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# Multiphase Oxidation of Aniline to Nitrosobenzene with Hydrogen Peroxide Catalyzed by Heteropolyacids

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Received 13 December 2007

**Abstract:** Keggin-type heteropolyacids have been used as catalyst for high-yielding oxidation reactions in multiphase conditions. This simple and efficient procedure promoted the conversion of anilines to the corresponding nitroso and nitro derivatives. In comparison with homogeneous system the oxidation from anilines to nitroso compounds and nitro compounds were more effective and the solvents used were not toxic.

**Key words:** multiphase system, Keggin polyoxometalate, hydrogen peroxide, oxidation, aniline

Nitroso compounds are very useful in organic chemistry as they undergo a variety of transformations such as nitroso aldol reactions,<sup>1</sup> nitroso ene reactions,<sup>2</sup> [2+2] and [2+3] cycloadditions,<sup>3</sup> addition of Grignard reagents,<sup>4</sup> and formation of azobenzenes.<sup>5</sup> Additionally, these compounds have been examined for their potential use as antiretroviral and antitumor agents.<sup>6</sup>

Nevertheless, a simple high-yielding procedure for the preparation of nitrosobenzenes remains unreported. Several oxidation methods for preparation of nitrosoarenes from anilines have been recently published, employing various oxidizing agents such as peracetic acid, 3-chloroperoxybenzoic acid, oxone and potassium permanganate.<sup>7</sup>

Alternatively, the use of aqueous hydrogen peroxide as an oxidant is very attractive and has previously been employed for the oxidation of anilines to nitroso compounds in the presence of rhenium,<sup>8</sup> tungsten<sup>9</sup> and molybdenum<sup>10</sup> catalysts, giving high yields of nitroso derivatives.

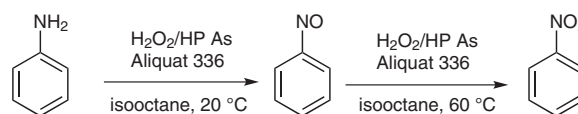
The demand for environmentally friendly processes has prompted researchers to investigate the use of heteropolyacids (HPAs) as catalysts, since they represent a green class of oxidation catalysts when they are used in the presence of aqueous hydrogen peroxide as an oxidizing agent.<sup>11</sup>

In the literature, several examples for the use of HPAs as oxidation catalysts have been described.<sup>12–14</sup> In the past few years, our research group has been studying the synthesis, characterization and application of new Keggin-

type HPAs for the oxidation reaction of phenols and sulfur, predominately under homogeneous conditions.<sup>15,16</sup>

Recently, we discovered a more convenient procedure for the oxidation of organic compounds using aqueous hydrogen peroxide promoted by HPAs in a triphasic system; comprising an aqueous solution of hydrogen peroxide, an organic solvent and an ionic liquid. Addition of Aliquat 336 to such a system, leads to formation of a third phase which resides between the aqueous phase and the organic phase. The oxidation reaction takes place in this third phase with the presence of HPA. Under these conditions, the observed selectivity is higher and the loss of hydrogen peroxide is dramatically reduced.<sup>17</sup> Such behavior renders the system suitable for a continuous process as the reaction components can be easily separated; the products reside in the organic phase, the oxidant in the aqueous phase and the catalyst within the Aliquat 336 phase.

In this paper we describe the selective oxidation of aniline to nitrosobenzene employing isooctane, aqueous hydrogen peroxide (35% p/V) and Aliquat 336 as an ionic liquid (Scheme 1). Several HPAs were examined as catalysts at ambient temperature, while additional control experiments were conducted using homogeneous conditions (acetonitrile), biphasic conditions (isooctane and H<sub>2</sub>O) and a triphasic system in the absence of a HPA. Additionally, the effect on selectivity by variation of the reaction temperature was investigated.



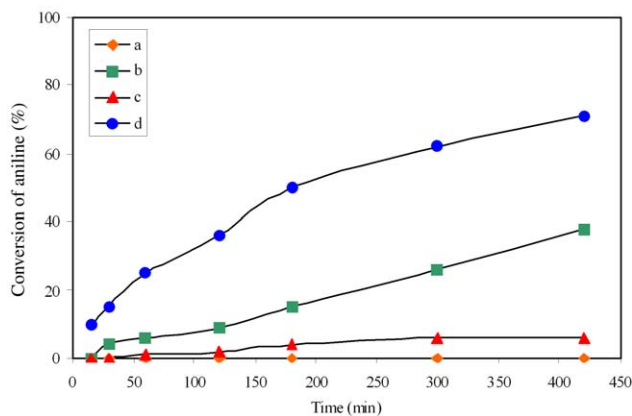
**Scheme 1** Oxidation of aniline in multiphasic system

The Keggin structure for all of the prepared catalysts<sup>18</sup> was verified by FT-IR; the spectral data were in agreement with those of the catalysts that we previously prepared and characterized by NMR, DRX, thermal analysis, TPR and voltamperometry.

The acidic properties of heteropolyacids were measured by potentiometric titration with *n*-butylamine.

A preliminary series of reactions was conducted using the heteropolyacid catalyst H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub> (M12P) and hydrogen peroxide as the oxidizing agent. Oxidation of aniline

to nitrosoaniline at ambient temperature was examined in various reaction systems. These were: (a) a homogeneous system using acetonitrile as solvent, (b) a biphasic system using isooctane and water, (c) a multiphasic system with isooctane, water and Aliquat 336 in the absence of catalyst and, (d) a multiphasic system as described in (c) with the presence of  $\text{H}_3\text{PMo}_{12}\text{O}_{40}$  as catalyst. The extent of conversion for the aforementioned reaction systems is depicted in Figure 1.<sup>19</sup>



**Figure 1** Selective oxidation of aniline to nitrosobenzene at 20 °C employing M12P as catalyst. The curves show the influence of the reaction media on conversion: (a) a homogeneous system, (b) a biphasic system, (c) a multiphasic system without catalyst and (d) a multiphasic system including catalyst

The reactions were carried out at 20 °C for seven hours. The catalyst M12P was employed in a 2-mmol% amount and hydrogen peroxide was used in a 35%-p/V solution.

With the exception of the reaction conducted in acetonitrile [system (a)], the selectivity ranged from 90–100% using conditions (b)–(d), with nitrosobenzene being the only observable by-product. No conversion was observed in the homogeneous acetonitrile system (a). In the biphasic system (b) the extent of conversion was 38% and the selectivity for nitrosobenzene was 90%, with the remaining 10% attributed to nitrobenzene. In the multiphasic system (c) which comprised isooctane, Aliquat 336 and water in the absence of catalyst, the extent of conversion was found to be 6% with no detectable by-products. In the same triphasic system with the inclusion of catalyst M12P [system (d)] the extent of conversion was 76% with a selectivity of 96%.

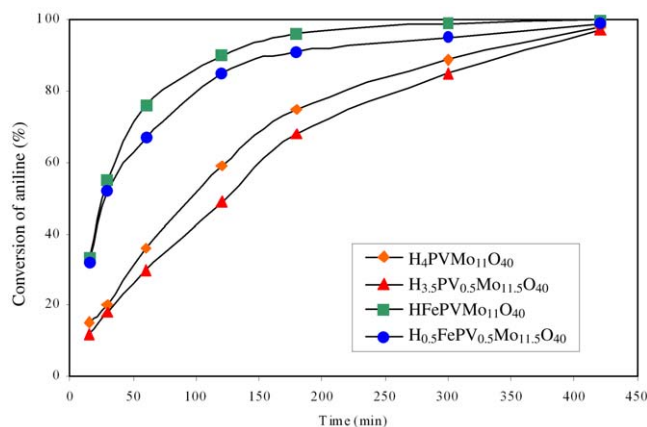
A series of experiments, performed in the multiphasic system (d), was then conducted in order to examine the performance of different heteropolyacids towards selective oxidation of aniline to nitrosobenzene. The HPA catalysts that were used,  $\text{H}_{3.5}\text{PV}_{0.5}\text{Mo}_{11.5}\text{O}_{40}$ ,  $\text{H}_4\text{PVMo}_{11}\text{O}_{40}$ ,  $\text{H}_9\text{PV}_6\text{Mo}_6\text{O}_{40}$ ,  $\text{H}_6\text{PAIMo}_{11}\text{O}_{40}$  and  $\text{H}_5\text{PA}_{10.5}\text{V}_{0.5}\text{Mo}_{11}\text{O}_{40}$  differed from M12P by inclusion of vanadium and/or aluminum. As shown in Table 1, inclusion of vanadium into the structure of the HPA improved the activity of the catalyst, which was attributed to an increase in the reduction potential which directly correlates with the amount of va-

nadium present in the structure.<sup>20</sup> Even more remarkable was the effect on conversion by incorporation of aluminum into the primary structure of the HPA; inclusion of one atom of aluminum increased the extent of conversion from 36 to 74%. However, the most active catalyst under the examined conditions contained both aluminum and vanadium within the heteropolyanion; the catalyst  $\text{M}_{11}\text{PA}_{10.5}\text{V}_{0.5}$  gave 90% conversion with 100% selectivity towards nitrosobenzene formation.

**Table 1** Selective Oxidation of Aniline to Nitrosobenzene at 20 °C (7 h), Employing Different HPAs as Catalysts in the Multiphasic System

Entry	Catalyst	Conv. (%)	PhNO (%)	PhNO <sub>2</sub> (%)
1	$\text{H}_3\text{PMo}_{12}\text{O}_{40}$	71	96	4
2	$\text{H}_6\text{PBMo}_{11}\text{O}_{40}$	98	97	3
3	$\text{H}_6\text{PAIMo}_{11}\text{O}_{40}$	100	93	7
4	$\text{H}_4\text{PVMo}_{11}\text{O}_{40}$	98	94	6
5	$\text{H}_6\text{PAI}_{0.5}\text{V}_{0.5}\text{Mo}_{11}\text{O}_{40}$	98	95	5
6	$\text{H}_7\text{PV}_2\text{Mo}_{10}\text{O}_{40}$	100	90	10
7	$\text{H}_9\text{PV}_6\text{Mo}_6\text{O}_{40}$	100	87	13
8	$\text{H}_{11}\text{PV}_8\text{Mo}_4\text{O}_{40}$	100	82	18
9	$\text{H}_5\text{PBiMo}_{11}\text{O}_{40}$	100	91	9

Further experiments were carried out to examine the influence of iron, by substitution of hydrogen within the HPA structure. The multiphasic reaction system (d) was employed with the following HPAs: the iron-containing catalysts  $\text{M}_{11.5}\text{PV}_{0.5}\text{Fe}$  and  $\text{M}_{11}\text{PVFe}$ , and for comparison,  $\text{M}_{11.5}\text{PV}_{0.5}$  and  $\text{M}_{11}\text{PV}$ . The results are reported in Figure 2.

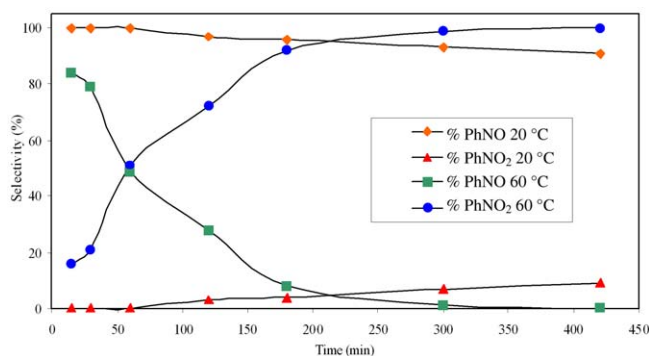


**Figure 2** Selective oxidation of aniline to nitrosobenzene at 20 °C after 7 h. The curves show the influence of iron within the structure of the catalyst on extent of conversion.

As illustrated in Figure 2, substitution of hydrogen with iron enhanced the activity of the catalyst, which resulted

in 76% conversion to nitrosobenzene in 60 minutes by use of M<sub>11</sub>PVFe. In contrast, a lower conversion of 36% was obtained with the use of M11PV after 60 minutes. Despite the differences in extent of conversion, 100% selectivity for nitrosobenzene was observed in both cases. Furthermore, the iron-substituted catalysts promoted higher conversions within shorter time frames also compared with the catalysts shown in Table 1. Such improved activity cannot be ascribed to the variation of reduction potentials, since the presence of iron does not affect this value; it is more likely to be due to the increased acidity of the catalysts, since potentiometric titrations of iron-substituted catalysts indicated higher electrode ionization potentials.

The results of the previous experiments conducted in the multiphase reaction system indicated that the iron-containing catalyst, M<sub>11</sub>PVFe, was the most active catalyst. Therefore, this catalyst was examined in further experiments at two different temperatures to establish the effect on selectivity. The reactions were carried out at 20 and 60 °C. As shown in Figure 3, the reaction conducted at 20 °C showed 100% selectivity for nitrosobenzene with 76% conversion after 60 minutes. In contrast, the reaction conducted at 60 °C showed 100% selectivity for nitrobenzene with 100% conversion after seven hours.



**Figure 3** Oxidation of aniline in the multiphase system using M<sub>11</sub>PVFe as catalyst. The curves show the influence of temperature on product selectivity.

Once the reaction conditions for the selective oxidation of aniline to nitroso and nitro derivatives had been optimized, the reaction was extended to other substrates. Table 2 shows the results for the selective oxidation of different anilines to nitroso compounds. In all cases the conversion to the related nitroso compound was completed in a short reaction time and the products were obtained in excellent yields (85–99%) and high selectivity. Table 3 reports the results for the selective oxidation of different anilines to nitro compounds. The reaction was performed at 60 °C and also in this case, yields were very high (99–100%) and the reaction was extremely selective.

In this work it was demonstrated that the multiphase system gives better results in the oxidation of aniline to nitrosobenzene using hydrogen peroxide as oxidant in the presence of Keggin-type HPAs as catalysts. This method represents a solution to the problem of incompatibility be-

**Table 2** Synthesis of Nitroso Derivatives in a Multiphase System at 20 °C Using as Catalyst HFePMo<sub>11</sub>VO<sub>40</sub> (Reaction Time: 7 h)

Entry	Substrate	Conv. (%)	PhNO (%)	PhNO <sub>2</sub> (%)
1	aniline	100	91	9
2	4-methylaniline	99	99	1
3	2-methylaniline	100	92	8
4	4-chloroaniline	98	92	8
5	4-methoxyaniline	100	85	15

**Table 3** Synthesis of Nitro Derivatives in a Multiphase System at 60 °C Using as Catalyst HFePMo<sub>11</sub>VO<sub>40</sub> (Reaction Time: 7 h)

Entry	Substrate	Conv. (%)	PhNO (%)	PhNO <sub>2</sub> (%)
1	aniline	100	–	100
2	4-methylaniline	100	–	100
3	2-methylaniline	100	1	99
4	4-chloroaniline	100	1	99
5	4-methoxyaniline	100	1	100

tween the oxidating aqueous phase and the organic phase of the substrate. In fact both catalyst's activity and selectivities improved in the presence of a third phase.

Several catalysts containing aluminum and vanadium in the primary structure of the heteropolyacid were studied. Moreover the effect of the substitution of hydrogen with iron atoms was reported. All substituted catalysts showed better activity than the commercial (M12P) one. The improved activity of the vanadium-containing HPAs is related to the corresponding increased redox potentials. On the other hand, the explanation for the increased activity of aluminum and/or iron-containing structures is more complicated and appears to be related to the increased acidity of catalysts.

The M<sub>11</sub>PVFe catalyst was employed to study the selectivity at two different temperatures. Keeping all the parameters same, the reactions were carried out at 20 and 60 °C; in the former case selectivity was 100% towards nitrosobenzene, while in the latter case it was 100% towards nitrobenzene, proving that selectivity is easily tunable by changing the reaction temperature. Moreover, in the multiphase conditions, no appreciable decomposition of hydrogen peroxide was recorded.

One of the advantages of this methodology is that H<sub>2</sub>O<sub>2</sub> as oxidant, as opposed to peracetic acid, 3-chloroperoxybenzoic acid, oxone and potassium permanganate,<sup>7</sup> does not produce any inorganic salts during the oxidation. Besides, compared to other systems employing H<sub>2</sub>O<sub>2</sub> as oxidant, in the multiphase system the catalyst is confined in one of the three phases, so allowing its recovery and reuse. Therefore a continuous flow condition can be easily applied to this procedure.

## Acknowledgment

The authors thank the Consorzio Interuniversitario Nazionale La Chimica per l'Ambiente (INCA), the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) and the University of La Plata.

## References and Notes

- (1) Oppolzer, W.; Tamura, O.; Sundarabau, G.; Signer, M. *J. Am. Chem. Soc.* **1992**, *114*, 5900.
- (2) Adam, W.; Krebs, O. *Chem. Rev.* **2003**, *103*, 4131.
- (3) Viehe, H. G.; Merenly, R.; Francotte, E.; Van Meersche, M.; Germani, G.; Declerq, J. P.; Bodart-Gilmont, J. *J. Am. Chem. Soc.* **1977**, *99*, 2340.
- (4) Kopp, F.; Sapountzis, I.; Knochel, P. *Synlett* **2003**, 885.
- (5) Goelitz, P.; de Meijere, A. *Angew. Chem.* **1977**, *16*, 854.
- (6) Rice, W. G.; Schaeffer, C. A.; Graham, L.; Bu, M.; McDougal, J. S.; Orloff, S. L.; Villinger, F.; Young, M.; Oroszlan, S.; Fesen, M. R.; Pommier, Y.; Mendelejev, J.; Kun, E. *Nature (London)* **1993**, *361*, 473.
- (7) (a) Gowenlock, B. G.; Richter-Addo, G. B. *Chem. Rev.* **2004**, *104*, 3315. (b) Yu, B.-C.; Shirai, Y.; Tour, J. M. *Tetrahedron* **2006**, *62*, 10303. (c) Priewisch, B.; Ruck-Braun, K. *J. Org. Chem.* **2005**, *70*, 2350.
- (8) Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 1326.
- (9) Giera, H.; Lange, W.; Meiers, M.; Pires, R. Eur. Patent Appl., EP1099683A1, **2001**.
- (10) (a) Tollari, S.; Cuscata, M.; Porta, F. *J. Chem. Soc., Chem. Commun.* **1993**, 1510. (b) Defoin, A. *Synthesis* **2004**, 706.
- (11) Alizadeha, M. H.; Tayebee, R. *J. Braz. Chem. Soc.* **2005**, *16*, 108.
- (12) Okujara, T.; Mizuno, M. *Appl. Catal. A: Gen.* **2001**, *222*, 63.
- (13) Corma, A. *Chem. Rev.* **1995**, *95*, 559.
- (14) (a) Risono, M. *Chem. Commun.* **2001**, 1141. (b) Simonova, M. V.; Zhizhina, E. G.; Russkikh, V. V.; Matveev, K. I. *Russ. Chem. Bull.* **2005**, *54*, 1532.
- (15) Villabrille, P. I.; Romanelli, G. P.; Vázquez, P. G.; Càceres, C. V. *Appl. Catal. A: Gen.* **2004**, *270*, 101.
- (16) Romanelli, G. P.; Vázquez, P. G.; Tundo, P. *Synlett* **2005**, 75.
- (17) Results not yet published.
- (18) The commercial catalyst, H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub> (M12P), was obtained from Aldrich. All the others were prepared according to conventional procedures described in ref. 16. Catalysts were characterized with a Bruker IFS 66 FT-IR equipment, employing KBr discs. The acidity was measured via potentiometric titration, adding little amounts of a solution of *n*-butylamine in MeCN (0.05 N) to the suspended solid (0.05 g) in MeCN (90 mL) stirred during the whole procedure. The difference of potential (mV) was recorded with a digital pHmeter (Instrumentalia S.R.L.), equipped with a combined electrode.
- (19) **General Procedure for Oxidation in Homogeneous Conditions:** Reactions were carried out in a 25-mL 3-necked round-bottomed flask, equipped with a refrigerator and thermostated at working temperature. In the reactor were charged aniline (1 mmol), a solution of *n*-decane in MeCN as internal standard (0.56 mL), MeCN to reach an overall volume of 5 mL, a solution of H<sub>2</sub>O<sub>2</sub> (35% p/V, 5 mL) and heteropolyacid (2 mmol%). The reaction mixture was stirred with a magnetic bar at 700 rpm.  
**General Procedure for Oxidation in Multiphasic Conditions:** The aforementioned procedure was employed for reactions in multiphasic conditions, with the addition of Aliquat 336 (2.32 mL) in isooctane (10% p/V) solution and employing isooctane instead of MeCN as organic solvent.  
**Samples Analysis:** Samples were withdrawn from the organic phase at 20 min time intervals during a total reaction period of 420 min. Each sample volume was approximately 20  $\mu$ L and it was diluted with 1–2 mL of isooctane or MeCN. The solution was stirred in the presence of silica gel and filtered to remove the Aliquat 336 before the injection in the GC. Concentrations were calculated with the internal standard method. Conversions were obtained with GC analysis performed with a Varian GC 3400 instrument, in the presence of *n*-decane as internal standard. The capillary column was a 30 m Chromopack CP Sil 8 CB, whose diameter was 0.32 mm. The identification of products was performed with GC-MS (detector HP 5971) for comparison with authentic samples.
- (20) Villabrille, P. I. *PhD Thesis*; Universidad Nacional de La Plata: Argentina, **2006**.