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One-pot palladium catalyzed synthesis of thioethers using borrowing hydrogen methodology

Avelino Corma*^[a], Javier Navas^[a], Tania Ródenas^[a], María J. Sabater*^[a]

Abstract: Palladium on magnesium oxide is able to perform a one-pot reaction to synthesize thioethers from thiols and aldehydes formed *in situ* from the respective alcohol by means of a *borrowing hydrogen* methodology. The reaction is initiated by

dehydrogenation of the alcohol to give a palladium hydride intermediate and an aldehyde. The latter reacts with a thiol involving most probably the intermediacy of a thionium ion $RCH=S^+R$, which can be reduced *in*

situ by the metal hydrides to afford thioethers.

Keywords: one-pot • palladium • thioether • borrowing hydrogen methodology • reductive thiolation • metal hydride

Introduction

The presence of sulphur containing compounds in chemicals and biologically active compounds has driven the development of carbon sulphur bond-forming reactions during the last decade [1]. Despite of that, the number of catalytic procedures for forming C-S bonds still remains scarce, as compared with the number of methods for forming C-O and C-N bonds, partly because of the of-cited belief that sulfur poisons metal catalysts. Fortunately, this apparent functional incompatibility is being surpassed in recent years with the merging of new metal catalytic strategies [2]. Work on the synthesis of aromatic thioethers has significantly increased since the resultant products are valuable synthetic intermediates frequently found in biologically and pharmaceutically active molecules. [3] For example, they have interest as precursors of the corresponding sulfoxides and sulfones contained in antifungal and anticancer agents, as well as in potential drug candidates for Alzheimer's disease or HIV [4]. Different synthesis strategies have been established for the synthesis of thioethers. Thioethers are typically prepared by addition of thiolate anions to organic halides, alkenes and alkynes [5-6], or by sulfur condensations of organolithium or Grignard reagents with chlorophenylsulphides [7]. Besides this, in the Pummerer rearrangement alkyl sulfoxides rearrange to α -acyloxy-thioethers in the presence of acetic anhydride [8,9]. In this reaction, sulfur is reduced while the adjacent carbon is oxidized.

Direct reductive sulfidations using a combination of a carbonyl compound, a mercaptan and a reducing agent have also been described [10]. In those cases, the formation of a hemithioacetalic (or in some cases a thionium ion) intermediate has been suggested, which is subsequently reduced using, for instance, lithium aluminium hydride/aluminium chloride, triethylsilane, or pyridine-borane in trifluoroacetic acid medium, to afford the sulfide [10]. However, most of processes are not suitable for large scale production because they are quite contaminant, require severe reaction conditions, or complex procedures. Thus, it would be of interest to develop a general and simple procedure that overcomes these limitations.

Within the context of direct reductive processes, the *borrowing hydrogen* methodology is an attractive concept that combines dehydrogenation/hydrogenation reactions (hydrogen transfer) with numerous interesting organic transformations in a single pot [11]. In that methodology there is a non sacrificial hydrogen donor compound which, after dehydrogenation by a metal catalyst, can undergo further transformations to give an intermediate compound that will be reduced by a metal hydride complex generated in the initial dehydrogenation step [11].

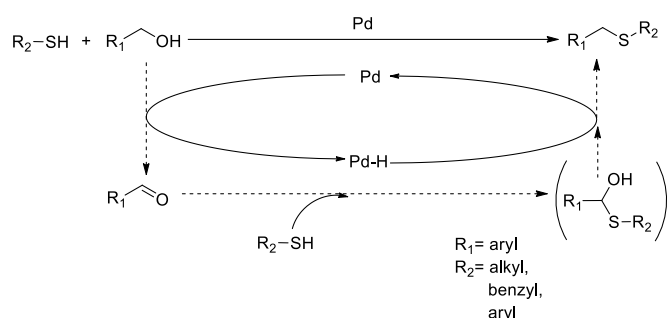
Many metals form very stable metal hydrides and are inefficient catalysts for the *borrowing hydrogen* methodology (also called hydrogen auto-transfer), as they are unable to release or transfer the hydrogen easily [12]. However, it has been shown that palladium is efficient for carrying out sequential processes based on hydrogen transfer from alcohols to afford C-N and C-C bonds [13]. The excellent catalytic ability of Pd is partly due to the large capacity of Pd nanoparticles to store hydrogen, something that is directly related to its specific electronic states, as well as to the high metal surface area that can be achieved when supporting Pd on high surface carriers [14].

In this study we will show that it is possible to achieve the self-supporting, one pot formation of C-S bonds with a solid catalyst that avoids the use of stoichiometric amounts of reducing agents.

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More specifically we report that Pd nanoparticles on high surface area MgO, efficiently catalyze the formation of thioethers starting with an alcohol and a thiol through a S-monoalkylation reaction (Scheme 1).

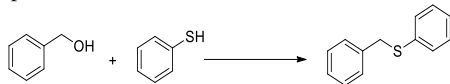


Scheme 1

The one-pot multistep reaction applies to benzylic alcohols which dehydrogenate on the metal surface to give a metal hydride complex and an aldehyde. The so-formed carbonyl compound is highly reactive towards the nucleophilic addition of thiols, also present in the same reaction medium, giving a hemithioacetal intermediate that will be most probably transformed into a thionium ion. The latter will be most probably then reduced *in situ* by the palladium hydrides to give the thioether (see reaction scheme 1).

Results and Discussion

The thioetherification reaction of benzyl alcohol and benzenethiol was selected as a model reaction to test the possibility of performing the multistep reaction as shown in scheme 2.



Scheme 2

In a preliminary experiment a metal/base Pd/MgO (0.8% Pd wt) catalyst (see characterization data in table 1S, supplementary information) was used working in trifluorotoluene (TFT) as solvent. Under these conditions thioether **1a** was obtained as main product without contamination by the symmetrical ether derived from benzyl alcohol (see entry 1, table 1). Besides **1a**, a lower amount of diphenyldisulfide **2a** was also obtained [15] (entry 1, table 1).

Table 1 S-monoalkylation reaction of benzenethiol with benzyl alcohol in one-pot^a

Entry	Catalyst	Time (h)	C(%) ^a	Yield(%) ^b		TON ^c
				1a	2a	
1 ^d	Pd/MgO (0.8% Pd)	24	90	67	23	207
2	Pd/MgO (0.8% Pd)	22	96	75	12	221
3 ^e	Pd/MgO (0.8% Pd)	24	90	82	<1	206
4 ^f	Pd/MgO (0.8% Pd)	45	34	2	32	78
5 ^g	Pd/MgO	24	37	7	30	85

	(0.8% wt Pd)					
6	Pd/Al ₂ O ₃ (1% wt Pd)	24	25	5	10	52
7	Pd/HT (0.8% wt Pd)	24	68	12	56	237
8	Pd/HAP (0.8% wt Pd)	15	11	0	11	72
9	Pd/C (Norit) (1% wt Pd)	24	50	15	30	179
10	Pd/CeO ₂ (1% wt Pd)	30	40	5	35	117
11	Au/CeO ₂ (1% wt Au)	30	55	32	13	167
12	Au/MgO (0.8% wt Au)	72	51	0	43	106
13	(Au,Pd)/MgO	48	67	58	3	--
14	Pt/MgO (1% wt Pt)	24	< 5	0	0	21
15	Ru/HT	24	0	0	0	0

a) Reaction conditions: 3 mmol PhCH₂OH, 1 mmol PhSH, 0.0075 mmol catalyst, T = 180°C, 1 ml TFT, N₂ atmosphere, dodecane was used as an internal standard; b) calculated by GC with respect to the amount thiol transformed; c) calculated as mmol thiol converted/mmol Pd surface atoms; d) reaction conditions: 1 mmol PhCH₂OH, 1 mmol PhSH, T = 180°C, 1 ml TFT, N₂; e) benzenethiol was added in 3 portions; f) reaction carried out at 100°C, g) PBN (1mmol) was added to the reaction mixture.

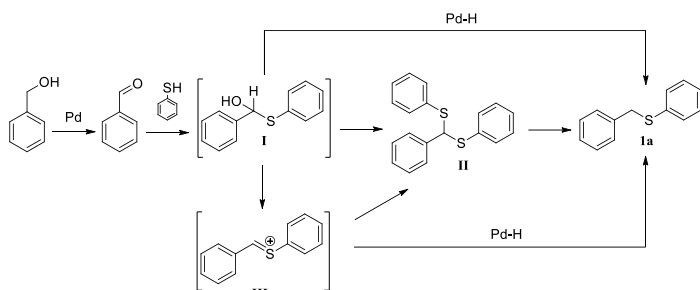
Since no dibenzyl ether but diphenyldisulphide was observed as sub-product, we performed the reaction with an excess of benzyl alcohol and the result (entry 2, table 1) indicated a moderate decrease in the formation of **2a** (see the evolution of reaction with time in figure 1s, supplementary material). A further decrease in the formation of **2a** was obtained by slowly adding the benzenethiol into an excess of the alcohol (entry 3, table 1).

When working at lower temperature (100°C), the catalyst was very chemoselective towards the undesired product **2a**, something that agrees with the fact that the metal catalyzed formation of disulfides usually involves lower activation energy than the formation of thioethers (entry 4, table 1) [15a]. Therefore from now on, and in order to selectively form the thioether **1a**, the working conditions were adjusted to 180°C while an excess of alcohol was always used.

It has been described that the formation of disulphides occur through the coupling of two sulphur radicals on the metal surface while the formation of thioethers from the aldehyde takes place by ionic intermediate species [15a]. If this is so, further decrease in the formation of **2a** could be achieved by adding into the reaction system a radical scavenger. Then, phenyl *N-tert*-butylnitron (PBN) was used as radical scavenger and, surprisingly selectivity to **2a** did not decrease but increased, while the rate of formation of thioether **1a** was strongly inhibited (entry 5, table 1) up to the point that in the presence of PBN, **2a** became the major reaction product. It can be then assumed that the strong inhibiting effect of PBN for the formation of the thioether is a clear indication that radical intermediates should be formed in some elementary step of the reaction. Following the above, and since the nucleophilic attack of the thiol to the aldehyde has been shown to proceed through ionic intermediates [15b], the obvious conclusion is that the dehydrogenation of benzyl alcohol to benzaldehyde must involve radical intermediates. This conclusion would be in agreement with mechanistic studies on the alcohol dehydrogenation reaction based on DFT calculations [13c]. Moreover, the fact that the formation of the disulfide **2a** was not affected by the presence of the radical scavenger indicates that this reaction involves partially ionic intermediates.

Mechanistically the formation of the thioether **1a** can be explained by nucleophilic attack of benzenethiol to the benzaldehyde formed after dehydrogenation of the alcohol, giving a hemithioacetal intermediate (RCH(OR)SR) (**I**) in equilibrium with a thioacetal **II**

(not detected by GC) if water is present (see Scheme 3). Taking into account that thioacetals can be desulfurized to the corresponding sulfides or hydrocarbons using diverse reducing agents (*vs.* H₂ and Raney nickel, pyridine-borane in trifluoroacetic, etc...) [16], it may very well occur that the final product **1a** could be formed by reductive hydrogenolysis of the thioacetal **II** by the metal hydrides formed on the metal surface, or even by reduction of the hemithioacetal **I** and/or of a thionium ion **III** intermediate formed during the reaction (see scheme 3).



Scheme 3

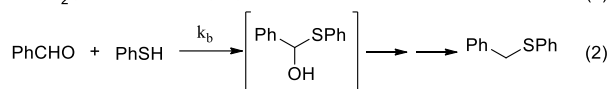
In order to test this hypothesis a fixed amount of Pd/MgO (0.8 % wt) was treated initially with H₂ (5 bar) at 180°C for 1 h to ensure the formation of metal hydrides from the very beginning. The total amount of palladium hydrides (0.6 mmol) was estimated on the basis of the decrease in hydrogen pressure. Then stoichiometric amounts of benzaldehyde and benzenethiol were reacted giving the expected thioether **1a** as major product, the hydrogenolysis product toluene as secondary product and traces of the hydrogenation product trifluoromethylcyclohexane. Disulfide **2a** was also detected just at the level of traces. These results confirm that formation of thioether **1a** will effectively occur through the direct reductive thiolation of *in situ* generated aldehydes with thiols by palladium hydride species according to Scheme 3. Then, in order to discern about the nature of the key intermediate that will be reduced during the reaction, compound **II** was synthesized [17] and it was reacted with 1 mmol of benzyl alcohol in the presence of Pd/MgO at 180°C. Under these experimental conditions thioacetal **II** remained unreacted after 8h reaction, albeit **1a** could be obtained with low yields (~5%) when the thioacetal was treated with H₂.

This experimental fact suggests that major pathway is most likely formation the thionium ion **III** from the hemithioacetalic compound **I**, followed by a very rapid hydrogenation of the former (**III**) by the palladium hydrides (see Scheme 3) [10]. In fact, these results are also consistent with the observed kinetics: first order dependence on benzaldehyde and first order dependence on benzenethiol (see Rate controlling step section)

Rate controlling step

The study of the reaction scheme and mechanism of the synthesis of thioethers through the direct reductive thiolation of *in situ* generated aldehydes as well as the scope of the reaction were carried out with a Pd(0.8%)/MgO catalyst (Pd average particle size, d: 2 nm) (See figure 3S Supporting Information). In a first approach, the elucidation of the rate determining step in the global process could be helpful to indicate what reaction step should be accelerated and consequently what modifications should be made on the catalyst to improve activity and selectivity.

To do that, the two elementary steps for the S-monoalkylation of benzenethiol with benzyl alcohol, *i.e.* alcohol dehydrogenation to afford benzaldehyde and reductive thiolation of the latter to form the thioether **1a**, have been formulated in equations 1-2, by assuming that the hemithioacetal (or the thionium ion), which was not detected by gas chromatography, is an intermediate that reacts very fast:



From the above chemical equations, two kinetic rate expressions were derived by assuming that the dehydrogenation of benzyl alcohol to give benzaldehyde and a metal hydride (equation 1), or the reductive S-thiolation (equation 2) was the overall rate controlling step, being the other in equilibrium (see table 2):

Table 2 Kinetic rate expressions obtained by considering that either dehydrogenation or the reductive thiolation reaction is the rate controlling step.

Entry	Rate controlling step	Reaction rate equation
1	1	$r_0 = k_a [\text{PhCH}_2\text{OH}]$
2	2	$r_0 = k_b [\text{PhCHO}] [\text{PhSH}] = K_a k_b [\text{PhCH}_2\text{OH}] [\text{PhSH}]$

a) Kinetic constants of first and second steps respectively: k_a , k_b b) K_a : steady state constant for dehydrogenation of benzyl alcohol.

When plotting the initial reaction rate *versus* the concentration of benzenethiol and benzyl alcohol determined experimentally (see Figure 2) it is possible to see that the initial rate for formation of thioether is a function of the concentration of the two reactants. There is a first order dependence on benzaldehyde and first order dependence on benzenethiol.

Therefore the controlling step of the reaction cannot be the dehydrogenation of alcohol (step 1) but the direct reductive thiolation (step 2) since in the former case the reaction rate will only be dependent on the concentration of alcohol (see entry 1, table 2).

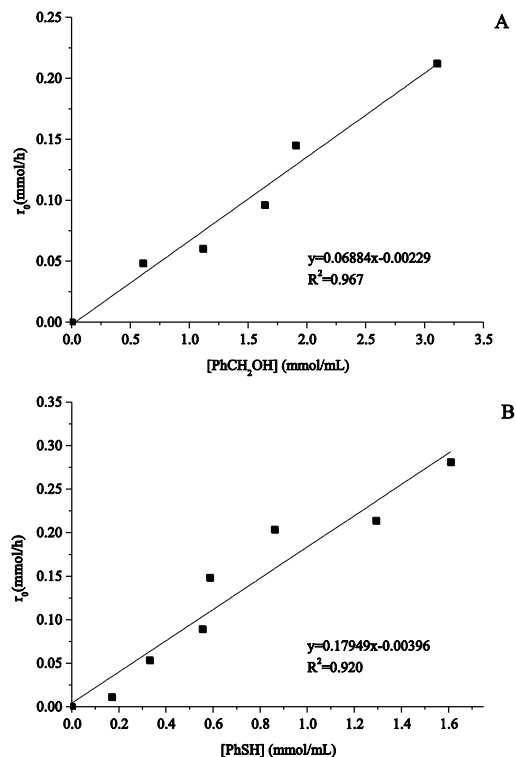


Figure 2 Graphic representations obtained when plotting A) r_0 versus [PhCH₂OH], and 1 mmol PhSH, and B) r_0 versus [PhSH], and 3 mmol [PhCH₂OH]) using Pd(0.8%)/MgO as catalyst.

It follows then that the direct reductive thiolation is the rate controlling step of the cascade reaction. If this is so, we can assume that the metal component of the catalyst performs a very fast

dehydrogenation of the alcohol which is, in any case, much faster than the reaction between the aldehyde and the thiol. If the above is true when a less effective dehydrogenation metal component is used, it may very well occur that the slowest reaction step will not be the thiolation anymore, but the dehydrogenation of benzylic alcohol.

Taking into account that dehydrogenation of alcohols [13] is a structure sensitive reaction, i.e. metal sites located at the crystal corners and edges of the crystallites are the most reactive, and that in a Pd/MgO catalyst prepared with larger metal particle sizes the amount of Pd atoms in corners and edges with respect to the total amount of Pd should decrease compared to smaller Pd crystals, we prepared a Pd(10%)/MgO catalyst with larger metal particle (average Pd particle size: 5.5 nm, instead of 2.2 nm of the original Pd/MgO catalyst) (see characterization data in table 1S and figure 3S in supplementary material) and the rate of the reaction was determined. Interestingly kinetic experiments with Pd(10%)/MgO as catalyst revealed that when plotting the initial reaction rate versus the concentration of benzenethiol and benzyl alcohol the initial reaction rate for formation of thioether did not depend on the concentration of benzenethiol or, even better, surface saturation for benzenethiol is very rapidly achieved (see Figure 3).

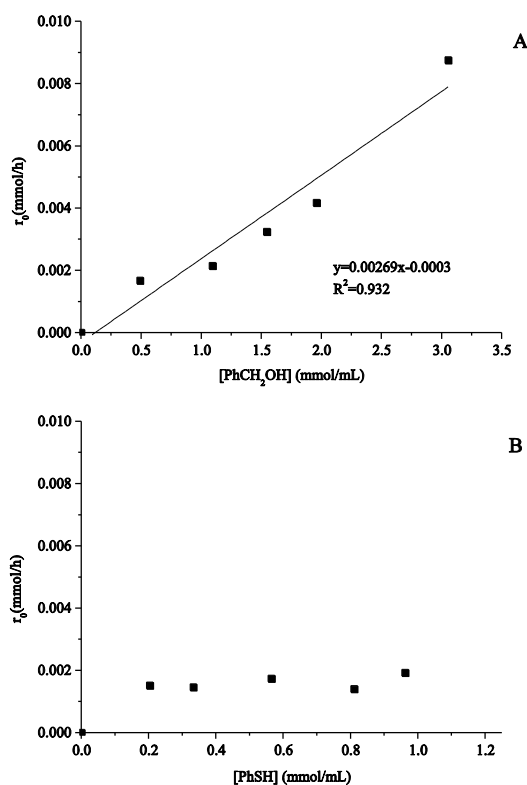


Figure 3 Graphic representations obtained when plotting A) r_0 versus [PhCH₂OH], and 1 mmol PhSH, and B) r_0 versus [PhSH], and 3 mmol [PhCH₂OH] using Pd(10%)/MgO as catalyst.

At this point, and with the Pd(0.8% Pd)/MgO catalyst, we proceeded to change the second catalyst component, i.e. the basic support. Thus, the reactivity of Pd on different basic supports such as Al-Mg hydroxalcite (HT) and hydroxyapatite (HAP) was also studied for the formation of thioethers (see table 1). In this case the results of activity and selectivity were always inferior to those obtained with MgO (entries 7-8, table 1).

In close connection with this and given the unusual stability of hemithioacetalic intermediates under basic/acid conditions as compared to their oxygenated analogs [18], we have also explored the possibilities of an acidic support, such as γ -Al₂O₃ (instead of the basic MgO) for forming thioethers. With this acidic support the activity and chemoselectivity values towards thioether **1a** were lower than those obtained with Pd/MgO (entry 6, table 1).

Palladium deposited on other supports (CeO₂ and C(Norit)) was less active and selective towards **1a** (entries 9-10, Table 1). Similarly gold deposited on CeO₂, MgO as well as a bimetallic Au/Pd/MgO catalyst were less active and selective towards the desired compound **1a** (entries 11-13, Table 1).

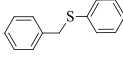
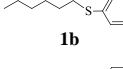
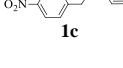
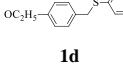
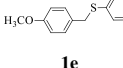
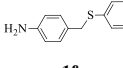
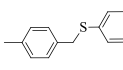
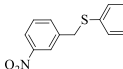
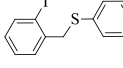
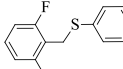
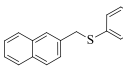
Finally other noble metals based-catalysts such as Pt/MgO and Ru/HT afforded also rather poor catalytic results (entries 14-15, Table 1).

Scope of the reaction

The same methodology has been extended to other alcohols and thiols and the results are given in Tables 3 and 4.

Table 3 Thioetherification reaction of alcohols with benzenethiol catalyzed by Pd/MgO (0.8 % wt) in one-pot.^a

$$\text{R}_1\text{-OH} + \text{C}_6\text{H}_5\text{-SH} \xrightarrow[\text{N}_2, 180^\circ\text{C}]{\text{Pd/MgO}} \text{R}_1\text{-S-C}_6\text{H}_5 + \text{C}_6\text{H}_5\text{-S-S-C}_6\text{H}_5$$
1a-k
2a

Entry	Thioether	C(%) ^b	Yield(%) ^c		TON ^d
			1a-k	2a	
1		96	75	12	221
2		0	0	0	0
3		98	81	12	225
4		93	78	11	214
5		84	70	10	193
6		86	73	10	198
7		31	17	9	71
8		10	8	0	23
9		3	0	0	7
10		12	5	7	28
11		8	5	0	18

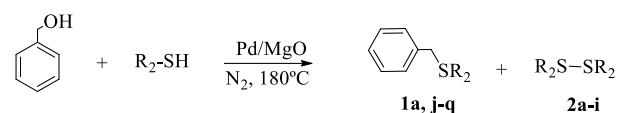
a) Reaction conditions: 3 mmol PhCH₂OH, 1 mmol PhSH, 0.0075 mmol catalyst, T = 180°C, 1 ml TFT, N₂; b) calculated by GC with respect to the amount thiol transformed; c) calculated by GC using dodecane as an internal standard; d) calculated as mmol thiol converted/mmol Pd surface atom.

As previously noticed, benzyl alcohol reacted with benzenethiol in the presence of Pd/MgO as catalyst to afford very good yields of the corresponding thioether **1a**, whereas the alkyl alcohol 1-hexanol was completely unreactive (see entry 2, table 3). This observation can be explained by considering the inability of aliphatic alcohols to dehydrogenate on the Pd metal surface to give the corresponding aldehydes [13a,b].

The influence of electron-withdrawing and electron-donating groups at different positions of the aromatic alcohol in the S-monoalkylation of benzenethiol was also studied. It was found that except for the methyl group, the introduction of electron-donating and electron-withdrawing groups at the *para* position of aromatic alcohol gave rise to high yields of thioethers (**1c-1g**, table 3), while the yield of the corresponding thioether strongly declined when the electron-withdrawing group, *i.e.* NO₂ group, was at the *meta* position (**1h**, table 3). Similarly, the presence of one and even two halogen groups at the *ortho* position led to a strong reduction in the yield of the corresponding thioethers **1i-1j** (table 3), owing not only to electronic but also to steric reasons. Similarly, the hindered naphthyl alcohol derivative, performed the S-monoalkylation with difficulty in part due to steric reasons (**1k**, table 3).

Interestingly, when reacting different thiol derivatives it could be observed that, unlike what occurs with alcohols, the reaction with different thiols was much more general so that the corresponding thioethers were obtained from moderate to very good yields with a wide range of different thiols as reactants (Table 4).

Table 4 Thioetherification reaction of benzyl alcohol with thiols catalyzed by Pd-MgO (0.8 % wt) in one-pot.^a



Entry	Thioether	C(%) ^b	Yield(%) ^c		TON ^d
			1a,j-k	2a-i	
1		96	75	12	221
2		91	71	15	209
3		99	78	17	227
4		99	83	10	227
5		75	52	33	172
6		60	37	21	138
7		88	69	16	202
8		87	68	19	200
9		86	66	12	198

a) Reaction conditions: 3 mmol PhCH₂OH, 1 mmol PhSH, 0.0075 mmol catalyst, T = 180°C, 1 ml TFT, N₂; b) calculated by GC with respect to the amount thiol transformed; c) calculated by GC using a response factor; d) calculated as mmol thiol converted/mmol Pd surface atoms.

According to results collected in table 4, the diversity of thiols that can be transformed in the one-pot two step reaction presented here, is much more extensive than that found for different alcohols. In fact, if one excludes for aliphatic thiols, which gave moderate yields of the corresponding thioether (see **1o**, Table 4), the rest of thiols afforded yields of the desired sulphur compounds which ranged from good to very good using Pd/MgO as catalyst (see Table 4). Finally the existence of a possible leaching process was studied. To this end the catalyst was removed by hot filtration after 20% benzenethiol conversion and the reaction was monitored by GC. At this point we noticed that in the absence of catalyst the reaction for formation of thioether did not occur, so that the existence of a possible metal leaching was definitively discarded (see figure 2S, supplementary material).

Conclusion

The borrowing hydrogen methodology has been applied for the formation of thioethers. The reaction is an adaptation of the reductive thiolation of aldehydes by palladium hydrides in which both reactants are formed and reacted *in situ* on the palladium surface giving thioethers. The reaction is accomplished in a single pot through dehydrogenation of a benzylic alcohol on the metal surface to give an aromatic aldehyde, which will react *in situ* with a mercaptan (either aromatic or aliphatic) to give a hemithioacetalic intermediate. The latter will form a thionium ion intermediate which will be rapidly hydrogenated by palladium hydride complexes formed also *in situ* on the metal surface to afford a thioether as major product.

The reaction can be considered general for thiols and benzylic alcohols.

Experimental section

Gas chromatography (GC) was performed with a Varian3900 apparatus equipped with an TRB-5MS column (5% phenyl, 95% polymethylsiloxane, 30 m, 0.25 mm × 0.25 μm, Teknokroma). GC/MS analyses were performed on an Agilent spectrometer equipped with the same column as the GC and operated at the same conditions. ESI-MS were performed on an Agilent Esquire 6000 instrument. Elemental analyses were performed on an EuroEA Elemental Analyser Eurovector.

Reagents and solvents were supplied by Aldrich and they were used as received. CeO₂ (Specific Surface Area, BET ≥ 252 m²/g) was supplied by Rhodia. MgO with a surface area of 670 m²/g and Al₂O₃ with a surface area ≥ 550 m²/g were purchased from NanoScale Materials. Carbon with a surface area of 1400 m²/g was purchased from Norit. Hydroxyapatite (HAP) and Hydrotalcite (HT) were prepared by following previously reported procedures [19].

Preparation of metal/MgO (metal= Pd, Pt, Au) catalysts: Pd/MgO (0.8%wt) was prepared according to a previously reported procedure [20].

Pt/MgO (1 wt% metal loading) was obtained by adding MgO (1 g, 670 m²g⁻¹) to a solution of [Pt (acac)₂] (24.01 mg, 0.078 mmol) in anhydrous dichloromethane (30 mL) while stirring for 12 h. After evaporation of the solvent at reduced pressure, the solid was dried overnight at 353 K. The sample was activated before reaction by heating the solid at 723 K under an atmosphere of air for 5 h and then for 5 h under nitrogen. Metal reduction was performed by heating the solid at 523 K in a flow of H₂/N₂ (90:10) for 2 h.

Au/MgO (1 wt% metal loading) was prepared by following a reported procedure, albeit with modifications [21]: MgO (1 g, 670 m²g⁻¹) was added to a solution of [Au(CH₃)₂ (acac)] (17.963 mg, 0.055 mmol) in ethanol (30 mL) while stirring for 12 h. The solvent was evaporated at reduced pressure. The solid was dried overnight at 353 K under vacuum. The sample was activated before reaction by heating the solid at 723 K under air for 5 h and then for 5 h under nitrogen. Metal reduction was performed by heating the solid at 523 K in a flow of H₂/N₂ (90:10) for 2 h.

Preparation of Pd supported catalysts (Pd/Al₂O₃, Pd/C, Pd/CeO₂): 1g of the support (Al₂O₃, C, CeO₂) was calcined (from 25 to 400°C at 5°C/min for 7h) and diluted in 30mL of anhydrous toluene containing Pd(acac)₂ (28 mg). The mixture was kept under vigorous stirring for 12 hours. The solvent was evaporated under vacuum and the resulting solid was dried (353K) under vacuum for 12 hours. The catalyst was calcined before reaction by heating the solid at 723 K under air for 5 h and then for 5 h under

nitrogen. Metal reduction was performed by heating the solid at 523 K in a flow of H₂/N₂ (90:10) for 2 h.

Preparation of Au/CeO₂: Au/CeO₂ (1%wt) was prepared according to a previously reported procedure [22].

Preparation of Pd/HAP: A 10⁻⁴ M solution of Pd(acac)₂ solution in acetone was added to 1g of HAP freshly prepared. The mixture was vigorously stirred during 3 hours at room temperature. The solid was then filtered, washed with acetone and dried (353K) under vacuum for 12 hours. Prior to use, the catalyst was calcined under flowing N₂ at 723K for 5.5h. The metal was reduced by heating the solid at 523 K in a flow of H₂ for 3 h.

Preparation of Pd/HT: A solution of PdCl₂ in deionized water (5·10⁻⁴ M) was added to a 1g of HT. The system was kept under vigorous stirring at room temperature for 1 hour. The solid was then filtered and was with deionized water until neutral pH was reached. Then the catalyst was dried under reduced pressure. Then, it was calcined in flowing air for 7 hours (723K) and flowing N₂ for additional 5.5h. The catalyst was kept under inert atmosphere until it was used in reaction.

Ru/HT catalyst, was prepared following the same procedure but employing RuCl₃ as the metal precursor.

(Au,Pd)/MgO (0.8 wt% Pd and 0.8 wt% Au) was prepared by co-impregnation of 1g of calcined MgO with two solutions of [Pd(acac)₂] (12.8 mg) and [Au (acac)] (13.3 mg) in acetone (15 mL). The mixture was stirred for 12 h at room temperature. The solvent was evaporated at reduced pressure and the solid was dried at 80°C for 12 h under vacuum. The material was calcined at 450°C under a N₂ flow for 4.5 h (5 °Cmin⁻¹). Metal reduction was performed by heating the solid at 523 K in a flow of H₂/N₂ (90:10) for 2 h.

Catalytic experiments

a) Catalyzed reductive thiolation of aldehydes:

A mixture of alcohol (3 mmol) and thiol (1 mmol), 0.0075 mmol catalyst, trifluorotoluene (1 ml) and n-dodecane (20 µl) as internal standard were placed into an autoclave. The resulting mixture purged with N₂ several times and vigorously stirred at 180°C. The reaction was monitored by GC.

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