can be followed by the disappearance of the peak at 436 nm and the appearance of a new peak at 590 nm corresponding to bromophenol blue, the tetrabrominated derivative.[16]

3. Results and Discussion

3.1. Synthesis and General Considerations

The ligand 1-methylimidazole-2-carboxylic acid (MeIm2COOH) has been prepared by carbonation of the 2-substituted lithium salt of 1-methylimidazole; however, the yield was very low (32 %).[17] Another synthetic route involved the electrophilic substitution of 1-methylimidazole by benzyl chloroformate followed by hydrogenation. The yield obtained using this method (59.2 %) was also relatively low.[18] In our method, we first prepared 1-methylimidazole-2-carboxaldehyde according to



Scheme 1
The reaction of imidazole-4-carboxylic acid (**1a**) and 1-methylimidazole-2-carboxylic acid (**1b**) with chloromethylated polystyrene to afford the polymer-anchored ligands **3a** and **3b**.

common method in relatively high yield (76.1 %).[19] This was then oxidised using hydrogen peroxide in water to afford the 2-carboxylic acid derivative quantitatively after evaporation of water. The ligands, Im4COOH and MeIm2COOH, were then linked to chloromethylated polystyrene through the more acidic carboxylic acid group leaving the imidazole nitrogen free for coordination to vanadium (Scheme 1).

The logic behind this synthesis was that by having free imidazole groups within the cross-linked polymer a coordination environment similar to the active site of VHPOs might be produced (Fig. 1). Reaction of the polymer-bound ligands with vanadyl sulphate gave the corresponding oxovanadium(IV) complex bound to the polymer via the imidazole ligand. Microanalysis results indicate a V/S ratio of approximately 1:1 for both **4a** and **4b** confirming the presence of cationic vanadium with a sulphate counter-ion. The V/N ratio of 1:6 suggests three imidazole units (2 nitrogen atoms per imidazole) per vanadyl centre, but it is unclear whether they are all coordinated or some are simply pendant. This might create an environment similar to that of the VHPO active site if one imidazole coordinates leaving two pendant (Fig. 1).

The coordination environments of the heterogeneous systems (**4a** and **4b**) are thus fundamentally different to that of the homogeneous systems (**2a** and **2b**). In the later compounds, the coordination is bidentate through the carboxylate oxygen and imidazole nitrogen, rendering a neutral *bis*-coordinated complex. The use of vanadium in the +4 oxidation state rather than the +5 state, as found in active VHPOs, does not bear any considerable consequence since upon addition of hydrogen peroxide vanadium(IV) is rapidly oxidised.

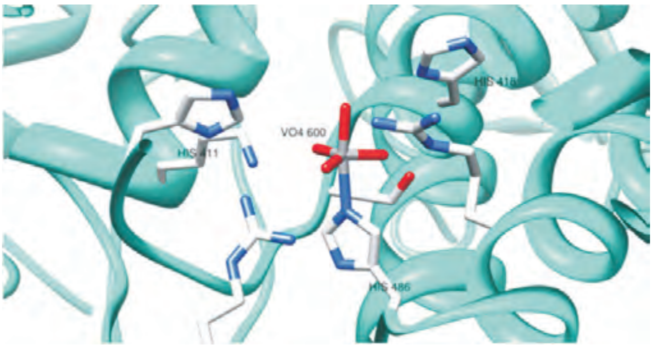


Figure 1 The active site of the bromoperoxidase from *Ascophyllum nodusum* showing vanadium coordinated to the imidazole group of a histidine residue (HIS 486) and the close proximity of two other histidine residues (HIS 418 and HIS 411).[3]

3.2. Characterisation of Catalysts

The connection of the ligands, Im4COOH and MeIm2COOH, to chloromethylated polystyrene was evidenced by the disappearance of the ν(C-Cl) vibration at 672 cm^{-1}.[20] The ν(C=O) at 1614 cm^{-1} for Im4COOH and 1655 cm^{-1} for MeIm2COOH, shifted to 1711 cm^{-1} in both **3a** and **3b** confirming the attachment of the ligands to the polymer via ester linkages. The appearance of bands at 972 cm^{-1} for **4a** and 983 cm^{-1} for **4b** are indicative of the ν(V=O) stretch and confirm the presence of the oxovanadium unit within the polymer.[8] The position of these bands was also different to that of complexes **2a** and **2b**, in which the ν(V=O) were observed at 981 cm^{-1} and 972 cm^{-1}, respectively. These divergences can be expected since, as already mentioned, the polymer-anchored and neat complexes share neither the same overall charge, nor the same coordination environment.

SEM was used to monitor morphological changes ocurring on the surface of the polymer beads during the various synthetic steps (Fig. 2). The images show a decrease in surface roughness from the ligand-bound polymer beads (**3a** and **3b**) to the oxovanadium-bound beads (**4a** and **4b**), a trend observed before.[10]

3.3. Catalytic Activity

The catalytic activity of the oxovanadium(IV) catalysts was investigated for the oxidation of thioanisole, styrene and ethylbenzene. The reaction progress was monitored using GC by comparing retention times to those of standards. The product identities were also confirmed using GC-MS. The haloperoxidases activity of the catalysts was also evaluated by following the conversion of phenol red to bromophenol blue spectrophotometrically. Hereafter, **4a** and **4b** may be inter-

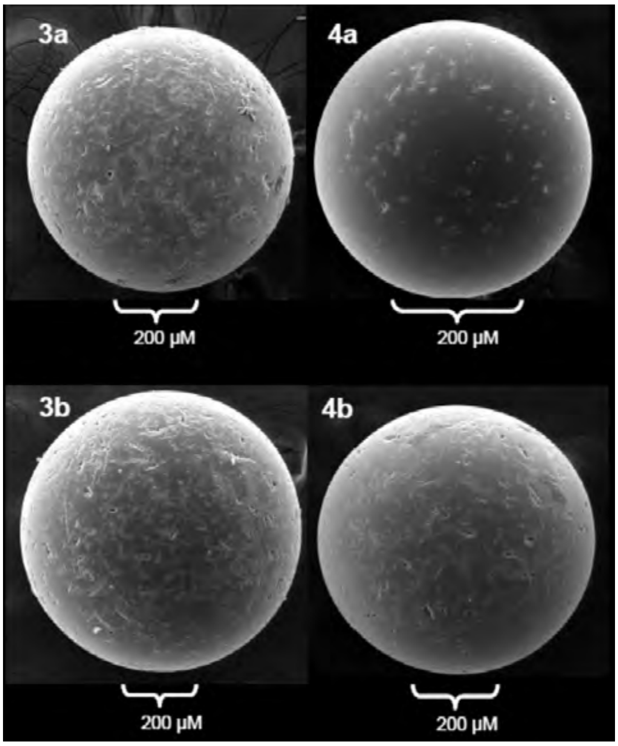
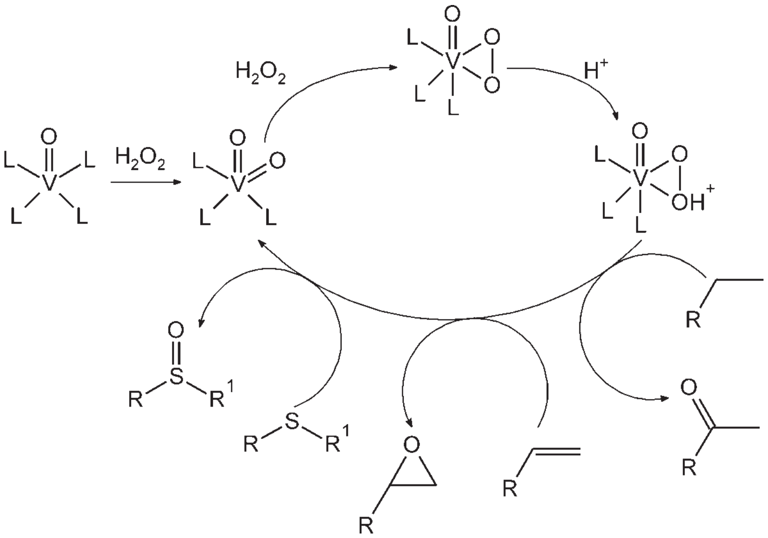


Figure 2 SEM micrographs of ligand-bound polymer beads (**3a** and **3b**) and oxovanadium-bound beads (**4a** and **4b**).



Scheme 2
A simplified catalytic mechanism for the oxidation of alkenes, alkanes and sulphides.[21,22] Here L refers to the donor atoms, which in the case of **2a** and **2b** would be N (imidazole) and O (carboxylic acid), while for **4a** and **4b** might be N (imidazole) as well as solvent molecules.

changeably referred to as the heterogeneous catalyst and **2a** and **2b** may be referred to as the homogeneous catalysts. The amount of **2a** (0.07 g, 0.02 mmol) and **2b** (0.08 g, 0.02 mmol) used in the homogeneous reactions, corresponded to the same amount of vanadium found in 0.025 g of the heterogeneous catalysts (0.02 mmol).

3.3.1. *Mechanism of Oxidation*

In the presence of hydrogen peroxide, vanadium(IV) readily converts to vanadium(V) along with the formation of monoperoxo and diperoxovanadium(V) complexes even when less than stoichiometric amounts of hydrogen peroxide are used.[21] All the reactions in this study were carried out in the presence of at least two-equivalents of H_2O_2 and so it is likely that mainly peroxo species exist. The peroxovanadium species are more reactive than H_2O_2 and are integral in the proposed catalytic mechanism as shown in Scheme 2.[21,22]

According to the mechanism outlined in Scheme 2, the first step involves the oxidation of vanadium(IV) followed by the formation of a peroxovanadium species which in acid media can form a reactive hydroxyl-peroxyvanadium(V) species, which subsequently oxidises the substrate. The first step of this process was confirmed by the spectrophotometric titration of **2a** with H_2O_2 (Fig. 3).

Before the addition of H_2O_2, three low-intensity peaks at 742 nm, 541 nm and 314 nm corresponding to the d-d transitions of a five-coordinate oxovanadium system were observed.[23] Upon addition of H_2O_2, these transitions disappeared and a charge transfer band appeared at 380 nm due to the formation of the d^0 dioxovanadium(V) species. Further addition of H_2O_2, produced a new band appearing at 325 nm which may be assigned the peroxo-vanadium charge transfer band ($\pi^*_v \rightarrow d\sigma^*$).[24,25]

3.3.2. *Oxidation of Thioanisole*

The oxidation of sulphides has become a valuable reaction due to the use of sulphoxides as intermediates in the synthesis of biologically active compounds.[26,27] Thioanisole, the sulphide used in this study, was oxidised to methyl phenyl sulphoxide which was further oxidised to methyl phenyl sulphone. This process was monitored using GC and the products confirmed by GC-MS.

The temperature as well as the amount of catalyst was varied until optimal conditions were obtained and the effect of these changes on overall conversion and product selectivity was evaluated. The amount of peroxide was kept constant at two-equivalents (relative to thioanisole), since it has been shown that maximal conversion is reached at this point.[6] Increasing the amount of **4a** from 0.025 g to 0.035 g resulted in a slight increase from 91.6 % to 99.5 % in the overall oxidation of thioanisole (Fig. 4). The same change for **4b** resulted in a slightly faster reaction along with a minor increase in overall conversion from 96.1 % to 97.7 %. When the same reaction was performed but in the absence of catalyst, a maximum conversion of around 25 % was observed.[10]

The heterogeneous catalysts, were collected and washed after being subjected to a 6-hour catalytic cycle. The similarity in colour of these recycled beads to the original beads suggested that the catalysts underwent a full cycle returning to the original +4 oxidation state. However, the infrared spectra of these beads reveals a change in the ν(V=O) probably due to the existence of new vanadium species. As shown in Fig. 5, the ν(V=O) for **4b** before a reaction shows a single band at 983 cm^{-1}. At the end of a typical thioanisole oxidation reaction, the ν(V=O) splits into two, one main band at 973 cm^{-1} with a shoulder at 941 cm^{-1}. It is likely that the shoulder was due to the formation of a dioxovanadium(V) species,[28] while the shift of the band at 983 cm^{-1} to 973 cm^{-1} may have been due to coordination of solvent or substrate to the regenerated vanadyl centre;[29] however, this is yet to be confirmed. Similar IR observations were found for **4a**.

The recycled heterogeneous catalysts were submitted to a new oxidation reaction and showed a reduced induction period (shown for **4a** in Fig. 6). This is consistent with the suspicion that the recycled beads contain the oxidised vanadium species. Even after three catalytic cycles, there was no appreciable loss in activity of the catalysts.

As shown in Scheme 3, thioanisole may be oxidised to the sulphoxide which can then be further oxidised to the sulphone.

For the heterogeneous catalysts, selectivity was in the order; sulphoxide > sulphone, when 2 eq of H_2O_2 was used and the reaction was performed at room temperature (shown for **4b** in Fig. 7).

The rate of reaction of the homogeneous catalysts was much faster than the heterogeneous catalysts, both **2a** and **2b** reached approximately 100 % conversion within 30 minutes. The forma-

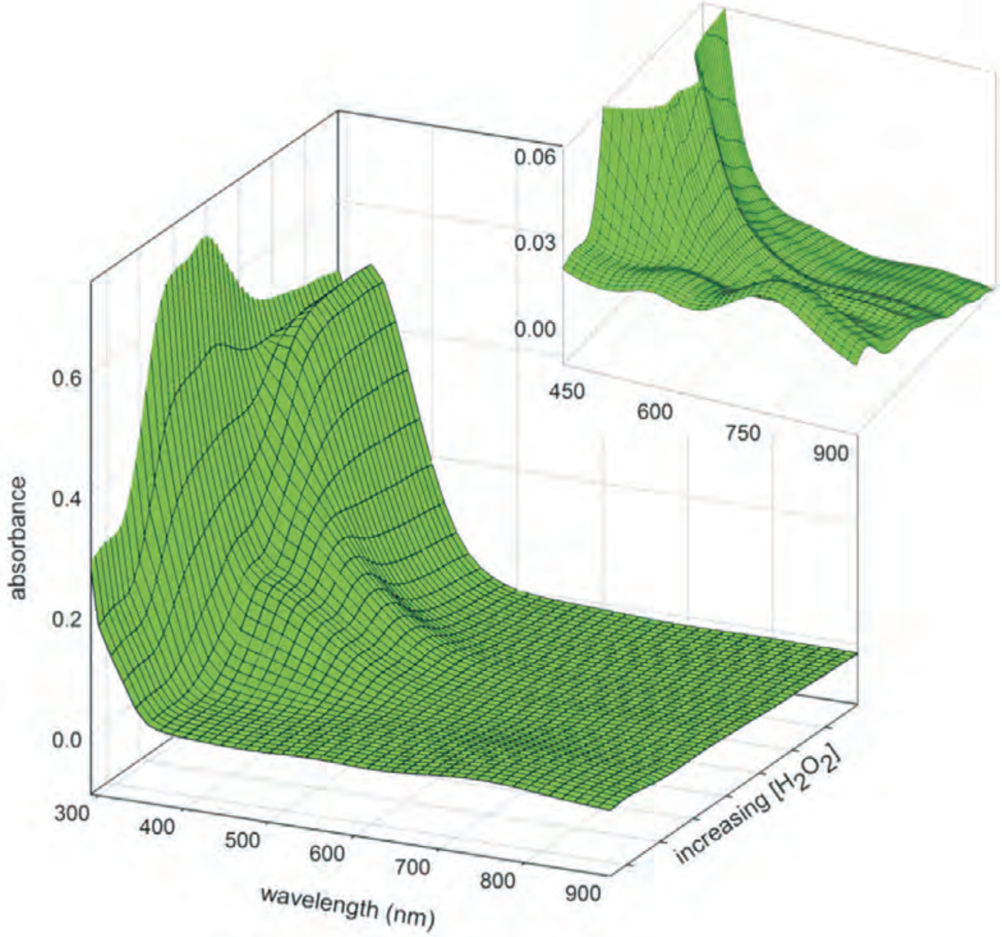


Figure 3 Spectrophotometric titration of **2a** (1×10^{-4} mM) with one-drop portions of H_2O_2 (5×10^{-2} mM) in water. The inset shows two of the d-d transitions which disappear upon addition of H_2O_2.

tion of the sulphoxide was rapid, reaching a maximum within 30 minutes and then decaying due to subsequent oxidation to the sulphone (shown for **2a** in Fig. 8). The product selectivity in the case of the homogeneous catalysts, after a 6-hour contact time, was sulphone > sulphoxide. To ascertain whether this improvement in activity was specific to **2a** and **2b**, or merely due to the homogeneity of the catalyst, we performed the same oxidation experiment using $VOSO_4$ (Fig. 8).

The fastest oxidation rate of thioanisole was observed with this vanadium salt. This confirmed that the reason for the improvement in activity was due mainly to the homogeneity of the catalysts and not necessarily specific to their coordination environment. The slower rate of reaction of **2a** and **2b** compared to $VOSO_4$ was probably due to the slightly lower solubility of these complexes in acetonitrile compared to $VOSO_4$.

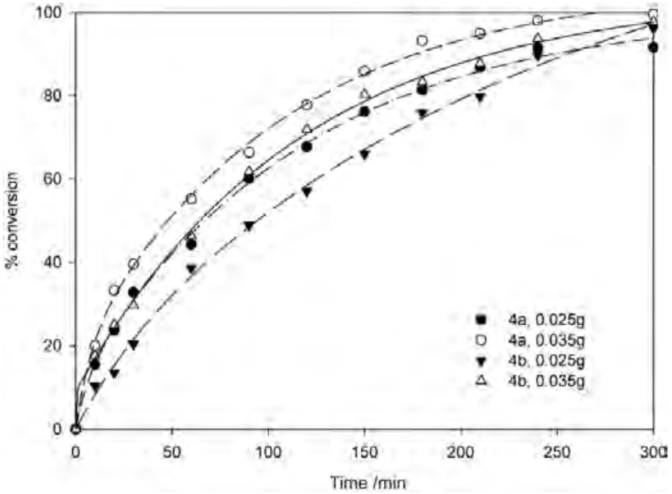


Figure 4 The effect of the catalyst amount on thioanisole oxidation. Reaction conditions: thioanisole (10 mmol), H_2O_2 (2 eq) and at room temperature.

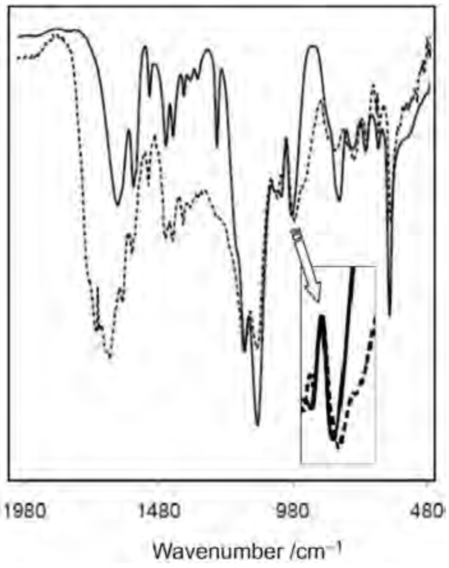


Figure 5 Overlaid infrared spectra of **4b** before (solid line) and after (dashed line) a 6-hour reaction. The region between 1000 and 900 cm^{-1} has been enlarged for clarity.

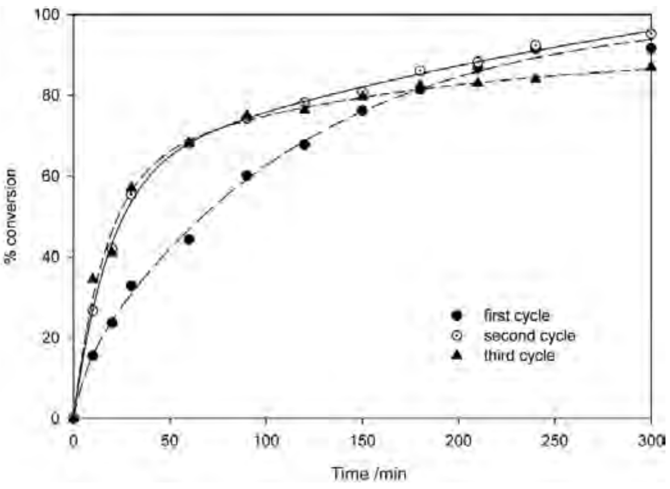


Figure 6 Recyclability of **4a** in the oxidation of thioanisole. Reaction conditions: catalyst **4a** (0.025 g), thioanisole (10 mmol), H_2O_2 (2 eq) and at room temperature.

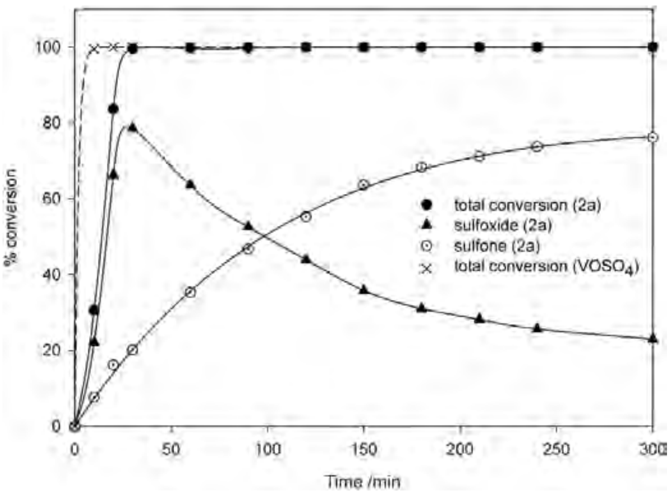


Figure 8 Oxidation of thioanisole by $VOSO_4$ (dashed line) and **2a** (solid line). Reaction conditions: **2a** (0.007 g, 0.023 mmol) or $VOSO_4$ (0.005 g, 0.0023 mmol), thioanisole (10 mmol), H_2O_2 (2 eq) and at room temperature.

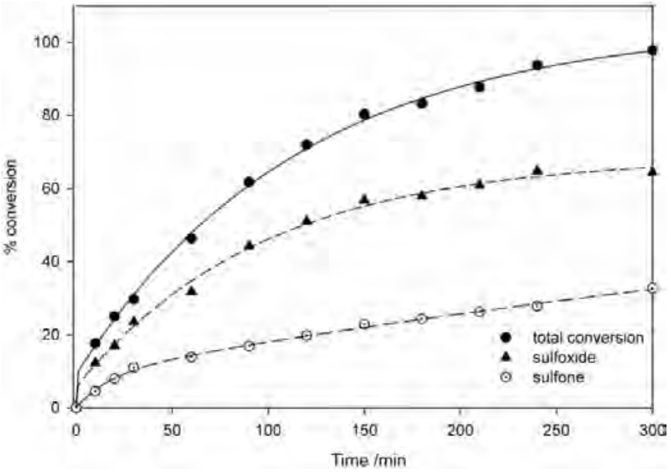


Figure 7 Overall oxidation and product selectivity of thioanisole by **4b**. Reaction conditions: **4b** (0.035 g), thioanisole (10 mmol), H_2O_2 (2 eq) and at room temperature.

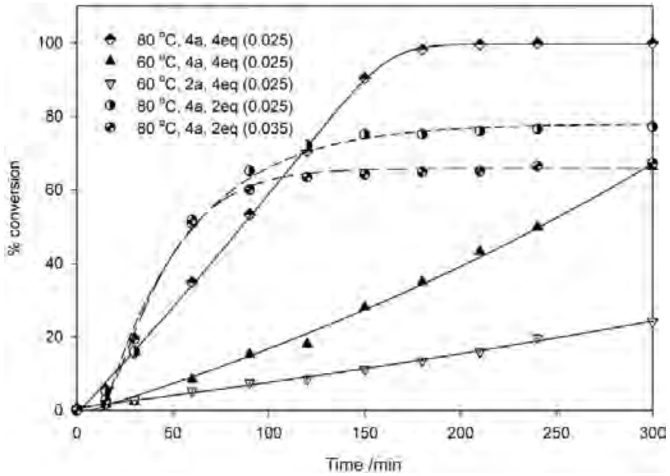
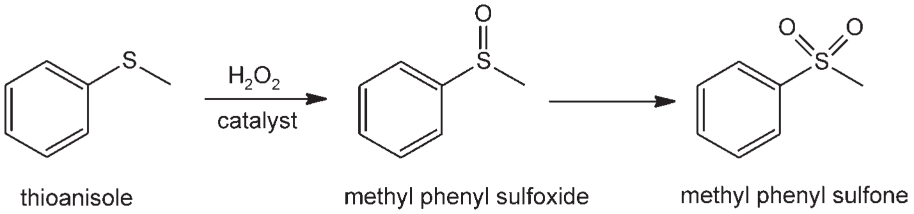


Figure 9 Effects of the amounts of catalyst and peroxide as well as temperature on the oxidation of styrene. Reaction conditions: **4a** (0.025 g and 0.035 g) or **2a** (0.007 g, 0.023 mmol), styrene (10 mmol).

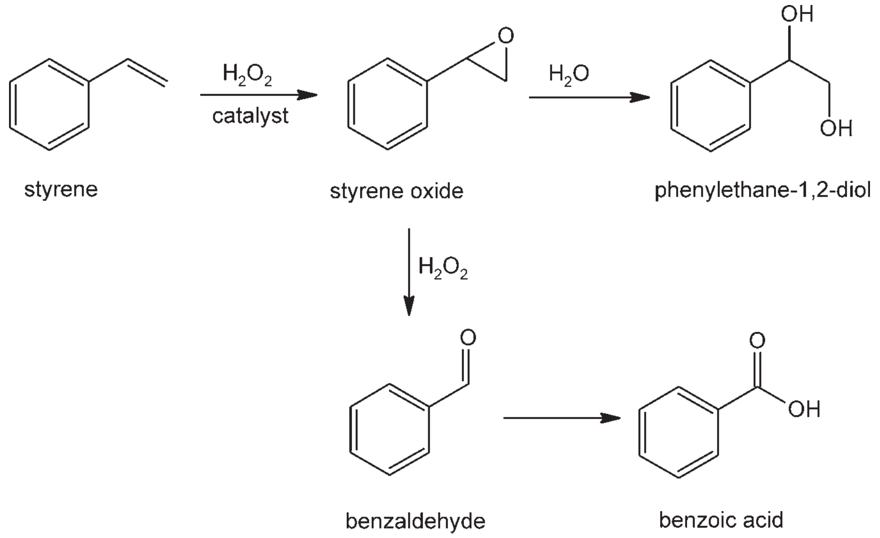
3.3.3. *Oxidation of Styrene*

The oxidation of styrene required much harsher conditions than that of thioanisole. Close to 100 % conversion was achieved in 3.5 h when using 4-equivalents of H_2O_2 at 80 °C. Under these conditions, however, the heterogeneous catalysts were unstable. For this reason milder conditions were employed despite the negative consequences on the overall conversion. Taking **4a** as an example; when the temperature was kept constant at 80 °C, and the amount of H_2O_2 was decreased from 4. eq to 2. eq, the overall conversion dropped to 77.1 % from 99.9 % (Fig. 9). The lower catalyst amount (0.025 g) achieved better overall conversion, but both amounts showed similar initial rates. Lowering the temperature to 60 °C, while keeping the amount H_2O_2 constant at 4 eq, also resulted in a reduced conversion of 66.2 % from 99.9 %. Unlike the trend observed for oxidation of sulphides, the homogeneous catalysts showed poorer activity than the heterogeneous catalysts. After a 6-hour reaction the homogeneous catalyst **2a** achieved a mere 24.1 % conversion of styrene at 60 °C using 4eq of H_2O_2 (Fig. 9).

As shown in Scheme 4, the first oxidation product of styrene is styrene oxide. This may then react with water via a ring opening mechanism to form phenylethane-1,2-diol. Wang and co-workers, have produced phenylethane-1,2-diol in 98 % yield by simply heating styrene oxide in pure water.[30] However, the



Scheme 3
The oxidation products of thioanisole.



Scheme 4
The oxidation products of styrene.

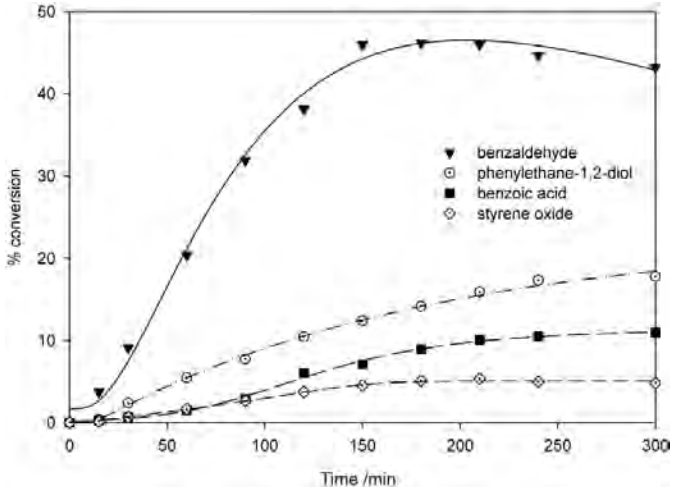


Figure 10 Product selectivity for the oxidation of styrene. Reaction conditions: **4a** (0.025 g), styrene (10 mmol), H_2O_2 (4 eq), 80 °C.

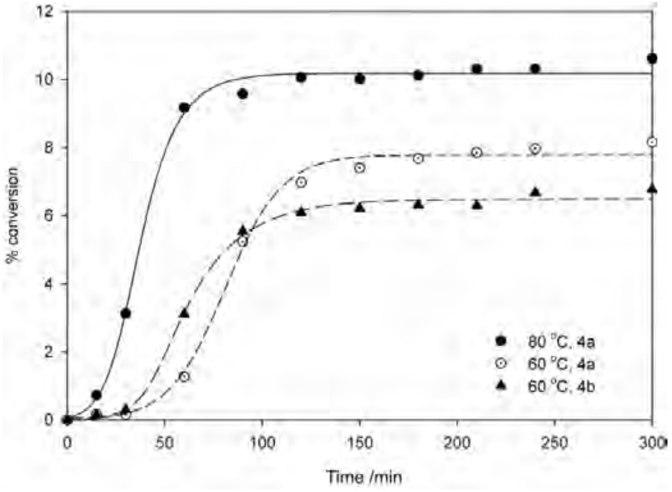


Figure 11 Overall conversion of ethylbenzene. Reaction conditions: **4a** or **4b** (0.035 g), ethylbenzene (10 mmol), H_2O_2 (4 eq), 60 °C.

predominant reaction occurring involves the oxidative cleavage of styrene to yield benzaldehyde.[31] Benzaldehyde may subsequently undergo further oxidation to yield benzoic acid. As shown in Fig. 10, the selectivity order for the oxidation of styrene was: benzaldehyde > phenylethane-1,2-diol > benzoic acid > styrene oxide.

3.3.4. *Oxidation of Ethylbenzene*

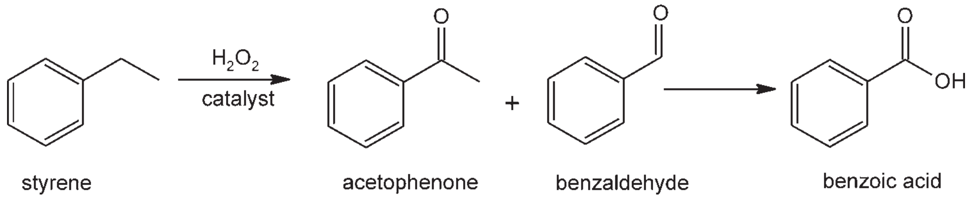
The oxidation of ethylbenzene was evaluated at 80 °C and 60 °C using two equivalents of peroxide (Fig. 11). Under these conditions, only low conversions of between 6.77 % and 10.6 % were attained. Unfortunately, increasing the amount peroxide or the temperature had detrimental effects on the stability of the catalyst.

For this reaction, the main product of oxidation was acetophenone along with some traces of benzaldehyde and benzoic acid according to Scheme 5. The formation of benzaldehyde and acetophenone from ethylbenzene has been addressed previously,[32] while benzoic acid forms from the oxidation of benzaldehyde.

3.3.5. *Oxidative Bromination of Phenol Red*

Vanadium compounds have been shown to catalyze the oxidative bromination of several organic molecules including; salicylaldehyde,[33] anisole,[34] 1,3,5-trimethoxybenzene[35] and phenol red[36], to name a few.

We have investigated the bromination activity of heterogeneous catalysts **4a** and **4b** as well as the homogeneous



Scheme 5
The oxidation products of ethylbenzene

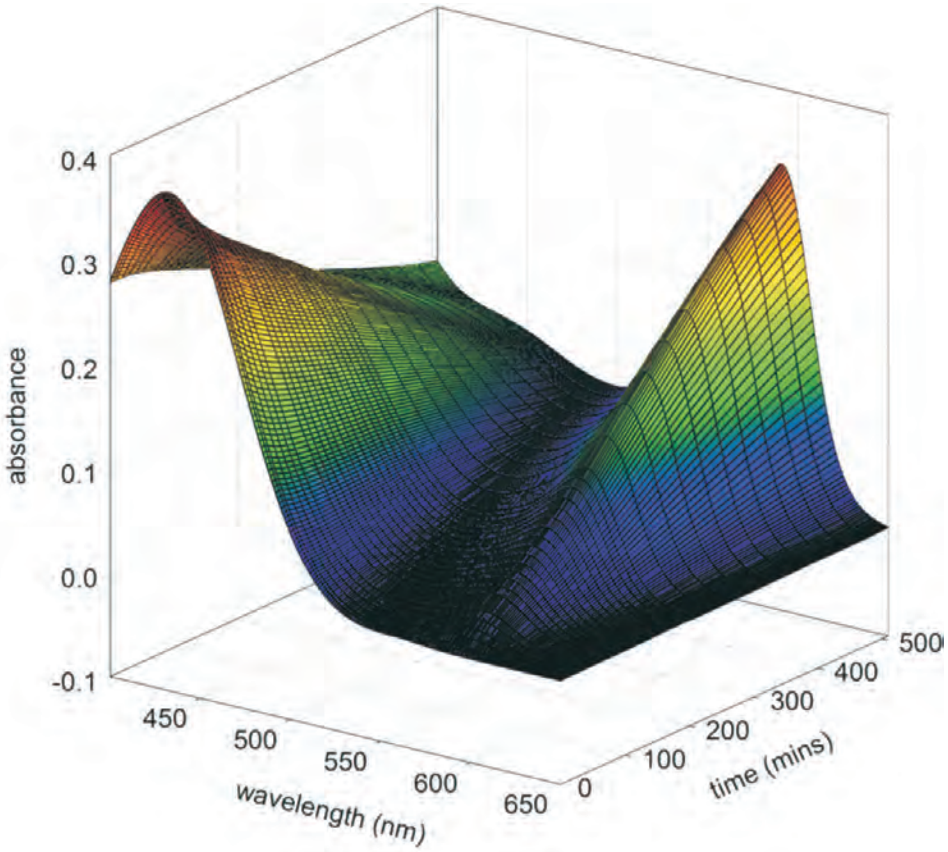


Figure 12 The change in the absorbance spectrum of phenol red due to the formation of bromophenol blue. Reaction conditions: **4b** (0.010 g), 25 mL of pH 5.5 phosphate buffer (50 mM), H_2O_2 (10 mM), KBr (1 M), phenol red (20 μM).

oxovanadium(IV) compounds **2a** and **2b**. This was done by monitoring the formation of bromophenol blue spectrophotometrically at 590 nm (Fig. 12). The reaction was performed at a pH of 5.5 since it has been shown that acidic conditionst assist vanadium-catalyzed brominations.[34] The concentrations of KBr and H_2O_2 were kept constant at 2.0 M and 10 mM, respectively. In the absence of catalyst no reaction was observed even after 3 h. However, addition of catalysts **4a** and **4b** resulted in the formation of bromophenol blue, albeit rather slow. There was no appreciable difference in activity between the two heterogeneous catalysts.

The neat oxovanadium(IV) complexes **2a** and **2b** showed improved activity over the heterogeneous counterparts. The reduced activity for the heterogeneous catalysts is likely to be due to the slow diffusion of reagents to the catalyst surface. The formation of bromophenol blue was slightly faster with catalyst **2a** compared to **2b** (Fig. 13).

3.4. Summary of Catalytic Activities

A summary of the results of the reactions can be found in Table 1. The percentage conversions correspond to the conversion after a 6-hour reaction. Likewise for the turnover frequencies (TOFs) unless a steady state was attained before the end of the 6-hour reaction, in which case they refer to the point at which a steady state was reached. The selectivity of the major products have also been included within this Table.

The catalysts were highly active in the oxidation of thioanisole, with the homogeneous catalysts proving to be more active than the heterogeneous. However, the heterogeneous catalysts showed excellent recyclability. Catalyst **4a** proved to be slightly more effective than **4b** for the oxidation of styrene and ethylbenzene. Considering the oxidation of styrene for example; when **4a** was used, a 67.2 % conversion was obtained compared to 49.1 % for **4b** (reaction conditions: 0.025 g of catalyst, 4 eq H_2O_2, 60 °C). Similarly **4a** proved to be more effect in the oxidation of ethylbenzene, reaching a maximum of 8.15 % compared to 6.7 % for **4b** (0.035 g of catalyst, 2 eq H_2O_2, 60 °C). For oxidative bromination, complex **2a** exhibited slightly better activity than complex **2b**.

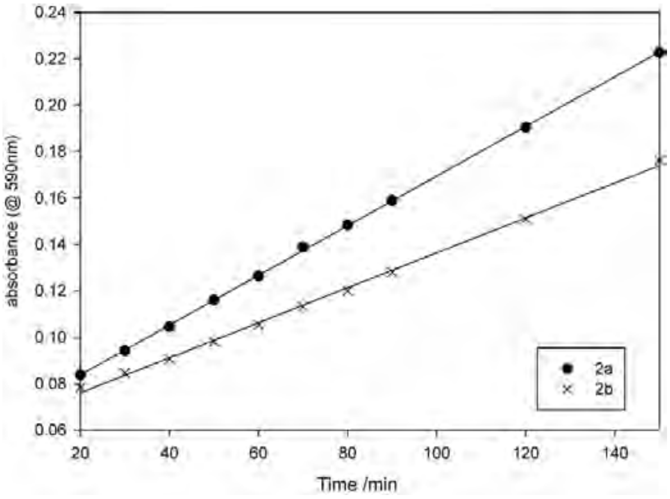


Figure 13 Plot of absorbance at 590 nm corresponding to the formation of bromophenol blue *vs.* time (min) for **2a** (R = 0.9999) and **2b** (R = 0.9982). Reaction conditions: **2a** (1.05 mg) or **2b** (1.15 mg), 25 mL of pH 5.5 phosphate buffer (50 mM), H_2O_2 (10 mM), KBr (1 M), phenol red (20 μM).

As noted earlier, the homogeneous catalysts display improved catalytic activity over the homogeneous counterparts for the

Table 1 Percentage conversion, turnover frequency (TOF) and product selectivity.

Substrate	Catalyst	Catalyst /g	H_2O_2 /eq	Temperature	TOF /h^{-1} [c]	Conversion	Product selectivity (major products)	
							Benzaldehyde	Phenylethane-1,2-diol
Styrene	**4a**	0.025	4	80	138	99.9 %	43.3 %	17.3 %
Styrene	**4a**	0.025	2	80	174	77.1 %	41.1 %	15.4 %
Styrene	**4b**	0.025	2	80	119	57.3 %	28.6 %	14.7 %
Styrene	**4a**	0.035	2	80	145	67.2 %	36.6 %	14.8 %
Styrene	**4a**	0.025	4	60	53	66.2 %	41.3 %	7.5 %
Styrene	**4b**	0.025	4	60	62	49.2 %	34.0 %	9.3 %
Styrene	**4b**	0.035	2	80	129	60.1 %	33.0 %	14.1 %
Styrene	2a	0.008	4	60	12	24.0 %	18.8 %	2.4 %
							Methyl phenyl sulphoxide	Methyl phenyl sulphone
Thioanisole	**4a**	0.025	2	60	485	100.0 %	68.2 %	30.5 %
Thioanisole	**4b**	0.025	2	60	911	100.0 %	65.7 %	33.0 %
Thioanisole	**4a**	0.025	2	25	88	91.6 %	65.8 %	29.9 %
Thioanisole	**4b**	0.025	2	25	73	96.1 %	67.0 %	27.9 %
Thioanisole	**4a**[a]	0.025	2	25	77	96.3 %	68.4 %	26.7 %
Thioanisole	**4a**[b]	0.025	2	25	72	90.0 %	61.3 %	27.2 %
Thioanisole	**4b**[a]	0.025	2	25	74	96.6 %	61.9 %	33.8 %
Thioanisole	**4a**	0.035	2	25	57	99.5 %	65.5 %	27.8 %
Thioanisole	**4b**	0.035	2	25	54	97.7 %	64.5 %	32.7 %
Thioanisole	**2a**	0.008	2	25	632	100.0 %	23.2 %	76.2 %
Thioanisole	**2b**	0.010	2	25	724	100.0 %	39.2 %	60.3 %
							Acetophenone	Benzaldehyde
Ethylbenzene	**4a**	0.025	2	80	23	10.60 %	3.6 %	1.2 %
Ethylbenzene	**4a**	0.035	2	60	10	8.15 %	4.7 %	1.1 %
Ethylbenzene	**4b**	0.035	2	60	10	6.77 %	3.9 %	0.6 %

[a] Catalyst after one full catalytic cycle.
[b] Catalyst after two full catalytic cycles.
[c] Determined as moles of substrate converted/moles of catalyst/time /h.

oxidation of thioanisole and oxidative bromination. However, at the elevated temperature used for the oxidation of styrene (60 °C), the heterogeneous catalyst proved more effective, possibly due to the extra stability imparted by the cross-linked polymeric support.[37]

4. Conclusions

The polymer-anchored oxovanadium(IV) catalysts (**4a** and **4b**) and homogeneous oxovanadium(IV) catalysts (**2a** and **2b**) display catalytic activity in the hydrogen peroxide facilitated oxidation of thioanisole, styrene and ethylbenzene and oxidative bromination of phenol red. Interestingly, the catalysts (**2a** and **4a**) containing the ligand Im4COOH were typically more active than those containing MeIm2COOH. This may be due to the structural similarity between Im4COOH and histidine, the amino acid found coordinated to vanadium in the active site of VHPOs.

For the oxidation of thioanisole, excellent conversions (above 90 %) were achieved under all reaction conditions tested. The homogeneous catalysts displayed significantly higher activity than the heterogeneous counterparts. Despite this, the heterogeneous catalysts are still a viable option since they were simple to separate and showed no appreciable loss in activity even after three catalytic reactions. The heterogeneous catalysts also proved to be effective for the oxidation of styrene. Unlike the trend observed for the oxidation of thioanisole, the heterogeneous catalysts were more active than their homogeneous counterparts in this reaction. Only low conversions were obtained for the oxidation of ethylbenzene. All catalysts displayed haloperoxidases activity as determined by the oxidative bromination of phenol red.

Acknowledgements

The authors would like to thank the DST/Mintek National Innovation Centre (Rhodes University) for microanalysis data as well as the Electron Microscopy Unit (Rhodes University) for SEM images. We also thank Sasol and NRF for financial support.

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