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# Polymer-supported molybdenyl thioglycolate as oxygen atom transfer reagent

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**Abstract**

Oxo-transfer reactions of a variety of substrates in DMF or methanol using polymer-supported molybdenyl thioglycolate (PSMT) have been investigated. The clean oxidation of $Me_2PhP$, *n*-butanethiol or benzoin to yield $Me_2PhPO$, disulfide or benzil, respectively, occurs in high yield. In the presence of air or pyridine N-oxide, a catalytic cycle is accomplished which goes on until the completion of the substrate. © 2000 Elsevier Science B.V. All rights reserved.

*Keywords:* Air oxidation; Molybdenum; Heterogeneous catalyst

## 1. Introduction

Interest in the synthesis and properties of polymer-supported catalysts has expanded significantly over the last two decades due to their applications in organic synthesis [1–4]. In all these applications, advantage is taken of the insolubility of the polymeric reagent and their by-products, which allows an easy removal of excess of reagent or spent materials from the desired product. These facts, along with the importance in organic synthesis of oxidation reactions that proceed under mild and neutral conditions, have led to the development of several polymer-supported oxidizing agents [5–13].

Recently, we have synthesized [14] a novel supported Mo(VI) catalyst named RTGA (from now on PSMT) in which 2-mercaptoacetic (thioglycolic) acid has been used as coligand for a molybdenum complex anchored to a Merrifield's resin. The well-documented dimerization of molybdate ions with an excess of thioglycolic acid [15,16] can be avoided by using polystyrene beads adjacent to the ligating nitrogen atoms. This supported complex catalyses alkene epoxidation with *tert*-butylhydroperoxide [14] shows a high stability of the supported reagent under these reaction conditions without molybdenum leaching.

We have previously reported [17,18] the syntheses of complexes whose ligands, containing thiolate and carboxylate groups, can mimic the behaviour of molybdenum hydroxylases which catalyse redox processes where an oxygen atom or a hydroxy group is added to or removed from

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the substrates. These complexes promote typical oxygen transfer reactions under catalytic homogeneous conditions, allowing the conversion of aliphatic thiols, $Me_2PhP$ or benzoin into the corresponding disulfide, $Me_2PhPO$ or benzil [19,20]. However, this method shows two disadvantages: specific ligands have to be prepared in order to avoid dimerization of the complex and purification of products from the complex along with catalyst recovery can be tedious. Polymer supported molybdenum complexes with thiolate and carboxylate groups should be an ideal means to solve these problems but, as far as we know, no molybdenum catalyst supported on Merrifield resins has been described for these reactions.

Taking into account the core similarities between PSMT and those homogeneous catalysts that promote oxygen transfer reactions, we decided to profit from the mild reaction conditions and low toxicity of the supported molybdenum complexes and we have focussed our attention on the development of oxidations using PSMT for organic synthesis. Here we report the behaviour of PSMT as a heterogeneous catalyst that allows a clean oxidation of $Me_2PhP$, thiols or benzoin at neutral pH to yield $Me_2PhPO$, disulfide or benzil, respectively. Using PSMT, these typical oxygen transfer reactions proceed in high to excellent yield with maximum purity. Regeneration and recycling of the molybdenyl resin was examined: in the presence of air or pyridine *N*-oxide, a catalytic cycle is accomplished which takes the reaction to complete the conversion of the substrate.

## 2. Experimental

### *2.1. Instrumentation*

Infrared spectra were recorded on a BIO-RAD FTS-7. Solid $^{13}C$ NMR spectra were recorded with a Varian Unity-300 spectrometer (operating frequency 299.95 MHz) using the CP-MAS technique. Liquid NMR spectra were recorded with a Varian Unity-400 (operating at 399.95, 161.90 and 100.58 MHz for $^{1}H$, $^{31}P$ and $^{13}C$) and a Varian Unity-300 spectrometer (operating at 299.95, 121.42 and 75.43 MHz for $^{1}H$, $^{31}P$ and $^{13}C$). Chemical shifts in the $^{1}H$ NMR are denoted in $\delta$ units (ppm) relative to tetramethylsilane as an internal standard at $\delta = 0$ and chemical shifts in the $^{13}C$ NMR are denoted in δ units (ppm) relative to deuterochloroform ($\delta = 76.9$). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Gas chromatography was performed using a KONIK 3000C with a flame ionisation detector. A commercial column S.G.E. 30QC2/BPX5 (phase BPX5 (non polar), fused silica, 30 m × 0.22 mm I.D, 0.33 mm OD) was used. Elemental microanalyses were determined by "Servicio de Semimicroanálisis del Centro de Investigación y desarrollo (CSIC) de Barcelona". Atomic absorption was performed on a UNICAM 939/959 with a molybdenum lamp at 313.3 nm using a nitrous oxide-acetylene flame (4.8 l/min).

### *2.2. Materials and methods*

PSMT was obtained according to Scheme 1 [14] (solid $^{13}C$ NMR $\delta$ 183.23, 143.76, 123.80, 63.19, 48.26, 41.60, 35.69, 26.82, 9.82 ppm). Dimethylformanide was dried and distilled over 4 A° molecular sieves. Some reactions were performed under a pure argon atmosphere. Solvents were purified, dried and deoxygenated where necessary using standard procedures. Pyridine N-oxide, *n*-butanethiol and $Me_2PhP$ (Aldrich) were used as received.

### *2.3. Oxidation of n-butanethiol*

PSMT (100 mg, weight equivalent to 0.14 mmol Mo) and *n*-butanethiol (0.28 mmol) were mixed with DMF (15 ml) at room temperature. The mixture was stirred for 24 h and filtered. The GC analysis shows the disappearance of the substrate and the quantitative formation of the

butyldisulfide (0.14 mmol) $^{1}$H NMR $\delta$ 2.68 (t, $J = 3.1$ Hz 2H); 1.48–1.60 (m 2H); 1.35–1.46 (m, 2H); 1.00 (t, 3H), $^{13}$C NMR $\delta$ 39.4, 32.4, 22.5, 14.0 ppm.

### 2.4. Oxidation of $Me_2PhP$

PSMT (100 mg, weight equivalent to 0.14 mmol Mo) and $Me_2PhP$ (0.14 mmol) were mixed with methanol (15 ml) at room temperature. The mixture was stirred for 24 h filtered and concentrated to give $Me_2PhPO$ in quantitative yield $^{1}$H NMR $\delta$ 1.78, 1.74, $^{13}$C NMR $\delta$ 16.70, 17.60, 129.60, 130.40, 130.60, 132.94, 132.96 ppm. $^{31}$P NMR $\delta$ 41.48 ppm.

### 2.5. Oxidation of benzoin

PSMT (100 mg, weight equivalent to 0.14 mmol Mo) and benzoin (0.14 mmol) were mixed with methanol (15 ml) at room temperature. The mixture was stirred for 24 h filtered and concentrated to give benzil in quantitative yield $^{13}$C NMR $\delta$ 129.2; 130.6; 134.4; 136.13; 196.2

### 2.6. Catalytic reactions between R (*n*-butanethiol, $Me_2PhP$ or benzoin) and XO

The reaction was carried in DMF or deoxygenated methanol with an excess of R and XO (air or pyridine N-oxide) and in the presence of PSMT as a catalyst (10:15:1 equiv.). The $^{1}$H, $^{31}$P and $^{13}$C NMR showed that *n*-butanethiol was completely consumed over a 72-h period for air and over 50 h for pyridine N-oxide, while $[BuS]_2$, and pyridine were generated. The excess of phosphine or benzoine after 48 h for air and 24 h for pyridine N-oxide had been completely oxidized to $Me_2PhPO$ or benzil. The GC analysis shows the disappearance of the substrate and the quantitative formation of the butyldisulfide or benzil (1.4 mmol) data were corrected for the relative response of the detector by integrating the response of each analyte against an internal standard (Naphthalene). The methanol solution of phosfine was concentrated and analysed by NMR. The reactions were carried out in glass systems at room temperature and, when pyridine N-oxide was used, under argon atmosphere.

### 2.7. Metal leaching

The sample was studied for atomic absorption spectrophotometry (AAS) to detect the Mo leaching at the end of reaction and the Molybdenum leached was lower than 0.1% expressed as a percentage of Mo originally present on the resin.

## 3. Results and discussion

### 3.1. Synthesis and structure of polymer-supported catalyst

The synthesis of PSMT is performed in three steps (Scheme 1). In the first step, ethylendiamine reacts with a 2% cross-linked chloromethylated polystyrene resin (4.3 mmol/g) in DMF to give R-AMIN in quantitative yield. The analyses for displaced chlorine by ion-exchange chromatography show a functional load of 4.17 mmol/g. In the second step, the obtained R-AMIN reacts with molybdenylacetylacetonate in the presence of DMF yielding R-ACAC in 95% yield. The presence and concentration of molybdenum was tested by atomic absorption spectrophotometry. The metal loading data and the elemental microanalysis are in concordance with a relation polymeric-ligand:metal 1:1. The IR band at 1658 $cm^{-1}$ due to carbonyl absorption and the absence of the peak at 1264 $cm^{-1}$ due to (C-C1) confirms the experimental facts. Finally, reaction of R-ACAC with TGA affords PSMT in 80% yield. During the substitution of acac by TGA, some molybdenum is removed from the polymer. However, the remaining loading of Mo is adequate for catalytic applications. Its elemental microanalysis along with atomic absorption spectrophotometry shows a 1:1.1 ligand-to-metal ratios, in agreement with a mono-

meric molybdenum complex. IR spectra of PSMT display a characteristic doublet for *cis* $MoO_2$, in the range 820–931 $cm^{-1}$ (see Scheme 1). Coordination of the carboxylate and thiolate groups is also consistent with large low-field shifts ($\sim$ 7 and 36 ppm, respectively) for their solid $^{13}C$ NMR signals when compared with those of the free ligand.

### 3.2. Oxidation of n-butanethiol by PSMT

We have recently demonstrated [19–21] that reaction of molybdenum thiocarboxylate complexes with an excess of *n*-butanethiol resulted in the formation of butyl disulfide. We find now that PSMT reacts in a similar form. We began by the oxidation of the *n*-butanethiol using a stoichiometric amount of PSMT in DMF under argon atmosphere. It was found that this reaction proceeds to virtual completion at room temperature in a few hours but only 1/2 equiv. of the disulfide could be obtained, as judged by $^1H$ and $^{13}C$ NMR spectroscopy. With 1 equiv. of PSMT and 2 equiv. of butanethiol, the reaction affords 1 equiv. of disulfide. Although no evidence was found for the Molybdenum oxidation state, the above stoichiometric ratio is consistent with the immediate formation of Mo(IV). Finally, the reaction between 1 equiv. of PSMT and 3 equiv. of *n*-butanethiol was tested, and resulted in the formation of 1 equiv. of disulfide in 24 h (as shown by $^1H$ and $^{13}C$ NMR spectroscopy and gas chromatography). The reaction was quantitatively examined by means of the clearly distinct signals for $-CH_2SH$ and $(-CH_2S)_2$ in their $^1H$ NMR. The stoichiometric ratio is consistent with the formation of a $Mo^{IV}O$ complex. So it is expected that the reduction of the PSMT core ($Mo^{VI}O_2$) with thiols yielded a $Mo^{IV}O$ species (PSMT reduced) following a two-electron redox process according to reaction (1).

$$\text{PSMT} + 2\,\text{BuSH} \rightarrow \text{PSMT (reduced)} + \text{BuS–SBu} + H_2O. \quad (1)$$

Filtration of the reaction mixture affords pure product and no further purification method is required. Elemental analysis of the reduced resin revealed the same sulphur loading as the initial PSMT. The molybdenum loading of this resin was determined by atomic absorption and the concentration was concordant with that of the original PSMT. Moreover, metal detection of the filtered solution has shown that no molybdenum leaching occurs during this process.

### 3.3. Phosphine oxidation by PSMT

It is well known that dioxo-molybdenum (VI) complexes will react with phosphines, transferring an O to P, producing oxo-molybdenum (IV) species [22–25]. Although these reactions cannot be considered as models for the enzymatic reactions, they do demonstrate a two-electron transfer of oxo groups and the influence of S ligands in promoting such transfers [26].

Stoichiometric amounts of PSMT and $Me_2PhP$ reacted under argon atmosphere to give $Me_2PhPO$ as shown by $^1H$, $^{13}C$ and $^{31}P$ NMR spectroscopy according to reaction (2).

$$\text{PSMT} + Me_2PhP \rightarrow \text{PSMT (reduced)} + Me_2PhPO \quad (2)$$

All $Me_2PhP$ signals ($^1H$, 2 $CH_3$, 1.28 and 1.27 ppm; $^{31}P$, 0.00 ppm) disappeared and signals of $Me_2PhPO$ ($^1H$, 2 $CH_3$, 1.78 and 1.74 ppm; $^{31}P$, 87.28 ppm) grew up in 24 h. When an excess of phosphine is present, quantitative analysis by gas chromatography and $^1H$, and $^{31}P$ NMR at the end of the reactions allowed us to calculate their stoichiometries, which appeared to be in agreement with a two-electron reduction of Mo(VI).

In conclusion, all the above studies indicate that PSMT is reduced by two-electron substrates to Mo(IV) species. Regeneration and recycling of the molybdenyl resin was also examined. After the first oxidation by *n*-butanethiol or $Me_2PhP$, the resin was recovered in quantitative

yield by filtration followed by washing with DMF methanol and ether. The recovered resin was reoxidised suspending the resin in DMF and stirring it in the presence of air or alternatively with pyridine N-oxide and the reaction was repeated with no loss of activity.

### 3.4. Catalytic reaction between n-butanethiol / phosphine and air or pyridine N-oxide

Taking into account that the reduction of PSMT to a Mo(IV) specie which can be oxidized by air or pyridine N-oxide to regenerate the original Mo(VI) according to Scheme 2. Oxo transfers to and from the substrate have been coupled to produce a catalytic system that turns over until completion in the presence of an excess of 20 equiv. for *n*-butanethiol or 10 equiv. for $Me_2PhP$. $^1H$ and $^{13}C$ NMR showed a complete consummation of *n*-butanethiol over a period of 72 h, 48 h for the phosphine, in the presence of air. With pyridine N-oxide, shorter reaction times, 50 and 24 h, respectively, were required. Pyridine formation was monitored and quantified by chromatography. When no PSMT is present there is no oxidation of *n*-BuSH or $Me_2PhP$ with air or pyridine N-oxide under these conditions.

Analysis of the pyridine at the end of the reaction indicates a stoichiometric ratio of the conversion that can be described by the following reactions:

$$PyrN{-}O + 2\,CH_3(CH_2)_3SH \rightarrow Pyr + \left[CH_3(CH_2)_3S\right]_2 + H_2O$$

$$PyrN{-}O + Me_2PhP \rightarrow Pyr + Me_2PhPO$$

After finishing these catalytic reactions, the PSMT retained their characteristic orange colour. The atomic absorption of the resulting polymer showed identical concentration of molybdenum to the initial PSMT. This observation is expected because the oxidant applied in this system is in excess over the reactant. However, catalytic systems do show signs of decreased activity after some time. For the system with PSMT and $Me_2PhP$ (15 equiv.) a contamination by $Me_2PhP=S$ can be detected after 48 h of reaction ($^{31}P$ NMR $\delta = 34.06$ ppm).

### 3.5. Other biochemical interesting substrates

Another interesting reaction is the catalytic air oxidation of benzoin to benzil in methanol in the presence of PSMT as a model reaction for C–H activation similar to the biological oxidations of xanthine or aldehydes by the corresponding oxidase [27–29]. These enzymes are known to utilize water as a source of oxygen atoms and dioxygen can be used as an oxidant [30,31]. Air oxidation of the C–H groups is important not only in biological energy transduction, but in organic synthesis as well, taking into account that the acyloin moiety is present in many natural products [32].

Stoichiometric reaction of 1 equiv. of PSMT and 2 equiv. of benzoin affords 1 equiv. of benzil after 10 h, which is in agreement with the formation of molybdenum (IV) species according to reaction (3).

$$PSMT + phCH(OH)CH(OH)ph \rightarrow PSMT\,(reduced) + phCOCOph + H_2O \quad (3)$$

Moreover, we have investigated the catalytic activity in the air oxidation of benzoin in a reaction mixture containing an excess of benzoin and PSMT (10:1). The complete oxidation of all benzoin occurred in 72 h, and benzil was found as the only oxidation product of benzoin. No reaction was detected without the presence of PSMT.

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