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Mercaptobenzoic acid-palladium(0) complexes as active catalysts for *S*-benzylation with benzylic alcohols *via* (η^3-benzyl)palladium(II) cations in water†

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Mercaptobenzoic acid-palladium(0) complexes show high catalytic activity for *S*-benzylation with benzylic alcohols *via* the (η^3-benzyl)palladium(II) cation in water. Notably, these palladium(0) complexes could play an important role in formation of active (η^3-benzyl)palladium(II) cation complexes followed by *S*-benzylation. Hammett studies on the rate constants of *S*-benzylation by various substituted alcohols show good correlation between $\log(k_X/k_H)$ and the σ^+ value of the respective substituents. From the slope, negative ρ values are obtained, suggesting that there is a build-up of positive charge in the transition state. Water plays an important role in the catalytic system for sp^3 C–O bond activation and stabilization of the activated Pd(II) cation species. The catalytic system can be performed using only 2.5 mol% $Pd_2(dba)_3$ without the phosphine ligand or other additives.

1. Introduction

(η^3-Benzyl)palladium catalysts are attracting increasing interest for the formation of carbon–carbon or carbon–nitrogen bonds.[1] However, the potentiality of these complexes is still unrealized compared to other well-established Tsuji–Trost reactions, merely due to their more recent development. Palladium-catalyzed benzylations with benzylic alcohols *via* the (η^3-benzyl)palladium(II) species are especially challenging, because the reactivity of benzylic alcohols towards Pd(0) is poor compared to benzylic halides, esters, carbonates, and phosphates. Therefore, the development of a direct substitution method for benzylic alcohols, which produces the desired products along with water as the sole co-product, is highly desired in organic chemistry. Only a few papers describe palladium-catalyzed benzylation with benzylic alcohols in aqueous media.[2] We have been developing a unique strategy for benzylation and C–H activation by the (η^3-benzyl)palladium(II) system from a palladium catalyst and benzyl alcohol in water.[3] Notably, water may activate the sp^3 C–O bond, then stabilize the Pd(II) cation species by hydration, which can then undergo innovative direct transformation reactions. Recently we reported a palladium-catalyzed selective *S*-benzylation of unprotected mercaptobenzoic acids with benzylic alcohols using $Pd(OAc)_2$/TPPMS (sodium diphenylphosphinobenzene-3-sulfonate) catalysts in water.[4] Classical approaches for *S*-benzylation with benzyl alcohols, which are activated by Lewis acids such as boron trifluoride etherates,[5] yttrium triflates,[6] ZnI_2,[7] and $ZrCl_4$,[8] have been reported.

Although palladium-catalyzed reactions of organosulfur compounds, *e.g.* thiols, are expected to be efficient methods for the synthesis of organosulfur compounds including the formation of new C–S bonds, the development of these methods is challenging due to poisoning of palladium catalysts by sulfur.[9] Recently, there have been many reports on the stabilization of palladium nanoparticles by thiol ligands due to the strong interaction between palladium and sulfur atoms.[10] Fornasiero and co-workers reported the synthesis of variably functionalized thiol-protected palladium nanoparticles (Pd-NPs).[10c] Palladium(II) complexes with a thiosalicylic acid ($HSC_6H_4CO_2H$) ligand have been synthesized and characterized.[10a,f–h]

In light of our ongoing efforts to develop new methods for direct substitution reactions of benzyl alcohols, this paper describes new insights into the chemistry of thiol-protected (η^3-benzyl)palladium(II) cation complexes for *S*-benzylation. Based on observations made in this investigation, we can now provide support for the cationic (η^3-benzyl)palladium(II) system in water. Notably, water-soluble mercaptobenzoic acid-Pd(0) species could play an important role in formation of active (η^3-benzyl)palladium(II) cation complexes followed by *S*-benzylation in our catalytic system, while benzenethiol is

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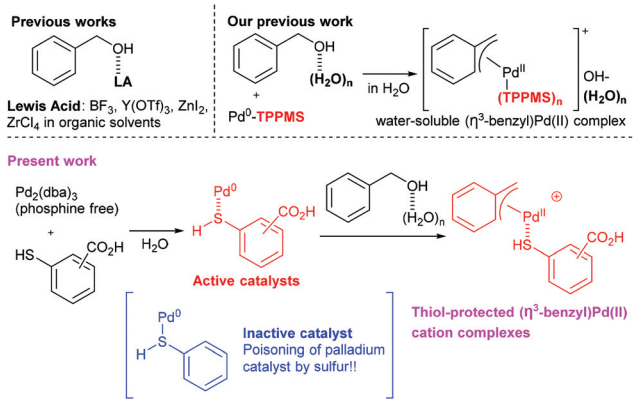


Scheme 1 Activation of the sp^3 C–O bond for *S*-benzylation. Classical approach and our approach.

ineffective due to poisoning of palladium catalysts by sulfur (Scheme 1). To the best of our knowledge, the phosphine-free palladium-catalyzed *S*-benzylation with benzyl alcohols *via* (η^3-benzyl)palladium(II) complexes in water was not described before.

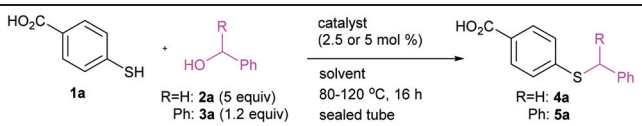
S-Benzylated thiophenyl structures are key units in a wide range of relevant pharmacophores with a broad spectrum of activities.[11] The most traditional *S*-benzylation method is the reaction of thiolate anions with benzyl halides.[11b,c,12] However, the use of excess benzyl halides leads to over-reaction of reactive functional groups. For example, the reaction of 2-mercaptobenzoic acid with 4-methylbenzyl chloride (2 equiv.) gives benzyl esters as the undesired products.[13] Protection of reactive functional groups such as amino, hydroxyl, or carboxyl groups is essential in organic synthesis, not only for suppressing side reactions, but also for easy handling by decreased polarity. However, protection sometimes causes serious problems, *e.g.* increasing the number of synthetic steps and difficulty in deprotecting unstable compounds. Therefore, the development of syntheses without protecting groups should lead to a breakthrough in organic synthesis.[14]

2. Results and discussion

2.1. Effects of catalysts and solvents on *S*-benzylation

First, a mixture of 4-mercaptobenzoic acid **1a** and benzyl alcohol (**2a**, 5 equiv.) in the presence of $Pd_2(dba)_3$ (2.5 mol%) in water was heated at 120 °C for 16 h in a sealed tube. *S*-Benzylated product **4a** was obtained in 81% conversion and 80% yield (Table 1, entry 1). The use of $Pd(PPh_3)_4$ also resulted in good yield (entry 2). Reduction of Pd(II) complexes in the presence of a phosphine ligand such as PPh_3 or TPPMS gave a Pd(0) species that could be used as a catalyst (entries 3 and 4). Since $Pd(OAc)_2$ instead of Pd(0) was ineffective (entry 5) and the reaction did not proceed in the absence of the palladium catalyst (entry 6), a S_N2 reaction mechanism was excluded in the formation of the *S*-benzylated product. The direct substitution of benzhydrol **3a** also afforded the desired **5a** in good yield (entries 7 and 8). Since using organic solvents such as DMF, EtOH or 1,4-dioxane resulted in no reaction (entries 9–11), water must play an important role in our catalytic system. To compare $Pd_2(dba)_3$ with other efficient catalysts, we tested the reaction using Brønsted acids such as $TsOH{\cdot}H_2O$,

Table 1 Effect of catalysts and solvents[a]



Entry	Catalyst (mol%)	Alcohols	Solvent	Temp. (°C)	Products	Conversion[b] (%)
1	$Pd_2(dba)_3$ (2.5)	**2a**	H_2O	120	**4a**	81 (80% yield)[c]
2	$Pd(PPh_3)_4$ (5)	**2a**	H_2O	120	**4a**	(87% yield)[c,d]
3	$PdCl_2(PPh_3)_2$ (5)	**2a**	H_2O	120	**4a**	(86% yield)[c,d]
4	$Pd(OAc)_2$ (5)/TPPMS (10)	**2a**	H_2O	120	**4a**	(88% yield)[c,d]
5	$Pd(OAc)_2$ (5)	**2a**	H_2O	120	**4a**	27
6	none	**2a**	H_2O	120	**4a**	0
7	$Pd_2(dba)_3$ (2.5)	**3a**	H_2O	80	**5a**	72
8	$Pd_2(dba)_3$ (2.5)	**3a**	H_2O	100	**5a**	85 (84% yield)[c]
9	$Pd_2(dba)_3$ (2.5)	**3a**	DMF	80	**5a**	0
10	$Pd_2(dba)_3$ (2.5)	**3a**	EtOH	80	**5a**	Trace
11	$Pd_2(dba)_3$ (2.5)	**3a**	1,4-Dioxane	80	**5a**	Trace
12	$TsOH{\cdot}H_2O$ (5)	**3a**	H_2O	80	**5a**	0
13	$Sc(OTf)_3$ (5)	**3a**	H_2O	80	**5a**	Trace
14	$Hf(OTf)_4$ (5)	**3a**	H_2O	80	**5a**	40
15	$CuCl_2$ (5)	**3a**	H_2O	80	**5a**	43
16	$Pd_2(dba)_3$ (2.5)	**3a**	NaOH aq. (1 equiv.)	80	**5a**	0

[a] Reaction conditions: 4-mercaptobenzoic acid **1a** (1 mmol), catalyst (2.5 or 5 mol%), benzylic alcohols (**2a**: 5 equiv. or **3a**: 1.2 equiv.), solvent (4 mL), 80–120 °C, 16 h in a sealed tube. [b] The conversion was determined by ^1H NMR analysis of the crude product using *p*-nitroanisole as an internal standard. [c] Yield of the isolated product in parenthesis. [d] 24 h.

and effective Lewis acids such as $Sc(OTf)_3$, $Hf(OTf)_4$, or $CuCl_2$. However, the reaction did not proceed or gave low yields (entries 12–15), clearly showing the superiority of $Pd_2(dba)_3$ for the *S*-benzylation of mercaptobenzoic acid **1a** with benzhydrol **3a** in water. In the presence of a base such as NaOH (1 equiv.), the reaction did not proceed (entry 16). Basset and co-workers reported that the π-allyl palladium intermediate was unstable under basic conditions.[15] Since our results were consistent with these reports on the palladium-catalyzed allylation with allylic alcohols, (η^3-benzyl)palladium was proposed to be an intermediate here in analogy to the allylic substitution reaction.

2.2. Scope of benzyl alcohols 2

Results for the *S*-benzylation of 4-mercaptobenzoic acid (**1a**) with a number of benzyl alcohols substituted by electron-withdrawing and electron-donating groups using $Pd_2(dba)_3$ in water are summarized in Table 2. The benzyl alcohols with electron-donating methoxy, methyl, and ethyl groups resulted in good yields (**4b**, 70%; **4c**, 86%; **4d**, 75%). The use of 4-fluorobenzyl alcohol also resulted in good yield (**4e**, 80%). The benzyl alcohols with bromo and chloro groups produced *S*-benzylated products in good yields with the carbon–halogen moiety left intact, which could be employed for further manipulation (**4f**, 79%; **4g**, 78%). The use of 3-methoxybenzyl alcohol also resulted in good yield (**4h**, 84%). A sterically demanding methyl group at the *ortho* position was tolerated in the *S*-benzylation (**4i**, 65%). A heteroaryl methyl alcohol, thienyl methyl, also resulted in good yield (**4j**, 85%; **4k**, 86%), although palladium-catalyzed reactions with heteroaryl methyl alcohol derivatives are extremely rare.[16] *S*-Benzylation with α-alkyl benzyl alcohols proceeded smoothly to give the desired product in good yields in spite of the possible formation of a vinylarene through β-hydride elimination from the benzylpalladium intermediate (**4l**, 80%).[17] A sterically demanding cyclic benzyl alcohol also gave good yield (**4m**, 77%). In contrast, the reaction using a substrate with a strong electron-withdrawing nitro group resulted in no reaction.

2.3. Scope of benzhydryl alcohols 3

Results for the reaction of 4-mercaptobenzoic acid (**1a**) with a number of benzhydryl alcohols **3** using $Pd_2(dba)_3$ in water are summarized in Table 3. The use of benzhydryl alcohols with electron-donating methoxy and methyl groups resulted in excellent yield (**5b**, 95%; **5c**, 83%; **5d**, 82%). In contrast, the reaction using substrates with electron-withdrawing chloro and fluoro groups proceeded slowly (**5e**, 62%; **5f**, 78%), and the strong electron-withdrawing decafluorophenyl group resulted in no reaction.

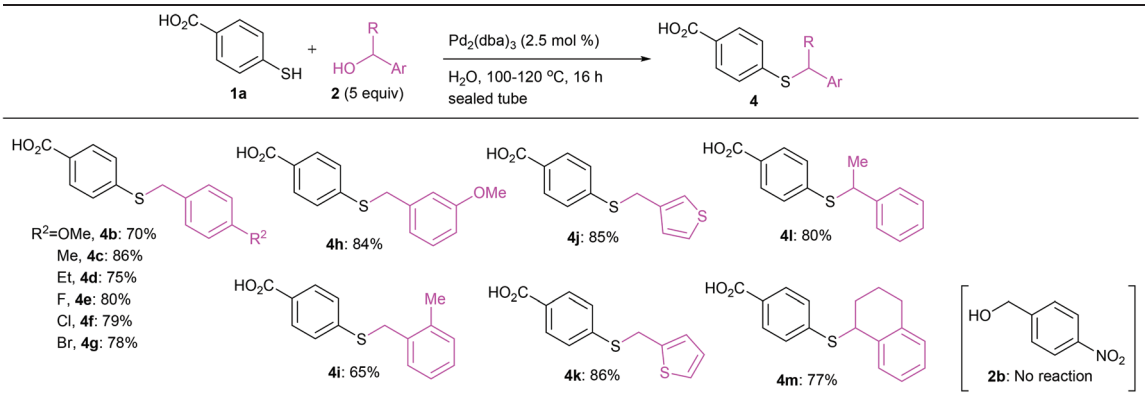
2.4. Scope of mercaptobenzoic acids 1

The reaction of 2-mercaptobenzoic acids with benzyl alcohol (**2a**) proceeded to give *S*-benzylated **4n–p** in overall yields ranging from 65 to 71% despite the steric effect of the carboxyl group at the *ortho*-position (Table 4). 3-Mercaptobenzoic acid smoothly underwent *S*-benzylation to give *S*-benzylated **4q** in 80% yield. The use of benzhydryl alcohol (**3a**) also resulted in good yields (**5g**, 65%; **5h**, 78%; **5i**, 68%). The reaction of 4-mercaptophenylcarboxylic acid or 4-mercaptohydrocinnamic acid instead of mercaptobenzoic acids resulted in moderate yields (**5j**, 50%; **5k**, 51%).

2.5. Hammett studies

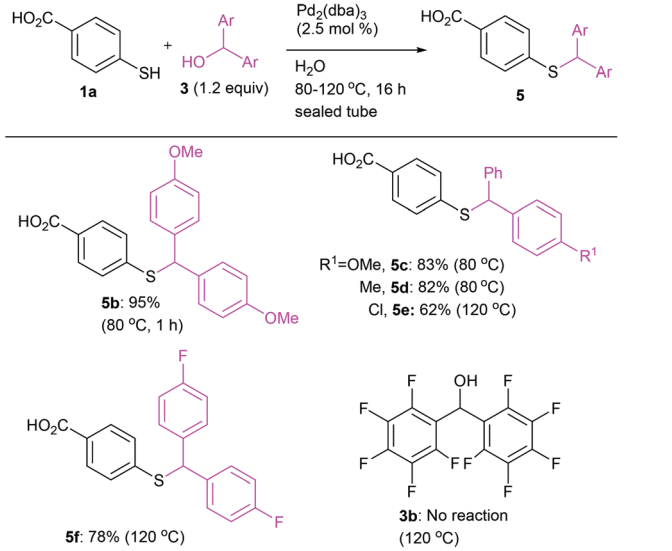
To demonstrate the electronic effect of substituents on the rates of the C–O bond cleavage and C–S bond formation reactions, a Hammett study was conducted on the reaction of **2a** or **3a** with substituted benzylic alcohols **2** or benzhydryl alcohols **3** in the presence of $Pd_2(dba)_3$ (2.5 mol%) to obtain the ratio of rate constants. The results are summarized in Fig. 1 (see Tables S1 and S2 in ESI†). The relative rates of coupling of 4-mercaptobenzoic acid (**1a**) with *para*-substituted benzylic alcohols (OMe, Me, Br, F, and Cl groups) were examined. Hammett plots show a good correlation (A: R^2 = 0.98; B: R^2 = 0.93) between the $\log(k_X/k_H)$ and the σ^+ value of the respective substituents that resulted in a negative ρ value of 2.7. These results suggested that a cationic (η^3-benzyl)palladium(II)

Table 2 Scope of benzyl alcohols **2**[a]



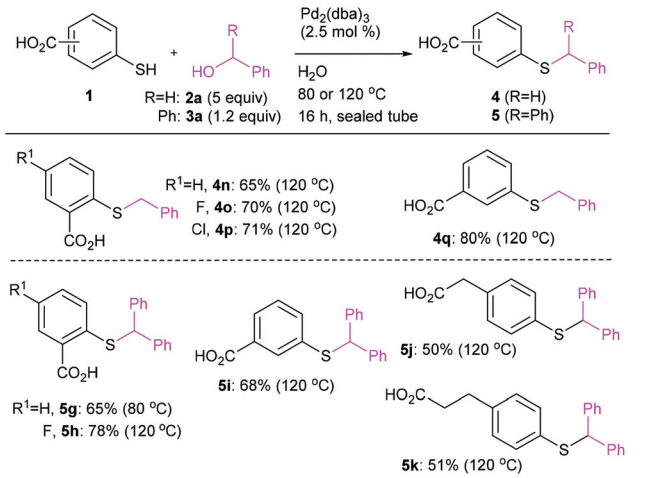
[a] Reaction conditions: 4-mercaptobenzoic acid **1a** (1 mmol), $Pd_2(dba)_3$ (2.5 mol%), benzyl alcohols **2** (1.2 equiv.), H_2O (4 mL), 100 or 120 °C, 16 h in a sealed tube. Yield of the isolated product.

Table 3 Scope of benzhydryl alcohols 3[a]



[a] Reaction conditions: **1** (1 mmol), $Pd_2(dba)_3$ (2.5 mol%), benzhydryl alcohols **3** (1.2 equiv.), H_2O (4 mL), 100–120 °C, 16 h in a sealed tube. Yield of the isolated product.

Table 4 Scope of mercaptobenzoic acid 1[a]



[a] Reaction conditions: **1** (1 mmol), $Pd_2(dba)_3$ (2.5 mol%), alcohol **2** or **3** (5 or 1.2 equiv.), H_2O (4 mL), 80–120 °C, 16 h in a sealed tube. Yield of the isolated product.

species was formed that played an important role in our catalytic system.

2.6. Role of the carboxyl group

To evaluate the role of the carboxyl group[18] of the mercaptobenzoic acids, *S*-benzylations of 2-mercaptobenzoic acid methyl ester (**6a**), 4-mercaptobenzoic acid methyl ester (**6b**), benzenethiol (**6c**), and 4-nitrobenzenethiol (**6d**) were carried out (Table 5). The reaction of ester **6a** or **6b** with benzhydryl alcohol (**3a**) using $Pd_2(dba)_3$ in water or toluene did not afford

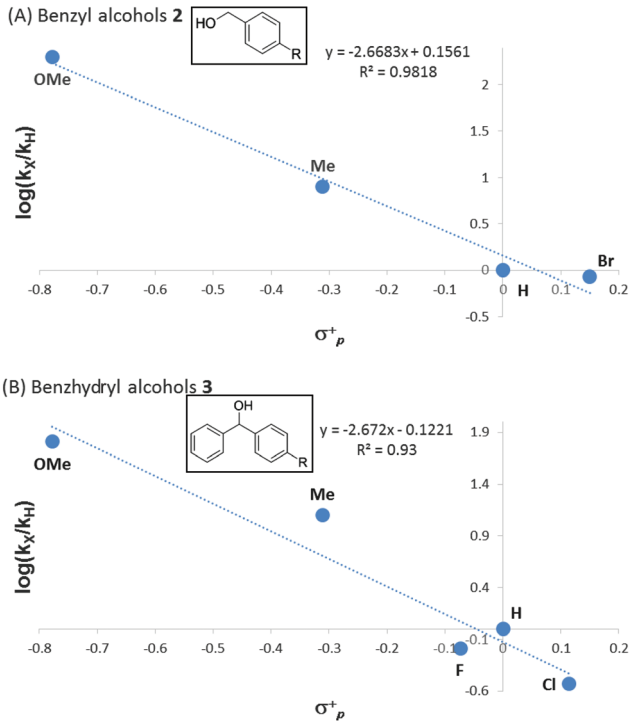


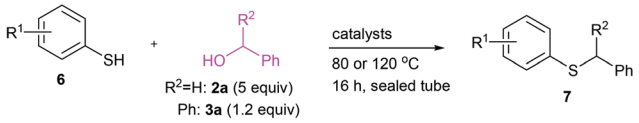
Fig. 1 Hammett plots for the rate constants of benzylation by various substituted benzylic alcohols (Tables S1–2 in ESI†).

the *S*-benzylated products **7** (entries 1 and 2). In the presence of AcOH (1 equiv.), the reaction also did not proceed (entry 3). In the presence of TPPMS, thiol **6a** or **6c** also did not afford *S*-benzylated **7**. In contrast, the use of benzenethiol with a strong electron-withdrawing nitro group afforded the desired **7a** in 69% yield (entry 6). These results suggested that the electron-withdrawing properties at the *para*-position on benzene rings causes an increase in the acidity of the mercapto groups, followed by formation of thiolate-Pd(II) species or thiolate anions as a nucleophile in our catalytic system. Indeed, while the carboxyl groups at the *ortho*- or *para*-position resulted in good yields (**5a**, 72%; **5g**, 68%), those at the *meta*-position resulted in low yield (**5i**, 48%) (Scheme 2). Additionally, mercaptophenylcarboxylic acid (**1c**) or 4-mercaptohydrocinnamic acid (**1b**) resulted in no reaction. However, 4-mercaptobenzoic acid **1a** (σ_p value: 0.45) resulted in good yield (72%), while the reaction of ester **6a** (σ_p value: 0.45) did not proceed (see Scheme 2 and Table 5). Therefore, the carboxylate anion **1a**′ as a base would play an important role in deprotonation of the mercapto group **9** in water (Scheme 3).

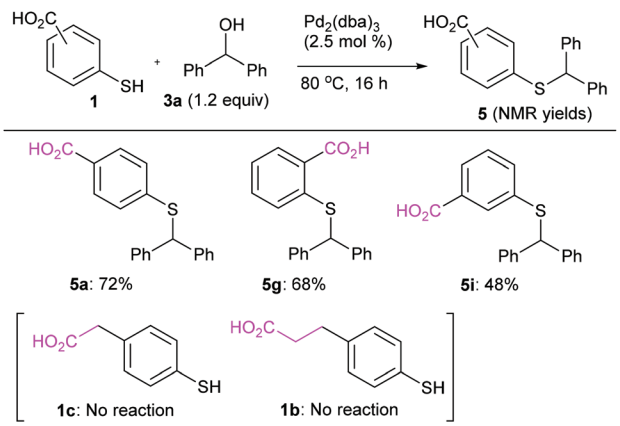
2.7. Mechanism

These results and our previous report suggest the following mechanism for the *S*-benzylation of 4-mercaptobenzoic acid **1a** with benzylic alcohols **2** using $Pd_2(dba)_3$ in water (Scheme 3). In the absence of a strong stabilizer such as a phosphine ligand for Pd(0), the low reactive precipitate of Pd black is produced. In contrast, $Pd_2(dba)_3$ ligates with thiol **1a** to form thiol-protected Pd(0) species **8**.[10] Next, oxidative addition of

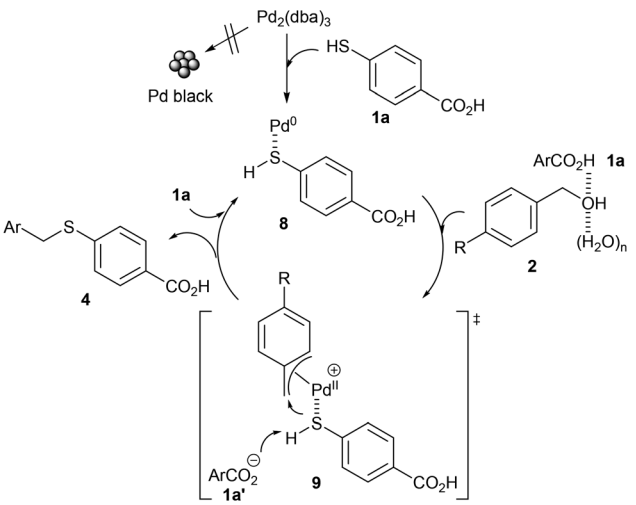
Table 5 Effect of carboxyl group



Entry	Catalysts (mol%)	R^1	Hammett const. σ_p values	R^2	Solvents	Temp. (°C)	Additive (equiv.)	Yield of 7 (%)
1	$Pd_2(dba)_3$ (2.5)	2-CO_2Me (**6a**)	—	Ph (**3a**)	H_2O or toluene	80	None	0
2	$Pd_2(dba)_3$ (2.5)	4-CO_2Me (**6b**)	0.45	Ph (**3a**)	H_2O	80	None	0
3	$Pd_2(dba)_3$ (2.5)	2-CO_2Me (**6a**)	—	Ph (**3a**)	H_2O	80	AcOH (1)	0
4	$Pd(OAc)_2$ (5)/TPPMS (10)	2-CO_2Me (**6a**)	—	H (**2a**)	H_2O	120	None or AcOH (1)	0
5	$Pd(OAc)_2$ (5)/TPPMS (10)	H (**6c**)	0	H (**2a**)	H_2O	120	None or AcOH (4)	0
6	$Pd_2(dba)_3$ (5)	NO_2 (**6d**)	0.778	Ph (**3a**)	H_2O	80	None	69 (**7a**)



Scheme 2 Effect of the position of carboxyl groups. Reaction conditions: **1** (1 mmol), $Pd_2(dba)_3$ (2.5 mol%), **3a** (1.2 equiv.), H_2O (4 mL), 80 °C, 16 h.

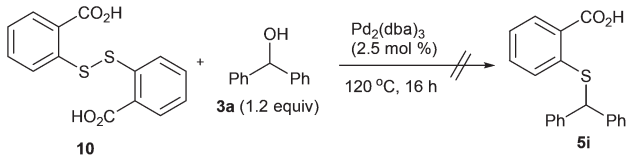


Scheme 3 Plausible mechanism.

alcohol **2** to thiol-Pd(0) species **8** affords the cationic (η^3-benzyl)palladium(II) complex **9**. These processes should be favored by electron-donating R groups on the intermediate **9**, since these will stabilize the positive charge on Pd(II). Hammett studies show a negative ρ value of 2.7, suggesting that there is a build-up of positive charge in the transition state. Indeed the benzylation using 4-nitrobenzyl alcohol **2b** or decafluorobenzhydryl alcohol **3b** does not proceed, since alcohols **2b** or **3b** cannot form cationic intermediates **9** (see Table 3). The carboxyl group of mercaptobenzoic acid and water activate the benzyl alcohol for the smooth generation of the cationic Pd(II) species **9**, which is stabilized by hydration. Indeed the reaction does not occur in organic solvents (see Table 1). Next, a thiolate-Pd(II) species is formed, then the nucleophilic thiolate anion ligand attacks the electrophilically active (η^3-benzyl) ligand of the intermediate **9** to afford the desired product **4** and regenerate Pd(0). Formation of the thiolate-Pd(II) species should be favored by electron-withdrawing R groups on the intermediate **9**, since these will stabilize the negative charge. Indeed, the use of benzene thiols with electron-withdrawing carboxyl groups at the *ortho*- or *para*-position proceeded smoothly compared with the *meta*-position (see Scheme 2).

Additionally, thiol-stabilized Pd nanoparticles featuring carboxylic functional end-groups at the edge of the self-assembled monolayer have been conveniently prepared starting from Pd(II) and 11-mercaptoundecanoic acid in aqueous media.[11c] Therefore, mercaptobenzoic acids (**1**) might form a monolayer in water, which is important in our catalytic system. Although the characterization of thiol-protected (η^3-benzyl)palladium(II) cation complexes are very difficult, there have been many reports on the stabilization of palladium nanoparticles by thiol ligands due to the strong interaction between palladium and sulfur atoms,[10] and palladium(II)/thiosalicylic acid complexes have been characterized.[10a,f–h] In addition, we could propose the formation of thiol-protected (η^3-benzyl)palladium(II) cation complexes by Hammett studies.

In general, thiols undergo oxidative homocoupling to produce disulfide byproducts. As shown in Scheme 4, disulfide **10** did not afford *S*-benzylated **5i**, suggesting that disulfide **10** was not an intermediate and oxidative homocoupling did not occur in our catalytic system. Additionally, although the direct use of thiols has drawbacks due to their foul smell, the use of mercaptobenzoic acid can solve this problem.[19]



Scheme 4 Pd-catalyzed reaction of disulphide **10**.

3. Conclusions

In summary, we have demonstrated a phosphine-free palladium-catalyzed *S*-benzylation with benzylic alcohols in water. The thiol-protected (η^3-benzyl)palladium(II) cation complexes are highly efficient catalysts for *S*-benzylation. Water-soluble mercaptobenzoic acid-Pd(0) species could play an important role in the formation of active (η^3-benzyl)palladium(II) cation complexes followed by *S*-benzylation in our catalytic system. Hammett studies on the rate constants of benzylation by various substituted alcohols show a good correlation. The negative ρ values showed that there is a build-up of positive charge in the transition state. Notably, our catalytic system and the proposed mechanism provide a scope for the development of palladium-catalyzed reactions for the direct modification of thiols, which are pharmaceutically active compounds, and electro materials.

4. Experimental

4.1. General procedure

A mixture of mercaptobenzoic acids **1** (1 mmol), $Pd_2(dba)_3$ (23 mg, 0.025 mmol) and benzylic alcohols (**2a**: 5 mmol or **3a**: 1.2 mmol) in H_2O (4 mL) was heated at 80–120 °C for 16 h in a sealed tube. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica gel, hexanes–EtOAc) to give the desired product **4** or **5**.

4-Benzylthiobenzoic acid 4a (Table 1).[4] 195 mg (80%); white solid; mp 188–190 °C; IR (KBr) (cm^{-1}) 3401, 2925, 1676, 1589, 1419, 1289; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.35 (s, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.32 (dd, J = 7.2, 7.2 Hz, 2H), 7.41 (d, J = 7.2 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 35.3, 126.4, 127.2, 127.4, 128.5, 128.8, 129.7, 136.8, 143.0, 166.9; MS (EI): m/z (%) 244 (M^+, 35.0), 91 (100).

4-(4-Methoxybenzylthio)benzoic acid 4b (Table 2).[4] 191 mg (70%); white solid; mp 200–202 °C; IR (KBr) (cm^{-1}) 2955, 1683, 1589, 1505, 1419, 1294; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H), 4.29 (s, 2H), 6.87 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 34.8, 55.0, 113.9, 126.4, 127.3, 128.4, 129.7, 130.0, 143.3, 158.4, 166.9; MS (EI): m/z (%) 274 (M^+, 9.4), 121 (100).

4-(4-Methylbenzylthio)benzoic acid 4c (Table 2).[4] 288 mg (86%); white solid; mp 210–212 °C; IR (KBr) (cm^{-1}) 2916, 1681, 1588, 1418, 1288; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.26 (s, 3H), 4.30 (s, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 20.6, 35.1, 126.4, 127.3, 128.7, 129.0, 129.7, 133.6, 136.4, 143.1, 166.9; MS (EI): m/z (%) 258 (M^+, 13.9), 105 (100).

4-(4-Ethylbenzylthio)benzoic acid 4d (Table 2).[4] 204 mg (75%); white solid; mp 203–205 °C; IR (KBr) (cm^{-1}) 2963, 1680, 1587, 1417, 1288; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.15 (t, J = 8.0 Hz, 3H), 2.56 (q, J = 8.0 Hz, 2H), 4.31 (s, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 15.5, 27.8, 35.0, 126.3, 127.3, 127.9, 128.8, 129.7, 133.9, 142.8, 143.2, 167.0; MS (EI): m/z (%) 272 (M^+, 12.4), 119 (100).

4-(4-Fluorobenzylthio)benzoic acid 4e (Table 2).[4] 210 mg (80%); off-white solid; mp 197–199 °C; IR (KBr) (cm^{-1}) 2821, 1675, 1589, 1503, 1415, 1286; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.35 (s, 2H), 7.14 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.45 (dd, J = 8.8, 5.6 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 34.5, 115.1, 115.4, 126.5, 127.5, 129.7, 130.8, 133.0, 133.1, 142.7, 160.1, 162.5, 166.9; MS (EI): m/z (%) 262 (M^+, 48.7), 109 (100).

4-(4-Chlorobenzylthio)benzoic acid 4f (Table 2).[4] 220 mg (79%); white solid; mp 210–212 °C; IR (KBr) (cm^{-1}) 2842, 1685, 1589, 1419, 1295; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.36 (s, 2H), 7.34–7.46 (m, 6H), 7.83 (d, J = 8.0 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 34.5, 126.6, 127.6, 128.4, 129.7, 130.7, 131.8, 136.1, 142.5, 166.9; MS (EI): m/z (%) 280 (M^+ + 2, 6.6), 278 (M^+, 17.2), 125 (100).

4-(4-Bromobenzylthio)benzoic acid 4g (Table 2).[4] 252 mg (78%); white solid; mp 222–224 °C; IR (KBr) (cm^{-1}) 2879, 1684, 1589, 1419, 1291; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.34 (s, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 34.5, 120.3, 126.6, 127.6, 129.7, 131.0, 131.3, 136.5, 142.5, 166.9; MS (EI): m/z (%) 324 (M^+ + 2, 17.8), 322 (M^+, 17.2), 169 (100).

4-(3-Methoxybenzylthio)benzoic acid 4h (Table 2). 230 mg (84%); white solid; mp 145–147 °C; IR (KBr) (cm^{-1}) 2834, 1675; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H), 6.82 (ddd, J = 8.3, 2.5, 0.9 Hz, 1H), 6.98–7.01 (m, 2H), 7.24 (dd, J = 4.8 Hz, 1H), 7.42 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.8, 55.5, 113.2, 115.0, 121.6, 126.9, 127.9, 130.1, 130.2, 138.8, 143.6, 159.8, 167.5; MS (EI): m/z (%) 274 (M^+, 26), 121 (100); Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; N, 0. Found: C, 65.44; H, 4.83; N, 0.

4-(2-Methylbenzylthio)benzoic acid 4i (Table 2).[4] 168 mg (65%); white solid; mp 173–175 °C; IR (KBr) (cm^{-1}) 2866, 1678, 1587, 1415, 1286; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.38 (s, 3H), 4.33 (s, 2H), 7.10–7.25 (m, 3H), 7.32 (d, J = 7.2 Hz, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 18.7, 34.1, 126.0, 126.6, 127.5, 127.6, 129.7, 130.4, 134.1, 136.7, 143.3, 167.0; MS (EI): m/z (%) 258 (M^+, 16.7), 105 (100).

4-(Thiophen-3-ylmethylthio)benzoic acid 4j (Table 2). 213 mg (85%); white solid; mp 188–190 °C; IR (KBr) (cm^{-1}) 2558, 1683; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.36 (s, 2H), 7.11 (dd, J = 5.0, 1.4 Hz, 1H), 7.41 (d, J = 8.7 Hz, 2H), 7.45 (s, 1H), 7.49 (dd, J = 5.0, 3.0 Hz, 1H), 7.83 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.6, 124.0, 126.8, 127.1, 127.8, 128.8, 130.2, 137.6, 143.6, 167.5; MS (EI): m/z (%) 250 (M^+, 19), 97 (100); Anal. Calcd for $C_{12}H_{10}O_2S_2$: C, 57.58; H, 4.03; N, 0. Found: C, 57.53; H, 3.79; N, 0.

4-(Thiophen-2-ylmethylthio)benzoic acid 4k (Table 2).[4] 215 mg (85%); off-white solid; mp 136–138 °C; IR (KBr) (cm^{-1}) 2838, 1678, 1589, 1417, 1290; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.60 (s, 2H), 6.93 (dd, J = 5.2, 3.6 Hz, 1H), 7.07 (d, J = 3.6 Hz, 1H), 7.40 (dd, J = 5.2, 1.2 Hz, 1H), 7.45 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.0 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 30.1, 125.6, 126.8, 126.9, 127.7, 129.7, 140.1, 142.2, 166.9; MS (EI): m/z (%) 250 (M^+, 30.7), 97 (100).

4-(1-Phenylethylthio)benzoic acid 4l (Table 2).[4] 207 mg (80%); white solid; mp 172–174 °C; IR (KBr) (cm^{-1}) 3430, 2974, 2920, 1683, 1591, 1426, 1301; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.59 (d, J = 6.8 Hz, 3H), 4.81 (q, J = 6.8 Hz, 1H), 7.23 (t, J = 7.2 Hz, 1H), 7.32 (t, J = 7.2 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 22.3, 44.6, 127.2, 127.3, 127.9, 128.2, 128.5, 129.6, 142.0, 142.5, 166.9; MS (EI): m/z (%) 258 (M^+, 57.5), 105 (100).

4-(1,2,3,4-Tetrahydronaphthalen-1-ylthio)benzoic acid 4m (Table 2).[4] 218 mg (77%); off-white solid; mp 169–171 °C; IR (KBr) (cm^{-1}) 2936, 1684, 1590, 1418, 1286; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.70–1.80 (m, 1H), 1.90–2.10 (m, 3H), 2.65–2.85 (m, 2H), 4.98 (s, 1H), 7.10–7.20 (m, 3H), 7.38 (d, J = 7.2 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.90 (dd, J = 8.4, 1.2 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 18.2, 27.9, 28.3, 44.6, 125.7, 127.2, 128.0, 129.1, 129.9, 130.4, 134.3, 137.5, 142.6, 166.9; MS (EI): m/z (%) 284 (M^+, 6.0), 131 (100).

2-Benzylthiobenzoic acid 4n (Table 4).[4] 159 mg (65%); white solid; mp 187–189 °C; IR (KBr) (cm^{-1}) 3413, 2920, 1674, 1459, 1411, 1262; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.21 (s, 2H), 7.18–7.23 (m, 1H), 7.27 (t, J = 6.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.40–7.60 (m, 2H), 7.48–7.52 (m, 2H), 7.89 (d, J = 7.6 Hz, 1H), 13.0 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 35.7, 124.0, 125.7, 127.1, 127.6, 128.5, 129.2, 130.9, 132.3, 136.6, 141.2, 167.4; MS (EI): m/z (%) 244 (M^+, 25.1), 91 (100).

2-Benzylthio-5-fluorobenzoic acid 4o (Table 4).[4] 184 mg (70%); white solid. mp 153–155 °C; IR (KBr) (cm^{-1}) 3034, 2912, 1690, 1465, 1424, 1246; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.21 (s, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.38–7.44 (m, 3H), 7.51 (dd, J = 9.0, 5.2 Hz, 1H), 7.63 (dd, J = 9.0, 2.8 Hz, 1H), 13.4 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 36.1, 117.0, 117.3, 119.3, 119.5, 127.2, 128.3, 128.4, 128.5, 129.1, 129.9, 130.0, 136.2, 136.5, 157.8, 160.2, 166.4; MS (EI): m/z (%) 262 (M^+, 18.7), 91 (100).

2-Benzylthio-5-chlorobenzoic acid 4p (Table 4).[4] 198 mg (71%); white solid; mp 162–164 °C; IR (KBr) (cm^{-1}) 2924, 1681, 1462, 1317, 1250; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.23 (s, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 6.0 Hz, 2H), 7.43 (d, J = 7.2 Hz, 2H), 7.51 (d, J = 8.6 Hz, 1H), 7.58 (dd, J = 8.6, 2.4 Hz, 1H), 7.84 (d, J = 2.4 Hz, 1H), 13.4 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 35.7, 127.3, 127.7, 128.5, 129.1, 130.1, 131.9, 136.3, 140.2, 166.2; MS (EI): m/z (%) 280 (M^+ + 2, 13.3), 278 (M^+, 35.8), 91 (100).

3-Benzylthiobenzoic acid 4q (Table 4).[4] 195 mg (80%); white solid; mp 129–131 °C; IR (KBr) (cm^{-1}) 2847, 1689, 1579, 1433, 1288; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.30 (s, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.35–7.39 (m, 2H), 7.42 (t, J = 8.0 Hz, 1H), 7.55–7.60 (m, 1H), 7.73 (dt, J = 8.0, 1.2 Hz, 1H), 7.84 (t, J = 1.6 Hz, 1H), 13.1 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 36.4, 126.7, 127.1, 128.4, 128.6, 128.8, 129.2, 131.5, 132.3, 136.9, 137.1, 166.8; MS (EI): m/z (%) 244 (M^+, 67.1), 91 (100).

4-(Benzhydrylthio)benzoic acid 5a (Table 1).[4] 269 mg (84%); off-white solid; mp 179–181 °C; IR (KBr) (cm^{-1}) 3021, 1685, 1591, 1488, 1417, 1282; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.13 (s, 1H), 7.23 (t, J = 7.2 Hz, 2H), 7.30–7.40 (m, 6H), 7.52 (d, J = 7.6 Hz, 4H), 7.75 (d, J = 8.4 Hz, 2H), 12.9 (brs, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ 53.3, 127.4, 127.8, 128.0, 128.7, 129.6, 140.5, 142.2, 166.8; MS (EI): m/z (%) 320 (M^+, 2.1), 167 (100).

4-[Bis(4-methoxyphenyl)methylthio]benzoic acid 5b (Table 3). 293 mg (95%); white solid; mp 160–162 °C; IR (KBr) (cm^{-1}) 2830, 1686, 1600; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 6H), 6.04 (s, 1H), 6.88 (d, J = 8.9 Hz, 4H), 7.34 (d, J = 8.7 Hz, 2H), 7.39 (d, J = 8.9 Hz, 4H), 7.74 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.6, 55.6, 114.5, 127.7, 128.1, 129.6, 130.1, 133.2, 143.3, 158.8, 167.4; MS (FAB): m/z 381 [M + H]$^+$; Anal. Calcd for $C_{22}H_{20}O_4S$: C, 69.45; H, 5.30; N, 0. Found: C, 69.18; H, 5.00; N, 0.

4-[(4-Methoxyphenyl)phenylmethylthio]benzoic acid 5c (Table 3). 291 mg (83%); white solid; mp 183–185 °C; IR (KBr) (cm^{-1}) 2841, 1684; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 3H), 6.08 (s, 1H), 6.88 (d, J = 8.7 Hz, 2H), 7.23 (tt, J = 7.3, 1.1 Hz, 1H), 7.32 (dd, J = 7.8, 7.8 Hz, 2H), 7.35 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.6, 54.9, 113.9, 127.2, 127.5, 127.8, 128.5, 129.1, 129.5, 132.2140.7, 142.4, 158.3, 166.7; MS (FAB): m/z 331 [M + H]$^+$; Anal. Calcd for $C_{21}H_{18}O_3S$: C, 71.98; H, 5.18; N, 0. Found: C, 71.98; H, 4.92; N, 0.

4-[Phenyl(*p*-tolyl)methylthio]benzoic acid 5d (Table 3). 274 mg (82%); white solid; mp 187–189 °C; IR (KBr) (cm^{-1}) 3025, 1676; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.24 (s, 3H), 6.09 (s, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.23 (dt, J = 7.3, 1.4 Hz, 1H), 7.28–7.42 (m, 6H), 7.49 (d, J = 7.1 Hz, 2H), 7.74 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.1, 53.5, 127.9, 128.3, 128.4, 128.5, 129.2, 129.8, 130.1, 137.2, 138.0, 141.2, 142.9, 167.4; MS (FAB): m/z 335 [M + H]$^+$; Anal. Calcd for $C_{21}H_{18}O_2S$: C, 75.42; H, 5.43; N, 0. Found: C, 75.28; H, 5.12; N, 0.

4-[(4-Chlorophenyl)phenylmethylthio]benzoic acid 5e (Table 3). 220 mg (62%); white solid; mp 173–175 °C; IR (KBr) (cm^{-1}) 3004, 1685; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.19 (s, 1H), 7.25 (dd, J = 6.4, 6.4 Hz, 1H), 7.30–7.47 (m, 6H), 7.49 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 53.0, 128.1, 128.5, 129.2,

129.3, 130.2, 130.4, 132.5, 140.1, 140.6, 142.3, 167.3; MS (FAB): *m*/*z* 357 $[M + 2 + H]^+$, 355 $[M + H]^+$; Anal. Calcd for $C_{20}H_{15}ClO_2S$: C, 67.70; H, 4.26; N, 0. Found: C, 67.44; H, 4.11; N, 0.

4-[Bis(4-fluorophenyl)methylthio]benzoic acid 5f (Table 3). 278 mg (78%); white solid; mp 179–181 °C; IR (KBr) (cm^{-1}) 2991, 1683; ^1H NMR (400 MHz, DMSO-d_6): δ 6.22 (s 1H), 7.17 (dd, *J* = 8.9, 8.9 Hz, 4H), 7.38 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.1, 116.1 (d, *J* = 21.0 Hz), 128.2, 128.6, 130.2, 130.5 (d, *J* = 7.6 Hz), 137.1 (d, *J* = 2.9 Hz), 142.3, 161.8 (d, *J* = 243 Hz), 167.3; MS (FAB): *m*/*z* 337 $[M + H]^+$; Anal. Calcd for $C_{20}H_{14}F_2O_2S$: C, 67.40; H, 3.96; N, 0. Found: C, 67.37; H, 3.94; N, 0.

2-(Benzhydrylthio)benzoic acid 5g (Table 4). 208 mg (65%); white solid; mp 209–211 °C; IR (KBr) (cm^{-1}) 3024, 1681; ^1H NMR (400 MHz, DMSO-d_6): δ 5.99 (s, 1H), 7.13 (dd, *J* = 6.9, 1.6 Hz, 1H), 7.24 (tt, *J* = 7.3, 1.1 Hz, 2H), 7.28–7.38 (m, 6H), 7.49 (dt, *J* = 8.0, 1.4 Hz, 4H), 7.84 (dd, *J* = 8.9, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 53.4, 124.7, 127.4, 127.8, 128.7, 128.8, 129.2, 131.3, 132.5, 140.7, 141.3, 168.0; MS (FAB): *m*/*z* 334 $[M + H]^+$; Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03; N, 0. Found: C, 74.61; H, 4.70; N, 0.

2-(Benzhydrylthio)-5-fluorobenzoic acid 5h (Table 4). 264 mg (78%); white solid; mp 166–168 °C; IR (KBr) (cm^{-1}) 3066, 1687; ^1H NMR (400 MHz, DMSO-d_6): δ 6.00 (s, 1H), 7.20–7.30 (m, 4H), 7.33 (dd, *J* = 7.3, 7.3 Hz, 4H), 7.47 (d, *J* = 7.1 Hz, 4H), 7.58 (dd, *J* = 9.4, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 53.9, 117.5 (d, *J* = 22.9 Hz), 119.7 (d, *J* = 21.9 Hz), 127.9, 128.7, 129.2, 130.2 (d, *J* = 7.6 Hz), 131.4 (d, *J* = 6.7 Hz), 135.5 (d, *J* = 2.9 Hz), 141.1, 159.6 (d, *J* = 243 Hz), 167.1; MS (FAB): *m*/*z* 339 $[M + H]^+$; Anal. Calcd for $C_{20}H_{15}FO_2S$: C, 70.99; H, 4.47; N, 0. Found: C, 70.80; H, 4.31; N, 0.

3-(Benzhydrylthio)benzoic acid 5i (Table 4). 218 mg (68%); white solid; mp 127–129 °C; IR (KBr) (cm^{-1}) 2559, 1693; ^1H NMR (400 MHz, DMSO-d_6): δ 6.02 (s, 1H), 7.22 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.28–7.38 (m, 5H), 7.50 (d, *J* = 7.3 Hz, 4H), 7.54 (dt, *J* = 8.7, 0.9 Hz, 1H), 7.69 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.82 (t, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.0, 127.7, 127.9, 128.6, 129.1, 129.6, 130.4, 131.9, 134.0, 136.8, 141.2, 167.2; MS (FAB): *m*/*z* 321 $[M + H]^+$; Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03; N, 0. Found: C, 74.74; H, 4.76; N, 0.

2-[4-(Benzhydrylthio)phenyl]acetic acid 5j (Table 4). 167 mg (50%); white solid; mp 99–101 °C; IR (KBr) (cm^{-1}) 3026, 1695; ^1H NMR (400 MHz, DMSO-d_6): δ 3.48 (s, 2H), 5.91 (s, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.15–7.28 (m, 4H), 7.31 (dd, *J* = 7.1, 7.1 Hz, 4H), 7.49 (d, *J* = 7.1 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 40.5, 55.3, 127.7, 128.6, 129.1, 129.8, 130.5, 133.8, 134.1, 141.7, 173.0; MS (FAB): *m*/*z* 334 $[M]^+$; Anal. Calcd for $C_{21}H_{18}O_2S{\cdot}0.2H_2O$: C, 74.62; H, 5.49; N, 0. Found: C, 74.70; H, 5.31; N, 0.

3-[4-(Benzhydrylthio)phenyl]propanoic acid 5k (Table 4). 178 mg (51%); white solid; mp 97–99 °C; IR (KBr) (cm^{-1}) 3026, 1707; ^1H NMR (400 MHz, DMSO-d_6): δ 2.61 (t, *J* = 8.0 Hz, 2H), 2.86 (t, *J* = 8.0 Hz, 2H), 5.49 (s, 1H), 7.01 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.18–7.24 (m, 2H), 7.29 (dd, *J* = 7.1, 7.1 Hz, 4H), 7.40 (d, *J* = 6.9 Hz, 4H), 7.84 (dd, *J* = 8.0, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.3, 35.4, 55.5, 127.7, 128.5, 129.1, 129.3, 130.2, 133.2, 139.8, 141.7, 174.2; MS (FAB): *m*/*z* 348 $[M]^+$; Anal. Calcd for $C_{22}H_{20}O_2S{\cdot}0.6H_2O$: C, 73.55; H, 5.95; N, 0. Found: C, 73.52; H, 5.63; N, 0.

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Notes and references

1 (*a*) S. Ueno, S. Komiya, T. Tanaka and R. Kuwano, *Org. Lett.*, 2012, **14**, 338–341; (*b*) P. Xie, Y. Xie, B. Qian, H. Zhou, C. Xia and H. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 9902–9905; (*c*) B. M. Trost and L. C. Czabaniuk, *J. Am. Chem. Soc.*, 2012, **134**, 5778–5781; (*d*) S. Zhang, Y. Wang, X. Feng and M. Bao, *J. Am. Chem. Soc.*, 2012, **134**, 5492–5495; (*e*) B. Peng, S. Zhang, X. Yu, X. Feng and M. Bao, *Org. Lett.*, 2011, **13**, 5402–5405; (*f*) S. L. Marquard and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2011, **50**, 7119–7123; (*g*) S. L. Marquard, D. C. Rosenfeld and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2010, **49**, 793–796; (*h*) B. M. Trost and L. C. Czabaniuk, *J. Am. Chem. Soc.*, 2010, **132**, 15534–15536; (*i*) R. Kuwano, *Synthesis*, 2009, 1049–1061; (*j*) A. M. Johns, M. Utsunomiya, C. D. Incarvito and J. F. Hartwig, *J. Am. Chem. Soc.*, 2006, **128**, 1828–1839; (*k*) R. Kuwano, Y. Konda and Y. Matsuyama, *J. Am. Chem. Soc.*, 2003, **125**, 12104–12105; (*l*) Y. Becker and J. K. Stille, *J. Am. Chem. Soc.*, 1978, **100**, 845–850.

2 (*a*) G. Verspui, G. Papadogianakis and R. A. Sheldon, *Catal. Today*, 1998, **42**, 449–458; (*b*) G. Papadogianakis, L. Maat and R. A. Sheldon, *J. Chem. Technol. Biotechnol.*, 1997, **70**, 83–91.

3 (*a*) H. Hikawa, N. Matsuda, H. Suzuki, Y. Yokoyama and I. Azumaya, *Adv. Synth. Catal.*, 2013, **355**, 2308–2320; (*b*) H. Hikawa and Y. Yokoyama, *RSC Adv.*, 2013, **3**, 1061–1064; (*c*) H. Hikawa, H. Suzuki, Y. Yokoyama and I. Azumaya, *Catalysts*, 2013, **3**, 486–500; (*d*) H. Hikawa, Y. Ino, H. Suzuki and Y. Yokoyama, *J. Org. Chem.*, 2012, **77**, 7046–7051; (*e*) H. Hikawa and Y. Yokoyama, *Org. Lett.*, 2011, **13**, 6512–6515.

4 H. Hikawa and Y. Yokoyama, *Org. Biomol. Chem.*, 2012, **10**, 2942–2945.

5 M. Jha, O. Enaohwo and A. Marcellus, *Tetrahedron Lett.*, 2009, **50**, 7184–7187.

6 M. Jha, O. Enaohwo and S. Guy, *Tetrahedron Lett.*, 2011, **52**, 684–687.

7 Y. Guindon, R. Frenette, R. Fortin and J. Rokach, *J. Org. Chem.*, 1983, **48**, 1357–1359.

8 H. Firouzabadi, N. Iranpoor and M. Jafarpour, *Tetrahedron Lett.*, 2006, **47**, 93–97.

9 Reviews: T. Kondo and T. Mitsudo, *Chem. Rev.*, 2000, **100**, 3205–3220.

10 (*a*) G. Corthey, A. A. Rubert, A. L. Picone, G. Casillas, L. J. Giovanetti, J. M. Ramallo-Lopez, E. Zelaya, G. A. Benitez, F. G. Requejo, M. Jose-Yacaman, R. C. Salvarezza and M. H. Fonticelli, *J. Phys. Chem. C*, 2012, **116**, 9830–9837; (*b*) E. Gao, F. Guan, X. Gao, M. Zhu, L. Liu, C. Wang, W. Zhang and Y. Sun, *J. Biol. Inorg. Chem.*, 2012, **17**, 263–274; (*c*) M. Cargnello, N. L. Wieder, P. Canton, T. Montini, G. Giambastiani, A. Benedetti, R. J. Gorte and P. Fornasiero, *Chem. Mater.*, 2011, **23**, 3961–3969; (*d*) F. Lu, J. Ruiz and D. Astruc, *Tetrahedron Lett.*, 2004, **45**, 9443–9445; (*e*) W. Henderson and B. K. Nicholson, *Inorg. Chem. Acta*, 2003, **346**, 7–11; (*f*) L. L. Maisela, A. M. Crouch, J. Darkwa and I. A. Guzei, *Polyhedron*, 2001, **20**, 3189–3200; (*g*) W. Henderson, L. J. McCaffrey and B. K. Nicholsn, *J. Chem. Soc., Dalton Trans.*, 2000, 2753–2760; (*h*) W. H. Meyer, R. Brull, H. G. Raubenheimer, C. Thompson and G. J. Kruger, *J. Organomet. Chem.*, 1998, **553**, 83–90.

11 (*a*) K. Islam, H. F. Chin, A. O. Olivares, L. P. Saunders, E. M. De La Cruz and T. M. Kapoor, *Angew. Chem., Int. Ed.*, 2010, **49**, 8484–8488; (*b*) A. S. Mehanna and J. Y. Kim, *Bioorg. Med. Chem.*, 2005, **13**, 4323–4331; (*c*) A. Zarghi, M. Faizi, B. Shafaghi, A. Ahadian, H. R. Khojastehpoor, V. Zanganeh, S. A. Tabatabai and A. Shafiee, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 3126–3129.

12 (*a*) F. Dai, S. Gong, P. Cui, G. Zhang, X. Qui, F. Ye, D. Sun, Z. Pang, L. Zhang, G. Dong and C. Zhang, *New J. Chem.*, 2010, **34**, 2496–2501; (*b*) N. Azizi, A. K. Amiri, M. Bolourtchian and M. R. Saidi, *J. Iran. Chem. Soc.*, 2009, **6**, 749–753; (*c*) A. Togninelli, C. Carmi, E. Petricci, C. Mugnaini, S. Massa, F. Corelli and M. Botta, *Tetrahedron Lett.*, 2006, **47**, 65–67; (*d*) B. C. Ranu and R. Jana, *Adv. Synth. Catal.*, 2005, **347**, 1811–1818.

13 G. Flouret, T. Majewski, L. Balaspiri, W. Brieher, K. Mahan, O. Chaloin, L. Wilson Jr. and J. Slaninova, *J. Pept. Sci.*, 2002, **8**, 314–326.

14 (*a*) H. Hikawa and Y. Yokoyama, *Org. Biomol. Chem.*, 2011, **9**, 4044–4050; (*b*) H. Hikawa and Y. Yokoyama, *J. Org. Chem.*, 2011, **76**, 8433–8439; (*c*) N. A. Afagh and A. K. Yudin, *Angew. Chem., Int. Ed.*, 2010, **49**, 262–310; (*d*) Y. Yokoyama, N. Takagi, H. Hikawa, S. Kaneko, N. Tsubaki and H. Okuno, *Adv. Synth. Catal.*, 2007, **349**, 662–668; (*e*) Y. Yokoyama, H. Hikawa, M. Mitsuhashi, A. Uyama, Y. Hiroki and Y. Murakami, *Eur. J. Org. Chem.*, 2004, 1244–1253; (*f*) Y. Yokoyama, H. Hikawa, M. Mitsuhashi, A. Uyama and Y. Murakami, *Tetrahedron Lett.*, 1999, **40**, 7803–7806.

15 J.-M. Basset, D. Bouchu, G. Godard, I. Karame, E. Kuntz, F. Lefebvre, N. Legagneux, C. Lucas, D. Michelet and J. B. Tommasino, *Organometallics*, 2008, **27**, 4300–4309.

16 (*a*) T. Mukai, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2010, **12**, 1360–1363; (*b*) C. C. Lindsey, B. M. O'Boyle, S. J. Mercede and T. R. R. Pettus, *Tetrahedron Lett.*, 2004, **45**, 867–868.

17 (*a*) J.-Y. Legros, G. Primault, M. Toffano, M.-A. Rivière and J.-C. Fiaud, *Org. Lett.*, 2000, **2**, 433–436; (*b*) J.-Y. Legros, M. Toffano and J.-C. Fiaud, *Tetrahedron*, 1995, **51**, 3235–3246.

18 Carboxylic acids enhance the formation of the π-allyl complex in aqueous media. (*a*) S.-C. Yang, Y.-C. Hsu and K.-H. Gan, *Tetrahedron*, 2006, **62**, 3949–3958; (*b*) K. Manabe and S. Kobayashi, *Org. Lett.*, 2003, **5**, 3241–3244.

19 M. Matoba, T. Kajimoto and M. Nobe, *Synth. Commun.*, 2008, **38**, 1194–1200.

