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One-Pot Palladium-Catalyzed Borrowing Hydrogen Synthesis of Thioethers

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Abstract: Palladium on magnesium oxide is able to allow a one-pot reaction to synthesize thioethers from thiols and aldehydes formed in situ from the respective alcohol by means of a borrowing hydrogen method. 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 hydride to afford thioethers.

Keywords: heterogeneous catalysis · hydrogen transfer · palladium · synthetic methods · thioethers

Introduction

The presence of sulfur-containing compounds in chemicals and biologically active compounds has driven the development of carbon–sulfur bond-forming reactions during the last decade.[1] In spite of that, the number of catalytic procedures for forming C–S bonds still remains scarce compared with the number of methods for forming C–O and C–N bonds, partly because of the reasoned belief that sulfur poisons metal catalysts. Fortunately, this apparent functional incompatibility has been surpassed in recent years with the emergence of new metal catalytic strategies.[2] Work on the synthesis of aromatic thioethers has increased significantly, 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 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 chlorophenylsulfides.[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 whereas 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 with, for instance, lithium aluminum hydride/aluminum chloride, triethylsilane, or pyridine-borane in trifluoroacetic acid medium to afford the sulfide.[10] However, most of these processes are not suitable for large-scale production because they are quite contaminating, and 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 method is an attractive concept that combines dehydrogenation/hydrogenation reactions (hydrogen transfer) with numerous interesting organic transformations in a single pot.[11] In that method there is a nonsacrificial 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.

Many metals form stable metal hydrides and are inefficient catalysts for the borrowing hydrogen method (also called hydrogen autotransfer), 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]

Herein, we 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. 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 an S-monoalkylation reaction (see Scheme 1).

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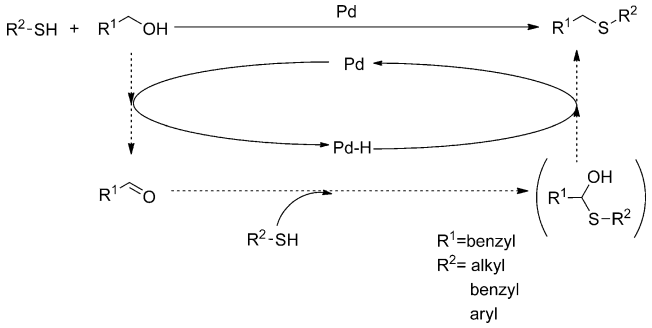
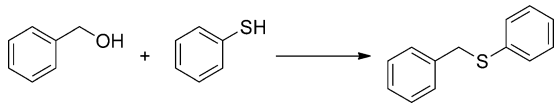


Scheme 1. Schematic representation of the one-pot synthesis of thioethers with a Pd catalyst.

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, thereby giving a hemithioacetalic intermediate that is most probably transformed into a thionium ion. The latter is then likely to be reduced in situ by the palladium hydrides to give the thioether.

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.

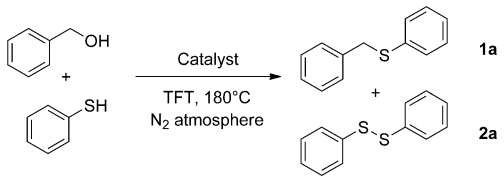


Scheme 2. Monoalkylation of benzenethiol with benzyl alcohol.

In a preliminary experiment a metal/base Pd/MgO (0.8 wt% Pd) catalyst (see characterization data in Table 1S in the Supporting Information) was used with 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 Table 1, entry 1). Besides **1a**, a lower amount of diphenyl disulfide **2a** was also obtained[15] (Table 1, entry 1).

As no dibenzyl ether but rather diphenyl disulfide was observed as subproduct, we performed the reaction with an excess of benzyl alcohol and the result (Table 1, entry 2) indicated a moderate decrease in the formation of **2a** (see the evolution of the reaction with time, Figure 1S in the Supporting Information). A further decrease in the formation of **2a** was obtained by slowly adding the benzenethiol to an excess of the alcohol (Table 1, entry 3).

Table 1. S-monoalkylation reaction of benzenethiol with benzyl alcohol in one pot.[a]



Entry	Catalyst ([wt%] metal)	Time [h]	Conversion [%][b]	Yield [%][c] 1a	2a	TON[d]
1[e]	Pd/MgO (0.8)	24	90	67	23	207
2	Pd/MgO (0.8)	22	96	75	12	221
3[f]	Pd/MgO (0.8)	24	90	82	<1	206
4[g]	Pd/MgO (0.8)	45	34	2	32	78
5[h]	Pd/MgO (0.8)	24	37	7	30	85
6	Pd/Al_2O_3 (1.0)	24	25	5	10	52
7	Pd/HT (0.8)	24	68	12	56	237
8	Pd/HAP (0.8)	15	11	0	11	72
9	Pd/C (1.0)	24	50	15	30	179
10	Pd/CeO_2 (1.0)	30	40	5	35	117
11	Au/CeO_2 (1.0)	30	55	32	13	167
12	Au/MgO (0.8)	72	51	0	43	106
13	(Au,Pd)/MgO (1.0,1.0)	48	67	58	3	–
14	Pt/MgO (1.0)	24	<5	0	0	21
15	Ru/HT (1.0)	24	0	0	0	0

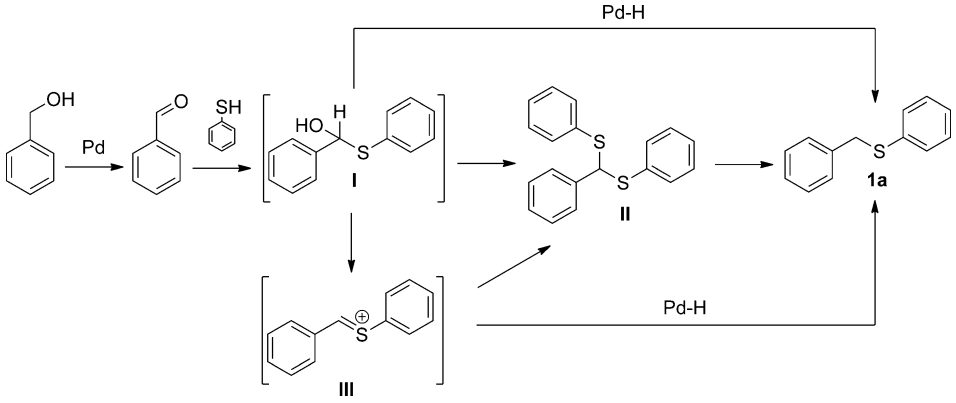
[a] Reaction conditions: $PhCH_2OH$ (3 mmol), PhSH (1 mmol), catalyst (0.75% mol), 180°C, TFT (1 mL), N_2 atmosphere, dodecane (0.2 mmol). [b] Calculated by GC with respect to the amount of thiol transformed using dodecane as an internal standard. [c] Determined by GC based on the amount of thiol converted. [d] Turnover number = [mmol thiol converted]/[mmol catalyst (surface Pd atoms)]. [e] Reaction conditions: $PhCH_2OH$ (1 mmol), PhSH (1 mmol), 180°C, TFT (1 mL), N_2 atmosphere. [f] Benzenethiol was added in three portions. [g] 100°C. [h] PBN (1 mmol) was added.

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 (Table 1, entry 4).[15a] Therefore, from now on, and to selectively form the thioether **1a**, the working conditions were adjusted to 180°C and an excess of alcohol was always used.

It has been described that the formation of disulfides occurs through the coupling of two sulfur radicals on the metal surface, whereas the formation of thioethers from the

aldehyde takes place through ionic intermediate species.[15a] If this is so, a further decrease in the formation of **2a** could be achieved by adding a radical scavenger to the reaction system. Then, phenyl *N-tert*-butylnitrone (PBN) was used as radical scavenger and, surprisingly, selectivity to **2a** did not decrease but increased, whereas the rate of formation of thioether **1a** was strongly inhibited (Table 1, entry 5) up to the point that in the presence of PBN, **2a** became the major reaction product. It can be assumed that the strong inhibiting effect of PBN for the formation of the thioether is a clear indication that radical intermediates are formed in some elementary step of the reaction. Following the above, and because 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 is 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, which gives a hemithioacetal intermediate (RCH(OR)SR; **I**) in equilibrium with thioacetal (**II**; not detected by gas chromatography (GC)) if water is present (see Scheme 3). Taking into account that thioacetals can be desulfurized to the corresponding sulfides or hydrocarbons by using diverse reducing agents (versus H_2 and Raney nickel, pyridine-borane in trifluoroacetic acid, and so forth),[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.



Scheme 3. Plausible mechanistic pathways for the palladium-catalyzed synthesis of **1a** starting from benzyl alcohol and benzenethiol.

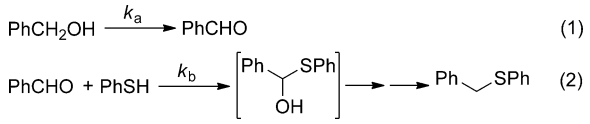
To test this hypothesis, a fixed amount of Pd/MgO (0.8 wt% Pd) was treated initially with H_2 (5 bar) at 180 °C for 1 h to ensure the formation of metal hydrides from the very beginning. The total amount of palladium hydrides (0.6 mmol) was estimated on the basis of the decrease in hydrogen pressure. Then, stoichiometric amounts of benzaldehyde and benzenethiol were reacted to give 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 at the trace level. 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, to discern the nature of the key intermediate that will be reduced during the reaction, compound **II** was synthesized[17] and reacted with benzyl alcohol (1 mmol) in the presence of Pd/MgO at 180 °C. Under these experimental conditions thioacetal **II** remained unreacted after 8 h, albeit **1a** could be obtained with low yields (≈5%) when the thioacetal was treated with H_2.

This experimental fact suggests that the major pathway is most likely formation of the thionium ion **III** from the hemithioacetalic compound **I**, followed by a very rapid hydrogenation of **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 below).

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 study of the scope of the reaction were carried out with a Pd(0.8 wt%)/MgO catalyst (Pd average particle size, $d=$ 2 nm; see Figure 3S in the 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, that is, alcohol dehydrogenation to afford benzaldehyde and reductive thiolation of the latter to form the thioether **1a**, have been formulated by assuming that the hemithioacetal (or the thionium ion), which was not detected by GC, is an intermediate that reacts very fast (see Scheme 4).

Two kinetic rate expressions were derived by assuming that the dehydrogenation of benzyl alcohol to give benzaldehyde and a metal hydride [Eq. (1)], or the reductive



Scheme 4. The two reaction steps and the kinetic constants k_a and k_b.

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[a,b]
1	(1)	Eq. (1): $r_0 = k_a$ [$PhCH_2OH$]
2	(2)	Eq. (2): $r_0 = k_b$ [PhCHO] [PhSH] $= K_a\, k_b$ [$PhCH_2OH$] [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.

S-thiolation [Eq. (2)] was the overall rate-controlling step, the other being in equilibrium (see Table 2).

Upon plotting the initial reaction rate versus the concentration of benzenethiol and benzyl alcohol determined experimentally (see Figure 1), it is possible to see that the initial rate for the 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 [Eq. (1)] but the direct reductive thiolation [Eq. (2)], since in the former case the reaction rate will only be dependent on the concentration of alcohol (see Table 2, entry 1).

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 be that the slowest reaction step will not be the thiolation anymore, but the dehydrogenation of benzyl alcohol.

Dehydrogenation of alcohols[13] is a structure-sensitive reaction, that is, metal sites located at the crystal corners and edges of the crystallites are the most reactive, and in a Pd/MgO catalyst prepared with larger metal particle sizes the number of Pd atoms in corners and edges with respect to the total amount of Pd should decrease relative to smaller Pd crystals. Therefore, we prepared a Pd(10 wt %)/MgO catalyst with larger metal particles (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 the Supporting Information) and the rate of the reaction was determined. Interestingly, kinetic experiments with Pd(10 %)/MgO as catalyst revealed that, on 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 2).

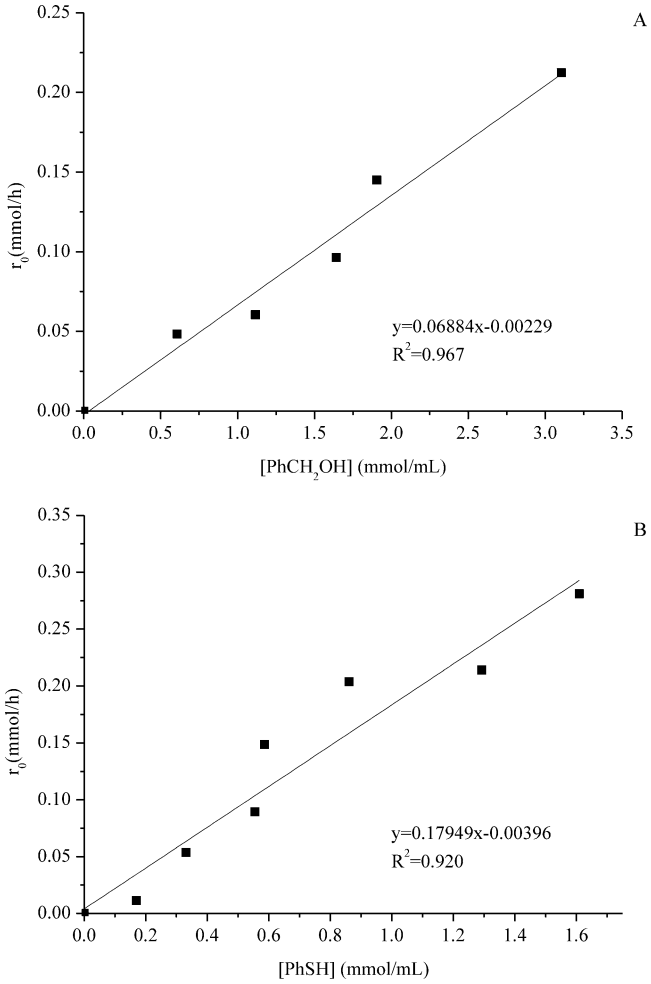


Figure 1. Graphical representations obtained when plotting A) r_0 versus [$PhCH_2OH$], and 1 mmol PhSH, and B) r_0 versus [PhSH], and 3 mmol [$PhCH_2OH$] using Pd(0.8 %)/MgO as catalyst.

At this point, and with the Pd(0.8 % Pd)/MgO catalyst, we proceeded to change the second catalyst component, that is, the basic support. Thus, the reactivity of Pd on different basic supports, such as Al-Mg hydrotalcite (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 (Table 1, entries 7 and 8).

In close connection with this and given the unusual stability of hemithioacetalic intermediates under basic/acid conditions relative to their oxygenated analogues,[18] we also explored the possibilities of an acidic support, such as γ-Al_2O_3 (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 (Table 1, entry 6).

Palladium deposited on other supports (CeO_2 and C (activated charcoal)) was less active and selective towards **1a**

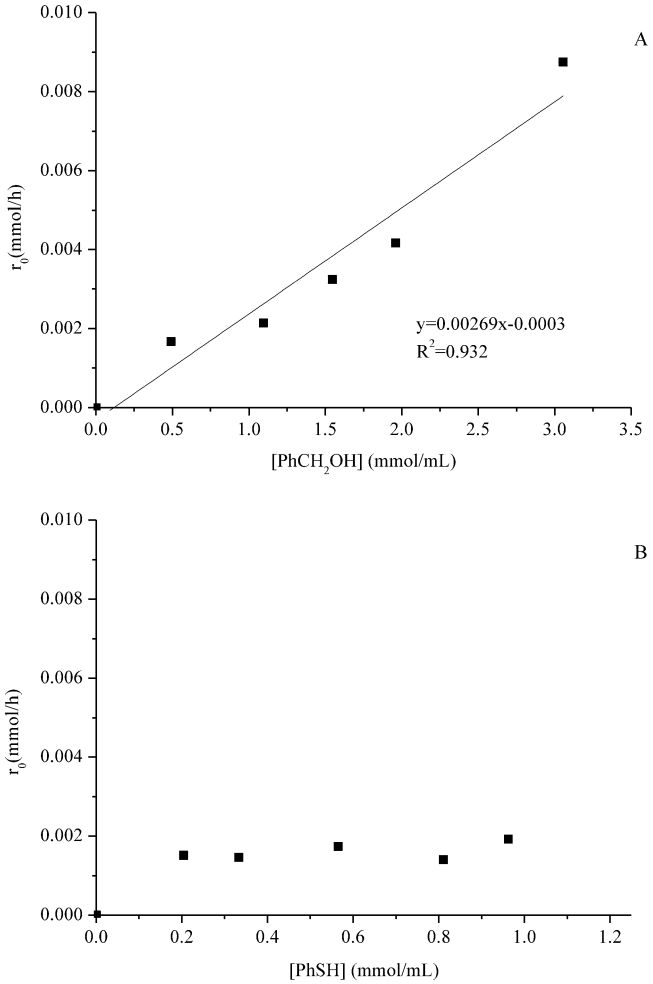


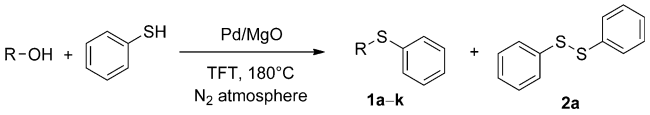
Figure 2. Graphical representations obtained when plotting A) r_0 versus [$PhCH_2OH$], and 1 mmol PhSH, and B) r_0 versus [PhSH], and 3 mmol $PhCH_2OH$ using Pd(10%)/MgO as catalyst.

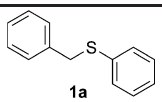
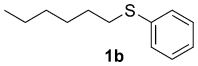
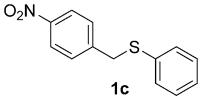
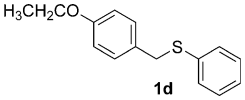
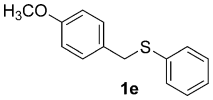
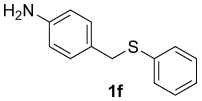
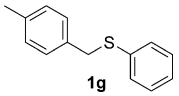
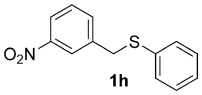
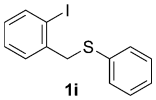
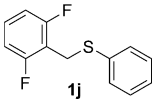
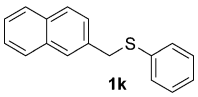
(Table 1, entries 9 and 10). Similarly, gold deposited on CeO_2 or MgO, as well as a bimetallic (Au,Pd)/MgO catalyst were less active and selective towards the desired compound **1a** (Table 1, entries 11–13). Finally, other noble-metal-based catalysts, such as Pt/MgO and Ru/HT, also afforded rather poor catalytic results (Table 1, entries 14 and 15).

Scope of the reaction: The same method was extended to other alcohols and thiols and the results are given in Tables 3 and 4. As previously noticed, benzyl alcohol reacted with benzenethiol in the presence of Pd/MgO as catalyst to afford good yields of the corresponding thioether **1a**, whereas the alkyl alcohol 1-hexanol was completely inactive (see Table 3, entry 2). 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 the aromatic alcohol gave rise to high yields of thioethers (**1c**–**g**, Table 3), whereas the yield of the corresponding thioether declined strongly when the electron-withdrawing group, that is, the NO_2 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** and **1j** (Table 3), owing not only to electronic but

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



Entry	Thioether	Conversion [%][b]	Yield [%][c] 1a–k	Yield [%][c] 2a	TON[d]
1	 **1a**	96	75	12	221
2	 **1b**	0	0	0	0
3	 **1c**	98	81	12	225
4	 **1d**	93	78	11	214
5	 **1e**	84	70	10	193
6	 **1f**	86	73	10	198
7	 **1g**	31	17	9	71
8	 **1h**	10	8	0	23
9	 **1i**	3	0	0	7
10	 **1j**	12	5	7	28
11	 **1k**	8	5	0	18

[a] Reaction conditions: alcohol (3 mmol), PhSH (1 mmol), catalyst (0.75 mol%), 180 °C, TFT (1 mL), N_2 atmosphere. [b] Calculated by GC with respect to the amount of benzenethiol transformed using dodecane as an internal standard. [c] Determined by GC based on the amount of benzenethiol converted. [d] Turnover number = [mmol benzenethiol converted]/[mmol catalyst (surface Pd atoms)].

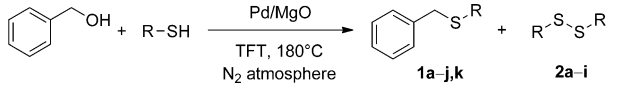
also to steric effects. Similarly, the hindered naphthyl alcohol derivative performed the S-monoalkylation with difficulty, in part for steric reasons (**1k**, Table 3).

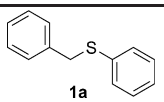
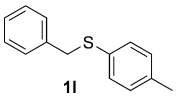
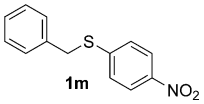
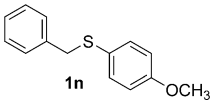
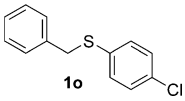
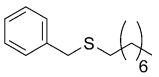
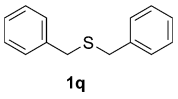
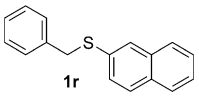
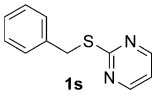
Interestingly, when reacting different thiol derivatives it could be observed that, unlike what occurs with alcohols, the reaction with different thiols was much more general so that the corresponding thioethers were obtained in moderate to very good yields with a wide range of different thiols as reactants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

According to the results collected in Table 4, the diversity of thiols that can be transformed in the one-pot two-step reaction presented herein is much more extensive than that found for different alcohols. In fact, if one excludes aliphatic thiols, which gave moderate yields of the corresponding thioether (see **1p**, Table 4), the rest of the thiols afforded yields of the desired sulfur compounds that ranged from good to very good on 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 the formation of thioether did not occur, so the existence of a possible metal leaching was definitively discarded (see Figure 2S in the Supporting Information).

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



Entry	Thioether	Conversion [%][b]	Yield [%][c] 1a,j,k	2a–i	TON[d]
1	 1a	96	75	12	221
2	 1l	91	71	15	209
3	 1m	99	78	17	227
4	 1n	99	83	10	227
5	 1o	75	52	33	172
6	 1p	60	37	21	138
7	 1q	88	69	16	202
8	 1r	87	68	19	200
9	 1s	86	66	12	198

[a] Reaction conditions: $PhCH_2OH$ (3 mmol), thiol (1 mmol), catalyst (0.75 mol%), 180 °C, TFT (1 mL), N_2 atmosphere. [b] Calculated by GC with respect to the amount of benzenethiol transformed using dodecane as an internal standard. [c] Determined by GC based on the amount of benzenethiol converted. [d] Turnover number = [mmol benzenethiol converted]/[mmol catalyst (surface Pd atoms)].

Conclusion

The borrowing hydrogen method 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 to give 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 reacts in situ with a mercaptan (either aromatic or aliphatic) to give a hemithioacetalic intermediate. The latter forms a thionium ion intermediate, which is rapidly hydrogenated by palladium hydride complexes also formed 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

General: Gas chromatography (GC) was performed with a Varian 3900 apparatus equipped with a 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 type as the chromatograph and operated under the same conditions.

Reagents and solvents were supplied by Aldrich and used as received. CeO_2 (specific surface area, BET $\geq 252\ m^2 g^{-1}$) was supplied by Rhodia. MgO with a surface area of $670\ m^2 g^{-1}$ and Al_2O_3 with a surface area $\geq 550\ m^2 g^{-1}$ were purchased from NanoScale Materials. Carbon with a surface area of $1400\ m^2 g^{-1}$ 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) to a solution of $[Pt(acac)_2]$ (acac = acetylacetonate; 24.01 mg, 0.078 mmol) in anhydrous dichloromethane (30 mL) with 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 a flow 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 H_2/N_2 (90:10) for 2 h.

Au/MgO (1 wt% metal loading) was prepared by following a reported procedure,[21] albeit with modifications. MgO (1 g) was added to a solution of $[Au(acac)(CH_3)_2]$ (17.963 mg, 0.055 mmol) in ethanol (30 mL) with stirring for 12 h. The solvent was evaporated at reduced pressure. The solid was dried overnight at 353 K under vacuum. The sample was acti-

vated 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 H_2/N_2 (90:10) for 2 h.

Preparation of supported Pd catalysts (Pd/Al_2O_3, Pd/C, Pd/CeO_2): The support (Al_2O_3, C, CeO_2; 1 g) was calcined (from 25 to 400 °C at 5 °C min^{-1} for 7 h) and diluted in anhydrous toluene (30 mL) containing [Pd(acac)$_2$] (28 mg). The mixture was kept under vigorous stirring for 12 h. The solvent was evaporated under vacuum and the resulting solid was dried (353 K) under vacuum for 12 h. 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 H_2/N_2 (90:10) for 2 h.

Preparation of Au/CeO_2: Au/CeO_2 (1 wt %) was prepared according to a previously reported procedure.[22]

Preparation of Pd/HAP: A [Pd(acac)$_2$] solution (10^{-4} M) in acetone was added to HAP (1 g). The mixture was stirred vigorously for 3 h at room temperature. The solid was then isolated by filtration, washed with acetone, and dried (353 K) under vacuum for 12 h. Prior to use, the catalyst was calcined under flowing N_2 at 723 K for 5.5 h. The metal was reduced by heating the solid at 523 K in a flow of H_2 for 3 h.

Preparation of Pd/HT: A solution of $PdCl_2$ in deionized water (5×10^{-4} M) was added to HT (1 g). The system was kept under vigorous stirring at room temperature for 1 h. The solid was isolated by filtration and washed with deionized water until neutral pH was reached. Then the catalyst was dried under reduced pressure. It was calcined in flowing air for 7 h (723 K) and flowing N_2 for an additional 5.5 h. The catalyst was kept under an inert atmosphere until use.

Ru/HT catalyst was prepared by following the same procedure but employing $RuCl_3$ as the metal precursor.

Preparation of (Au,Pd)/MgO (0.8 wt % Pd and 0.8 wt % Au): This material was prepared by co-impregnation of calcined MgO (1 g) with 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 N_2 flow for 4.5 h (5 °C min^{-1}). Metal reduction was performed by heating the solid at 523 K in a flow of H_2/N_2 (90:10) for 2 h.

Catalyzed reductive thiolation of aldehydes: Alcohol (3 mmol), thiol (1 mmol), catalyst (0.0075 mmol), trifluorotoluene (1 mL), and *n*-dodecane (20 μL) as internal standard were placed into an autoclave. The resulting mixture was purged with N_2 several times and stirred vigorously at 180 °C. The reaction was monitored by GC.

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